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The association between anxiety and alcohol versus cannabis abuse disorders among adolescents in primary care settings

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Background. Both clinical and population-based studies show that anxiety disorders and substance misuse frequently co-occur in adults, whereas among adolescents, less examination of this association has been done. Adolescence is frequently the time of substance use initiation and its subsequent interaction with anxiety disorders has not been fully explored. It is unknown in adolescents whether anxiety is more related to alcohol abuse versus cannabis abuse. In addition, as depression has been implicated in adolescents with both anxiety and substance misuse, its role in the association should also be considered.

Objective. To test the association between current anxiety with alcohol versus cannabis abuse disorders.

Method. Cross-sectional, clinician-administered, structured assessment—using the Primary Care Evaluation of Mental Disorders—to evaluate anxiety, mood and substance abuse disorders among 632 adolescents recruited from primary care settings.

Results. Results show a strong association between current anxiety and alcohol [odds ratio = 3.8; 95% confidence interval (CI) 1.2–11.8], but not cannabis (odds ratio = 1.4; 95% CI 0.4–4.7) abuse.

Conclusion. This association in adolescents reflects the importance for increased awareness of anxiety symptoms and alcohol use patterns in primary care. The lack of association of anxiety with cannabis abuse in this group may reflect differences in cannabis' anxiolytic properties or that this young group has had less exposure thus far. Given adolescence is a time of especially rapid psychosocial, hormonal and brain development, primary care may provide an opportunity for further investigation and, potentially, early screening and intervention.

Keywords. Adolescents, alcohol abuse, anxiety, cannabis abuse, family medicine, primary care.

Background

In youth, the co-occurrence of other mental disorders along with anxiety disorders and symptoms has been associated with a more menacing course of anxiety disorders, characterized by suicidal events[1,2] and serious disability/impairment.[3] Studies of youth aged 8–18 years have found that the progression of anxiety disorders to other psychiatric co-morbidity complicates the clinical picture of both the primary and secondary disorders, rendering both more difficult to detect, diagnose, treat and further from the reach of prevention efforts.[3–5]

Though the research in adolescents compared to adults is sparse, the limited number of studies has shown overlap between anxiety disorders and

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substance use disorders. They have generally examined anxiety and 'substance misuse in general'.[6–9] Shrier *et al.*[7] examined psychiatric co-morbidity across three groups of substance use diagnoses (substance use disorders, substance use problems, no substance use) in 538 adolescents aged 14–18 (68% female) in a hospital-based adolescent clinic. They found that ~70% of males and females had anxiety in the substance use disorder group compared to ~55% in the non-substance use group. Rao *et al.*[6] followed-up depressed adolescents (without substance use disorders at baseline) 7 years later and found that anxiety traits were associated with the development of substance use disorders.

Other studies have examined anxiety in association with a 'specific substance' (e.g. cannabis or alcohol).[10–12] With respect to cannabis, in a birth cohort of 3239 people from the general population followed until age 21, Hayatbakhsh *et al.*[10] found that cannabis use before age 15 years and frequent use at 21 were associated with more anxiety and depression. In another study that followed 1601 students aged 14–15 for 7 years, Patton *et al.*[12] found that daily cannabis use in females was associated with a 5-fold risk elevation for anxiety/depression, while weekly use was associated with a ~2-fold increase. Also, Wittchen *et al.*[11] followed 1395 adolescents for 10 years and found that baseline anxiety was associated with later cannabis abuse/dependence.

With respect to alcohol, similar associations have been found with anxiety.[13–15] Fidalgo *et al.*[13] studied 84 adolescents from clinics who were grouped by frequency of alcohol use [daily users, mild users (who used >1 per week, but not daily), non-users] and found that 50% of daily users had anxiety. Schmidt *et al.*[14] prospectively studied 404 youth aged 16–24 (from high schools, college and the community) over 2 years and found that high anxiety sensitivity in male youths was strongly associated with development of alcohol use disorders. Finally, in a study that examined 1747 18- to 23-year olds from the National Comorbidity Survey, Lopez *et al.*[15] found that anxiety disorders were associated with the presence of alcohol dependence and that the anxiety disorders preceded the onset of alcohol dependence. This association was independent of other co-occurring mental disorders.

There are, however, studies that do not find replication of these associations between cannabis or alcohol and anxiety.[16–19] Furthermore, some studies have not considered the well-established overlap of anxiety and mood disorders[3] as a common potential confounder, despite evidence showing that anxiety disorders are risk factors for secondary depression.[4] Other types of evidence for association between anxiety and substance use disorders have been demonstrated by reports of co-aggregation of these disorders within families.[20] However, biological correlates[6,21,22] have been found only within proposed subgroups of samples. Thus, precise elucidation of the relationship between anxiety and cannabis and alcohol misuse remains unresolved.

The examination of anxiety and alcohol/cannabis abuse in adolescents in primary care settings is important for several reasons. First, for most young people, primary care is the only professional care they will access for a mental disorder.[23] Second, primary care offers an opportunity to assess symptoms in a context where adolescents have not already been identified as having stigmatizing mental health problems.[24] Thirdly, primary care may represent an opportunity for screening and early intervention as some adolescents are required to have regular visits to their physicians for school attendance purposes. Psychiatric disorders detected at this point may not have developed secondary psychiatric complications and may be more amenable for intervention and prevention.[25] Fourth, with respect to study methodology, if adolescents attending clinics are actively symptomatic, symptom reporting is less prone to recall bias.[26] Fifthly, anxiety frequently presents with physical symptoms of a medical disorder. Those that have both anxiety and co-morbid physical illness have greater disabilities, a poorer quality of life and may be high utilizers of care.[27–30] This study uses a large sample of adolescents from primary care settings to test the association between current anxiety and alcohol and cannabis abuse disorders.

Methods

Sample

The sample consisted of 632 English-speaking adolescent, primary care patients (32.8% male, 67.2% female) between the ages of 13 and 19 years (mean age = 16.1 years, SD = 1.24). Individuals with evidence of mental retardation or a mental disorder due to a medical illness were excluded from the study. Participating clinics and school sites were selected from urban, suburban and rural areas in the Eastern, Midwestern and Western regions of the US to maximize the demographic representativeness of the sample. Participants were recruited from two primary care sources: (i) the greater Sacramento region through the University of California Davis Health System Primary Care Network and (ii) the primary care and school nurse offices in Ohio, New Jersey and New York (see Table 1).

California subjects were identified using centralized appointment records available through a centralized practice management system, between November 1997 and June 1998. Letters describing the study and requesting written consent were sent to parents/guardians of all adolescents. For participants who were less than 18 years of age, parents provided informed

TABLE 1 *Sample characteristics*

	Total sample (N = 632)	Female (N = 425) (67.2% of total)	Male (N = 207) (32.8% of total)
Mean age (years, SD and range)	16.1 (1.2, 13–19)	16.1 (1.1, 13–19)	15.9 (1.2, 13–19)
Age (%)			
13- to 14-year olds	8.1 (51)	5.4 (23)	13.5 (28)
15- to 16-year olds	52.6 (333)	52.9 (225)	52.2 (108)
17- to 19-year olds	39.3 (248)	41.7 (177)	34.3 (71)
Ethnicity (%)			
White or Caucasian	473 (74.8)	74.4 (316)	75.8 (157)
Hispanic or Latino	81 (12.8)	13.8 (59)	10.6 (22)
Black or African American	37 (5.9)	5.9 (25)	5.8 (12)
Asian, American Indian, other	41 (6.5)	5.9 (25)	7.8 (16)
Sites of Sampling			
New York, Ohio, New Jersey	403 (63.8)	67.1 (285)	57.0 (118)
University of California Davis Primary Care Network	229 (36.2)	32.9 (140)	43.0 (89)

written consent and participants provided youth assent. In response to over 900 letters, parental consent was returned for 285 adolescents (32%); assent forms and self-report measures were then sent directly to the adolescent by mail. Of the 285 adolescents contacted, 254 adolescents (89%) completed and returned the questionnaires and consent. Completed telephone interviews were conducted with 229 subjects.

In New York, New Jersey and Ohio, adolescents were informed about the study by their physicians or school nurses. Potential subjects were recruited between December 1995 and May 1997. Those who were interested in participating were given a packet that included questionnaires, a letter describing the study procedures, participant consent, parental consent and youth assent forms. Participants returned the packet by mail to the study team in a stamped, self-addressed envelope that was also included. Four hundred and forty-two participants completed and returned the questionnaire packets. Complete interviews were conducted in 403 (91%) of these subjects.

Study procedures were approved by the Institutional Review Boards in accordance with review procedures at New York State Psychiatric Institute, Columbia-Presbyterian Medical Center and University of California Davis School of Medicine. In all, 43% (269/632) of the total sample visited their primary care physician or nurse for a regular medical check up. Further methodological details have been previously reported.[31]

Interview procedures

Following collection of parental consent and participant consent/youth assent, a participant's contact details were given to interviewers. All interviews were conducted by telephone by masters- or doctorate-level, trained mental health professionals. Research has supported the validity of telephone-administered structured clinical interviews.[32] All interviewers contacted participants within a week of receiving a participant's contact details. After the clinical interview was completed, each participant was mailed a payment of $20.00. A certificate of confidentiality was obtained, and information was not divulged to anyone by the study investigators. The confidentiality of the information collected in the protocol was not compromised at any stage. The doctors and clinics did not have access to the information in the study protocol. Therefore, study participation or refusal did not influence a participant's care. There was no sharing of data by investigators.

Measures

The Primary Care Evaluation of Mental Disorders (PRIME-MD)[33] is a structured diagnostic interview with specific modules that assess according to the Diagnostic and Statistical Manual of Mental Disorders' (fourth edition)[34] criteria for anxiety, eating, mood disorders and substance abuse or dependence. Research findings have supported the reliability and validity of diagnoses produced using the PRIME-MD system[33] and that PRIME-MD diagnoses are associated with substantial impairment and disability, in addition to elevated health care utilization.[35]

The anxiety disorders included in the interview were panic disorder, generalized anxiety disorder and anxiety disorder not otherwise specified. The mood disorders included major depressive episode, dysthymia and minor depression. The substances assessed for use and abuse were cannabis, hashish, alcohol, hallucinogens, sedatives, cocaine/'crack', stimulants, opiates and inhalants. All disorders assessed were current. Disorders were therefore required to meet various durational criteria depending on the disorder; for example, major depression had to be within the last 2 weeks, dysthymia for the last 2 years; for the anxiety disorders, the last 6 months for generalized anxiety

and last month for panic disorder and for substance abuse, the last 6 months.

Differences in the *DSM-IV* diagnostic criteria between adolescents and adults among the disorders were few and minor. For example, duration of dysthymia is 2 years in adults and 1 year in adolescents. In this case, interviewers were trained to consider a dysthymia diagnosis if the adolescent criteria of 1 year duration was met. The PRIME-MD has been frequently used in studies examining adolescent subjects from primary care, psychiatric and other specialty settings to assess mood, anxiety and substance disorders.[36–40]

Statistical analyses

Chi-square tests were conducted to compare the frequencies of mental disorders between males and females and between mental disorders. Odds ratios with 95% confidence intervals (CIs) were estimated from logistic regression models using alcohol and cannabis abuse as outcomes in two separate models. Both models used anxiety disorder as the main effect while controlling for mood disorder, gender, age, ethnicity and sampling site. The mood disorder variable was a dichotomous variable which included any major depressive episode, dysthymia or minor depression. Age was used a continuous variable in years. Ethnicity was a categorical variable including the possible responses of White/Caucasian, Hispanic/Latino, Black/African American or Asian/American Indian/other. Sampling site was a dichotomous variable (NY/NJ/OH versus CA). All statistical analyses were conducted using SPSS 15.0 (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL).

Results

Table 2 reports the rates of current mental disorders among the adolescents. In all, 7% reported symptoms consistent with a diagnosis of an anxiety disorder. Nearly 10% of the sample reported having a substance abuse disorder, with males reporting a slightly higher rate of 13.0% versus females with 7.5% (P-value = 0.0270). Alcohol and cannabis abuse rates were about equal at 5–6%, with no gender difference. Mood disorders, which have been well-established to co-occur with anxiety disorders, were also prominent among the sample with 14.1% of the adolescents affected.

Table 3 shows the overlap between anxiety, alcohol and cannabis abuse disorders. Among those adolescents who were anxious, 11% were found to have alcohol abuse, while 9% had cannabis abuse. Among those with alcohol abuse 15% had anxiety, compared to 11% with anxiety among cannabis abusers. About one-third of those who reported alcohol abuse also abused cannabis and vice versa. Over half of those with anxiety were also found to have a mood disorder, and one-third of those with a mood disorder had anxiety.

Table 4 contrasts the association between anxiety and alcohol versus cannabis abuse. Anxiety disorder diagnosis was significantly associated with alcohol abuse [OR = 3.8, 95% CI 1.2–11.8], but in contrast, there was

TABLE 2 *Prevalence of current psychiatric disorders*

Psychiatric disorder	Total sample (N = 632), % (n)	Females (N = 425), % (n)	Males (N = 207), % (n)	Odds ratio[a] (95% CI)
Anxiety disorder	7.0 (44)	8.2 (35)	4.3 (9)	2.0 (0.9–4.2)
Panic disorder	1.9 (12)	2.4 (10)	1.0 (2)	2.5 (0.5–11.4)
Generalized anxiety disorder	1.9 (12)	2.4 (10)	1.0 (2)	2.5 (0.5–11.4)
Any anxiety not otherwise specified	3.8 (24)	4.5 (19)	2.4 (5)	1.9 (0.7–5.1)
Substance abuse disorder	9.3 (59)	7.5 (32)	13.0 (27)	0.5 (0.3–0.9)*
Alcohol	5.2 (33)	4.5 (19)	6.8 (14)	0.6 (0.3–1.3)
Cannabis	5.7 (36)	4.7 (20)	7.7 (16)	0.6 (0.4–1.2)
Mood disorder	14.1 (89)	15.5 (66)	11.1 (23)	1.5 (0.9–2.4)

[a]Males are the reference group.
*P-value < 0.05.

TABLE 3 *Psychiatric disorder co-morbidity*

	Anxiety disorder	Alcohol abuse	Cannabis abuse	Mood disorder
	% (n/44)	% (n/33)	% (n/36)	% (n/89)
Anxiety disorder		15.2 (5/33)	11.1 (4/36)	30.3 (27/89)
Alcohol abuse	11.4 (5/44)		30.6 (11/36)	4.5 (4/89)
Cannabis abuse	9.1 (4/44)	33.3 (11/33)		9.0 (8/89)
Mood disorder	61.4 (27/44)	12.1 (4/33)	22.2 (8/36)	

TABLE 4 *Association between anxiety and alcohol and cannabis abuse disorders*

	Alcohol abuse	Cannabis abuse
	Odds ratio (95% CI)	Odds ratio (95% CI)
Main effect		
Anxiety disorder	3.8 (1.2–11.8)	1.4 (0.4–4.7)
Covariates		
Mood disorder	0.6 (0.2–2.0)	2.0 (0.8–4.8)
Sex (0 = male, 1 = female)	0.6 (0.3–1.2)	0.5 (0.2–1.0)
Age	1.2 (0.9–1.6)	1.7 (1.2–2.3)
Ethnicity	0.7 (0.5–1.1)	0.8 (0.5–1.2)
Sampling site	1.0 (0.9–1.2)	1.1 (0.5–1.1)

no association with cannabis abuse (OR = 1.4, 95% CI 0.4–4.7). The presence of a co-morbid mood disorder did not change the association of anxiety with either alcohol or cannabis abuse, nor did adolescents' age, gender, ethnicity or the sampling site.

Discussion

The major finding of this report is the significant association between current anxiety with alcohol abuse and not cannabis abuse. This study extends previous literature by contrasting the specific relationship of anxiety with alcohol versus cannabis abuse disorders, while controlling for mood disorders, a common confounder. The study's sample size is also larger than previous primary care studies and employs multiple centers for recruitment with direct clinician assessment, rather than self-report measures. The main finding that anxiety is associated with alcohol abuse is in general agreement with other findings derived from primary care, in- and out-patient psychiatry settings.[7,9,41] However, no previous studies have directly compared current anxiety in relation to alcohol versus cannabis abuse.

Given the paucity of standard, widely accepted, mental disorder rates among primary care settings of adolescents, a comparison of this study's rates of disorders was made with recent, nationally representative, population-based surveys in order to examine the generalizability of these findings. This study's rates of anxiety, mood, alcohol and cannabis abuse disorders were 7%, 14%, 5% and 5%, respectively. The National Comorbidity Survey—Replication reported 12-month rates among the total sample (age-specific rates were not reported) of 18% for any anxiety (which included 'all' anxiety disorders) and 10% for any mood disorder.[42] The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) reported rates of 7% for alcohol abuse[43] and 3% for cannabis abuse among 18- to 29-year olds.[44] A recent study of ~4100 adolescents aged 11–17 from a metropolitan area found the rates of anxiety, mood, alcohol and cannabis abuse disorders to be 7%, 3%, 3% and 3%, respectively.[45] These population-based rates are in general agreement with this study's rates, with some expected variation given differences in methodologies (e.g. population versus primary care sampling, use of structured versus semi-structured instruments, clinical versus lay-trained interviewers, etc.) and purposes of the studies. The co-morbidity between the disorders (mood, anxiety and substance misuse) in the national samples and ours was also in general agreement.

The findings of this study support the need for ongoing research among adolescents to further delineate the association between anxiety and alcohol misuse. Due to the cross-sectional design of this study, evidence supporting the pathway or evolution to this association cannot be provided here. There is little research in the age group of 13–17 given alcohol use is illegal in North America and most parts of Europe. However, research on the next older age group (young adults) may shed some light on certain aspects of the association.

Research in young adults (~18 to early 20s) has shown complexity in the relationship between anxiety, motives to drink (e.g. for coping/stress management) and alcohol use.[14,46–48] Some findings have supported social anxiety as a risk for alcohol use, whereas others have not. Two large nationally representative epidemiologic studies have examined the perspective that anxiety plays a primary role leading to alcohol misuse, also known as 'alcohol as self-medication for anxiety'. Bolton *et al.*[49] observed that in a sample of ~8000 persons (aged 15–54) those with anxiety who self-medicated with drinking had higher rates of alcohol abuse. Falk *et al.*[50] looked at the temporal sequencing of the onset of specific anxiety and mood disorders with respect to alcohol misuse (abuse and dependence) in the NESARC sample of nearly 20 000 (over-sampled for 18- to 24-year olds). They found that specific phobia and social anxiety were the only two disorders to precede alcohol misuse, while panic disorder and generalized anxiety disorder increased the risk of persistent alcohol dependence.

In adolescents, the association between alcohol and anxiety is likely to depend on and involve the adolescent's age; the dose, nature and timing (chronic versus episodic) of alcohol intake; developmental stage; familial risk and peer contexts. Research is already underway on interventions that target high school students for alcohol misuse.[51] Finally, research in animal models of adult versus adolescent rats also show that adolescent rats experience less negative effects of alcohol withdrawal and are able to clear alcohol faster[52,53] which may set a context with which self-medication of anxiety would increase the risk for alcohol abuse.

The lack of association between anxiety and cannabis abuse may be due to several reasons.

Delta-9-tetrahydrocannabinol, the psychoactive ingredient of cannabis, may have less anxiolytic properties compared to alcohol in this age group and stage of brain development rendering it less effective for those using it as a substance to self-medicate anxiety. Also, the types of anxiety assessed in this study—mainly panic (characterized by unexpected, episodic attacks) and generalised anxiety disorder (chronic, increased basal anxiety) may be more amenable to alleviation with alcohol. This is in contrast to social anxiety or specific phobias where the feared cue is known. In addition, the anxiety disorder thresholds employed may not refined sufficiently to detect anxiety symptom alleviation associated with cannabis use. Finally, these adolescents may have also had less exposure to cannabis (since it is illegal and less accessible) compared to alcohol in their lifetime thus far and therefore have not had a chance to develop cannabis abuse. However, recent literature on trajectories of cannabis and alcohol use has shown preference of adolescents for one substance over the other.[54]

Strengths and limitations

Strengths of this report include the use of a well-validated instrument designed to diagnose mental disorders in primary care settings; the use of clinically experienced interviewers with standardized assessment tools rather than self-reports; the close temporal relationship between treatment seeking in the clinic and psychiatric assessment; a sizeable, multi-site sample and the adjustment for mood disorders in the analyses.

Limitations of this study include its cross-sectional nature, limiting its ability to draw any causal conclusions; the anxiety disorder assessment of the PRIME-MD did not distinguish between primary versus substance-induced anxiety disorder; the sample size was underpowered to examine specific subtypes of anxiety, in addition, the rates of substance abuse cases themselves were low; male adolescents may also be under-represented in this sample and subjects may have not fully disclose about illegal substance (cannabis) use.

Implications

Findings would suggest that promoting awareness of anxiety and alcohol use patterns within primary care settings may lead to greater case detection and potentially a role for prevention. If complaints of anxiety symptoms arise from adolescents, alcohol use patterns should be queried and, vice versa, if problematic alcohol use presents, anxiety symptoms should be queried. Adolescents' perceptions of their anxiety and alcohol use, and ways they cope with stress, can be further follow-up questions as their responses may provide potential targets of education and intervention. In addition, inquiry about other substance use and depressive symptoms may also be considered.

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References

[1] Boden JM, Fergusson DM, Horwood LJ. Anxiety disorders and suicidal behaviours in adolescence and young adulthood: findings from a longitudinal study. *Psychol Med* 2007; **37:** 431–440.
[2] Foley DL, Goldston DB, Costello EJ, Angold A. Proximal psychiatric risk factors for suicidality in youth: the Great Smoky Mountains Study. *Arch Gen Psychiatry* 2006; **63:** 1017–1024.
[3] Costello EJ, Egger HL, Angold A. The developmental epidemiology of anxiety disorders: phenomenology, prevalence, and comorbidity. *Child Adolesc Psychiatr Clin N Am* 2005; **14:** 631–648., vii.
[4] Wittchen HU, Beesdo K, Bittner A, Goodwin RD. Depressive episodes—evidence for a causal role of primary anxiety disorders? *Eur Psychiatry* 2003; **18:** 384–393.
[5] Costello EJ, Egger H, Angold A. 10-Year research update review: the epidemiology of child and adolescent psychiatric disorders: I. Methods and public health burden. *J Am Acad Child Adolesc Psychiatry* 2005; **44:** 972–986.
[6] Rao U, Ryan ND, Dahl RE *et al*. Factors associated with the development of substance use disorder in depressed adolescents. *J Am Acad Child Adolesc Psychiatry* 1999; **38:** 1109–1117.
[7] Shrier LA, Harris SK, Kurland M, Knight JR. Substance use problems and associated psychiatric symptoms among adolescents in primary care. *Pediatrics* 2003; **111:** e699–e705.
[8] Goodwin RD, Lieb R, Hoefler M *et al*. Panic attack as a risk factor for severe psychopathology. *Am J Psychiatry* 2004; **161:** 2207–2214.
[9] Deas D. Adolescent substance abuse and psychiatric comorbidities. *J Clin Psychiatry* 2006; **67 suppl 7):** 18–23.
[10] Hayatbakhsh MR, Najman JM, Jamrozik K, Mamun AA, Alati R, Bor W. Cannabis and anxiety and depression in young adults: a large prospective study. *J Am Acad Child Adolesc Psychiatry* 2007; **46:** 408–417.
[11] Wittchen HU, Frohlich C, Behrendt S *et al*. Cannabis use and cannabis use disorders and their relationship to mental disorders: a 10-year prospective-longitudinal community study in adolescents. *Drug Alcohol Depend* 2007; **88 (suppl 1):** S60–S70.
[12] Patton GC, Coffey C, Carlin JB, Degenhardt L, Lynskey M, Hall W. Cannabis use and mental health in young people: cohort study. *BMJ* 2002; **325:** 1195–1198.
[13] Fidalgo TM, da Silveira ED, da Silveira DX. Psychiatric comorbidity related to alcohol use among adolescents. *Am J Drug Alcohol Abuse* 2008; **34:** 83–89.
[14] Schmidt NB, Buckner JD, Keough ME. Anxiety sensitivity as a prospective predictor of alcohol use disorders. *Behav Modif* 2007; **31:** 202–219.
[15] Lopez B, Turner RJ, Saavedra LM. Anxiety and risk for substance dependence among late adolescents/young adults. *J Anxiety Disord* 2005; **19:** 275–294.
[16] Monshouwer K, Vand S, Verdurmen J, Bogt TT, DEG R, Vollebergh W. Cannabis use and mental health in secondary school

children. Findings from a Dutch survey. *Br J Psychiatry* 2006; **188:** 148–153.

[17] Hofstra MB, van der Ende J, Verhulst FC. Child and adolescent problems predict DSM-IV disorders in adulthood: a 14-year follow-up of a Dutch epidemiological sample. *J Am Acad Child Adolesc Psychiatry* 2002; **41:** 182–189.

[18] Pardini D, White HR, Stouthamer-Loeber M. Early adolescent psychopathology as a predictor of alcohol use disorders by young adulthood. *Drug Alcohol Depend* 2007; **88 (suppl 1):** S38–S49.

[19] Roberts RE, Roberts CR, Xing Y. Comorbidity of substance use disorders and other psychiatric disorders among adolescents: evidence from an epidemiologic survey. *Drug Alcohol Depend* 2007; **88 (suppl 1):** S4–S13.

[20] Nurnberger JI Jr, Wiegand R, Bucholz K *et al*. A family study of alcohol dependence: coaggregation of multiple disorders in relatives of alcohol-dependent probands. *Arch Gen Psychiatry* 2004; **61:** 1246–1256.

[21] Enoch MA, White KV, Harris CR, Rohrbaugh JW, Goldman D. Alcohol use disorders and anxiety disorders: relation to the P300 event-related potential. *Alcohol Clin Exp Res* 2001; **25:** 1293–1300.

[22] Meade Eggleston A, Woolaway-Bickel K, Schmidt NB. Social anxiety and alcohol use: evaluation of the moderating and mediating effects of alcohol expectancies. *J Anxiety Disord* 2004; **18:** 33–49.

[23] Zimmer-Gembeck MJ, Alexander T, Nystrom RJ. Adolescents report their need for and use of health care services. *J Adolesc Health* 1997; **21:** 388–399.

[24] Thornicroft G, Rose D, Kassam A. Discrimination in health care against people with mental illness. *Int Rev Psychiatry* 2007; **19:** 113–122.

[25] Pinfold V, Toulmin H, Thornicroft G, Huxley P, Farmer P, Graham T. Reducing psychiatric stigma and discrimination: evaluation of educational interventions in UK secondary schools. *Br J Psychiatry* 2003; **182:** 342–346.

[26] Wacholder S, McLaughlin JK, Silverman DT, Mandel JS. Selection of controls in case-control studies. I. Principles. *Am J Epidemiol* 1992; **135:** 1019–1028.

[27] Ford JD, Trestman RL, Tennen H, Allen S. Relationship of anxiety, depression and alcohol use disorders to persistent high utilization and potentially problematic under-utilization of primary medical care. *Soc Sci Med* 2005; **61:** 1618–1625.

[28] Kroenke K, Spitzer RL, Williams JB, Monahan PO, Lowe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Ann Intern Med* 2007; **146:** 317–325.

[29] Leiknes KA, Finset A, Moum T, Sandanger I. Current somatoform disorders in Norway: prevalence, risk factors and comorbidity with anxiety, depression and musculoskeletal disorders. *Soc Psychiatry Psychiatr Epidemiol* 2007; **42:** 698–710.

[30] McCauley E, Katon W, Russo J, Richardson L, Lozano P. Impact of anxiety and depression on functional impairment in adolescents with asthma. *Gen Hosp Psychiatry* 2007; **29:** 214–222.

[31] Lavan H, Johnson JG. The association between axis I and II psychiatric symptoms and high-risk sexual behavior during adolescence. *J Personal Disord* 2002; **16:** 73–94.

[32] Rohde P, Lewinsohn PM, Seeley JR. Comparability of telephone and face-to-face interviews in assessing axis I and II disorders. *Am J Psychiatry* 1997; **154:** 1593–1598.

[33] Spitzer RL, Williams JB, Kroenke K *et al*. Utility of a new procedure for diagnosing mental disorders in primary care. The PRIME-MD 1000 study. *JAMA* 1994; **272:** 1749–1756.

[34] American Psychiatric Association. (1994): Diagnostic and Statistical Manual of Mental Disorders. 4th edn., Washington, DC: American Psychiatric Association Press.

[35] Spitzer RL, Kroenke K, Linzer M *et al*. Health-related quality of life in primary care patients with mental disorders. Results from the PRIME-MD 1000 Study. *JAMA* 1995; **274:** 1511–1517.

[36] Carballo JJ, Bird H, Giner L *et al*. Pathological personality traits and suicidal ideation among older adolescents and young adults with alcohol misuse: a pilot case-control study in a primary care setting. *Int J Adolesc Med Health* 2007; **19:** 79–89.

[37] Goldney RD, Fisher LJ. Double depression in an Australian population. *Soc Psychiatry Psychiatr Epidemiol* 2004; **39:** 921–926.

[38] Persoons P, Luyckx K, Desloovere C, Vandenberghe J, Fischler B. Anxiety and mood disorders in otorhinolaryngology outpatients presenting with dizziness: validation of the self-administered PRIME-MD Patient Health Questionnaire and epidemiology. *Gen Hosp Psychiatry* 2003; **25:** 316–323.

[39] Kumar G, Kim AH, Krefetz D, Steer RA. Screening for major depressive disorders in adolescent psychiatric inpatients with the mood modules from the Primary Care Evaluation of Mental Disorders and the Patient Health Questionnaire. *Psychol Rep* 2001; **89:** 274–278.

[40] Carson AJ, Ringbauer B, MacKenzie L, Warlow C, Sharpe M. Neurological disease, emotional disorder, and disability: they are related: a study of 300 consecutive new referrals to a neurology outpatient department. *J Neurol Neurosurg Psychiatry* 2000; **68:** 202–206.

[41] Swadi H, Bobier C. Substance use disorder comorbidity among inpatient youths with psychiatric disorder. *Aust N Z J Psychiatry* 2003; **37:** 294–298.

[42] Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry* 2005; **62:** 617–627.

[43] Hasin DS, Stinson FS, Ogburn E, Grant BF. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry* 2007; **64:** 830–842.

[44] Stinson FS, Ruan WJ, Pickering R, Grant BF. Cannabis use disorders in the USA: prevalence, correlates and co-morbidity. *Psychol Med* 2006; **36:** 1447–1460.

[45] Roberts RE, Roberts CR, Xing Y. Rates of DSM-IV psychiatric disorders among adolescents in a large metropolitan area. *J Psychiatr Res* 2007; **41:** 959–967.

[46] Hussong AM, Galloway CA, Feagans LA. Coping motives as a moderator of daily mood-drinking covariation. *J Stud Alcohol* 2005; **66:** 344–353.

[47] Lewis MA, Hove MC, Whiteside U *et al*. Fitting in and feeling fine: conformity and coping motives as mediators of the relationship between social anxiety and problematic drinking. *Psychol Addict Behav* 2008; **22:** 58–67.

[48] Ham LS, Bonin M, Hope DA. The role of drinking motives in social anxiety and alcohol use. *J Anxiety Disord* 2007; **21:** 991–1003.

[49] Bolton J, Cox B, Clara I, Sareen J. Use of alcohol and drugs to self-medicate anxiety disorders in a nationally representative sample. *J Nerv Ment Dis* 2006; **194:** 818–825.

[50] Falk DE, Yi HY, Hilton ME. Age of onset and temporal sequencing of lifetime DSM-IV alcohol use disorders relative to comorbid mood and anxiety disorders. *Drug Alcohol Depend* 2008; **94:** 234–245.

[51] Conrod PJ, Stewart SH, Comeau N, Maclean AM. Efficacy of cognitive-behavioral interventions targeting personality risk factors for youth alcohol misuse. *J Clin Child Adolesc Psychol* 2006; **35:** 550–563.

[52] Doremus TL, Brunell SC, Varlinskaya EI, Spear LP. Anxiogenic effects during withdrawal from acute ethanol in adolescent and adult rats. *Pharmacol Biochem Behav* 2003; **75:** 411–418.

[53] Varlinskaya EI, Spear LP. Acute ethanol withdrawal (hangover) and social behavior in adolescent and adult male and female Sprague-Dawley rats. *Alcohol Clin Exp Res* 2004; **28:** 40–50.

[54] Patton GC, Coffey C, Lynskey MT *et al*. Trajectories of adolescent alcohol and cannabis use into young adulthood. *Addiction* 2007; **102:** 607–615.