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Association of respondent psychiatric comorbidity with family history of comorbidity: Results from the National Epidemiologic Survey on Alcohol and Related Conditions-III

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Abstract

Objective—Substance use disorders and major psychiatric disorders are common, highly comorbid with each other, and familial. However, the extent to which comorbidity is itself familial remains unclear. The purpose of this study is to investigate associations between comorbidity among respondents with family history of comorbidity.

Methods—We analyzed data from the National Epidemiologic Survey on Alcohol and Related Conditions-III to study the associations of family history (FH) of comorbidity among alcoholism, drug problems, depression, antisocial behavior, and anxiety disorders in parents and maternal and paternal grandparents with corresponding DSM-5 diagnostic comorbidity among respondents. We utilized multivariable multinomial logistic regression models controlling for age, sex, race, education, family income, marital status, and adverse childhood experiences (ACEs).

Results—All comorbid associations of any two disorders with FH were statistically significant; almost all adjusted odds ratios (ORs) for respondent comorbidity in the presence of FH of the parallel comorbidity exceeded 10. ORs involving antisocial behavior in relatives and antisocial personality disorder in respondents were consistently larger than any other pairs of disorders. After further adjustment for ACEs, most patterns of association were similar but the ORs were reduced two to threefold. ACEs may be mediators in relationships between familial and respondent comorbidities.

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Conclusion—Further investigations of relationships among familial comorbidity, ACEs, and respondents' diagnoses may improve understanding of comorbidity.

Keywords

family history; comorbidity; psychiatric epidemiology; alcohol use disorder; drug use disorder; major depression

1. Introduction

Substance use disorders and major psychiatric disorders, including mood, anxiety, and personality disorders, are common and highly comorbid with each other [1–4]. Such comorbidity is associated with greater clinical severity and complexity, as well as poor treatment outcomes [1, 5,6]. In addition, all substance use disorders and major psychiatric disorders are familial [7, 8]. However, the extent to which comorbidity between specific disorders (e.g., alcohol (AUD) and drug use disorders (DUD) and antisocial personality disorder (ASPD), and borderline personality disorder) is itself familial and, if so, via what underlying mechanisms, remains unclear. Drawing on the work of Klein and Riso (1994) [9], Neale and Kendler (1995) [10] elaborate a range of theoretical models of comorbidity. In addition to chance, sampling bias, and population stratification, these include alternate form (two disorders as alternate manifestations of a single underlying liability), multiformity (having one disorder can generate symptoms of the other) correlated liability, causation, and the comorbid condition as a distinct clinical entity.

Weissman et al. [11] found that comorbid panic disorder plus MDD reflected two separate disorders that are highly comorbid within individuals and independently transmitted in families, with the comorbid state representing a clinically heterogeneous entity, rather than a distinct, specifically transmitted syndrome. Findings reported by Horwath et al. [12] suggested that elevated rates of social phobia in relatives of probands with panic disorder reflected the combination of high familiality of panic disorder plus the tendency for panic disorder to occur with social phobia in individuals. Both these sets of findings appear compatible with multiformity models. Twin studies suggest that correlated liabilities, MD as a cause of GAD, and reciprocal causation best account for comorbidity between these two disorders [10]. Conversely, there is evidence suggesting that at least some subsets of co-occurring conditions such as AUD and DUD (e.g., [13]), DUD plus ASPD (e.g., [14]), and attention-deficit/hyperactivity disorder plus conduct disorder [15,16] may be specifically transmitted, distinct clinical entities. Among clinically ascertained adolescents, Rhee et al. [17] found strongest support for alternate form and correlated liabilities models of the comorbidity between alcohol and illicit drug dependence.

Previous studies addressing the familiality of comorbidity have been generally drawn on clinically ascertained, adoptee, twin, or otherwise highly selected samples. To our knowledge, no study has yet investigated whether particular constellations of comorbidity are specifically transmitted within families among the general population. Findings that comorbidity is itself familial may reflect familial environmental, nonfamilial environmental, or genetic or epigenetic factors associated with vulnerability to one or both disorders. Each

of these mechanisms carries potential implications for revisions to diagnostic classifications. In addition, the results of this study may inform the design of new studies that could generate new knowledge about etiology. Both in their own right and by informing new etiologic research, they could also contribute to the development of improved prevention and treatment approaches, and the tailoring of existing ones, to take account of both intraindividual and within-family comorbidities, e.g. to extent that interventions might be differentially effective for individuals at familial risk for pure versus comorbid presentations of specific disorders.

Accordingly, the goal of this study was to investigate associations of family history (FH) of comorbidity among alcoholism (ALC), drug problems (DP), depression (DEP), antisocial behavior (ASB), and anxiety disorder (ANX) with the corresponding DSM-5 diagnostic comorbidity among respondent probands in the 2012–2013 National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC-III) after controlling for sociodemographics and adverse childhood experiences. We hypothesized that comorbidity of any two psychiatric disorders is positively associated with FH of comorbidity involving the corresponding pairs, and also is positively associated with a family history of each disorder occurring singly.

2. Method

2.1 Sample

The NESARC-III is a nationally representative survey of the non-institutionalized civilian U.S. adult population 18 years and older. Multistage probability sampling was used to select respondents. Primary sampling units (PSUs) were individual counties or groups of contiguous counties, secondary sampling units (SSU) were groups of Census-defined blocks, and tertiary sampling units were households within SSUs. Finally, eligible adults within sampled households were randomly selected. Hispanics, Blacks, and Asians were oversampled, and in households with ≥4 eligible minority persons (n=1661), 2 respondents were selected. The total sample size was 36,309. Data were adjusted for oversampling and nonresponse, then weighted to represent the US civilian population based on the 2012 American Community Survey [18]. When participants were compared to the total eligible sample, including nonrespondents, no significant differences were found in percent Hispanic, Black, or Asian population subgroups, population density, vacancy rate, proportion of population in group quarters or proportion of renters at the segment level. At the individual level, there were no differences between respondents and the total eligible sample on Hispanic ethnicity. Respondents included a slightly higher percentage of men than the total eligible sample (48.1% versus 46.2%, $p<0.01$). NESARC-III respondents also included a significantly greater percentage of those aged 60–69 years (13.7% versus 12.6%) and smaller percentages of those aged 40–49 (18.1% versus 18.3%) and 30–39 (16.7% versus 17.4%) than the total eligible sample. Protocol and consent procedures were approved by the institutional review boards of the National Institutes of Health and Westat, Inc.

2.2. Assessment

The diagnostic interview was the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule-5 (AUDADIS-5), designed to measure DSM-5 alcohol (AUD), nicotine (NUD), other specific drug use disorders (DUDs), and selected mood, anxiety, trauma-related, eating and personality disorders (PDs). For the present study, respondent diagnoses of lifetime AUD, DUD (sedatives/tranquilizers, cannabis, amphetamine, cocaine, club drug, opioid, heroin, hallucinogens, solvents/inhalants, other drug use disorders), major depressive disorder (MDD), any anxiety disorder, and antisocial personality disorder (ASPD) were considered.

Test-retest reliability of DSM-5 AUD and DUD diagnoses (kappa (κ) =0.40–0.62) and corresponding dimensional scales (intraclass correlation coefficient (ICC) =0.45–0.85) were fair to excellent in a large general population sample. Test-retest of MDD diagnoses (κ=0.40) and its associated dimensional scale (ICC=0.59) were fair to good as were reliabilities for anxiety disorder diagnoses (κ=0.35–0.51) and their dimensional counterparts (ICC=0.74–0.79). Reliability of the ASPD diagnoses was fair (κ=0.46), but higher for its dimensional counterpart (ICC=0.60) [19]. Procedural validity of DSM-5 diagnoses was assessed through blind clinical reappraisal using the clinician-administrated semi-structured psychiatric research interview, DSM-5 (PRISM-5) version [20]. The clinical reappraisal, conducted in a large general population sample showed fair to good concordance for AUD and DUD (κ=0.36–0.58), MDD (κ=0.35–0.36), and anxiety disorders (κ=0.20–0.56) and generally greater concordance for their dimensional scales (ICC>0.64) [20, 21].

2.3. Family History

The AUDADIS-5 also assessed family history of alcoholism (ALC), drug problems (DP), depression (DEP), antisocial behavior (ASB), and anxiety (ANX) among six categories of respondent probands' biologic relatives: father, mother, and maternal and paternal grandfathers and grandmothers using the family history method. Family history of each condition was assessed using a single question applicable to each type of relative. For example, family history of alcohol problems was assessed with the following question: "Has your [*RELATIVE*] been an alcoholic or problem drinker at any time in his life?" A relative was considered an "alcoholic or problem drinker" if a respondent answered affirmatively to questions operationalizing DSM-5 AUDs: whether the relative had physical or emotional problems because of drinking; problems with a spouse, family, or friends because of drinking; problems at work or school because of drinking; problems because of driving after drinking or seemed to spend a lot of time drinking or being hung over.

Analogously, DEP was considered positive among a relative if the respondent answered affirmatively a question about whether that relative felt down, sad, blue or didn't care about things and also ate or slept too little or too much, moved more slowly than usual, were tired or agitated, had trouble concentrating, making decisions or doing things, or felt worthless or thought about suicide. Test-retest reliability of the DEP family history question among parents and grandparents ascertained in a large general population sample were good to excellent (κ =0.56–0.78) [22]. Family history of any anxiety disorder was considered positive if the respondent answered affirmatively to the question about whether the relative

had times when they were tense, nervous or anxious for at least three months, had panic attacks, were very frightened of objects or situations or avoided them, or had bad reactions to a traumatic or stressful event. Relatives were considered positive for ASPD if the respondent answered affirmatively to the DSM-5 ASPD question about whether the relative was cruel to people or animals, fought or destroyed property, had trouble keeping a job or paying bills, was impulsive, reckless or did not plan ahead, lied or conned people or got arrested, did not seem to care if they hurt others and had problems at an early age such as truancy, staying out all night or running away.

A positive FH of comorbidity was indicated by any one person in any of the six categories of relatives having lifetime histories of both conditions of interest, e.g., ALC and DEP. While family histories were assessed individually for each parent and grandparent, those of siblings, offspring, and maternal and paternal aunts and uncles were each queried in the aggregate ("How many [*RELATIVES*] are now, or were in the past, alcoholics or problem drinkers?"). Because we could not determine comorbidity within individual relatives in these categories, we excluded them from the present analyses. We classified three additional groups according to family history status: two disorders without comorbidity (e.g., ALC in mother and DEP in paternal grandfather), either single disorder of interest in any family members but no instance of the other (e.g., ALC in one or more relatives but none with DEP), and neither disorder of interest. The same classification was applied to pairs of these five disorders.

2.4. Statistical Analysis

Weighted cross-tabulations estimated prevalences of lifetime DSM-5 disorders of interest and their corresponding FH designations adjusted for sociodemographic characteristics. Adjusted odds ratios (ORs) were derived from multivariable multinomial logistic regression models that test for associations between explanatory variables (e.g., family history of particular types of problems) and a response variable (e.g., respondent diagnostic status) with more than two levels. To illustrate, and as described above, analyses of comorbid AUD and DEP in respondents and FH of ALC and DEP categorized respondent diagnosis as comorbid AUD + DEP, AUD (Disorder X) and DEP (Disorder Y) occurring singly, with respondents diagnosed as having neither as the referent group. In parallel, FH was categorized as comorbid ALC plus DEP, both ALC (Disorder X) and DEP (Disorder Y) within the family but not comorbid in any one relative, ALC only, and DEP only, with family history of neither ALC nor DEP as the FH referent group. Multinomial models adjusted for sociodemographic characteristics such as age, sex, race, education, family income, and marital status.

In addition, adverse childhood experiences (ACE), including sexual, physical, and verbal abuse, physical and emotional neglect, and having a battered mother, and a household member with a mental health or substance use disorder or who was incarcerated, or who attempt/commit suicide, when respondents were younger than 18 years old, constitute strong risk factors for a broad range of substance use disorders and other psychiatric disorders [23–25] and associated with family histories of psychopathology [26]. Therefore, we fit additional models in which we further adjusted for ACE as well as sociodemographic

characteristics to examine the extent to which ACE explained associations of FH comorbidity with respondent comorbidity. We assessed childhood abuse and neglect using items adapted from the Conflict Tactics Scale and the Childhood Trauma Questionnaire [27, 28]. Respondents were considered positive for physical abuse if they reported that a parent or caregiver had at “sometimes,” “fairly often,” or “very often” physically harmed or injured them. Respondents were analogously considered positive for emotional abuse, sexual abuse, physical neglect, and exposure to a battered mother if the respective harmful behaviors occurred at least “sometimes.” Emotional neglect was considered positive if respondents’ family never, rarely, or only sometimes encouraged their success, made them feel special, was a source of strength and support, believed in them, or if it was never, rarely, or only sometimes true that the family was close-knit. Parental suicide or attempt, mental health disorder, substance use disorder, and incarceration of adult household members when respondents were younger than 18 were queried dichotomously. The sum of ACEs coded positive was converted into a categorical variable based on the empirical distribution: none, 1, 2 or 3, and 4 or more [29, 30].

All analyses examined comorbidity among respondents and family history of comorbidity among parents and grandparents. When analyses were restricted to comorbidity among parents only, the results were remarkably consistent with slight attenuation of the observed odds ratios (analytic results available upon request). All analyses utilized SUDAAN, version 11.0, which accounts for the NESARC-III's complex sample design.

3. Results

3.1. Prevalences of comorbid disorders with family history of comorbidity

Table 1 shows the prevalence of lifetime comorbidity of respondents with family history of parallel comorbidity by sociodemographic characteristics. Prevalences of lifetime AUD and other four comorbid disorders among respondents with FH of the corresponding comorbid disorders are about 2%, AUD + DEP being the most prevalent. Prevalences of DUD and other comorbid disorders are less than 1% except for DUD + AUD. The prevalence of comorbid DEP plus ANX among respondents with FH of this comorbidity is 4%, the highest across all pairs. The rates of comorbid substance use disorder plus ASPD were greater among males. Native Americans have the highest prevalence rates across all combinations of comorbid disorders, in turn Whites were higher than Blacks and Asians. Overall, respondents in the youngest age group and those with annual incomes <$20,000 has the highest prevalence. Those never married or those with ≤ high school education show higher prevalences for most pairs of disorders.

3.2. Association of psychiatric disorders and their comorbidity with family history

Table 2 shows adjusted odds ratios (ORs) derived from multivariable multinomial logistic regression models controlling for age, sex, race, education, family income, and marital status. All comorbid associations of any two disorders with FH were statistically significant. Except in the cases of respondent DUD without AUD, DEP without AUD, and ASPD without DUD, in which the largest ORs were associated with both singly occurring disorders among different relatives, the largest ORs for both comorbid and singly occurring

respondent disorders were observed in the presence of comorbidity in one or more of the queried relatives. All but one OR (DEP plus ANX) for respondent comorbidity in the presence of FH comorbidity exceeded 10, and those for comorbidity involving ASPD in respondents and ASB in relatives were the largest. ORs associated with FH of both singly occurring disorders among different relatives were smaller than those for FH of comorbidity, and higher than having only one of the two disorders occurring among the assessed relatives. For each of the two disorders occurring singly in the respondent, ORs were higher with FH of the parallel singly occurring disorder, absent FH of the other, than for FH of the other singly occurring disorder: i.e., Disorder X without Disorder Y in the respondent, and parallel FH of Disorder X without Disorder Y; and similarly, Disorder Y without Disorder X in the respondent, and parallel FH of Disorder Y without Disorder X.

Table 3 illustrates adjusted odds ratios (ORs) derived from multinomial regression models controlling for ACE in addition to the sociodemographic variables. Most patterns of associations were similar to those shown in Table 2 except that ORs were two- to threefold smaller than those in models adjusting only for sociodemographic variables. Furthermore, ORs of respondent ASPD plus AUD, ASPD plus DEP were modestly larger in FH for the two disorders occurring singly than in FH of comorbidity, while those of respondent ASPD with DUD, and ASPD with ANX remained largest among four groups of FH. In addition, ORs of AUD plus ASPD occurring singly in a relative were highest for respondents with ASPD occurring singly. Association involving FH of ASB were more strongly attenuated by adjustment for ACE.

4. Discussion

The purpose of this study was to investigate familial comorbidity involving ALC, DP, DEP, ASPD, and ANX as a risk factor for comorbidity of parallel pairs of DSM-5 psychiatric disorders in a national survey of the general adult US population. Having a FH of two comorbid disorders had the highest ORs with the corresponding respondent comorbidity, followed by both disorders occurring singly in different relatives after adjustment only for sociodemographic variables. FH involving comorbidity with ASPD was consistently more strongly associated with the corresponding comorbidity than FH of DEP and ANX or that of substance disorders and other psychiatric disorders. After adjustment for ACE in addition to sociodemographic variables, most patterns of associations were similar, but ORs of respondents with ASPD and AUD and ASPD plus DEP were higher when FH for the two disorders occurred singly than with FH for comorbidity of the disorders. One possible explanation for the strong associations involving ASPD is that children with antisocial parents or grandparents may be more likely to experience maltreatment, or may witness violence in the home [31]. More generally, however, ACEs constitute risk factors for many psychiatric disorders. The reductions in ORs after adjustment for ACEs, combined with highly significant log-likelihood ratio test (LRT) statistics comparing models with and without ACE variables across any pairs of disorders of interest, suggest that ACEs may constitute intervening variables in relationships between familial and respondent comorbidities.

Our findings with respect to associations of FH of comorbid alcohol and drug problems with comorbidity of AUD and DUD in respondents, and drug problems and ASPD with comorbid DUD plus ASPD in respondents, are compatible with those reported previously by Dick et al. [13] and Van den Bree et al. [14], respectively, suggesting that at least some subsets of comorbid cases of these pairs of disorders may reflect specifically transmitted, distinct clinical entities. However, our findings of familial comorbidity contrast with those reported by, for example, Weissman et al. [11] with respect to comorbid panic disorder plus MDD, Horwath et al. [12] regarding comorbid panic disorder plus social phobia, and Coelho et al. [32] with respect to comorbid generalized social phobia plus generalized anxiety disorder in all-female sample. We are unable to utilize the study designs reported by Weissman et al. [11] and Coelho et al. [32] in part due to lack of family history ascertained, for example, for specific anxiety disorders versus anxiety disorders in the aggregate. More generally, discrepancies between present findings and those from both family history and family study designs [33, 34] identifying specific and independent transmission of disorders that may be highly comorbid within individuals may be explained by methodological differences, including sample ascertainment. For example, our study is based on a large, nationally representative epidemiologic survey, rather than ascertainment of probands specifically for having particular disorders. The large sample size affords power to investigate FH of singly and comorbidly occurring disorders and eliminates potential biases resulting from samples selected for psychiatric morbidity, comorbidity, family affectedness, or treatment seeking.

We used the family history method (FHM) of investigating psychopathology in relatives in which NESARC-III respondents were interviewed about DSM-5 symptoms of AUD, DUD, MDD, any anxiety disorder, and ASPD among their parents and grandparents. In contrast, the family study method (FSM) entails direct interviews with all available relatives. In general, the FHM has shown good interrater and test-retest reliability and concordance with clinical reappraisals, and when compared with FSMs, show good to excellent specificity but modest sensitivity for AUD, DUD, MDD, anxiety disorders, and ASPD [34–42]. Although modest sensitivity suggests the possibility of underreporting by the FHM used in this study, the FHM of investigating psychopathology in relatives is far more cost- and time-efficient than the family study method (FSM), in which all available relatives are directly assessed [33, 34, 43]. Indeed, the FSM would be both prohibitively resource intensive and logistically infeasible in a nationally representative general population survey [8]. Further, when parents, and especially grandparent, are deceased, or otherwise unavailable, for interview, the FHM is the only available method. Importantly, associations of FH of comorbid disorders and comorbidity among NESARC-III respondents were strong, suggesting that the potential for underreporting in the FHM likely attenuated the associations found in this study.

5. Conclusions

In conclusion, we found that respondent-probands' psychiatric comorbidity was strongly associated with parallel comorbidity as ascertained by the FHM in six categories of relatives. All comorbid associations of any two disorders with FH were statistically significant. Childhood adversity appear to explain some of the association between FH and respondent comorbidity, but significant and generally moderate to substantial associations between FH and respondent status persisted after adjustment for ACEs. These results lay the groundwork

for further large general population studies testing alternative models of respondent-probands and familial comorbidity that incorporate covariates including childhood adversity [44] to improve understanding of etiologic factors underlying comorbidity. The findings also suggest the future need to develop family-based prevention and intervention program for comorbid disorders.

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References

1. Merikangas KR, Kalaydjian A. Magnitude and impact of comorbidity of mental disorders from epidemiologic surveys. Curr Opin Psychiatry. 2007; 20:353–358. [PubMed: 17551350]
2. Goes FS, McCusker MG, Bienvenu OJ, Mackinnon DF, Mondimore FM, Schweizer B, National Institute of Mental Health Genetics Initiative Bipolar Disorder Consortium. Depaulo JR, Potash JB. Co-morbid anxiety disorders in bipolar disorder and major depression: familial aggregation and clinical characteristics of co-morbid panic disorder, social phobia, specific phobia and obsessive-compulsive disorder. Psychol Med. 2012; 42:1449–1459. [PubMed: 22099954]
3. Goodwin RD, Hamilton SP. Lifetime comorbidity of antisocial personality disorder and anxiety disorders among adults in the community. Psychiatry Res. 2003; 117:159–166. [PubMed: 12606017]
4. Lai HM, Cleary M, Sitharthan T, Hunt GE. Prevalence of comorbid substance use, anxiety and mood disorders in epidemiological surveys, 1990–2014: A systematic review and meta-analysis. Drug Alcohol Depend. 2015; 154:1–13. [PubMed: 26072219]
5. Kessler RC. The epidemiology of dual diagnosis. Biol. Psychiatry. 2004; 56:730–737. [PubMed: 15556117]
6. O'Brien CP, Charney DS, Lewis L, Cornish JW, Post RM, Woody GE, Zubieta JK, Anthony JC, Blaine JD, Bowden CL, Calabrese JR, Carroll K, Kosten T, Rounsaville B, Childress AR, Oslin DW, Pettinati HM, Davis MA, Demartino R, Drake RE, Fleming MF, Fricks L, Glassman AH, Levin FR, Nunes EV, Johnson RL, Jordan C, Kessler RC, Laden SK, Regier DA, Renner JA Jr, Ries RK, Sklar-Blake T, Weisner C. Priority actions to improve the care of persons with co-occurring substance abuse and other mental disorders: a call to action. Biol Psychiatry. 2004; 56:703–713. [PubMed: 15556110]
7. Kendler KS, Edwards A, Myers J, Cho SB, Adkins A, Dick D. The predictive power of family history measures of alcohol and drug problems and internalizing disorders in a college population. Am J Med Genet B Neuropsychiatr Genet. 2015; 168B:337–346. [PubMed: 25946510]
8. Kendler KS, Davis CG, Kessler RC. The familial aggregation of common psychiatric and substance use disorders in the National Comorbidity Survey: a family history study. Br J Psychiatry. 1997; 170:541–548. [PubMed: 9330021]
9. Klein, DN.; Riso, LP. Psychiatric disorders: problems of boundaries and comorbidity. In: Costello, CG., editor. Basic issues in psychopathology. Guilford, New York: 1994. p. 19-66.
10. Neale MC, Kendler KS. Models of comorbidity for multifactorial disorders. Am. J. Hum. Genet. 1995; 57:935–953. [PubMed: 7573055]
11. Weissman MM, Wickramaratne PJ, Adams PB, Lish JD, Horwath E, Charney D, Woods SW, Leeman E, Frosch E. The relationship between panic disorder and major depression: a new family study. Arch Gen Psychiatry. 1993; 50:767–780. [PubMed: 8215801]

12. Horwath E, Wolk SI, Goldstein RB, Wickramaratne P, Sobin C, Adams P, Lish JD, Weissman MM. Is the comorbidity between social phobia and panic disorder due to familial cotransmission or other factors? Arch Gen Psychiatry. 1995; 52:574–582. [PubMed: 7598634]
13. Dick DM, Agrawal A, Wang JC, Hinrichs A, Bertelsen S, Bucholz KK, Schuckit M, Kramer J, Nurnberger J Jr, Tischfield J, Edenberg HJ, Goate A, Bierut LJ. Alcohol dependence with comorbid drug dependence: genetic and phenotypic associations suggest a more severe form of the disorder with stronger genetic contribution to risk. Addiction. 2007; 102:1131–1139. [PubMed: 17567401]
14. Van den Bree MB, Svikis DS, Pickens RW. Genetic influences in antisocial personality and drug use disorders. Drug Alcohol Depend. 1998; 49(3):177–187. [PubMed: 9571383]
15. Christiansen H, Chen W, Oades RD, Asherson P, Taylor EA, Lasky-Su J, Zhou K, Banaschewski T, Buschgens C, Franke B, Gabriels I, Manor I, Marco R, Müller UC, Mulligan A, Psychogiou L, Rommelse NN, Uebel H, Buitelaar J, Ebstein RP, Eisenberg J, Gill M, Miranda A, Mulas F, Roeyers H, Rothenberger A, Sergeant JA, Sonuga-Barke EJ, Steinhausen HC, Thompson M, Faraone SV. Co-transmission of conduct problems with attention-deficit/hyperactivity disorder: familial evidence for a distinct disorder. J Neural Transm. 2008; 115:163–175. [PubMed: 18200434]
16. Doyle AE, Faraone SV. Familial links between attention deficit hyperactivity disorder, conduct disorder, and bipolar disorder. Curr Psychiatry Rep. 2002; 4:146–152. [PubMed: 11914177]
17. Rhee SH, Hewitt JK, Young SE, Corley RP, Crowley TJ, Neale MC, Stallings MC. Comorbidity between alcohol dependence and illicit drug dependence in adolescents with antisocial behavior and matched controls. Drug Alcohol Depend. 2006; 84(1):85–92. [PubMed: 16413148]
18. Grant BF, Goldstein RB, Saha TD, Chou SP, Jung J, Zhang H, Pickering RP, Ruan WJ, Smith SM, Huang B, Hasin DS. Epidemiology of DSM-5 Alcohol Use Disorder: Results From the National Epidemiologic Survey on Alcohol and Related Conditions III. JAMA Psychiatry. 2015; 72(8):757–766. [PubMed: 26039070]
19. Grant BF, Goldstein RB, Smith SM, Jung J, Zhang H, Chou SP, Pickering RP, Ruan WJ, Huang B, Saha TD, Aivadyan C, Greenstein E, Hasin DS. The Alcohol Use Disorder and Associated Disabilities Interview Schedule-5 (AUDADIS-5): reliability of substance use and psychiatric disorder modules in a general population sample. Drug Alcohol Depend. 2015; 48:27–33.
20. Hasin DS, Shmulewitz D, Stohl M, Greenstein E, Aivadyan C, Morita K, Saha T, Aharonovich E, Jung J, Zhang H, Nunes EV, Grant BF. Procedural validity of the AUDADIS-5 depression, anxiety and post-traumatic stress disorder modules: Substance abusers and others in the general population. Drug Alcohol Depend. 2015; 152:246–256. [PubMed: 25939727]
21. Hasin DS, Greenstein E, Aivadyan C, Stohl M, Aharonovich E, Saha T, Goldstein R, Nunes EV, Jung J, Zhang H, Grant BF. The Alcohol Use Disorder and Associated Disabilities Interview Schedule-5 (AUDADIS-5): procedural validity of substance use disorders modules through clinical re-appraisal in a general population sample. Drug Alcohol Depend. 2015; 148:40–46. [PubMed: 25604321]
22. Ruan WJ, Goldstein RB, Chou SP, Smith SM, Saha TD, Pickering RP, Dawson DA, Huang B, Stinson FS, Grant BF. The alcohol use disorder and associated disabilities interview schedule-IV (AUDADIS-IV): reliability of new psychiatric diagnostic modules and risk factors in a general population sample. Drug Alcohol Depend. 2008; 92(1–3):27–36. [PubMed: 17706375]
23. Kessler RC, Davis CG, Kendler KS. Childhood adversity and adult psychiatric disorder in the US National Comorbidity Survey. Psychol Med. 1997; 27:1101–1119. [PubMed: 9300515]
24. Pirkola S, Isometsa E, Aro H, Kestila L, Hamalainen J, Veijola J, Kiviruusu O, Lönnqvist J. Childhood adversities as risk factors for adult mental disorders: results from the Health 2000 study. Soc Psychiatry Psychiatr Epidemiol. 2000; 40:769–777.
25. Chapman DP, Whitfield CL, Felitti VJ, Dube SR, Edwards VJ, Anda RF. Adverse childhood experiences and the risk of depressive disorders in adulthood. J Affect Disord. 2004; 82:217–225. [PubMed: 15488250]
26. Oladeji BD, Makanjuola VA, Gureje O. Family-related adverse childhood experiences as risk factors for psychiatric disorders in Nigeria. Br J Psychiatry. 2010; 196:186–191. [PubMed: 20194539]

27. Bernstein DP, Fink L, Hondelsman L, Foote J, Lovejoy M. Initial reliability and validity of a new retrospective measure of child abuse and neglect. Am. J. Psychiatry. 1994; 151:1132–1136. [PubMed: 8037246]
28. Straus, M.; Gelles, RJ. Physical Violence in American Families: Risk Factors and Adaptations to Violence in 8145 Families. New Brunswick, NJ: Transaction Press; 1990.
29. Schüssler-Fiorenza Rose SM, Xie D, Stineman M. Adverse childhood experiences and disability in U.S. adults. PM R. 2014; 6:670–680. [PubMed: 24486921]
30. Kerker BD, Zhang J, Nadeem E, Stein RE, Hurlburt MS, Heneghan A, Landsverk J, McCue Horwitz S. Adverse Childhood Experiences and Mental Health, Chronic Medical Conditions, and Development in Young Children. Acad Pediatr. 2015; 15:510–517. [PubMed: 26183001]
31. Glenn AL, Johnson AK, Raine A. Antisocial personality disorder: a current review. Curr Psychiatry Rep. 2013; 15:427. [PubMed: 24249521]
32. Coelho HF, Cooper PJ, Murray L. A family study of co-morbidity between generalized social phobia and generalized anxiety disorder in a non-clinic sample. J Affect Disord. 2007; 100:103–113. [PubMed: 17113155]
33. Kendler KS, Silberg JL, Neale MC, Kessler RC, Heath AC, Eaves LJ. The family history method: whose psychiatric history is measured? Am J Psychiatry. 1991; 148:1501–1504. [PubMed: 1928463]
34. Andreasen NC, Endicott J, Spitzer RL, Winokur G. The family history method using diagnostic criteria. Reliability and validity. Arch Gen Psychiatry. 1977; 34:1229–1235. [PubMed: 911222]
35. Andreasen NC, Rice J, Endicott J, Reich T, Coryell W. The family history approach to diagnosis. How useful is it? Arch Gen Psychiatry. 1986; 43:421–429. [PubMed: 3964020]
36. Vandeleur CL, Rothen S, Jeanprêtre N, Lustenberger Y, Gamma F, Ayer E, Ferrero F, Fleischmann A, Besson J, Sisbane F, Preisig M. Inter-informant agreement and prevalence estimates for substance use disorders: direct interview versus family history method. Drug Alcohol Depend. 2008; 92(1–3):9–19. [PubMed: 17643870]
37. Hardt J, Franke P. Validity, reliability and objectivity of the family history method in psychiatry: a meta analysis. Eur Psychiatry. 2007; 22:49–58. [PubMed: 17188848]
38. Weissman MM1, Wickramaratne P, Adams P, Wolk S, Verdeli H, Olfson M. Brief screening for family psychiatric history: the family history screen. Arch Gen Psychiatry. 2000; 57:675–682. [PubMed: 10891038]
39. Rougemont-Buecking A, Rothen S, Jeanprêtre N, Lustenberger Y, Vandeleur CL, Ferrero F, Preisig M. Inter-informant agreement on diagnoses and prevalence estimates of anxiety disorders: direct interview versus family history method. Psychiatry Res. 2008; 157:211–223. [PubMed: 17881063]
40. Prescott CA, Sullivan PF, Myers JM, Patterson DG, Devitt M, Halberstadt LJ, Walsh D, Kendler KS. The Irish Affected Sib Pair Study of Alcohol Dependence: study methodology and validation of diagnosis by interview and family history. Alcohol Clin Exp Res. 2005; 29:417–429. [PubMed: 15770118]
41. Reich JH. A family history method for DSM-III anxiety and personality disorders. Psychiatry Res. 1988; 26(2):131–139. [PubMed: 3237910]
42. Cuijpers P, Smit F. Assessing parental alcoholism: a comparison of the family history research diagnostic criteria versus a single-question method. Addict Behav. 2001; 26:741–748. [PubMed: 11676383]
43. Kosten TA, Anton SF, Rounsaville BJ. Ascertaining psychiatric diagnoses with the family history method in a substance abuse population. J Psychiatr Res. 1992; 26:135–147. [PubMed: 1613680]
44. Rhee SH, Neale MC, Corley RC, Hewitt JK. The inclusion of measured covariates in the Neale and Kendler model fitting approach. Behav Genet. 2007; 37(2):423–432. [PubMed: 17171532]

Table 1

Prevalence of Lifetime comorbidity among respondents and family history of comorbidity controlling for Socio-demographic Characteristics, % (SE)

Characteristic	AUD				DUD			DEP		ASB
	DUD	DEP	ASB	ANX	DEP	ASB	ANX	ASB	ANX	ANX
Total	1.56 (0.09)	2.78 (0.13)	2.14 (0.10)	1.99 (0.11)	0.75 (0.07)	0.78 (0.06)	0.72 (0.07)	1.40 (0.09)	3.99 (0.15)	1.33 (0.07)
Sex										
Male	1.75 (0.11)	2.27 (0.14)	2.26 (0.11)	1.58 (0.15)	0.63 (0.07)	0.80 (0.08)	0.62 (0.06)	1.14 (0.09)	2.26 (0.14)	0.81 (0.09)
Female	1.39 (0.11)	3.26 (0.18)	2.03 (0.15)	2.37 (0.14)	0.87 (0.10)	0.77 (0.08)	0.82 (0.10)	1.63 (0.13)	5.60 (0.25)	1.82 (0.11)
Race/ethnicity										
White	1.68 (0.12)	3.48 (0.20)	2.29 (0.13)	2.31 (0.15)	0.86 (0.09)	0.77 (0.07)	0.75 (0.09)	1.54 (0.11)	4.76 (0.21)	1.45 (0.10)
Black	1.25 (0.17)	1.03 (0.12)	1.60 (0.18)	0.91 (0.14)	0.72 (0.12)	0.82 (0.15)	0.61 (0.13)	1.13 (0.18)	2.19 (0.19)	1.11 (0.16)
Native American	3.87 (0.70)	5.53 (0.78)	6.50 (1.57)	7.46 (1.30)	1.20 (0.33)	2.69 (1.26)	3.70 (0.87)	3.76 (0.82)	7.25 (1.22)	4.30 (0.98)
Asian	0.44 (0.11)	0.55 (0.20)	0.39 (0.13)	0.17 (0.07)	0.05 (0.05)	0.15 (0.10)	0.10 (0.06)	0.40 (0.16)	1.24 (0.26)	0.29 (0.15)
Hispanic	1.48 (0.19)	1.62 (0.16)	2.12 (0.26)	1.57 (0.16)	0.54 (0.10)	0.85 (0.17)	0.60 (0.12)	1.11 (0.17)	2.72 (0.23)	1.10 (0.16)
Age, y										
18–29	3.07 (0.25)	3.58 (0.29)	3.24 (0.24)	2.79 (0.29)	1.65 (0.20)	1.73 (0.18)	1.40 (0.19)	2.20 (0.18)	4.03 (0.29)	1.99 (0.18)
30–44	2.39 (0.20)	3.75 (0.27)	2.80 (0.20)	2.45 (0.20)	1.00 (0.11)	1.17 (0.14)	0.95 (0.13)	1.80 (0.21)	4.31 (0.32)	1.64 (0.15)
45–64	0.77 (0.08)	2.64 (0.19)	1.85 (0.16)	1.90 (0.14)	0.35 (0.07)	0.28 (0.06)	0.49 (0.08)	1.19 (0.13)	4.62 (0.26)	1.20 (0.12)
≥65	0.07 (0.04)	0.67 (0.12)	0.43 (0.10)	0.52 (0.12)	0.06 (0.04)	0.06 (0.03)	0.01 (0.01)	0.23 (0.07)	2.22 (0.20)	0.33 (0.10)
Family income, $										
0–19,999	2.67(0.22)	3.47(0.27)	2.88(0.24)	2.99(0.24)	1.45(0.16)	1.59(0.20)	1.59(0.20)	2.10(0.18)	4.54(0.27)	2.16(0.19)
20,000–34,999	1.84(0.18)	2.39(0.20)	2.55(0.24)	1.81(0.17)	0.74(0.11)	0.92(0.14)	0.57(0.10)	1.62(0.20)	3.98(0.29)	1.39(0.17)
35,000–69,999	1.46(0.14)	2.59(0.20)	2.18(0.20)	2.07(0.19)	0.71(0.10)	0.68(0.11)	0.62(0.10)	1.36(0.16)	4.03(0.25)	1.28(0.15)
≥70,000	0.67(0.10)	2.68(0.20)	1.32(0.15)	1.30(0.15)	0.29(0.06)	0.21(0.05)	0.27(0.06)	0.77(0.11)	3.56(0.25)	0.74(0.11)
Marital status										
Married/cohabiting	1.14(0.09)	2.52(0.16)	1.92(0.12)	1.71(0.12)	0.56(0.07)	0.60(0.06)	0.46(0.06)	1.06(0.09)	3.70(0.17)	1.04(0.09)
Widowed/separated/divorced	1.43(0.18)	3.04(0.23)	1.96(0.17)	2.25(0.19)	0.68(0.11)	0.64(0.17)	0.76(0.12)	1.64(0.17)	4.96(0.27)	1.63(0.17)
Never married	2.78(0.22)	3.23(0.27)	2.88(0.20)	2.50(0.25)	1.33(0.17)	1.38(0.17)	1.36(0.19)	2.03(0.19)	3.89(0.26)	1.82(0.17)
Education										
Less than high school	1.90(0.26)	2.14(0.25)	2.17(0.24)	2.00(0.29)	1.03(0.15)	0.93(0.17)	0.81(0.14)	1.24(0.19)	3.03(0.25)	1.24(0.19)

Characteristic	AUD				DUD				DEP			ASB
	DUD	DEP	ASB	ANX	DEP	ASB	ANX	ASB	ANX	ANX
High school	1.86(0.16)	2.53(0.22)	2.77(0.21)	1.94(0.15)	0.93(0.14)	1.04(0.12)	0.79(0.12)	1.51(0.20)	3.69(0.28)	1.44(0.15)
Some college or higher	1.37(0.11)	3.02(0.16)	1.87(0.11)	2.01(0.14)	0.62(0.07)	0.65(0.08)	0.68(0.08)	1.38(0.10)	4.32(0.19)	1.31(0.08)

Table 2

Adjusted Odds ratios of comorbidity by family history of comorbidity and Socio-demographic Characteristics, OR, 95% confidence interval

			Family history			
			Disorder X and Y comorbid	**Disorder X OR Y not comorbid**	**Disorder X only**	**Disorder Y only**
Disorder X	Disorder Y	respondents				
AUD	DUD	Comorbid	**10.07 (8.5. 11.9)**	8.37 (6.5,10.8)	3.22 (2.8,3.6)	2.89 (2.1,4.1)
		Disorder X	**2.87 (2.5,3.2)**	2.61 (2.0,3.4)	2.06 (1.9,2.2)	1.56 (1.2,1.9)
		Disorder Y	4.76 (3.6,6.2)	**4.87 (3.1,7.6)**	2.37 (2.0,2.7)	4.42 (2.9,6.7)
	DEP	Comorbid	**12.45 (10.5,14.7)**	9.38 (7.9,11.1)	3.00 (2.5,3.5)	4.56 (3.8,5.5)
		Disorder X	**3.31 (3.0,3.7)**	2.69 (2.3,3.1)	2.22 (2.0,2.4)	1.59 (1.4,1.8)
		Disorder Y	4.08 (3.5,4.7)	**4.35 (3.8,5.0)**	1.62 (1.4,1.8)	3.68 (3.3,4.1)
	ASB	Comorbid	**14.36 (11.3,18.2)**	12.94 (7.6,21.9)	3.56 (3.0,4.3)	6.48 (4.8,8.7)
		Disorder X	**2.92 (2.7,3.2)**	2.33 (1.8,3.1)	2.12 (1.9,2.3)	1.98 (1.7.2.2)
		Disorder Y	**9.92 (7.6,13.0)**	9.64 (5.3,17.6)	2.14 (1.6,2.9)	6.01 (4.1,8.9)
	ANX	Comorbid	**10.87 (9.2,12.8)**	7.76 (6.3,9.5)	2.86 (2.4,3.4)	3.96 (3.5,4.5)
		Disorder X	**3.18 (2.8,3.7)**	2.40 (2.0,2.9)	2.23 (2.1,2.4)	1.44 (1.3,1.6)
		Disorder Y	**4.44 (3.8,5.2)**	4.14 (3.5,4.9)	1.54 (1.4,1.7)	2.85(2.5,3.3)
DUD	DEP	Comorbid	**12.28 (9.7,15.6)**	8.88 (6.1,13.0)	4.01 (2.9,5.8)	4.62 (3.9,5.5)
		Disorder X	**5.73 (4.8,6.8)**	4.03 (2.8,5.8)	2.95 (2.3,3.7)	2.01(1.7,2.3)
		Disorder Y	**3.84 (3.4,4.4)**	3.15 (2.4,4.2)	1.56 (1.2,2.0)	3.44 (3.2,3.7)
	ASB	Comorbid	**14.23 (10.7,18.8)**	11.85 (6.5,21.6)	5.29 (3.9,7.2)	5.85 (4.4,7.8)
		Disorder X	**4.34 (3.7,5.0)**	2.99 (1.6,5.6)	3.05 (2.5,3.7)	2.06 (1.8,2.4)
		Disorder Y	6.51 (5.0,8.5)	**9.78 (4.1,23.1)**	2.26 (1.7,3.1)	5.73 (4.8,6.9)
	ANX	Comorbid	**13.02 (10.4,16.4)**	7.14 (4.9,10.4)	3.99 (3.2,5.0)	4.02 (3.4,4.8)
		Disorder X	**4.60 (3.7,5.8)**	4.17 (3.0,5.9)	3.69 (3.1,4.4)	1.80 (1.5,2.1)
		Disorder Y	**3.73 (3.1,4.5)**	3.71 (2.8,4.9)	1.59 (1.3,1.9)	2.96 (2.7,3.2)
DEP	ASB	Comorbid	**17.80 (12.7,25.0)**	17.26 (10.5,28.3)	4.36 (3.3,5.8)	6.84 (4.3,10.9)
		Disorder X	**4.19 (3.7,4.7)**	4.08 (3.4,4.9)	3.4 (3.1,3.7)	2.10 (1.7,2.6)
		Disorder Y	**8.60 (6.6,11.2)**	7.09 (4.8,10.4)	2.15 (1.7,2.7)	5.64 (4.2,7.5)

			Family history			
			Disorder X and Y comorbid	Disorder X OR Y not comorbid	Disorder X only	Disorder Y only
	ANX	Comorbid	**9.98 (8.8,11.3)**	5.66 (4.1,7.9)	4.38 (3.8,5.1)	2.77 (2.3,3.4)
		Disorder X	**3.78 (3.3,4.3)**	3.27 (2.3,4.7)	3.18 (2.9,3.5)	1.99 (1.7,2.3)
		Disorder Y	**4.67 (4.2,5.2)**	2.93 (2.0,4.2)	2.10 (1.9,2.3)	2.36(2.0,2.7)
ASB	ANX	Comorbid	**26.94 (20.5,35.4)**	10.82 (7.0,16.7)	6.25 (4.6,8.5)	4.13 (3.1,5.4)
		Disorder X	**7.71 (5.8,10.2)**	5.94 (3.9,9.1)	4.52 (3.4,5.9)	1.79 (1.4,2.3)
		Disorder Y	**4.90 (4.3,5.5)**	4.36 (3.6,5.3)	2.17 (1.9,2.5)	2.68(2.4,2.9)

Table 3

Adjusted Odds ratios of comorbidity by family history of comorbidity and Socio-demographic Characteristics and categorized ACE, OR, 95% confidence interval

			Family history			
			Disorder X and Y comorbid	**Disorder X OR Y not comorbid**	**Disorder X only**	**Disorder Y only**
Disorder X	Disorder Y	respondents				
AUD	DUD	Comorbid	**5.52(4.6,6.6)**	4.98(3.8,6.6)	2.36(2.1,2.7)	1.85(1.3,2.6)
		Disorder X	**2.14(1.9,2.5)**	2.06(1.6,2.7)	1.78(1.7,1.9)	1.28(1.0,1.6)
		Disorder Y	2.69(2.0,3.6)	**2.98(1.8,4.9)**	1.72(1.4,2.1)	2.91(1.9,4.4)
	DEP	Comorbid	**7.11(5.9,8.6)**	6.37(5.3,7.7)	2.29(1.9,2.7)	3.81(3.2,4.6)
		Disorder X	**2.43(2.1,2.7)**	2.19(1.9,2.5)	1.92(1.7,2.1)	1.46(1.3,1.6)
		Disorder Y	2.77(2.4,3.3)	**3.36(2.9,3.8)**	1.34(1.2,1.5)	3.27(2.9,3.6)
	ASB	Comorbid	3.93(3.0,5.1)	**4.65(2.6,8.2)**	1.87(1.5,2.3)	2.65(1.9,3.7)
		Disorder X	**2.14(1.9,2.4)**	1.79(1.3,2.4)	1.80(1.7,2.0)	1.60(1.4,1.8)
		Disorder Y	2.99(2.2,4.0)	**3.58(1.9,6.8)**	1.16(0.9,1.6)	2.60(1.7,4.0)
	ANX	Comorbid	**5.03 (4.2,6.1)**	4.07 (3.3,5.0)	1.80 (1.5,2.1)	3.10 (2.7,3.6)
		Disorder X	**2.42 (2.1,2.8)**	1.91 (1.6,2.3)	1.89 (1.7,2.1)	1.33 (1.2,1.5)
		Disorder Y	2.60 (2.2,3.1)	**2.65 (2.2,3.2)**	1.12 (1.0,1.3)	2.43 (2.1,2.8)
DUD	DEP	Comorbid	**5.99(4.7,7.7)**	4.75 (3.3,6.9)	2.65 (1.9,3.6)	3.43 (2.9,4.1)
		Disorder X	**3.40 (2.8,4.1)**	2.56 (1.8,3.7)	2.15 (1.7,2.7)	1.61 (1.4,1.9)
		Disorder Y	2.63 (2.3,3.1)	2.28 (1.7,3.1)	1.24 (1.0,1.6)	**2.96 (2.7,3.2)**
	ASB	Comorbid	**4.23 (3.1,5.8)**	3.52 (1.8,6.9)	2.56 (1.8,3.5)	2.23 (1.6,3.1)
		Disorder X	**2.69 (2.3,3.1)**	1.82 (1.0,3.5)	2.31 (1.9,2.8)	1.40 (1.2,1.6)
		Disorder Y	2.28 (1.7,3.0)	**3.42 (1.4,8.6)**	1.22 (0.9,1.7)	2.51 (2.0,3.1)
	ANX	Comorbid	**5.48 (4.4,6.8)**	3.48 (2.4,5.1)	2.26 (1.8,2.9)	2.83 (2.4,3.4)
		Disorder X	**2.83 (2.2,3.6)**	2.78 (1.9,4.0)	2.67 (2.2,3.2)	1.50 (1.3,1.8)
		Disorder Y	2.19 (1.8,2.7)	**2.42 (1.8,3.2)**	1.12 (0.9,1.4)	2.44 (2.2,2.7)
DEP	ASB	Comorbid	5.12 (3.5,7.5)	**5.58 (3.2,9.6)**	2.80 (2.1,3.7)	2.60 (1.6,4.3)
		Disorder X	2.85 (2.5,3.2)	2.85 (2.3,3.5)	**2.99 (2.8,3.2)**	1.57 (1.3,1.9)

			Family history			
			Disorder X and Y comorbid	Disorder X OR Y not comorbid	Disorder X only	Disorder Y only
		Disorder Y	**2.94 (2.2,4.0)**	2.66 (1.8,4.0)	1.49 (1.2,1.9)	2.47 (1.8,3.3)
	ANX	Comorbid	**6.61 (5.8,7.6)**	4.17 (3.0,5.9)	3.52 (3.0,4.1)	2.33 (1.9,2.9)
		Disorder X	**3.05 (2.7,3.5)**	2.78 (1.9,4.1)	2.85 (2.6,3.2)	1.82 (1.6,2.1)
		Disorder Y	**3.37 (3.0,3.8)**	2.30 (1.6,3.3)	1.76 (1.6,2.0)	2.06 (1.8,2.4)
ASB	ANX	Comorbid	**7.58 (5.5,10.5)**	3.39 (2.1,5.5)	2.30 (1.7,3.2)	2.72 (2.1,3.6)
		Disorder X	**2.79 (2.0,3.8)**	2.36 (1.5,3.7)	2.05 (1.5,2.7)	1.31 (1.0,1.7)
		Disorder Y	**2.98 (2.6,3.4)**	2.79 (2.3,3.4)	1.48 (1.3,1.7)	2.34 (2.1,2.6)