

SPECIAL SECTION INTRODUCTION

Studying Fine-Grained Elements of Psychopathology to Advance Mental Health Science

Miriam K. Forbes¹, Eiko I. Fried², and Uma Vaidyanathan³¹ School of Psychological Sciences, Macquarie University² Clinical Psychology Unit, Leiden University³ Sublimus LLC, Washington, DC, United States

Given the now well-recognized limitations of traditional classification systems for research, this editorial proposes to advance mental health science by focusing research efforts on studying fine-grained elements of mental health and illness such as symptoms, mechanisms, and processes. Our own perspectives are informed by three approaches in particular that have gained traction over the last decade: the Hierarchical Taxonomy of Psychopathology, the network or systems approach, and the National Institute of Mental Health Research Domain Criteria. Drawing on these and other perspectives as well as the diverse views of the author teams that contributed to this Special Section, we summarize the state of the field and propose an ambitious plan for the way ahead. Specifically, we propose that embracing pluralistic, multimethod, and multisystem approaches offers a way forward. This will require strategies to reduce research waste and much stronger channels for communication to identify confluence, discoveries, and dead ends within and between disciplines. We are optimistic this will lead to a better understanding of the mechanisms underpinning psychopathology and ultimately to more effective interventions.

General Scientific Summary

In this editorial, we introduce a Special Section focused on investigating fine-grained elements of mental health and illness such as individual symptoms, symptom clusters, or detailed mechanisms and processes. We summarize a variety of viewpoints reflected in the Special Section and propose paths forward.

Keywords: psychopathology, symptoms, Hierarchical Taxonomy of Psychopathology, systems, Research Domain Criteria

Categorical diagnostic systems such as the *Diagnostic and Statistical Manual of Mental Disorders (DSM)* and *International Classification of Diseases (ICD)* were developed with clinical utility strongly in mind: Diagnoses should be clinically useful and usable by stakeholders. It is therefore unsurprising that such systems are not a perfect fit for many research situations.

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One limitation they have is heterogeneity in the diagnoses they catalog: The “checklist” approach in the *DSM* means two people with the same diagnosis may share many or few symptoms—or, in some cases, no symptoms at all (e.g., Fried & Nesse, 2015). How do we better design research studies to embrace interindividual differences of people with mental health problems? A second limitation is overlap: The hundreds of *DSM-5* diagnoses comprise approximately 680 unique symptoms, many of which feature across a broad range of disorders (Forbes et al., 2023)—for example, depressed mood is part of 15 disorders, and insomnia part of 22. This raises the question of how to best deal with transdiagnostic mechanisms that influence the onset and maintenance of a variety of mental health problems. Third, many people exhibit mental health problems close to diagnostic thresholds but do not fully meet *DSM* criteria. This invites questions about operationalizing mental disorders as categories when there is very little evidence for this conceptualization (e.g., Haslam et al., 2020). All three limitations challenge the value of case-control studies in general, and go hand in hand with disappointing progress in the last few decades: The prevalence of mental health problems has, if anything, increased; gold-standard treatments for many diagnoses have remained the same; and treatment efficacy has not improved (e.g., Jorm et al., 2017; Khan & Brown, 2015; van Zoonen et al., 2014).

A growing body of research has thus been moving beyond traditional categorical diagnoses over the last decade or more, reconsidering how

Miriam K. Forbes  <https://orcid.org/0000-0002-6954-3818>

Eiko I. Fried  <https://orcid.org/0000-0001-7469-594X>

Uma Vaidyanathan  <https://orcid.org/0009-0003-4970-1262>

All authors contributed equally to this work. Contributing authors' and editors' responses to the questions reported in the second section of the editorial are available in full on the Open Science Framework page for this Special Section: <https://osf.io/jhd9m/>.

Correspondence concerning this article should be addressed to Miriam K. Forbes, School of Psychological Sciences, Australian Hearing Hub, Macquarie University, Sydney, NSW 2109, Australia. Email: miriam.k.forbes@gmail.com

mental health science ought to progress. Our own perspectives are informed by three approaches in particular that have gained traction over the last decade. First, the Hierarchical Taxonomy of Psychopathology (HiTOP) conceptualizes covariation among symptoms, signs, traits, and syndromes as reflecting often transdiagnostic dimensions of psychopathology. Second, network or systems approaches understand such covariation to derive from mutual causal interactions among these elements. Finally, the National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) is agnostic to current disorder categories, but promotes research that starts with known neurobehavioral domains and constructs associated with functioning in a view to understand how they may go awry in psychopathology.

These and other approaches (e.g., process-based therapy and clinical staging; Hofmann & Hayes, 2019; McGorry et al., 2006) challenge the field to move beyond a focus on *DSM*-defined diagnoses. Although the frameworks all originate from similar critiques of *DSM*-based diagnoses, such as their low reliability and validity (e.g., Borsboom, 2017; Cuthbert & Kozak, 2013; Kotov et al., 2017), the proposed paths for progress are rather different. Studying fine-grained elements of mental health and illness is one potential path that aligns with numerous frameworks, and the focus of our Special Section (<https://osf.io/jhd9m/>)—building on past Special Sections on the reconceptualization of psychopathology (Krueger et al., 2016; MacDonald & Krueger, 2013) and embracing the complexity and underlying processes in mental health problems (e.g., Fried & Robinaugh, 2020; Patrick & Hajcak, 2016). Specifically, this Special Section showcases research on fine-grained psychopathology constructs from a variety of viewpoints, featuring works aimed to provide new perspectives that leverage intersections among different approaches to understanding, modeling, predicting, and treating mental illness. In this editorial, we bring together these different views and propose ways forward.

Perspectives on Studying Fine-Grained Phenomena

Concretely, how might research on fine-grained elements of mental health progress toward informing our theories and treatments? We asked all author teams and editors of the Special Section to answer three questions centered around this topic:

1. What do you see as the “grains” (constructs of interest) of psychopathology, and why is that type of granularity important?
2. What does a fine-grained perspective offer that is better or different from other approaches?
3. What do you see as the essential next steps for this approach to achieve the aim of advancing mental health science?

Given the variety of perspectives of research teams contributing to this special section as well as our choice of open-ended questions, it was unsurprising that there was no clear consensus in responses to any of the questions. However, broad themes did emerge among the responses that we summarize at a high level in the following paragraphs. The full response sets are available at <https://osf.io/jhd9m/>.

In response to the first question, several author teams suggested symptoms as the starting point for fine-grained investigations—either those that are explicitly included in the *DSM*, or those that are a part of models such as the tripartite model of anxiety and depression (e.g., Rowe et al., 2023). This approach is interesting to consider in light

of the limitations of the extant diagnostic systems described above. Indeed, it can be convincingly argued that symptoms make a logical starting point for evolution and no doubt capture some phenomena of importance to mental health and illness, albeit imperfectly and incompletely (see Levin-Aspenson, 2023). Others expanded the notion of “grains” beyond symptoms, focusing on dynamic processes such as stability and change over time (e.g., Olthof et al., 2023), or the way various elements of the biopsychosocial model relate to each other. Teams also set different priorities regarding methodological and measurement approaches, with some focusing on repeated observations and ambulatory assessment methods, while others highlighted the importance of integrating information across various modalities, including self-report measures and biological circuits.

Among the answers for question two, one theme that emerged on the benefits offered by a fine-grained perspective was the opportunity to examine transdiagnostic symptoms, processes, or mechanisms (e.g., sleep or irritability; Karlovich et al., 2023), as well as elements that may be unique to particular forms of psychopathology (e.g., syndromes nested within traditional constructs; Waldman & Poore, 2023). Such perspectives afford the opportunity to untangle the heterogeneity in traditional diagnostic constructs and provide a clearer understanding of treatment mechanisms, biomarkers, risk factors, and consequences of specific symptoms or syndromes. Studies designed to conduct head-to-head comparisons with traditional diagnostic constructs can start to determine whether and for what purposes these alternative approaches improve on the status quo. In addition to the richer information afforded through the more comprehensive conceptualization of the constructs we study, several author teams highlighted the opportunities presented by a more detailed understanding of dynamic change within individuals, and the potential to use this knowledge for practices such as personalized just-in-time interventions. In keeping with these different perspectives on what a fine-grained approach entails, a couple of responses noted that defining a grain and evaluating the potential advantages of the approach would depend on the question—that is, we may need to focus on different grains for different use cases such as identifying treatment targets, improving diagnostic specificity, or defining constructs for research. Taken together, the responses underscored that studying fine-grained mechanisms could paint a richer picture of the individuals and the constructs we study.

In response to the third question, the overarching theme evident in the ideas on immediate next steps for advancing mental health science was that of integration. Many research teams emphasized the need to explore and understand the extent to which intra- and interindividual processes and constructs mapped onto each other. Indeed, while there are some differences between HiTOP, network approaches, and RDoC, the majority of work conducted has been focused on the interindividual of concepts and constructs with the assumption that such results can be applied at the individual level as well (ergodicity; see Fisher et al., 2018; Molenaar, 2004)—a premise that has not been tested adequately. Several respondents also noted a critical need to integrate various frameworks for psychopathology such as HiTOP and RDoC to ensure there were no redundancies between them (e.g., Michelini et al., 2021) and to allow for rigorous measurement and testing of constructs advanced by each system. Similarly, the importance of integrating the multimethod approaches to the measurement between frameworks was clear, although the small intercorrelations among various measurement modalities pose a challenge here—for example, self-report symptoms correlated more highly with other self-report symptoms than

they do electroencephalogram (EEG), magnetic resonance imaging (MRI), or genetics, and vice versa (see Stange et al., 2023, and Pasion et al., 2023, for examples of such studies). The commentary by Joyner and Perkins (2023) discusses this topic in greater detail as well.

A significant hurdle in integrating the various frameworks and the concepts they are organized around is the need for shared terminology. This has been a challenge in psychology as a field more broadly over decades. While there is general agreement on notions of broadly used constructs such as “fear,” “anxiety,” or “cognition,” it has proved much more difficult to specifically define these in a standardized way that is accepted universally. In fact, terminology systems such as the Systematized Nomenclature of Medicine (SNOMED)—mandated in several countries for the electronic exchange of health information—struggle in defining disorder constructs beyond those specified in the *DSM* and *ICD*. If we move away from the clearly specified diagnostic criteria and constructs in the *DSM* and *ICD* as the defining frameworks for our field, we will need to find new anchors for research that facilitate crosswalks among studies’ findings, but it is not yet clear what these should be. Empirically derived dimensions in HiTOP? Elements or layers of dynamic systems? Specific biobehavioral domains of functioning? Something entirely different from all the above?

Ways Forward

Evidently, the problems we are working to solve are complex, with no obvious solutions. One proposal might be a unifying framework to homogenize research efforts in the field. But given that different frameworks work toward different goals, the question is how useful or even feasible such an approach would be. Instead, we propose to embrace a pluralistic, multimethod, and multisystem approach to advance mental health science and benefit from the richness that diverse perspectives will bring.

We see two fundamental threats to the success of this pluralistic approach. First, with a profusion of approaches comes a stretching of already scarce resources and the need for efficiency in each research program. Second, if various research programs head in different directions it will be easy to lose sight of emerging confluence in studies’ findings, and the field at large may overlook generalizable limitations identified within a specific subfield. Below, we suggest potential solutions that could provide a path forward for both challenges.

To address the scarcity of resources, studies need to be conducted in ways that progress our body of knowledge, whether through novel insights or meaningful null findings. Guiding principles of rigor, transparency, and robustness can all increase the likelihood from the outset that dead ends are recognized, errors are identified, and research outputs make meaningful (and perhaps even lasting) contributions in each of the rapidly evolving literature. Concretely, this means that we should (a) be clearer about and explicate the theories we are testing so that they can be meaningfully amended or rejected (e.g., Robinaugh et al., 2021); (b) share data and code so that others can reproduce, verify, and extend our findings (e.g., Martone et al., 2018); and (c) instead of conducting many studies in small samples that easily fall prey to false positives, publication bias, and file drawer effects, we should invest our resources in fewer high-powered studies—preferably leveraging large-scale collaborations and team-science (e.g., Moshontz et al., 2018). Together, these and related initiatives will considerably reduce research waste and ensure research money is spent in ways that yield health dividends for both patients and the public (see Lancet 2014 series on research waste).

To integrate discoveries and identify dead ends on the profusion of paths we pursue, we also need to develop stronger channels for communication both within and between subfields. Hubs for many frameworks already exist with varying degrees of formality (e.g., the HiTOP Consortium, the Psychosystems Lab, and the NIMH RDoC Unit), and a formalization of these structures for communication of research findings could further increase efficiency in the research programs within each subfield. Furthermore, research summits that act as meeting points for researchers from various frameworks could provide opportunities for rapid advancements that capitalize on the diverse research approaches and outputs among the subfields.

For example, there was a panel discussion in Berlin in 2022 with participants from six research frameworks—including HiTOP, systems, and RDoC along with the *ICD*, the Alternative Model of Personality Disorders, and process-based therapy. This exchange of ideas resulted in new insights for at least some of the panelists (i.e., two of the authors of this editorial were present) and a collaborative discussion paper on points of agreement regarding how best to proceed with (re-)conceptualizing psychopathology (Rief et al., under review). Similarly, in early 2020, proponents of varied approaches including the HiTOP, network theory, RDoC, the *DSM*, a “*p*-factor,” clinical staging, and complex systems met in Amsterdam seeking to integrate their perspectives and methods into a new psychiatric nosology. While that ambitious aim has not yet been achieved, these kinds of meetings offer a direct route to building stronger connections and pathways for communication within and between fields. Such pathways—as well as formal research collaborations (e.g., Eaton et al., 2023, representing HiTOP, network, and clinical staging approaches)—can facilitate new discoveries and minimize research waste in the process. For example, by reducing jingle-jangle fallacies between fields that stymie progress, and providing opportunities for direct crosswalks between frameworks when researchers from different approaches have access to shared resources like data.

Ultimately, we all started with the same motivations and have many shared aims (e.g., improving conceptualization of psychopathology, understanding of mechanisms, and improvement of treatment outcomes), but studying individual pieces of a phenomenon as complex as psychopathology can only get us so far. We believe it is the differences in our approaches that will provide the depth of understanding that can lead us to new insights. If we embrace these differences and still come together to share ideas, discoveries, failures, and resources, we could forge a path to understanding the mapping between individuals’ presenting symptoms, the specific mechanisms at work, and the best-suited interventions.

References

- Borsboom, D. (2017). A network theory of mental disorders. *World Psychiatry*, 16(1), 5–13. <https://doi.org/10.1002/wps.20375>
- Cuthbert, B. N., & Kozak, M. J. (2013). Constructing constructs for psychopathology: The NIMH research domain criteria. *Journal of Abnormal Psychology*, 122(3), 928–937. <https://doi.org/10.1037/a0034028>
- Eaton, N. R., Bringmann, L. F., Elmer, T., Fried, E. I., Forbes, M. K., Greene, A. L., Krueger, R. F., Kotov, R., McGorry, P. D., Mei, C., & Waszczuk, M. A. (2023). A review of approaches and models in psychopathology classification research. *Nature Reviews Psychology*. Advance online publication. <https://doi.org/10.1038/s41159-023-00218-4>
- Fisher, A. J., Medaglia, J. D., & Jeronimus, B. F. (2018). Lack of group-to-individual generalizability is a threat to human subjects research.

- Proceedings of the National Academy of Sciences of the United States of America*, 115(27), E6106–E6115. <https://doi.org/10.1073/pnas.1711978115>
- Forbes, M. K., Neo, B., Nezami, O. M., Fried, E. I., Faure, K., Michelsen, B., Twose, M., & Dras, M. (2023). *Elemental psychopathology: Distilling constituent symptoms and patterns of repetition in the diagnostic criteria of the DSM-5*. PsyArXiv. <https://doi.org/10.31234/osf.io/u56p2>
- Fried, E. I., & Nesse, R. M. (2015). Depression is not a consistent syndrome: An investigation of unique symptom patterns in the STAR*D study. *Journal of Affective Disorders*, 172, 96–102. <https://doi.org/10.1016/j.jad.2014.10.010>
- Fried, E. I., & Robinaugh, D. J. (2020). Systems all the way down: Embracing complexity in mental health research. *BMC Medicine*, 18(1), 1–4. <https://doi.org/10.1186/s12916-020-01668-w>
- Haslam, N., McGrath, M. J., Viechtbauer, W., & Kuppens, P. (2020). Dimensions over categories: A meta-analysis of taxometric research. *Psychological Medicine*, 50(9), 1418–1432. <https://doi.org/10.1017/S003329172000183X>
- Hofmann, S. G., & Hayes, S. C. (2019). The future of intervention science: Process-based therapy. *Clinical Psychological Science*, 7(1), 37–50. <https://doi.org/10.1177/2167702618772296>
- Jorm, A. F., Patten, S. B., Brugha, T. S., & Mojtabai, R. (2017). Has increased provision of treatment reduced the prevalence of common mental disorders? Review of the evidence from four countries. *World Psychiatry*, 16(1), 90–99. <https://doi.org/10.1002/wps.20388>
- Joyner, K., & Perkins, E. R. (2023). Challenges and ways forward in bridging units of analysis in clinical psychological science. *Journal of Psychopathology and Clinical Science*, 132(7), 888–896. <https://doi.org/10.1037/abn0000879>
- Karlovich, A. R., Shaughnessy, S., Simmons, K., & Evans, S. C. (2023). Toward greater specificity in the nonspecific: Estimating the prevalence of diagnostic irritability and sleep symptoms in adolescents. *Journal of Psychopathology and Clinical Science*, 132(7), 820–832. <https://doi.org/10.1037/abn0000870>
- Khan, A., & Brown, W. A. (2015). Antidepressants versus placebo in major depression: An overview. *World Psychiatry*, 14(3), 294–300. <https://doi.org/10.1002/wps.20241>
- Kotov, R., Krueger, R. F., Watson, D., Achenbach, T. M., Althoff, R. R., Bagby, R. M., Brown, T. A., Carpenter, W. T., Caspi, A., Clark, L. A., Eaton, N. R., Forbes, M. K., Forbush, K. T., Goldberg, D., Hasin, D., Hyman, S. E., Ivanova, M. Y., Lynam, D. R., Markon, K., ... Zimmerman, M. (2017). The Hierarchical Taxonomy of Psychopathology (HiTOP): A dimensional alternative to traditional nosologies. *Journal of Abnormal Psychology*, 126(4), 454–477. <https://doi.org/10.1037/abn0000258>
- Krueger, R. F., Tackett, J. L., & MacDonald, A., III. (2016). Toward validation of a structural approach to conceptualizing psychopathology: A special section of the Journal of Abnormal Psychology. *Journal of Abnormal Psychology*, 125(8), 1023–1026. <https://doi.org/10.1037/abn0000223>
- Levin-Aspenson, H. F. (2023). To fully leverage fine-grained clinical phenomena, we have to think beyond DSM-based concepts and the presumption of diagnostic kinds. *Journal of Psychopathology and Clinical Science*, 132(7), 881–887. <https://doi.org/10.1037/abn0000876>
- MacDonald, A. W., III, & Krueger, R. F. (2013). Mapping the country within: A special section on reconceptualizing the classification of mental disorders. *Journal of Abnormal Psychology*, 122(3), 891–893. <https://doi.org/10.1037/a0033996>
- Martone, M. E., Garcia-Castro, A., & VandenBos, G. R. (2018). Data sharing in psychology. *American Psychologist*, 73(2), 111–125. <https://doi.org/10.1037/amp0000242>
- McGorry, P. D., Hickie, I. B., Yung, A. R., Pantelis, C., & Jackson, H. J. (2006). Clinical staging of psychiatric disorders: A heuristic framework for choosing earlier, safer and more effective interventions. *Australian & New Zealand Journal of Psychiatry*, 40(8), 616–622. <https://doi.org/10.1080/j.1440-1614.2006.01860.x>
- Michelini, G., Palumbo, I. M., DeYoung, C. G., Latzman, R. D., & Kotov, R. (2021). Linking RDoC and HiTOP: A new interface for advancing psychiatric nosology and neuroscience. *Clinical Psychology Review*, 86, Article 102025. <https://doi.org/10.1016/j.cpr.2021.102025>
- Molenaar, P. C. M. (2004). A manifesto on psychology as idiographic science: Bringing the person back into scientific psychology, this time forever. *Measurement: Interdisciplinary Research and Perspectives*, 2(4), 201–218. https://doi.org/10.1207/s15366359mea0204_1
- Moshontz, H., Campbell, L., Ebersole, C. R., Ilzerman, H., Urry, H. L., Forscher, P. S., Grahe, J. E., McCarthy, R. J., Musser, E. D., Antfolk, J., Castille, C. M., Evans, T. R., Fiedler, S., Flake, J. K., Forero, D. A., Janssen, S. M. J., Keene, J. R., Protzko, J., Aczel, B., ... Chartier, C. R. (2018). The psychological science accelerator: Advancing psychology through a distributed collaborative network. *Advances in Methods and Practices in Psychological Science*, 1(4), 501–515. <https://doi.org/10.1177/2515245918797607>
- Olthof, M., Hasselman, F., Aas, B., Lamoth, D., Scholz, S., Daniels-Wredenhagen, N., Weinans, E., Strunk, G., Schiepek, G., Bosman, A., & Lichtwarck-Aschoff, A. (2023). The best of both worlds? General principles of psychopathology in personalized assessment. *Journal of Psychopathology and Clinical Science*, 132(7), 808–819. <https://doi.org/10.1037/abn0000858>
- Pasion, R., Ribes-Guardiola, P., Patrick, C., Stewart, R. A., Palva, T. O., Macedo, I., Barbosa, F., Brislin, S. J., Martin, E. A., Blain, S. D., Cooper, S. E., Ruocco, A. C., Tiego, J., Wilson, S., Goghari, V. M., & HiTOP Neurobiological Foundations Workgroup. (2023). Modeling relations between event-related potential factors and broader versus narrower dimensions of externalizing psychopathology. *Journal of Psychopathology and Clinical Science*, 132(7), 867–880. <https://doi.org/10.1037/abn0000856>
- Patrick, C. J., & Hajcak, G. (2016). Reshaping clinical science: Introduction to the special issue on psychophysiology and the NIMH research domain criteria (RDoC) initiative. *Psychophysiology*, 53(3), 281–285. <https://doi.org/10.1111/psyp.12613>
- Rief, W., Hofmann, S. G., Berg, M., Forbes, M. K., Pizzagalli, D. A., Zimmerman, J., Fried, E., & Reed, G. M. (under review). *Should we change the way we classify psychopathology? A discussion paper*.
- Robinaugh, D. J., Haslbeck, J. M., Ryan, O., Fried, E. I., & Waldorp, L. J. (2021). Invisible hands and fine calipers: A call to use formal theory as a toolkit for theory construction. *Perspectives on Psychological Science*, 16(4), 725–743. <https://doi.org/10.1177/1745691620974697>
- Rowe, J., Poppenk, J., Squires, S., Mazurka, R., Nogovitsyn, N., Hassel, S., Zamyadi, M., Arnott, S. R., Rotzinger, S., Kennedy, S. H., Milev, R. V., & Harkness, K. L. (2023). Anxious arousal predicts within-person changes in hippocampal volume in adults with a history of childhood maltreatment: A CAN-BIND4 report. *Journal of Psychopathology and Clinical Science*, 132(7), 797–807. <https://doi.org/10.1037/abn0000864>
- Stange, J. P., Li, J., Xu, E. P., Zapetis, S. L., Phanord, C. S., Wu, J., Sellery, P., Keefe, K., Forbes, E., Mermelstein, R. J., Trull, T. J., & Langenecker, S. A. (2023). Autonomic complexity dynamically indexes affect regulation in everyday life. *Journal of Psychopathology and Clinical Science*, 132(7), 847–866. <https://doi.org/10.1037/abn0000849>
- van Zoonen, K., Buntrock, C., Ebert, D. D., Smit, F., Reynolds, C. F., III, Beekman, A. T., & Cuijpers, P. (2014). Preventing the onset of major depressive disorder: A meta-analytic review of psychological interventions. *International Journal of Epidemiology*, 43(2), 318–329. <https://doi.org/10.1093/ije/dyt175>
- Waldman, I. D., & Poore, H. E. (2023). Evaluating alternative models of youth externalizing using quantitative genetic analyses. *Journal of Psychopathology and Clinical Science*, 132(7), 833–846. <https://doi.org/10.1037/abn0000874>

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