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Aggregation of Lifetime Axis I Psychiatric Disorders through Age 30: Incidence, Predictors, and Associated Psychosocial Outcomes

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Abstract

Longitudinal data from representative birth cohorts on the aggregation of psychiatric disorders, or the cumulative number of unique diagnosed disorders experienced by persons within a circumscribed period, are limited. Consequently, risk factors for and psychosocial implications of lifetime disorder aggregation in the general population remain largely unknown. This research evaluates the incidence, predictors, and psychosocial sequela of lifetime disorder aggregation from childhood through age 30. Over a 14-year period, participants in the Oregon Adolescent Depression Project (probands; $N = 816$) were repeatedly evaluated for psychiatric disorders and assessed with multiple measures of psychosocial functioning. First-degree relatives of probands ($N = 2,414$) were also interviewed to establish their lifetime psychiatric history. The cumulative prevalence of common lifetime psychiatric disorders for the proband sample was 71%. Three-quarters of all proband psychiatric disorders occurred among 37% of the sample, and 82% of all disorder diagnoses were made among persons who met criteria for at least one other lifetime disorder. Lifetime disorder aggregation in probands was predicted by lifetime psychiatric disorder densities among first-degree relatives and was related to heterotypic comorbidity patterns that included disorders from both internalizing and externalizing domains, most notably major depressive and alcohol use disorders. By age 30, disorder aggregation was significantly associated with mental health care service utilization and predictive of personality disorder pathology and numerous indicators of poor psychosocial functioning. Possible implications of disorder aggregation on the conceptualization of lifetime psychiatric disorder comorbidity are discussed.

Keywords

Disorder aggregation; cumulative prevalence; familial risk; mental health care utilization; functional response domains

Shortly after the advent of semi-structured clinical interviews for assessing psychiatric disorders, researchers observed that diagnostic categories co-occurred at rates substantially greater than would be expected by chance (Boyd et al., 1984; Wolf et al., 1988). Since then, diagnostic comorbidity has been a central focus of clinical research, with emphasis placed on relations among pairs or subsets of disorders to inform etiologic theories, suggest

refinements in disorder definitions, and aid prevention- or treatment-related decisions (Maser & Cloninger, 1990; Krueger & Markon, 2006; Watson, 2005). The related topic of *disorder aggregation*, or the cumulative number of unique diagnosed disorders experienced by persons within a circumscribed period (Angold, Costello, & Erkanli, 1999), however, has received comparatively little attention in the research literature.

Much of extant research on disorder aggregation comes from cross-sectional community-based surveys. These studies suggest that about half of all persons with a psychiatric disorder will meet criteria for at least one additional disorder within a 12-month period (Kessler et al., 2005b; WHO World Mental Health Survey Consortium, 2004). Importantly, in the National Comorbidity Survey Replication (NCS-R; Kessler et al., 2005b), 77% of all mental disorders within a 12-month period occurred among persons diagnosed with more than one mental disorder, and 56% of all disorders occurred among persons diagnosed with 3 or more disorders. In the initial NCS (Kessler et al., 1994), where data on *lifetime* disorder aggregation were reported, 54% of all lifetime diagnoses were concentrated among 14% of the sample, with 79% of all lifetime disorders diagnosed among persons who met criteria for at least two lifetime disorders.

Research based on longitudinal studies of representative birth cohorts similarly suggests that lifetime psychiatric disorders are common and frequently comorbid with other conditions. Findings from the Great Smoky Mountains Study (Copeland, Shanahan, Costello, & Angold, 2011), for example, indicated that 61% of participants by age 21 were diagnosed with well-defined *DSM* psychiatric disorder, with an additional 21% meeting criteria for a “not otherwise specified” (or NOS) disorder. In the Dunedin Multidisciplinary Health and Development Study (Kim-Cohen et al., 2003), 82% of the sample that was diagnosed with a disorder within a 12-month period at age 26 had at least one other psychiatric disorder at an earlier age. In combination, these findings suggest that lifetime psychiatric disorders are prevalent in community samples, and that disorder aggregation is also quite common among young adults with current disorder diagnoses.

Despite the potential importance of disorder aggregation for epidemiology, treatment program development, and prevention efforts, relatively little is known about individuals who are diagnosed with multiple distinct psychiatric disorders over the lifetime. Additionally, cross-sectional studies that have reported data on disorder aggregation (Boyd et al., 1984; Kessler et al., 2005b; Kessler et al., 1994; WHO World Mental Health Survey Consortium, 2004) have been limited by the heterogeneous age composition of the samples and exclusive reliance on retrospective reports to estimate lifetime disorder frequency. Although age heterogeneity is a desirable methodological feature when generalizing from sample to population, this sampling feature can be problematic when estimating the prevalence of disorders that are especially common during certain developmental periods (Wittchen, Höfler, & Merikangas, 1999). Because most psychiatric disorders are first diagnosed before age 30 (Kessler et al., 2005a; Kessler et al., 2005b), the timeframe for lifetime disorder assessment for older persons in cross-sectional studies is longer than for younger participants, thus introducing a possible age-related recall bias as retrospective reports over extended periods are known to produce substantial underestimates of some disorder occurrences (Moffitt et al., 2010; Olino et al., 2012; Wells & Horwood, 2004). Pertinent longitudinal studies (Copeland et al., 2011; Kim-Cohen et al., 2003) have similarly been limited by comparatively small assessment windows (3- or 12-months) relative to the full duration of the longitudinal period, thus also likely resulting in underestimates of positive lifetime disorder histories and disorder aggregation.

This Study

The present research focuses on lifetime disorder aggregation, or counts of individual lifetime disorders, based on a combination of repeated prospective and retrospective assessments conducted over a 14-year interval with a representative community cohort. These assessments produced diagnostic data for each proband for each year of age, spanning the continuum from early childhood to age 30.

If disorder aggregation is common, questions arise about the meaning of such observations for etiological theories and nosology. High rates of disorder aggregation, for example, might indicate common causes among subsets of disorders (Kessler & Price, 1993; Rutter, 2009). Alternatively, high levels of disorder aggregation might reflect the effects of multiple underlying liability dimensions. Recent developments in psychopathology research, for example, converge on the observation that a large number of common psychiatric disorders can be described with reference to broad-band latent domains, internalizing (i.e., anxiety and mood disorders; eating disorders) and externalizing (i.e., oppositional, attentional, and disruptive disorders of childhood; adult antisocial behavior; substance use disorders) (e.g., Beesdo-Baum et al., 2009; Farmer, Seeley, Kosty, & Lewinsohn, 2009; Forbush et al., 2010; Krueger, 1999; Krueger & Markon, 2006; Seeley, Kosty, Farmer, & Lewinsohn, 2011; Slade & Watson, 2006; Vollebergh et al., 2001). A common interpretation of such findings is that these higher-order factors represent “liability spectra,” whereby certain psychiatric disorders are regarded as expressions of latent liabilities that, in turn, explain diagnostic comorbidity or the increased risk for spectrum-related disorders during one’s lifetime (Krueger & Markon, 2006; Watson, 2005). High levels of disorder aggregation might reflect latent level associations with both internalizing and externalizing domains, which would be evident in the patterns of comorbidity observed among persons with two or more lifetime disorders (Angold et al., 1999). As used here, *homotypic aggregation* is most clearly indicated when a domain of related disorders (e.g., internalizing disorders) constitutes an increased risk for disorders within the same domain (e.g., specific anxiety disorders, major depressive disorder). *Heterotypic aggregation*, in contrast, is evident when a domain of related disorders is associated with an increased risk for disorders from another domain (e.g., major depressive disorder, alcohol dependence disorder). In the present study, we will evaluate if disorder aggregation by age 30 is associated with complex patterns of disorder associations from these two domains.

If a majority of diagnosed disorders in a sample were preceded by an earlier disorder, one implication would be that most disorders have foundations established earlier in life. In addition to our examination of this issue in the present research, we also evaluate the association between the onset age associated with the first onset of a psychiatric disorder and subsequent lifetime disorder aggregation. Consistent with prior research (e.g., Copeland et al., 2011; Kim-Cohen et al., 2003), we expect that age at first disorder onset will predict subsequent lifetime aggregation, with those who have a first episode at a younger age being at an especially high risk. Although we have no firm predictions about the association of gender with overall disorder aggregation, we expect based on prior research (e.g., Angst et al., 2005; Copeland et al., 2011; Kim-Cohen et al., 2003) that women compared to men will have more extensive histories of internalizing disorders whereas men will have more lifetime externalizing disorders.

In the present research, we also evaluate whether various forms psychopathology among first-degree relatives (e.g., lifetime histories of mood, anxiety, disruptive behavior, and substance use disorders) significantly account for lifetime disorder aggregation in probands. Milne and colleagues (Milne et al., 2009) previously reported a significant association between family disorder density and disorder recurrence in probands, which suggests that

family disorder density may also have implications for disorder aggregation. Although we expect that more extensive histories of psychopathology among first-degree family members will be positively associated with disorder aggregation in probands, the present research is primarily focused on whether some sets of family-based disorders represent an especially high risk for aggregation.

Finally, in this research we investigate the extent to which lifetime disorder aggregation significantly predicts a wide range of indicators of psychosocial functioning, including mental health care service utilization, personality disorder symptomatology, and several indicators of functional impairment assessed during the last assessment wave (~ age 30). Findings from these analyses will provide information concerning the consequences of lifetime disorder aggregation from a personal and public health perspective. In connection with the primary focus on lifetime disorder aggregation in this research, we will also compute and report the cumulative prevalence of common psychiatric disorders from childhood to age 30. Based on relevant extant research (Copeland et al., 2011; Kim-Cohen et al., 2003; Moffitt et al., 2010), we expect that cumulative rates of lifetime psychiatric disorders over the age range studied will be considerable, with a large majority of cohorts having a history of at least one lifetime psychiatric disorder.

METHOD

Probands

The proband sample for this research was from the Oregon Adolescent Depression Project (OADP; Lewinsohn, Hops, Roberts, Seeley & Andrews, 1993). Initial participant recruitment took place at 9 randomly selected high schools within western Oregon. Figure 1 depicts the study's participation, selection, and attrition rates at each assessment wave. The first assessment wave (T₁) involved a cohort of 1,709 adolescents between the ages of 14 and 19 ($M = 16.6$, $SD = 1.2$), who were again reassessed about one year later (T₂) with a retention rate of 88% ($n = 1,507$). The third assessment wave (T₃) occurred as participants approached their 24th birthday. Due to the extensive costs of reassessing all probands, a stratified sampling procedure was implemented at T₃ whereby all persons with a positive psychiatric history by T₂ ($n = 644$) and a randomly selected subgroup of persons who were negative for any history of mental disorder by T₂ ($n = 457$ of 863 persons) were recruited. To strengthen the ethnic diversity of the sample, all non-Caucasian T₂ participants were recruited for T₃ regardless of T₁ or T₂ diagnostic status. Of the 1,101 probands recruited for a T₃ interview following the implementation of stratification procedures, 941 (85%) completed the evaluation. As T₃ participants approached their 30th birthday, they were recruited to participate in a fourth assessment (T₄). Seventy-four percent of eligible T₂ participants ($n = 816$; 59% women) were reassessed at T₄. This latter group completed each of the 4 assessment waves and served as the reference sample for this research. Most persons within this sample self-identified as Caucasian (89%) and currently married (53%), and a minority of participants (41%) reported having earned a bachelor's degree or a higher. As detailed by Rohde and colleagues (Rohde et al., 2007), attrition over assessment waves was small. Individuals with externalizing behavior disorders or from lower socioeconomic groups were slightly but significantly more likely to discontinue participation.

Axis I Psychiatric Disorder Assessments among Probands

Probands participated in four waves of diagnostic assessments, with the first of these occurring at ~ age 16 (T₁). This interview assessed both current symptoms and lifetime histories (from early childhood) of common Axis I disorders. Beginning with the second assessment wave (T₂), all diagnostic interviews assessed both current and past (since last interview) symptoms of psychiatric disorders. For the first 3 waves, psychiatric disorders

among probands were assessed with the Present Episode and Epidemiologic versions of the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS; Chambers et al., 1985; Orvaschel, Puig-Antich, Chambers, Tabrizi, & Johnson, 1982). At T₄, the Structured Clinical Interview for Axis I *DSM-IV* Disorders–Non-Patient Edition (SCID-NP; First, Spitzer, Gibbon, & Williams, 1994) was used for diagnostic assessments. These interviews were supplemented with the Longitudinal Interval Follow-Up Evaluation (Keller et al., 1987) to assess disorder presence and course since the previous assessment. Symptom reports were evaluated with respect to *DSM-III-R* diagnostic criteria and decision rules at T₁ and T₂ and *DSM-IV* criteria and rules at T₃ and T₄.

Taped interviews were randomly selected from each wave (T₁ = 263, T₂ = 162, T₃ = 190, and T₄ = 124) and evaluated for inter-rater reliability. Diagnostic agreement, as assessed by kappa (κ), was evaluated in instances where disorders were diagnosed at least 10 times by both raters combined. For disorders that met this minimal threshold, the level of agreement among raters was generally good to excellent (*range of* κ = .56 to .89 for 15 separate diagnostic categories; *median* κ = .77; see Farmer et al., 2009, and Seeley et al., 2011, for additional details concerning the reliability analyses).

Psychiatric Disorder Assessments among First-Degree Relatives

Within the T₃ assessment period, first-degree relatives of probands were also evaluated for current and past psychiatric disorders. Diagnostic data were available for 732 of 816 proband families (90%), or 2,414 first-degree relatives (730 biological mothers, 719 biological fathers, 476 female siblings, 489 male siblings).

When feasible, we conducted direct (in-person or phone-based) diagnostic history interviews with family members. Direct interviews were conducted with the SCID-NP for adult relatives and the K-SADS modified for *DSM-IV* for adolescent relatives aged 14 to 18 years and, whenever possible, supplemented with reports from a second family member. When direct interviews were not possible, informant interviews with family members were conducted. These interviews usually involved at least two knowledgeable family members who were questioned individually about another family member's diagnostic history. Informant interviews were based on the Family Informant Schedule and Criteria modified for *DSM-IV* (Mannuzza & Fyer, 1990). All interviews were conducted blind to proband diagnoses. As described in Klein (Klein, Lewinsohn, Seeley, & Rohde, 2001), the best estimate method (Leckman, Sholomskas, Thompson, Belanger, & Weissman, 1982) was used for determining lifetime psychiatric diagnoses for family members. Inter-rater reliability was good to excellent for all diagnostic categories (κ > .69).

Relationships between Disorder Aggregation and Indicators of Psychosocial Functioning at T₄ (~ Age 30)

Mental health care utilization among probands—If a proband received a psychiatric diagnosis during any assessment, interviewers inquired as to whether therapy services were sought or psychotropic medications prescribed and used for mental health-related concerns.

Therapy participation was coded as present if the proband received at least one session in any format (e.g., individual, family, group) for mental health-related issues offered by a range of providers (e.g., psychologist, psychiatrist, school counselor, clergy) in any setting (e.g., inpatient or outpatient). Use of physician-prescribed medications for mental health-related concerns was coded as positive for pharmacotherapy. A composite variable was also generated that corresponded to ever having received any form of treatment (therapy or medications) for mental health reasons.

Personality disorder (Axis II) symptomatology—To help clarify the implications of lifetime disorder aggregation of common Axis I psychiatric disorders, we examined the association that aggregation had with personality disorder pathology among probands. At T₄, symptoms of three personality disorders were assessed with the International Personality Disorder Examination (IPDE; Loranger et al., 1994): antisocial, borderline, and depressive. Because the weighted prevalence of these individual disorder categories was very small in some instances (n s = 17, 4, and 11, respectively), personality disorder dimensional scores rather than diagnoses were used as the primary outcome measures. Interrater reliabilities of dimensional scores, as indexed by intraclass correlation coefficients, were .68, .88, and .88 for antisocial, borderline, and depressive personality disorder dimensional scores, respectively.

Proband psychosocial functioning—Several indicators related to psychosocial functioning were assessed at T₄. These included annual household income, unemployment during the past year (rated on a 6-point scale according to the number of weeks unemployed), history of divorce or separation, relationship quality with family (Perceived Social Support from Family scale; α = .90) (Procidano & Heller, 1983), level of social adjustment during the past two weeks (Social Adjustment Scale; α = .70; higher scores indicate poorer adjustment) (Weissman & Bothwell, 1976), self-reported suicide attempt since T₃, and current functioning as assessed by the *DSM-IV* Global Assessment of Functioning scale.

Statistical Analyses

Participant weighting—Because of the unequal stratified sampling strategy implemented at T₃, Caucasian participants without a psychiatric diagnosis by T₂ were under-sampled at T₃ and T₄. To adjust for this sampling procedure, Caucasian participants with no lifetime diagnosis by T₂ were assigned a weight that reflected the probability of this subgroup being sampled during T₃ and T₄ assessments. The Taylor series linearization method was also implemented in SUDAAN to appropriately adjust standard errors and confidence intervals for the parameter estimates. To avoid artificially inflating our sample size, we computed normalized sampling weights. To derive these, original weights for each participant were multiplied by the size of the reference sample, and then divided by the sum of the original sampling weights. Unless otherwise specified, all findings subsequently presented are based on weighted data.

Disorder aggregation analyses—For probands, the aggregate number of lifetime psychiatric disorders was indexed by the sum of distinct diagnostic categories for which probands met *DSM*-defined criteria. In the computation of this variable, all individual Axis I psychiatric disorder were considered regardless of the presence of other lifetime disorders from the same broad diagnostic domain (e.g., mood disorders; anxiety disorders; disorders usually first diagnosed in infancy, childhood, or adolescence). When participants met lifetime criteria for both abuse and dependence diagnoses in the same substance category (alcohol, cannabis, hard drug), however, the substance use disorder was counted once rather than twice. Recurring episodes of the same disorder were treated as a single occurrence given our focus on disorders rather than episodes, and *DSM* hierarchical diagnostic decision rules were followed when specified.

The proportion (density) of first-degree relatives of probands who met lifetime criteria for specific diagnostic categories was calculated. To derive a family density score for a given disorder, first-degree relatives with a positive history for that disorder were assigned a count of 1, with these counts summed over all first-degree relatives and then divided by the total number of first-degree family members. A similar procedure was used to derive sums for

sets of related disorders (e.g., any anxiety disorder), whereby a count of 1 was assigned to a family member if any disorder within a set of related disorders was diagnosed. This approach, as described in detail in Milne et al. (2008), takes into account family size in the computation of density variable.

Regression analyses were primarily used to evaluate associations with lifetime disorder aggregation. When the predicted variable was based on count data with a preponderance of zero counts, as was the case with the disorder aggregation variable, Poisson regression methods were used.

RESULTS

Proband Attrition over the Study Duration

Across waves, 88% (T_1 to T_2), 85% (T_2 to T_3), and 74% (T_2 to T_4) of eligible participants completed the assessments, with the latter two percentages based on the T_2 panel of 1,507 participants minus the 406 participants from this panel who were deselected as a result of the sample stratification procedures implemented at T_3 . The cumulative rate of attrition over the full duration of the study (T_1 through T_4), however, was more substantial (37% of all eligible participants; see Figure 1). We tested whether attrition was related to disorder aggregation, with the attrition group comprised of participants who (a) dropped out between T_1 and T_2 , (b) were recruited at T_3 but did not participate, or (c) dropped out between T_3 and T_4 . Specifically, we compared the T_4 panel ($n = 816$) to the attrition group ($n = 488$) with respect to disorder aggregation and lifetime prevalence rates for any disorder at T_1 using a Poisson regression and contingency table analyses, respectively. The T_4 panel was not statistically different from the attrition group with respect to disorder aggregation at T_1 ($M = 0.68$, $SD = 1.06$ and $M = 0.76$, $SD = 1.15$, respectively; $\beta = 0.11$, $t = 1.20$, $p = .23$). Similarly, no significant differences were observed in the lifetime prevalence rates for any psychiatric disorder at T_1 between the T_4 panel and the attrition group, which were 48.5% and 48.7%, respectively ($\chi^2 [1, n = 1,303] < 0.01$, $p = .965$).

Distribution and Cumulative Prevalence of Lifetime Psychiatric Disorders among Probands

The lifetime rates of psychiatric disorders among probands through age 30.0 are presented in Table 1. The weighted cumulative lifetime prevalence rate for experiencing any psychiatric disorder listed in the Table is 71%.

Table 2 summarizes lifetime disorder occurrence and aggregation from childhood to age 30. Among probands who met criteria for any lifetime disorder ($n = 580$; 235 men, 345 women), 41% had one lifetime diagnosis, 25% had two, 18% had three, and 16% had 4 or more diagnoses.

A different perspective on lifetime disorder comorbidity can be achieved through a consideration of counts of individual disorder occurrences. Of the 1,310 total diagnosed disorders in the proband sample through age 30, a large majority ($n = 1,081$, or 82.5%) were comorbid with other lifetime disorders; that is, more than 4 out of every 5 psychiatric disorders diagnosed in the sample occurred among persons with a history of at least one other lifetime disorder. Furthermore, most diagnoses were disproportionately concentrated among a subset of the sample: 50% of all lifetime disorders occurred among 19% of the sample, and 75% of all disorders occurred among 36% of the sample.

Gender and Age of Onset of First Psychiatric Disorder as Predictors of Lifetime Disorder Aggregation

Among the 580 persons with positive lifetime disorder histories, weighted rates corresponding to the first incidence of *any* psychiatric disorder for each age range specified are as follows: childhood through age 13.9 = 25.2%; ages 14 to 18.9 = 39.1%; ages 19 to 23.9 = 24.1%; and ages 24 to 30 = 11.6%. When the distribution of all diagnosed lifetime disorders was examined with respect to these age ranges, 17% ($n = 226$) of all disorder onsets occurred prior to age 14.0. Cumulative values increased to 53% ($n = 693$) by age 18.9 and to 81% ($n = 1,061$) by age 23.9. Only 19% ($n = 249$) of the total number of lifetime disorders occurred between ages 24.0 and 30.0.

Poisson regression methods were used to evaluate the prediction of lifetime disorder aggregation from proband gender and age at first disorder onset. The main effect of age emerged as a significant unique predictor of lifetime disorder aggregation ($\beta = -.05$, $X^2 = 44.85$, $p < .001$, $pseudo R^2 = .052$). The main effect of gender ($\beta = .18$, $X^2 = 1.46$, $p = .226$, $pseudo R^2 = .002$) and the interaction of age at first disorder onset and gender ($\beta = -.01$, $X^2 = 1.36$, $p = .244$, $pseudo R^2 = .002$), however, were not statistically significant.

Disorder Aggregation Associations with Disorder Domains

Disorder occurrence and aggregation were also examined with respect to anxiety, mood, disruptive behavior, substance abuse, and eating disorder diagnostic domains as identified in Table 1. Women compared to men received a greater number of lifetime anxiety ($M = 0.37$, $SD = 0.75$ and $M = 0.14$, $SD = 0.41$, respectively; $\beta = 0.98$, $t = 5.51$, $p < .001$), mood ($M = 0.73$, $SD = 0.60$ and $M = 0.39$, $SD = 0.55$, respectively; $\beta = 0.61$, $t = 7.19$, $p < .001$), and eating disorder diagnoses ($M = 0.04$, $SD = 0.22$ and $M = 0.01$, $SD = 0.08$, respectively; $\beta = 1.94$, $t = 2.50$, $p = .013$). Men, when compared with women, received more disruptive behavior ($M = 0.13$, $SD = 0.38$ and $M = 0.06$, $SD = 0.25$, respectively; $\beta = -0.77$, $t = -3.35$, $p < .001$) and substance use ($M = 0.75$, $SD = 0.94$ and $M = 0.56$, $SD = 0.89$, respectively; $\beta = -0.30$, $t = -3.00$, $p = .003$) disorder diagnoses. Very low-base rates of psychotic disorders precluded gender comparisons for this domain.

In addition to the association between disorder aggregation and the above disorder categories, we also examined disorder aggregation based on internalizing (i.e., mood and anxiety disorders, bulimia nervosa) and externalizing (i.e., childhood disruptive behavior disorders, substance use disorders) domain distributions. This analysis involved a series of contingency table analyses to evaluate the frequency of lifetime heterotypic comorbidity (i.e., histories that include lifetime diagnoses from both internalizing *and* externalizing domains) as a function of disorder aggregation category. Among those with only 1 lifetime disorder, internalizing disorders (69.7%) were more commonly diagnosed than externalizing disorders (30.3%). For those with 2, 3, and 4 lifetime disorders, with these groups partially overlapping, the rates of heterotypic comorbidity were 66.1%, 76.4%, and 91.5%, respectively. As anticipated, more extensive lifetime disorder histories are characterized by an incrementally higher likelihood of demonstrating greater liability for the two major domains of psychopathology examined here.

Table 3 presents a more fine-grained analysis of the likelihood of a given psychiatric disorder given membership in one of the four aggregation categories associated with a positive psychiatric history (i.e., 1, 2, 3, 4 lifetime disorders). All disorders listed in the table displayed a significant linear association with the aggregation variable. Lifetime disorder categories 2, 3, and 4 displayed similar patterns whereby the most common lifetime disorders for each of these three groups were major depressive disorder (MDD) and alcohol use disorders (AUD). The group with 3 lifetime disorders ($n = 105$) resembled the

group with 4 lifetime disorders ($n = 94$) in that the four most probable diagnoses were the same for both groups: MDD, AUD, cannabis use disorders (CUD), and hard drug use disorders (DRG). The main difference between these latter two groups was found in the probability of each of the three substance use disorder diagnoses, with AUD, CUD, and DRG each significantly more likely in the 4 lifetime disorder group compared to the group with 3 lifetime disorders. Overall, these findings suggest that harmful substance abuse patterns coupled with major depressive disorder are common features among those with more extensive lifetime disorder histories.

Density of Psychiatric Disorders among First-Degree Relatives as Predictors of Lifetime Disorder Aggregation in Probands

Lifetime prevalence rates of specific psychiatric disorders among first-degree relatives, and kappa coefficients that index their reliability of assessment, are presented in Table 4. Within a set of Poisson regression analyses, the family densities of specific psychiatric disorder domains with values $> .01$ were evaluated as predictors of the aggregate number of lifetime disorders among probands. Family densities of these domains were first evaluated individually after controlling for proband gender. Family densities of anxiety ($\beta = .56$, $X^2 = 16.96$, $p < .001$, $\text{pseudo } R^2 = .022$), mood ($\beta = .70$, $X^2 = 56.78$, $p < .001$, $\text{pseudo } R^2 = .072$), disruptive behavior ($\beta = .98$, $X^2 = 23.80$, $p < .001$, $\text{pseudo } R^2 = .028$), and substance use ($\beta = .83$, $X^2 = 79.37$, $p < .001$, $\text{pseudo } R^2 = .100$) disorders were each individually related to lifetime disorder aggregation in probands.

As a follow-up to the above analyses, unique effects associated with each family density domain after controlling for gender were evaluated with hierarchical Poisson regression procedures. Substance use ($\beta = .67$, $X^2 = 45.13$, $p < .001$, $\text{pseudo } R^2 = .059$), mood ($\beta = .53$, $X^2 = 26.84$, $p < .001$, $\text{pseudo } R^2 = .035$), and disruptive behavior ($\beta = .67$, $X^2 = 10.72$, $p = .001$, $\text{pseudo } R^2 = .013$) disorders emerged as significant unique predictors. When all family density predictors were entered into the same multivariate model to derive the overall magnitude of predictor effects, the model was significant ($X^2 = 132.22$, $p < .001$, $\text{pseudo } R^2 = .147$). Relationships between Disorder Aggregation and Indicators of Psychosocial Functioning at T_4

History of mental health care utilization—There was an incremental relationship between the number of lifetime diagnoses and the likelihood of receiving either therapy or psychotropic medication (Table 5). Among those who received services, disproportionately more were women (60%) than men (40%), ($X^2 = 23.06$, $p < .001$, odds ratio = 2.28, 95% confidence interval = 1.62 – 3.19).

Personality disorder pathology at T_4 —We evaluated the associations between disorder aggregation and antisocial, depressive, and borderline personality dimensional scores assessed at T_4 with a series of multiple regression models in which personality disorder dimensional scores were regressed on disorder aggregation in probands after controlling for proband gender. Dimensional scores for antisocial ($\beta = .08$, $t = 2.33$, $p = .020$, $R^2 = .007$), depressive ($\beta = .39$, $t = 11.93$, $p < .001$, $R^2 = .147$), and borderline personality disorders ($\beta = .51$, $t = 16.85$, $p < .001$, $R^2 = .259$) were each independently related to lifetime disorder aggregation in probands.

Unique effects were investigated in a series of sequential multiple regression models. Gender and dimensional scores from the remaining two personality disorders, other than the predicted score, were entered as covariates in the first step to control for covariation with other forms of personality disorder pathology. Disorder aggregation was entered in the second step. Disorder aggregation significantly predicted dimensional scores for depressive

($\beta = .13$, $t = 3.95$, $p < .001$, $R^2 = .013$) and borderline ($\beta = .34$, $t = 11.62$, $p < .001$, $R^2 = .094$) personality disorders after controlling for gender and the remaining personality disorder dimensional scores. Disorder aggregation had a more sizeable effect on borderline personality disorder features than depressive personality disorder features as indicated by associated R^2 values.

Other indicators of psychosocial functioning or impairment at T₄—Lifetime disorder aggregation was evaluated with respect to the prediction of T₄-assessed psychosocial functioning. In a series of hierarchical regression analyses, the sum of lifetime psychiatric disorders served as the predictor variable, with the predicted variable in each analysis corresponding to an impairment- or psychosocial functioning-related variable. Variance due to proband gender was controlled prior to the evaluation of predictor variables. As illustrated in Table 6, all ordinal impairment-related variables were significantly related to disorder aggregation. Two dichotomous variables, ever divorced/separated ($\beta = .28$, $X^2 = 27.56$, $p < .001$, *pseudo* $R^2 = .033$; odds ratio = 1.32, 95% confidence interval = 1.20 – 1.48) and suicide attempt since T₃ ($\beta = .64$, $X^2 = 46.71$, $p < .001$, *pseudo* $R^2 = .055$; odds ratio = 1.90, 95% confidence interval = 1.58 – 2.29), were both significantly predicted by disorder aggregation in separate logistic regression analyses.

DISCUSSION

There were five primary sets of findings that emerged from this research. First, over 70% of the proband cohort had a lifetime psychiatric disorder by age 30. This finding and similar findings reported by others (Copeland et al., 2011; Kim-Cohen et al., 2003; see also Moffitt et al., 2010) suggest that the experience of psychiatric disorders up to age 30 is very common in the general population.

Second, and consistent with findings from cross-sectional studies (Kessler et al., 2005b; Kessler et al., 1994; WHO World Mental Health Survey Consortium, 2004), lifetime psychiatric disorders were highly concentrated among a relatively small subset of the sample. Three-quarters of all psychiatric disorders occurred among 37% of the sample, and 4 out of 5 disorders occurred among persons who met criteria for at least one other lifetime disorder. Consistent with other reports (Copeland et al., 2011; Kim-Cohen et al., 2003; Kessler et al., 2005a), findings from this study also indicate that (a) a majority of individuals with a positive lifetime psychiatric history experienced their first disorder onset during or before adolescence, (b) most diagnosed disorders occurred between the ages of 14 to 24, and (c) age of first disorder onset significantly predicted the degree of subsequent lifetime disorder aggregation by age 30.

Third, and consistent with similar findings from cross-sectional (Kessler et al., 2005b; Seedat et al., 2010) and longitudinal studies of representative birth cohorts (Angst et al., 2005; Copeland et al., 2011; Kim-Cohen et al., 2003), women by age 30 were more likely to than men to have histories of internalizing disorders (i.e., anxiety, mood, and eating disorders) whereas men were more likely than women to have externalizing disorders (i.e., disruptive behavior and substance use disorders). Although gender did not predict overall disorder aggregation in the present research, increasing levels of disorder aggregation were associated with incrementally greater degrees of heterotypic aggregation, as defined by the lifetime comorbidity of domain-related internalizing and externalizing disorders. Major depressive disorder and alcohol use disorder were the two most commonly occurring diagnoses among those with histories of 2, 3, or 4+ psychiatric disorders.

Fourth, lifetime disorder aggregation in probands was significantly associated with lifetime psychiatric disorder densities among first-degree relatives. These findings are similar to

those reported by Milne and colleagues (Milne et al., 2009) who found an association between family disorder density and disorder recurrence in probands. Apart from family-based anxiety disorders that provided only redundant information to the prediction of proband disorder aggregation, there is little evidence of risk specificity associated with sets of family-based disorders in relation to disorder aggregation. Family-based mood, substance use, and disruptive behavior disorders were each unique and significant predictors of disorder aggregation in probands, although the magnitude of overall effects was greatest for substance use disorders.

Finally, lifetime disorder aggregation predicted several indicators of psychosocial functioning at T₄. Among these were findings from adjusted analyses that indicated that depressive and borderline personality disorder dimensional scores were significantly predicted by disorder aggregation, with scores from the latter disorder category demonstrating a greater overall effect. Antisocial personality disorder features were likely not predicted by disorder aggregation after controlling depressive and borderline dimensional scores because this disorder is robustly associated with the externalizing domain of Axis I psychopathology (Farmer et al., 2009; Krueger & Markon, 2006; Røysamb et al., 2011). In contrast, borderline personality disorder (Eaton et al., 2011; Røysamb et al., 2011; Zimmerman & Mattia, 1999) and depressive personality disorder (McDermut, Zimmerman, & Chelminski, 2003; Røysamb et al., 2011) have high rates of comorbidity with a broad range of Axis I disorders, including those that belong to both internalizing and externalizing disorder domains. Since higher levels of disorder aggregation in this study were linked to more frequent instances of heterotypic aggregation involving both internalizing and externalizing disorders, it is perhaps not surprising that personality disorder constructs with extensive associations with both broadband domains were significantly predicted by disorder aggregation.

Lifetime disorder aggregation also evidenced a dose-response relationship with the utilization of mental health care services, whereby the presence of an additional lifetime disorder was associated with an incrementally higher probability of receiving some mode of treatment. This finding mirrors the observation that disorder severity is often correlated with the probability of receiving some form of therapy (Bijl et al., 2003; WHO World Mental Health Survey Consortium, 2004), and is consistent with suggestions psychiatric disorders in clinical samples are accompanied by greater overall psychopathology when compared with psychiatric disorders observed community samples (Berkson, 1946; Cohen & Cohen, 1984). A noteworthy related finding, one similar to observations reported with other community samples (Kessler et al., 1994), is that most persons in the present study who met criteria for one or two lifetime disorders did not receive any mental health treatment related to their diagnoses.

Although there are several strengths associated with this research, there are also limitations. First, the racial and ethnic diversity of the sample, although representative of the race/ethnic distribution of the region sampled, is nonetheless limited. Second, different interview methods and versions of *DSM* were used to assess and diagnose disorders across waves. Changes in diagnostic criteria and assessment approaches could have introduced method bias into the study that, in turn, differentially influenced decisions concerning disorder occurrences. Third, multiple diagnostic assessments over 14-year span likely reduced biases associated with retrospective recall. Nonetheless, such biases likely influenced responding to some degree given the time interval (~ 6 years) between some assessment waves and, particularly, for disorders that occurred during childhood, which were first evaluated with retrospective assessments at ~ age 16. Fourth, although overall sample attrition was relatively modest, it did favor persons with externalizing disorders and from lower socioeconomic groups. We note, however, that attrition after T₁ was unrelated to disorder

aggregation at T₁, suggesting that aggregation alone may not have been a significant source of bias in participant attrition over time. Fifth, youth self-reports of symptoms associated with childhood externalizing behavior disorders often result in lower symptom endorsements when compared to parent or teacher reports (e.g., Fabrega, Ulrich, & Loeber, 1996; Youngstrom, Loeber, & Stouthamer-Loeber, 2000). Among adolescents, however, the accuracy of symptom reports may be greater when based on youth self-reports versus reports from knowledgeable informants (Cantwell, Lewinsohn, Rohde, & Seeley, 1997). In the present study, the lifetime prevalence of childhood externalizing behavior disorders is lower than reported elsewhere (e.g., Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Merikangas et al., 2010), suggesting that several participants with histories of these behavior disorders were not detected. Such under-detection is most likely a joint consequence of the exclusive use of youth self-reports in the assessment of childhood externalizing disorder symptoms and the extensive age gap between the developmental period during which these disorders typically first emerge and the age at which probands were first assessed (e.g., Moffitt et al., 2010). Sixth, because of the right-hand censoring of the data at age 30, and because new disorder occurrences are frequently observed after this age (Kessler et al., 2005a), lifetime disorder incidence and aggregation rates reported here are likely underestimates compared to what would be observed had assessments been extended through old age. Collectively, these latter four study limitations (modest participant attrition favoring individuals with externalizing disorders, lengthy time intervals between some diagnostic assessments, likely underreporting or under-detection of externalizing disorder histories, right-hand censoring of data) strongly suggest that the cumulative lifetime prevalence of psychiatric disorders and lifetime disorder aggregation rates from childhood through the full range of adulthood are substantially greater than reported here.

Overall, findings presented here and related observations presented elsewhere (Copeland et al., 2011; Kim-Cohen et al., 2003; Kessler et al., 2005b; WHO World Mental Health Survey Consortium, 2004) suggest that lifetime disorder aggregation is relatively common, typically begins before adulthood, and should be regarded as a relevant consideration in etiological theories, disorder taxonomies, prevention programs, and treatment models. Future research might consequently emphasize the identification of possible underlying mechanisms that account for lifetime disorder aggregation. Possible mechanisms are suggested from behavioral views of response covariation, specifically the concept of *functional response domains*. Functional responses domains consist of groups of behaviors that, although different in form or how they are expressed, share functional relatedness in the outcomes they produce (Follette, Naugle, & Linnerooth, 2000; Hayes, Wilson, Gifford, Follette, & Strosahl, 1996). Although the psychiatric disorders evaluated in the present research are topographically distinct (i.e., they vary in form or surface level features as evident in the diverse sets of diagnostic criteria), the constellation of behaviors, experiences, and symptoms that define these categories may be instrumental in producing similar outcomes. Three partially overlapping functional response domains, in particular, may contribute to the risk for disorder aggregation: (a) behavioral excesses, (b) escape and avoidance response repertoires, and (c) approach deficits. These response domains have been implicated as having roles in the onset, experience, and maintenance of a wide variety of psychiatric disorders and associated problem behaviors (Aldao, Nolen-Hoeksema, & Schweizer, 2010; Barlow, 2000; Hayes et al., 1996; Scotti, Morris, McNeil, & Hawkins, 1996; Trew, 2011), including the most prevalent disorders among those with especially pronounced aggregation histories in the present research (i.e., major depressive disorder, panic disorder, post-traumatic stress disorder, and alcohol-, cannabis-, and hard drug-use disorders).

Behavioral excesses refer to forms of behavior that are excessive in terms of frequency, intensity, and/or duration. Behaviors associated with this functional response domain are maintained by the positive reinforcing consequences they produce, which include the

activation of endogenous reward centers in the case of some substance use and behavior disorders (e.g., Bandelow, Schmahl, Falkai, & Wedekind, 2010; Brewer & Potenza, 2008; Leshner, 1997) and the provision of social reinforcers (e.g., attention, notice from others) for some childhood and adult internalizing and externalizing behaviors (e.g., Kearney & Albano, 2004; Nock & Prinstein, 2004; Scotti et al., 1996; Wedig & Nock, 2010).

Given the functional properties typically associated with behavioral excesses, it is perhaps not surprising that the most successful therapies for behavioral or psychiatric disorders within this functional domain include those that remove or alter the reinforcing properties of problematic behaviors targeted for weakening or elimination. Examples of such interventions include the use of opioid receptor antagonists for disorders associated with the activation endogenous reward centers (e.g., Bandelow et al., 2010; Krupitsky et al., 2011; Pettinati et al., 2006), response cost interventions that result in the removal of social reinforcers contingent on displays of targeted behaviors (e.g., the time out procedure [Friman & Finney, 2003], which has been adapted for use in reducing high priority target behaviors in treatment approaches such as dialectical behavior therapy [Linehan, 1993]), and differential reinforcement procedures (e.g., as exemplified by voucher-based contingency management programs for substance use disorders [Higgins, Heil, & Sigmon, 2013; Iguchi, Belding, Morral, Lamb, & Husband, 1997]).

Escape and avoidance response domains can be divided into at least two overlapping subcategories: behavioral avoidance and experiential avoidance. Behavioral avoidance refers to actions that result in avoiding, evading, or escaping situations, events, persons, or things experienced as aversive. Behavioral avoidance can be either active (e.g., fleeing the mall upon noticing the first signs of a possible panic attack) or passive (e.g., not responding to an invitation to join co-workers at a picnic for someone with significant social anxiety). Experiential avoidance is characterized by an unwillingness to remain in contact with private experiences such as troubling physiological sensations (e.g., elevated heart rate, shortness of breath, dizziness) and painful emotions, thoughts, or memories (Hayes et al., 1996), and can vary in the extent to which avoidance is active (e.g., consuming alcohol to alter painful emotions) or passive (e.g., dissociating in response to upsetting memories).

When avoidance-related behaviors are effective in attenuating or terminating aversive experiences, they often become negatively reinforced behaviors due to the short-term relief they produce. Avoidance coping, however, precludes the opportunity to actively address or solve life problems and inevitably results in the avoidance of an increasingly wider range of contexts and the expansion of behavioral avoidance repertoires. Avoidance has a central role in several theories of the development and maintenance of anxiety disorders (e.g., Barlow, 2000; Gray & McNaughton, 2000), depressive disorders (e.g., Ferster, 1973; Lewinsohn, 1974; Trew, 2011), and substance use disorders (e.g., Aldao et al., 2010; Hayes et al., 1996), and the blocking of avoidance tendencies is a central feature of many effective therapies for these conditions (e.g., exposure therapy in the treatment of post-traumatic stress disorder [Foa et al., 2005] and panic disorder [Barlow & Craske, 1994]; behavioral activation therapy for depression [Dimidjian, Barrera, Martell, Muñoz, & Lewinsohn, 2011]; exposure to drinking urges and cravings in the treatment of alcohol use disorders [Vollstädt-Klein et al., 2011; Witkiewitz, Bowen, & Donovan, 2011]).

Approach deficits refer to low rates of participation in actions that increase the likelihood of positive reinforcement or rewarding outcomes. Individuals who generally refrain from engaging in approach behaviors are consequently less likely to obtain rewards or positive reinforcers for behavior (e.g., experience pleasant events, have success experiences, achieve goals, realize long-term plans). Approach deficits are central features in theories of anxiety and associated disorders (e.g., Fowles, 2001; Gray & McNaughton, 2000). In addition to

blocking escape and avoidance response tendencies, exposure therapies for anxiety disorders also usually involve assisting clients in developing action tendencies (i.e., approach behavior) inconsistent with anxiety-based response tendencies (Barlow, Allen, & Choate, 2004). Approach deficits have also figured prominently in several behavioral theories of depression, namely by their effect of limiting access to potential rewards or positive reinforcers (e.g., Dimidjian, Barrera, Martell, Muñoz, & Lewinsohn, 2011; Ferster, 1973; Jacobson, Martell, & Dimidjian, 2001; Lewinsohn, 1974; Trew, 2011). Given their theoretical relevance to depression development and maintenance, approach deficits constitute a core target in behavioral interventions for depression (Lewinsohn, Antonuccio, Steinmetz-Breckenridge, & Teri, 1984; Martell, Dimidjian, & Herman-Dunn, 2010). Approach deficits may also have a role in exacerbating hazardous substance use. Acute negative affect often precedes substance use occasions (e.g., Cooper, Skinner, Frone, & Mudar, 1992; Witkiewitz & Villarroel, 2009), for example, particularly among persons with fewer supportive or intimate relationships (Hussong, Hicks, Levy, & Curran, 2001) or who have positive expectancies concerning the reinforcing effects of substance use (Cooper, Skinner, Frone, & Mudar, 1992). Because substance consumption can provide relief from negative mood states and potentiate feelings of euphoria, addictions treatment specialists have stressed the need to counter the reinforcing effects of substance use with the development of alternative approach repertoires that produce a broad range of naturally reinforcing outcomes (e.g., the community reinforcement approach; Miller, Forcehimes, & Zweben, 2011).

Extensive disorder aggregation among some persons might reflect the influence of one or more of these functional response domains. Careful idiographic assessments followed by the application of relevant domain-related interventions might be particularly useful among multi-problem clients with extensive disorder histories. Other possible etiologically-relevant factors, such as early exposure to childhood adversities (Green et al., 2010), vulnerability to traits such as neuroticism or negative emotion (Lahey, 2008), or the activities of dissociable neural substrates that mediate the expression of related clinical signs or symptoms (Corr, 2008; Depue & Lenzenweger, 2006) might also be examined for their contribution to lifetime disorder aggregation.

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REFERENCES

- Aldao A, Nolen-Hoeksema S, Schweizer S. Emotion-regulation strategies across psychopathology: A meta-analytic review. *Clinical Psychology Review*. 2010; 30:217–237. [PubMed: 20015584]
- Angold A, Costello EJ, Erkanli A. Comorbidity. *Journal of Child Psychology and Psychiatry*. 1999; 40:57–87. [PubMed: 10102726]
- Angst J, Gamma A, Neuenschwander M, Ajdacic-Gross V, Eich D, Rössler W, Merikangas KR. Prevalence of mental disorders in the Zurich Cohort Study: a twenty year prospective study. *Epidemiologia e Psichiatria Sociale*. 2005; 14:68–76. [PubMed: 16001703]
- Bandelow B, Schmahl C, Falkai P, Wedekind D. Borderline personality disorder: A dysregulation of the endogenous opioid system? *Psychological Review*. 2010; 117:623–636. [PubMed: 20438240]
- Barlow DH. Unraveling the mysteries of anxiety and its disorders from the perspective of emotion theory. *American Psychologist*. 2000; 55:1247–1263. [PubMed: 11280938]
- Barlow DH, Allen LB, Choate ML. Toward a unified treatment for emotional disorders. *Behavior Therapy*. 2004; 35:205–230.
- Barlow, DH.; Craske, MG. *Mastery of your anxiety and panic – II*. Graywind/Psychological Corporation; San Antonio, TX: 1994.

- Beesdo-Baum K, Höfler M, Gloster AT, Klotsche J, Lieb R, Beauducel A, et al. The structure of common mental disorders: A replication study in a community sample of adolescents and young adults. *International Journal of Methods in Psychiatric Research*. 2009; 18:204–220. [PubMed: 20024895]
- Berkson J. Limitations of the application of fourfold table analysis to hospital data. *Biometrics Bulletin*. 1946; 2:47–53. [PubMed: 21001024]
- Bijl RV, de Graaf R, Hiripi E, Kessler RC, Kohn R, Offord DR, et al. The prevalence of treated and untreated mental disorders in five countries. *Health Affairs*. 2003; 22:122–133. [PubMed: 12757277]
- Boyd JH, Burke JD Jr, Gruenberg E, Holzer CE, Rae DS, George LK, et al. Exclusion criteria of DSM-III: A study of co-occurrence of hierarchy-free syndromes. *Archives of General Psychiatry*. 1984; 41:983–989. [PubMed: 6477056]
- Brewer JA, Potenza MN. The neurobiology and genetics of impulse control disorders: Relationships to drug addictions. *Biochemical Pharmacology*. 2008; 75:63–75. [PubMed: 17719013]
- Cantwell DP, Lewinsohn PM, Rohde P, Seeley JR. Correspondence between adolescent report and parent report of psychiatric diagnostic data. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1997; 36:610–619. [PubMed: 9136495]
- Chambers WJ, Puig-Antich J, Hirsch M, Paez P, Ambrosini PJ, Tabrizi MA, et al. The assessment of affective disorders in children and adolescents by semistructured interview: Test-retest reliability of the Schedule for Affective Disorders and Schizophrenia for School-Age Children, present episode version. *Archives of General Psychiatry*. 1985; 42:696–702. [PubMed: 4015311]
- Cohen P, Cohen J. The clinician's illusion. *Archives of General Psychiatry*. 1984; 41:1178–1182. [PubMed: 6334503]
- Cooper ML, Russell M, Skinner JB, Frone MR, Mudar P. Stress and alcohol use: Moderating effects of gender, coping, and alcohol expectancies. *Journal of Abnormal Psychology*. 1992; 101:139–152. [PubMed: 1537960]
- Copeland WE, Shanahan L, Costello EJ, Angold A. Childhood and adolescent psychiatric disorders as predictors of young adult disorders. *Archives of General Psychiatry*. 2010; 66:764–772. [PubMed: 19581568]
- Copeland WE, Shanahan L, Costello EJ, Angold A. Cumulative prevalence of psychiatric disorders by young adulthood: a prospective cohort analysis from the Great Smoky Mountains Study. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2011; 50:252–261. [PubMed: 21334565]
- Corr, PJ. *The reinforcement sensitivity theory of personality*. Cambridge University Press; New York: 2008.
- Costello EJ, Mustillo S, Erkanli A, Keeler G, Angold A. Prevalence and development of psychiatric disorders in childhood and adolescence. *Archives of General Psychiatry*. 2003; 60:837–844. [PubMed: 12912767]
- Depue, RA.; Lenzenweger, MF. A multidimensional neurobehavioral model of personality disturbance. In: Krueger, RF.; Tackett, JL., editors. *Personality and psychopathology*. Guilford Press; New York: 2006. p. 210-261.
- Dimidjian S, Barrera M, Martell C, Muñoz RF, Lewinsohn PM. The origins and current status of behavioral activation treatments for depression. *Annual Review of Clinical Psychology*. 2011; 7:1–38.
- Eaton NR, Krueger RF, Keyes KM, Skodol AE, Markon KE, Grant BF, Hasin DS. Borderline personality disorder co-morbidity: relationship to the internalizing-externalizing structure of common mental disorders. *Psychological Medicine*. 2011; 41:1041–1050. [PubMed: 20836905]
- Fabrega H, Ulrich R, Loeber R. Adolescent psychopathology as a function of informant and risk status. *Journal of Nervous and Mental Disease*. 1996; 184:27–34. [PubMed: 8551286]
- Farmer RF, Seeley JR, Kosty DB, Lewinsohn PM. Refinements of the hierarchical structure of externalizing psychiatric disorders: Patterns of lifetime liability from mid-adolescence through early adulthood. *Journal of Abnormal Psychology*. 2009; 118:699–710. [PubMed: 19899840]
- Fergusson DM, Boden JM. Cannabis use and later life outcomes. *Addiction*. 2008; 103:969–976. [PubMed: 18482420]

- Ferster CB. A functional analysis of depression. *American Psychologist*. 1973; 28:857–870. [PubMed: 4753644]
- First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. Structured clinical interview for Axis I DSM-IV disorders, Non-patient Edition. Biometrics Research Department; New York: 1994.
- Foa EB, Hembree EA, Cahill SP, Rauch SAM, Riggs DS, Feeny NC, et al. Randomized trial of prolonged exposure for posttraumatic stress disorder with and without cognitive restructuring: Outcome at academic and community clinics. *Journal of Consulting and Clinical Psychology*. 2005; 73:953–964. [PubMed: 16287395]
- Follette, WC.; Naugle, AE.; Linnerooth, PJN. Functional alternatives to traditional assessment and diagnosis. In: Dougher, MJ., editor. *Clinical behavior analysis*. Context Press; Reno, NV: 2000. p. 99-125.
- Forbush KT, South SC, Krueger RF, Iacono WG, Clark LA, Keel PK, Legrand LN, Watson D. Locating eating pathology within an empirical diagnostic taxonomy: Evidence from a community-based sample. *Journal of Abnormal Psychology*. 2010; 119:282–292. [PubMed: 20455601]
- Fowles, DC. Biological variables in psychopathology: A psychobiological perspective. In: Sutker, PB.; Adams, HE., editors. *Comprehensive handbook of psychopathology*. 3rd ed. Kluwer/Plenum; New York: 2001. p. 85-104.
- Friman, PC.; Finney, JW. Time-out (and time-in). In: O'Donohue, W.; Fisher, JE.; Hayes, SC., editors. *Cognitive behavior therapy: Applying empirically supported techniques in your practice*. Wiley; Hoboken, NJ: 2003. p. 429-435.
- Gray, JA.; McNaughton, N. *The neuropsychology of anxiety*. 2nd ed. Oxford University Press; London: 2000.
- Green JG, McLaughlin KA, Berglund PA, Gruber MJ, Sampson NA, Zaslavsky AM, et al. Childhood adversities and adult psychiatric disorders in the National Comorbidity Survey Replication I: Associations with first onset of DSM-IV disorders. *Archives of General Psychiatry*. 2010; 67:113–123. [PubMed: 20124111]
- Hayes SC, Wilson KG, Gifford EV, Follette VM, Strosahl K. Experiential avoidance and behavioral disorders: A functional dimensional approach to diagnosis and treatment. *Journal of Consulting and Clinical Psychology*. 1996; 64:1152–1168.
- Higgins, ST.; Heil, SH.; Sigmon, SC. Voucher-based contingency management in the treatment of substance use disorders. In: Madden, GJ., editor. *APA handbook of behavior analysis*. Vol. Vol. 2. American Psychological Association; Washington, DC: 2013. p. 481-500.
- Hussong AM, Hicks RE, Levy SA, Curran PJ. Specifying the relations between affect and heavy alcohol use among young adults. *Journal of Abnormal Psychology*. 2001; 110:449–461. [PubMed: 11502088]
- Iguchi MY, Belding MA, Morral AR, Lamb RJ, Husband SD. Reinforcing operants other than abstinence in drug abuse treatment: An effective alternative for reducing drug use. *Journal of Consulting and Clinical Psychology*. 1997; 65:421–428. [PubMed: 9170765]
- Jacobson NS, Martell CR, Dimidjian S. Behavioral activation treatment for depression: Returning to contextual roots. *Clinical Psychology: Science and Practice*. 2001; 8:255–270.
- Kearney CA, Albano A.M. The functional profiles of school refusal behavior: Diagnostic aspects. *Behavior Modification*. 2004; 28:147–161. [PubMed: 14710711]
- Keller MB, Lavori PW, Friedman B, Nielsen E, Endicott J, McDonald-Scott PA. The Longitudinal Interval Follow-up Evaluation: A comprehensive method for assessing outcome in prospective longitudinal studies. *Archives of General Psychiatry*. 1987; 44:540–548. [PubMed: 3579500]
- Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry*. 2005a; 62:593–602. [PubMed: 15939837]
- Kessler RC, Chiu W-T, Demler O, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry*. 2005b; 62:617–627. [PubMed: 15939839]
- Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: Results from the

- National Comorbidity Survey. *Archives of General Psychiatry*. 1994; 51:8–19. [PubMed: 8279933]
- Kessler RC, Ormel J, Petukhova M, McLaughlin KA, Green JG, Russo LJ, et al. Development of lifetime comorbidity in the World Health Organization World Mental Health Surveys. *Archives of General Psychiatry*. 2011; 68:90–100. [PubMed: 21199968]
- Kessler RC, Price R. Primary prevention of secondary disorders: A proposal and agenda. *American Journal of Community Psychology*. 1993; 21:607–631. [PubMed: 8192124]
- Kim-Cohen J, Caspi A, Moffitt TE, Harrington H, Milne BJ, Poulton R. Prior juvenile diagnoses in adults with mental disorder: Developmental follow-back of a prospective-longitudinal cohort. *Archives of General Psychiatry*. 2003; 60:709–717. [PubMed: 12860775]
- Klein DN, Lewinsohn PM, Seeley JR, Rohde P. Family study of major depressive disorder in a community sample of adolescents. *Archives of General Psychiatry*. 2001; 58:13–20. [PubMed: 11146753]
- Krueger RF. The structure of common mental disorders. *Archives of General Psychiatry*. 1999; 56:921–926. [PubMed: 10530634]
- Krueger RF, Markon KE. Reinterpreting comorbidity: A model-based approach to understanding and classifying psychopathology. *Annual Review of Clinical Psychology*. 2006; 2:111–133.
- Krupitsky E, Nunes EV, Ling W, Illeperuma A, Gastfriend DR, Silverman BL. Injectable extended-release naltrexone for opioid dependence: a double-blind, placebo-controlled, multicentre randomised trial. *Lancet*. 2011; 377:1506–1513. [PubMed: 21529928]
- Lahey BB. The public health significance of neuroticism. *American Psychologist*. 2008; 64:241–256. [PubMed: 19449983]
- Lahey BB, Rathouz PJ, Van Hulle C, Urbano RC, Krueger RF, Applegate B, et al. Testing structural models of DSM-IV symptoms of common forms of child and adolescent psychopathology. *Journal of Abnormal Child Psychology*. 2008; 36:187–206. [PubMed: 17912624]
- Leckman JF, Sholomskas D, Thompson D, Belanger A, Weissman MM. Best estimate of lifetime psychiatric diagnosis: A methodological study. *Archives of General Psychiatry*. 1982; 39:879–883. [PubMed: 7103676]
- Leshner AI. Addiction is a brain disease, and it matters. *Science*. 1997; 278:45–37. [PubMed: 9311924]
- Lewinsohn, PM. A behavioral approach to depression. In: Friedman, RM.; Katz, MM., editors. *The psychology of depression: Contemporary theory and research*. Wiley; New York: 1974. p. 157-185.
- Lewinsohn, PM.; Antonuccio, DO.; Steinmetz-Breckenridge, J.; Teri, L. *The coping with depression course*. Castalia; Eugene, OR: 1984.
- Lewinsohn PM, Hops H, Roberts RE, Seeley JR, Andrews JA. Adolescent psychopathology: I. Prevalence and incidence of depression and other DSM-III-R disorders in high school students. *Journal of Abnormal Psychology*. 1993; 102:133–144. [PubMed: 8436689]
- Linehan, MM. *Cognitive-behavioral treatment of borderline personality disorder*. Guilford; New York: 1993.
- Loranger AW, Sartorius N, Andreoli A, Berger P, Buchheim P, Channabasavanna SM, et al. The International Personality Disorder Examination: The World Health Organization/Alcohol, Drug Abuse, and Mental Health Administration international study of personality disorders. *Archives of General Psychiatry*. 1994; 51:215–224. [PubMed: 8122958]
- Mannuzza, S.; Fyer, AJ. *Family informant schedule and criteria (FISC)*, July 1990 revision. Anxiety Disorders Clinic, New York State Psychiatric Institute; New York: 1990.
- Markon KE. Modeling psychopathology structure: a symptom-level analysis of Axis I and II disorders. *Psychological Medicine*. 2010; 40:273–288. [PubMed: 19515267]
- Martell, CR.; Dimidjian, S.; Herman-Dunn, R. *Behavioral activation for depression: A clinician's guide*. Guilford Press; New York: 2010.
- Maser, JD.; Cloninger, CR. *Comorbidity of mood and anxiety disorders*. American Psychiatric Press; Washington, DC: 1990.
- McDermut W, Zimmerman M, Chelminski I. The construct validity of depressive personality disorder. *Journal of Abnormal Psychology*. 2003; 112:49–60. [PubMed: 12653413]

- Merikangas KR, He J-P, Burstein M, Swanson SA, Avenevoli S, Cui L, Benjet C, et al. Lifetime prevalence of mental disorders in U.S. adolescents: Results from the National Comorbidity Survey Replication--Adolescent Supplement (NCS-A). *Journal of the American Academy of Child & Adolescent Psychiatry*. 2010; 49:980–989. [PubMed: 20855043]
- Miller, WR.; Forcehimes, AA.; Zweben, A. Treating addiction: A guide for professionals. Guildford Press; New York: 2011.
- Milne BJ, Caspi A, Harrington H, Poulton R, Rutter M, Moffitt TE. Predictive value of family history on the severity of illness: The case for depression, anxiety, alcohol dependence, and drug dependence. *Archives of General Psychiatry*. 2009; 66:738–747. [PubMed: 19581565]
- Milne BJ, Moffitt TE, Crump R, Poulton R, Rutter M, Sears MR, et al. How should we construct psychiatric family history scenes? A comparison of alternative approaches from the Dunedin Family Health History Study. *Psychological Medicine*. 2008; 38:1793–1802. [PubMed: 18366822]
- Moffitt TE, Caspi A, Kokaua J, Milne BJ, Polanczyk G, Poulton R. How common are common mental disorders? Evidence that lifetime prevalence rates are doubled by prospective *versus* retrospective ascertainment. *Psychological Medicine*. 2010; 40:899–909. [PubMed: 19719899]
- Nock MK, Prinstein MJ. A functional approach to the assessment of self-mutilative behavior. *Journal of Consulting and Clinical Psychology*. 2004; 72:885–890. [PubMed: 15482046]
- Olino TM, Klein DN, Shankman SA, Seeley JR, Pettit JW, Farmer RF, Lewinsohn PM. Lifetime rates of psychopathology in single versus multiple diagnostic assessments: Comparison in a community sample of probands and siblings. *Journal of Psychiatric Research*. 2012; 46:1217–1222. [PubMed: 22739001]
- Orvaschel H, Puig-Antich J, Chambers WJ, Tabrizi MA, Johnson R. Retrospective assessment of prepubertal major depression with the Kiddie-SADS-E. *Journal of the American Academy of Child Psychiatry*. 1982; 21:392–397. [PubMed: 7119313]
- Pettinati HM, O'Brien CP, Rabinowitz AR, Wortman SP, Oslin DW, Kampman KM, Dackis CA. The status of naltrexone in the treatment of alcohol dependence: specific effects on heavy drinking. *Journal of Clinical Psychopharmacology*. 2006; 26:610–625. [PubMed: 17110818]
- Procidano ME, Heller K. Measures of perceived social support from friends and from family: Three validation studies. *American Journal of Community Psychology*. 1983; 11:1–24. [PubMed: 6837532]
- Rohde P, Lewinsohn PM, Seeley JR, Klein DN, Andrews JA, Small JW. Psychosocial functioning of adults who experienced substance use disorders as adolescents. *Psychology of Addictive Behaviors*. 2007; 21:155–164. [PubMed: 17563135]
- Røysamb E, Kendler KS, Tambs K, Orstavik RE, Neale MC, Aggen SH, Torgersen S, et al. The joint structure of DSM-IV Axis I and Axis II disorders. *Journal of Abnormal Psychology*. 2011; 120:198–209. [PubMed: 21319931]
- Rutter M. Understanding and testing risk mechanisms for mental disorders. *Journal of Child Psychology and Psychiatry*. 2009; 50:44–52. [PubMed: 19220588]
- Scotti JR, Morris TL, McNeil CB, Hawkins RP. DSM-IV and disorders of childhood and adolescence: Can structural criteria be functional? *Journal of Consulting and Clinical Psychology*. 1996; 64:1177–1191. [PubMed: 8991304]
- Seedat S, Scott KM, Angermeyer MC, Berglund P, Bromet EJ, Brugha TS, et al. Cross-national associations between gender and mental disorders in the World Health Organization World Mental Health Surveys. *Archives of General Psychiatry*. 2010; 66:785–795. [PubMed: 19581570]
- Seeley JR, Kosty DB, Farmer RF, Lewinsohn PM. The modeling of internalizing disorders on the basis of patterns of lifetime comorbidity: Associations with psychosocial functioning and psychiatric disorders among first-degree relatives. *Journal of Abnormal Psychology*. 2011; 120:308–321. [PubMed: 21401216]
- Slade T, Watson D. The structure of common DSM-IV and ICD-10 mental disorders in the Australian general population. *Psychological Medicine*. 2006; 36:1593–1600. [PubMed: 16882356]
- Trew JL. Exploring the roles of approach and avoidance in depression: An integrative model. *Clinical Psychology Review*. 2011; 31:1156–1168. [PubMed: 21855826]

- Vollebergh WAM, Iedema J, Bijl RV, de Graaf R, Smit F, Ormel J. The structure and stability of common mental disorders: The NEMESIS study. *Archives of General Psychiatry*. 2001; 58:597–603. [PubMed: 11386990]
- Vollstädt-Klein S, Loeber S, Kirsch M, Bach P, Richter A, Bühler M, et al. Effects of cue-exposure treatment on neural cue reactivity in alcohol dependence: A randomized trial. *Biological Psychiatry*. 2011; 69:1060–1066. [PubMed: 21292243]
- Watson D. Rethinking mood and anxiety disorders: A quantitative hierarchical model for DSM-V. *Journal of Abnormal Psychology*. 2005; 114:522–536. [PubMed: 16351375]
- Wedig MM, Nock MK. The functional assessment of maladaptive behaviors: A preliminary evaluation of binge eating and purging among women. *Psychiatry Research*. 2010; 178:518–524. [PubMed: 20537726]
- Weissman MM, Bothwell S. Assessment of social adjustment by patient self-report. *Archives of General Psychiatry*. 1976; 33:1111–1115. [PubMed: 962494]
- Wells JE, Horwood LJ. How accurate is recall of key symptoms of depression? A comparison of recall and longitudinal reports. *Psychological Medicine*. 2004; 34:1001–1011. [PubMed: 15554571]
- WHO World Mental Health Survey Consortium. Prevalence, severity, and unmet need for treatment of mental disorders in the World Health Organization World Mental Health Surveys. *Journal of the American Medical Association*. 2004; 291:2581–2590. [PubMed: 15173149]
- Witkiewitz K, Bowen S, Donovan DM. Moderating effects of a craving intervention on the relation between negative mood and heavy drinking following treatment for alcohol dependence. *Journal of Consulting and Clinical Psychology*. 2011; 79:54–63. [PubMed: 21261434]
- Witkiewitz K, Villarroel NA. Dynamic association between negative affect and alcohol lapses following treatment. *Journal of Consulting and Clinical Psychology*. 2009; 77:633–644. [PubMed: 19634957]
- Wittchen H-U, Frölich C, Behrendt S, Günther A, Lieb R, Perkonig A, et al. Cannabis use and cannabis use disorders and their relationship to mental disorders: A 10-year prospective-longitudinal study in adolescents. *Drug and Alcohol Dependence*. 2007; 88:60–70.
- Wittchen H-U, Höfler M, Merikangas K. Toward the identification of core psychopathological processes? *Archives of General Psychiatry*. 1999; 56:929–931. [PubMed: 10530635]
- Wolf AW, Schubert DSP, Patterson MB, Grande TP, Brocco KJ, Pendleton L. Associations among major psychiatric diagnoses. *Journal of Consulting and Clinical Psychology*. 1988; 56:292–294. [PubMed: 3372837]
- Youngstrom E, Loeber R, Stouthamer-Loeber M. Patterns and correlates of agreement between parent, teacher, and male adolescent ratings of externalizing and internalizing problems. *Journal of Consulting and Clinical Psychology*. 2000; 68:1038–1050. [PubMed: 11142538]
- Zimmerman M, Mattia JJ. Axis I diagnostic comorbidity and borderline personality disorder. *Comprehensive Psychiatry*. 1999; 40:245–252. [PubMed: 10428182]

Figure 1.

Sample participation, selection, and attrition at each assessment wave ($T_1 - T_4$).

Notes. The sum of persons lost to attrition over the 4 assessment waves (excluding those deselected based on stratification) is 488. When this value is divided by the T_1 sample ($n = 1,709$) minus those excluded as a result of stratification procedures implemented at T_2 ($n = 406$), or 1,303 participants total, the overall sample attrition rate is 37% (i.e., $488/1,303 = .3745$).

Table 1

Lifetime Prevalence of Psychiatric Disorders and Diagnostic Agreement (Probands, through age 30.0: N = 816)

Psychiatric disorder	Waves disorder assessed	Unweighted lifetime prevalence % (SE)	Weighted lifetime prevalence: % (SE)
<i>Anxiety Disorders</i>			
Separation Anxiety (SAD)	All	5.4 (0.8)	3.9 (0.7)
Simple/Specific Phobia (PHOB)	All	4.3 (0.7)	3.3 (0.6)
Generalized Anxiety (GAD)	All	2.2 (0.5)	2.0 (0.5)
Obsessive–Compulsive (OCD)	All	1.3 (0.4)	1.0 (0.3)
Panic (PAN)	All	6.6 (0.9)	5.6 (0.8)
Agoraphobia without Panic (AGOR)	All	0.5 (0.3)	0.4 (0.2)
Post-Traumatic Stress (PTSD)	T ₃ , T ₄	8.6 (1.0)	7.0 (0.9)
Social Phobia (SOC)	All	4.4 (0.7)	3.6 (0.7)
<i>Any Anxiety Disorder</i>		24.8 (1.5)	20.3 (1.4)
<i>Mood Disorders</i>			
Major Depressive (MDD)	All	58.5 (1.7)	50.8 (1.8)
Dysthymia (DYS)	All	5.6 (0.8)	4.1 (0.7)
Bipolar Disorders (BIP)	All	3.7 (0.7)	3.1 (0.6)
<i>Any Mood Disorder</i>		60.0 (1.7)	52.3 (1.7)
<i>Disruptive Behavior Disorders</i>			
Attention-Deficit/Hyperactivity (ADHD)	All	3.2 (0.6)	2.3 (0.5)
Oppositional Defiant (ODD)	T ₁ , T ₂ , T ₃	3.4 (0.6)	2.6 (0.6)
Conduct (CD)	All	5.0 (0.8)	3.8 (0.7)
<i>Any Disruptive Behavior Disorder</i>		10.2 (1.1)	7.7 (0.9)
<i>Substance Use Disorders</i>			
Alcohol Use (AUD)	All	37.0 (1.7)	34.2 (1.7)
Cannabis Use (CUD)	All	21.2 (1.4)	19.1 (1.4)
Hard Drug (DRG)	All	13.7 (1.2)	11.0 (1.1)
<i>Any Substance Use Disorder</i>		44.1 (1.7)	40.4 (1.7)
<i>Eating Disorders</i>			
Anorexia Nervosa (AN)	All	1.0 (0.3)	0.8 (0.3)
Bulimia Nervosa (BN)	All	2.5 (0.5)	1.8 (0.5)
<i>Any Eating Disorder</i>		3.2 (0.6)	2.5 (0.5)
<i>Psychotic Disorders</i>			
Schizophrenia or Schizoaffective (SCHZ)	All	0.4 (0.2)	0.3 (0.2)
<i>Any Lifetime Psychiatric Disorder</i>		77.8 (1.5)	71.1 (1.6)

Notes. Weighted lifetime prevalence rates are adjusted for the stratified sampling procedures introduced at T₃ and continued through T₄.

Table 2

Lifetime Psychiatric Disorder Aggregation

Number of lifetime disorders	Unweighted		Weighted ^a	
	Number of cases	% (SE)	Number of cases	% (SE)
0	181	22.2 (1.5)	236	28.9 (1.6)
1	229	28.1 (1.6)	235	28.8 (1.6)
2	157	19.2 (1.4)	146	17.9 (1.3)
3	126	15.4 (1.3)	105	12.9 (1.2)
4	124	15.2 (1.3)	94	11.5 (1.1)

^a Values are based on weighted data adjusted for sampling stratification procedures implemented at T3.

Table 3

Probabilities of Common Disorder Categories (1% Weighted Lifetime Prevalence) as a Function of the Number of Lifetime Disorders

Diagnostic Category	Number of lifetime disorders				Mantel-Haenszel χ^2 Test
	1	2	3	4	
<i>Internalizing Disorders:</i>					
Separation Anxiety (SAD)	.02 _a	.04 _a	.07 _{ab}	.14 _b	21.94 ^{***}
Specific Phobia (PHOB)	.02 _a	.03 _{ab}	.09 _{bc}	.13 _c	21.29 ^{***}
Generalized Anxiety (GAD)	.01 _a	.02 _a	.02 _a	.10 _b	15.90 ^{***}
Obsessive–Compulsive (OCD)	.00 _a	.00 _a	.02 _{ab}	.05 _b	11.93 ^{***}
Panic (PAN)	.01 _a	.05 _a	.10 _a	.26 _b	51.51 ^{***}
Post-Traumatic Stress (PTSD)	.02 _a	.08 _{ab}	.18 _{bc}	.24 _c	48.51 ^{***}
Social Phobia (SOC)	.01 _a	.03 _a	.06 _a	.18 _b	35.70 ^{***}
Major Depressive (MDD)	.59 _a	.76 _b	.76 _b	.90 _b	31.96 ^{***}
Dysthymia (DYS)	.00 _a	.03 _{ab}	.10 _{bc}	.19 _c	46.39 ^{***}
Bipolar Disorders (BIP)	.02 _a	.02 _a	.03 _a	.15 _b	19.47 ^{***}
Bulimia Nervosa (BN)	.01 _a	.02 _a	.02 _a	.09 _b	14.83 ^{***}
<i>Externalizing Disorders:</i>					
Attention-Deficit/Hyperactivity (ADHD)	.01 _a	.03 _{ab}	.04 _{ab}	.08 _b	8.70 ^{**}
Oppositional Defiant (ODD)	.01 _a	.03 _{ab}	.05 _{ab}	.09 _b	12.59 ^{***}
Conduct (CD)	.00 _a	.03 _{ab}	.08 _b	.19 _c	47.70 ^{***}
Alcohol Use (AUD)	.23 _a	.53 _b	.63 _b	.86 _c	117.54 ^{***}
Cannabis Use (CUD)	.04 _a	.23 _b	.45 _c	.69 _d	162.28 ^{***}
Hard Drug Use (DRG)	.00 _a	.05 _a	.26 _b	.59 _c	178.37 ^{***}

Notes. Values represent the percentage of persons within aggregation categories who met lifetime criteria for a given disorder. Percentages that share the same subscript within rows are not significantly different ($p < .05$) according to the Scheffé test. A significant Mantel-Haenszel χ^2 test indicates a linear association between the row and column variables.

*
 $p < .05$,

**
 $p < .01$,

 $p < .001$.

Table 4

Family Densities of Lifetime Psychiatric Disorders and Diagnostic Agreement (First-degree relatives: N = 2,414)

Psychiatric disorder	Lifetime family density ^a (SD)	Interrater reliability (κ)
<i>Anxiety Disorders</i>		
Simple/Specific Phobia (PHOB)	.03 (.10)	.91
Generalized Anxiety (GAD)	< .01 (.03)	.90
Obsessive–Compulsive (OCD)	.01 (.04)	.76
Panic Disorder (PAN)	.03 (.11)	.92
Agoraphobia without Panic (AGOR)	< .01 (.02)	.91
Post-Traumatic Stress (PTSD)	.04 (.13)	.98
Social Phobia (SOC)	.03 (.11)	.93
<i>Any Anxiety Disorder</i>	.12 (.20)	.93
<i>Mood Disorders</i>		
Major Depressive (MDD)	.26 (.28)	.91
Dysthymia (DYS)	.04 (.12)	.89
Bipolar Disorders (BIP)	.01 (.06)	.69
<i>Any Mood Disorder</i>	.29 (.30)	.91
<i>Substance Use Disorders</i>		
Alcohol Use Disorder (AUD)	.29 (.28)	.97
Cannabis Use Disorder (CUD)	.12 (.21)	.97
Hard Drug Use Disorder (DRG)	.10 (.19)	.93
<i>Any Substance Use Disorder (SUD)^b</i>	.36 (.30)	.97
<i>Eating Disorders</i>		
Anorexia Nervosa (AN)	< .01 (.04)	1.00
Bulimia Nervosa (BN)	.01 (.06)	.91
<i>Any Eating Disorder</i>	.01 (.07)	.96
<i>Disruptive Behavior Disorders</i>		
Attention-Deficit/ Hyperactivity (ADHD)	.03 (.11)	.89
Conduct (CD)	.02 (.07)	.77
<i>Any Disruptive Behavior Disorder</i>	.04 (.12)	.87
<i>Psychotic Disorders</i>		
Schizophrenia or Schizoaffective (SCHZ)	< .01 (.05)	.96
<i>All Psychiatric Disorders</i>	.53 (.33)	.95

^aValues in this column are based on the proportion of first-degree relatives who had a given disorder or any disorder within a set of related disorders.

^bSUD includes the abuse of or dependence on alcohol, cannabis, or other substances.

Table 5

Lifetime Mental Health Treatment Utilization as a Function of Disorder Aggregation

Treatment modality	Number of lifetime disorders ^a			
	1	2	3	4
Medication	18.7 _a	20.8 _a	30.0 _a	52.7 _b
Consultation/therapy	37.6 _a	45.0 _{ab}	58.8 _{bc}	79.3 _c
Any mental health treatment	40.4 _a	46.5 _{ab}	60.2 _{bc}	82.4 _c

^aValues within each frequency category represent the percentage of persons who participated in a particular treatment modality. Percentages that share the same subscript within rows are not significantly different ($p < .05$) according to the Scheffé test.

Table 6

The Prediction of T₄-Assessed Continuous Impairment-Related Variables from Lifetime Disorder Aggregation

Outcome	Semi-partial		
	β	p	r
Unemployment (weeks during past year)	.164	<.001	.162
Household income (past year)	-.297	<.001	-.294
Relationship quality	-.200	<.001	-.201
Poor social adjustment	.295	<.001	.293
Global functioning (GAF)	-.442	<.001	-.438

Note. All regression coefficients (β) are standardized and were computed following the control of proband gender entered in Step 1.