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Classification of psychopathology: conceptual and historical background

In their paper in this issue of the journal, Krueger et al¹ consider two different approaches to the classification of psychopathology. Here I would like to focus on the conceptual and historical background of these approaches.

What the authors call “authoritative” nosology – represented currently in the US by the DSM-5 system² – evolved from classificatory efforts starting in the late 17th century, when large numbers of patients began to be collected in asylums in Central and Western Europe. These efforts were based on earlier attempts to classify general medical conditions, which were in turn heavily influenced by systems that classified animal and plant species as part of the beginning of zoology and botany as descriptive sciences³. So, I agree with the authors that the DSM is an historically influenced document, but I see this more positively than they do.

Medicine has worked by a gradual evolutionary process of the articulation of broad syndromes, many of which, with advancing knowledge, become divided up into more homogeneous entities that then develop into what we might call “disorders” and eventually “diseases”. In psychiatry, this process has been slower and more difficult than in most areas of medicine, but still represents an accumulated wisdom that typically works pretty well in the real world of patient care. How well it serves the goals of research is another matter.

As this brief history suggests, categories are inextricably intertwined with the world of clinical medicine. Individuals in care need to be given diagnoses because of the key dichotomies that exist in this world – to treat or not to treat, to discharge (from an emergency room) or hospitalize, to qualify for a particular treatment algorithm or not, to bill or not and, if to bill, with what specific code. This does not, of course, preclude quantitative measures, the focus of the nosologic approach advocated by the authors. These too are woven into the fabric of medicine. Think of temperature, pulse rates, fasting blood sugar, white blood cell counts and bone densities. These measures happily co-exist with the diagnostic world and are used nearly universally to monitor health and illness and guide therapy.

I worry that underneath this debate about continua versus categories there is a confusion between the “levels” of underlying physiology/etiology and clinical manifestation. Let me illustrate this by a “thought experiment”:

A steep south-facing slope in the high mountains received a heavy snowfall. The next morning dawns warm with a clear sky and strong sun. The temperature – a classical quantitative variable – at the lower levels of the snow pack starts to rise and melting increases gradually throughout the morning. Suddenly, in mid-afternoon,

the snow pack starts to slide, ending in a dramatic avalanche.

This example illustrates a natural quantitative process – snow melting with increasing temperature – and a dramatic threshold effect. If you work for the ski patrol to prevent avalanches, you need to understand both processes.

Turning to medical applications, consider a femur with increasing levels of strain – a quantitative trait. At some point, the bone breaks with dramatic health consequences. Think of a coronary artery with increasing occlusions as cholesterol plaques increase. At some point, the blood flow and associated delivery of oxygen slips below a critical level. Heart tissue starts to die and a myocardial infarct occurs.

I agree that taxometric methods provide at most modest evidence for discrete diagnostic categories in psychiatry. But I want to add to this discussion a different and informative perspective – within individual analyses. Like when seeing an avalanche, when seeing an acute patient presenting in the emergency room with a broken femur or an active myocardial infarction, it is difficult to conclude that one should only be concerned with the underlying quantitative process. Something clinically dramatic and “categorical” has occurred that calls for immediate intervention. Consider the following brief psychiatric vignettes:

A vulnerable individual, who stopped his antipsychotic medication four weeks ago, over 48 hours transitions from a non-psychotic state to a full-blown psychosis characterized by active auditory hallucinations and persecutory delusions about which he is quite preoccupied.

An individual with prior bipolar illness in good remission, after traveling across five time zones and experiencing several nights of poor sleep, the next day, “flips” into a fully syndromal mania.

You observe a friend with panic disorder in a crowded restaurant go from a calm, collected state in less than a minute to one of acute distress with sweating, panting, shaking and fear of dying.

While not all psychiatric disorders have such dramatic “avalanche-like” transitions, they are fairly common in clinical psychiatry and challenge the authors’ conclusions that there is little viable evidence that psychiatric disorders need to be understood from a categorical perspective.

Let me turn to a quite different issue. I was concerned by the manner in which the authors characterize the DSM pro-

cess: “group discussions and associated political processes”, manifesting “sociopolitical dynamics”, issuing *ex cathedra* decisions with the final diagnoses resulting from “presumed authority and fiat”. This tone will not aid interdisciplinary discourse. The authors imply that they are the objective scientists while those who worked on DSM are, by comparison, bogged down in political discourse and constrained by old-fashioned historical dictates. While this is not the place to discuss this in detail, any organized effort in science to develop classifications involves “sociopolitical dynamics”. Readers who think otherwise might consult a history of the decision of the International Astronomical Union to remove Pluto from the official list of planets⁴.

I want to conclude by talking about standards of diagnostic validation. At the risk of over-simplification, the Hierarchical Taxonomy of Psychopathology (HiTOP) program emphasizes psychometric methods in its typological proposals. Such methods have been key in the history of psychology, for example in the development of personality typologies and measures of various cognitive skills. So, it is sensible that they should be applied in the area of psychopathology. However, this approach differs considerably from the medical tradition emphasized by DSM. Put simply, the medical tradition wants diagnoses that tell us a lot about the patient – the course, the likely etiologic process, the best treatment, etc.. We organize our literature around our diagnoses, from cohort studies to randomized controlled trials.

The specific articulation of this viewpoint in psychiatry was first given by Robins and Guze⁵ with their list of validators, substantially expanded since then. Since DSM-III, the role of the evaluation of validators in diagnostic change has, albeit some-

what unevenly, gradually increased. The main approach has been the use of literature reviews trying to summarize available information on validators. These questions were the specific focus of the Scientific Review Committee that evaluated every proposed diagnostic change in DSM-5⁶. The procedures developed for change in DSM-5 by the American Psychiatric Association’s Steering Committee are empirically rigorous and data driven⁷.

It is not surprising that the scientific disciplines of psychiatry and clinical psychology have developed different approaches to the creation and evaluation of diagnostic entities/dimensions. Optimal communication between these two disciplines, however, requires an understanding of the similarities and differences in these approaches, the relative strengths and limitations of each approach, and the acceptance by both sides that each is likely to be able to contribute meaningfully to the difficult challenge of designing an optimal psychiatric classification.

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1. Krueger RF, Kotov R, Watson D et al. *World Psychiatry* 2018;17:282-93.
2. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*, 5th ed. Arlington: American Psychiatric Association, 2013.
3. Kendler KS. *Psychol Med* 2009;39:1935-41.
4. Zachar P, Kendler KS. *Philos Ethics Humanit Med* 2012;7:4.
5. Robins E, Guze SB. *Am J Psychiatry* 1970;126:983-7.
6. Kendler KS. *Psychol Med* 2013;43:1793-800.
7. First MB, Kendler KS, Leibenluft E. *JAMA Psychiatry* 2017;74:115-6.

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Progress in achieving quantitative classification of psychopathology

Robert F. Krueger¹, Roman Kotov², David Watson³, Miriam K. Forbes⁴, Nicholas R. Eaton⁵, Camilo J. Ruggero⁶, Leonard J. Simms⁷, Thomas A. Widiger⁸, Thomas M. Achenbach⁹, Bo Bach¹⁰, R. Michael Bagby¹¹, Marina A. Bornovalova¹², William T. Carpenter¹³, Michael Chmielewski¹⁴, David C. Cicero¹⁵, Lee Anna Clark³, Christopher Conway¹⁶, Barbara DeClercq¹⁷, Colin G. DeYoung¹, Anna R. Docherty¹⁸, Laura E. Drislane¹⁹, Michael B. First²⁰, Kelsie T. Forbush²¹, Michael Hallquist²², John D. Haltigan¹¹, Christopher J. Hopwood²³, Masha Y. Ivanova⁹, Katherine G. Jonas², Robert D. Latzman²⁴, Kristian E. Markon²⁵, Joshua D. Miller²⁶, Leslie C. Morey²⁷, Stephanie N. Mullins-Sweatt²⁸, Johan Ormel²⁹, Praveetha Patalay³⁰, Christopher J. Patrick³¹, Aaron L. Pincus²², Darrel A. Regier³², Ulrich Reininghaus³³, Leslie A. Rescorla³⁴, Douglas B. Samuel³⁵, Martin Sellbom³⁶, Alexander J. Shackman³⁷, Andrew Skodol³⁸, Tim Slade³⁹, Susan C. South³⁵, Matthew Sunderland³⁹, Jennifer L. Tackett⁴⁰, Noah C. Venables¹, Irwin D. Waldman⁴¹, Monika A. Waszczuk², Mark H. Waugh⁴², Aidan G.C. Wright⁴³, David H. Zald⁴⁴, Johannes Zimmermann⁴⁵

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Shortcomings of approaches to classifying psychopathology based on expert consensus have given rise to contemporary efforts to classify psychopathology quantitatively. In this paper, we review progress in achieving a quantitative and empirical classification of psychopathology. A substantial empirical literature indicates that psychopathology is generally more dimensional than categorical. When the discreteness versus continuity of psychopathology is treated as a research question, as opposed to being decided as a matter of tradition, the evidence clearly supports the hypothesis of continuity. In addition, a related body of literature shows how psychopathology dimensions can be arranged in a hierarchy, ranging from very broad “spectrum level” dimensions, to specific and narrow clusters of symptoms. In this way, a quantitative approach solves the “problem of comorbidity” by explicitly modeling patterns of co-occurrence among signs and symptoms within a detailed and variegated hierarchy of dimensional concepts with direct clinical utility. Indeed, extensive evidence pertaining to the dimensional and hierarchical structure of psychopathology has led to the formation of the Hierarchical Taxonomy of Psychopathology (HiTOP) Consortium. This is a group of 70 investigators working together to study empirical classification of psychopathology. In this paper, we describe the aims and current foci of the HiTOP Consortium. These aims pertain to continued research on the empirical organization of psychopathology; the connection between personality and psychopathology; the utility of empirically based psychopathology constructs in both research and the clinic; and the development of novel and comprehensive models and corresponding assessment instruments for psychopathology constructs derived from an empirical approach.

Key words: Psychopathology, mental disorder, personality, nosology, classification, dimensions, clinical utility, Hierarchical Taxonomy of Psychopathology, ICD, DSM, RDoC

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Throughout the history of psychiatric classification, two approaches have been taken to delineating the nature of specific psychopathologies¹. A first one might be termed authoritative: experts gather under the auspices of official bodies, and delineate classificatory rubrics through group discussions and associated political processes. This approach characterizes official nosologies, such as the DSM

and the ICD. It also often characterizes official efforts to influence the constructs and conceptualizations that frame the perspectives of funding bodies. For example, the US National Institute of Mental Health’s Research Domain Criteria (RDoC) effort involved the delineation of constructs that were shaped and organized by panels of experts².

A second approach might be termed

empirical. In this approach, data are gathered on psychopathological building blocks. These data are then analyzed to address specific research questions. For example, does a specific list of symptoms delineate a single psychopathological entity or, by contrast, do those symptoms delineate multiple entities? This approach is sometimes characterized as more “bottom up”, compared

with the more “top down” approach of official nosologies. This is because the approach generally starts with basic observations and works to assemble them into classificatory rubrics, rather than working from a set of assumed rubrics to fill in the detailed features of those rubrics.

Obviously, these approaches, although distinguishable, are not entirely separable. Authoritative classification approaches have relied on specific types of empiricism as part of their construction process, and an empirical approach begins with the expertise needed to assemble and assess specific psychopathological building blocks (e.g., signs and symptoms). Nevertheless, it is clear that authoritative approaches tend to weigh putative expertise, disciplinary background, and tradition heavily.

To pick a specific example, the construction of DSM-5 was primarily a psychiatric endeavor, by virtue of the disciplinary background of most participants and by the nature of the body that served to generate and publish the manual (i.e., the American Psychiatric Association). As part of the DSM-5 construction process, field trials were undertaken to evaluate the reliability of specific mental disorder diagnoses. Interestingly, these trials produced a wide range of reliability estimates, encompassing evidence of weak reliability for many common diagnostic entities, such as major depressive disorder and generalized anxiety disorder³. In spite of questionable reliability, these constructs remain enshrined in DSM-5 and constitute the official “diagnostic criteria and codes” in Section II of the manual.

Because of these types of sociopolitical dynamics (e.g., asserting the existence of specific psychopathological categories *ex cathedra* despite questionable evidence), authoritative approaches have come under increased scrutiny. Many types and sources of scrutiny coalesce around the scientific disappointments that have accompanied research on diagnostic categories. Simply put, the categories of official nosologies have not provided compelling guidance in the search for etiology and pathophysiology. As a result, the empirical approach to classification

is now attracting great interest as a potential alternative to diagnosis by presumed authority and fiat.

In the present paper, we summarize some key types of evidence that have emerged from the burgeoning literature on empirical approaches to psychiatric classification. We focus in particular on: a) evidence pertaining to the continuous versus discrete nature of psychopathological constructs; b) evidence for the hierarchical organizational structure of psychopathological constructs; and c) evidence for specific empirically-based organizational rubrics.

In our discussion of specific empirically-based organizational rubrics, we focus on a consortium that has recently formed to organize and catalyze empirical research on psychopathology, the Hierarchical Taxonomy of Psychopathology (HiTOP) Consortium. As we discuss the work of this consortium, we consider major issues that confront an empirical approach to classification, as it continues to evolve. These issues correspond to existing workgroups in the consortium, and hence, we use the foci of those workgroups to organize our discussion.

Specifically, those workgroups and our discussion are organized around: a) continued research on the organization of broad spectra of psychopathology; b) the connection between personality and psychopathology; c) the utility of constructs derived from an empirical approach (e.g., the ability of these constructs to organize research on pathophysiology); d) translation of empirical research into clinical practice; e) the development of novel and comprehensive models and corresponding assessment instruments for constructs derived from an empirical approach.

THE CONTINUOUS VS. DISCRETE NATURE OF PSYCHOPATHOLOGICAL PHENOTYPES

Perhaps the most fundamental difference between current authoritative psychiatric nosologies and empirical research on psychopathology classification per-

tains to the continuous vs. discrete nature of constructs. Through tradition and putative authority, authoritative nosologies claim that psychopathologies are organized into discrete diagnostic entities. By contrast, an empirical approach to classification treats the discrete vs. continuous nature of psychopathology as a research question⁴. When treated as a research question, evidence points toward the generally continuous nature of psychopathological variation.

Taxometric evidence

Taxometric methods originated in the writings of P. Meehl, and evaluate the possibility that a set of symptoms (or other indicators of psychopathology) delineate a discrete group. These methods have been used extensively, such that there is now a considerable literature on their application. This literature was summarized quantitatively by Haslam et al⁵. Based on findings from 177 articles, encompassing data from over half a million research participants, psychopathological variation was found to be continuous as opposed to discrete, i.e., there was little consistent evidence for taxa.

Subsequent taxometric reports in diverse areas also tend to reveal greater evidence for continuity as opposed to discreteness. For example, recent taxometric investigations have provided evidence for the continuity of subclinical paranoia and paranoid delusions⁶, adolescent substance use⁷, and depression in youth⁸. Occasional evidence for potential discreteness is also reported^{9,10}, emphasizing the importance of ongoing quantitative summaries of this literature.

Psychometric studies of putative taxa are important to establish their validity, such as evaluating stability over time. That is, longitudinal stability of putative taxon membership is also a key means of evaluating a taxonic conjecture, inasmuch as psychopathology taxon membership is conceptualized as a stable property over modest time intervals (e.g., weeks or months). For example, Waller and Ross¹¹ reported evidence that patho-

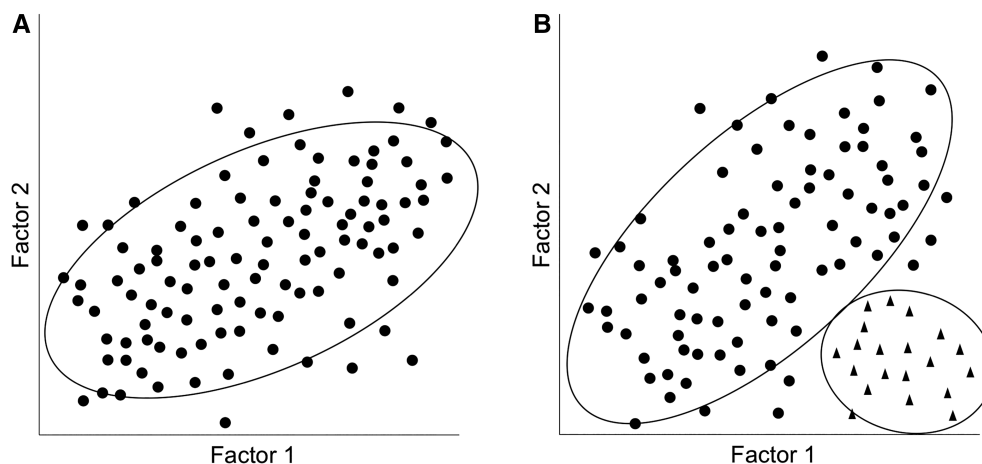


Figure 1 Illustration of hypothetical data compatible with fully continuous and partially discrete models of psychopathological variation. In Panel A, the data points are generally well captured by positing a single group, in which Factor 1 and Factor 2 are positively correlated. In Panel B, the data are better captured by positing two groups, one in which Factor 1 and Factor 2 are positively correlated (the circles), and a second smaller group in which Factor 1 and Factor 2 are weakly negatively correlated (the triangles).

logical dissociation might be taxonic. Watson¹² investigated this putative taxon and found that taxon membership was not stable across a two-month interval, whereas continuous indicators of dissociation were strongly stable.

In sum, extensive evidence suggests that the likelihood of identifying discrete psychopathology groups empirically via taxometrics is not high. By contrast, the taxometrics literature generally points to the continuity of psychopathological variation, emphasizing the greater relative utility and empirical accuracy of continuous as opposed to discrete conceptualizations of psychopathology.

Model-based evidence

Taxometric procedures originally evolved to some extent outside of the mainstream statistical literature. Within the more mainstream literature, approaches have emerged that rely on the ability to fit models to raw data on symptom patterns, and to use all of the extensive information in those data to adjudicate between continuous, discrete and hybrid accounts of psychopathology constructs. These approaches are often termed *model-based*, because they rely on formal

statistical models that describe the distributional form of the constructs that underlie symptoms.

Generally, direct comparison of continuous and discrete models via these approaches have indicated that psychopathological constructs tend to be more continuous than discrete^{13–19}. Nevertheless, there are also occasional suggestions of potentially meaningful discontinuities, particularly as conceptualized in models that have both continuous and discrete features^{20–22}.

For example, Figure 1 depicts a bivariate distribution similar to the results found in Forbes et al²⁰. Panel A shows a sample where the two continuous factors are moderately correlated for all participants (i.e., all participants are drawn from a single underlying population, akin to the results Forbes et al found for the relationships among depression, anxiety and sexual dysfunctions for women). In contrast, Panel B shows a discontinuity in the data where two groups emerge: the majority of the sample has a strong positive correlation between the factors, but a subgroup of the sample has a weak negative correlation (i.e., participants are drawn from two distinct underlying populations, akin to the results Forbes et al found for men). Generally speaking, the

development and comparison of models of latent structure remains a profitable and active area of inquiry, because this approach provides an empirical means of directly comparing and potentially integrating categorical and continuous conceptions of psychopathology^{23,24}.

However, similar to the situation with potential taxa, the discontinuities need to map truly discrete features of psychopathology (i.e., be reliable and replicable) to be meaningful. Consider, for example, how these requirements played out in a project reported by Eaton et al²⁵. In this project, *model based clustering* was used to discern potential discrete personality disorder groups. This approach works well in a variety of scientific areas, when there are actual discontinuities to be detected (e.g., character recognition, tissue segmentation; see <http://www.stat.washington.edu/mclust/>). Eaton et al therefore applied this approach to a large data set (N=8,690) containing samples from four distinguishable populations (clinical, college, community and military participants). Potential discontinuities observed in each sample were not replicated across samples. By contrast, a dimensional model of the data was readily replicated across the samples. The authors interpreted these findings as suggesting that personality dis-

order features did not delineate replicable discontinuities, but instead, represented replicable continuities.

In sum, efforts to identify potential discontinuities on the basis of data are important endeavors, because they continue to expose dimensional conjectures to risky and direct tests. Nevertheless, similar to what has been learned from decades of taxometric research, the bulk of the existing model-based evidence points to the dimensional nature of psychopathology.

Implications of dimensionality

Evidence to date, stemming from multiple empirical approaches, generally points to the continuity of psychopathological phenotypes. As a result, contemporary empirical approaches often conceptualize psychopathological constructs as dimensional, which has a number of implications. For example, it highlights the extent to which the categories of official nosologies are out of sync with data on the dimensional nature of psychopathology. This disparity is well recognized, and also, very challenging to navigate in a sociopolitical sense, because so many professional endeavors are firmly intertwined with the category labels enshrined in official nosologies²⁶. In this paper, we do not detail specific events that have recently played out surrounding this challenge (e.g., pertaining to DSM-5 and ICD-11), but we do note that the challenge needs to be faced head-on if official nosologies aim to be founded on solid empirical footing²⁷.

We also note here another key implication of the dimensional nature of psychopathology, pertaining to relations between manifest psychopathology and its correlates. Specifically, the continuous nature of psychopathological variation provides a framework for understanding the form and nature of relations between cumulative risk factors, manifest psychopathology, and important outcomes²⁸. Consider distal and putatively etiologic correlates, such as specific genetic and environmental risk factors. Continuous phenotypic variation suggests (but does not prove) that the relevant etiologic

elements are likely multiple and numerous. Multiple relatively independent causes give rise to continuous phenotypic variation, as is observed with many human phenotypes, e.g. height^{29,30}. Similar to physical phenotypes, psychopathological phenotypes are likely the result of specific mixtures of numerous etiologic influences, with both proportions of influence and the resulting phenotypes varying continuously across persons³¹.

In sum, the concept of continuous variation among persons in etiologic mixture dovetails well with the observation of continuous phenotypic variation, and provides generative strategies for etiologic research. For example, persons with similar phenotypic values may have arrived at those values in distinct ways. Hence, profitable research strategies might focus less on “cases” and “controls”, and more on developing multivariate models of the joint distribution of etiologic (e.g., genomic polymorphisms) and continuous phenotypic observations in larger samples³².

Turning from causes to consequences, thinking about continuous variation and the public health consequences of psychopathology may also provide novel insights. Although psychopathology appears to be a continuous predictor, the nature of its relationship with public health consequences could take numerous forms, at least in theory. Thinking about this situation may provide insights that go well beyond an artificial “cases vs. controls” research strategy. For example, continuous psychopathology may very well show a monotonically-increasing and generally linear relationship with impairment^{33,34}. Or, the relationship could have non-linear features, e.g., accelerating in a certain region of continuous psychopathological variation^{22,35}.

Again, the key point here is that these possibilities are empirically tractable when psychopathology is modeled dimensionally, yet obscured through the artificial dichotomization that characterizes traditional psychiatric nosologies. Somewhat ironically, continuous measurement of psychopathology is essential to evaluating the possibility that there are meaningful thresholds, beyond which social

and occupational dysfunction becomes increasingly more likely.

HIERARCHICAL ORGANIZATIONAL STRUCTURE OF PSYCHOPATHOLOGICAL DIMENSIONS

One perennial issue in developing an empirically-derived and dimensional approach to psychopathology pertains to general organizing principles. In traditional authoritative and categorical approaches to classification, this issue is tacitly addressed by the organizational structure of the classificatory effort. For example, the specific workgroup structure of the DSM-5 construction effort implies an organization of psychopathology into rubrics that reflect the workgroup names, and that structure trickles down into the chapter structure of the printed classification.

Might organizational issues also be addressed empirically? Evidence described in the foregoing section stems from asking if a specific set of signs and symptoms delineates a specific dimension as opposed to a specific category. This evidence suggests that psychopathology is generally dimensional in nature, but how many dimensions are there, and how are these dimensions organized?

Work in this area has generally progressed from asking “what is the correct number of dimensions” to realizing that this question is somewhat specious, because individual difference dimensions (e.g., individual differences in the propensity to experience specific psychopathological signs and symptoms) are organized *hierarchically*. This understanding has been important in resolving a variety of classificatory conundrums, typically focused in areas where two or more psychopathological constructs contain variation that is both shared and unique.

Perhaps the most classic example pertains to anxiety and depression³⁶. The tendency to experience pathological anxiety is clearly correlated with the tendency to experience pathological depression, yet these tendencies are also distinguishable. Categorical nosologies

have difficulty managing these situations, because they tend to lead to proposals of “mixed categories” (e.g., a category of mixed anxiety and depression that is putatively distinguishable from a category of anxiety only and a category of depression only). If anxiety and depression are more dimensional than categorical, as well as correlated but not perfectly correlated, then most patients will not fit neatly into any of these three categories. This tends to lead to difficulties making categorical diagnostic determinations in practice. For example, a mixed anxiety-depression category was proposed for DSM-5, but did not emerge from the field trials as a reliable diagnosis³⁷.

The key to resolving these sorts of dilemmas is to realize that the evidence is most readily compatible with conceptualizing anxiety and depressive phenomena (as well as other dimensional phenomena) as encompassed by *hierarchically organized dimensions*. To illustrate this point concretely, consider a model developed by Waszczuk et al³⁸, portrayed in Figure 2. This model, which is based on extensive data, shows how specific anxiety and depressive phenomena are associated with continuous degrees of similarity and distinctiveness, across four hierarchically arranged levels of generality vs. specificity. These hierarchical levels reflect the overall degree of empirical co-occurrence vs. distinctiveness of the phenomena encompassed by the model. Concepts higher in the figure are more general and broad, whereas concepts lower in the figure are more specific and narrow.

At the most general level, diverse anxious and depressive phenomena are understood to be aspects of a general domain of internalizing psychopathology. However, as is apparent in both data and clinical work in this area, although anxious and depressive phenomena are indeed correlated, they are not perfectly correlated and, therefore, are distinguishable from one another. Hence, one level down, distinctions emerge among distress, fear, and obsessive-compulsive (OCD)/manic phenomena. Note that this is a more refined and empirically based understanding when compared with DSM chapter headings, because, rather than

being delineated by individual committees, this model uses data to encompass the breadth of phenomena that fall into the internalizing domain.

Accordingly, at a third level of specificity, key distinctions emerge among aspects of the three distress, fear and OCD/mania domains. OCD and mania are distinguishable at this level, as are specific aspects of these broader domains, such as the cognitive and vegetative aspects of depression. Indeed, considered across levels, these patterns have fundamental conceptual and clinical implications. For example, these patterns highlight the connection between OCD and manic phenomena, as well as their distinctiveness from distress and fear. This may be traceable to the connection that OCD and manic phenomena share with the broad spectrum of psychosis, and how this psychotic aspect both drives OCD and mania together, and separates them from other parts of the internalizing spectrum³⁹. Finally, at the lowest level of the hierarchy lie specific symptom clusters, such as checking, lassitude, and so on.

In sum, the Figure 2 model solves the problem of “comorbidity between anxiety and depression” by using data to model the empirical organization of emotional disorder phenomena. Rather than forcing these phenomena into committee-derived categories, they are modeled as they are in nature. As a result, “complex presentations” (e.g., persons who present with a mix of emotional disorder symptoms) are handled because these presentations can be readily represented by a specific profile of problems. This understanding then drives case conceptualization in the clinic⁴⁰, and strategies for identifying key correlates (e.g., neural response) in the laboratory⁴¹.

Evidence for dimensional hierarchies can be found throughout psychopathology, and is not limited to anxiety and mood phenomena. Indeed, this evidence is sufficiently comprehensive that it has formed the basis for a consortium of researchers interested in empirical approaches to psychopathology, the HiTOP Consortium⁴². We turn now to describe the main features of the model that frames HiTOP, as well as the issues and topics

that are currently being pursued within HiTOP.

EVIDENCE FOR SPECIFIC EMPIRICALLY-BASED ORGANIZATIONAL RUBRICS

Given evidence that psychopathological phenotypes are dimensional in nature, and that these dimensions are organized hierarchically, what types of classificatory rubrics emerge in an empirical hierarchy of psychopathological dimensions? The HiTOP Consortium focuses on these and related issues.

The consortium currently consists of 70 investigators with backgrounds in diverse disciplines (e.g., psychology, psychiatry and philosophy), and this group has proposed a working dimensional and hierarchical model, derived from the literature on empirical psychopathology classification. This model is portrayed in Figure 3.

The model is not intended to be the final word on empirical psychopathology classification. Indeed, the purpose of articulating this model was to provide a first draft that might frame continued inquiry, and thereby move discourse away from tendentious debates about various reified classification schemes. Nevertheless, the model does summarize a substantial literature, reviewed by Kotov et al⁴³ as background for the hierarchical structure portrayed in Figure 3. Here, we will briefly outline the main features of the model, and then turn to discuss various workgroups within the consortium, which formed to address major issues in the field of empirical psychopathology classification.

As portrayed in Figure 3, the working HiTOP model is hierarchical in nature. Constructs higher in the figure summarize the tendencies for constructs lower in the figure to co-occur in specific patterns. For example, consistent with Figure 2, the broad internalizing spectrum in Figure 3 encompasses more specific “sub-spectra” such as the fear, distress and mania spectra. However, the model in Figure 3 was intended to synthesize the entire available literature on empiri-

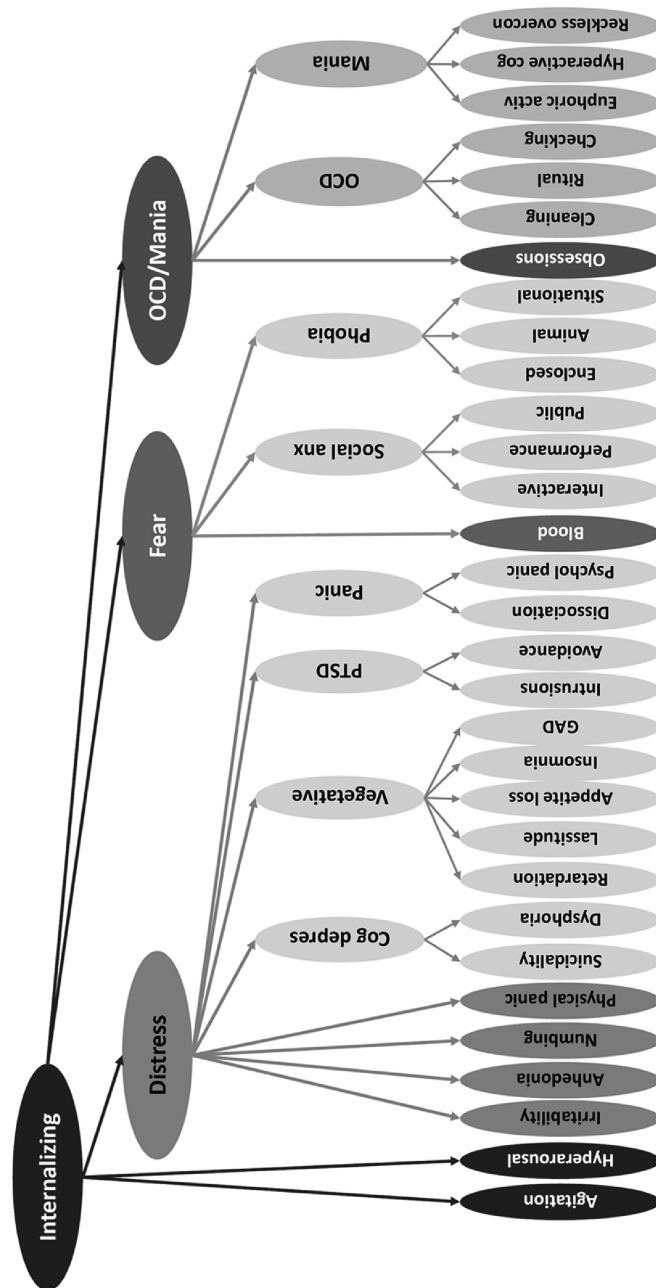


Figure 2 Illustration of an empirically based model of the internalizing spectrum. Constructs higher in the figure are broader and more general, whereas constructs lower in the figure are narrower and more specific (adapted from Waszczuk et al³⁸). PTSD – post-traumatic stress disorder, Social anx – social anxiety, OCD – obsessive-compulsive disorder, GAD – generalized anxiety disorder, Cog depress – cognitive depression, Psychol panic – psychological panic, Euphoric activ – euphoric activation, Hyperactive cog – hyperactive cognition, Reckless overcon – reckless overconfidence.

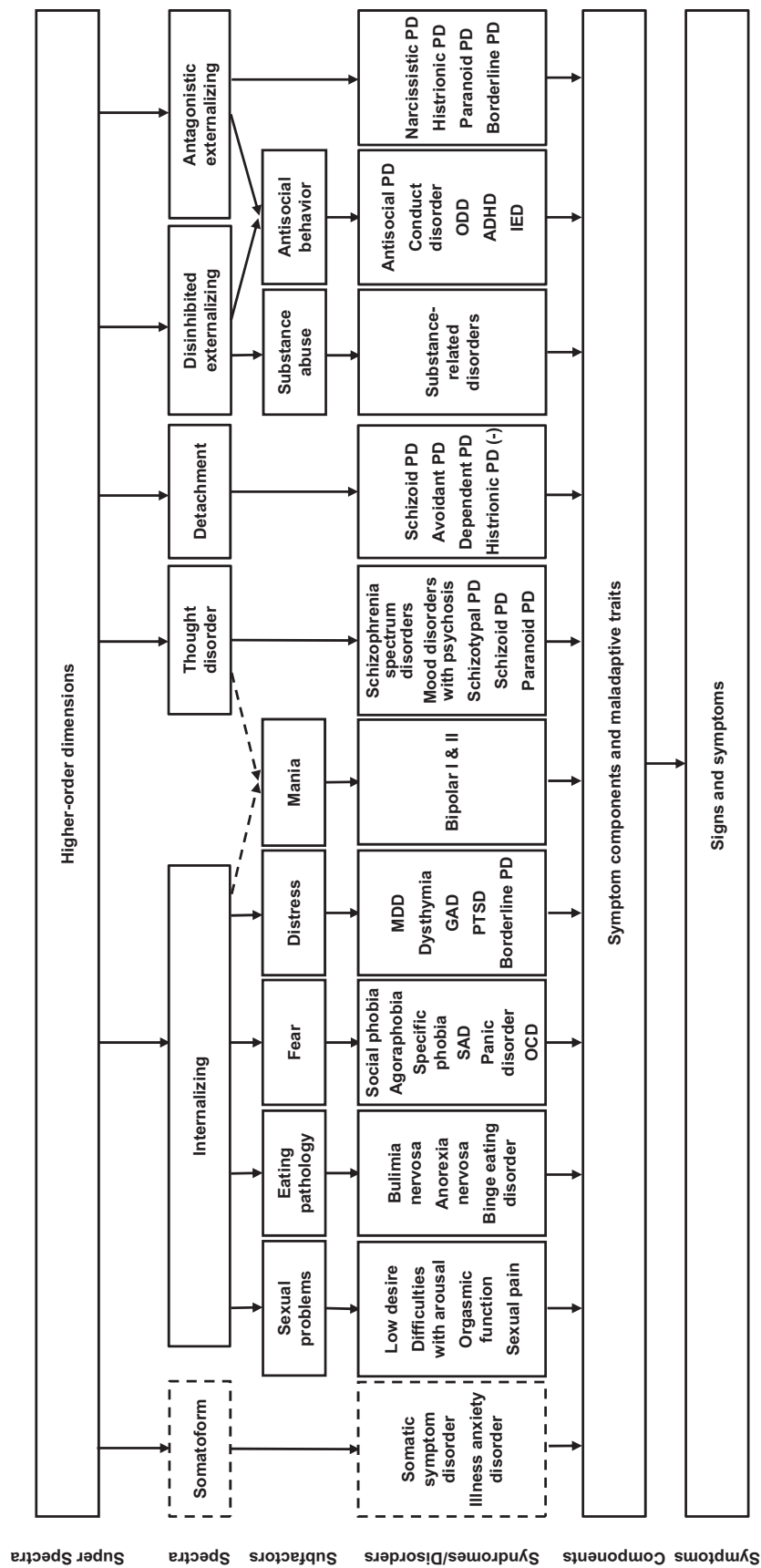


Figure 3 Working Hierarchical Taxonomy of Psychopathology (HiTOP) consortium model. Constructs higher in the figure are broader and more general, whereas constructs lower in the figure are narrower and more specific (adapted from Kotov et al⁴³). SAD – separation anxiety disorder, OCD – obsessive-compulsive disorder, MDD – major depressive disorder, GAD – generalized anxiety disorder, PTSD – post-traumatic stress disorder, PD – personality disorder, ODD – oppositional defiant disorder, ADHD – attention-deficit/hyperactivity disorder, IED – intermittent explosive disorder.

cal classification and, as a result, its scope and breath is considerably larger than the Figure 2 model, which was designed specifically to delineate the internalizing spectrum.

Consider spectra adjacent to internalizing in the Figure 3 model. In addition to the internalizing spectrum, five other major empirical divisions of psychopathology are portrayed on the same level. Currently, the model posits major spectra labeled *somatoform*, *thought disorder*, *detachment*, *disinhibited externalizing*, and *antagonistic externalizing*. These concepts are reminiscent of, but not necessarily coterminous with, similar constructs in existing authoritative nosologies such as the DSM and ICD. For example, the current HiTOP model posits the existence of a somatoform spectrum that is separable from other major psychopathology spectra, and roughly similar in content to somatoform diagnoses in DSM-5.

While the evidence for the somatoform spectrum is limited (as indicated by the dashed lines in Figure 3), this spectrum illustrates a general principle of empirical classification research. Phenomena that are not explicitly considered within a specific scope can be considered by expanding that scope accordingly. For example, somatoform constructs are not as heavily researched as other phenomena on the level of major spectra (e.g., internalizing and externalizing), and this provides an important opportunity for targeted and focused research⁴⁴. Specifically, how closely do somatoform concepts align with other spectrum concepts, and what are the shared and distinguishing features of these concepts?

Rather than being handled in relatively insular literatures aligned with traditional classificatory rubrics, the HiTOP framework provides novel opportunities for more targeted and synthetic research on key empirical questions in classification. For example, how do somatoform phenomena covary with other phenomena in the HiTOP model? Are they better understood as an aspect of the broader internalizing spectrum, or are they sufficiently distinguished to form their own separate spectrum? If they have both shared and distinctive features, are in-

tervention efforts more effective if focused on the shared features, or on the distinctive features? Such questions are posed and framed by thinking about somatoform phenomena in the context of psychopathology broadly, in ways that go well beyond a more piecemeal approach to parsing and conceptualizing psychopathology.

Similar to the situation with the somatoform spectrum, other constructs on the spectra level have varying volumes of associated literature, as well as being associated with specific arrangements portrayed in Figure 3. Recognizing these hypothesized arrangements provides generative avenues for novel research. Consider examples pertinent to each of the spectra in Figure 3. The thought disorder spectrum reflects the close empirical connections among psychotic phenomena that have historically been divided between more dispositional vs. more acute manifestations^{45,46}. This empirical distinction thereby becomes a topic for continuing empirical inquiry, and not an issue presumably settled by the unfortunate tradition of studying personality and clinical disorders in separate literatures⁴⁷.

For example, the ICD-11 proposal for personality disorders does not encompass a psychoticism domain, not because psychotic phenomena are outside of a comprehensive multivariate model of maladaptive personality, but rather because tradition places them in a different chapter within the ICD (and in contrast with the DSM, which assigns schizotypal disorder primarily to the personality disorders chapter, with a secondary assignment as part of the schizophrenia spectrum in the schizophrenia and other psychotic disorders chapter⁴⁸). Likewise, antisocial personality disorder is assigned both to the personality disorder and the disruptive, impulse control and conduct disorders chapter. In the HiTOP approach, these sorts of fundamental issues become topics for empirical inquiry.

Similar issues are addressed by the two externalizing spectra portrayed in Figure 3. The current HiTOP model reflects the distinction between the two major aspects of externalization: antagonism (hurting others intentionally) and

disinhibition (acting on impulse or in response to a current stimulus, with little consideration of consequences⁴⁹). As such, it also reflects the ways in which these separable aspects are both present in traditional DSM diagnostic criteria sets. For example, DSM-IV defined antisocial personality disorder, and similar DSM diagnostic concepts, represent a mix of antagonistic and disinhibited features⁵⁰. The HiTOP model posits that separating these empirically-based features may result in greater clarity regarding the classification of specific phenomena. For example, the model posits a closer connection between substance related disorders and disinhibition than between substance related disorders and antagonism. In addition, the model ties together closely aligned externalizing phenomena that are spread throughout DSM chapters and various literatures (e.g., child and adult manifestations of basic antagonistic tendencies, as well as phenomena such as intermittent explosive disorder).

Finally, consider the detachment (avoidance of socioemotional engagement) spectrum portrayed in Figure 3. Similar to somatoform phenomena, detachment phenomena have not been as heavily studied as other major spectra. In addition, similar to externalizing phenomena, detachment has been somewhat diffused throughout traditional nosologies, being captured within the features of a number of traditional personality disorders. The HiTOP model recognizes the evidence that detachment appears to be a major spectrum of adult psychopathology. As such, the model underlines the importance of understanding the public health significance of pathological socioemotional avoidance, as opposed to spreading this feature across constructs that have attracted relatively less clinical and research attention, compared with more florid manifestations of psychopathology.

Below the level of spectra in Figure 3 are levels encompassing subfactors and disorders. These concepts reflect a mix of more traditional and more empirically based rubrics. The presence of traditional diagnostic labels on Figure 3 is not to reify these concepts (many of which are highly heterogeneous, and therefore in need of

empirical refinement), but rather, to provide a cross walk to traditional and familiar DSM-style labels. As the model implies, the heterogeneity of these phenomena provides important opportunities for clarifying investigations.

Consider, for example, borderline personality disorder (BPD), which is listed below both the distress and antagonistic externalizing rubrics in the working HiTOP model. BPD encompasses a number of distinguishable elements and, as a result, tends to be associated with diverse psychopathology spectra^{51,52}. Indeed, the majority of the variance in BPD is shared with other forms of psychopathology (rather than being unique to it), emphasizing the importance of reducing BPD and similar constructs to their constituent elements, and working to reconstitute those elements in an empirical manner.

This type of refinement endeavor has been clarifying in specific literatures where it has been undertaken. For example, empirical efforts underlie large segments of the DSM-5 alternative personality disorder model, and frame the essential structure of the ICD-11 personality disorder approach, in ways that go fundamentally beyond traditional personality disorder rubrics. Thinking broadly, the HiTOP model underlines the general utility of this type of empirical refinement endeavor, pursued with regard to psychopathology writ large.

THE HIERARCHICAL TAXONOMY OF PSYCHOPATHOLOGY CONSORTIUM (HiTOP) AS A FRAMEWORK FOR CONTINUED PROGRESS

HiTOP is intended to serve as a consortium to organize and stimulate progress on an empirical approach to classifying psychopathology. To facilitate this progress, the consortium is organized into a series of workgroups. The workgroup rubrics do not exhaust all the important issues that might be addressed in empirical psychopathology classification. Nevertheless, they do reflect themes that have emerged to organize current HiTOP efforts. Importantly, membership

in HiTOP is not closed, and there are many opportunities to get involved in various aspects of the endeavor⁴².

Higher-order dimensions workgroup

A significant challenge posed by the model in Figure 3 is its breadth. As implied by the distinction between Figure 2 and Figure 3 (i.e., the distinction between detail and breadth), many empirical classification efforts have been understandably focused on specific spectra of psychopathology. Above the level of internalizing in Figure 3 is the “super spectra” level, which is currently open, largely because relations among various psychopathology spectra remains an active area of empirical inquiry. For example, there has been recent interest in a general psychopathology dimension, akin to the general dimension found in the cognitive abilities literature^{53,54}.

Although there is little doubt that variation in psychopathology spectra is generally correlated (i.e., multi-morbidity is encountered frequently), important issues remain to be addressed in contemplating the organizational structure of psychopathology above the spectrum level. For example, for a hierarchical construct to be “truly general”, its influence on constructs below it in a hierarchy should be relatively uniform. Contrary to this conceptualization, the magnitude of influence of the general psychopathology factor on specific constructs below it has not been necessarily uniform. For example, Caspi et al⁵³ modeled a general factor of psychopathology and found it to be associated primarily with psychotic phenomena. Lahey et al⁵⁴ also modeled a general factor of psychopathology, but found it to be associated primarily with phenomena that fall generally into the distress subdomain of internalizing (albeit they did not specifically study psychotic phenomena).

These distinctions between various representations of the general factor of psychopathology may relate to important technical issues surrounding the meaning and interpretation of a general factor. For example, technical issues have arisen

in the literature on individual differences in cognitive test performance. In that literature, it is now understood that ways of modeling general factors (e.g., using a bifactor versus a hierarchical structural model), and ways of comparing models (e.g., based on fit indices), differ in subtle but important ways from many traditional approaches to structural modeling⁵⁵⁻⁵⁷. These issues have yet to be addressed thoroughly in the psychopathology literature, and are therefore a focus of current activity in the higher order workgroup.

Furthermore, we note that the breadth of psychopathology in various studies of potential general factors is less than the breadth of psychopathology encompassed in Figure 3. How to efficiently assess (and thereby have the opportunity to model) the entire breadth of psychopathology covered by Figure 3 presents an important – and daunting – challenge. In addition, the current model does not encompass the neurodevelopmental spectrum (e.g., intellectual disability, autism spectrum disorders, learning disorders), the neurocognitive disorders, and the paraphilic disorders.

Measures development workgroup

Many existing measures assess different aspects of the HiTOP scheme (see <https://psychology.unt.edu/hitop>). Nevertheless, as of this writing, a comprehensive measure designed to assess the entire breadth of psychopathology covered in Figure 3 does not exist. The measures development workgroup in HiTOP was created to address this issue directly. The related but distinct goals of the measurement workgroup are to: a) simultaneously develop measures for all proposed symptom dimensions and personality traits encompassed by HiTOP in the service of empirically refining the model through psychometrically rigorous structural work, and b) based on this work, developing clinical useful tools designed to permit researchers and mental health practitioners to reliably, validly and efficiently assess all components of the HiTOP model.

In the service of building clinically useful tools, which is an important translational goal of HiTOP more generally, a number of fundamental measurement issues arise. We list just a few here to give a feel for some of the challenges ahead. For example, if the conceptualization of psychopathology is dimensional, should skip-outs (or other adaptive techniques) be employed to enhance the efficiency of assessment (akin to skip-outs designed on a rational basis to enhance the efficiency of traditional category assessment via structured interview)? Traditionally, dimensional approaches to psychopathology have been more closely associated with questionnaire as opposed to interview assessment strategies (because of the close intellectual and historical connections between psychometrics and questionnaire development). How can interview approaches – often favored in clinical research contexts – be developed that reflect more dimensional conceptualizations (e.g., the Structured Interview for the Five Factor Model⁵⁸ and the Interview for Mood and Anxiety Symptoms³⁸)? In addition, assessment of traditional categories via interview is typically modularized; only specific modules are used in many assessments, consistent with the constructs targeted. Can or should dimensional assessment be similarly modularized? Is this even possible or desirable, given the evidence portrayed in Figure 3, that all varieties of psychopathology are positively correlated? Finally, how can transient symptom manifestations and chronic maladaptive trait characteristics be seamlessly integrated within a single instrument?

Normal personality workgroup

The resemblance between the model portrayed in Figure 3 and well-established models of human personality variation, particularly the prominent Five Factor Model⁵⁹, is clear. This resemblance is not accidental, but rather reflects the ways in which personality forms the empirical psychological infrastructure for the development of specific varieties of psychopathological symptoms⁵⁹. Nevertheless,

a number of interesting and important issues arise in recognizing the intertwined nature of variation in personality and psychopathology.

For example, as noted earlier, the model in Figure 3 reflects empirical connections based on extant literature that was framed by constructs that vary in their associated presumed periodicity. By tradition, DSM frames some disorders as more episodic (e.g., mood disorders), and other disorders are more dispositional (e.g., personality disorders). Stepping back from this act of historical fiat, what in actuality are the distinctions between more dispositional personality constructs, and more acute symptom constructs? Both seem important in comprehensive case conceptualization but, practically and empirically, what strategies might help to parse similarities and differences, yet also unify them in a more comprehensive model? These are the sorts of issues that fall into the bailiwick of the HiTOP normal personality workgroup.

Utility workgroup

Implicit in articulating the type of model portrayed in Figure 3 is the idea that this model has utility, i.e., that it can do some useful work in the world that will help to propel research and clinical practice. The role of the utility workgroup is to realize this potential explicitly. A number of examples might be mentioned, but those that seem particularly salient involve connections of empirical psychopathological phenotypes with neural mechanisms and genomic variants, given contemporary funding priorities. The biomedical research enterprise (e.g., the basic paradigm framing funding bodies such as the US National Institutes of Health) prioritizes the role of fundamental biological processes in addressing issues in public health. This prioritization reflects the success of this paradigm in addressing many health problems during the 20th century. Accordingly, there is substantial interest and financial investment in understanding the neural bases of manifest psychopathology.

HiTOP constructs have a key role to play in furthering this endeavor. For example, the RDoC initiative has sometimes been criticized for providing limited guidance in conceptualizing clinical psychopathology *per se*. This may in some ways reflect a disjunction between what RDoC has aimed to achieve, and what investigators are seeking. To our reading, RDoC aimed to focus attention and effort on more fundamental neurobiological constructs as promising topics for research. The intent was not necessarily to re-conceptualize phenotypic psychopathology⁶⁰. In this way, HiTOP represents a necessary and desirable counterpart to RDoC. The interface between the neurobiological constructs of RDoC and the more phenotypic constructs of HiTOP represents a key means of connecting structure and process in understanding psychopathology.

Clinical translation workgroup

Although traditional nosologies are framed by their category labels, dimensional approaches to psychopathology are also clearly part and parcel of clinical practice. Psychosocial and pharmacological intervention strategies often are effective because they track clinically salient clusters of symptom dimensions⁶¹. Indeed, dimensional conceptualization and corresponding intervention strategies are arguably (if not always explicitly) the essence of clinical practice⁶². Triage is often a matter of matching the intensity of the presentation with the intensity of intervention. In routine clinical practice, the key decision is not typically “to treat or not to treat”. Rather, the key decision is “what level of intervention best suits this level of need?”.

To pick a specific example, persons presenting with substance use problems are not clinically homogenous in their level of problems and corresponding need for a specific treatment approach (indeed, the DSM-5's more dimensional conceptualization of substance use disorder reflects this reality). Instead, milder presentations can often be treated effectively through outpatient detoxification (assuming medi-

cal stabilization); more severe presentations often benefit from more structured approaches (e.g., partial hospitalization); and very severe presentations often require at least an initial inpatient stay (e.g., for purposes of medical stabilization). As this example makes clear, conceptualizing substance use presentations as “present vs. absent” would be fundamentally at odds with routine and responsible clinical practice⁶³. The clinical translation workgroup serves to make these sorts of dimensional considerations more explicit, and to help disseminate specific dimensionally-oriented approaches to front-line clinicians.

SUMMARY AND CONCLUSIONS

There has been considerable recent interest in empirical approaches to psychopathology classification. This interest has arisen for various reasons, but arguably, the overarching consideration and motive is to place classification on an empirical playing field, as opposed to relying more on the political considerations that influence traditional nosological endeavors, such as the DSM revision process.

This empirical classification movement is well intended, but numerous challenges remain. For example, will progress result more from a distributed approach, or from a more centrally organized approach? In many sciences, a distributed approach facilitates progress. Laboratories compete for resources, and seek to replicate other laboratories’ work. Classification of psychopathology, however, presents different kinds of scientific and practical challenges. For example, there is a need for coherence in conceptualizing the entire breadth of the subject matter. This need is arguably more acute than in many more focal scientific endeavors. That is, a piecemeal classification would have limited utility in portraying the entire picture, and portraying the entire picture is a key goal in addressing the limitations of extant schemes (e.g., the generally piecemeal nature of category-driven research efforts).

The HiTOP Consortium formed as a way of addressing this need for breadth and coherence, closely tethered to data. However, HiTOP, like endeavors before it, is a consortium of human clinicians, scientists and scholars, each with their own unique perspectives, in addition to their shared goals. Although focused squarely on the role of data in adjudicating nosological controversies via its principles⁴², how will HiTOP navigate new evidence, which, after all, is not self-interpreting? We are optimistic that these challenges can (and indeed must) be surmounted, because moving toward a more empirical approach is critical to the ultimate intellectual health and credibility of the field.

The next phase in the development of HiTOP and the broader field of empirical psychopathology classification may prove to be a watershed in arriving at a data-based approach to age old questions in classification, and therefore, a system that bridges and unifies both research and clinical practice in mental health.

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REFERENCES

1. Blashfield R. The classification of psychopathology: neo-kraepelinian and quantitative approaches. Berlin: Springer, 1984.
2. Cuthbert BN. The RDoC framework: facilitating transition from ICD/DSM to dimensional approaches that integrate neuroscience and psychopathology. *World Psychiatry* 2014;13:28-35.
3. Regier DA, Narrow WE, Clarke DE et al. DSM-5 field trials in the United States and Canada, Part II: test-retest reliability of selected categorical diagnoses. *Am J Psychiatry* 2013;170:59-70.
4. Lubke GH, Miller PJ. Does nature have joints worth carving? A discussion of taxometrics, model-based clustering and latent variable mixture modeling. *Psychol Med* 2015;45:705-15.
5. Haslam N, Holland E, Kuppens P. Categories versus dimensions in personality and psychopathology: a quantitative review of taxometric research. *Psychol Med* 2012;42:903-20.

6. Elahi A, Perez Algorta G, Varese F et al. Do paranoid delusions exist on a continuum with subclinical paranoia? A multi-method taxometric study. *Schizophr Res* 2017;190:77-81.
7. Liu RT. Substance use disorders in adolescence exist along continua: taxometric evidence in an epidemiological sample. *J Abnorm Child Psychol* 2017;45:1577-86.
8. Liu RT. Taxometric evidence of a dimensional latent structure for depression in an epidemiological sample of children and adolescents. *Psychol Med* 2016;46:1265-75.
9. Morton SE, O’Hare KJM, Maha JKL et al. Testing the validity of taxonomic schizotypy using genetic and environmental risk variables. *Schizophr Bull* 2017;43:633-43.
10. Witte T, Holm-Denoma J, Zuromski K et al. Individuals at high risk for suicide are categorically distinct from those at low risk. *Psychol Assess* 2017;29:382-93.
11. Waller NG, Ross CA. The prevalence and biometric structure of pathological dissociation in the general population: taxometric and behavior genetic findings. *J Abnorm Psychol* 1997;106:499-510.
12. Watson D. Investigating the construct validity of the dissociative taxon: stability analyses of normal and pathological dissociation. *J Abnorm Psychol* 2003;112:298-305.
13. Carragher N, Krueger RF, Eaton NR et al. ADHD and the externalizing spectrum: direct comparison of categorical, continuous, and hybrid models of liability in a nationally representative sample. *Soc Psychiatry Psychiatr Epidemiol* 2014;49:1307-17.
14. Conway C, Hammen C, Brennan PA. A comparison of latent class, latent trait, and factor mixture models of DSM-IV borderline personality disorder criteria in a community setting: implications for DSM-5. *J Pers Disord* 2012;26:793-803.
15. Krueger RF, Markon KE, Patrick CJ et al. Externalizing psychopathology in adulthood: a dimensional-spectrum conceptualization and its implications for DSM-V. *J Abnorm Psychol* 2005;114:537-50.
16. Vrieze SI, Perlman G, Krueger RF et al. Is the continuity of externalizing psychopathology the same in adolescents and middle-aged adults? A test of the externalizing spectrum’s developmental coherence. *J Abnorm Child Psychol* 2012;40:459-70.
17. Walton KE, Ormel J, Krueger RF. The dimensional nature of externalizing behaviors in adolescence: evidence from a direct comparison of categorical, dimensional, and hybrid models. *J Abnorm Child Psychol* 2011;39:553-61.
18. Wright AGC, Krueger RF, Hobbs MJ et al. The structure of psychopathology: toward an expanded quantitative empirical model. *J Abnorm Psychol* 2013;122:281-94.
19. Eaton NR, Krueger RF, Markon KE et al. The structure and predictive validity of the internalizing disorders. *J Abnorm Psychol* 2013;122:86-92.
20. Forbes MK, Baillie AJ, Schniering CA. Where do sexual dysfunctions fit into the meta-structure of psychopathology? A factor mixture analysis. *Arch Sex Behav* 2016;45:1883-96.
21. Kramer MD, Arbisi PA, Thuras PD et al. The class-dimensional structure of PTSD before and after deployment to Iraq: evidence from direct comparison of dimensional, categorical, and hybrid models. *J Anxiety Disord* 2016;39:1-9.

22. Klein DN, Kotov R. Course of depression in a 10-year prospective study: evidence for qualitatively distinct subgroups. *J Abnorm Psychol* 2016;125:337-48.
23. Lubke GH, Luningham J. Fitting latent variable mixture models. *Behav Res Ther* 2017;98:91-102.
24. Masyn KE, Henderson CE, Greenbaum PE. Exploring the latent structures of psychological constructs in social development using the dimensional-categorical spectrum. *Soc Dev* 2018;12:82-6.
25. Eaton NR, Krueger RF, South SC et al. Contrasting prototypes and dimensions in the classification of personality pathology: evidence that dimensions, but not prototypes, are robust. *Psychol Med* 2011;41:1151-63.
26. Zachar P, Krueger R, Kendler K. Personality disorder in DSM-5: an oral history. *Psychol Med* 2015;46:1-10.
27. Hopwood CJ, Kotov R, Krueger RF et al. The time has come for dimensional personality disorder diagnosis. *Personal Ment Health* 2018;12:82-6.
28. Forbes M, Tackett J, Markon K et al. Beyond comorbidity: toward a dimensional and hierarchical approach to understanding psychopathology across the life span. *Dev Psychopathol* 2016;28:971-86.
29. Lello L, Avery SG, Tellier L et al. Accurate genomic prediction of human height. *bioRxiv* (in press).
30. von Eye A, DeShon RP. Directional dependence in developmental research. *Int J Behav Dev* 2012;36:303-12.
31. Kendler KS. A joint history of the nature of genetic variation and the nature of schizophrenia. *Mol Psychiatry* 2015;20:77-83.
32. Okbay A, Baselmans B, De Neve J et al. Genetic variants associated with subjective well-being, depressive symptoms, and neuroticism identified through genome-wide analyses. *Nat Genet* 2016;48:624-33.
33. Markon KE. How things fall apart: understanding the nature of internalizing through its relationship with impairment. *J Abnorm Psychol* 2010;119:447-58.
34. Jonas K, Markon K. A model of psychosis and its relationship with impairment. *Soc Psychiatry Psychiatr Epidemiol* 2013;48:1367-75.
35. Wakschlag LS, Estabrook R, Petittlerc A et al. Clinical implications of a dimensional approach: the normal: abnormal spectrum of early irritability. *J Am Acad Child Adolesc Psychiatry* 2015;54:626-34.
36. Clark LA, Watson D. Tripartite model of anxiety and depression: psychometric evidence and taxonomic implications. *J Abnorm Psychol* 1991;100:316-36.
37. Möller HJ, Bandelow B, Volz HP et al. The relevance of 'mixed anxiety and depression' as a diagnostic category in clinical practice. *Eur Arch Psychiatry Clin Neurosci* 2016;266:725-36.
38. Waszczuk M, Kotov R, Ruggero C et al. Hierarchical structure of emotional disorders: from individual symptoms to the spectrum. *J Abnorm Psychol* 2017;126:613-34.
39. Chmielewski M, Watson D. The heterogeneous structure of schizotypal personality disorder: item-level factors of the schizotypal personality questionnaire and their associations with obsessive-compulsive disorder symptoms, dissociative tendencies, and normal personality. *J Abnorm Psychol* 2008;117:364-76.
40. Barlow DH, Farchione TJ, Bullis JR et al. The unified protocol for transdiagnostic treatment of emotional disorders compared with diagnosis-specific protocols for anxiety disorders: a randomized clinical trial. *JAMA Psychiatry* 2017;74:875-84.
41. Venables NC, Yancey JR, Kramer MD et al. Psychoneurometric assessment of dispositional liabilities for suicidal behavior: phenotypic and etiological associations. *Psychol Med* 2018;48:463-72.
42. Stony Brook School of Medicine. The Hierarchical Taxonomy of Psychopathology (HiTOP). <https://medicine.stonybrookmedicine.edu/HiTOP>.
43. Kotov R, Krueger RF, Watson D et al. The Hierarchical Taxonomy of Psychopathology (HiTOP): a dimensional alternative to traditional nosologies. *J Abnorm Psychol* 2017;126:454-77.
44. Forbes M, Kotov R, Ruggero C et al. Delineating the joint hierarchical structure of clinical and personality disorders in an outpatient psychiatric sample. *Compr Psychiatry* 2017;79:19-30.
45. Carpenter WT, Bustillo JR, Thaker GK et al. The psychoses: cluster 3 of the proposed meta-structure for DSM-V and ICD-11. *Psychol Med* 2009;39:2025-42.
46. Guloksuz S, van Os J. The slow death of the concept of schizophrenia and the painful birth of the psychosis spectrum. *Psychol Med* 2018;48:229-44.
47. Kotov R, Watson D, Krueger RF et al. Thought disorder spectrum of the Hierarchical Taxonomy of Psychopathology (HiTOP): bridging psychosis and personality pathology. Submitted for publication.
48. Tyrer P, Crawford M, Mulder R. Reclassifying personality disorders. *Lancet* 2011;377:1814-5.
49. Krueger RF, Markon KE, Patrick CJ et al. Linking antisocial behavior, substance use, and personality: an integrative quantitative model of the adult externalizing spectrum. *J Abnorm Psychol* 2007;116:645-66.
50. Krueger R, Tackett J. The externalizing spectrum of personality and psychopathology: an empirical and quantitative alternative to discrete disorder approaches. In: Beauchaine T, Hinshaw S (eds). *Oxford handbook of externalizing disorders*. Oxford: Oxford University Press, 2015:79-89.
51. Eaton NR, Krueger RF, Keyes KM et al. Borderline personality disorder co-morbidity: relationship to the internalizing-externalizing structure of common mental disorders. *Psychol Med* 2011;41:1041-50.
52. Sharp C, Wright AG, Fowler JC et al. The structure of personality pathology: both general ('g') and specific ('s') factors? *J Abnorm Psychol* 2015;124:387-98.
53. Caspi A, Houts RM, Belsky DW et al. The p factor: one general psychopathology factor in the structure of psychiatric disorders? *Clin Psychol Sci* 2014;2:119-37.
54. Lahey BB, Krueger RF, Rathouz PJ et al. Validity and utility of the general factor of psychopathology. *World Psychiatry* 2017;16:142-4.
55. Morgan GB, Hodge KJ, Wells KE et al. Are fit indices biased in favor of bi-factor models in cognitive ability research?: a comparison of fit in correlated factors, higher-order, and bi-factor models via Monte Carlo simulations. *Intelligence* 2015;3:2-20.
56. Eid M, Geiser C, Koch T et al. Anomalous results in G-factor models: explanations and alternatives. *Psychol Methods* 2017;22:541-62.
57. Murray AL, Johnson W. The limitations of model fit in comparing the bi-factor versus higher-order models of human cognitive ability structure. *Intelligence* 2013;41:407-22.
58. Trull TJ, Widiger TA, Burr R. A structured interview for the assessment of the five-factor model of personality: facet-level relations to the axis II personality disorders. *J Pers* 2001;69:175-98.
59. Widiger TA, Presnall JR. Clinical application of the five-factor model. *J Pers* 2013;81:515-27.
60. Clark LA, Cuthbert B, Lewis-Fernández R et al. Three approaches to understanding and classifying mental disorder: ICD-11, DSM-5, and the National Institute of Mental Health's Research Domain Criteria (RDoC). *Psychol Sci Public Interest* 2017;18:72-145.
61. Waszczuk MA, Zimmerman M, Ruggero C et al. What do clinicians treat: diagnoses or symptoms? The incremental validity of a symptom-based, dimensional characterization of emotional disorders in predicting medication prescription patterns. *Compr Psychiatry* 2017;79:80-8.
62. Helzer J, Kraemer H, Krueger R. The feasibility and need for dimensional psychiatric diagnoses. *Psychol Med* 2006;36:1671-80.
63. Gastfriend DR, Mee-Lee D. The ASAM patient placement criteria: context, concepts and continuing development. *J Addict Dis* 2003;1:1-8.

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Quantitative classification as (re-)descriptive psychopathology

Consider these contrasts identified in Krueger et al's paper¹: authoritative vs. empirical, *ex cathedra* (dogmatic) vs. evidence-based, and tradition vs. empiricism. It is powerful verbiage, suggesting that the members of the Hierarchical Taxonomy of Psychopathology (HiTOP) consortium are arguing for their generation's Copernican turn in distinction to the system that preceded it.

Freud famously described his achievement as an intellectual revolution², the neo-kraepelinians used revolutionary idioms against the psychoanalysts that preceded them³, and now they are being used against the neo-kraepelinians.

Doubtlessly, readers will have a range of reactions to these contrasts. If the reaction "this is a coup by clinical researchers to replace the DSM and ICD with the factor analytic, dimensional models used in psychological testing" formed one end of a bipolar continuum, the other end would be "this is a heroic scientific revolution". I doubt many readers would assent to either pole wholeheartedly, but they may lean more toward one side or the other. I will argue that "coup" is too antagonistic an attribution and the proposed transition would be more appealing to psychiatrists if diplomatic alternatives to the "revolution" metaphor were used.

With respect to the coup, importing research traditions from scientific psychology into psychiatry not only has historical precedent; it has been historically important. To illustrate, consider E. Kraepelin, a groundbreaking architect of psychiatric classification, and R. Spitzer, who was the driving force behind the DSM-III and DSM-III-R.

Kraepelin's career plan was inspired by his contact with the founder of scientific psychology, W. Wundt. From his earliest days in the field, Kraepelin wanted to orient psychiatry away from speculative anatomical hypotheses and reductionism, and replace them with the experimental methods and concepts used in scientific psychology⁴. His descriptive psychopathology owed much to Wundt's

strategy of decomposing complex psychological states into components that are more measurable.

Spitzer majored in psychology at Cornell University. In her biography of him, H. Decker⁵ reports that Spitzer was trained as a psychoanalyst, but his interests lay in developing structured interviews and rating scales. He began his academic career at the New York State Department of Mental Hygiene in the Biometrics Research Unit, under the psychologist J. Zubin. The unit's purpose was to advance the quantitative study of psychopathology⁶. The psychological nature of Spitzer's early work is further documented by his collaborations with J. Endicott – a psychologist who had training in psychometrics.

In current terms, Kraepelin and Spitzer each had an interdisciplinary focus. With respect to classification, it has not been such a bad thing for psychiatry to occasionally take note of what the scientific psychologists are doing and rethink current practices – and it does not require a coup.

Turning to the revolution, many psychiatrists, including Spitzer⁷, would assert that they are aware that psychiatric distress occurs with degrees of severity and that the distinction between normal and abnormal can be fuzzy. Indeed, one could argue that a manifest dimensionality is fundamental to descriptive psychopathology. Understanding it is a prerequisite for the competent use of a categorical classification system. If so, rather than a revolution, the HiTOP model is better seen as an attempt to translate common background knowledge of psychopathology into something more precise and substantive. One disadvantage of revolutionary talk is that it emphasizes the discontinuity between past and present, often drawing attention away from the many continuities⁸.

Illuminated by the light of dimensionality, our understanding of psychopathology can be expanded in useful and interesting ways. Krueger et al's paper emphasizes an expansion in the scope of

research questions asked. Here I would like to discuss another area of expansion. In doing so I will explain what is meant by my title "Quantitative classification as (re-)descriptive psychopathology".

I begin by giving an example of descriptive psychopathology: the depiction of panic disorder. After imipramine was introduced in the late 1950s, working at Hillside Hospital on Long Island, D. Klein and M. Fink began prescribing the drug to patients to learn about its mode of action⁹. In a historical retrospective based on interviews with Klein, F. Callard¹⁰ recounts Klein and Fink's treatment of the man who would become the ur-patient for panic disorder.

The referring therapist believed that this patient had schizophrenia, but Klein disagreed, describing him as anxious, dependent and demanding. After four weeks of treatment with imipramine, neither the patient, his resident therapist, nor the supervising psychiatrist believed that the medication had made any difference. The ward staff did not concur, but they were not sure why. Eventually one nurse noticed that the patient no longer ran to the nurse's station several times a day asking for help because he feared he was dying.

For much of the 20th century, the symptoms of panic were a commonly manifested feature in the population of psychiatric phenotypes, but they were seen as parts of a coherent anxiety neurosis. Klein and Fink re-described these symptoms by putting a boundary around them, thus separating what they called episodic anxiety from anticipatory anxiety. With this re-description, even though panic had long been a background feature of the psychiatric landscape, it came into the foreground.

Descriptive psychopathology has been derided as a shallow emphasis on surface features. A successful re-description, however, is also a conceptual achievement of a synthetic nature in Kant's sense – it guides the way to the acquisition of information that is not contained in the description itself. For example, once Klein

and Fink saw panic as distinct from worry and avoidance, they learned that the primary problem in agoraphobia is not fear of open spaces, but fear of having another panic attack. Their discovery that the same patients also avoided crowded theaters would have been a puzzling feature of agoraphobia, but not of panic disorder.

The Research Domain Criteria (RDoC) initiative, with its focus on causality, might represent the abandonment of descriptive psychopathology, but it is equally consistent with RDoC's anti-reductionist aspiration that mechanisms will be maps for locating new descriptions in the psychiatric landscape. The same is true for HiTOP. Proposing a meta-structure for how things fit together affords some options for recognizing new patterns. HiTOP has an immediate advantage over RDoC because it does not have to translate biological findings into psychological descriptions; it is already psychological.

Using a taxonomy, however, is only a part of understanding psychopathology, including descriptive psychopathology.

It is unrealistic, therefore, to expect that statistical correlations can do all the descriptive work. With respect to panic disorder, Klein claimed that the ward nurse who reported that the ur-patient no longer ran to the nurse's station was a good observer. This was their first clue to describing what they called a psychiatric reaction pattern. It was followed by prolonged observations of what the patient did and said, how he reacted to others, and how others reacted to him.

Hopefully, good observers will notice some of the clues that a comprehensive dimensional hierarchy presents, recognize patterns, and subject them to validation studies. Concepts like borderline and narcissistic personality disorder are so entrenched that they assert themselves when certain features are present. HiTOP offers a way to take a second look. Ideally, clinicians and scientists could learn to see anew something that has been there before them all along – and let it guide them to other things that they did not recognize before.

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1. Krueger RF, Kotov R, Watson D et al. *World Psychiatry* 2018;17:282-93.
2. Freud S. A general introduction to psychoanalysis. New York: Liveright, 1920.
3. Wender PH, Klein DF. *Mind, mood, and medicine*. New York: Farrar Straus Giroux, 1981.
4. Engstrom EJ, Kendler KS. *Am J Psychiatry* 2015; 172:1190-6.
5. Decker HS. The making of DSM-III: a diagnostic manual's conquest of American psychiatry. New York: Oxford University Press, 2013.
6. Zubin J, Salzinger K, Fleiss JL et al. *Annu Rev Psychol* 1975;26:621-71.
7. Spitzer RL. *Schizophr Bull* 1982;8:592.
8. Zachar P. In: Kendler KS, Parnas J (eds). *Philosophical issues in psychiatry II: Nosology – definition of illness, history, validity, and prospects*. New York: Oxford University Press, 2012:21-34.
9. Klein DF, Fink M. *Am J Psychiatry* 1962;119: 432-8.
10. Callard F. *Osiris* 2016;31:203-26.

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Dimensions fit the data, but can clinicians fit the dimensions?

Krueger et al's paper¹ is impressive and erudite. One might say it is too erudite, because the average clinician will find it difficult to anchor his or her clinical practice to the attachments offered. But the arguments put forward are scientifically incontrovertible; the data for almost, if not all, psychiatric disorders indicate that their dimensional description is nearer to truth than a categorical one.

The key section in this paper to most readers in practice is "clinical translation", and here the work group is going to have to work extra hard. To what extent can the dimensional system be adapted, transformed, or forced, depending on your starting point, into clinical decision-making?

There is an interesting historical parallel here. In the UK, in the late 1950s and early 1960s, there was what is com-

monly called the Platt-Pickering debate, played out in the columns of *The Lancet*. This pitted the cerebral (dimensional) champion, G. Pickering, in one corner, against the clinical (categorical) pugilist, R. Platt, in the other. Although there were no apparent knockout blows, the debate was a riveting spectacle, illustrated by rapier-like thrusts and counter-punches by two austere but slightly irritable protagonists, always polite but each showing incredulity at the apparent stupidity of the other.

Their debate was over the classification of high blood pressure. Was it best regarded as a continuous variable² or better described as two categorical populations, a larger one with normal blood pressure, and a smaller one with hypertension³? Pickering made the case that blood pressure is a continuously distributed characteristic with no clean sep-

aration between abnormal and normal. Platt insisted that those with very high blood pressure were a discrete group who represented the disease, hypertension, and that this fact could potentially be explained by genetic characteristics; he proposed a Mendelian dominant gene. This genetic theory was not supported and the Pickering power-house swept away the old arguments: "The new view, for which we and our colleagues are largely responsible, is that essential hypertension represents a quantitative and not a qualitative deviation from the norm"⁴.

This resonates strongly with the current debate about dimensions in psychiatry. In the Platt-Pickering debate, the clinicians – and, dare one say, *The Lancet* itself⁵ – were on Platt's side. After all, if he was right, it would make their job so much easier. Clean categorical diagno-

sis is always better than a dimensional fudge. What the Hierarchical Taxonomy of Psychopathology (HiTOP) investigators need to do is to show the clinician that there is genuine clinical value in the dimensional approach; that it is not a fudge. We have some clues. Thus, in the case of personality disorder, shortly to be a dimensional diagnosis in ICD-11 and regarded as a genuine paradigm shift⁶, it is important to know that the more severe the disorder the greater its persistence and its impact on long-term social functioning⁷.

But this only describes prognosis. Can a dimensional diagnosis help treatment? Again we have some encouraging findings. Sub-clinical depression is not a formal diagnosis but it causes a lot of suffering. It is easily accommodated on a dimensional continuum and could be a suitable condition for treatment, and in a recent meta-analysis there is some evidence, not yet strong, that psychological treatments are effective here⁸. Would this apply to drug treatment too? Probably not, and, for this to be appropriate, a higher point on the dimension would probably have to be chosen⁹.

Clinicians are naturally conservative when it comes to diagnosis and classification, and change is always resisted at first. But if it can be shown that there is definite advantage in a dimensional approach, that it can lead to better and more fine-tuning of management, then it may win approval. It would probably be necessary to have parallel systems at first to allow comparisons to be made between categorical and dimensional approaches.

But there will be continuing concerns in clinical practice if there are not clear indications for decision-making offered

by the diagnostic system. Krueger and his colleagues rightly note that the recent elegant Research Domain Criteria proposals, whatever their value in identifying neurobiological constructs, do not help such decision-making. Although the HiTOP team may go further and succeed in their aim of “connecting structure and process” in explaining psychopathology, the clinician at the coal-face can only look on with bemusement at any system which, however well grounded in empirical science, still does not provide answers to key questions. When is apparent pathology within the range of normality? At what stage in a dimensional system of a major diagnosis is coercion justified in management? When is it right to regard co-occurrence of disorders as comorbidity or instead as part of the same spectrum (e.g., anxiety-depression)?

These are not academic talking points. Therapeutic advancement often happens by serendipity, but we also need to have a classification system that helps empirical science to focus on specific aspects of efficacy. So, instead of psychiatry using the current pot-pourri of general interventions into heterogeneous populations giving equivocal results, we could look forward to “focused diagnosis-specific gain”. The possible value of quinine in malaria was discovered by chance but, because malaria was a clearly identified disease, it was possible, even in the mid-1860s, to show that all the cinchona alkaloids – quinine, quinidine, cinchonine and cinchonidine – were equally effective in treating the disease. Remember, at this time in history, malaria was identified by the same procedures that we use in psychiatry today.

The HiTOP investigators may feel it is far outside their remit to enter the ther-

apeutic and other intervention arenas, but they need to be aware of their importance. The oldest and most successful classification in psychiatry has been the dimensional one of intellectual disability based on IQ. Although this has been rightly modified in several ways to take account of adaptive functioning, for more than a century this classification has allowed appropriate placement, support and management to take place for people in each of the dimensional groups.

What about the long-term outcome of the Platt-Pickering debate, which Pickering was generally assumed to have won? Currently the most common diagnosis in cardiology in the ICD-10 classification is essential hypertension, so the Platt supporters may now claim some sort of victory. So, in 60 years hence, will it be seen that dimensions have triumphed or will psychiatric classification be essentially the same as now? If Krueger and his colleagues can come forward with more clinical meat to add to their helping of science, things will certainly change.

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1. Krueger R, Kotov R, Watson D et al. *World Psychiatry* 2018;17:282-93.
2. Pickering G. *Lancet* 1960;275:170.
3. Platt R. *Lancet* 1959;274:1092.
4. Oldham PD, Pickering G, Fraser Roberts JA et al. *Lancet* 1960;275:1085-93.
5. Editorial. *Lancet* 1959;274:895-6.
6. Widiger TA, Oltmanns JR. *Personal Ment Health* 2016;10:120-2.
7. Tyrer P, Tyrer H, Yang M et al. *Personal Ment Health* 2016;10:76-83.
8. Cuijpers P, Koole SL, van Dijke A et al. *Br J Psychiatry* 2014;205:268-74.
9. Maj M. *Br J Psychiatry* 2011;199:85-6.

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HiTOP must meet the use requirements of the ICD before it can aspire to replace it

As described by Krueger et al¹, the approach being taken by the Hierarchical Taxonomy of Psychopathology (HiTOP)

consortium in attempting to elucidate the underlying dimensions of psychopathology is an important one. I agree par-

ticularly about the immediate importance of identifying connections between overt expressions of psychopathology

and neural mechanisms and genomic variance, and believe that HiTOP has an important contribution to make in this regard.

At the same time, I do not believe that HiTOP can be successful as a sole approach. As with the Research Domain Criteria (RDoC) project promoted by the US National Institute of Mental Health (NIMH), it seems important not to oversell HiTOP or to pretend that it describes a classification system *per se* that will be capable of replacing the ICD or the DSM at any point in the immediate future. Although the NIMH has walked back its initial rhetoric² to clarify that RDoC is actually a framework for research³, Krueger et al's paper makes the same mistake with HiTOP.

The paper is also marred by tendentious repetition of the claim that the ICD and the DSM are "consensus-based", "authoritative", "political" classifications, in contrast to HiTOP, which is "empirical" and "scientific". Such characterizations, although perhaps rhetorically useful in promoting a new approach, are actually inaccurate, as with the widely repeated and false characterization of DSM-I and DSM-II as psychoanalytic⁴, or the initial messaging about RDoC that characterized the DSM explicitly and the ICD by implication as responsible for the lack of dramatic breakthroughs in understanding the etiology of mental disorders and providing curative treatments². This paper's similar denigration of "authoritative" as opposed to "empirical" classification systems appears to be based, thinly, on the facts that: a) the ICD-11 and DSM-5 (and RDoC) are institutionally sponsored; b) expert working groups developed the initial proposals for changes to the previous versions of the classifications; and c) there was an institutional demand for some degree of continuity across versions.

With regard to the first point, the development and maintenance of international classifications for health and the standardization of diagnostic procedures are core constitutional functions assigned to the World Health Organization (WHO) through international treaty by 194 member states. It is unclear why being a "con-

sortium" without a clear formal authority structure or a responsible institution would make HiTOP inherently superior in relation to these tasks. With regard to the second point, an explicit charge of working groups for both the ICD-11 and the DSM-5 was to perform a rather rigorous analysis of the state of the current evidence. Krueger et al are correct, though, that the range of possibilities for transforming the classifications was to some extent limited by the adoption of *a priori* elements of the existing structure, such as the existence of separate groupings of mood disorders and anxiety disorders.

Most of the results presented in the paper in support of HiTOP's hierarchical dimensional models are based on a set of inter-related techniques including taxometric analysis, latent class analysis, cluster analysis, and factor analysis. While these can be powerful and sophisticated statistical tools, they do not serve up the truth like Venus on a clamshell. They still require interpretation by human experts. The fact that HiTOP's authority structure and the specific criteria for evaluation are not transparent or explicit (at least based on this paper) does not mean that the evidence is not being synthesized and interpreted based on expert judgments.

For the WHO, a demand for explicit continuity between the ICD-10 and the ICD-11, at a minimum in the form of clear cross-walking, is based on one of the ICD's main purposes – to provide a framework for the collection and reporting of health statistics – as well as on the need for longitudinal global, national and local health information. The governments of WHO member states have increasingly integrated the ICD into clinical processes and policies related to health care coverage and reimbursement, social services, and disability benefits⁵, and are also concerned about the continuity of health data and the continuous application of laws and policies. However, the paper suffers from a lack of familiarity with the functioning of the WHO and the purposes of the ICD-11. Even though Krueger et al include the ICD-11 in the sweep of their characterizations, all of the specific information in the paper about "traditional", "authoritative" clas-

sifications is taken from the DSM-5. This perhaps reflects the fact that only ten of the paper's 45 authors are from outside the US and none is from a developing country.

The WHO does not, in fact, "claim, through tradition and putative authority, that psychopathologies are organized into discrete diagnostic entities". We have recently written explicitly and at great length about the better correspondence of dimensional approaches to the observed data³. The categorical nature of the ICD system is necessary for its application in global health statistics and in many instances for its use in clinical settings (e.g., eligibility, treatment selection). In most countries, provision of medical care other than routine examinations and preventive services is contingent on a qualifying diagnosis. Other relevant decisions are typically categorical (yes/no); even if the information that underlies them is dimensional, a threshold must be imposed. Inclusion of mental disorders in the ICD facilitates coordination with the classification of other disorders, as well as the search for related mechanisms of etiology, pathophysiology and comorbidity of disease processes. It also provides a basis for parity of mental disorders with other types of health conditions⁵. Mental disorders in the ICD-11 must follow the same set of structural and taxonomic rules as the rest of the classification.

Within the constraints of a categorical system, the ICD-11 has gone to considerable lengths to integrate dimensional constructs into the classification of mental disorders, which has been made possible by specific structural innovations as compared to the ICD-10. One example that is discussed in the paper is the incorporation of a dimensional classification of personality disorders^{6,7}. Similarly, the ICD-10 subtypes of schizophrenia (e.g., paranoid, hebephrenic, catatonic) have been replaced by a set of symptom ratings (e.g., positive symptoms, negative symptoms, cognitive symptoms) that may be applied to all primary psychotic disorders⁸. A category for anxious depression based on two correlated but distinct dimensions has been incorporated into the

version of the ICD-11 classification of mental disorders for primary care settings⁹. These innovations will push the ICD-11 in the direction envisioned by HiTOP, but it is possible that they may be experienced as more complex than the purely categorical approach they are replacing, which may stimulate resistance among clinicians and health systems.

While the WHO does appear to be facing this challenge head-on within the structural and taxonomic constraints of the ICD, there is a considerable amount that HiTOP might take on board in order to facilitate further transformations of this nature. Assuming that the correct dimensions have been identified, much work is necessary to translate group-

level research results into measures and cutoffs that are predictive at the individual level³. Although Krueger et al claim “greater relative utility and empirical accuracy of continuous conceptualizations of psychopathology”, very little work has been conducted aimed at developing tools that can be demonstrated as robustly valid as a basis for making individual health care decisions.

Any dimensional system that would seek to replace “authoritative” classifications would need to demonstrate that it is fit for purpose across the range of functions for which the world uses the ICD.

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1. Krueger RF, Kotov R, Watson D et al. *World Psychiatry* 2018;17:282-93.
2. Insel T. Transforming diagnosis. <https://www.nimh.nih.gov>.
3. Clark LA, Cuthbert B, Lewis-Fernández R et al. *Psychol Sci Public Interest* 2017;18:72-145.
4. Cooper R, Blashfield RK. *Psychol Med* 2016;46:449-56.
5. International Advisory Group for the Revision of ICD-10 Mental and Behavioural Disorders. *World Psychiatry* 2011;10:86-92.
6. Tyrer P, Reed GM, Crawford MJ. *Lancet* 2015;385:717-26.
7. Hopwood CJ, Kotov R, Krueger RF et al. *Personal Ment Health* 2018;12:82-6.
8. Gaebel W. *Schizophr Bull* 2012;38:895-8.
9. Goldberg DP, Reed GM, Robles R et al. *J Affect Disord* 2017;213:199-206.

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“Throwing out the baby with the bathwater”? Conceptual and methodological limitations of the HiTOP approach

More sophisticated explorations of the higher-order dimensional and hierarchical structure of psychopathology have become an exciting complementary way towards developing an improved classification of mental disorders and reducing artefactual comorbidity.

The impressive work of the Hierarchical Taxonomy of Psychopathology (HiTOP) Consortium with their mission paper¹ provides evidence for considerable advances as compared to previous suggestions, and underscores the potential of such approaches not only for improved future classificatory models with increased utility for research and practice, but also for the development of improved psychometric assessment instruments for psychopathology. However, as impressive such an approach might appear at first sight, there is a need of pointing out several limitations that caution against the use of this model.

On the *conceptual level*, we emphasize first of all that comorbidity is not “a problem”, but a clinical characteristic of patients meaningful for treatment and management². The belief that people suffer from only one underlying condition is im-

plausible and misleading. The value of the HiTOP Consortium approach might be in reducing a certain degree of what has been called “artefactual” comorbidity, due to overlapping criteria in our current classification systems.

Second, the suggested hierarchical structural model has a serious limitation: it is based almost exclusively on traditional assessment instruments (dimensional scales, interviews) from cross-sectional studies. Leaving aside the vast array of inherent general psychometric problems, we highlight that such scales merely reflect a subjective-verbal “snapshot” picture of the level of symptom-distress that a person reports at the time of investigation. As essential such a snapshot might be for a first “impressionistic” step of a syndromal diagnosis, it certainly does not allow to decide on a diagnosis relevant for treatment without taking into account the patient’s history (e.g., depressive syndromes cannot be equated with diagnoses of major depression or even of any affective or any mental disorder).

Third, the HiTOP approach does not grab appropriately the nature of mental disorders as dysfunctions – up to now in-

sufficiently understood – of basic psychological processes as well as associated “perturbations” in brain functions at the cell and systems level³. The former are centrally involved in the behavioral, cognitive-affective and somatic symptom processes currently used to define mental disorders. The latter “perturbations” can be best described as various types of fluctuating dysfunctions in complex structural and functional neural circuits involved in information processing and emotion regulation.

The identification of common causal pathways is of core relevance for an improved diagnostic system. They allow identifying the factors and mechanisms responsible for the onset, progression and maintenance of mental disorders. Proposed models based on such mechanisms provide guidance for improved research strategies and the derivation of improved interventions, targeted to interrupt the causal pathways³.

Promising examples come from psychosis research. In a clinical staging framework, the at-risk or symptomatic state of a patient can be evaluated to derive tailored interventions spanning from

primary selective prevention in asymptomatic subgroups (stage 0) and high-risk subjects (stage 1), over early treatment in first episode (stage 2) or relapsing psychotic patients (stage 3), to maintenance treatment in unrelapsing patients (stage 4)⁴.

Such frameworks also exist for other facets of psychopathology such as anxiety, depression or substance use, providing specific guidance on early targeted interventions. The “symptom progression - comorbidity development” model^{3,5} emphasizes the early signs and symptoms of fear and anxiety in the development of psychopathology and a staging based on “comorbid” escalations from circumscribed manifestations in childhood to more complex diagnostic constellations (multiple anxiety disorders, comorbid depression and substance disorders) later in adolescence or adulthood. Besides a range of vulnerability factors at various levels and in different developmental periods, the initial psychopathology itself entails a causal cascade (e.g., increasing demoralization and inactivity due to avoidance promoting depression)⁶. This model has direct implications for therapeutic and preventive interventions.

Therefore, the first caveat of higher-order taxonomies such as the one suggested by the HiTOP Consortium is that they are at best a complementary piece of descriptive evidence that might prove useful in reducing artefactual comorbidity. But they do not reflect the true dynamic developmental nature of mental disorders and might even be an obstacle for developing improved targeted causal interventions.

Regarding *methodological constraints*, we do not refer here to the numerous mathematical and statistical limitations of the higher-order dimensional and hierarchical approaches that call for caution^{7,8}. Beyond these, the strongest evidence against such models comes from prospective-longitudinal investigations, revealing the instability of the assumed higher-order structure and spectra over time⁷. Along the developmental axis, the

structure of higher-order dimensions changes significantly, both within factors and across spectra. The assumption that this instability might be due to a limited reliability of assessments is implausible and would actually also argue against such higher-order models in general.

Furthermore, the statement that dimensional measures are advantageous over categorical data is trivial. They simply provide more information and are thus preferable in any approach⁹. Assuming that hierarchical structural models based on dimensional data may lead *per se* to an improved classification of mental disorders and “solve the problem of comorbidity” is like “throwing out the baby with the bathwater” and obscures important issues, given the underlying assumptions and the lack of developmental considerations. This does not invalidate the additional utility and the potential of such approaches, but suggests that these models are at best complementary to other principles and sources of evidence.

Undoubtedly, as compared to previous simpler models, the HiTOP model has increased in breadth and specificity (e.g., spectra for thought disorder and detachment). However, the extensions also cause new inconsistencies, such as enhancing the “distance” between internalizing and externalizing dimensions, although externalizing disorders might involve preceding internalizing pathways (and vice versa). Moreover, as attractive and impressive the visual depiction of a new taxonomy of psychopathology may be, using new words for old ones might increase the risk that already established research findings lack consideration in the future.

Further, “somatoform” diagnoses (dismissed in DSM-5) are reintroduced without explaining the rationale. This particular cluster also serves as an example for the difficulty – even cross-sectionally – to find a coherent general structure of psychopathology. Somatoform syndromes are differentially (i.e., by gender and age group) associated with a broad range of conditions which are spread out in the

HiTOP model (anxiety, psychosis, hypomania, post-traumatic stress disorder, and many other diagnoses not mentioned in the framework)⁷, which complicates the implementation of the model.

To conclude, higher-order dimensional and hierarchical models of psychopathology such as the ambitious HiTOP model are at best a complementary way towards developing an improved classification of mental disorders for research and practice. Their potential value lies in reducing artefactual comorbidity and deriving improved cross-sectional psychometric assessment instruments.

However, HiTOP provides little specific guidance towards our ultimate goal, namely, a classification of mental disorders based on causal factors and mechanisms involved in the first development of psychopathology and its progression over time. Its inherent weakness remains the overemphasis on cross-sectional psychopathology and the neglect of dynamic developmental pathways and differential diagnostic issues relevant to treatment and management.

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1. Krueger RF, Kotov R, Watson D et al. World Psychiatry 2018;17:282-93.
2. Fava GA, Tossani E, Bech P et al. Int J Methods Psychiatr Res 2014;23:92-101.
3. Wittchen H-U, Knappe S, Andersson G et al. Int J Methods Psychiatr Res 2014;23:28-40.
4. Fusar-Poli P, McGorry PD, Kane JM. World Psychiatry 2017;16:251-65.
5. Shear MK, Bjelland I, Beesdo K et al. Int J Methods Psychiatr Res 2007;16(Suppl. 1):S52-64.
6. Beesdo K, Bittner A, Pine DS et al. Arch Gen Psychiatry 2007;64:903-12.
7. Wittchen H-U, Beesdo-Baum K, Gloster A et al. Int J Methods Psychiatr Res 2009;18:189-203.
8. Wittchen H-U, Beesdo K, Gloster AT. Psychol Med 2009;39:2083-9.
9. Wittchen H-U, Höfler M, Gloster AT et al. In: Regier DA, Narrow WE, Kuhl EA et al. (eds). The conceptual evolution of DSM-5. Washington: American Psychiatric Publishing, 2010:119-43.

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The dialectic of quantity and quality in psychopathology

Krueger et al¹ provide a novel and challenging perspective on the perennial divide between the categorical and dimensional approaches to the conceptualization and classification of psychopathological phenomena.

Writing on behalf of the recently established Hierarchical Taxonomy of Psychopathology (HiTOP) Consortium, they address critically the “official nosology”, especially as exemplified in the DSM-5. The latter manual is criticized for being “authoritative”, guided by psychiatrists, and not immune against “socio-political” considerations in preserving and presenting an *ex cathedra* view of psychopathology as consisting of discrete nomothetic entities or taxa. In contrast, the authors highlight the likely empirical advantages of adopting the alternative position on psychopathology as a continuum of quantitative variation that can be organized hierarchically into several higher-order spectra and dimensions.

Krueger et al claim that recent research, methodologically stronger than its predecessors, overwhelmingly supports the quantitative-dimensional model of psychopathology, and believe that the latter is now fit to be ubiquitously translated into clinical practice. They advocate placing this model of classifying psychopathology on “an empirical playing field” instead of perpetuating the “traditional” nosology, exemplified by the DSM revision process.

Much of the evidence in support of these proposals stems from the comprehensive quantitative review of published taxometric research by Haslam et al². This review was based on a detailed examination and secondary analysis of 177 articles which, when combined, reported a total of 39.9% taxonic results. However, the authors concluded that, after statistically controlling for confounds, the “true” prevalence of taxonic findings was only 14%, mostly involving the domains of schizotypy, autism and substance use disorders. They contended that historical improvements in the methodological quality of taxometric studies,

especially the use of simulated comparison data and the linked comparison curve fit index, have contributed to the marked decline of taxonic findings.

There are two possible caveats to this line of reasoning. First, the purely statistical analysis and interpretation of the data is no substitute for a well-designed, real-life comparative study of clinical populations assessed according to both the hierarchical dimensional model illustrated by Krueger et al and the “traditional” categorical nosology of ICD-10 or DSM-5. The outcome criteria in such a hypothetical study should include choice of treatment, prognosis and functional status of the participants. As far as I am aware, no such study has yet been designed or conducted.

My second caveat concerns the applicability of the quantitative dimensional scheme to the bulk of psychotic disorders (marginally mentioned in Krueger et al’s paper). Historically, the evolution of the classification of these disorders has taken a path in reverse to that of the common non-psychotic disorders. The theory of the “unitary psychosis” has been dominant in European psychiatry around the middle of the 19th century, being associated with the names of its first proponent A. Zeller and its first critics W. Griesinger and K. Kahlbaum. It postulated a continuum of different stages within a unitary morbid process, terminating ultimately in a complete disintegration of mental life. It was against this background that E. Kraepelin synthesized the three pre-existing entities of hebephrenia, catatonia and paranoid dementia into a single concept, and proposed in 1896 the dichotomy of the unitary spectrum into the discrete entities of dementia praecox and manic-depressive insanity. Renamed as schizophrenia by E. Bleuler in 1908, the former entity was further described as “the group of schizophrenias”, to be split further by K. Leonhard into systematic and unsystematic forms, each containing many discrete subtypes³. Notably, there has been a recent revival of the continuum mod-

el of psychotic disorders⁴, which in its turn has been criticized as “scientifically unproven and clinically impractical”⁵.

At this point, I shall add my own take on the problem: can a classification of mental disorders be biologically anchored? This is doubtful, at least in the foreseeable future, because: a) the objects classified in psychiatry are explanatory concepts, i.e. abstract entities rather than physical organisms; b) the taxonomic units of “disorders” in DSM-IV, DSM-5 and ICD-10 do not form hierarchies; c) the current psychiatric classifications contain no supraordinate, higher-level organizing concepts. Leaving aside the vexing issue of validity of the categories, the criteria for evaluating psychiatric classifications should at present focus pragmatically on their clinical relevance and utility⁶: capacity of discriminating between syndromes and between degrees of their expression in individual patients; adaptability to different populations and cultural environments; reliability; cognitive ease of use; and reducing stigma. My prediction is that the quantitative/dimensional and the taxonic/discrete approaches to the classification of mental disorders will remain dialectically interconnected as the “yin” and “yang”.

A methodological tool eminently suited for empirical research is the grade of membership (GoM) latent structure analysis⁷, which enables the aggregation of clinical and/or neurocognitive measures into a parsimonious number of “pure types” (taxons) which represent fuzzy sets, rather than discrete categories, and assigns to each individual a quantitative affinity score indexing the degree to which he/she resembles each one of the taxons. My research group has been using the GoM to split a large cohort of schizophrenia patients into subtypes based on neurocognitive measures and to specify each patient’s affinity to any one of the taxons⁸.

I am reminded of the Hegelian postulate⁹ about the transition (“phase shift”) of the accumulation of quantitative changes into a new quality. This sums

up my impression of the stimulating argumentation presented in the paper by Krueger et al.

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1. Krueger RF, Kotov R, Watson D et al. *World Psychiatry* 2018;17:282-93.
2. Haslam N, Holland E, Kuppens P. *Psychol Med* 2012;42:903-20.
3. Leonhard K. *Classification of endogenous psychoses and their differentiated etiology*. Wien: Springer, 1999.
4. van Os J, Linscott RJ, Myin-Germeys I et al. *Psychol Med* 2009;39:179-95.
5. Lawrie SM, Hall J, McIntosh AM et al. *Br J Psychiatry* 2010;197:423-5.
6. Kendell R, Jablensky A. *Am J Psychiatry* 2003;160:4-12.
7. Woodbury MA, Manton KC. *Soc Methods Res* 1978;18:126-63.
8. Hallmayer J, Kalaydjieva L, Badcock J et al. *Am J Hum Genet* 2005;77:468-76.
9. Hegel GWF. *Phenomenology of spirit*. Oxford: Oxford University Press, 1977.

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After the failure of DSM: clinical research on psychiatric diagnosis

Clinical research on psychiatric diagnosis has failed from 1980 until now. In the DSM-III onwards era, clinical nosology research has been irrelevant. Contrary to the claims made in 1980 with DSM-III, diagnostic reliability did not lead to diagnostic validity, because reliability became an end in itself. The psychiatric profession congratulated itself on agreeing about how to define psychiatric diagnoses, and refused to make any further changes. The process was reified in DSM-III and DSM-IV, such that major changes were infrequent, and when they did occur, they were based on winds of opinion rather than solid, replicated scientific research. Minor changes were fought with passion, despite reasonable scientific data in their support¹.

In short, the greatest obstacle to scientific progress is, and has been, the DSM system of diagnosis. In 1980, DSM-III promised to push psychiatry forward, defining clear criteria for improvement with research. Now, DSM-5 is based on unscientific definitions which the profession's leadership refuses to change based on scientific research.

This perspective can be seen as heretical, as it is still not accepted by the mainstream of the American Psychiatric Association (APA). Yet, not all American psychiatry agrees with the APA. Importantly, the US National Institute of Mental Health (NIMH) leadership strongly criticized DSM-5 upon its publication, and announced it would no longer fund research using DSM criteria. Instead, the NIMH leadership proposed an alternative approach for research: the Research

Domain Criteria (RDoC). The main problem with the latter approach is that it gives up on clinical research about diagnosis altogether, claiming that research should begin with brain-based concepts. Both extremes are questionable: the DSM approach is clinical but unscientific; the NIMH approach is scientific but not clinical. The profession still awaits a scientific approach to clinical research on diagnosis.

Krueger et al's paper² reflects a positive response to this unfortunate state of affairs. The key leaders of this consortium were involved with the unhappy personality traits vs. disorders controversy in DSM-5³. They are researchers who advocated for following scientific data towards a change in personality nosology in favor of traits. They failed. Now they propose a consortium to conduct and promote an empirically-based nosology in psychiatry. This project is long overdue.

Our current dilemma was predictable. We can learn from early critics of DSM, like H. van Praag. In 1993, while the DSM-IV process was in full swing, he wrote⁴: "Today's classification of the major psychiatric disorders is as confusing as it used to be some 30 years ago. All things considered, the present situation is worse. Then, the psychiatrists were at least aware that diagnostic chaos reigned and many of them had not high opinion of diagnosis, anyhow. Now the chaos is codified and thus much more hidden... There is nothing wrong in basing the first draft of an operationalized taxonomy on expert opinion... One should

abstain, however, from proceeding further on that route. Yet, this is exactly what happened... I strongly feel that 1) an immediate moratorium should be laid on any further expert-opinion-based alterations in [diagnosis]... and that 2) future changes should be based on research only".

An important feature of the DSM ideology is the rejection of the concept of a hierarchy of diagnosis, on the debatable ground that we cannot have hierarchies in the absence of etiology. If we do not know causes of diseases, we cannot say which ones should be diagnosed preferentially to others. This perspective ignores the importance of differentiating diseases with many symptoms from those with fewer. If a symptom occurs as one of twenty in one illness, and one of two in another, then the first should be ruled out before the second is diagnosed. It is not biologically sound to diagnose "comorbid" panic disorder every time someone has a panic attack in the setting of a depressive or manic episode. The panic symptoms are often caused by mood states, rather than being a separate independent disease. We already take this approach with delusions and hallucinations; if they occur in mood states, we do not diagnose schizophrenia. This is an exception in the DSM system, though, which refuses to use the same logic for other psychopathological states.

Hence two problems result, again as van Praag described decades ago: "nosologomania"⁵ (i.e., the creation of many scientifically invalid diagnostic definitions) and many false "comorbidities"⁶.

In fact, the concept of “comorbidity” was introduced by Feinstein in 1970 as meaning the simultaneous co-occurrence of two independent, unrelated diseases⁷. The co-occurrence of anxiety and depression does not qualify for comorbidity; either they are symptoms of the same condition (like neurotic depression), or they reflect one condition causing another (as in mixed depression, where anxiety is caused by the mixed state).

The hierarchy proposed by this consortium grows out of the personality literature. It includes concepts that may be relevant to personality, but which are less relevant to mood or psychotic diseases. Dimensionality is relevant in both cases, but perhaps in different ways. For instance, the best clinical research supports the dichotomy between schizophrenia and manic-depressive illness. Further, the externalizing/internalizing concepts do not capture many of the features of manic-depressive illness, such as the presence of mixed states. The placement of “mania” as part of an “internalizing” disorder is questionable. The distinction between bipolar illness and “unipolar” depression is assumed in the hierarchical taxonomy, whereas this distinction has questionable validity based on the best available clinical research.

Thus, the proposal of a quantitative hierarchy is welcome, but how it is set up will require more attention to some clinical research that does not appear to

have been included in the working taxonomy provided in Krueger et al’s paper.

An alternative approach growing out of research on mood and psychotic diseases has been proposed dating back to the 1970s⁸. I have suggested a modernized version of that approach⁹. In this proposal, the hierarchy of psychopathology would involve manic states (bipolar illness) at the top of the pyramid of diagnosis, followed by depressive states (unipolar depression), followed by schizophrenia, then anxiety diagnosis (like obsessive-compulsive disease), then personality “disorders” (such as borderline and antisocial), then attention deficit disorder and narrowly defined diagnoses (such as eating disorders or paraphilias). The general concept is that conditions higher on the hierarchy are polysymptomatic, and cause the symptoms of conditions lower on the hierarchy, and thus the former should be ruled out before the latter are diagnosed.

This is standard medical teaching. Core medical training involves using symptoms to identify diagnoses, and not just converting symptoms into diagnoses, as is the case with DSM-III onwards. Then those diagnoses are organized in a differential diagnosis, where higher order ones are ruled out before lower order ones are made. The opposite approach is taken with the DSM system, which is powerful evidence for an important observation: contrary to what many of the post-mod-

ernist and anti-biological critics of DSM claim, the DSM system is not at all representative of the “medical model”. In fact, it is quite anti-medical, as shown in its rejection of the hierarchy concept.

In sum, Krueger et al’s effort is very worthwhile, but essentially limited to concepts in the personality literature. If expanded to capture affective and psychotic conditions, it could begin to put the profession on the road to a better clinical nosology for the future, leaving DSM in the rearview mirror.

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1. Ghaemi SN. *World Psychiatry* 2013;12:210-2.
2. Krueger RF, Kotov R, Watson D et al. *World Psychiatry* 2018;17:282-93.
3. Zachar P, Krueger RF, Kendler KS. *Psychol Med* 2016;46:1-10.
4. van Praag HM. *Make-believes in psychiatry or the perils of progress*. New York: Brunner Mazel, 1992.
5. van Praag HM. *World J Biol Psychiatry* 2000;1: 151-8.
6. van Praag HM. *Br J Psychiatry* 1996;168(Suppl. 30):129-34.
7. Feinstein AR. *J Chronic Dis* 1970;23:455-68.
8. Surtees PG, Kendell RE. *Br J Psychiatry* 1979; 135:438-43.
9. Ghaemi SN. *Mood disorders: a practical guide*, 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2007.

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Internalizing disorders: the whole is greater than the sum of the parts

The Hierarchical Taxonomy of Psychopathology (HiTOP) consortium is a group of investigators working to advance the empirical classification of psychopathology. In a previous issue of this journal they published a concise account of the work of their consortium¹, and now they put forward a statement of intent and a summary of progress².

Practitioners in the mental health field act as though each mental disorder is a discrete category – Mrs. Smith has panic

disorder; Mr. Brown has major depressive disorder – and consider that treatment and future developments will naturally follow from the diagnosis. At one level this is appropriate and necessary for the orderly management of treatment for individual patients, but at a higher level this is not correct: the defining symptoms of each mental disorder exist on dimensions that extend from very mild and incomplete sets consistent with wellness to the very severe, complete sets that dis-

able and distress and are incompatible with being well.

The classifications of mental disorders – DSM-5 and ICD-10 – are, at the simplest level, definitions of the threshold at which a set of symptoms becomes sufficiently complete, disabling or distressing to be of clinical concern, and an indicator of the need for treatment. The point on a dimension of increasing severity where a diagnosis is warranted is not indicated by any external measure

such as a sudden change in pathophysiology or of distress or disability. The threshold for a diagnosis in each classification is made by experts convened to define it and hence is somewhat arbitrary. There is broad consensus that mental disorders exist on dimensions, not categories, and in 2008 two members who would later join the HiTOP consortium convened a meeting and edited a seminal book, *Dimensional Approaches in Diagnostic Classification*, as part of work on refining the research agenda for DSM-5³.

Multivariate research has indicated that a latent general liability – *internalizing* – accounts for higher-than-chance levels of mood and anxiety disorder comorbidity, a finding that has been replicated and extended many times in different data sets and cultures (note that half of people who meet criteria for an anxiety or depressive disorder have a second diagnosis, and a quarter meet criteria for three or more).

For example, within the HiTOP consortium, Eaton et al⁴ modelled seven internalizing disorders in a nationally representative sample of 43,093 individuals. The study used a structured diagnostic interview optimized to cover the DSM-IV defining characteristics of these disorders. They found that a two-dimensional (distress-fear) liability structure for internalizing fit best and replicated across gender, assessment waves, and lifetime and 12-month diagnoses. These internalizing liabilities, *not the individual disorders*, predicted future internalizing pathology, suicide attempts, angina, and ulcer.

Waszczuk et al⁵ conducted a study based on the Interview for Mood and Anxiety Symptoms that assessed, without the usual skip outs, DSM-IV and ICD-10 emotional disorder symptoms and other manifestations of emotional disorders such as hopelessness, desperation, loss of libido, social withdrawal, and self-harm. In a series of analyses that ranged from symptom components to latent structures, they reported that dimensional components are better predictors of functioning than categorical DSM-IV diagnoses, even though impair-

ment is explicitly included in clinical diagnoses but is not part of those symptom components.

There are two implications from this body of work. First, that considering groups of disorders may be more informative than considering individual diagnoses. Second, that opening up research to include symptoms not presently included in classifications may point to new disorders or new arrangements of existing disorders and reduce the circularity of reanalyzing data from interviews designed to inform existing classifications.

There has been other work on classification independent of the HiTOP consortium that is relevant to the current Forum. As part of the work for DSM-5 and ICD-11, a working group⁶, including two members who would later join the HiTOP consortium, explored the feasibility of a meta-structure based on eleven validating criteria comprising both clinical features and risk factors (i.e., shared genetic risk factors; familiarity; shared specific environmental risk factors; shared neural substrates; shared biomarkers; shared temperamental antecedents; shared abnormalities of cognitive or emotional processing; symptom similarity; high rates of comorbidity; course of illness; treatment response). DSM-IV disorders were allocated to one of five clusters as a starting premise. Teams of experts then reviewed the literature to determine within-cluster similarities on the eleven predetermined validating criteria and discovered that those similarities were consistently greater than between-cluster similarities.

The five clusters were neurocognitive (identified principally by neural substrate abnormalities), neurodevelopmental (identified principally by early and continuing cognitive deficits), psychosis (identified principally by clinical features and biomarkers for information processing deficits), emotional/internalizing (identified principally by the temperamental antecedent of negative emotionality), and externalizing (identified principally by the temperamental antecedent of disinhibition). The working group considered that there could be advantages for

clinical practice, public administration and principally from the adoption of such an organizing principle. The chapter order in DSM-5 was changed to reflect this.

Computerized cognitive behavioural therapy (CBT) has a long history of focusing on the internalizing disorders as a group. Newby et al⁷ identified seventeen randomized controlled trials. Results showed that “transdiagnostic” computerized CBT outperformed control conditions on all outcome measures at post-treatment, with large effect sizes for depression ($g=0.84$), and medium effect sizes for anxiety ($g=0.78$) and quality of life ($g=0.48$), comparable to the benefits seen in diagnosis specific studies⁸.

Lastly, and again using “transdiagnostic” computerized CBT, Mewton et al⁹ assessed changes in the internalizing construct using a longitudinal latent trait framework that compared internalizing factor means at pre- and post-treatment. The standardized mean reduction in the internalizing construct with treatment was large (effect size 1.23, $SE=0.09$, $p<0.001$).

We conclude that treatment aimed at the internalizing construct is to be preferred to disorder specific treatment. In the internalizing disorders, whether one is investigating prognosis, impairment or response to treatment, the whole is greater than the sum of the parts.

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1. Kotov R, Krueger RF, Watson D. *World Psychiatry* 2018;17:24-5.
2. Krueger RF, Kotov R, Watson D et al. *World Psychiatry* 2018;17:282-93.
3. Helzer JE, Kraemer HC, Krueger RF et al. *Dimensional approaches in diagnostic classification*. Arlington: American Psychiatric Association, 2008.
4. Eaton NR, Krueger RF, Markon KE et al. *J Abnorm Psychol* 2013;122:86-92.
5. Waszczuk M, Kotov R, Ruggero C et al. *J Abnorm Psychol* 2017;126:613-34.
6. Andrews G, Goldberg DP, Krueger RF et al. *Psychol Med* 2009;39:1993-2000.
7. Newby JM, Twomey C, Yuan Li SS et al. *J Affect Disord* 2016;199:30-41.
8. Andrews G, Basu A, Cuijpers P et al. *J Anxiety Disord* (in press).
9. Mewton L, Hobbs MJ, Sunderland M et al. *Behav Res Ther* 2014;63:132-8.

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Categorical and/or continuous? Learning from vascular surgery

R. Krueger and his impressive international team of co-authors offer a clear and comprehensive review of current issues in dimensional approaches to classifying psychopathology¹. They make a challenging case for the advantages of this approach, as embodied in their Hierarchical Taxonomy of Psychopathology (HiTOP) model, over the categorical classifications widely adopted in psychiatry.

The issues as such are not new. They were widely discussed in the 1960s and 1970s. The British psychiatrist and epidemiologist R. Kendell covered much the same ground in his now classic book *The Role of Diagnosis in Psychiatry*². Then as now the question was whether psychopathology could be “cut at the joints” into distinct categories or whether it was better described quantitatively along one or more dimensions of continuous change. Then as now the answer depended in part on the kind of psychopathology in question and in part on the statistical methods adopted. Then as now opinion remained divided largely along professional lines, with psychiatrists favouring categorical and psychologists favouring dimensional approaches (Krueger, like a majority of his co-authors, is a psychologist).

There are, certainly, as Krueger and his colleagues point out, new factors in play, some positive, others negative. On the positive side, there have been important methodological advances. Statistical methods have progressed dramatically with developments in computing science. Formal logic, too, has a novel role to play: the British philosopher and psychologist P. Koralus’ semantic modelling of decision making, for example, offers potentially exciting applications to psychopathology³. On the negative side, fifty years of experience with symptom-based psychopathological categories have been disappointingly thin on aetiological insights. The promise of early 20th century advances (with discoveries such as neurosyphilis and Alzheimer’s disease) remains, despite all the power of contemporary neuroscience, largely unfulfilled.

Should we then be persuaded by Krueger et al’s case that categorical classifications of psychopathology should be abandoned in favour of dimensional description? Experience from other areas of medicine suggests that we should not.

Vascular surgery offers a case in point. As a relatively new specialty (the Vascular Surgical Society of Great Britain and Ireland was founded in 1966), vascular surgery adopted from the start an explicitly evidence-based approach and remains strongly research-led. In this respect, its predominantly categorical classification of disease entities has (as in most other areas of bodily medicine) served it well. Where psychiatry has suffered fifty years of frustration, vascular surgery has made significant and sustained progress in understanding the pathophysiology of a whole range of categorically-defined disorders, ranging from aortic aneurysm to varicose veins, with corresponding advances in both surgical and non-surgical management options.

So far so good then, it would seem, for traditional disease entities. However, closer inspection shows that, while the objects of scientific interest in vascular surgery are indeed categorically defined disorders, the science of vascular surgery has been in many instances dimensional in character. Progress in the treatment of aortic aneurysm, for example, has depended critically on quantitative studies of the relative risk of death respectively from vascular surgery and from aneurysm rupture. The key variable in these studies is the diameter of the aneurysm. The risk of rupture increases as the aneurysm expands. In most people this happens slowly, and international guidelines recommend annual monitoring until the diameter of the patient’s aneurysm reaches five and a half centimeters, this being the point at which the risk of rupture within the next twelve months (5%) is sufficient to justify the risks of surgery⁴.

Vascular surgical science has thus made progress by combining categorical with dimensional approaches. Similar com-

bined approaches continue to be adopted in ongoing research on the management of aortic aneurysm. The object of interest remains the categorically defined disease entity “aortic aneurysm”; the key variables remain the essentially dimensional variables of relative risk.

Psychopathology, it is true, is different from and in certain respects more complex than vascular pathology. There are, for example, no counterparts in vascular pathology of the conceptual challenges presented by comorbidity in psychopathology (reflected in the difficulties described by Krueger et al in establishing a stable hierarchical structure for their dimensional approach). Comorbidities are, of course, common in vascular pathology, but the requisite divisions and distinctions are largely unproblematic. Similarly unproblematic in vascular pathology are criteria of functioning. Descriptively similar experiences of voice hearing, for example, may be for one person functionally impairing and for another empowering^{5,6}. A swelling aorta, by contrast, is a functionally impaired aorta for anyone.

Such differences, though, make the example of vascular pathology more rather than less pertinent for psychopathology. If progress in vascular pathology has been achieved with a combined categorical and dimensional approach, it is at the very least likely that a similar approach will be needed if progress is to be made with the more complex challenges of psychopathology. The point, anyway, is general. All sciences make progress through quantification. But progress through quantification has usually been by way of addition, not substitution. This is evident throughout the medical and biological sciences. It is evident, too, in physics, surely the paradigm of a successful quantitative science (think of wave/particle dualism in quantum mechanics). So why should psychopathology be any different?

Krueger et al might reply: “because this is where the science leads”. In the opening paragraphs of their paper, they claim in support of their HiTOP model

the high ground of empirical science, contrasting this with what they describe as the received authority of the DSM. But this is tendentious. The scientific basis specifically of DSM-5 has indeed been widely criticized⁷. But the criticism is precisely that DSM-5 has departed from the explicitly evidence-based principles on which earlier revisions of the DSM (and ICD) were based. Notably, the Research Domain Criteria project, although bracketed by Krueger et al with DSM-5, was in fact inspired by much the same aims as HiTOP for a return to empiricism in psychopathological research⁸.

We should thus welcome the advances in quantification of psychopathology described by Krueger et al. But we should welcome these advances as adding to rather than displacing categorical classi-

fications as the basis of psychopathological science. More will be required for effective translation of psychopathological science into practice. In vascular surgery, translation has required teamwork rather than competition between professionals, and attention to values as well as evidence⁹. But, as to the science, the example of vascular surgery suggests that it is time for a change of conjunction. For fifty years the focus of debate in psychopathology has been “categorical *or* continuous”. The example of vascular surgery suggests that its time to think instead “categorical *and* continuous”.

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1. Krueger RF, Kotov R, Watson D et al. *World Psychiatry* 2018;17:282-93.
2. Kendell RE. *The role of diagnosis in psychiatry*. Oxford: Blackwell, 1975.
3. Parrott M, Korulus P. *J Cogn Neuropsychiatry* 2015;20:398-415.
4. The UK Small Aneurysm Trial Participants. *Lancet* 1998;352:1649-55.
5. Jackson M, Fulford KWM. *Philos Psychiatry Psychol* 1997;4:41-66.
6. Daalman K, Diederens K, Derks E et al. *Psychol Med* 2012;42:2475-84.
7. Frances A. *Saving normal: an insider's revolt against out-of-control psychiatric diagnosis, DSM-5, big pharma, and the medicalization of ordinary life*. New York: Morrow, 2013.
8. Insel TR. *Transforming diagnosis*. www.nimh.nih.gov.
9. Handa IA, Fulford-Smith L, Barber ZE et al. *The importance of seeing things from someone else's point of view*. *BMJ Careers*, August 15, 2016.

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