Reinterpreting Comorbidity Among Common Mental Disorders Using Latent Class Analysis

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DEDICATION

I would like to dedicate this dissertation to my family. I am not sure mere words can capture all that I want to say. So, I'll keep it simple - thank you for everything. It was definitely my luckiest day when I was born into our family.

ABSTRACT

Comorbidity among mental disorders has long been a conundrum to researchers. While factor analytic models that divide psychopathology into internalizing and externalizing syndromes have helped to clarify the picture somewhat, much remains to be done. For example, evidence from factor analytic, behavior-genetic, and longitudinal modeling studies all suggest significant overlap between internalizing and externalizing disorders. Likewise, research also indicates that though structural models treat psychopathological syndromes as monothetic entities, far more heterogeneity exists among subjects with disorders such as depression, post-traumatic stress disorder, social phobia, and psychosis. These lines of work point to the need for alternative, complementary ways of examining psychopathology. In service of this, the current study examined psychopathology from a person-oriented approach. It utilized latent class analysis to characterize patterns of comorbidity among subjects from two different epidemiological samples – the National Comorbidity Survey (N=5877) and the National Comorbidity Survey-Replication (N=3197) – into groups (or classes) based on diagnoses of common mental disorders. Results from both samples indicated that subjects could be divided into 5 distinct latent classes, the profiles of which were almost identical across samples. Validation data including demographics, and medication and treatment-related variables also revealed distinct patterns of homogeneity and heterogeneity across latent classes. Results from this study provide a basis for understanding psychopathology from a novel perspective and have potential for a range of applications including understanding the genetics of psychopathological syndromes and even treatment research.

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Introduction

Structural models of psychiatric diagnostic data have revealed two distinct (albeit correlated) higher-order factors—internalizing and externalizing—accounting for the extensive comorbidity among common mental disorders occurring in individuals in the community (Krueger, 1999). Internalizing disorders encompass anxiety and mood syndromes, whereas externalizing disorders encompass child and adult components of antisocial personality along with alcohol and drug problems. Structurally, internalizing disorders can be further organized around two highly correlated, but distinct subfactors: one reflecting close associations among fear-related disorders (the phobias and panic disorder) and the other reflecting close relations among distress-related disorders (major depression, generalized anxiety disorder, and dysthymia).

This basic model has been shown to replicate across varying samples (Krueger, 1999; Slade & Watson, 2006; Vollebergh et al., 2001). Further, behavior genetic studies focusing on this structural model have demonstrated high heritability for the broad internalizing and externalizing factors, and also for the fear and distress subfactors of internalizing (Kendler, Prescott, Myers, & Neale, 2003). In addition, though further research along these lines is needed to support firm conclusions, some recent work has pointed to distinctive neurobiological correlates of these differing thematic clusters of disorders – for example, differing patterns of electroencephalographic (EEG) lateralization and differing parameters of startle reflex reactivity in relation to fear versus distress variants of internalizing (Heller & Nitschke, 1998; Vaidyanathan, Patrick, & Cuthbert, 2009), and reduced P300 brain potential response in relation to varying types of externalizing disorders (Iacono, Carlson, Malone, & McGue, 2002; Patrick et al., 2006).

In addition, there is evidence that certain classes of medications are effective with varying disorders within one or the other domains (e.g., selective serotonin reuptake inhibitors or SSRIs with varying internalizing disorders, particularly those of the distress type; see Hellerstein, Kocsis, Chapman, Stewart, & Harrison, 2000; naltrexone with varying forms of externalizing, in particular, those involving addictive tendencies; see Crabtree, 1984; J. E. Grant & Kim, 2002; Swift, 1995). Thus, research to date indicates that broad latent factors account for the systematic overlap (covariance) among differing subgroups of disorders within the DSM, with affiliated evidence pointing to distinctive genetic and neurobiological substrates for these broad factors.

Based on such work, it has been proposed that the upcoming editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) and the International Classification of Diseases (ICD-11) should group psychopathological syndromes into distinct clusters of disorders (Andrews, Goldberg et al., 2009). A recent attempt to do this by established investigators in the diagnostic comorbidity area arrived at a "metastructure" of 5 clusters (see special issue of *Psychological Medicine*, December 2009; Andrews, Goldberg et al., 2009; Andrews, Pine, Hobbs, Anderson, & Sunderland, 2009; Carpenter et al., 2009; Goldberg, Krueger, Andrews, & Hobbs, 2009; Krueger & South, 2009; Sachdev, Andrews, Hobbs, Sunderland, & Anderson, 2009). Under this system, most internalizing disorders are classified into a large "emotional cluster" (Goldberg et al., 2009), while externalizing disorders are demarcated in a separate "externalizing cluster" (Krueger & South, 2009). However, a point acknowledged by contributing authors (Andrews, Goldberg et al., 2009) and highlighted in accompanying

commentaries (First, 2009; Jablensky, 2009; Wittchen, Beesdo, & Gloster, 2009) was that further empirical evidence is required to support a move in this direction:

> This exercise is limited in the following ways. It is not based on systematic reviews; to perform such a review for each disorder would have been a Herculean task even if the appropriate data (disorder versus controls versus all other disorders within cluster versus all disorders in other clusters) were available for all disorders. They are not. It did not rely on statistical procedures to identify broad disorder groupings although the latent structures in the emotional and externalizing clusters did go some way along this path. (p. 1997)

In addition to the lack of an adequate empirical foundation for such a move at this time, there are other reasons to proceed cautiously. For one thing, though such a structure may seem superficially appealing due to its simplicity, considerable evidence from structural, behavior genetic, and longitudinal studies indicates that there is systematic overlap between disorders in the internalizing and externalizing domains (Fu et al., 2002; Kim-Cohen et al., 2003; Koenen et al., 2005; Krueger, 1999; Slade & Watson, 2006; Subbarao et al., 2008; Vollebergh et al., 2001; Watson, 2005). Further research is needed to clarify the nature and bases of this overlap. In addition, whereas research in this area has tended to treat specific disorders as loading on only one latent factor or subfactor (e.g., phobias on the fear subfactor, depression on the distress subfactor, etc.), a substantial body of literature demonstrates that distinct subgroups of individuals exist even within apparently monothetic diagnoses such as PTSD (Breslau, Reboussin, Anthony, & Storr, 2005), eating disorders (Keel et al., 2004), major depression (Sullivan,

Kessler, & Kendler, 1998), and psychosis (Kendler, Karkowski, & Walsh, 1998), and social phobia (Kessler, Stein, & Berglund, 1998). The implication is that there is more heterogeneity within these disorders than previously thought. Similarly, others have noted that the latent factors underlying various mental disorders as depicted in structural models may not necessarily reflect a common etiology (Wittchen, Hofler, & Merikangas, 1999). Yet another point emphasized by key researchers in the field, is that interrelations among common mental disorders may in actuality be more complex than the simple additive associations assumed by factor analytic models (Kessler, Chiu, Demler, & Walters, 2005). Thus, though the various dimensions underlying psychopathology provide a useful starting point, it is unclear how these manifest at an individual level.

These varying issues point to the need for an alternative approach to understanding mental disorder comorbidity that complements the factor-analytic/structural-modeling approach—one that focuses on *subgroups of individuals* exhibiting distinctive patterns of disorder co-occurrence. The current study was undertaken as a step in this direction. Specifically, the current study sought to characterize patterns of comorbidity among mental disorders within the domains of internalizing and externalizing using latent class analysis (LCA), a statistical method that groups individuals into discrete classes on the basis of specified characteristics (in this case, presence versus absence of varying disorders). Compared with other agglomerative techniques such as cluster analysis and factor analysis, LCA is a non-parametric statistical approach that requires few assumptions about variables used in the analyses such as normality, linearity, or type of variable (e.g., continuous, categorical, etc.). It does, however, require conditional independence – i.e., variables in any particular class

should not be related due to any other reason apart from the underlying latent class, such as complete criterion overlap or nesting of diagnoses within one another (e.g., conduct disorder nested within antisocial personality disorder; alcohol abuse nested within dependence); violation of this assumption may lead to spurious classes.

Three previous studies that applied LCA to lifetime and 12-month diagnoses of DSM disorders reported optimal solutions ranging from 6 – 8 latent classes (Kessler, 1997; Kessler, Chiu et al., 2005; Sullivan & Kendler, 1998). While some similarities do exist across results from these investigations, direct comparisons are not entirely possible due to the use of different sets of disorders (e.g., variable inclusion of disorders such as bipolar disorder, eating disorders, and intermittent explosive disorder; use of lifetime diagnoses versus 12-month diagnoses) and different samples in the various studies. As it not entirely clear where disorders such as bipolar disorder or anorexia fit into existing structural models of disorders, it is difficult to draw any firm conclusions based on these analyses. Furthermore, some studies omitted use of more rigorous goodness-of-fit indices such as the Bayesian Information Criterion (BIC) when evaluating the fit of alternative models (Kessler, 1997; Sullivan & Kendler, 1998) or failed to control for issues such as local dependence among disorders (e.g., entering alcohol abuse and dependence as separate variables within the same model (Kessler, 1997).

Thus, while there is some evidence for the existence of distinct subgroups of individuals that are prone to particular types of disorder, there is no clear consensus as to what these subgroups are. The current study attempted to address this and other crucial questions noted above by (a) testing for the presence of latent classes of individuals exhibiting distinct patterns of comorbidity among variants of mental disorder most

commonly included in structural modeling studies (i.e., major depression, generalized anxiety disorder, dysthymia, post-traumatic stress disorder, panic disorder, social phobia, specific phobia, agoraphobia, drug dependence, alcohol dependence, and conduct disorder/antisocial personality disorder), and (b) using statistically rigorous techniques to determine optimal model fit. To examine the replicability of the solution obtained, the same models were fit and compared across two different epidemiological samples – the National Comorbidity Survey (NCS), and the National Comorbidity Survey – Replication sample.

The major question addressed by the current study was whether patterns of comorbidity evident among subgroups of individuals identified by LCA would mirror patterns of comorbidity emerging from dimensional-structural analyses of varying disorders. If the structure of internalizing and externalizing symptoms is assumed to be similar across all subjects, LCA results should indicate the same profile of disorders in all clusters, but with increasing levels of severity (i.e., mild, moderate, severe, etc.). Alternatively, if factor analytic models adequately capture relations between disorders in the internalizing and externalizing disorders, then one or more internalizing domains, one or more externalizing classes, and one or more comorbid internalizing-externalizing classes would be expected. Any deviations from this pattern would suggest that interactions or associations exist between internalizing and externalizing disorders that are not being captured adequately by factor analytic models.

Method

Participants

The National Comorbidity Survey (NCS) and the National Comorbidity Survey Replication (NCS-R) are two separate nationally representative surveys (Ns= 8098 and 9282, respectively) of mental health diagnoses conducted in the United States between 1990-1992 and 2001-2003, respectively, with response rates of 82.6% and 70.9%. Further details regarding the recruitment, consent, sampling strategy, have been covered extensively in other publications (Kessler et al., 2004; Kessler, Berglund et al., 2005; Kessler et al., 1994; Kessler & Merikangas, 2004; Wittchen, 1994). A summary of the sampling strategy utilized in both studies is described in Appendix A.

Assessment of Mental Disorders

Lifetime diagnoses were utilized for all analyses from both the NCS and NCS-R datasets. Lifetime diagnoses, rather than past year or 30-day diagnoses were utilized for two reasons. First, one of the goals of this project was to compare results directly with those obtained by Krueger (1999), which primarily used lifetime diagnoses. Second, research has yet to demonstrate any conclusive evidence regarding the sequential progress of different types of psychopathology in relation to each other. Thus, using past year diagnoses or 30-day diagnoses which only capture a limited time period in an individual's life might not be that informative. Both NCS and NCS-R diagnoses are based on the World Mental Health Survey Initiative Version of the World Health Organization Composite International Diagnostic Interview (WMH-CIDI; World Health Organization, 1992), a structured diagnostic interview. This interview yielded *DSM-IIIR* (American Psychiatric Association, 1987) diagnoses for NCS data and *DSM-IV* (American Psychiatric Association, 1994) diagnoses for NCS-R data. Disorders utilized

in the current analyses include those that are most frequently diagnosed in the general population: specific phobia, social phobia, agoraphobia, panic disorder, post-traumatic stress disorder (PTSD), major depressive disorder, generalized anxiety disorder (GAD), dysthymia, alcohol dependence, drug dependence, and conduct disorder/antisocial personality disorder. As diagnoses of panic disorder and agoraphobia sometimes overlapped in both samples (e.g., agoraphobia with or without panic disorder, panic disorder with or without agoraphobia), to avoid double-entry of subjects, subjects in both samples were reclassified into those diagnosed with panic disorder only, agoraphobia only, and those with panic disorder and agoraphobia. Details regarding assessment procedures for all disorders are covered elsewhere (Kessler, Berglund et al., 2005; Kessler et al., 1994). As understanding comorbidity among different disorders was one of the key aims of this study, non-hierarchical diagnoses were utilized for all analysis.

Statistical Analyses

LCA was carried out using the Latent Gold 4.5 software package (Vermunt & Magidson, 2007; see Appendix B for a brief overview of LCA). Classes ranging from 1 to 10 were compared. Model fit was assessed using the Bayesian Information Criterion (BIC; Schwarz, 1978), the Akaike Information Criterion (AIC; Akaike, 1974), and the "consistent" Akaike Information Criterion (CAIC; Bozdogan, 1987). All three are model selection indices that balance model fit and parsimony, but penalize model complexity to different degrees. Their formulae are as follows:

BIC = -2 log likelihood of current model + k ln(N)

AIC = -2 log likelihood of current model + 2 k

CAIC = -2 log likelihood of current model + k ln(N +1)

where k is the number of parameters in the model and N is the sample size.

When comparing models, generally, lower values of all three models are preferred (Raftery, 1995). Difference in χ^2 values were not used for comparison purposes, as generally χ^2 values tend to be smaller for more complex models. It must be noted here however, that model fit indices do not always unanimously agree on a "best-fitting" model. In such cases, other heuristics such as size of latent classes and a scree-plot like test of model fit indices (i.e., where values begin to level off) may be utilized to determine optimal model fit (Bradshaw, Buckley, & Ialongo, 2008; Sclove, 1987; Uebersax, 2000a). Additionally, it must be noted that there are some studies suggesting that the BIC outperforms the AIC with regard to latent class models (Nylund, Asparouhov, & Muthen, 2007). However, the optimal fit index for arbitrating among competing models remains a much debated area. Thus, a combination of all the above-mentioned factors were taken into account when deciding on the optimal model for sample. Each model was run with 50 different starting values to avoid problems with local maxima.

To address the issue of local dependence, a number of steps were taken. First, though a previous study elected to collapse dysthymia and depression into one variable to control for possible local dependence (Kessler, Chiu et al., 2005), we chose not to do so based on previous research that shows that despite their co-occurrence, these disorders

differ appreciably in chronicity and patterns of comorbidity with other disorders (Klein et al., 1995; Klein, Schwartz, Rose, & Leader, 2000; Klein, Shankman, & Rose, 2006; Klein, Taylor, Harding, & Dickstein, 1988; Pepper et al., 1995). A second issue was the division of subjects into agoraphobia only, panic disorder only, and panic disorder with agoraphobia categories. This also led to a form of local dependence – i.e., subjects with any one of these disorders could not be diagnosed with either of the other two. To deal with this, we examined the relationship between the residuals of pairs of variables once their association due to a common latent class was accounted for; the Latent Gold software refers to these as bivariate residuals. Bivariate residuals with a value greater than 3.84 (i.e., $p < .05$ for a χ^2 with df = 1) suggest that the association between the residuals of two observed variables is statistically significant. Latent Gold also allows the user to specify direct effects (Hagenaars, 1988) between these two variables in such cases, and rerun the model. For the purposes of the current study, both the relative magnitude and presence of such variables across the various datasets we utilized were taken into account before adding direct effects terms and re-evaluating the model. For all samples, models both with and without direct effects terms were compared to assess the effects of such terms (i.e., were there any extra latent classes in the absence of direct effects?).

With regard to the datasets and diagnoses that were available for analyses, in the NCS sample, information regarding antisocial personality disorder (including child and adult criteria) was available for the entire sample; however, PTSD was assessed only in a subsample of subjects (N=5877). Conversely, in the NCS-R, PTSD diagnoses were available for the full sample, but full diagnoses of antisocial personality disorder were not

a part of the publicly available dataset; however, lifetime diagnoses of conduct disorder were available for a subset of the NCS-R (N=3197), ranging in age from 18-44 years. To permit direct comparison of findings across the two samples, conduct disorder was used in place of antisocial personality disorder for the subset of subjects from each sample (Ns = 5877 and 3197, respectively) for whom data on this diagnosis was available along with data for the diagnosis of PTSD. In addition, to allow comparisons to be made with previous structural modeling studies that utilized data for the full (N = 8098) NCS sample (Krueger, 1999), we also evaluated LCA models in this full participant sample. Thus, we undertook LCA in three different sets of subjects:

1.) Subset of NCS for whom PTSD and conduct disorder were assessed (N=5877)
2.) Subset of NCS-R for whom PTSD and conduct disorder were assessed (N=3197)
3.) Full NCS sample for whom antisocial personality disorder, but not PTSD, were assessed (N=8098)

Following determination of the best-fitting LCA model, validation analyses were undertaken to examine the characteristics of the differing latent classes using additional data from the NCS and NCS-R datasets. The Latent Gold software allows for the classification of subjects into different classes based on modal probability. Following classification in this manner, the following criterion variables were compared across the various classes for each sample:

1) prevalence of the DSM disorders utilized in the LCA;

2) prevalence of additional DSM disorders not utilized in the LCA (bipolar I disorder, bipolar II disorder, manic and hypomanic episodes, attention-deficit disorder, oppositional defiant disorder, intermittent-explosive disorder, and nicotine dependence);
3) demographic variables (age, sex, marital status, income); and
4) treatment and medication-related variables

For each of the above-noted criterion variables, multinomial logistic regression was used to predict class membership based on that variable. For categorical predictor variables assessing endorsement of a symptom or disorder, variables were interpreted in the direction of endorsement relative to non-endorsement; for variables with multiple categories (e.g., marital status, education), one of the categories was picked as a referent; continuous predictor variables were z-scored before being utilized in analyses to account for skew. Odds ratios and standard errors are reported for all logistic regression analyses. Means and standard deviations are also reported for continuous variables that were z-scored for analyses. Statistical significance was evaluated at $p < .01$.

Results

Latent Class Analysis

A 5-class model was found to be the best-fitting solution for all three samples. While BIC and CAIC values for all three samples were the lowest for the 5-class model, the AIC stopped decreasing in magnitude sharply, and appeared to trail off after 5-

classes. Thus, based on the criteria outlined earlier, the 5-class model emerged as the optimal model across samples.

An examination of bivariate residuals in all three samples revealed significant associations between pairwise combinations of agoraphobia without panic disorder, panic disorder without agoraphobia, and panic disorder with agoraphobia. As these three associations were the greatest in magnitude and the most consistent across all three samples, direct effect paths for all three were specified and LCA models ranging from 1-10 classes were re-evaluated in all samples. Results once again indicated that the 5-class solution was the optimal one in all three samples. While parameter estimates changed slightly after including direct effects in all samples, the five latent classes were virtually identical to those without direct effects. For the sake of greater accuracy, all results from this point onward are based on the models with direct effects. Model fit indices for models with direct effects are presented in both tabular and graphical forms in Table 1 and Figures 1, 2, and 3.

Profiles of the parameter estimates for the optimal 5-class model that emerged for both the NCS and NCS-R samples are presented in Figures 4, 5, and 6. As can be seen, there are striking similarities between the profiles of the various latent classes across the samples, despite the fact that the NCS and NCS-R were collected a decade apart and used slightly different diagnostic criteria (DSM IIIR and DSM IV, respectively). As the primary purpose of using LCA in the full NCS sample was to ensure that we obtained the same solution regardless of whether we used conduct disorder or antisocial personality disorder in our analyses, for the sake of brevity, results from the full NCS sample are not discussed in detail for the remainder of the analyses. Instead, we focus on the NCS and

NCS-R subsamples for the remainder of the analyses presented, because the use of identical sets of disorders in these two latent class models allowed for direct comparisons of findings across these two samples.

Using modal classification, results indicated that latent class 1, the largest of the five classes, consisted of subjects who showed evidence of few disorders. The median number of disorders in the NCS in this latent class was zero, while in the NCS-R sample the median number was one (see Tables 2 and 3; note that 49.1 % of subjects in the NCS-R sample in this class had no disorder). In both samples, most subjects were diagnosed with a maximum of two or fewer disorders; however a smaller percentage of subjects in the NCS-R sample (.4%) were diagnosed with three disorders. Out of those diagnosed with some form of psychopathology, the most prevalent disorders were major depression, followed by social phobia, and then by specific phobia. Other disorders were present at low rates as well.

Latent class 2 was comprised of subjects with modal diagnoses of phobias and depression; interestingly, the prevalence of other distress disorders such as GAD and dysthymia was quite low in this class, implying the presence of fear disorders without accompanying distress disorders aside from depression. For the NCS and NCS-R samples, the median number of disorders for subjects in this class was two and three, respectively. Latent class 3 consisted predominantly of subjects diagnosed with depression along with GAD and dysthymia. In contrast with latent class 2, the prevalence of phobias in this class was lower, suggesting the presence of predominant distress without high levels of accompanying cue-specific fear. The median number of disorders in this class was two in the NCS sample and three in the NCS-R sample.

Latent class 4 comprised subjects who demonstrated high levels of both internalizing and externalizing forms of psychopathology with high overall rates of diagnoses (median number of disorders: NCS = 5; NCS-R = 6). Subjects in this class had a minimum of at least 3-4 disorders. Lastly, latent class 5 was characterized by a high prevalence of externalizing disorders along with some comorbid distress disorders (PTSD, GAD, major depression), with three being the median number of diagnoses in both samples. All subjects in this last class had at least one externalizing disorder diagnosis, suggesting this was the only class (apart from latent class 1) in both samples that was closest to resembling pure externalizing. However, most of these subjects had at least one other internalizing disorder diagnosis (in the NCS-R, 81.7% of subjects had at least one internalizing disorder, while in the NCS, 58.7% had at least one internalizing disorder). Conversely, in both samples, latent classes 5 and 1 were the only classes in which subjects with no internalizing disorder diagnoses were present.

Prevalence of Disorders in Each Class

Tables 2 and 3 detail the odds of belonging to each class relative to the referent class based on the diagnosis of a particular disorder. The referent class in most cases was the large disorder-free class; however, when certain variables (e.g., dysthymia) were not present in this class at all, then the fear class was used as the referent class. In such cases, to facilitate comparisons between the NCS and NCS-R datasets, the fear class was used as the referent class in both datasets, even if the other dataset had data for all classes. Because the large sample sizes of the current study ensured significance of even modest effects, odds ratios greater than 5 and less than .5 are bolded in Table 2 and 3 to highlight

effects of larger magnitude that are consistent across samples. Results presented in these tables mirror the profiles of the various disorders presented in Figures 5 and 6, with phobias and panic disorder being characteristic of the fear class; PTSD, GAD, dysthymia and major depressive episode of the depressed class; multimorbidity for all disorders as a key feature of the comorbid internalizing-externalizing class; and conduct disorder, alcohol and drug dependence, along with some distress disorders (PTSD, GAD, major depression) comprising the externalizing-distress class. In both samples, these groups will be referred to as the normal, fear, depressed, multimorbid, and externalizing-distress classes respectively, throughout the remainder of this manuscript.

Additional noteworthy results were that dysthymia was completely absent in the normal class in both samples (see Tables 3 and 4), implying its presence suggests greater prevalence or proneness to other forms of psychopathology. Interestingly, dysthymia combined with major depression was prevalent only in the depressed and multimorbid classes, whereas depression without dysthymia was manifested by individuals in the fear and externalizing-distress classes. Similarly, drug and alcohol dependence were associated primarily with the more severe multimorbid and externalizing-distress classes. Likewise, being diagnosed with panic disorder with agoraphobia greatly increased the odds of belonging to the multimorbid class in both samples. Agoraphobia alone without panic disorder was more indicative of the fear and multimorbid classes, while the evidence for panic disorder was more mixed. Lastly, in both samples, while having PTSD increases the odds of belonging to the multimorbid class, it predicted memberships for *all* 4 psychopathology-prone classes, suggesting that PTSD was not restricted to the distress-

syndromes (i.e., major depression, dysthymia, and GAD) alone. A similar pattern was seen for depression, which was also present in all classes.

Validation Analyses

Validation data for all classes for the entire sample are presented in Tables 5 - 11. Being diagnosed with a manic episode or with bipolar I disorder increased the odds of being classified in the multimorbid class (see Table 5). In the NCS-R dataset, which assessed for both bipolar I and bipolar II disorders, bipolar II disorder increased the odds of belonging to the depressed as well as the multimorbid class, while bipolar I disorder was more selective to the multimorbid class. Intriguingly, nonaffective psychoses were also most prevalent in the multimorbid class within the NCS dataset. Psychosis was not assessed directly in the NCS-R, and therefore we used a proxy for psychosis here, consisting of prescribed use of antipsychotic medication in the previous 12 months; this indication of the presence of psychosis again greatly increased the odds of belonging to the multimorbid class. These results suggest that psychosis and bipolar I disorder tend to co-occur with one another and with other internalizing and externalizing disorders, rather than forming their own separate classes, though future analyses including these in LCA models will need to confirm this. Another noteworthy result was that attention-deficit disorder was most indicative of the multimorbid class, whereas nicotine dependence and oppositional defiant disorder were indicative of the multimorbid and externalizing-distress classes. Hypomanic episodes and intermittent explosive disorder were less specific to any one single class.

Demographic data for both NCS and NCS-R subsamples (see Table 6) indicated that subjects in the depressed and multimorbid classes tended to be older than the normal class. Females were more likely to be in the fear, depressed, and multimorbid classes, while males were more likely to be in the externalizing-distress class. Being separated/widowed/divorced was generally predictive of individuals in all four psychopathology-prone classes. A household income of < $20,000 was particularly predictive of being in the multimorbid class in both datasets.

As shown in the Tables 7 and 8, surprisingly, comparison of age of onset of disorders across groups revealed few consistent results across both samples. The only disorder that differentiated subjects in the various classes was major depression, which tended to onset earlier in the multimorbid and externalizing-distress classes. Somewhat intriguingly, among those with panic disorder and agoraphobia, the mean age of onset of agoraphobia in *both* samples was earlier than the mean age of onset of panic disorder, suggesting an opposite pattern than would be expected based on DSM diagnostic criteria. Along similar lines, as depicted in Tables 9 and 10, comparison of treatment-related variables suggested few significant differences between groups, though there appeared to be a general trend among those in the externalizing-distress classes in both samples to utilize mental-health related services earlier than the other classes. This may partly be due to the criteria or outcome of disorders in that class such as conduct disorder (which requires a diagnosis before 15) or drug dependence (which may cause more functional impairment than a disorder such as specific phobia).

Table 11 shows that being prescribed most types of medication in the year prior to the survey (sleeping pills, antidepressants, tranquilizers, anti-psychotics, etc.) tended to

increase the odds of belonging to the multimorbid classes, suggesting that subjects in these classes are utilizing a variety of medications. Interestingly, using prescription medication generally did not increase the odds of belonging to the externalizing-distress class in the NCS subsample, but did so in the NCS-R sample, suggesting perhaps an increased tendency in recent years to prescribe medication for most mental health disorders.

Discussion

This article examined the typology of individuals with various common mental health disorders in two large-scale epidemiological samples. Results revealed that across both samples, subjects could be divided into 5 distinct groups that were almost identical across both samples. While sample size and replication across two different datasets collected a decade apart from each other are significant strengths of the current study, some notable weaknesses include the fact that diagnoses were determined by interviews administered by lay-persons, retrospective recall of information was utilized in the case of disorders such as conduct disorder, and the fact that only noninstitutionalized subjects were part of both samples.

Nevertheless, despite these limitations, the results from this study are in concordance with previous research that has attempted to examine comorbidity using factor analysis or behavior genetics (Kendler et al., 2003; Krueger, 1999; Slade & Watson, 2006; Vollebergh et al., 2001). Similar to the models specified in these studies, distinct classes of subjects with just phobias, or with more pervasive distress, emerged from the analyses. However, in contrast with previous research, no group with just

externalizing disorders was apparent in this sample. In fact, externalizing appeared to co-occur with internalizing in two separate groups – one with high levels of all internalizing disorders and one with just moderately elevated levels of distress disorders including depression, PTSD, dysthymia and GAD. There was little comorbidity with externalizing disorders in just the fear or depressed classes. Thus, our results suggest that the overlap between internalizing and externalizing appears to be restricted to specific subgroups of subjects. Noteworthy is the fact that the 5 latent classes tended to have very specific correlates in terms of demographics and odds ratios of other DSM disorders. This pattern of results suggests that these latent classes do not appear to be simply profiles of subjects progressing in severity of disorders, but rather indicate distinct types of subjects who are prone to differing types of disorders. However, as our analyses were conducted with lifetime diagnoses, and as we did not have longitudinal data on our subjects, this possibility cannot be ruled out completely.

Links to Neurobiology

Findings from the current study are congruent with evidence from the neurobiological literature indicating distinct patterns of neurobiological activity and subsystems related to fear disorders, depressive syndromes, mixed anxiety-depressive syndromes, and externalizing disorders (Heller & Nitschke, 1998; Iacono et al., 2002; Olvet & Hajcak, 2008; Patrick et al., 2006; Vaidyanathan et al., 2009). Thus, there appear to be distinct subsystems in the brain that contribute differentially to internalizing and externalizing disorders. As discussed in the next section, the findings of the current study provide insight into the basis of the association between internalizing and externalizing

and may be of value for understanding relations of these forms of psychopathology with varying neurobiological indicators, and their amenability to differing pharmacologic interventions.

Overlap between Internalizing and Externalizing

An intriguing feature of our results was that no distinct pure externalizing class emerged from our analyses, though there were subjects in the normal and externalizing-distress classes who were diagnosed who had diagnoses of externalizing disorders alone. A number of reasons can be posited for this. Perhaps, the disorders we used in the current study were not pure indicators of externalizing – i.e., if we had included disorders such as attention deficit hyperactivity disorder, intermittent explosive disorder, etc., as part of the LCA, they might have led to a separate externalizing group. On the other hand, this could be a function of the nature of the samples used in the study, which were both epidemiological and utilized non-institutionalized participants. It is possible that externalizing disorders that do not co-occur with internalizing disorders may be more common within particular clinical samples such as incarcerated offenders, where the prevalence of criminal psychopathy is high. Alternatively, as other studies have shown an association between conduct disorder and major depression (Subbarao et al., 2008), or between substance use and anxiety disorders (B. F. Grant et al., 2004; Merikangas et al., 1998), the current results may be more than just a function of the disorders included in the model or the subjects – i.e., externalizing and internalizing may be linked in some fundamental manner. Interestingly, the basis of overlap between internalizing and externalizing disorders appears to distress disorders rather than the fear disorders. This is

in accordance with structural models (Krueger, 1999), that reflect stronger associations between these two factors. Additional evidence for this is also provided by psychophysiological studies that indicate that *both* depression and externalizing tendencies appear to be related to reduced visual P300 (Houston, Bauer, & Hesselbrock, 2003; Patrick et al., 2006). Similarly, though evidence is mixed, pharmacological research suggests that SSRIs can be used to treat depression as well as substance dependence problems (Cornelius, Salloum, Ehler, Jarrett, & al, 1997; Naranjo & Knoke, 2001; Nunes et al., 1998; Schmitz et al., 2001).

Homogeneity and Heterogeneity of Disorders

A notable feature in our analyses is that most disorders were present in at least two or more of the classes suggesting marked heterogeneity in the etiology of several syndromes, even if they appear to be subsumed under one diagnosis. This was particularly the case for major depression, PTSD, and to some extent, social phobia – all three of which were present in all classes in both samples. Such findings are not unique to this study. For example, research has shown that the presentation of major depressive episodes in isolation varies from that associated with comorbid internalizing or externalizing syndromes (Small et al., 2008). Similarly, other studies have noted that major depression and conduct disorder appear to be correlated at the genetic level (Subbarao et al., 2008). Our results provide additional support to such studies by showing different profiles of disorders associated with depression in each class. PTSD is another disorder that has likewise evinced correlations with both internalizing and externalizing disorders (Cox, Clara, & Enns, 2002; Watson, 2005, 2009), leading to difficulty in its

classification. Based on the results from the current study, this seems to be due to the fact that PTSD exhibits different patterns of comorbidity in the different classes that were examined in the current study.

The implication of these findings may be that amongst the various DSM disorders, major depression, social phobia, and PTSD, may be normative. That is to say, it may not be that unusual for an individual to experience symptoms of social fear, or symptoms of PTSD after traumatic events, or depression as an outcome after some form of life stress, and that these may be common psychopathological processes or states. In the case of individuals who are a part of the latent classes with high levels of psychopathology, they may be more prone to such states given that they already appear to be experiencing much distress. Thus, these disorders appear somewhat nonspecific. What would distinguish between the latent classes that individuals that experience these disorders belong to would be the accompanying comorbid psychopathology and not these disorders in and of themselves.

While such heterogeneity may seem somewhat surprising initially, a further examination of the results reveals deeper ties to the extant literature. For example, there has long been much debate about how to categorize different subtypes of depression and a number of schemes have been proposed including endogenous vs. reactive, psychotic vs. neurotic, unipolar vs. bipolar, and dysthymia vs. major depression, etc.. To some extent, all these classifications are supported by the current data. With regard to the endogenous vs. reactive distinction, the depressed class and the multimorbid class seem to manifest more of the endogenous type of depression in that they also show comorbid dysthymia and generalized anxiety disorder. Subjects in these classes appear to have

some sort of underlying tendency to experience more severe or prolonged forms of depression as compared to those in the fear and the externalizing-distress classes. On the other hand, it could be hypothesized that subjects in these latter two classes are demonstrating more of the reactive type of depression, as the incidence of dysthymia and GAD are far lower in these classes. This implies that if and when depression occurs in these classes, it tends to manifest as discrete episodes rather than over more prolonged periods. Likewise, while the need for dysthymia as a diagnosis distinct from depression has been debated (Akiskal, 1994; Waintraub & Guelfi, 1998a, 1998b), findings from the current study indicate that it is an alternative indicator of the endogenous vs. reactive distinction. Similarly, the distinction between unipolar and bipolar depression seems to be relatively straightforward as well in that individuals in the multimorbid class appear to be most prone to bipolar I disorder, while unipolar depression is present in all the other classes. Thus, the heterogeneity of depression in our results is not without precedent.

A similar argument can be made with regard to PTSD, where previous researchers have suggested that there appear to be both internalizing and externalizing forms of PTSD (Miller, Greif, & Smith, 2003; Miller, Kaloupek, Dillon, & Keane, 2004). Along similar lines, an in-depth examination of the criteria for PTSD reveals some interesting patterns that relate to the classes obtained in the current analysis. The criteria for PTSD are divided into three sets – the re-experiencing of trauma and reactivity upon exposure to trauma, avoidance and numbing reactions, and symptoms of increased arousal including irritability, anger, exaggerated startle, etc. While no single criterion is a pure indicator of any of the classes obtained in this study, the avoidance and physiological and psychological distress upon exposure to trauma seem to correspond more to the fear

class; the re-experiencing of trauma, and the emotional numbing reactions correspond more to the depressed class, while reactions such as irritability, anger, difficulty concentrating may index symptoms of those in the externalizing-distress class. Studies of dimensional models of psychopathology support a similar interpretation in that they show that PTSD loads on all three fear, distress, and externalizing factors (Cox et al., 2002; Watson, 2005). Thus, the reason for such heterogeneity in the criteria for PTSD makes sense if PTSD is viewed as a disorder that attempts to capture abnormalities in emotional reactivity across different types of individuals after they are exposed to some traumatic event.

Lastly, with regard to the heterogeneity of social phobia in both samples in the current study, it is not immediately apparent what this may reflect. One hypothesis is that since it is normative to experience some level of social fear, psychopathology-prone individuals may just have greater levels of it, given that they already have high levels of negative affect. Alternatively, their psychopathology could act in a reciprocal manner with their social phobia in that such individuals may feel self-conscious and alienated from others due to their psychopathology. On the other hand, different variants of social phobia might be associated with the different latent classes. Some preliminary evidence is provided for this hypothesis by a study that undertook a latent class analysis of subjects with social phobia (Kessler et al., 1998) and yielded two different groups – one that endorsed primarily speaking fears, while the other showed more generalized social fears, in addition to speaking fears. Their results indicated that in general the presence of multiple social fears increased the odds of being diagnosed with any other anxiety or mood disorder, or antisocial personality disorder. Additionally, when the authors divided

those with speaking fears into a group with public speaking fears alone and those with other speaking fears such as “talking to people when you might have nothing to say or might sound foolish” or “talking in front of a small group of people”, the former group was less likely to have any comorbid mood disorder or antisocial personality disorder. Extending these results to the current study, it is possible that perhaps those in the normal and fear classes might have more restricted public speaking fears, while those in the other classes might demonstrate other forms of social fears.

In contrast to the ubiquity of PTSD, depression, and social phobia as discussed above, an examination of our results from the opposite viewpoint also reveals interesting patterns of homogeneity among particular disorders. Specific phobia and agoraphobia without panic disorder, appear to be primarily prevalent in either the fear class or the multimorbid class. Panic disorder without agoraphobia appears more nonspecific and is prevalent to some extent in all classes; however, panic disorder with agoraphobia is found mostly in the multimorbid classes in both the NCS and NCS-R samples. Similarly, alcohol dependence and drug dependence are found at elevated levels only in 2 out of 5 classes in both datasets. These results are in line with both structural modeling research (e.g., Krueger, 1999) and genetic research (Kendler et al., 2003), which show the presence of distinct “fear factor” and externalizing factors that are heritable.

The multimorbid class obtained in this study appeared to have high rates of all the disorders utilized in the LCA models, as well as disorders such as bipolar I disorder, and schizophrenia-spectrum disorders. These results are not entirely surprising as several studies have shown that both these disorders are highly comorbid with other internalizing and externalizing disorders (Buckley, Miller, Lehrer, & Castle, 2009; Krishnan, 2005;

McMillan, Enns, Cox, & Sareen, 2009; Simon et al., 2004). In fact, the DSM attempts to circumvent this issue by specifying complex hierarchical and exclusionary criteria – e.g., a diagnosis of bipolar disorder supercedes major depression; dysthymia and depression cannot be assigned as a diagnosis of they occur only during schizophrenia, or if they are not accounted for schizoaffective disorder, etc. Thus, the results we found are not an entirely unusual phenomenon. However, the obvious question that comes to mind in relation to this particular class is what it represents, since it appears almost nonspecific to any disorder. No easy answers are available at this point. To some extent, the patterns of deficits seen in disorders such as schizophrenia and bipolar mirror this class where anomalies in these disorders are observed in multiple domains including emotional, cognitive, and neurobiological (Berns & Nemeroff, 2003; Blumberg et al., 2003; Heinrichs, 2005; Lieberman, 1999; Mandal, Pandey, & Prasad, 1998; Ng, Lau, Graham, & Sim, 2009). This seems to suggest some sort of greater, wider, systemic problem rather than those observed in phobias alone or depression alone.

Another possibility is that this multimorbid class indexes some sort of tendency to experience severe levels of distress, where individuals in one of the other classes who have experienced multiple adverse life circumstances might possibly develop all disorders, akin to the concept of multiple organ system failure in medical disorders. There is some tentative evidence for this in that subjects in this class in both the NCS and NCS-R appear to be earning less money and are more likely to be divorced (see Table 6) – i.e., suggesting that they may be experiencing more life stress; however, somewhat paradoxically, they do not appear to seek out mental health services significantly earlier

than subjects in the other classes (see Tables 9 and 10). Thus, this line of reasoning is speculative at best.

Lastly, it is worth noting that both the NCS and NCS-R samples are comprised of noninstitutionalized subjects. Because of this, subjects who are likely experiencing the most severe forms of psychopathology (e.g., inpatient populations, prisoners, homeless individuals, etc.) were not a part of these analyses. Thus, there may not have been enough variation among subjects in this multimorbid class to present a clearer picture of the patterns of psychopathology they may be experiencing. In fact, studies that have focused on subjects with schizophrenia-spectrum disorders as opposed to more broader epidemiological samples (Boks, Leask, Vermunt, & Kahn, 2007; Kendler et al., 1998) have yielded latent classes of subjects characterized by psychotic symptoms occurring both with and without mood disorders. Thus, including more of such subjects in future epidemiological samples may provide additional insight into the nature of the multimorbid classes obtained in the current study.

Categories, Dimensions, or Prototypes?

An important question that arises out of our findings is whether they support dimensional or categorical models of psychopathology. Though our results suggest that latent classes appear to exist among subjects with psychopathology, they do not necessarily provide conclusive evidence that current models of psychopathology should be redefined in terms of classes. Additionally and relatedly, while LCA does enable division of subjects into various groups, it does not capture variation within those groups either. These caveats must be borne in mind when interpreting the results presented in

this paper. However, despite these shortcomings, what is noteworthy here is that the pattern of psychopathology that is being demonstrated in the current study is not identical to the internalizing-externalizing hierarchical scheme portrayed by factor-analytic models, suggesting that these latter models may not be capturing all interrelationships among mental disorders. Future research will need to confirm this by performing more direct comparisons between dimensional and categorical models of psychopathology. Recent advances in the statistical modeling world have also given way to another type of model – mixtures of factor analyzers – which allow for both categorical and continuous latent variables in the same structural model. These will provide an additional intriguing comparison to both dimensional and categorical models.

Secondly, to some extent, latent class models and latent trait models may not even necessarily have to be pitted against each other. If one wishes to construe the results presented here as simply the inversion or "flip" of the internalizing-externalizing structural model (Krueger, 1999), and the classes presented here as representing subjects who are on the extremes of the dimensions of that model, the current results still provide a valuable addition to prior research. The dimensional model of internalizing-externalizing disorders, while useful, does not provide information on how the various latent factors (fear, anxious-misery, externalizing) manifest at an individual level. It is unclear at what point psychopathology begins and how to characterize those individuals at the extremes of those dimensions. The results from this study could help bridge that gap by suggesting *prototypes* for such subjects.

Lastly, another interpretation could be that results from this study and from the internalizing-externalizing model represent the same data at different levels. For example,

if one were to take symptoms such as fever and headaches, which are common to disorders as different as influenza and meningitis, and apply a structural model, results would yield correlated “fever” and “headache” factors. This does not mean that influenza and meningitis are the same; however, neither does it mean that the fever and headache symptoms are unimportant. While it is valuable to know what the syndrome or disorder is present so that the appropriate overall treatment can be applied (e.g., antibiotics, antivirals, or other medication), it may also be necessary to treat the individual symptoms (e.g., fever) in each case as well. Thus, information from both levels (i.e., cause and manifestation) is important to understand and treat the disorder. A similar case can be made for psychopathological syndromes as well.

Possible Clues to Psychiatric Genetics

Though highly speculative and based on very preliminary results, some of our findings could lead to clues to elucidating candidate genes for psychiatric genetics, a field where results have been notoriously difficult to replicate. For example, there has been recent controversy regarding the association between the serotonin transporter gene and major depression (Caspi et al., 2003; Risch et al., 2009). While it is not entirely clear why some studies show a relationship between the two, while others fail to, one possible reason might be the heterogeneity of depression among the various classes seen in the current sample. Similarly, studies have also shown that subjects with comorbid alcohol and drug dependence show specific associations with candidate genes, whereas those with alcohol dependence alone do not (Dick et al., 2007). Likewise, bipolar disorder with comorbid panic disorder appears to have different genetic correlates as opposed to bipolar

disorder diagnosed alone (Rotondo et al., 2002). In our analyses, the odds ratios for both these disorders were greatest in the multimorbid class, as compared to the other classes. Similarly, recent studies have also shown that bipolar disorder and schizophrenia appear to have common genetic bases – the two disorders that were again most prevalent in the multimorbid class (International Schizophrenia Consortium, 2009). These findings appear to suggest that different patterns of comorbidity between the various DSM disorders are associated with different genes. Results from the current study provide additional targets for such research by showing distinct patterns of comorbidity within different individuals (i.e., the latent classes we obtained). Such individuals could provide useful data for genetic research regardless of whether the latent classes we obtained are truly categorical, dimensional, or prototypical in nature.

Implications for DSM-V and ICD-11

The analyses presented in this article suggest that the scheme proposed for DSM-V and ICD-11 (see Psychological Medicine, December 2009 issue; Andrews, Goldberg et al., 2009) will likely need to be modified. First, since major depression is present in almost every class, including the externalizing-distress class, classifying it as purely an emotional disorder is not supported by the data presented here. Second, though we did not include them as part of the variables used for identifying latent classes, rates of disorders such as bipolar disorder and psychotic disorders demonstrate very specific relationships to some of the classes we obtained. They tended to co-occur with several internalizing and externalizing disorders, and not in isolation. Though this is not conclusive proof that these disorders do belong to these specific classes, since their

association with specific classes is far greater than chance and is not equal across all classes (as would be expected, if they were unrelated to the disorders we used in this sample), suggesting separate clusters for these classes does not appear to be supported by the current analyses. Rather, what is required here is to elucidate the associations between common neurobiological factors and processes between psychopathological syndromes such as bipolar disorders, schizophrenia, and the "emotional" disorders and "externalizing" disorders, before classifying them in their own separate clusters. Lastly, based on our results, what truly distinguished subjects in the various classes we obtained in our analyses were their *patterns of comorbidity.* This suggests that if there is a compelling need to reorganize the DSM and ICD in the immediate future, perhaps the simpler and more cautious way to go without attempting to reorganize entire diagnostic schemes, or introduce dimensional criteria, might be to classify patterns of comorbidity among individuals presenting for mental health problems. For example, one approach might be to refer to these patterns as syndromes – i.e., classify individuals with multiple phobias and depression as having a "fear" syndrome, those with depression, dysthymia, and GAD alone, as a "depressed" syndrome, and so on. In other words, rather than considering each disorder as a separate disease state in and unto itself, it could be treated as a sign or symptom of an underlying disease state. Conceptualizing disorders in this manner might prove useful in elucidating common genetic and neurobiological bases for all DSM disorders, while still retaining much of the original structure of the DSM-IV TR.

In conclusion, our analyses extend previous work significantly by showing that there exist different groups of individuals that are prone to different types of internalizing

and externalizing forms of psychopathology. Future research will need to focus on the developmental and genetic correlates of these various subgroups of subjects, as well as further investigate typologies associated with relatively rare syndromes such as bipolar disorder, eating disorders, personality disorders, etc.. Ultimately, research that integrates both the structural and typological associations between various disorders is likely to shed the most light on mental disorders.

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Table 1.Model fit indices for latent class analysis (LCA) models in the full National Comorbidity Survey (NCS) sample, National Comorbidity Survey (NCS) subsample, and National Comorbidity Survey – Replication (NCS-R) subsample.

Model Fit Indices	BIC	AIC	CAIC	BIC	AIC	CAIC	BIC	AIC	CAIC
Sample	**NCS Full Sample (N=8098)**			**NCS Subsample (N=5877)**			**NCS-R Subsample (N=3197)**		
# of classes									
1	46383.38	46285.39	46397.38	47733.32	47633.14	47748.32	25334.08	25243.03	25349.08
2	42813.28	42631.30	42839.28	45334.34	45147.34	45362.34	23984.99	23815.03	24012.99
3	42279.86	42013.88	42317.86	44826.14	44552.31	44867.14	23783.28	23534.41	23824.28
4	42028.31	41678.34	42078.31	44582.87	44222.22	44636.87	23750.69	23422.91	23804.69
5	**41839.34**	**41405.37**	**41901.34**	**44437.82**	**43990.34**	**44504.82**	**23712.88**	**23306.19**	**23779.88**
6	41865.67	41347.71	41939.67	44470.72	43936.42	44550.72	23751.04	23265.44	23831.04
7	41939.39	41337.44	42025.39	44535.10	43913.98	44628.10	23822.48	23257.97	23915.48
8	42020.05	41334.11	42118.05	44609.03	43901.07	44715.03	23899.59	23256.17	24005.59
9	42102.95	41333.02	42212.95	44690.46	43895.68	44809.46	23978.91	23256.59	24097.91
10	42187.08	41333.16	42309.08	44769.29	43887.68	44901.29	24065.83	23264.59	24197.83

Note. LL = Log-likelihood
AIC = Akaike Information Criterion
BIC = Bayesian Information Criterion
CAIC = Consistent Akaike Information Criterion
Indices for optimal model are bolded

Table 2. Percentage of subjects with DSM disorders in each class in the National Comorbidity Survey (NCS) subsample, and National Comorbidity Survey – Replication (NCS-R) subsample.

# of Disorders	Normal	Fear	Depressed	Multimorbid	Externalizing-Distress
NCS Subsample (N=5877)					
0	**56.4**	-	-	-	-
1	38.4	-	10.5	-	-
2	5.1	**54.9**	**45.1**	-	37.5
3	-	30.9	34.0	2.1	**32.1**
4	-	12.1	9.1	22.2	22.0
5	-	2.1	1.4	**30.5**	6.8
6	-	-	-	25.7	1.5
7	-	-	-	11.8	-
8	-	-	-	6.5	-
9	-	-	-	.6	-
10	-	-	-	.6	-
NCS-R Subsample (N=3197)					
0	49.1	-	-	-	-
1	**39.0**	1.8	.7	-	-
2	11.5	32.3	35.8	-	26.8
3	.4	**43.0**	**40.8**	-	**30.8**
4	-	20.8	18.8	1.8	21.0
5	-	2.2	3.9	20.9	17.0
6	-	-	-	**38.2**	4.5
7	-	-	-	22.7	-
8	-	-	-	11.8	-
9	-	-	-	3.6	-
10	-	-	-	.9	-

Note. Median number of disorders in each group is bolded.

Table 3. Odds ratios of disorders in each latent class in optimal solution (5-class) in National Comorbidity Survey (NCS) dataset.

	Normal *(n=3884)*	Fear *(n=572)*	Depressed *(n=497)*	Multimorbid *(n=338)*	Externalizing-Distress *(n=586)*
Specific Phobia	1	**47.12*** **(37.33-59.48)**	**.17*** **(.06-.46)**	**50.56*** **(38.27-66.80)**	1.74* (1.24-2.45)
Social Phobia	1	**19.05*** **(15.51-23.39)**	1.44 (1.06-1.96)	**22.03*** **(17.12-28.36)**	2.82* (2.23-3.58)
Agoraphobia Only	**.04*** **(.03-.06)**	1	**.14*** **(.09-.21)**	.71 (.52-.97)	**.07*** **(.04-.11)**
Panic Disorder Only	1	**15.44*** **(9.50-25.09)**	**11.34*** **(6.70-19.17)**	**22.50*** **(13.55-37.36)**	3.50* (1.78-6.88)
Panic disorder with agoraphobia	**.09*** **(.04-.22)**	1	.82 (.36-1.86)	**10.41*** **(5.76-18.82)**	**.14*** **(.03-.60)**
PTSD	1	**10.86*** **(8.09-14.60)**	**17.63*** **(13.22-23.51)**	**32.40*** **(23.93-43.85)**	**9.31*** **(6.89-12.57)**
GAD	1	3.72* (2.32-5.99)	**25.25*** **(17.93-35.57)**	**77.87*** **(54.93-110.40)**	4.34* (2.77-6.81)
Dysthymia	-	1	**68.05*** **(40.03-115.69)**	**32.37*** **(18.85-55.59)**	3.60* (2.04-6.36)
Major Depression	1	**5.38*** **(4.40-6.58)**	**31.62*** **(25.01-39.99)**	**81.49*** **(56.52-117.48)**	2.85* (2.28-3.54)
Alcohol Dependence	1	.58* (.41-.82)	.75 (.54-1.05)	**8.74*** **(6.90-11.06)**	**57.20*** **(43.88-74.55)**
Drug Dependence	1	2.07* (1.29-3.33)	3.98* (2.66-5.96)	**30.90*** **(22.56-42.32)**	**77.08*** **(58.25-101.99)**
Conduct Disorder	1	2.09* (1.61-2.71)	.89 (.62-1.29)	**6.25*** **(4.85-8.06)**	**23.94*** **(19.43-29.48)**

Note. * $p < .01$. Odds rations greater than 5 or less than .5 are in boldface.
- = disorder not present in class.

Table 4. Odds ratios of disorders in each latent class in optimal solutions (5-class) in National Comorbidity Survey – Replication (NCS-R) dataset.

	Normal *(n=2302)*	Fear *(n=279)*	Depressed *(n=282)*	Multimorbid *(n=110)*	Externalizing-Distress *(n=224)*
Specific Phobia	1	**26.02* (19.08-35.49)**	1.49 (1.07-2.09)	**32.76* (19.86-54.04)**	2.26* (1.62-3.15)
Social Phobia	1	**28.42* (20.88-38.68)**	2.28* (1.66-3.14)	**41.34* (24.77-69.00)**	4.70* (3.47-6.38)
Agoraphobia Only	-	1	**.05* (.02-.17)**	.72 (.38-1.37)	**.11* (.04-.29)**
Panic Disorder Only	1	**9.78* (6.76-14.14)**	2.51* (1.50-4.20)	**11.76* (7.22-19.16)**	3.05* (1.80-5.16)
Panic disorder with agoraphobia	-	1	**.04* (.01-.30)**	4.77* (2.64-8.61)	**.25* (.10-.68)**
PTSD	1	4.47* (3.00-6.68)	**13.37* (9.60-18.61)**	**65.17* (40.89-103.87)**	**6.91* (4.67-10.22)**
GAD	1	4.14* (2.78-6.12)	**30.17* (22.04-41.31)**	**29.91* (19.45-45.97)**	4.60* (3.04-6.95)
Dysthymia	-	1	**37.74* (15.10-94.30)**	**76.24* (29.13-199.57)**	2.29 (.76-6.95)
Major Depression	1	2.53* (1.94-3.28)	**282.12* (104.59-761.03)**	**442.47* (61.61-3177.89)**	3.16* (2.38-4.19)
Alcohol Dependence	1	.27 (.07-1.13)	1.99 (1.09-3.61)	**24.40* (15.37-38.73)**	**125.75* (83.97-188.30)**
Drug Dependence	1	-	1.36 (.30-6.12)	**100.72* (50.51-200.82)**	**364.32* (193.89-684.55)**
Conduct Disorder	1	2.51* (1.76-3.57)	1.24 (.80-1.92)	**10.59* (7.05-15.90)**	**9.53* (7.00-12.96)**

Note. * $p < .01$. Odds rations greater than 5 or less than .5 are in boldface.
- = disorder not present in class.

Table 5. Odds ratios of prevalence of disorders not utilized in latent class analyses in National Comorbidity Survey (NCS) and National Comorbidity Survey - Replication (NCS-R) datasets.

	Normal	Fear	Depressed	Multimorbid	Externalizing-Distress
National Comorbidity Survey (N=5877)					
Manic episode	1	**13.67*** **(2.50-74.80)**	**15.75*** **(2.88-86.20)**	**71.45*** **(15.92-320.59)**	**23.47*** **(4.86-113.23)**
Bipolar I disorder	1	**7.90*** **(3.92-15.91)**	**8.58*** **(4.22-17.47)**	**47.97*** **(26.70-86.16)**	**11.02*** **(5.74-21.12)**
Non-affective Psychoses	1	3.67* (1.47-9.29)	**6.11*** **(2.67-14.02)**	**20.73*** **(10.34-41.55)**	**7.29*** **(3.41-15.58)**
National Comorbidity Survey - Replication (N=3197)					
Manic episode	1	3.38* (2.22-5.14)	3.00* (1.94-4.62)	**20.97*** **(13.62-32.28)**	4.66* (3.07-7.08)
Hypomanic Episode	1	2.72* (1.32-5.62)	1.32 (.51-3.43)	.67 (.09-4.97)	1.67 (.64-4.36)
Bipolar I disorder	1	3.46* (1.58-7.58)	3.03* (1.33-6.86)	**27.40*** **(14.70-51.06)**	**6.91*** **(3.48-13.70)**
Bipolar II disorder	1	2.78 (1.00-7.72)	**9.17*** **(4.48-18.76)**	**33.88*** **(16.80-68.35)**	**5.65*** **(2.37-13.47)**
Prescribed antipsychotics in last 12 months	1	3.22 (1.14-9.11)	1.89 (.54-6.68)	**23.58*** **(10.65-52.22)**	2.39* (.68-8.44)
Attention Deficit Disorder	1	2.51* (1.76-3.58)	2.41* (1.68-3.45)	**10.09*** **(6.71-15.19)**	3.28* (2.28-4.71)
Nicotine Dependence	1	1.38 (.89-2.15)	2.32* (1.60-3.37)	**5.27*** **(3.36-8.27)**	**7.50*** **(5.45-10.34)**
Oppositional Defiant Disorder	1	2.12* (1.50-2.99)	1.73* (1.20-2.49)	**8.09*** **(5.41-12.12)**	**6.39*** **(4.71-8.68)**
Intermittent Explosive Disorder	1	2.15* (1.58-2.91)	1.87* (1.37-2.56)	4.46* (2.98-6.68)	2.95* (2.16-4.04)

Note. * $p < .01$. Odds rations greater than 5 or less than .5 are in boldface.

Table 6. Odds ratios of demographics for each latent class National Comorbidity Survey (NCS) and National Comorbidity Survey - Replication (NCS-R) datasets in optimal solution.

	Normal	Fear	Depressed	Multimorbid	Externalizing-Distress
National Comorbidity Survey (N=5877)					
Age:	1				
M = 32; SD = 10.60	M=31.16	1.12* (1.03-1.23)	1.63* (1.48-1.79)	1.44* (1.29-1.61)	1.07 (.98-1.16)
Sex	1				
Male	50.1%	.42* (.35-.51)	.46* (.38-.56)	.54*(.43-.68)	2.82* (2.32-3.43)
Female	49.9%	-	-	-	-
Income	1				
$0-$19,999	28.8%	1.76* (1.27-2.44)	1.85* (1.29-2.66)	2.64* (1.71-4.10)	1.93* (1.40-2.67)
$20,000-$34,999	24.9%	1.42 (1.01-2.00)	1.95* (1.35-2.81)	1.64 (1.03-2.62)	1.61* (1.15-2.25)
$35,000-$69,999	32.8%	1.57* (1.14-2.18)	1.60 (1.11-2.29)	1.58 (1.01-2.48)	1.40 (1.01-1.94)
$\geq$ $70,000	13.5%	-	-	-	-
Marital Status	1				
Marr./Cohab	49.4%	1.31* (1.08-1.59)	1.45* (1.15-1.82)	1.59* (1.21-2.10)	1.18 (.97-1.43)
Sep./Div./Wid.	12.0%	1.50* (1.13-1.98)	4.02* (3.10-5.22)	3.97* (2.90-5.44)	1.61* (1.24-2.10)
Never married	38.6%	-	-	-	-
National Comorbidity Survey - Replication (N=3197)					
Age:	1				
M = 31.29; SD = 7.86	M=30.93	1.06 (.93-1.20)	1.30* (1.14-1.47)	1.37* (1.13-1.67)	1.13 (.98-1.29)
Sex	1				
Male	45.7%	.52* (.40-.68)	.41* (.31-.55)	.53* (.35-.80)	1.55* (1.18-2.05)
Female	54.3%				
Income	1				
$0-$19,999	17.9%	1.30 (.91-1.87)	1.07 (.75-1.54)	4.51* (2.49-8.15)	1.80* (1.22-2.67)
$20,000-$34,999	15.9%	1.03 (.69-1.54)	1.10 (.76-1.59)	2.54* (1.30-4.97)	1.11 (.70-1.76)
$35,000-$69,999	34.0%	1.24 (.91-1.69)	.98 (.72-1.34)	2.02 (1.11-3.69)	1.45 (1.02-2.07)
$\geq$ $70,000	32.3%	-	-	-	-
Marital Status	1				
Marr./Cohab	54.7%	1.13 (.85-1.49)	1.22 (.91-1.63)	.73 (.47-1.13)	1.05 (.78-1.43)
Sep./Div./Wid.	10.2%	1.83* (1.24-2.70)	2.82* (1.96-4.07)	2.64* (1.59-4.37)	1.63 (1.06-2.52)
Never married	35.1%	-	-	-	-

Note. * $p < .01$.

Table 7. Odds ratios of age of onset[†] of disorders in latent classes in National Comorbidity Survey (NCS) dataset.

Disorder	*N*	*Mean*	*SD*	*Normal*	*Fear*	*Depressed*	*Multimorbid*	*Externalizing-Distress*
Specific Phobia	861	13.93	10.06	1	1.06 (.88-1.27)	2.08 (1.03-4.18)	1.05 (.86-1.27)	.59 (.38-.94)
Social Phobia	1043	14.96	7.98	1	1.13 (.97-1.32)	.95 (.69-1.30)	1.13 (.95-1.34)	.86 (.67-1.10)
Panic Disorder Only	167	24.65	10.09	1	.97 (.60-1.56)	1.13 (.68-1.89)	.62 (.37-1.05)	.41 (.18-.91)
Agoraphobia Only	361	18.57	9.94	.88 (.66-1.19)	1	1.36 (.93-1.99)	1.19 (.91-1.55)	1.12 (.67-1.85)
Panic Disorder with Agoraphobia	105	PD: 24.84	9.71	2.09 (.84-5.23)	1	2.94 (1.19-7.26)	2.24 (1.15-4.37)	1.68 (.35-8.08)
		AG:21.48	9.74	2.07 (.86-4.99)	1	2.15 (.92-5.06)	1.33 (.72-2.47)	.82 (.16-4.30)
PTSD	591	17.98	9.67	1	.88 (.66-1.17)	1.12 (.86-1.46)	.96 (.73-1.25)	.98 (.74-1.31)
GAD	407	25.44	10.53	1	1.01 (.63-1.62)	.82 (.59-1.14)	.55* (.39-.76)	.40* (.25-.65)
Dysthymia	563	25.40	10.35	-	1	1.66 (.96-2.86)	1.29 (.74-2.25)	1.11 (.61-2.02)
Major Depressive Episode	1403	23.71	9.82	1	.78* (.67-.93)	1.03 (.89-1.18)	.68* (.58-.80)	.67* (.55-.83)
Alcohol Dependence	1193	21.93	6.68	1	.97 (.70-1.33)	1.51* (1.18-1.92)	.99 (.84-1.18)	.71* (.62-.82)
Drug Dependence	624	21.07	6.21	1	1.40 (.95-2.04)	1.13 (.80-1.60)	1.12 (.86-1.44)	.60* (.47-.78)

Note. [†]Age of onset for each disorder was z-scored across subjects for that particular disorder for analyses.
PTSD = Post-traumatic stress disorder; GAD = Generalized anxiety disorder; PD = Panic Disorder; AG = Agoraphobia.
- Not utilized in analyses as no subject in that class had that disorder
* $p < .01$

Table 8. Odds ratios of age of onset[†] of disorders in latent classes in National Comorbidity Survey - Replication (NCS-R) dataset.

Disorder	*N*	*Mean*	*SD*	*Few Disorders*	*Fear*	*Depressed*	*Multimorbid*	*Externalizing-Distress*
Specific Phobia	687	7.46	5.25	1	.85 (.71-1.02)	.84 (.60-1.17)	.74 (.55-.99)	.81 (.58-1.13)
Social Phobia	682	11.33	5.67	1	.99 (.82-1.20)	1.21 (.93-1.58)	1.03 (.81-1.32)	1.11 (.87-1.43)
Panic Disorder Only	200	18.96	8.65	1	.96 (.68-1.35)	.90 (.54-1.48)	.79 (.51-1.24)	.70 (.41-1.19)
Agoraphobia Only	69	15.55	8.79	-	1 (.34-3.41)	1.07 (.65-2.09)	1.17 (.27-2.20)	.77
Panic Disorder with Agoraphobia	PD: 62	19.76	8.48	-	1 (.37-24.67)	3.03 (.52-1.56)	.90 (.38-2.64)	1.00
	AG: 62	16.44	9.72	-	1 (.03-5.82)	.43 (.36-2.36)	.92 (.37-1.12)	.64
PTSD	341	16.35	8.45	1	.87 (.60-1.28)	.94 (.70-1.27)	.75 (.55-1.04)	1.08 (.76-1.53)
GAD	387	21.36	9.26	1	.63 (.42-.93)	1.13 (.87-1.46)	.89 (.64-1.23)	1.09 (.74-1.61)
Dysthymia	193	19.91	9.59	-	1 (.48-3.00)	1.20 (.35-2.28)	.90 (.33-3.07)	1.00
Major Depressive Episode	1047	20.85	8.90	1	.77 (.62-.95)	.85 (.73-.99)	.54* (.42-.68)	.69* (.55-.87)
Alcohol Dependence	290	20.71	5.82	1	1.30 (.39-4.28)	1.70 (1.06-2.73)	.63 (.40-1.00)	.90 (.67-1.21)
Drug Dependence	199	20.24	5.81	1	-	1.16 (.34-4.01)	.89 (.50-1.58)	.67 (.40-1.14)
Conduct Disorder	385	11.61	3.50	1	.94 (.68-1.30)	1.00 (.65-1.51)	1.05 (.77-1.45)	1.04 (.81-1.33)

Note. [†]Age of onset for each disorder was z-scored across subjects for that particular disorder for analyses
PTSD = Post-traumatic stress disorder; GAD = Generalized anxiety disorder; PD = Panic Disorder; AG = Agoraphobia.
- Not utilized in analyses as no subject in that class had that disorder
* p <.01

Table 9. Odds ratios of treatment-related variables in latent classes in National Comorbidity Survey (NCS) dataset.

Treatment-related variable	*N*	*Normal*	*Fear*	*Depressed*	*Multimorbid*	*Externalizing-Distress*
Age of 1st self-help treatment	737 M=28.28 SD=8.91	1	.89 (.67-1.17)	1.16 (.92-1.46)	1.02 (.82-1.28)	.71* (.59-.86)
Age 1st time saw general practitioner	658 M=28.41 SD=9.04	1	.98 (.77-1.24)	1.17 (.95-1.45)	.94 (.75-1.18)	.77 (.58-1.00)
Age 1st saw psychiatrist	595 M=26.60 SD=9.95	1	1.02 (.29-1.33)	1.14 (.91-1.43)	1.14 (.90-1.44)	.75 (.57-.97)
Age 1st saw psychologist	611 M=27.72 SD=9.73	1	.92 (.70-1.21)	.99 (.79-1.22)	.84 (.65-1.07)	.62* (.47-.82)
Age 1st saw social worker	256 M=26.64 SD=9.98	1	.71 (.45-1.13)	1.19 (.83-1.71)	.92 (.65-1.31)	.69 (.47-1.01)
Age 1st saw counselor	819 M=25.13 SD=9.40	1	.96 (.76-1.21)	1.27 (1.03-1.57)	1.13 (.92-1.39)	.86 (.71-1.05)
Age 1st hospitalized for emergency related to emotions/alcohol/drugs	195 M=28.07 SD=9.55	1	1.24 (.75-2.04)	1.31 (.81-2.12)	1.29 (.86-1.95)	.76 (.48-1.23)
Age 1st used psychiatric outpatient clinic	326 M=27.08 SD=9.60	1	.91 (.65-1.27)	1.07 (.78-1.47)	.87 (.63-1.19)	.56* (.37-.83)
Age 1st used drug/alcohol outpatient clinic	155 M=27.26 SD=8.22	1	1.07 (.48-2.35)	1.63 (.79-3.36)	1.17 (.72-1.89)	.54* (.36-.83)
Age 1st went to doctor's private office for emotions/alcohol/drugs	1045 M=27.44 SD=9.35	1	.96 (.79-1.16)	1.24 (1.05-1.46)	1.04 (.87-1.26)	.85 (.68-1.06)

Note. †Age of onset for each variable was z-scored across subjects for that particular variable for analyses.
* p <.01

Table 10. Odds ratios of treatment-related variables in latent classes in National Comorbidity Survey – Replication (NCS-R) dataset.

Treatment-related variable	*N*	*Normal*	*Fear*	*Depressed*	*Multimorbid*	*Externalizing-Distress*
Age 1st hospitalized overnight for mental health/sub use	140 M=21.39 SD=7.69	1	1.02 (.61-1.71)	.73 (.38-1.39)	1.04 (.66-1.65)	.64 (.39-1.06)
Age 1st self-help group for emotions	318 M=24.58 SD=7.61	1	1.02 (.71-1.46)	1.28 (.91-1.80)	1.06 (.73-1.54)	1.00 (.73-1.36)
Age 1st session of psych counsel/therapy	1382 M=21.77 SD=8.73	1	.91 (.76-1.09)	1.05 (.89-1.23)	.90 (.72-1.13)	.77* (.64-.92)
Age 1st prescription for emotions	903 M=25.46 SD=8.64	1	1.00 (.82-1.23)	1.06 (.88-1.28)	.97 (.76-1.23)	.74* (.59-.92)
Age 1st talk to psychiatrist about emotion/mental health	680 M=21.52 SD=8.90	1	1.28 (1.01-1.63)	1.06 (.85-1.32)	1.15 (.90-1.49)	.81 (.64-1.03)
# visits to psychiatrist for emotions/sub use past year	196 M=8.35 SD=10.57	1	1.11 (.63-1.94)	1.10 (.59-2.04)	1.78* (1.16-2.73)	1.49 (.89-2.49)
Age 1st saw medical doctor for mental health/sub use	713 M=25.05 SD=8.80	1	.89 (.71-1.11)	.98 (.79-1.22)	.72 (.54-.97)	.75 (.57-.99)
Age 1st saw psychologist about mental health/sub use	576 M=21.67 SD=8.45	1	.84 (.64-1.10)	1.20 (.94-1.53)	1.03 (.75-1.40)	.84 (.64-1.11)
Age 1st saw social worker for mental health/sub use	241 M=21.53 SD=8.78	1	.67 (.42-1.06)	1.03 (.71-1.51)	.91 (.60-1.37)	.86 (.60-1.25)
Age 1st saw counselor for mental health/sub use	755 M=21.25 SD=8.70	1	.85 (.67-1.09)	1.08 (.85-1.37)	.74 (.56-.99)	.82 (.65-1.03)

Note. †Age of onset for each variable was z-scored across subjects for that particular variable for analyses.
* p <.01

Table 11. Odds ratios of medication-related variables in latent classes in National Comorbidity Survey (NCS) and National Comorbidity Survey – Replication (NCS-R) datasets.

Medication Type	N	Normal	Fear	Depressed	Multimorbid	Externalizing-Distress
National Comorbidity Survey (N=5877)						
In the past 12 months, subject took medication under supervision of doctor:						
Sleeping pills or other sedative (Halcion, Dalmane)	76	1	2.68 (1.24-5.83)	4.51* (2.27-8.96)	**13.99*** **(7.89-24.81)**	1.45 (.55-3.82)
Antidepressants	164	1	**5.51*** **(3.42-8.88)**	**7.73*** **(4.89-12.21)**	**16.68*** **(10.82-25.72)**	.99 (.42-2.36)
Other tranquilizers (Librium, Valium)	99	1	2.66* (1.36-5.22)	4.67* (2.59-8.41)	**10.36*** **(6.07-17.66)**	2.60* (1.33-5.09)
Amphetamines or other stimulants	Not evaluated as only 4 out of 5877 subjects endorsed being prescribed amphetamines					
Analgesics or painkillers	79	1	3.15* (1.54-6.47)	4.66* (2.40-9.07)	**11.74*** **(6.55-21.04)**	1.94 (.83-4.53)
Anti-psychotic medications	17	-	1	1.15 (.29-4.63)	3.44 (1.03-11.52)	.24 (.03-2.18)
National Comorbidity Survey - Replication (N=3197)						
Took following medications in past 12 months:						
Sleeping pills/sedatives	191	1	2.84* (1.80-4.46)	2.92* (1.87-4.56)	**9.88*** **(6.16-15.86)**	2.87* (1.76-4.69)
Anti-depressants	411	1	3.32* (2.43-4.54)	2.64* (1.91-3.67)	**9.22*** **(6.17-13.78)**	2.39* (1.65-3.46)
Tranquilizers	135	1	3.36* (2.04-5.53)	2.24* (1.27-3.95)	**10.41*** **(6.19-17.50)**	2.11 (1.12-3.99)
Amphetamines/stimulants	30	1	2.22 (.73-6.75)	1.64 (.47-5.69)	2.82 (.64-12.49)	4.19* (1.61-10.91)
Anti-psychotics	37	1	3.22 (1.14-9.11)	1.89 (.54-6.68)	**23.58*** **(10.65-52.22)**	2.39 (.68-8.44)

Note. Odds ratios > 5 are in boldface.
- Not utilized in analyses as no subject in that class endorsed that variable.
* p <.01

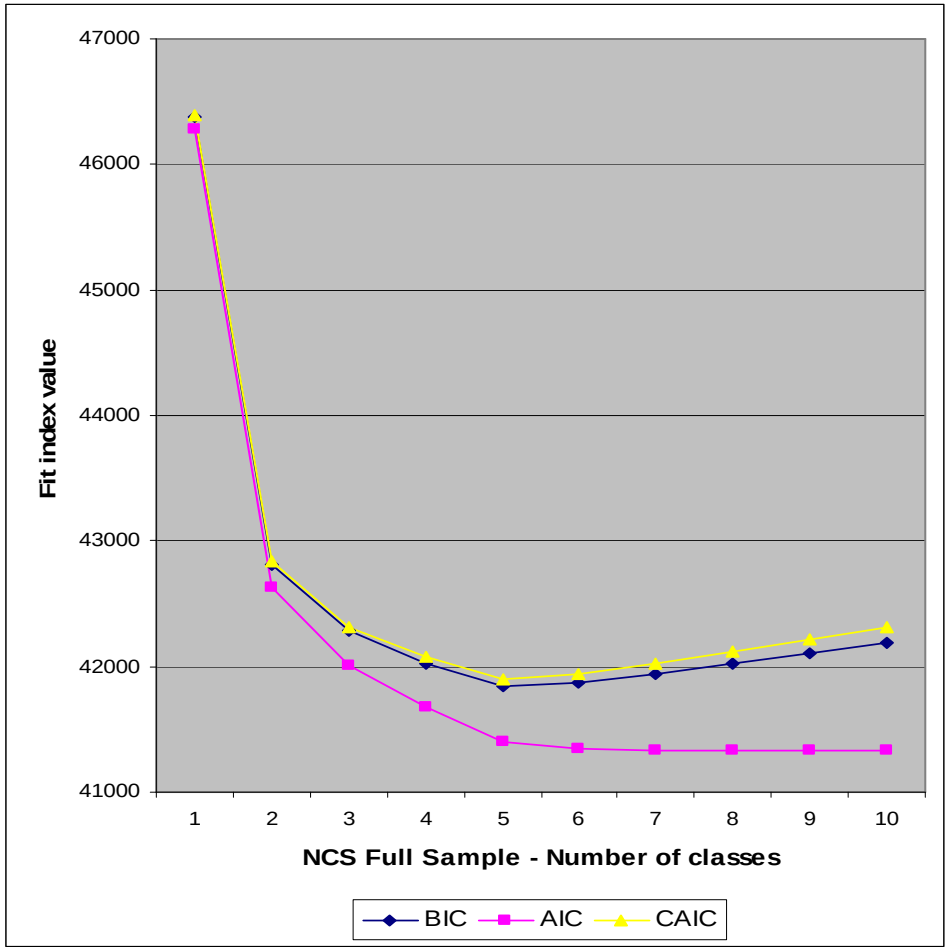

Figure 1. Graphical representation of model fit indices for latent class models showing optimal fit for 5-class model for National Comorbidity Survey (NCS) full sample (N=8098).

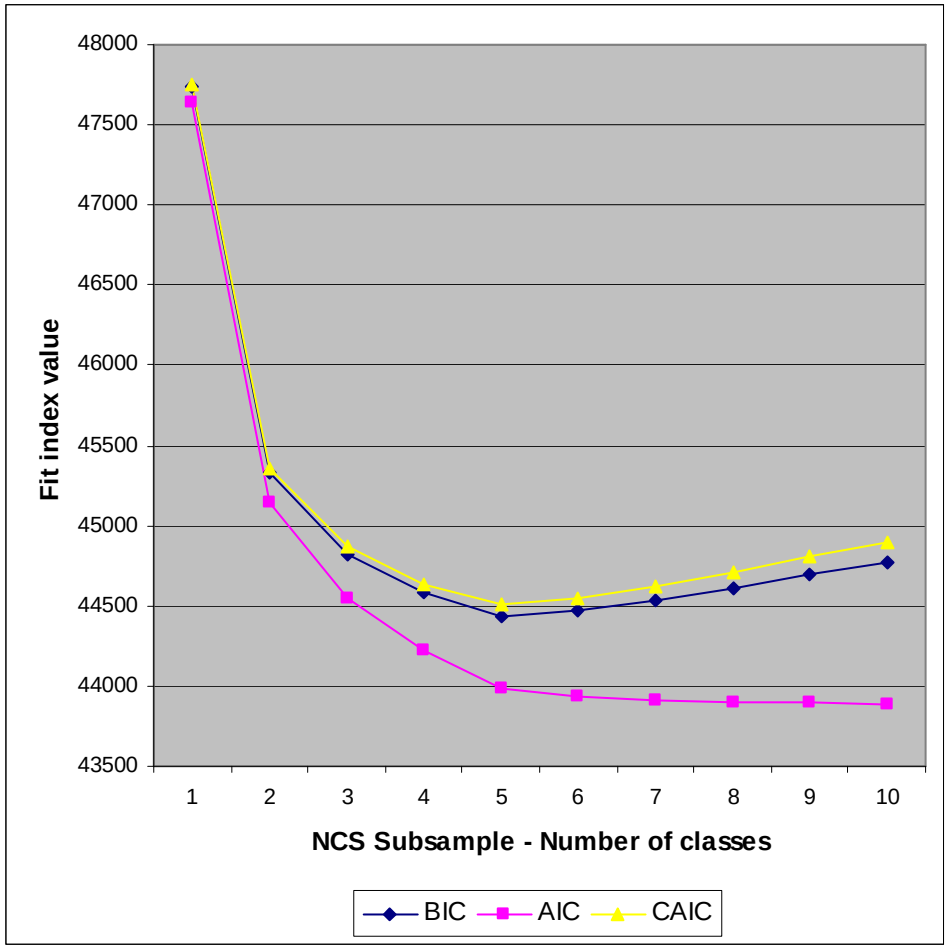

Figure 2. Graphical representation of model fit indices for latent class models showing optimal fit for 5-class model for National Comorbidity Survey (NCS) subsample (N=5877).

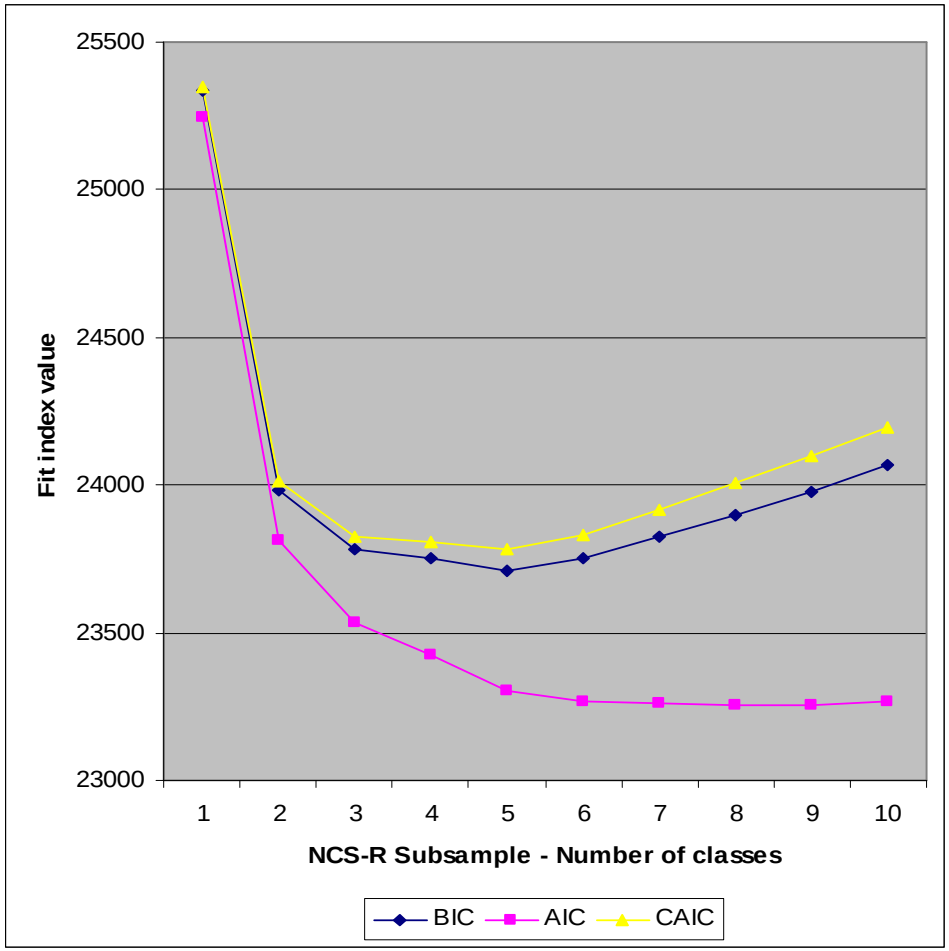

Figure 3. Graphical representation of model fit indices for latent class models showing optimal fit for 5-class model for National Comorbidity Survey - Replication (NCS-R) subsample (N=3197).

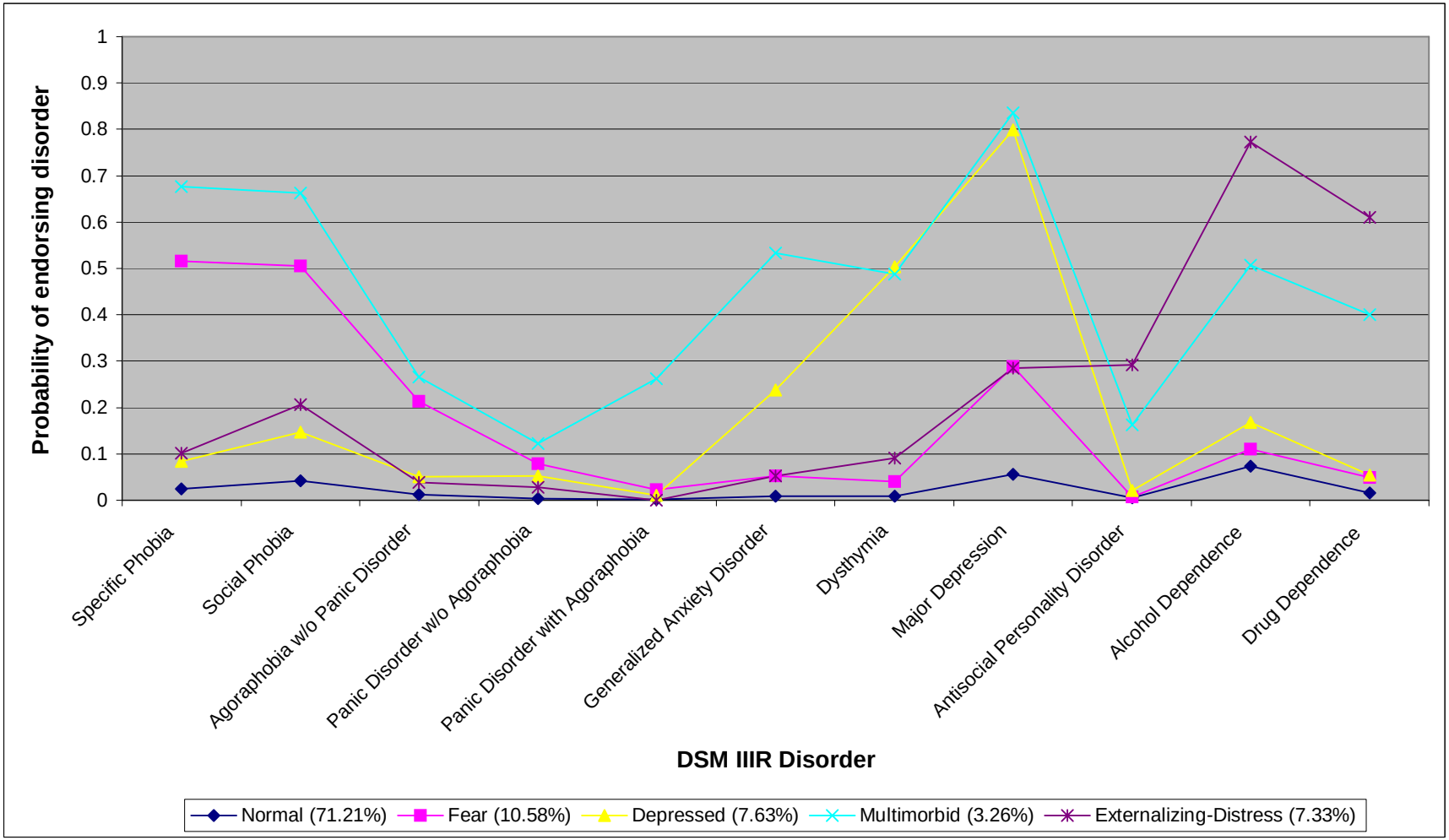

Figure 4. Profile of classes for optimal 5-class model in the National Comorbidity Survey (NCS) full sample (N=8098).

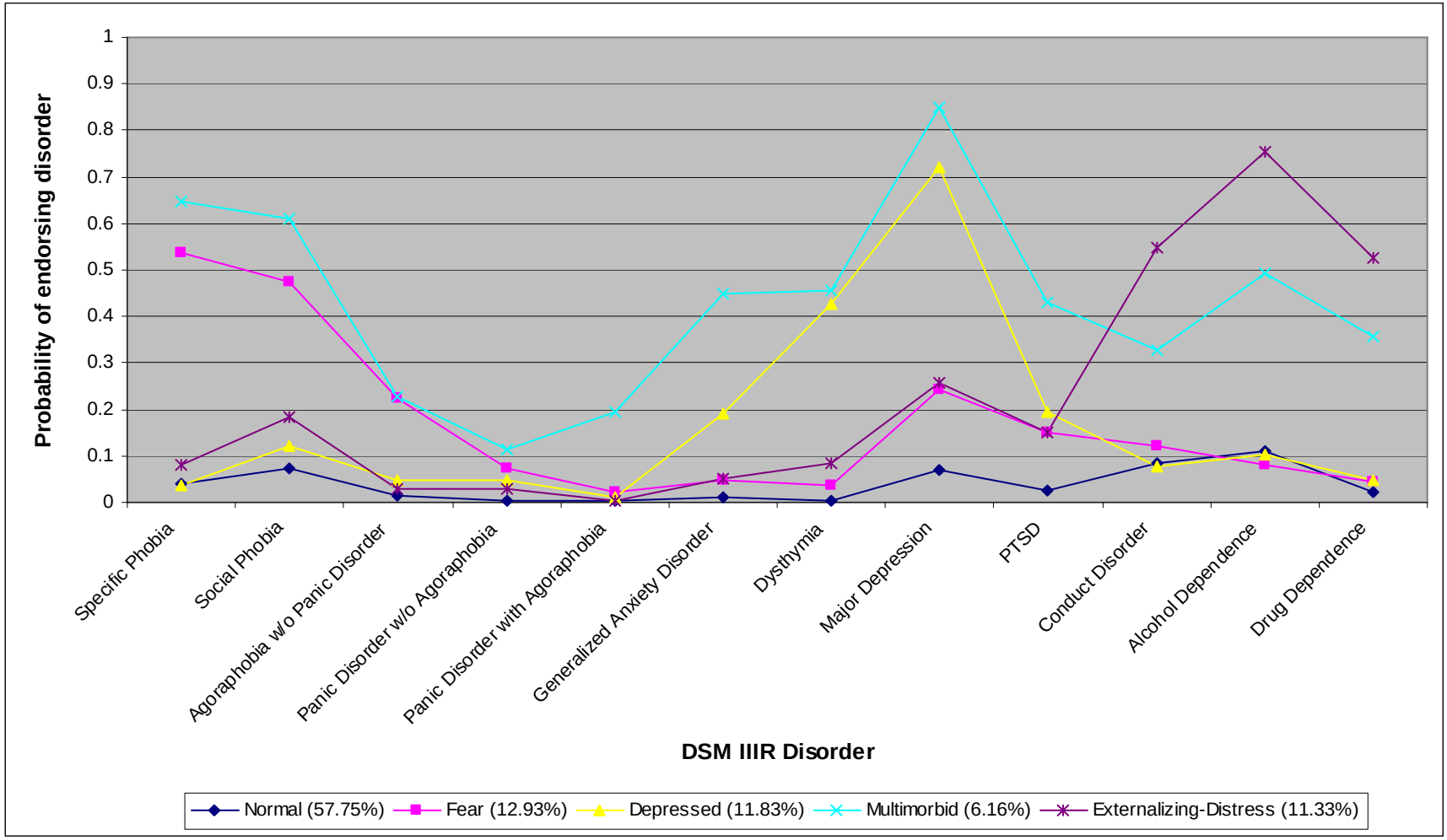

Figure 5. Profile of classes for optimal 5-class model in the National Comorbidity Survey (NCS) subsample (N=5877).

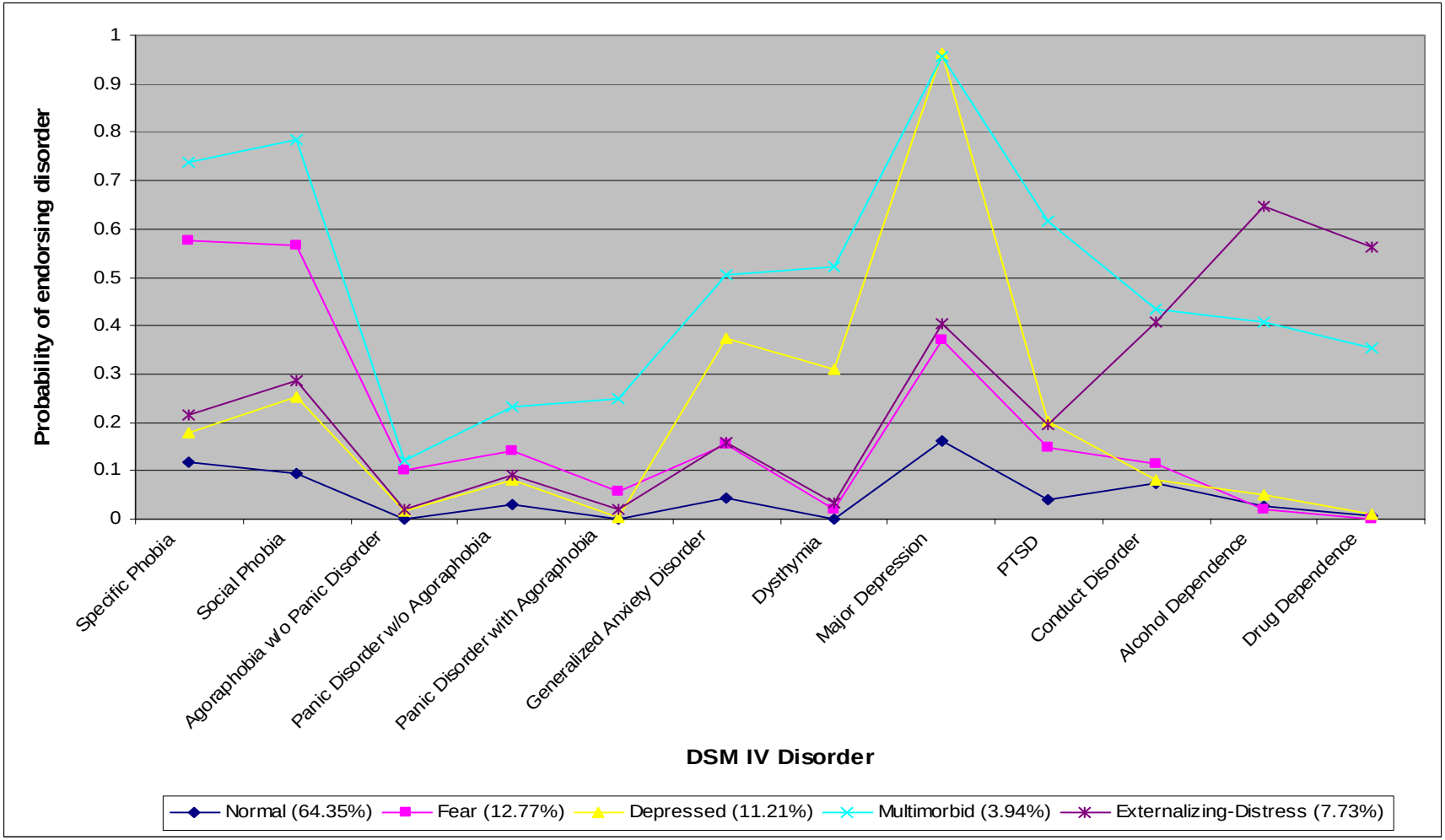

Figure 6. Profile of classes for optimal 5-class model in the National Comorbidity Survey - Replication (NCS-R) subsample (N=3197).

Appendix A

Subject Samples and Methods Utilized in the NCS and NCS-R Datasets

The samples utilized in the current study – the National Comorbidity Survey (NCS), and the National Comorbidity Survey – Replication (NCS-R) – are two nationally representative epidemiological datasets that contain a variety of information related to mental health problems in the United States. The NCS survey was conducted from 1990-1992, while the NCS-R was conducted almost a decade later, from 2001-2003, and utilized a completely different sample, though a similar recruitment strategy. Both studies used a stratified, multistage area, probabilistic sampling approach to recruit subjects, who were comprised of noninstitutionalized US civilians. Interviewers in both studies were trained staff of the Survey Research Center (SRC) of the Institute for Social Research at the University of Michigan. They visited the homes of all subjects to conduct face-to-face interviews using a modified version of the World Health Organization's (WHO) Composite International Diagnostic Interview (CIDI). In the case of the NCS, this was done a using a paper-and-pencil version of the interview (PAPI), while the NCS-R utilized a computer-assisted personal interview (CAPI). Subjects in both studies were offered financial incentives to complete the interview. Informed consent was obtained from all participants.

Subjects in the NCS sample ranged in age from 15 – 54, while those in the NCS-R were 18 or older. Great care was taken to ensure that subjects were representative of all regions of the United States, socioeconomic status, ages, and gender in both studies. Weights were calculated for each dataset to account for these variables along with other

factors such as household size, nonresponse, etc.. These weights are provided with each dataset to allow for the calculation of precise statistics. All interviewers underwent extensive training before administering interviews. Their fieldwork was carefully monitored to ensure reliability of data. NCS-R documentation also notes that interviewers were provided incentives to gather as much data as possible during interviews (e.g., they were paid by the hour rather than per interview). Also, in the NCS-R, the use of the CAPI minimized errors in interviews due to skip logic. Overall response rates in the NCS and NCS-R were 82.6% and 70.9%, respectively. The final sample of the NCS was comprised of 8098 subjects, while the NCS-R consisted of 9282 subjects. Diagnoses in the NCS were assigned using DSM-IIIR criteria, while the NCS-R utilized DSM-IV criteria. With regard to the completeness of information that was obtained, if subjects did not endorse some of the stem questions for particular disorders, then the relevant disorders were not assessed. During coding, however, all diagnoses were coded as endorsed/non-endorsed leading to a complete dataset with no missing data. However, individual items were coded as missing if subjects were unaware of, chose not to answer, or were not eligible for some question.

Interviews in both the NCS and NCS-R were carried out in several stages. All mood and anxiety disorder diagnoses, with the exception of PTSD, were assessed in the first part in both samples (Ns for Part 1: NCS = 8098; NCS-R = 9282). While the NCS assessed for substance use problems and antisocial personality disorder in addition to these core disorders in Part 1 of the interview, the NCS-R did not. Part 2 in both studies included assessment of risk factors, as well as other diagnoses such as PTSD, which were considered time-consuming to assess. Though the NCS-R did assess for substance use

problems at this stage (i.e., Part 2), antisocial personality disorder was not included among the NCS-R diagnoses at all. Subjects for Part 2 included subjects from Part 1 who met criteria for significant psychopathology and a random sample of the remaining Part 1 subjects (total N's for Part 2: NCS = 5877; NCS-R = 5692). This strategy led to oversampling subjects who had significant mental health issues in Part 2. A different set of weights for each sample were calculated to accommodate this issue. Thus, each sample has two weights – one that can be utilized for Part 1 variables, and one that can be utilized for Part 2 variables.

The NCS-R had a further, third subsample of subjects ranging in age from 18 – 44 amongst those from Part 2 (N = 3197), that were assessed for impulse-control disorders such as conduct disorder, oppositional-defiant disorder, attention deficit hyperactivity disorder, and separation anxiety disorder. These diagnoses were restricted to this particular age group out of concerns regarding recall bias among older subjects. Separate weights were not provided for this subsample. Instructions provided with the NCS-R note that Part 2 weights should be used for this sample as well.

In addition to the above diagnoses, the NCS also assessed for bipolar I disorder, while the NCS-R assessed for bipolar I and II disorders. Both studies attempted to measure the prevalence of psychosis in their respective samples as well, where they collapsed several diagnostic categories including schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, and atypical psychosis into a summary variable labeled "nonaffective psychosis". While this diagnosis was provided with the NCS dataset, subsequent analysis of the NCS-R revealed that the prevalence rates of these disorders appeared to be lower than that assessed in other surveys, raising

some questions about the validity of this category (Kessler, Birnbaum et al., 2005). Thus, this variable was eliminated from the publicly available NCS-R dataset. Likewise, though the NCS-R also attempted to diagnose obsessive-compulsive disorder, a problem with the skip logic during the interview lead to lower rates of OCD in this dataset, leading to its elimination from the publicly available dataset as well (*NCS-R: Answers to Frequently Asked Questions*).

In addition to variables regarding diagnoses, both datasets also contain item-level information for each disorder, as well as a wide variety of variables regarding treatment, medication use, and other sociodemographic data. The variables utilized for comparison in the current study were chosen since they contributed most to the aims of this project; it would have been an almost impossible, as well as an impractical endeavor to compare subjects on all available variables. Both datasets along with relevant documentation regarding coding and weights are currently available online for public use. The NCS dataset is stored in archival form on the Substance Abuse and Mental Health Data Archive (SAMHDA) website - http://webapp.icpsr.umich.edu/cocoon/SAMHDA-STUDY/06693.xml. The NCS-R subset is available on the Collaborative Psychiatric Epidemiology Surveys website - http://www.icpsr.umich.edu/CPES/ .

Issues regarding the use of weights in the NCS and NCS-R datasets

Results using weighted data are not presented in the current study. As noted above, while the appropriate weights were provided for NCS and NCS-R Parts 1 and 2, separate weights were not provided for the subsample that had conduct disorder diagnoses in the NCS-R. While the NCS-R instructions note that Part 2 weights should be

used for this subsample, this seemed inappropriate to us because of the following reason. The purpose of weighting is to ensure that subjects accurately represent the population they are drawn from – e.g., certain genders, ages, parts of the country (urban vs. rural areas), etc. – are not under- or over-represented. Weights for each subject are generally calculated based on the joint product of the inverse probability of being selected into the sample for each variable of interest. An additional post-stratification weight is then applied to match these subjects to some larger dataset (in this case, the US census). The NCS-R survey authors (Kessler et al., 2004) note that they undertook this procedure and that the post-stratification weight "….was based on comparisons of age, sex, race-ethnicity, education, marital status, region, and urbanicity in the weighted ……sample and the 2002 CPS sample for persons ages 18+ in the continental US" (p. 82). An additional weight was then created for the probability of being selected into the Part 2 sample (N for Part 1 = 9282; N for Part 2 = 5692). However, the NCS-R subsample that was utilized in the current study (i.e., the sample that had conduct disorder which we will refer to as Part 3, with N=3197) was a subsample of the Part 2 sample (specifically, only those that ranged in age from 18-44). Thus, not everyone in Part 2 had an equal probability of being selected into this Part 3 subsample. This is why it seemed inappropriate to apply Part 2 weights to the Part 3 subjects, just as it would have been inappropriate to use Part 1 weights for the Part 2 subjects, even though all these samples are nested within Part 1. Additionally, we could not simply weight each subject by the inverse probability of being selected into Part 3, due to the stratified sampling strategy utilized in the study. Consequently, we have contacted the NCS-R helpline regarding this

issue, who then referred us directly to the authors. However, as of the time of the writing of this dissertation, the authors have yet to respond to us.

On a more practical level, to examine how this issue affected data, LCA models for the current study were fit in both the NCS and NCS-R samples with and without the recommended weights. Weighted and unweighted data yielded highly similar solutions for the two NCS datasets (i.e., a 5-class model). However, for the NCS-R Part 3 subsample (N=3197) while the unweighted data converged to a 5-class solution, model fit indices for the weighted data indicated a 3- or 4-class model, implying that the weights recommended by the NCS-R authors (i.e., the Part 2 weights) were interacting with the data in some manner, and thus, perhaps not appropriate.

To ensure that the change in the optimal model was not restricted to the NCS-R data alone, we undertook two further steps. First, we fit additional weighted and unweighted models to the Part 2 NCS-R dataset (i.e., all diagnoses utilized in the current study except conduct disorder; N=5692). The optimal model in this case was a 5-class solution in both weighted and unweighted data, with profiles of latent classes that were highly similar to other models presented in the results section of the current study. Second, we fit models to weighted Part 3 NCS-R subsample ***without*** conduct disorder as part of the LCA variables. This was to ensure that the change in the optimal model was not because of the inclusion of conduct disorder. Similar to the weighted models with conduct disorder, fit indices for models without conduct disorder suggested a 3- or 4-class model. This suggested that merely including conduct disorder in the LCA were not affecting results. Thus, in light of this evidence, and due to most of the results being in

favor of the 5-class model (weighted or unweighted), we elected to utilize unweighted data for all the analyses in the current study.

Appendix B

A Brief Overview of Latent Class Analysis (LCA)

Latent class analysis (LCA) is a statistical technique that partitions subjects into underlying groups or classes based on certain observed characteristics (Lazarsfeld & Henry, 1968; McCutcheon, 1987). It is similar to factor analysis in that it assumes a latent structure to the variables being assessed in the model, but instead of treating them dimensionally, it treats them categorically. This technique groups subjects into distinct classes or clusters of disorders based on observed response patterns of the variables being assessed. Thus, rather than using the variance-covariance matrix as the basis for model-fitting (e.g., as in factor analyses), frequencies of response patterns across subjects are utilized instead. This gives it an advantage over factor analysis in that it is not affected by the non-normality of the variables used in the analysis. The tradeoff however, is that LCA assumes that there is no variation within a class – i.e., all members within a particular class are considered equal – an assumption that may or may not be true.

The basic latent class model attempts to estimate two sets of parameters:
(1) the mixing proportions (or the size of each class), and
(2) given a particular mixing proportion, the probability that a member of that class responds a particular way to a particular observed variable (e.g., in the current study, the probability of a subject being diagnosed with social phobia given that they belong to a particular class in a 5-class model).

Using these parameters, LCA attempts to capture all the different response patterns observed in the dataset. Parameters are estimated using maximum likelihood estimation techniques, which attempts to find the model that has the greatest likelihood of fitting the observed data. Model fit indices are then used to calculate how well these parameters are able to do so.

Some precautions must be taken when attempting to estimate LCA models. The first of these is related to the issue of local maxima. Given a particular set of parameters, local maxima are those that result when the estimation technique happens to chance upon data that appear to maximize the likelihood of the model, while the true maximum of the data may be further away. Such parameter estimates may be misleading. To counter this problem, LCA models must be run several times, each time with a different set of starting values for the parameters. If they converge on the same solution every time, this provides stronger support for the model in question. In the current study, we used 50 different sets of starting values for each model. Another problem encountered with LCA models is that of local dependence. If two observed variables in a model are related for any other reason apart from the latent class they share (e.g., because of very similar diagnostic criteria, as in this particular study), this may lead to the formation of spurious classes. A variety of methods have been advocated to cover these (Uebersax, 2000b). For the purposes of the current study, we utilized bivariate residuals among disorders to assess for local dependence after fitting models.

Again, it is worth bearing in mind that LCA does not conclusively prove or disprove whether the dataset in question is truly categorical or dimensional. It merely does what the user wants it to do – i.e., divide the dataset into latent classes or groups.

However, to the extent that it does *not* merely result in identical profiles with progression in severity among classes (implying artificial segmentation of a dimension into classes), it can provide an alternative view of the data being modeled. As with any other model, substantive interpretation of such results ultimately depends on the user.