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## Defining Psychiatric Disease

To the Editor: In his review of Horwitz and Wakefield's book on anxiety in the January issue of the *Journal* (1), Dr. Kenneth Kendler rightly points out two major problems with definitions of disorder or disease based on putative "dysfunction of an evolved mind/brain mechanism," namely, 1) it is almost impossible to confirm or refute claims about such evolved mechanisms through any empirical studies, and 2) the "evolved mechanisms" concept cannot be applied coherently to individual genomes, which may differ markedly in their sensitivity to environmental stimuli. But Dr. Kendler may be too willing to yield to the "harmful dysfunction" model advocated by Horwitz and Wakefield ("I cannot suggest a much better approach…").

Historically, the concept of human "disease" (etymologically, dis-*ease*) arose in response to various instances of prolonged or intense suffering and incapacity not due to an obvious wound or a deliberate attack (2). Thus, disease is not a biological or even etiological term, but rather a term of ordinary language (3), often first applied to the suffering and incapacitated person by family or friends. Only subsequent to the recognition of disease does our system of classification become relevant, insofar as it aims to identify the *type* of disease at hand. Applied to anxiety, a patient has psychiatric disease or disorder when his or her anxiety is such that it causes prolonged or intense suffering and incapacity—which we may define by whatever measures we care to specify. We need not invoke unverifiable evolutionary mechanisms at all (4).

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## Commentary on the Application of DSM-5 Criteria for Autism Spectrum Disorder

To the Editor: In the introduction of the article by Huerta et al. in the October 2012 issue of the *Journal* (1), the authors cite several published studies indicating that the proposed DSM-5 criteria for autism spectrum disorder (ASD) would exclude approximately 10%–50% of patients currently meeting DSM-IV criteria. These patients would become ineligible for services if clinics required a rediagnosis meeting the new criteria (a common occurrence), and a similar proportion of newly diagnosed patients would be "dropped out" and denied services.

To assess this serious issue, Huerta et al. set out to determine the sensitivity and specificity of the proposed DSM-5 criteria relative to the DSM-IV criteria. They utilized three data sets including 4,453 children with a DSM-IV clinical diagnosis of pervasive developmental disorder (PDD) and 690 with non-PDD diagnoses (e.g., language disorder). They reported an overall sensitivity of 0.91 and a specificity of 0.53 for the proposed DSM-5 criteria.

The authors concluded, "Our findings indicate that the majority of children with DSM-IV PDD diagnoses would continue to be eligible for an ASD diagnosis under DSM-5," thus implying that their data support instituting the proposed DSM-5 changes.

We respectfully disagree with their opinion regarding the usefulness of the proposed DSM-5 criteria based on their data. Abandoning criteria that have been in worldwide use for decades for new ones that may eliminate from 9% (their data) to >40% (prior reports) of previously diagnosed patients is neither scientifically nor morally justified.

Also, the specificity values they computed for the new criteria averaged only 0.53. This figure is unacceptably low by typical medical test standards.

It is also important to point out that the data set used by the authors contained only 238 case subjects with Asperger's disorder among all 4,453 children meeting DSM-IV criteria. Thus, only a small number (0.53%) of those compared with the DSM-5 criteria were those most likely to be eliminated according to the prior studies they cited. This makes the observed specificity and sensitivity higher than they would have been if those known to be most likely to be excluded were in fact excluded before the study began.

We also wish to point out another serious unintended consequence of instituting the proposed DSM-5 criteria—the obvious problem posed to all researchers when selection criteria for subjects are changed. We have amassed large, detailed, uniformly diagnosed subject pools at great effort and expense over the past four decades. Changing diagnostic criteria would make those subject data pools incompatible and unusable for studies involving individuals diagnosed by

new criteria who will be enrolled in our ongoing and future clinical and biomedical research projects.

In conclusion, the results presented by the authors do not support instituting the DSM-5 criteria and can cause harm to our patients and research projects. Furthermore, the proposed changes rest on clinical data, and any changes should be postponed until new, replicable biomedical data warrant such a major undertaking.

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## Response to Ritvo and Ritvo Letter

TO THE EDITOR: The goal of our article (1) was to examine the impact of the new DSM-5 criteria for autism spectrum disorder (ASD) in three large samples of children with DSM-IV-defined ASD and non-ASD disorders. Using items from the Autism Diagnostic Interview–Revised and the Autism Diagnostic Observation Schedule to match DSM-5 criteria, we found that the new criteria correctly classified a large majority of children with ASD (91%), including very young children, girls, and children without language impairments. We also found that the specificity of the new criteria represented an improvement over existing DSM-IV criteria.

Ritvo and Ritvo's commentary about our article and about the upcoming changes to DSM criteria center on two main concerns: 1) that the changes introduced by DSM-5 will affect the sensitivity of the diagnostic criteria and 2) that the changes to DSM-5 criteria will limit the usefulness of ASD data banks.

The possibility of decreased sensitivity in diagnostic criteria is a valid concern. In fact, the initial motivation for our study was to examine whether children with previous DSM-IV diagnoses of any pervasive developmental disorder (PDD) would be incorrectly left out by the new criteria. As Ritvo and Ritvo note, when based on parent-reported symptoms only, approximately 9%−10% of our sample meeting DSM-IV criteria for ASD was not correctly classified by DSM-5 criteria. However, it is important to reiterate that the sensitivity of identification was much more likely affected by the methods of the study—using diagnostic instruments not designed to address the specific revisions in DSM-5—than by the DSM-5 criteria. Our results show that relying on clinical observation in addition to parental report of symptoms improved the sensitivity of the proposed DSM-5 criteria, and in many cases this resulted in sensitivities similar to those for DSM-IV criteria (see Table 2 in our article [1]).

Ritvo and Ritvo expressed particular concern about the sensitivity of the new criteria for Asperger's disorder because of the relatively small proportion of our sample for whom this DSM-IV diagnosis was used. However, we reiterate that separate analyses were performed with 261 case subjects with Asperger's disorder and 971 case subjects with PDD not otherwise specified (PDD-NOS), and similar results were obtained when both parental report and clinical observation were used. As for previous studies that reported DSM-5 criteria to have poor sensitivity, we refer the reader to Swedo and colleagues' commentary (2) for a full discussion on the limitations of those studies. To assess the true sensitivity of the new criteria, field trials are necessary.

A second and important issue raised by Ritvo and Ritvo involves the effect of the new criteria on the utility of previously collected phenotypic and genetic ASD samples. They speculate that the changes in diagnostic criteria will make these samples "incompatible and unusable." The authors assume that some of the existing cases will lose their ASD classification. However, our study results indicate that this is unlikely to be true. The new DSM-5 criteria now explicitly state that individuals with a well-informed clinical diagnosis of any of the previous PDD subtypes, including PDD-NOS and Asperger's disorder, do not have to be rediagnosed but are assumed to fall under the new larger category of ASD. Importantly, the revisions in DSM-5 provide researchers and clinicians an alternative system for coding dimensions both within ASD and from other areas, including intellectual disabilities, language disorders, and other disorders such as attention deficit hyperactivity disorder, through clinical specifiers. This system should result in more accurate and meaningful descriptions of individuals (see Grzadzinski et al. [3]).

In closing, we remind the reader that the upcoming changes to the DSM criteria reflect the growing body of empirical work showing that the existing classification system needs improvement. Comparisons of DSM-IV subtypes do not reveal consistent differences in clinical presentation (4), and longitudinal studies indicate that these categorical distinctions are not predictive of outcome (5). More recently, research has demonstrated that DSM-IV categorical diagnoses are not reliably made across clinical and research sites (6). With our current classification system, what diagnosis you get (e.g., ASD or Asperger's disorder) is more related to where you go for the diagnosis than to the pattern of presenting symptoms. Thus, while we respect the concerns outlined by Ritvo and Ritvo, the evidence indicates that it is neither scientifically nor clinically justifiable to continue using DSM-IV criteria in the face of data indicating its significant limitations in describing individuals with ASD.

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