

# New Dimensions in the Quantitative Classification of Mental Illness

Roman Kotov, PhD; Camilo J. Ruggero, PhD; Robert F. Krueger, PhD; David Watson, PhD; Qilong Yuan, PhD; Mark Zimmerman, MD

**Context:** Patterns of comorbidity among mental disorders are thought to reflect the natural organization of mental illness. Factor analysis can be used to investigate this structure and construct a quantitative classification system. Prior studies identified 3 dimensions of psychopathology: internalizing, externalizing, and thought disorder. However, research has largely relied on common disorders and community samples. Consequently, it is unclear how well the identified organization applies to patients and how other major disorders fit into it.

**Objective:** To analyze comorbidity among a wide range of Axis I disorders and personality disorders (PDs) in the general outpatient population.

**Design:** Clinical cohort study.

**Setting:** A general outpatient practice, the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project.

**Participants:** Outpatients (N=2900) seeking psychiatric treatment.

**Main Outcome Measures:** The Structured Clinical Interview for DSM-IV and the Structured Interview for DSM-IV Personality.

**Results:** We tested several alternative groupings of the 25 target disorders. The DSM-IV organization fit the data poorly. The best-fitting model consisted of 5 factors: internalizing (anxiety and eating disorders, major depressive episode, and cluster C, borderline, and paranoid PDs), externalizing (substance use disorders and antisocial PD), thought disorder (psychosis, mania, and cluster A PDs), somatoform (somatoform disorders), and antagonism (cluster B and paranoid PDs).

**Conclusions:** We confirmed the validity of the 3 previously found spectra in an outpatient population. We also found novel somatoform and antagonism dimensions, which this investigation was able to detect because, to our knowledge, this is the first study to include a variety of somatoform and personality disorders. The findings suggest that many PDs can be placed in Axis I with related clinical disorders. They also suggest that unipolar depression may be better placed with anxiety disorders than with bipolar disorders. The emerging quantitative nosology promises to provide a more useful guide to clinicians and researchers.

*Arch Gen Psychiatry.* 2011;68(10):1003-1011

## Author Affiliations:

Department of Psychiatry, Stony Brook University, Stony Brook, New York (Drs Kotov and Yuan); Department of Psychology, University of North Texas, Denton (Dr Ruggero); Department of Psychology, University of Minnesota, Minneapolis (Dr Krueger); Department of Psychology, University of Notre Dame, Notre Dame, Indiana (Dr Watson); and Department of Psychiatry and Human Behavior, Brown Medical School, Rhode Island Hospital, Providence (Dr Zimmerman).

**C**OMORBIDITY AMONG MENTAL disorders in clinical and community populations is extensively documented.<sup>1-7</sup> It complicates research design and clinical decision making but provides an opportunity to improve psychiatric classification.<sup>6,8,9</sup> Patterns of comorbidity are thought to reflect the underlying structure of psychopathology, and analyses of these patterns may reveal the natural classification of mental illness.<sup>8-11</sup>

This proposal inspired a significant number of studies that seek to construct a new, quantitative nosology with the aid of factor analysis, a procedure designed to elucidate the structure of the data based on relations among variables (eg, comor-

bidity). Indeed, there is a long tradition of factor-analytically derived classification systems, especially in child psychiatry.<sup>12-14</sup> This research consistently identified 2 fundamental dimensions of mental illness: the internalizing and externalizing spectra. Recent factor analyses<sup>11,15,16</sup> of community surveys extended the quantitative approach to adult populations. They focused on 11 common mental disorders and replicated the 2 fundamental dimensions.<sup>6</sup> The internalizing spectrum included depressive and anxiety disorders. The externalizing spectrum was composed of substance use disorders (SUDs), conduct disorder, and adult antisocial behavior. These dimensions have been found in many cultures.<sup>17,18</sup> Some studies<sup>6,11,15</sup> also

identified 2 subgroups within the internalizing spectrum: a distress cluster (consisting of major depressive disorder, dysthymic disorder, generalized anxiety disorder, and posttraumatic stress disorder) and a fear cluster (panic disorder, obsessive-compulsive disorder, and phobic disorders). However, these clusters sometimes are so highly correlated that they do not emerge as separate elements within the internalizing spectrum.<sup>17,18</sup>

This research produced valuable insights into the natural organization of mental illness, but it has been limited in 2 respects. First, most studies of adults have been restricted to community samples. Findings of general population surveys do not necessarily generalize to clinical samples. Indeed, it is unclear how well the identified organization applies to psychiatric patients. Factor-analytic studies have begun examining specific patient populations, namely, self-identified patients, treatment-seeking veterans, and inpatients with psychosis.<sup>11,19,20</sup> The present investigation sought to extend this work by evaluating a general outpatient sample.

Second, the existing literature focused on common diagnoses, namely SUDs, anxiety and depressive disorders, and antisocial personality disorder (PD). It is uncertain whether the previously identified spectra will be confirmed when a broader range of diagnoses is considered and whether additional dimensions are needed to capture less-common disorders. Several investigations have sought to extend the 2-spectrum model. One<sup>17</sup> reported that symptoms of somatization and hypochondriasis belong to the internalizing cluster, although they are less central to it than anxiety and depression. Another study<sup>21</sup> found that eating disorders are part of the internalizing dimension. A third investigation<sup>20</sup> observed that schizophrenia and schizotypal PDs form a distinct thought disorder spectrum. Finally, borderline PD was linked to both internalizing and externalizing dimensions.<sup>22,23</sup> These findings require replication but suggest hypotheses for the present study.

Other factor-analytic investigations have examined comorbidity among PDs. O'Connor<sup>24</sup> cumulated data from 33 studies and found support for 2 structures. The first model consisted of dimensions that can be identified as externalizing (composed of cluster B and paranoid PDs) and internalizing (cluster C, cluster A, and borderline). The second model included the same externalizing factor but split the cluster A PDs—disorders linked to the thought disorder dimension—from the other internalizing conditions. Thus, factor analyses of PDs appear to replicate the spectra found in studies centered on Axis I disorders.

However, only joint analyses of Axis I and Axis II disorders can link the 2 sets of findings. Few such investigations have been undertaken. Beyond antisocial PD, there are some initial data on borderline and schizotypal diagnoses, but virtually nothing is known about placement of other PDs in the overall quantitative classification. The most comprehensive study<sup>25</sup> to date analyzed various Axis I and Axis II symptoms in a British community sample and found 4 broad dimensions: internalizing, externalizing, thought disorder (symptoms of psychosis and cluster A PDs), and pathological introversion (symptoms of avoidant and dependent PDs). It appears

that the first 3 dimensions cut across Axis I and Axis II symptomatology, whereas pathological introversion is specific to the latter axis. It is uncertain, however, whether the same dimensions would be found in analyses of the corresponding disorders.

The aim of the present investigation was to broaden the quantitative nosology by examining a wide range of Axis I and Axis II conditions, many of which have not been considered in this framework. In particular, we sought to integrate personality pathology fully into this system and to explicate the nature of the relations between the axes. Moreover, we planned to evaluate the generalizability of the previously identified spectra to the outpatient population using a large, unselected sample diagnosed with state-of-the-art procedures. We hypothesized that the current *DSM-IV* organization of disorders would fit the data poorly. We further predicted that the internalizing, externalizing, and thought disorder spectra would be confirmed in this sample. We also planned to test whether the same spectra cut across Axis I and Axis II. Finally, we sought to examine the distinction between fear and distress disorders observed within the internalizing cluster in several studies.<sup>6,11,15,16</sup> Given that the present analyses go well beyond previous research, we made modifications to our a priori models when such changes were clearly indicated by the data.

## METHODS

### SAMPLE AND PROCEDURE

Data were obtained from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project, a clinical program created to integrate research assessments into routine care.<sup>26</sup> Participants presenting at a community-based outpatient psychiatric practice underwent a comprehensive diagnostic assessment. The practice predominantly treats individuals with medical insurance (including Medicare) on a fee-for-service basis. The main referral sources are primary care physicians, psychotherapists, and family members or friends. All individuals seeking treatment at this practice were asked to participate in the MIDAS project. Exclusion criteria were age younger than 18 years, inability to understand English, and severe cognitive impairment. Nonparticipants were compared with participants using self-administered symptom inventories, and no significant differences were found, suggesting that this sample is representative of the population served by the clinic with regard to psychopathology.<sup>27,28</sup> The Rhode Island Hospital's institutional review board approved the research protocol, and all participants provided written informed consent.

The sample included the 2900 consecutive patients evaluated in the MIDAS project since it began. Their mean (SD) age was 38.5 (13.0) years; the majority were female and white (**Table 1**). Of these patients, 2151 completed the PD assessment. This component was not introduced until the study was under way and the procedures for incorporating research interviews into clinical practice had been well established. As a result, 749 participants were missing PD data. There were no significant differences between participants with and those without PD assessment on any demographic characteristics or Axis I diagnoses except that the latter were more likely to have a psychotic disorder (12.3% vs 6.7%,  $P < .001$ ) and less likely to have generalized anxiety disorder (18.8% vs 30.6%,  $P < .001$ ). Thus, missing data likely had little systematic effect on the results. We addressed missing

data with the Full Information Maximum Likelihood method,<sup>29</sup> which uses all available information without deleting any records and is recommended for such missing data patterns.

## MEASURES

Lifetime Axis I diagnoses were made using the Structured Clinical Interview for *DSM-IV* (SCID),<sup>30</sup> which was modified to relax certain hierarchical exclusion rules and thus allow some nonhierarchical diagnoses. Lifetime rather than current diagnoses were chosen for consistency with the PD assessment. Axis II conditions were measured with the Structured Interview for *DSM-IV* Personality (SIDP).<sup>31</sup> Each *DSM-IV* PD criterion was rated on a 0 (not present) to 3 (strongly present) scale, with a score of 2 (present) or higher considered positive. The SIDP questions are grouped thematically to reduce halo effects (ie, ratings for a criterion are influenced by how other criteria of that diagnosis are rated).

Both assessments were administered by highly trained interviewers (including C.J.R.) who were monitored throughout the study to minimize rater drift. Interviewers typically were PhD-level psychologists. Every diagnostician underwent intense training lasting 3 to 4 months.<sup>26</sup> The raters were required to demonstrate exact agreement with a senior diagnostician on 5 consecutive evaluations. Ongoing supervision by one of the investigators (M.Z.) included weekly case conferences and review of written reports and item ratings of every case. Fourteen raters performed joint interviews to assess the diagnostic reliability of the SCID (based on 65 participants) and SIDP (based on 47 participants). The SCID reliability estimates ( $\kappa$ ) ranged from 0.64 to 1.00 (median, 0.88). Reliability of any PD on the SIDP was 0.90. Individual disorders were too rare to compute  $\kappa$  coefficients, but intraclass correlation coefficients for criterion counts ranged from 0.82 to 0.97 (median, 0.94).

The SCID covers 7 *DSM-IV* sections: SUDs and mood, psychotic, anxiety, somatoform, adjustment, and eating disorders. In selecting variables for the analyses, we considered both frequency and hierarchical exclusion rules. Disorders with low frequency (defined as <20 cases) were excluded because their associations with other variables cannot be estimated reliably. Diagnoses affected by hierarchical rules could not be analyzed because those rules prohibit certain combinations of diagnoses and therefore would dictate the structure, leading to spurious findings.

Consequently, we examined mood episodes (major depressive and manic) rather than mood disorders, as these diagnoses contain exclusion rules. We used a nonhierarchical generalized anxiety disorder diagnosis. Psychosis—defined as the presence of definite psychotic symptoms, including psychosis during mood episodes—was analyzed as a single category and could not be subdivided because individual psychotic disorders incorporate complex hierarchical rules. For the same reason, we examined a broad eating-disorder group that consisted of anorexia nervosa, bulimia nervosa, and binge eating disorder. In addition, the undifferentiated somatoform disorder group included cases with somatization disorder, which represents an extreme form of this condition. Body dysmorphic disorder was too infrequent to be analyzed. Adjustment disorders were not considered because all involved hierarchical rules that could not be relaxed. Not otherwise specified diagnoses were not counted in any of the categories. Overall, 15 Axis I conditions were selected (Table 1).

The SIDP assesses all 10 PDs, but several diagnoses had low frequency. To ensure comprehensive coverage of personality pathology, we expanded PD categories to include subthreshold cases. Specifically, we required 1 criterion less than *DSM-IV* thresholds and thus were able to analyze all 10 resulting PD

**Table 1. Demographic Characteristics and Diagnoses of the Analysis Sample**

	No. (%)
Sex	
Male	1132 (39.0)
Female	1768 (61.0)
Educational level	
<High school	267 (9.2)
Graduated high school	1813 (62.5)
Graduated college or more	820 (28.3)
Marital status	
Married/cohabitating	1359 (46.9)
Formerly married	631 (21.8)
Never married	910 (31.4)
Race	
White	2538 (87.5)
Black	128 (4.4)
Other	234 (8.1)
Axis I conditions <sup>a</sup>	
Psychosis	236 (8.1)
Manic episode	96 (3.3)
Major depressive episode	2100 (72.4)
Generalized anxiety disorder	799 (27.6)
Posttraumatic stress disorder	610 (21.0)
Panic disorder	721 (24.9)
Social phobia	883 (30.4)
Specific phobia	337 (11.6)
Obsessive-compulsive disorder	258 (8.9)
Eating disorder	224 (7.7)
Undifferentiated somatoform disorder	97 (3.3)
Hypochondriasis	35 (1.2)
Pain disorder	37 (1.3)
Alcohol use disorder	1159 (40.0)
Drug use disorder	735 (25.3)
Axis II traits <sup>a,b</sup>	
Paranoid	154 (7.1)
Schizoid	55 (2.6)
Schizotypal	28 (1.3)
Antisocial	258 (9.6)
Conduct problems	171 (9.5)
Borderline	449 (16.1)
Histrionic	53 (2.5)
Narcissistic	80 (3.7)
Dependent	84 (3.9)
Obsessive-compulsive	343 (15.9)

<sup>a</sup>Diagnoses are not mutually exclusive.

<sup>b</sup>Because of missing data, the prevalence of these conditions was estimated for available cases. Antisocial symptoms are represented with adult antisocial traits and childhood conduct problems variables. Avoidant traits were excluded because of redundancy with social phobia.

traits. Similar to prior studies,<sup>6,20</sup> we treated adult antisocial traits and childhood conduct problems as separate variables instead of combining them into antisocial PD, which allowed us to test rather than assume this link. We also found that avoidant PD was highly overlapping with social phobia (tetrachoric  $r=0.81$ ). This is consistent with reports arguing that avoidant PD is an extreme form of social phobia.<sup>32-34</sup> Given this problematic redundancy, avoidant PD was excluded from the analysis.

All study variables were dichotomous. They were sufficiently common to be analyzed, with frequencies of 28 or more (Table 1).

## DATA ANALYSIS

Bivariate associations among target conditions were computed as tetrachoric correlations, which is the standard ap-

proach for factor-analytic studies of diagnoses and other dichotomous variables. Alternative classifications were compared using confirmatory factor analysis. First, we examined the fit of the 7-factor model, in which disorders were grouped according to the *DSM-IV*. Next, we tested the internalizing-externalizing model. Variables were assigned to factors based on findings of prior investigations. Conditions that had not been studied within this organization (manic episode and psychosis) were allowed to load on both dimensions. We also evaluated the hypothesized internalizing-externalizing thought-disorder model, with the latter dimension defined by psychosis, manic episode, and cluster A PDs.

Next, we examined modifications to these basic models as outlined in the first section of this article. The basic models assumed that the previously identified PD factors<sup>24</sup> map onto the Axis I dimensions.<sup>6,20</sup> To test this assumption, we first split the externalizing spectrum into Axis I and Axis II components and compared fit of the resulting organization with the original model. We then did the same with the internalizing spectrum. We were not able to split the thought disorder cluster because there were too few markers to define its Axis I component. Finally, we examined the structure within the internalizing spectrum by moving fear disorders (panic disorder, social anxiety, specific phobia, and obsessive-compulsive disorder) to a separate fear factor.

The models were analyzed with commercial software (*Mplus* version 5).<sup>35</sup> In comparing these models, we considered 7 fit indices: the  $\chi^2$  goodness-of-fit statistic, the comparative fit index (CFI), the Tucker-Lewis index (TLI), the root-mean-square error of approximation (RMSEA), the Akaike information criterion (AIC), the Bayesian information criterion (BIC), and the sample-size adjusted BIC (ABIC).<sup>36-38</sup> Although there are no strict criteria for evaluating these fit indices, conventional guidelines<sup>38</sup> suggest that TLI and CFI of 0.90 or more indicates adequate fit and 0.95 or more indicates excellent fit; RMSEA of 0.08 or lower indicates adequate fit and 0.06 or lower indicates excellent fit. There are no absolute cutoffs on the AIC, BIC, and ABIC, but these indices can be used to compare models, with lower values representing better fit.<sup>39,40</sup> Conventional guidelines<sup>40</sup> suggest that a difference of less than 6 is small, 6 to 10 is substantial, and more than 10 is very substantial.

## RESULTS

### BIVARIATE ASSOCIATIONS AMONG TARGET CONDITIONS

Tetrachoric correlations (**Table 2**) revealed strong associations among SUDs, antisocial traits, and conduct problems, with correlations ranging from 0.42 to 0.64. This pattern implies the presence of the externalizing spectrum in our data. Other cluster B syndromes and paranoid traits also correlated strongly with antisocial conditions and with each other (range, 0.35-0.62). However, their associations with SUDs were much weaker. Hence, it is unclear whether all these conditions define a single externalizing spectrum or the structure is more complex.

Correlations among mood, anxiety, and somatoform disorders were not as strong, although several were substantial (9 coefficients were  $>0.30$ ). Of note, somatoform conditions correlated appreciably with each other (range, 0.27-0.36), but showed only weak associations with mood and anxiety disorders (all  $r$  values  $\leq 0.20$ ). This pattern may indicate a somatoform cluster that is distinct from the internalizing spectrum. In contrast, de-

pendent and borderline traits had many notable links with mood and anxiety disorders.

Psychosis showed a close connection with schizotypal traits and was substantially associated with other cluster A conditions, which suggests the existence of a coherent thought disorder spectrum. However, the strongest correlate of psychosis was mania. Moreover, the 2 variables correlated more highly with each other than mania did with major depression (0.60 vs 0.30). This pattern indicates that these variables should be placed on the same factor.

### COMPARISON OF BASIC MODELS

First, we examined a 7-factor model based on the *DSM-IV*. The factors were somatoform, anxiety, mood, psychotic, eating, substance use, and personality. The conditions were assigned to factors according to their placement into *DSM-IV* classes. Confirmatory factor analysis indicated that this organization fit the data poorly. The CFI and TLI were not acceptable, and this model was the worst on all fit indices (**Table 3**).

Next, we considered an internalizing-externalizing model, which was specified according to prior research.<sup>6,17,21,24,25</sup> The internalizing spectrum included somatoform and anxiety disorders, major depressive episode, eating disorder, and cluster A and cluster C traits. The externalizing spectrum was composed of SUDs and cluster B traits. Borderline and paranoid traits were allowed to load on both dimensions because they did so in previous studies.<sup>22-24</sup> To our knowledge, manic episode and psychosis have not been investigated within this framework, and we therefore allowed them to cross-load rather than making assumptions about their placement. This model performed better than the *DSM-IV* organization on all fit indices, although the CFI and TLI did not reach the acceptable level. The 2 dimensions correlated only moderately ( $r=0.29$ ). All factor loadings were larger than 0.30, which indicates good placement of variables in the model,<sup>41</sup> with 2 exceptions. First, manic episode and psychosis had very weak loadings on the externalizing factor (0.12 each), in contrast to their appreciable loadings on the internalizing factor (0.39 and 0.34, respectively). Evidently, these conditions can be placed in the internalizing cluster and their externalizing loadings can be constrained to zero. Second, all somatoform disorders had low loadings (range, 0.21-0.29), which indicates that they did not fit clearly in the 2-spectrum model. To capture these conditions, we had to specify an additional somatoform factor.

The resulting 3-factor model was identical to the internalizing-externalizing organization except that somatoform disorders went on the third dimension rather than the internalizing factor. In addition, manic episode and psychosis were allowed to load only on the internalizing dimension. These changes resulted in significantly better fit, as indicated by the AIC, BIC, and ABIC. The CFI and TLI improved but remained just below the threshold for acceptable fit. All somatoform disorders were well captured by the model, with their factor loadings ranging from 0.49 to 0.61. The correlation between the internalizing and somatoform factors was modest ( $r=0.43$ ),

**Table 2. Tetrachoric Correlations Among 15 Axis I Conditions and 10 Axis II Traits<sup>a</sup>**

Conditions	Tetrachoric Correlations																								
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	
<b>Axis I Conditions</b>																									
1. Psychosis																									
2. Manic episode	<b>0.60</b>																								
3. MDE	-0.03	<b>0.30</b>																							
4. GAD	-0.03	0.08	<b>0.34</b>																						
5. PTSD	0.27	0.23	<b>0.40</b>	0.16																					
6. Panic D/O	0.13	0.14	0.25	<b>0.30</b>	<b>0.31</b>																				
7. Social phobia	0.11	0.06	0.28	<b>0.34</b>	0.19	0.21																			
8. Specific phobia	0.13	0.10	0.16	0.23	0.20	0.23	<b>0.30</b>																		
9. OCD	0.20	0.27	0.21	0.13	0.18	0.25	0.25	0.17																	
10. Eating D/O	0.21	0.15	0.22	0.21	0.23	0.17	0.17	0.08	0.26																
11. USD	0.09	-0.09	0.03	0.16	0.18	0.20	0.11	0.12	0.19	-0.02															
12. Hypochondriasis	0.22	-0.13	0.06	0.19	0.09	0.19	0.18	0.05	0.11	0.14	<b>0.36</b>														
13. Pain D/O	0.12	-0.03	0.15	-0.01	0.08	0.09	0.11	0.12	-0.02	0.13	<b>0.35</b>	0.27													
14. Alcohol D/O	0.10	0.15	0.08	0.09	0.18	0.06	0.09	0.01	-0.01	0.07	-0.06	0.06	-0.02												
15. Drug D/O	0.15	0.17	0.11	0.12	0.24	0.09	0.14	0.08	0.08	0.05	-0.07	-0.03	-0.08	<b>0.64</b>											
<b>Axis II Traits</b>																									
16. Paranoid	<b>0.32</b>	0.24	0.27	0.27	0.28	0.21	0.23	<b>0.33</b>	0.28	0.16	0.23	<b>0.35</b>	0.10	0.14	0.26										
17. Schizoid	<b>0.38</b>	-0.09	0.11	0.09	0.04	0.00	<b>0.31</b>	0.13	0.15	0.08	0.01	-0.06	0.07	0.01	-0.05	0.29									
18. Schizotypal	<b>0.52</b>	0.27	0.04	0.02	<b>0.32</b>	0.18	0.17	0.29	0.24	0.14	0.01	0.04	0.06	<b>0.30</b>	0.19	<b>0.54</b>	<b>0.58</b>								
19. Antisocial	0.21	0.18	0.08	0.08	0.20	0.03	0.06	0.08	0.17	0.05	-0.01	-0.09	0.05	<b>0.42</b>	<b>0.53</b>	<b>0.41</b>	0.07	0.27							
20. Conduct problems	0.13	0.03	0.06	0.12	0.26	0.04	0.00	0.11	0.12	0.06	-0.06	0.16	0.01	<b>0.48</b>	<b>0.52</b>	<b>0.36</b>	0.10	0.23	<b>0.60</b>						
21. Borderline	0.29	0.27	<b>0.37</b>	<b>0.33</b>	<b>0.37</b>	0.22	<b>0.33</b>	<b>0.34</b>	0.29	<b>0.36</b>	0.11	0.07	0.20	0.27	0.32	<b>0.62</b>	0.15	<b>0.42</b>	<b>0.57</b>	<b>0.40</b>					
22. Histrionic	0.13	0.26	0.22	0.06	0.00	0.10	-0.12	0.17	0.19	<b>0.32</b>	-0.10	-0.06	0.07	0.29	0.24	<b>0.32</b>	-0.16	<b>0.31</b>	<b>0.50</b>	<b>0.35</b>	<b>0.54</b>				
23. Narcissistic	0.11	0.05	0.06	0.10	0.03	-0.01	-0.01	0.10	0.19	0.18	0.09	-0.12	0.23	0.26	0.24	<b>0.51</b>	0.08	0.24	<b>0.46</b>	<b>0.37</b>	<b>0.44</b>	<b>0.62</b>			
24. Dependent	0.09	-0.04	0.29	<b>0.34</b>	0.21	0.22	<b>0.38</b>	0.14	0.22	0.28	-0.07	0.11	-0.12	0.16	0.07	0.17	0.14	<b>0.36</b>	0.23	0.24	<b>0.48</b>	0.20	0.05		
25. O-C	0.14	0.21	0.18	0.28	0.15	0.08	0.20	0.12	0.29	0.21	0.20	0.16	0.09	0.19	0.20	<b>0.38</b>	0.23	0.20	0.08	0.04	<b>0.30</b>	0.11	<b>0.39</b>	0.12	

Abbreviations: D/O, disorder; GAD, generalized anxiety disorder; MDE, major depressive episode; O-C, obsessive-compulsive traits; OCD, obsessive-compulsive disorder; PTSD, posttraumatic stress disorder; USD, undifferentiated somatoform disorder.  
<sup>a</sup>Bold-faced type indicates *r* values of 0.30 or larger.

**Table 3. Fit Indices for Confirmatory Factor Analyses**

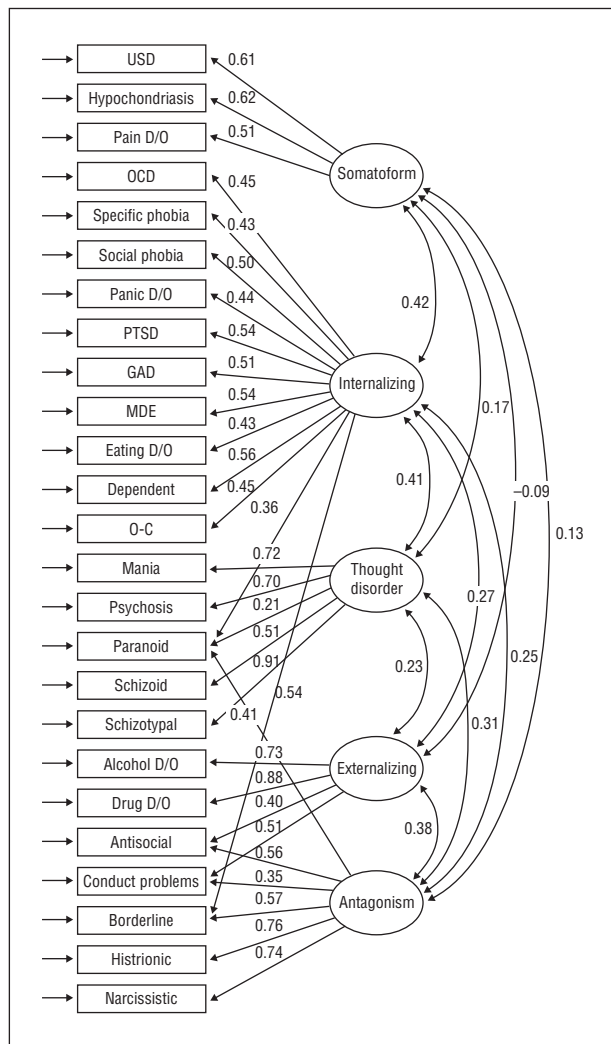
Model <sup>a</sup>	df	$\chi^2$	CFI	TLI	RMSEA	AIC	BIC	ABIC
<b>Basic models</b>								
<i>DSM-IV</i> (7-factor)	142	593.98	0.858	0.859	0.033	727.98	1128.13	915.25
2-Factor	149	516.69	0.885	0.891	0.029	626.69	955.18	780.42
3-Factor	149	502.68	0.889	0.895	0.029	612.68	941.16	766.41
4-Factor	149	417.24	0.916	0.920	0.025	535.24	887.61	700.15
<b>Modifications</b>								
5-Factor	147	313.84	0.948	0.950	0.020	443.84	<b>832.05</b>	<b>625.52</b>
6-Factor A	145	301.67	0.951	0.952	0.019	441.67	859.74	637.33
6-Factor B	144	301.17	0.951	0.952	0.019	<b>441.17</b>	859.24	636.83

Abbreviations: ABIC, sample size—adjusted BIC; AIC, Akaike information criterion; BIC, Bayesian information criterion; CFI, comparative fit index; RMSEA, root-mean-square error of approximation; TLI, Tucker-Lewis index.  
<sup>a</sup>Data shown in bold-faced type indicate best relative fit indices. The *DSM-IV* model assigned conditions to 7 factors according to their placement into *DSM-IV* classes. The 2-factor model assigned somatoform, anxiety, and mood disorders, as well as cluster A and C traits, to the internalizing dimension; substance use disorders and cluster B traits were assigned to the externalizing factor; manic episode, psychosis, paranoid, and borderline traits were allowed to cross-load. The 3-factor model was identical to the 2-factor model except that somatoform disorders loaded on the somatoform rather than the internalizing dimension. The 4-factor model differed from the 3-factor model only in that manic episode, psychosis, and cluster A traits were moved to the thought disorder dimension; paranoid traits were allowed to cross-load on internalizing and externalizing factors. The 5-factor model split externalizing conditions of the 4-factor organization into externalizing and antagonism factors (Figure). The 6-factor A model replicated the last organization but separated Axis I internalizing conditions (major depressive episode, eating disorders, and anxiety disorders) and Axis II internalizing traits (paranoid, borderline, dependent, and obsessive-compulsive) on 2 factors. The 6-factor B model is a modification of the 5-factor organization in which fear disorders (panic disorder, social anxiety, specific phobia, and obsessive-compulsive disorder) formed a separate factor from the internalizing factor.

which is further evidence of a separate somatoform spectrum. Additional refinements were necessary given the marginal fit of this organization.

Next, we specified a 4-factor model by splitting psychosis, manic episode, and cluster A traits from the internalizing group and placing them on the thought disorder dimension, as hypothesized.<sup>20,24,25</sup> Paranoid traits

were allowed to cross-load on internalizing and externalizing factors, as they did in prior research.<sup>24</sup> This model showed much better fit on all indices. The TLI and CFI were now in the adequate range, and the RMSEA was excellent. All variables loaded well. The thought disorder and internalizing factors were related but clearly distinct ( $r=0.43$ ). Overall, there was substantial support for



**Figure.** The best-fitting model. The arrows along the left margin indicate residual variance. D/O indicates disorder; GAD, generalized anxiety disorder; MDE, major depressive episode; O-C, obsessive-compulsive traits; OCD, obsessive-compulsive disorder; PTSD, posttraumatic stress disorder; and USD, undifferentiated somatoform disorder.

the thought disorder spectrum. However, the fit of the model was not uniformly excellent, and it was based on the assumption that the same dimensions cut across Axis I and Axis II.

### MODIFICATIONS TO BASIC MODELS

To test this assumption, we first split externalizing conditions into Axis I externalizing (SUDs) and Axis II externalizing (cluster B and paranoid traits). Antisocial traits and conduct problems were allowed to cross-load between the 2 factors because they are well-established members of both groups. The resulting 5-factor model was by far superior to the other organizations considered and showed excellent or near-excellent fit on all indices. All variables loaded well and all factors were distinct, with intercorrelations ranging from  $-0.09$  to  $0.42$  (Figure). In particular, the association between the 2 externalizing factors was modest ( $r=0.38$ ), which further strengthened the case for differentiating them. It appears that Axis II externalizing actu-

ally is a distinct dimension, which we labeled *antagonism* in accord with terminology proposed for DSM-5.<sup>42</sup>

Next, we modified the resulting organization by splitting the internalizing spectrum into Axis I internalizing (major depressive episode, eating disorder, and anxiety disorders) and Axis II internalizing (paranoid, borderline, dependent, and obsessive-compulsive traits). This 6-factor model (6-factor A in Table 3) fit the data worse than the 5-dimension organization, as indicated by the BIC and ABIC. Thus, the slight improvement in absolute fit (ie, the CFI, TLI, and RMSEA) was not sufficient to justify the model's increased complexity. Moreover, the correlation between Axis I internalizing and Axis II internalizing factors was  $0.96$ , indicating that they are essentially the same dimension. Hence, this model was rejected in favor of the 5 spectra.

We also examined the possibility of separating fear disorders from other internalizing conditions. This 6-factor organization (6-factor B) fit the data similarly to the 6-factor A model. It was slightly better than the 5-factor organization on the AIC, but this difference was very small. In contrast, the BIC and ABIC clearly indicated that the 5-factor model is superior. The fear and internalizing factors correlated  $0.93$ , which suggests that they should be combined. Thus, the 5-spectrum organization was more parsimonious and emerged as the best classification scheme in our analyses.

### COMMENT

This study extended research on the quantitative nosology in several ways. First, it confirmed the internalizing, externalizing, and thought disorder spectra in a clinical population. These clusters have been observed in community and inpatient samples, and we now have replicated them in outpatients. Second, we examined Axis I and Axis II disorders jointly and found that, although most personality pathology fits into the 3 spectra discussed herein, some conditions (cluster B and paranoid PD) reflect a distinct antagonism dimension. Third, our analyses included several Axis I conditions that were not studied previously in the quantitative framework, namely, mania and somatoform disorders. The former was linked to the thought disorder spectrum, whereas the latter formed a separate cluster. Overall, this investigation represents a significant advance in classification research; it is the most comprehensive study to date and was performed in a large, carefully diagnosed outpatient sample.

Our hypotheses were generally supported. As predicted, we found that the DSM-IV organization fits the data poorly. It had the worst fit of the models considered, despite being the most elaborate. The internalizing, externalizing, and thought disorder spectra emerged as hypothesized. We also observed 2 additional dimensions: antagonism and somatoform. These spectra are defined by high negative affect (internalizing), extreme trait disinhibition (externalizing), odd/eccentric cognition and behavior (thought disorder), callous antipathy (antagonism), and maladaptive responses to somatic symptoms (somatoform).<sup>42,43</sup> We replicated the 3 personality pathology dimensions reported by O'Connor.<sup>24</sup> His model

did not include somatoform and externalizing spectra, which are defined primarily by Axis I conditions and could not have been identified in analyses restricted to PDs. O'Connor's dimensions mapped onto the internalizing and thought disorder spectra as expected, whereas the antagonism dimension was unique to Axis II.

The present investigation builds on Markon's<sup>25</sup> analysis of Axis I and Axis II symptoms. In addition to the internalizing, externalizing, and thought disorder spectra observed by Markon, we found somatoform and antagonism dimensions. We were able to detect these additional spectra because we had better coverage of somatoform and cluster B conditions. We did not observe Markon's pathological introversion factor, likely because he evaluated several relevant symptoms, whereas we analyzed diagnoses, which provided few clear markers of that dimension.

Overall, our syndrome-based analysis confirmed the major symptom dimensions. The 2 approaches are complementary. Syndrome-based analyses directly inform a diagnostic system but are tied to diagnoses specified within it. A symptom-based approach is not bound by a particular system and can address heterogeneity within disorders. Convergence between these approaches provides important evidence of the spectra's fidelity.

A distinct fear cluster within the internalizing spectrum is well documented, although not all studies find it.<sup>17,18,25</sup> Our results were somewhat equivocal in that splitting off the fear factor improved model fit slightly on some fit indices, but other indices indicated that this improvement did not justify the model's increased complexity. Fear and distress disorders are closely related, and the distinction between them may be useful in some—but not all—contexts.

We also found that some disorders need to be assigned to multiple spectra. Specifically, antisocial, conduct, borderline, and paranoid traits all split between multiple clusters. Each of these splits has been reported<sup>24</sup> and likely reflect the heterogeneity of the corresponding diagnoses. For example, borderline PD is defined both by emotional and interpersonal instability,<sup>44</sup> which are relevant to the internalizing and antagonism clusters, respectively.

Mania had only a moderate association with major depression. Although lifetime depression was prevalent in patients with lifetime mania (90.6%), depressive episodes were similarly common in several internalizing disorders (eg, posttraumatic stress disorder, dependent traits). In addition, the prevalence of mania was not elevated in patients with lifetime depression (4.1%) but was high in the schizotypal (10.7%) and psychosis (19.1%) groups. These findings are consistent with proposals to dissolve the mood disorders class and research suggesting that bipolar disorder differs from unipolar depression on many validators.<sup>45,46</sup> Mania may fit better on the thought disorder spectrum. Indeed, mania shares features with these conditions, including frank psychosis (observed in 47% of our patients with bipolar I disorder), disorganized thought, tangential speech, and bizarre behavior. However, mania does not show the negative symptoms common in schizoid PD and some forms of schizophrenia. Hence, relations within the spectrum are complex and require further study. We could not investigate them here because we lacked data on spe-

cific psychotic syndromes due to hierarchical rules of the *DSM-IV*. Different assessment strategies can overcome this limitation.<sup>20</sup>

The emerging quantitative classification ultimately may provide a more useful guide to the field than the *DSM-IV*. Indeed, factor-analytically derived spectra appear to reflect core genetic vulnerabilities. Twin studies<sup>47-53</sup> have reported that shared genetic factors underlie each of the 5 dimensions observed in the present investigation. Thus, an explicit focus on these spectra can aid research on genetic etiologies. In fact, molecular genetic studies are beginning to identify specific genes contributing to the 3 established spectra.<sup>54-56</sup> We hope that our findings will stimulate parallel work on the somatoform and antagonism dimensions. Research on other diagnostic validators, such as neurobiological underpinnings and treatment response, produced preliminary support for the usefulness of internalizing, externalizing, and thought disorder clusters.<sup>57-59</sup> More such research is needed on all 5 spectra.

Strengths of the study include the large sample size and diagnostic ascertainment by clinicians who used state-of-the-art semistructured interviews. Nevertheless, these findings need to be considered against the limitations. Although our approach was firmly grounded in prior studies, we examined many disorders not considered previously, and our analyses were, in part, exploratory. Indeed, 2 of the identified dimensions are novel and require replication. However, the current investigation was limited to 25 conditions even though it was much broader than prior studies. Future research needs to examine many more disorders to explicate a comprehensive quantitative classification system. In addition, we had to exclude avoidant PD for analytic reasons, but given its high overlap with social phobia, avoidant PD clearly belongs on the internalizing spectrum. Factor-analytic studies, including ours, analyze nonhierarchical syndromes. Nosologists will need to refine identified organizations and add hierarchical rules whenever a syndrome may be secondary to other conditions. Finally, the present study was conducted in a single clinical practice in which patients were predominantly white and female and had health insurance. This may have affected the results, and the study should be replicated in clinical samples with different demographic characteristics and presenting concerns.

In conclusion, this study is the most comprehensive investigation of the quantitative nosology to date, and thus it was able to identify novel somatoform and antagonism spectra. We also confirmed the internalizing, externalizing, and thought disorder spectra in an outpatient population, providing crucial evidence of their validity in clinical settings. These 3 dimensions are gaining recognition and have been included in a proposed meta-structure for *DSM-5*.<sup>43</sup> Current findings underscore the need to reorganize the diagnostic system, especially since the *DSM* model fit the data so poorly. Our results are consistent with proposals to relocate PDs to Axis I in *DSM-5*,<sup>3,33</sup> because we observed close links between PDs and clinical disorders: cluster A with psychotic disorders, cluster C and borderline with depressive and anxiety disorders, and antisocial disorder with SUDs. However, we found that cluster B PDs define a distinct group. An antagonism class may need to be added

to Axis I or an antagonism trait domain included on Axis II. Our findings also indicate that unipolar depression clusters with anxiety disorders rather than with bipolar disorders, which reinforces the calls to dissolve the mood disorders class.<sup>43,45</sup> Some of the present findings require replication, and other disorders need to be incorporated into this system. Ultimately, these advances are expected to enhance the validity and practical usefulness of psychiatric diagnosis.

**Submitted for Publication:** February 7, 2011; final revision received April 21, 2011; accepted May 1, 2011.

**Correspondence:** Roman Kotov, PhD, Department of Psychiatry, Putnam Hall–South Campus, Stony Brook University, Stony Brook, NY 11794 (roman.kotov@stonybrook.edu).

**Author Contributions:** Dr Kotov had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Financial Disclosure:** None reported.

**Funding/Support:** Feldstein Medical Foundation (Dr Kotov).

**Role of the Sponsor:** The funder had no role in the design and conduct of the study; in the collection, management, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

## REFERENCES

- Andrews G, Slade T, Issakidis C. Deconstructing current comorbidity: data from the Australian National Survey of Mental Health and Well-Being. *Br J Psychiatry*. 2002;181:306-314.
- Bijl RV, Ravelli A, van Zessen G. Prevalence of psychiatric disorder in the general population: results of the Netherlands Mental Health Survey and Incidence Study (NEMESIS). *Soc Psychiatry Psychiatr Epidemiol*. 1998;33(12):587-595.
- Clark LA. Assessment and diagnosis of personality disorder: perennial issues and an emerging reconceptualization. *Annu Rev Psychol*. 2007;58:227-257.
- Grant BF, Stinson FS, Dawson DA, Chou SP, Dufour MC, Compton W, Pickering RP, Kaplan K. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry*. 2004;61(8):807-816.
- Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62(6):617-627.
- Krueger RF, Markon KE. Reinterpreting comorbidity: a model-based approach to understanding and classifying psychopathology. *Annu Rev Clin Psychol*. 2006;2:111-133.
- Mineka S, Watson D, Clark LA. Comorbidity of anxiety and unipolar mood disorders. *Annu Rev Psychol*. 1998;49:377-412.
- Watson D. Rethinking the mood and anxiety disorders: a quantitative hierarchical model for DSM-V. *J Abnorm Psychol*. 2005;114(4):522-536.
- Markon KE, Krueger RF. Categorical and continuous models of liability to externalizing disorders: a direct comparison in NESARC. *Arch Gen Psychiatry*. 2005;62(12):1352-1359.
- Brown TA, Barlow DH. Comorbidity among anxiety disorders: implications for treatment and DSM-IV. *J Consult Clin Psychol*. 1992;60(6):835-844.
- Krueger RF. The structure of common mental disorders. *Arch Gen Psychiatry*. 1999;56(10):921-926.
- Achenbach TM, Rescorla LA. *Manual for the ASEBA School-Age Forms & Profiles*. Burlington: University of Vermont, Research Center for Children, Youth and Families; 2001.
- Lahey BB, Applegate B, Waldman ID, Loft JD, Hankin BL, Rick J. The structure of child and adolescent psychopathology: generating new hypotheses. *J Abnorm Psychol*. 2004;113(3):358-385.
- Lahey BB, Rathouz PJ, Van Hulle C, Urbano RC, Krueger RF, Applegate B, Gariock HA, Chapman DA, Waldman ID. Testing structural models of DSM-IV symptoms of common forms of child and adolescent psychopathology. *J Abnorm Child Psychol*. 2008;36(2):187-206.
- Slade T, Watson D. The structure of common DSM-IV and ICD-10 mental disorders in the Australian general population. *Psychol Med*. 2006;36(11):1593-1600.
- Vollebergh WAM, Iedema J, Bijl RV, de Graaf R, Smit F, Ormel J. The structure and stability of common mental disorders: the NEMESIS study. *Arch Gen Psychiatry*. 2001;58(6):597-603.
- Krueger RF, Chentsova-Dutton YE, Markon KE, Goldberg D, Ormel J. A cross-cultural study of the structure of common psychopathological syndromes in the general health care setting. *J Abnorm Psychol*. 2003;112(3):437-447.
- Kessler RC, Ormel J, Petukhova M, McLaughlin KA, Green JG, Russo LJ, Stein DJ, Zaslavsky AM, Aguilar-Gaxiola S, Alonso J, Andrade L, Benjet C, de Girolamo G, de Graaf R, Demyttenaere K, Fayyad J, Haro JM, Hu C, Karam A, Lee S, Lepine J-P, Matchsinger H, Mihaescu-Pintia C, Posada-Villa J, Sagar R, Ustun TB. Development of lifetime comorbidity in the World Health Organization world mental health surveys. *Arch Gen Psychiatry*. 2011;68(1):90-100.
- Miller MW, Fogler JM, Wolf EJ, Kaloupek DG, Keane TM. The internalizing and externalizing structure of psychiatric comorbidity in combat veterans. *J Trauma Stress*. 2008;21(1):58-65.
- Kotov R, Chang SW, Fochtmann LJ, Mojtabai R, Carlson GA, Sedler MJ, Bromet EJ. Schizophrenia in the internalizing-externalizing framework: a third dimension [published online March 31, 2010]? *Schizophr Bull*. doi:10.1093/schbul/sbq024.
- Forbush KT, South SC, Krueger RF, Iacono WG, Clark LA, Keel PK, Legrand LN, Watson D. Locating eating pathology within an empirical diagnostic taxonomy: evidence from a community-based sample. *J Abnorm Psychol*. 2010;119(2):282-292.
- Eaton NR, Krueger RF, Keyes KM, Skodol AE, Markon KE, Grant BF, Hasin DS. Borderline personality disorder comorbidity: relationship to the internalizing-externalizing structure of common mental disorders [published online September 14, 2010]. *Psychol Med*. doi:10.1017/S0033291710001662.
- James LM, Taylor J. Revisiting the structure of mental disorders: borderline personality disorder and the internalizing/externalizing spectra. *Br J Clin Psychol*. November 2008;47(pt 4):361-380.
- O'Connor BP. A search for consensus on the dimensional structure of personality disorders. *J Clin Psychol*. 2005;61(3):323-345.
- Markon KE. Modeling psychopathology structure: a symptom-level analysis of Axis I and II disorders. *Psychol Med*. 2010;40(2):273-288.
- Zimmerman M. Integrating the assessment methods of researchers in routine clinical practice: the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project. In: First MB, ed. *Standardized Evaluation in Clinical Practice*. Arlington, VA: American Psychiatric Publishing; 2003:29-74.
- Zimmerman M, Mattia JI. Psychiatric diagnosis in clinical practice: is comorbidity being missed? *Compr Psychiatry*. 1999;40(3):182-191.
- Zimmerman M, Mattia JI. A self-report scale to help make psychiatric diagnoses: the Psychiatric Diagnostic Screening Questionnaire. *Arch Gen Psychiatry*. 2001;58(8):787-794.
- Schafer JL, Graham JW. Missing data: our view of the state of the art. *Psychol Methods*. 2002;7(2):147-177.
- First MB, Spitzer RL, Gibbon M, Williams JBW. *Structured Clinical Interview for DSM-IV Axis I Disorders—Patient Edition (SCID-IP, Version 2.0)*. New York: Biometrics Research Department, New York State Psychiatric Institute; 1995.
- Pfohl B, Blum N, Zimmerman M. *Structured Interview for DSM-IV Personality*. Washington, DC: American Psychiatric Press; 1997.
- Chambless DL, Fydrich T, Rodebaugh TL. Generalized social phobia and avoidant personality disorder: meaningful distinction or useless duplication? *Depress Anxiety*. 2008;25(1):8-19.
- Tyrer P, Gunderson JG, Lyons M, Tohen M. Extent of comorbidity between mental state and personality disorders. *J Pers Disord*. 1997;11(3):242-259.
- Widiger TA. Generalized social phobia versus avoidant personality disorder: a commentary on three studies. *J Abnorm Psychol*. 1992;101(2):340-343.
- Muthén LK, Muthén BO. *Mplus: Statistical Analyses With Latent Variables: User's Guide*. 5th ed. Los Angeles, CA: Muthén & Muthén; 2007.
- Hu L, Bentler PM. Fit indices in covariance structure modeling: sensitivity to underparameterized model misspecification. *Psychol Methods*. 1998;3:424-453. doi:10.1037/1082-989X.3.4.424.
- Hu L, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. *Struct Equ Modeling*. 1999;6(1):1-55.
- Marsh HW, Hau KT, Wen Z. In search of golden rules: comment on hypothesis-testing approaches to setting cutoff values for fit indexes and dangers in overgeneralizing Hu and Bentler's (1999) findings. *Struct Equ Modeling*. 2004;11(3):320-341.



39. Akaike H. A new look at the statistical model identification. *IEEE Trans Automat Contr*. 1974;19(6):716-723.
40. Burnham KP, Anderson DR. *Model Selection and Multimodel Inference: A Practical Information-Theoretic Approach*. 2nd ed. New York, NY: Springer-Verlag; 2002.
41. Fabrigar LR, Wegener DT, MacCallum RC, Strahan EJ. Evaluating the use of exploratory factor analysis in psychological research. *Psychol Methods*. 1999; 4:272-299. doi:10.1037/1082-989X.4.3.272.
42. Krueger RF, Eaton NR, Clark LA, Watson D, Markon KE, Derringer J, Skodol A, Livesley WJ. Deriving an empirical structure of personality pathology for *DSM-5*. *J Pers Disord*. 2011;25(2):170-191.
43. Andrews G, Goldberg DP, Krueger RF, Carpenter WT Jr, Hyman SE, Sachdev P, Pine DS. Exploring the feasibility of a meta-structure for *DSM-V* and *ICD-11*: could it improve utility and validity? *Psychol Med*. 2009;39(12):1993-2000.
44. Livesley J. Toward a genetically-informed model of borderline personality disorder. *J Pers Disord*. 2008;22(1):42-71.
45. Clark LA, Watson D. Distress and fear disorders: an alternative empirically based taxonomy of the "mood" and "anxiety" disorders. *Br J Psychiatry*. 2006;189: 481-483.
46. Goldberg DP, Andrews G, Hobbs MJ. Where should bipolar disorder appear in the meta-structure? *Psychol Med*. 2009;39(12):2071-2081.
47. Hicks BM, Krueger RF, Iacono WG, McGue M, Patrick CJ. Family transmission and heritability of externalizing disorders: a twin-family study. *Arch Gen Psychiatry*. 2004;61(9):922-928.
48. Kato K, Sullivan PF, Evengård B, Pedersen NL. A population-based twin study of functional somatic syndromes. *Psychol Med*. 2009;39(3):497-505.
49. Kendler KS, Aggen SH, Knudsen GP, Røysamb E, Neale MC, Reichborn-Kjennerud T. The structure of genetic and environmental risk factors for syndromal and sub-syndromal common *DSM-IV* Axis I and all Axis II disorders. *Am J Psychiatry*. 2011; 168(1):29-39.
50. Kendler KS, Prescott CA, Myers J, Neale MC. The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. *Arch Gen Psychiatry*. 2003;60(9):929-937.
51. Lichtenstein P, Yip BH, Björk C, Pawitan Y, Cannon TD, Sullivan PF, Hultman CM. Common genetic determinants of schizophrenia and bipolar disorder in Swedish families: a population-based study. *Lancet*. 2009;373(9659):234-239.
52. Torgersen S, Czajkowski N, Jacobson K, Reichborn-Kjennerud T, Røysamb E, Neale MC, Kendler KS. Dimensional representations of *DSM-IV* cluster B personality disorders in a population-based sample of Norwegian twins: a multi-variate study. *Psychol Med*. 2008;38(11):1617-1625.
53. Livesley WJ, Jang KL. The behavioral genetics of personality disorder. *Annu Rev Clin Psychol*. 2008;4:247-274.
54. Dick DM, Aliev F, Wang JC, Grucza RA, Schuckit M, Kuperman S, Kramer J, Hinrichs A, Bertelsen S, Budde JP, Hesselbrock V, Porjesz B, Edenberg HJ, Bierut LJ, Goate A. Using dimensional models of externalizing psychopathology to aid in gene identification. *Arch Gen Psychiatry*. 2008;65(3):310-318.
55. Hetttema JM, An SS, Bukszar J, van den Oord EJ, Neale MC, Kendler KS, Chen X. Catechol-*O*-methyltransferase contributes to genetic susceptibility shared among anxiety spectrum phenotypes. *Biol Psychiatry*. 2008;64(4):302-310.
56. Owen MJ, Craddock N, Jablensky A. The genetic deconstruction of psychosis. *Schizophr Bull*. 2007;33(4):905-911.
57. Goldberg DP, Krueger RF, Andrews G, Hobbs MJ. Emotional disorders: cluster 4 of the proposed meta-structure for *DSM-V* and *ICD-11*. *Psychol Med*. 2009; 39(12):2043-2059.
58. Krueger RF, South SC. Externalizing disorders: cluster 5 of the proposed meta-structure for *DSM-V* and *ICD-11*. *Psychol Med*. 2009;39(12):2061-2070.
59. Carpenter WT Jr, Bustillo JR, Thaker GK, van Os J, Krueger RF, Green MJ. The psychoses: cluster 3 of the proposed meta-structure for *DSM-V* and *ICD-11*. *Psychol Med*. 2009;39(12):2025-2042.