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Mental Disorders as Homeostatic Property Clusters
A Narrative Review

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IMPORTANCE Psychiatric classification faces longstanding challenges, including heterogeneous diagnostic categories, high comorbidity rates, limited interrater reliability, and modest clinical utility. Successive revisions of systems such as the *DSM* since 1980 have done little to resolve these issues. How to move forward?

OBSERVATIONS This narrative review draws an analogy to biology, which has grappled for centuries with the hard problem of species classification. Following Darwin's insights that species are not fixed categories, contemporary theorists of classification have moved away from the natural kind view toward understanding species as homeostatic property clusters (HPCs): sets of properties contingently clustered in nature because the presence of some properties favors the presence of others. Probabilistic associations among these properties lead to imperfect aggregations and gray areas between species. This work adapts the HPC view for mental disorders, where probabilistic associations among biopsychosocial mental health properties form statistical aggregations: property clusters. These clusters are just as messy as in biology and usually lack sharp boundaries. Similar to species, diagnostic structures cannot be straightforwardly discovered in this space—they must be superimposed. To advance this view, a research agenda is outlined for mapping out a mental health atlas by identifying properties, their associations, and their dynamics and illustrating this idea using example data.

CONCLUSIONS AND RELEVANCE The HPC view accounts for many robust phenomena in mental health science, turning classification challenges from isolated anomalies into natural consequences of superimposing structure on the landscape of mental health problems. It aligns with major clinical and research frameworks—including Engel's biopsychosocial model, network and systems approaches, the Hierarchical Taxonomy of Psychopathology, and the Research Domain Criteria project—highlighting its role as a mental health science meta-framework. Doing so, it helps sidestep unproductive debates over the best universal classification system. Clinicians, researchers, and policymakers have different priorities and constraints, and no single classification system will optimally serve all stakeholders.

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Supplemental content

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For centuries, biologists have tried to bring order to the vast complexity of the animal kingdom. This has resulted in species categories such as giraffes, crocodiles, and beavers, as well as broader taxonomic groups such as mammals, reptiles, and fish. Some of these have passed the test of time: modern genetics has shown that mammals, for example, form a coherent evolutionary group. All mammals descend from a single common ancestor and include all its descendants. Fish, however, do not exist. They were grouped together based on superficial resemblance but they do not form a sensible class on the tree of life. Some fish, like the lungfish, are more closely related to cows than to many other fish.[1]

Psychiatric nosology has long faced a similarly difficult task: to classify the many different thoughts, feelings, and behaviors people experience in relation to mental health. Like biologists, we have come up with specific diagnoses (species) and broader diagnostic (taxonomic) groups, which has led to systems like the *DSM*. Such manuals are crucial tools for clinical care, communication and standardization, research and epidemiology, education and training, and public health policy. Unfortunately, they also pose many problems, including highly heterogeneous categories that lack sharp boundaries, high comorbidity rates, problematic interrater reliability for many common disorders, validity issues, and limited clinical utility.[2-6]

I view the *DSM* as an important paper plane held together by screws, matches, and chewing gum added by very thoughtful clinicians and scholars over many decades to keep it flying.[7,8] But *DSM* categories are largely based on superficial resemblance, and therefore, like fish, necessarily limited. Changes to the *DSM* since its third iteration in 1980 have not done much to change this: fixing a wing, replacing a wheel, or adding yet another propeller. These revisions have not resolved the core challenges *DSM-5* is facing. How to move forward?

In what follows, I use the analogy of species to showcase what biology, a field with centuries of fruitful work on the hard problem of species classification, can teach us. Specifically, I first review biological approaches to species classification, moving from essentialist views to contemporary accounts of species as homeostatic property clusters (HPCs). I then develop an initial sketch of this framework for mental health science.

Biological Species as Natural Kinds

So let us start with the question of what biological species are. One traditional view is that giraffes, crocodiles, and beavers are natural kinds: categories discovered in nature, in much the same way we discovered elements like hydrogen and oxygen. Natural kinds have fixed essences, necessary and sufficient properties that clearly define kind membership. Hydrogen atoms always have one proton, and everything with 1 proton is hydrogen. Giraffes have long necks, crocodiles have sharp teeth, and beavers build dams.

This species concept is intuitive but false; species do not have essences.[9,10] Instead, species are moving targets: they evolve and merge and split over time. Furthermore, 2 crocodiles could not produce viable offspring if they did not differ in some aspects. Finally, crocodiles do not have necessary and sufficient properties that define kind membership, such as sharp teeth: wolves are not crocodiles despite having sharp teeth, and a crocodile without teeth is still a crocodile.

For these reasons, species classification in biology remains difficult. Different classification frameworks for species have been developed, each bringing their own diagnostic tools for identifying distinct species.[11] I will focus on the phenetic species concept, grouping animals by similarity of phenotypic traits. This is based on numerical taxonomy, counting overlapping traits of animals (**Figure 1**).

There are other species frameworks as well, such as the biological species concept, grouping animals based on interbreeding; the ecological species concept, grouping animals based on the occupation of ecological niches; and the phylogenetic species concept, grouping animals based on common ancestry. Some approaches, like the biological species concept, tend to result in fewer overall categories (ie, lumping), whereas others like the phylogenetic concept produce more categories (ie, splitting). Interestingly, different classification manuals in biology rely on different species concepts: the *International Code of Zoological Nomenclature* is based on the biological species concept. But because genetic or reproductive data are not always available for botany or paleontology, the *International Code of Nomenclature for Algae, Fungi, and Plants* also uses morphological data. For bacteria, species are often defined by genomic similarity rather than reproductive isolation. Overall, difficult questions about classifying a complex space, overlapping phenotypes, discussions about splitting vs lumping, and diverging classification frameworks must sound eerily familiar to psychiatric nosologists.

Biological Species as Property Clusters

If biological species are not what our intuition tells us—clear categories discovered in nature—then what are they? Boyd conceptualized species as HPCs,[12,13] a framework with immense explanatory power for mental health science that has been only scarcely discussed.[14,15] Note that I set aside aspects of HPCs that do not lend themselves to a productive analogy for mental health science, such as the idea of evolutionary principles driving homeostasis.

Animals have properties, including phenotypic (giraffes have long necks), genetic (cheetahs have alleles for fast-twitch muscle fibers), ecological (coral reefs create habitats for marine life), developmental (butterflies undergo metamorphosis), anatomical (elephants have trunks), perceptual (bats use echolocation), and behavioral (beavers build dams). These properties are contingently clustered in nature. Giraffes have long necks and specialized cardiovascular adaptations with exceptionally powerful hearts. They also have prehensile tongues and eat from trees. Why do properties cooccur? Because the presence of some properties favors the presence of others. A very long neck requires an exceptionally strong heart, and a prehensile tongue helps with eating leaves from trees.

Associations among properties are usually probabilistic rather than deterministic: taller animals tend to weigh more. Such probabilistic associations lead to giraffes being rather similar to each other, but not identical: property clusters are imperfect aggregations, which results in a "gray area between species."[1]

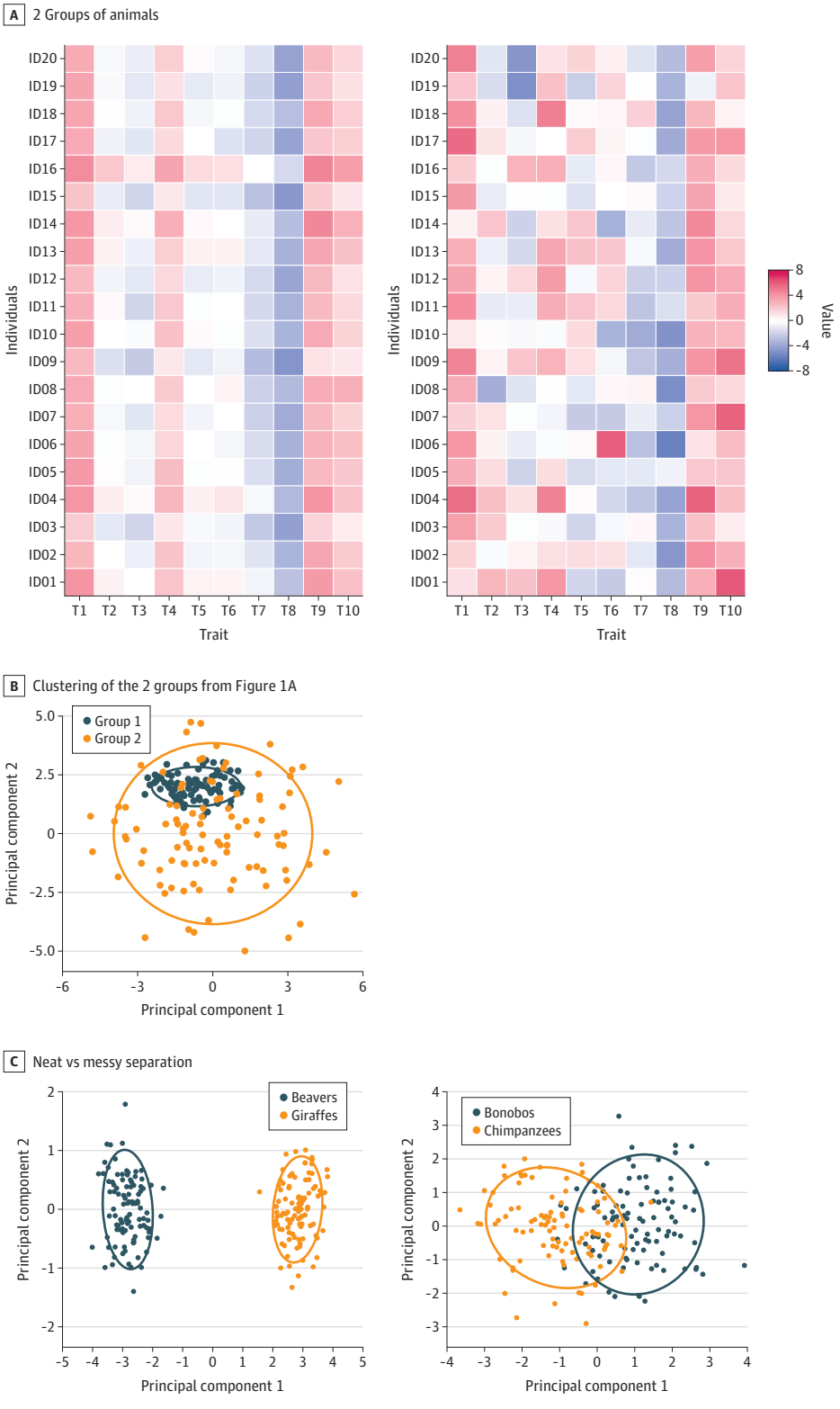
Now assume we measure each animal in the world on a few million properties—genetic, ecological, developmental, anatomical, perceptual, and behavioral—and plot each animal as a dot in the resulting n-dimensional space. We would see messy and overlapping point clouds emerge: property clusters. In this space, some species pairs would be much easier to distinguish than others (Figure 1). The correlated nature of properties would also lead to combinations that are unlikely or impossible, resulting in zones of rarity (ie, areas without dots): there are no large insects (due to respiratory system constraints) or cold-blooded mammals (due to metabolic constraints).

These point clouds do not by themselves give us species: they are just statistical patterns in data. But we can use these property clusters as a basis for classification, by superimposing categorical species onto this messy map. This is how numerical taxonomy works.[16]

Mental Health Problems as Property Clusters

Moving from clustering animals to clustering people who experience mental health problems, we start with mental health properties. Our discipline has focused predominantly on symptom properties over the last century, but there are many other important features. Remember the lesson that fish taught us—to not cluster based on superficial traits alone. For this reason, my working definition for mental health properties is that they show interindividual differences and are related to mental health broadly. As such, they include differences in genotype and phenotype, brain anatomy and functioning, neurotransmitter and hormone levels, psychological traits, lifestyle, coping mechanisms, beliefs about the world, life history, treatment response, and so on. There are no objective sets of properties: common frameworks separate properties into biological, psychological, and social domains,[17] but one could conceive of others, such as environmental (eg, noise pollution), cultural (eg, collective norms around emotion expression), or spiritual (eg, sense of purpose).

Figure 1. Heat Map and Scatterplots Showing Biological Species Heterogeneity and Separation in Simulated Data



A, The 20 animals (ID01-ID20) in group 1 are more similar to each other on each of the 10 traits (T1 to T10) than the 20 animals in group 2 are. B, Reducing this 10-dimensional trait-space to 2 principal components reveals that the animals in group 1 cluster more tightly than those in group 2, suggesting they may be a better candidate for a coherent species. C, Applying this framework to real species, beavers and giraffes can be more neatly distinguished than bonobos and chimpanzees. Simulation code is available at https://osf.io/vnxd5.

Mental health properties tend to cluster, just like animal properties: severe fears cluster with avoidance; sad mood with suicidal thoughts; and hallucinations with delusions. Going beyond symptoms, neuroticism tends to go together with internalizing disorders[18]; perfectionism with eating disorders[19]; cancer with depression[20]; smoking with schizophrenia[21]; and lower socioeconomic status, as well as hypothalamic-pituitary-adrenal axis dysfunction, with all sorts of difficulties.[22,23] Properties like social support and self-efficacy are inversely related to mental health problems.[24] Although associations between properties are stronger within domains (such as psychological), properties also cluster across domains.[25-27]

Properties cluster because the presence of some properties favors the presence of others. For example, lack of concentration tends to follow sleepless nights. Associations are usually probabilistic: there is variability in how people respond to a night of bad sleep. Such probabilistic associations lead to imperfect aggregations, which means that if we accept the HPC view, diagnoses will by their very nature encompass individuals that differ in important aspects, similar to meaningful differences among a group of giraffes. Correlations among properties also lead to zones of rarity: severe sleep problems and sustained high performance rarely cooccur, as do severe suicidal ideation and elevated positive affect.

There are various reasons for correlated properties, but all have in common some underlying causal structure. For example, insomnia causally explains variance in concentration problems. Such links will usually be moderated or mediated by a host of further processes. This, in turn, relates to causal structures such as third variable explanations, like the link between having a diagnosis of depression and experiencing loss of libido, which may be due to taking antidepressants. There are also cohesion-inducing mechanisms—common causes such as traumatic experiences or low socioeconomic status—that generate correlations among many properties. This is also known as endogeneity in epidemiology, where correlations among a set of features are inflated unless the common cause, in our case some unmeasured shared etiology of various mental health properties, is taken into account. Such etiological features are of particular interest from a causal perspective.

We can also distinguish more global from more local associations.[28] Global associations likely generalize better: lack of sleep always decreases vigilance. Other, more local associations may depend on the time of day they are experienced, cultural norms, language groups, or climate regions. For example, the association between socioeconomic status and mental health problems varies across both time and place.[29,30]

Mapping Out a Mental Health Atlas

Suppose we could obtain data on all mental health properties in all people. Based on the idea of HPCs, we could now map out the statistical associations among all mental health properties in an atlas of mental health. This atlas would provide a large-scale, descriptive, nomological network: a starting point for further interrogation. What properties cluster together, and what does the resulting map of clustered properties look like? Do clean property clusters emerge, or is the resulting map largely messy? Do some clusters more cleanly separate than others, and can we identify hierarchies of clusters? What mental health properties play important roles across many clusters, and what are the most prominent cohesion-inducing mechanisms for the largest clusters? Are the most important properties evenly spread across biopsychosocial domains? And what are the most temporally stable and unstable clusters?

Answers to these and related questions would provide crucial inroads to mechanistic research, theory building and testing, and, in turn, psychiatric classification as a whole. Below, I sketch a 5-point research agenda to pursue this idea further.

Data Collection

First, I propose we collect data in large, representative samples with varying degrees of mental health problems. We start with a pragmatic set of mental health properties, such as an abridged version of the transdiagnostic symptom set developed by Forbes.[31] We extend this set to include other important biopsychosocial properties, including social determinants that are under researched in mental health science.[22] This extension is necessary because symptoms no longer form a sensible category of mental health properties; what ties them together as a group is their definition as passive indicators of underlying diseases, an outdated causal model.[32-34] Including etiology and other features in clustering may also help overcome problems of symptom heterogeneity; it is plausible that 2 groups of people require different types of treatment despite experiencing very similar symptoms. Such groups could potentially be identified by validators outside of symptom sets. The extension may also help tackle one of the core problems of the *DSM*: that diagnostic categories provide poor guidance to studying etiology.

Variable-Centered Mapping

Second, equipped with some data, we use statistical models to map out associations among properties, including zero-order correlations (**Figure 2**) and conditional-dependence associations (**Figure 3**). This results in a vast nomological network of properties—a variable-centered projection of the atlas—showcasing which variables cooccur together.

Person-Centered Mapping

Third, we can summarize the associations among variables in several dimensions (**Figure 4**) and then derive a person-centered projection of the atlas that shows individual people as dots on a map (**Figure 5**). Correlated properties in this space result in property clusters, allowing us to study who goes with whom and what people who cluster have in common.

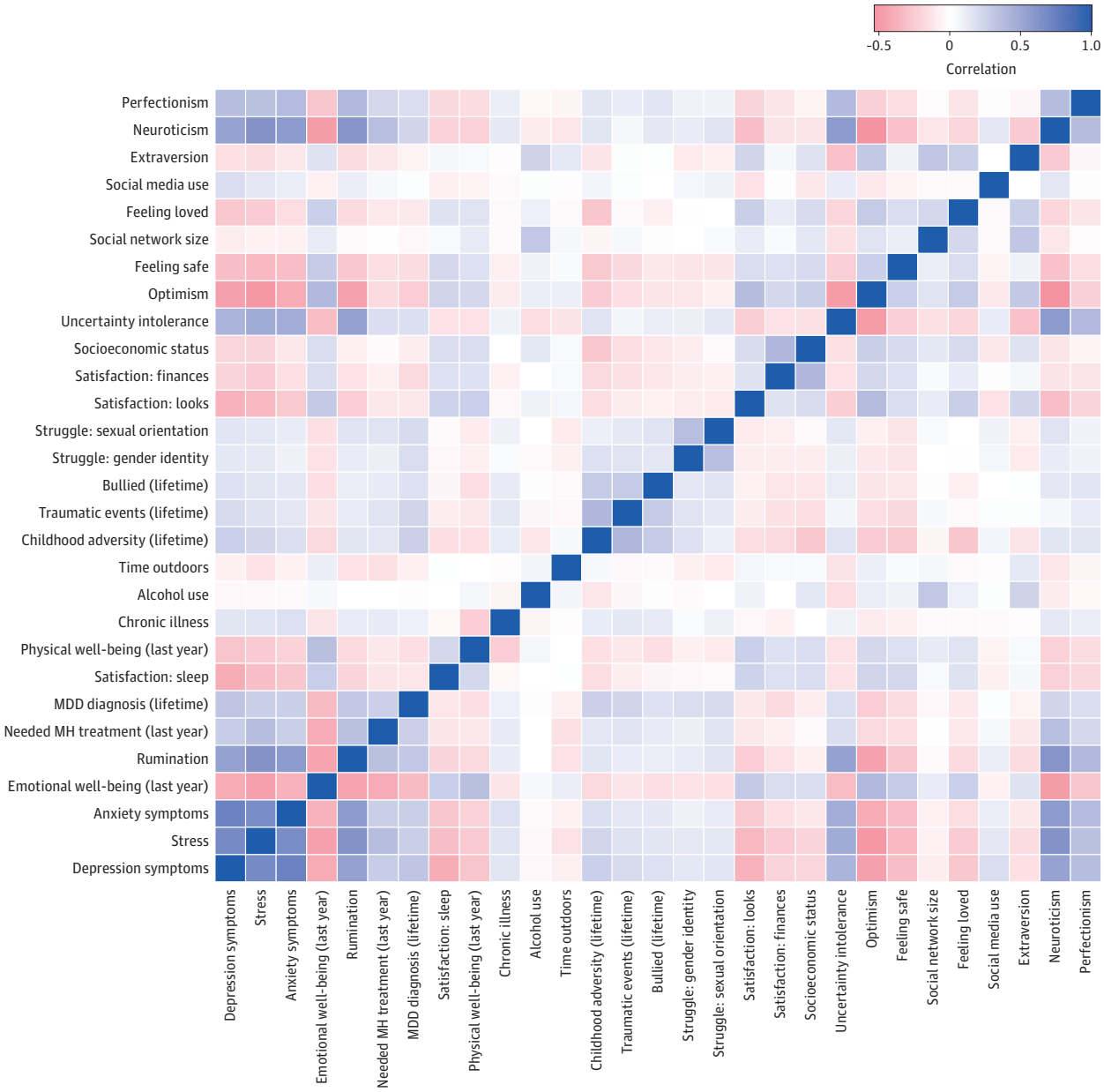
Zooming In

To construct more local maps, we can also limit the space of variables or people to subsets we are particularly interested in. For example, we can focus only on biological properties, or only on people seeking help for mental health problems. We can also compare local maps—for example, to figure out the role of the cohesion-inducing mechanism socioeconomic status across different countries.

Time

Most prior work in mental health science can be interpreted as contributions to mapping out the atlas[33,35-38]: identifying relevant mental health properties, their associations, and their dynamics. This last part highlights a core challenge: that mental health problems are

Figure 2. Heat Map Showing Correlations of 29 Psychosocial Mental Health Properties From the WARN-D Study (N = 1193)

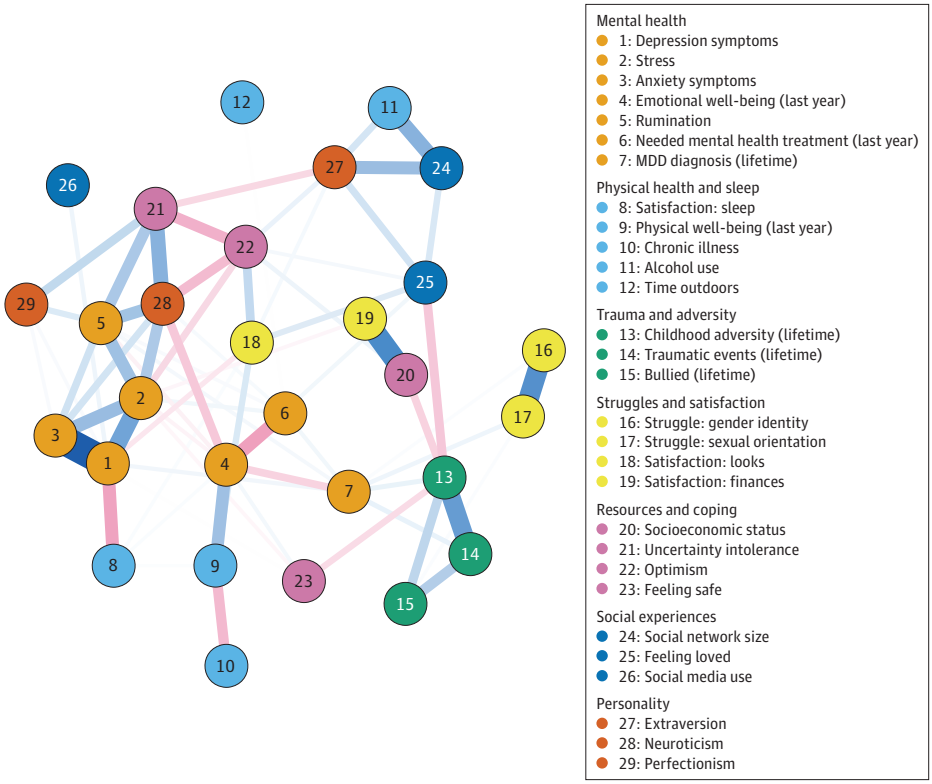


All variables are part of the baseline assessment of WARN-D[42] and were collected as general ("I see myself as someone who…") or present (current depression symptoms) items, except for variables denoted as lifetime and last year. See the eAppendix in the Supplement for details about data, measures, and methods. Simulation code is available at https://osf.io/vnxd5.
MDD indicates major depressive disorder; MH, mental health.

dynamic and cannot be fully understood cross-sectionally. The HPC view allows us to extend the atlas into time-varying versions, such as a point cloud of people that can move over time. Assume a person is in a healthy, stable state of mental health, self-reinforced by a system of financial resources, a supportive social network, adaptive coping mechanisms, personality features, and so on. We can use mathematical models to infer this person's safe operating space[39]: a certain region of the atlas in which the person can move around without risk. If a person moves beyond that space, they may transition to an alternative stable state, such as a depressive or manic episode. Mapping this out for a group of people diagnosed with bipolar disorder, for example, may show them rather rapidly switch between several different atlas regions—mania, depression, health, and perhaps mixed mania—in turn offering inroads for tools and concepts from complexity science.[34,40-42]

With advances in ambulatory assessment tools[43] such as smartphone-based ecological momentary assessment[44] and wearable-based passive sensing,[45] tracking people over time has become feasible at large scale to detect potential changes in stable states.[42,46] While this relatively new line of work raises more questions than it

Figure 3. Network Diagram Showing Conditional Dependence of 29 Psychosocial Mental Health Properties From the WARN-D Study (N = 1193)



All variables are part of the baseline assessment of WARN-D[42] and were collected as general ("I see myself as someone who…") or present (current depression symptoms) items, except for variables denoted as lifetime and last year. See the eAppendix in the Supplement for details about data, measures, and methods. Simulation code is available at https://osf.io/vnxd5. Blue edges depict positive associations; red edges, negative associations. MDD indicates major depressive disorder.

currently answers, it offers a promising path for mental health science to incorporate time-varying features of data as a central component of clustering efforts.

Empirical Demonstration

Figures 2, 3, 4, and 5 showcase an empirical demonstration of this mapping, using convenience data of 29 psychosocial variables in a sample of 1193 students from the WARN-D study.[42] Given the lack of comprehensive data and open questions that will need to be further developed in future work, this is an illustration only, intended not to derive empirical insights but to use visualizations as a heuristic tool for clarifying the conceptual framework of HPCs.

Overall, the variable-centered projections in Figure 2 (correlations) and Figure 3 (partial correlations) showcase heterogenous associations among properties, with associations both within (eg, symptom screeners) and across (eg, mental health, resources, social experiences, and personality) domains. The strongest principal components in Figure 4 are C1 (internalizing problems), C2 (lifetime trauma, low socioeconomic status, and financial concerns), and C3 (alcohol use, social network size, and extraversion). In Figure 5, we can see where individuals with depression cluster in the person-centered projection of this map.

Superimposing Structure

For centuries, biologists have studied animal properties and developed the foundational theory of evolution. Yet, despite the ability to interbreed animals experimentally and the access to millions of years of fossils, imposing species categories that form sharp boundaries remains challenging because "there are many different, (approximately) equally methodologically important ways of demarcating species, each corresponding to a different legitimate way of understanding species level taxa."[13]

There is no reason to believe that mental disorders should form neater categories than species. From the HPC perspective, diagnoses, just like species, are obtained not by discovering them in data, but by superimposing a structure on the complex landscape of properties.[32,47] Crucially, "this does not make symptoms and impairments of psychiatric disorders or their underlying etiology or pathophysiology less real, any more than Ptolemaic astronomy made stars and planets less real."[47] Instead, it means that there is more than one empirically grounded, scientifically accurate and robust way to slice the cake of mental disorders.

Another complication is that mental health problems and associated labels are moving targets that must be interpreted in light of cultural, contextual, and historical factors—shell shock, neurasthenia, hysteria, Hikikomori, internet gaming disorder, and climate

Figure 4. Heat Map of Loadings From a Principal Components Analysis of 29 Psychosocial Mental Health Properties From the WARN-D Study (N = 1193)

All variables are part of the baseline assessment of WARN-D[42] and were collected as general ("I see myself as someone who…") or present (current depression symptoms) items, except for variables denoted as lifetime and last year. See the eAppendix in the Supplement for details about data, measures, and methods. Simulation code is available at https://osf.io/vnxd5. C1 indicates component 1; C2, component 2; C3, component 3; MDD indicates major depressive disorder; MH, mental health.

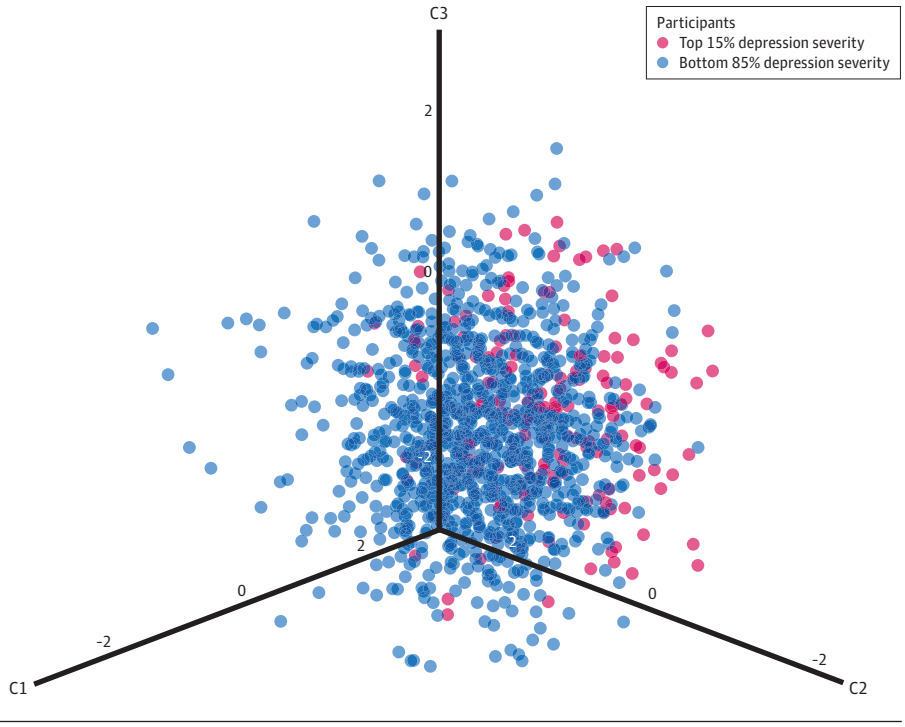
anxiety are good examples. Having a clear goal in mind helps to adjudicate between different ways of clustering the property space, and a crucial goal is clinical utility, providing information about clinical presentation, etiology, treatment specificity, prognosis, and treatment outcomes.[5] For this reason, variables beyond symptoms such as etiology and treatment response should be included to begin with. But there are other goals for comprehensive classification, too: justifying billing and coverage, determining service eligibility and criminal responsibility, prevalence estimation, investigating pathophysiology, or defining study populations. We should take seriously the idea of developing different classification frameworks that maximize utility for different purposes. Biological species offer a fruitful analogy here once again, where different species concepts carve up the same biological reality but serve somewhat different scientific goals—including quantitative classification (phenetic species concept), evolutionary explanation (biological species concept), ecological differentiation (ecological species concept), and taxonomic classification (phylogenetic species concept).

Conclusions

To reiterate, the HPC view for mental health science has 3 core premises: (1) there are many interrelated mental health properties; (2) clustering is driven by probabilistic associations, which leads to fuzzy groups; and (3) diagnoses cannot be discovered in this space, they must be defined. What kind of world would emerge if these 3 premises held? It would be one where monocausal explanations of mental health problems have largely failed. Instead, there would be hundreds of biopsychosocial risk and resilience factors, explaining only modest amounts of variance in isolation. Categorical diagnoses would be plagued by heterogeneity, high comorbidity, limited interrater reliability, and variable treatment efficacy. Interventions targeting specific problems (eg, sleep) would show efficacy across diagnostic boundaries (eg, mood and anxiety disorders), because they would target shared processes rather than diagnostic labels. And we would find many dimensional traits underlying categorical disorders, alongside persistent disagreements over mental health theories, measurement, and classification.[2-4,31,48] In other words, the HPC view accounts for many robust phenomena in mental health science that are often treated as separate challenges but that can be understood as natural consequences of a probabilistically structured property space and superimposed diagnoses.

Second, the HPC view connects to and integrates many clinical and research frameworks.[36] We can situate it within Engel's biopsychosocial model[17] and see clear associations to network and system approaches that conceptualize mental health problems as states that emerge out of complex associations, leading to clustering of variables and people.[32-34,40] It also resonates with dimensional approaches, such as the Hierarchical Taxonomy of Psychopathology,

Figure 5. Point Cloud of Individuals on 3 Principal Components Derived From 29 Psychosocial Mental Health Properties in the WARN-D Study (N = 1193)



Depression severity is based on the 9-item Patient Health Questionnaire. See the eAppendix in the Supplement for details about data, measures, and methods of the WARN-D study. Simulation code is available at https://osf.io/vnxd5. Components (C1-C3) are derived from Figure 4. The lines show standardized component scores.

which summarize statistical spaces of interest via latent variable models.[37] These latent variables can operate as organizing principles, denser areas in statistical space that require explanation.[49] This, in turn, relates closely to Cronbach and Meehl's nomological networks, where a construct is defined by its associations with other constructs[50]: the atlas is an extension of this idea. The HPC view further aligns with frameworks focused on understanding and targeting transdiagnostic mechanisms (eg, Research Domain Criteria, Unified Protocol, process-based cognitive behavioral therapy[38,51,52]), which serve as stabilizing forces or cohesion-inducing properties. Because property clusters are imperfect aggregations, the HPC view dovetails with idiographic approaches to mental health treatment, encouraging treatment plans based on individual property profiles, which can substantially differ across people, even within the same cluster.[53,54] Further, the notion of establishing rather than discovering diagnoses is consistent with modern pragmatic accounts of psychopathology.[55] Finally, the view connects to recent efforts to construct formal theories for mental disorders, which can be understood as zooming into the space of the atlas containing the most relevant mental health properties, associations, and dynamics for a particular phenotype or diagnosis, such as panic disorder or suicidal ideation.[56,57]

Third, the HPC view reframes the complex nature of the mental health landscape not as a problem, but as flexibility. It helps us sidestep the unproductive debates over the best approach by embracing pluralism[2,48]: no single classification system will optimally serve all stakeholders. This is because clinicians, researchers, and policymakers have different priorities and face different constraints. If categories are superimposed rather than truths discovered, then it is essential to develop multiple coexisting frameworks, each tailored to its pragmatic function, rather than championing a universal taxonomy.

Fourth, the HPC view refocuses our attention on the core question of why variables and people aggregate in statistical spaces. Importantly, such clusters and associated labels require explaining, they do not do the explaining. An animal does not have a long neck because it is a giraffe—we label the animal as a giraffe due to its long neck. In the same way, a person's diagnosis of generalized anxiety disorder does not make them sleep badly—their problems are summarized as generalized anxiety disorder.[58]

Ultimately, data-driven classification efforts are reminiscent of the earliest efforts to understand species: numerical taxonomy, counting overlapping features. Modern species concepts, based on ecological niches, reproduction, and shared ancestry, all critically rely on Darwin's theory of evolution. At a time when both classification manuals like the *DSM* and research frameworks like the Hierarchical Taxonomy of Psychopathology are proudly agnostic, the HPC view reminds us that successful classification may require strong theories that explain clustering, reorienting the field toward theory building and testing.[57,59]

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