university of groningen

NWO
Netherlands Organisation for Scientific Research

Topics in Scientific Philosophy
UC Irvine 2018

Resiliency in Psychiatric Science

⋆

Jan-Willem Romeijn
University of Groningen

Disease classification

Classification schemes for mental illness serve a large variety of goals.

- Medical doctors use classification schemes to design and apply treatments.
- Researchers employ them to design studies and carry them out.
- Patients and their families and friends fall back on classifications for explanation and understanding.

How can we best serve these goals? When is a classification scheme “good”?

This talk

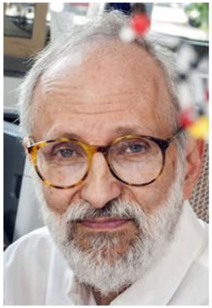
I consider what function psychiatric classifications have, and how they perform this function best.

- Classification involves conventions. Disease concepts need to be coordinated to empirical fact.
- A good classification supports predictions and interventions, by helping us to determine reliable chances.
- Chances can be understood as resilient degrees of belief, and their resilience is a fact about the world.
- Viewing classifications in this way invites an anti-reductionist view on psychiatric science.

Contents

Joint work

Sections 1 and 2 of this talk are based on work with Hanna van Loo and several other psychiatrists.

1 Comorbidity

In psychiatry it often occurs that patients suffer from multiple disorders at the same time.

	Country	N	DSM	12 mth any dx (in%)	1 dx	2 dx	3 dx	> 3 dx	% pts > 1dx
Bijl 1998	NL	7076	III-R	23,3	15,3	4,4	1,9	1,9	35
Jacobi 2004	BRD	4181	IV	31,1	18,8	6,3	2,8	3,2	40
Kessler 2005	USA	9282	IV	26,2	14,4	5,8	6,0		45

Having one disorder invites the manifestation of other disorders.

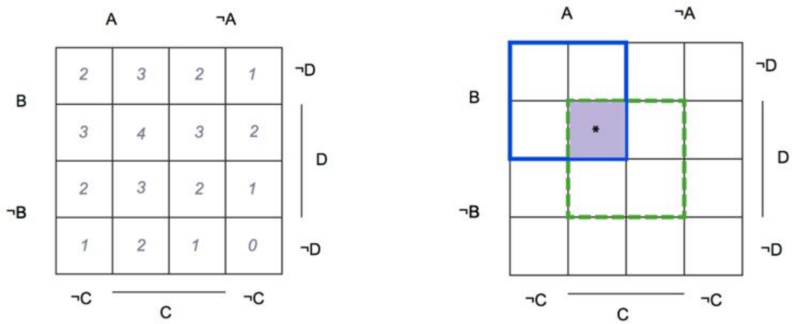
Why study comorbidity?

Understanding this phenomenon is important, both practically and theoretically.

- Patients with comorbid disorders have disproportional functional disability and react less well to treatment.
- A better understanding of comorbidity will contribute to a sensible debate over theoretical issues that surround the DSM.
- Comorbidity serves as a magnifying glass for philosophical concerns about scientific categorisation.

Comorbidity as overlap

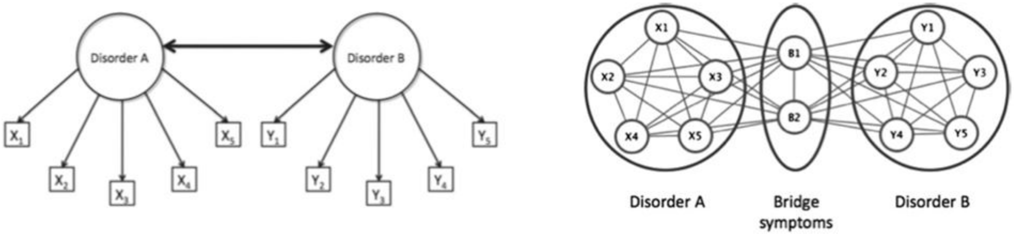
It may be an artefact of the DSM that some people are diagnosed with multiple disorders, e.g. MDD and GAD.



Comorbidity might merely signal that the disease definitions are sloppy.

Comorbidity as causal

The co-occurrence of two disorders may also signal that they promote each other causally.



(Figures from Cramer *et al*, BBS 2010)

In that case comorbidity signals something important about the disorders themselves.

Realism vs constructivism

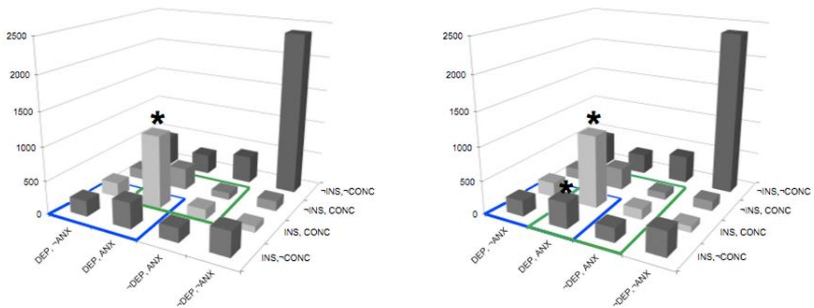
The discussion over comorbidity has focused on what it tells us.

- Constructivists argue that it results from definitional choices.
- Realists maintain that it reveals genuine facts about diseases.

The distinctions used in the debate hark back to the “science wars”. Can we escape this stalemate?

2 Conventionalism

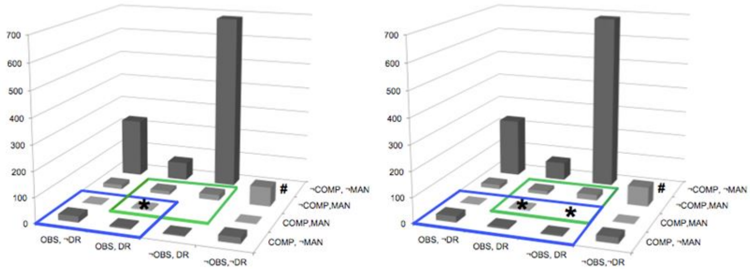
In empirical studies we find an interplay between constructs and empirical reality. Comorbidity might increase from 43% to 54% when widening a disease definition.



(Data from NEMESIS study n=7076)

Empirical study of comorbidity

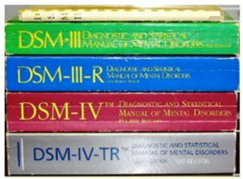
But depending on the empirical facts, comorbidity might also decrease from 7% to 6% with a widened definition.



(Data from NEMESIS study n=7076)

DSM as a "convention"

Comorbidity is definitional, but it also reveals robust empirical facts about diseases.



The role of the DSM is similar to that of a ruler or a thermometer: on the one hand indicative, on the other constitutive.

Coordinative definitions

Mental disorders obtain the role of “coordinative definitions” that we know from Reichenbach and Poincaré.

The pertinent question is: what conventions are best for psychiatric practice?

3 Reference classes

A good classification scheme is one that generates the right reference classes.

- We want to select characteristics, and thus identify patient groups, that allow us to reliably determine chances pertaining to those patients.
- Such characteristics arguably provide us with a natural disease classification, and thereby with an understanding of the nature of psychiatric disease.
- On this basis we may hope to predict the outcome of treatment and hence intervene reliably.

This suggests a reorientation of current classification efforts.

Model selection

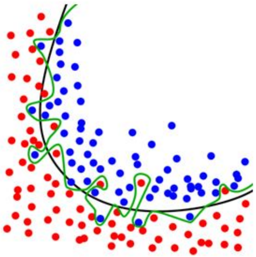
When viewed in this way, the problem of psychiatric disease classification becomes largely statistical.

- The search for salient characteristics comes down to the choice for a set of statistical variables, and hence the determination of a statistical model.
- In statistical model selection, the choice of variables is regulated by expected predictive performance. The choice of a model is thereby data-driven.

This link with model selection offers a particular grip on disease classification.

Overfitting

An important property of model selection tools is that they guard against so-called overfitting.



Increasing the number of characteristics may improve the fit to data, but it will make predictions less reliable.

Causal modelling

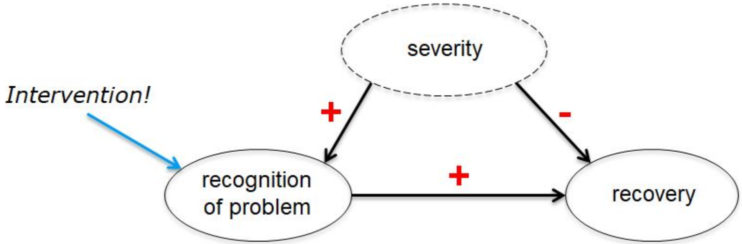
Perhaps the most important application of classification is in designing treatment programs and allocating patients to them.

- We want to define mental disorders in such a way that they facilitate maximally effective clinical interventions.
- In psychiatry interventions are mostly stochastic, i.e., they merely raise the chance of some desired outcome.

The link to causal modeling offers another important handle on the problem of disease classification.

Causally relevant classifications

Searching for confounders helps to determine classifications that support better predictions and interventions.



This idea is applicable across a variety of validators and levels of description.

4 Probabilistic resiliency

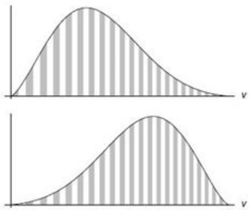
Skyrms’ 1977 paper on chance offers an insightful perspective on the classification problem, understood as the search for reference classes.

- Chances are best understood as degrees of belief that are resilient under learning any further information.
- Whether or not some degree of belief may count as a chance is dependent on the specifics of the system under scrutiny.

We can develop this further by reusing some ideas from von Mises’ frequentism.

Arbitrary functions and multiple realizability

Other sources of inspiration are Hopf's method of arbitrary functions and Putnam's notion of radical multiple realizability.



The general idea is that some stochastic properties of macroscopic states do not reduce to probability assignments over microscopic states.

Resilience and random events

We call an event S *random* relative to a reference class R and some algebra $\mathcal{X}$ iff for all refinements X_i from this algebra we have

$$P(S|R \cap X_i) = P(S|R).$$

The resulting probability assignment is then *resilient*: adding further information from $\mathcal{X}$ to a reference class R does not alter the chances for S.

5 Employing frequentism

We can provide a formal underpinning of this notion of resilience that relies on ideas from frequentism. Recall the definition of the limiting relative frequency F of a sequence s:

$$F(s) = \lim_{n \to \infty} \frac{\Sigma_{t=1}^{n} s(t)}{n},$$

where $s(t)$ is the digit at position t in the sequence. Note: the denotation of the sequence by s, while uppercase S is a set, is not a coincidence.

Place selections

We can use a second sequence x_i to select elements from the sequence s, and construct the relative frequency of a subsequence:

$$F(s; x_i) = \lim_{n\to\infty} \frac{\Sigma_{t=1}^{n} s(t) x_i(t)}{\Sigma_{t=1}^{n} x_i(t)}.$$

The sequence s is random relative to a set $\mathcal{X}$ of sequences, or selection rules, if for all $x_i \in \mathcal{X}$ we have:

$$F(s) = F(s; x_i).$$

We might say that the set of sequences $\mathcal{X}$ contains "no information" about the original sequence s.

Sequences and place selections as sets

Sequences and place selections can be viewed as sets of natural numbers. For binary sequences we have:

$$S_s = \{t \mid t \in \mathbb{N} \text{ and } s(t) = 1\}.$$

Similar relations between a sequence s and a set S can be determined when we consider S to be a set in a continuous space. This is easiest if S is a countable set of points in the space.

Random sets and resilience

We can now apply the same notion of invariance under place selection in the richer context of events: the set S is random relative to a lower-level algebra $\mathcal{X}$ iff for all X_i we have

$$P(S) = P(S|X_i).$$

We thus employ the mathematical machinery of place selections to arrive at a notion of randomness for an event S, and hence at the resilience of the probability assignment $P(S)$ relative to $\mathcal{X}$.

Full resilience

The ultimate version of resilience has the event S distributed uniformly over the space X. Consider the σ-algebra $\mathcal{X}$ generated by

$$B[x,\delta] = \{x' : x' \in (x, x+\delta)\}$$

where the δ can be arbitrarily small, and stipulate that

$$P(S|B[x,\delta]) = P(S).$$

That is, no amount of fine-graining will offer additional information on the event S, making the probability "fully resilient".

6 Objective chances?

We can construct such a random set by employing a simple ergodic dynamical system. Consider a set R with elements indexed by t,

$$R(t) = 2^t R(0) \pmod 1.$$

where $R(0) \in [0,1]$ is the starting position generating the set. For a given initial state $R(0)$, we can label all the points $R(t)$ by 0 if $R(t-1) \leq 1/2$ and by 1 if $R(t-1) > 1/2$. The set of points labelled 1 we call S.

Full resilience: example

Assuming that $R(0)$ is a collective with a relative frequency σ, the limiting relative frequency of points of S within R is

$$P(S|R) = \sigma.$$

The set R is dense everywhere in $[0, 1]$. Moreover, for any interval $X_i \subset [0, 1]$, however small, we have

$$P(S|R \cap X_i) = P(S|R).$$

But every point x in the space X, or in the class R, is or is not a member of S so we do not violate determinism.

The correct reference class

The proposal is to call a reference class R correct for a chance ascription to S if $P(S|R)$ is fully resilient in the above sense. Notice:

- There are many variations on the randomness of the event S, and the correctness of the reference class R depending on the details of the algebra $\mathcal{X}$. This runs parallel to the randomness of sequences.

- It seems that a natural line is drawn by the algebra $\mathcal{X}_S$ corresponding to "Kurtz randomness": whether or not a point x is a member of an element $X \in \mathcal{X}$ must be effectively computable.

- This leaves room for the random events S and R to be the result of an effective procedure, which makes their physical realization conceivable.

Discussion

There are many loose ends in this picture of resilient probabilities on the macro-level.

- The foregoing may explain what the ultimate aim of statistical model selection is: to find the set R for which $P(S|R)$ is fully resilient.
- Nothing guarantees that random events, like S in R, actually obtain. The foregoing offers an extreme case of resilient probability but the reality of chances may fall short of this.
- Chances are only truly objective if our choice for the algebra $\mathcal{X}_S$ can be given a further motivation.

7 Back to psychiatry

I hope that the above insights can be of use in the hunt for improvements of disease classification.

- The conventionalist view clears the way for trying out revisions to disease classification.
- Viewing disease classification as a reference class problem invites an empiricist and pragmatic approach.
- It directs us to the use of model selection and causal modeling, and suggests that we search for resilient probabilities.

Anti-reductionism

It is perfectly possible that the classification employs characteristics from a several different levels of description.

This offers an alternative to classifications that are based on an assumed metaphysics, e.g., strictly neuro-scientific.

Words of caution

Admittedly, statistical tools alone will not deliver answers to the classification questions.

- For long-term improvements it may be beneficial to adhere to a metaphysics, or a specific disciplinary matrix, when designing a classification.
- Classification schemes serve many different goals. I have focused on prediction and intervention as objectives but this is a substantive choice.
- The statistical methods and tools that I advertized are too generic and abstract. They need to be tailored to the case at hand.

Papers in psychiatry

- “Psychiatric classification and the reference class problem”, in Conceptual Issues in Psychiatry, ed. K. Kendler and J. Parnas, Oxford University Press, to appear 2018.
- “Measuring and defining: the double role of the DSM-criteria for psychiatric disorders”, with H. van Loo, Psychological Medicine, 2017.
- “Psychiatric comorbidity does not only depend on diagnostic thresholds: an illustration with major depressive disorder and generalized anxiety disorder”, with H. van Loo, P. de Jonge, K.S. Kendler, and R.S. Schoevers, Depression and Anxiety, DOI 10.1002/da.22453, 2015.
- “Comorbidity: fact or artefact?”, with H. van Loo, Theoretical Medicine and Bioethics 36(1), pp. 41–60, 2015.
- “Psychiatric comorbidity and causal disease models”, with H.M. van Loo, P. de Jonge, R.A. Schoevers, Preventive Medicine, 57(6), pp. 748-752, 2013.
- “Data-driven subtypes of major depressive disorder: a systematic review”, with H.M. van Loo, P. de Jonge, R.C. Kessler, and R.A. Schoevers, BMC medicine 10: 156, 2012.

Thanks for your attention

This talk will be available at `http://www.philos.rug.nl/~romeyn`. For comments and questions, email j.w.romeijn@rug.nl.