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Alcohol and tobacco use disorders in a general population: short-term and long-term associations from the St. Louis Epidemiological Catchment Area Study

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Abstract

Background—Although research using clinical and convenience samples has shown alcohol use disorders (AUD) to be highly comorbid with tobacco dependence (TD), little work has examined this association prospectively using population-based data. The AUD–TD association was prospectively examined using data from the St. Louis Epidemiological Catchment Area (ECA) Study and its 1-year follow-up as well as from a 16-year follow-up on a subsample of ECA data.

Method—Respondents were 3004 (2564, 85%, at Wave 2) participants in the St. Louis household ECA sample, including 444 participants at Year 16 follow-up. At baseline, the sample was predominately White (58%; 38% Black), female (60%), and 44.3 years. Past-year AUD and TD were diagnosed at all waves according to DSM-III criteria.

Results—AUDs and TDs were cross-sectionally associated at Years 1, 2, and 16. Controlling for demographics, Year 1 TD prospectively predicted Year 2 AUD, and Year 1 AUD prospectively predicted Year 16 TD. We found evidence for prediction of onset and persistence of both AUD and TD at short-term but not long-term follow-up. Prospective findings were reduced and no longer reached significance when concurrent diagnoses at follow-up were included in the regression models.

Conclusions—We observed short-term and long-term associations between AUD and TD. These associations were mediated through concurrent diagnoses with the other substance use disorder.

Keywords

Alcoholism; Alcohol use disorder; Tobacco dependence; Comorbidity; Epidemiology; Prospective

1. Introduction

Many individuals who are diagnosed with alcohol use disorders (AUD) have a history of other psychiatric disorders. Data from general population-based samples such as the National Comorbidity Survey (NCS) and the Epidemiological Catchment Area (ECA) Study have demonstrated high comorbidity between alcohol abuse/dependence and psychiatric disorders (Helzer and Pryzbeck, 1988; Kessler et al., 1997; Regier et al., 1990). In the ECA, 47% of

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alcoholics met criteria for at least one other psychiatric disorder (e.g. antisocial personality disorder, mania; Helzer and Pryzbeck, 1988). As with AUDs, nicotine dependence and lifetime and current smoking rates are higher among those with psychiatric disorders (Breslau, 1995; Lasser et al., 2000), even when adjusted for age, sex, and region of the country (Lasser et al., 2000). The relationship between alcoholism and tobacco dependence (TD) has not been explored with ECA data because only one ECA site (St. Louis) collected data on TD. In this report, we take advantage of St. Louis ECA data on both TD and AUDs, as well as a long-term follow-up study of a sub-sample of the St. Louis ECA, to investigate both cross-sectionally and prospectively the nature of comorbidity between AUD and TD

1.1. Alcohol-tobacco comorbidity

The positive relation between alcohol consumption and tobacco use is a robust one. Social drinkers as well as alcoholics are more likely to smoke than non-drinkers (Bien and Burge, 1990; Gulliver et al., 1995; Istvan and Matarazzo, 1984; Martin et al., 1996; Rohde et al., 1995). Similarly, smokers are more likely to drink than non-smokers (Bien and Burge, 1990; DiFranza and Guerrero, 1990; Fleming et al., 1989).

Most of the research documenting the association between alcohol and tobacco use disorders (i.e. alcohol abuse, alcohol dependence and TD) has been conducted using clinical populations (e.g. Mintz et al., 1985; York and Hirsch, 1995) or college students (e.g. Jackson et al., 2000). These samples have limited generalizability, and tend to underrepresent minority groups. To date, little research has examined the association between alcohol and tobacco use disorders using population-based, representative samples in a longitudinal time frame. Prospective data permit greater exploration of the direction of effect. For example, having an AUD at Time 1 might predispose the individual to have a TD diagnosis at Time 2; alternately, having TD at Time 1 might predispose the individual to have an AUD diagnosis at Time 2. The relation between AUDs and TD might also be bi-directional, or may be due to the common influence of other variables.

Individuals who experience a diagnostic episode of a disorder are more likely to have subsequent episodes (Krueger et al., 1998), and substance use disorders are often conceptualized as a “chronic relapsing disease” (Platt, 1995). Previous work in our lab using a college sample (Jackson et al., 2000) showed that the covariation between alcohol and tobacco use disorders appeared to conform to a traitlike (as opposed to a timebound, directional) process. Work in behavior genetics, in fact, has demonstrated evidence for common genetic mechanisms underlying alcohol and tobacco use (e.g. Koopmans et al., 1997; Swan et al., 1997) and dependence (e.g. Prescott and Kendler, 1995; True et al., 1999). If, as this evidence suggests, alcohol and tobacco use disorders operate as stable traits, then the association between the two may exist at the level of the trait, and hence the association over a long-term interval should have a similar magnitude to that of a short-term interval than would be expected by a timebound, stochastic process. To our knowledge, no studies to date have examined the magnitude of association of comorbidity between alcohol and tobacco use disorders as a function of follow-up interval using structured diagnostic interviews and standard diagnostic criteria within a large, multi-ethnic sample.

1.2. Moderators of the alcohol–tobacco use disorder association

Across all ages, the prevalence of AUDs is greater among men than women (Hesselbrock and Hesselbrock, 1997; Kessler et al., 1994; Regier et al., 1990). Among epidemiological samples, male-to-female ratios for alcohol dependence range from 2.0 to 5.0 (Bucholz, 1999). Conversely, there are equal or higher rates of daily cigarette use¹ and tobacco use disorders among women than men, both among young adults (Johnston et al., 1998) and older adults (Breslau et al., 2001; Centers of Disease Control, 1999; Kandel and Chen, 2000). The alcohol–

tobacco association, however, appears to be relatively robust across gender (Istvan and Matarazzo, 1984; Simon et al., 1995), even in the context of these opposing relations. Additionally, racial differences have been observed for alcohol dependence (Caetano and Schafer, 1996; Robins and Regier, 1991) and TD (Andreski and Breslau, 1993; Breslau et al., 2001; Kandel and Chen, 2000) and smoking (Centers of Disease Control, 1999) such that African Americans tend to exhibit lower rates of alcohol and tobacco involvement than do Whites or Mexican Americans. Although the alcohol–tobacco use association was comparable across racial group among adolescents (Jackson et al., 2002), the moderating effect of race on comorbidity has not yet been examined in adults using diagnostic criteria for substance use disorders.

In addition, past-year alcohol and tobacco use disorders exhibit varying prevalence rates throughout the life course. Both overall ECA and NHIS data show that both lifetime and past-year alcohol abuse/dependence rates increase up to age 29 and then drop thereafter (Bucholz, 1992); similarly, NLAES data show that 18–24-year-olds report the highest rates of alcohol dependence (Grant, 1997). Research also shows age-related declines in alcohol consumption (Fillmore et al., 1991; although see Grant, 1997, who shows a slight increase from age 25 to 34 before a decline) as well as in heavy drinking and problem drinking (Fillmore, 1988). In addition, although TD tends to be least common among those who are younger (under age 24; Anthony et al., 1994), other recent data on smoking show that report of any past-year smoking tends to decrease after age 24 (Department of Health and Human Services, 1999). In addition, Jennison (2000) found that as women age, smoking quantity was more likely to be associated with drinking quantity and less likely to be associated with drinking frequency. Given these inconsistencies, it is not clear what influence age might have on the association between AUDs and TD.

1.3. Overview

We examined the directional association between past-year alcohol and tobacco use disorders using prospective data from the St. Louis ECA Study. In this study, a community-based representative sample was interviewed with a structured diagnostic assessment of psychiatric disorders, with a 1 year follow-up assessment. Data from both the 1 year follow-up and an additional follow-up of a subsample of the St. Louis ECA respondents approximately 16 years following the initial study were used in order to examine the extent to which the association between alcohol and tobacco use disorders reflects a traitlike (vs. timebound) process. In addition, we examined the association as a function of age group, gender and race.

2. Method

2.1. Participants and procedure

We used data from the household sample of the St. Louis ECA Study (Regier et al., 1984; Robins and Regier, 1991) because St. Louis was the only ECA site to assess TD. At baseline, complex, multistage, random sampling techniques were utilized to select community and institutional residents aged 18 or older. Sampled areas corresponded with Mental Health Catchment areas, within which blocks were selected, with an over-sampling of blocks that contained Black residents. Households were then sampled within blocks and one individual per household was randomly selected to be interviewed. Each interview was comprised of a structured psychiatric interview (the Diagnostic Interview Schedule, version III), which permitted recovery of lifetime and current psychiatric diagnoses according to DSM-III criteria, which was the diagnostic nomenclature in effect at that time (American Psychiatric

¹We would like to note that in recent years, smoking rates for young women have caught up to and have even surpassed rates for young men (Johnston et al., 1998), but this was not so at the time of baseline ECA collection and is likely not true of older cohorts.

Association, 1980; Robins et al., 1981). Participants were interviewed at baseline, and about 85% (2564 of 3004) were interviewed 1 year later, from 1981 to 1983. At Year 1, 58% of the sample was White, 38% was black, 60% was female, and mean age was 44.3 years (S.D. = 19.2).

In 1998, a follow up study using St. Louis ECA respondents was undertaken, approximately 15.9 years after their last ECA interview, the primary purpose of which was to compare current health services use and costs in a group of lifetime alcoholics, compared with nonalcoholics and unaffected individuals (Bucholz and Grazier, 2001; Grazier and Bucholz, 2001). 444 respondents were re-interviewed (62% of the 711 targeted participants; 79% of the 565 living targeted participants). Based on their AUD diagnoses at ECA Years 1 and 2, three groups were sampled: stable ECA alcoholics (those who met lifetime DSM-III AUD diagnosis at both Year 1 and 2; 33%), non-alcoholic but heavy or problem drinkers (34%), and those who had no AUD at either ECA interview (33%). The majority of this sample was White (78%; 20% Black), male (79%), and were on average age 50.1 at follow-up. Respondents completed a structured telephone interview that repeated alcohol abuse and dependence items from the original ECA interview as well as items from the Diagnostic Interview Schedule, DSM-IV version (Robins et al., 1997). TD history, current and lifetime depression, and drug use histories were also included.

The current study was reviewed by the University of Missouri Institutional Review Board (IRB) and also the IRB for Washington University School of Medicine under the auspice of the Data Management and Methodology Core of the Missouri Alcoholism Research Center, with which the authors are associated. Both IRBs gave exemption to the project on the basis that the current study consisted of secondary analysis of pre-existing data sets.

2.2. Measures

2.2.1. Alcohol use disorder—Diagnostic classification was limited in this report to Diagnostic and Statistical Manual of Mental Disorders (third ed.; DSM-III; American Psychiatric Association, 1980) alcohol abuse or dependence, termed herein “alcohol use disorder” (AUD). We combined alcohol abuse and dependence in our analyses because under DSM-III classification, the concepts of alcohol abuse and alcohol dependence are quite different from those in later versions of the DSM. Unlike DSM-III-R and DSM-IV, where alcohol abuse is considered a residual diagnosis, and for which only a few symptoms count, the DSM-III version of abuse contains many of the problem behaviors that count toward dependence in the later classification systems (e.g. pathological use such as health problems from drinking, blackouts, inability to abstain, and impairment in social functioning), and individuals were permitted to meet criteria for both simultaneously. Alcohol dependence under DSM-III required either tolerance or withdrawal, again very unlike the later diagnostic definitions where these were not considered necessary for diagnosis. As such, the constructs of alcohol abuse and dependence are substantively different from the constructs of the same names in the later nosologies. For these reasons, we adopt the definition used in the ECA of considering alcoholism abuse and/or dependence.

At Years 1 and 2, past-year and lifetime DSM-III alcohol dependence and abuse were assessed using the Diagnostic Interview Schedule (DIS) Version III-A (Robins et al., 1985). At 16 year follow-up, items from the ECA were preserved, so that DSM-III diagnoses were recoverable for alcohol abuse/dependence. In addition, items to permit recovery of alcohol abuse and dependence from DSM-IV were added. For analyses reported here, alcohol abuse and/or dependence was scored according to DSM-III criteria, so that across the various timepoints the diagnosis definition would be consistent². Alcohol abuse was diagnosed if an individual showed a pattern of pathological alcohol use (e.g. wanted to stop drinking but could not) and impairment in social or occupational functioning (e.g. family objected to drinking). Alcohol

dependence was diagnosed if the individual showed either pathological use or social impairment, and reported tolerance or withdrawal symptoms. AUD was defined as present if a participant met criteria for alcohol abuse or alcohol dependence. For Years 1 and 2, past-year diagnoses were scored if a respondent endorsed past-year recency on a single item assessing recency across a list of symptoms. For Year 16, past-year diagnoses were based on the set of items used to construct DSM-III AUD that had recency information available; if a symptom occurred in the past-year, past-year AUD was scored. Unfortunately, it was not possible to get recency on each particular symptom or syndrome. For the current study, unless otherwise noted, all references to AUD are based on a past-year timeframe. Prevalence (weighted) of past-year DSM-III AUD was 6% at Year 1, 7% at Year 2, and 6% for the Year 16 sample.

2.2.2. Tobacco dependence—Past-year and lifetime DSM-III TD were assessed using the DIS Version III-A (Robins et al., 1985) at Years 1 and 2, and DIS Version-IV (Robins et al., 1997) at Year 16. TD was diagnosed if an individual showed current daily use of cigarettes for at least a month and had unsuccessfully tried to quit or reduce smoking, experienced withdrawal symptoms while attempting to quit, and/or continued to smoke despite a serious physical condition known to be exacerbated by smoking. For Years 1 and 2, past-year diagnoses were scored if the respondent endorsed having smoked at least half-pack per day in the past-year. As a parallel item was not available at Year 16, recency was scored based on an item assessing cigarette use in the past-year (however, only 11 of 178 smokers reported having smoked fewer than ten cigarettes per day, suggesting that this item was a very good proxy for half-pack recency). Again, unless otherwise noted, all references to TD are based on a past-year timeframe. Prevalence (weighted) of past-year DSM-III TD was 29% at Year 1, 28% at Year 2, and 22% at Year 16.

2.2.3. Background variables—Sex, race, age, and SES, indicated by total past-year household income and highest level of education, were assessed at Time 1 and Time 16. For analytic purposes, race was given two dummy codes (Black and White), with Other as the reference group.

2.3. Weighting for full ECA sample and long-term follow-up

ECA data were collected using a complex, multistage, random sampling procedure, which leads to larger variance than would be expected from a simple random sample. We downweighted the full (St. Louis) ECA sample to the size of a simple random sample with the same variance using the Woodbury downweight (Robins and Regier, 1991), which compensates for artifacts resulting from the stratification. All analyses using Year 1 and the Year 2 follow-up have been weighted. To obtain unbiased variance estimates, we adjusted for complex sampling in all analyses using STATA 7.0 (StataCorp, 2001), with the exception of the attrition analyses.

Given selection criteria consistent with the goals of the study, participants in the Year 16 follow-up differed from the rest of the baseline sample on baseline respondent characteristics. Those in the Year 16 sample were more likely to be male, Caucasian, younger, more educated, from a higher-income family, and more likely to be diagnosed with AUD and TD. Based on the biased nature of the sampling frames for follow-up, response propensity weights were assigned to participants on the basis of their selection probability. Logistic regression analyses predicting non-response were conducted to construct weights following the method of Heath et al. (1998). From the logistic regressions, the probability of participating in the follow-up study (p_i) was computed for each respondent, and the sample was weighted for analysis using

²DSM-III scoring was approximate for the Year 16 follow-up, given that not all DSM-III symptoms were covered in the given assessment. This may account for the low prevalence for DSM-III past-year AUD at Year 16 (5.5%; see Table 2).

the reciprocal of p_i . Given that the Year 16 sample was not originally selected to be representative of the ECA population as a whole, and our inferences are specific to the Year 16 sample, we did not downweight the sample again for the complex sampling design of the original ECA. With the exception of attrition analyses, all follow up analyses reported below incorporate these weights, and again, variance estimates were adjusted using STATA (with the exception of the attrition analyses, and the examination of mortality rates). Note that descriptive information on age, sex, and race is unweighted when reported in text but weighted when presented in tables.

3. Results

First, we describe differences between those who did versus did not complete the follow-up among the respondents who were targeted for follow-up at Years 2 and 16. Then, we examined the association between alcohol and tobacco use disorders both cross-sectionally and prospectively (over a 1 year interval and over a 15 year interval), and explored possible moderating effects of age, sex, and race.

3.1. Attrition analyses

3.1.1. One-year follow-up—2564 (85%) of the original 3004 respondents were reassessed at Year 2. Using χ^2 -analyses (for categorical variables) and analyses of variance (for continuous variables), analyses were conducted to determine the extent to which responders significantly differed from non-responders on substantively important baseline (Year 1) variables (see Table 1, left panel). Respondent's race, age, family income, AUD prevalence, and tobacco use disorder prevalence did not differ between Year 2 responders and non-responders. However, women were more likely to be followed than were men, and higher education was positively associated with retention. Although these latter two associations have small effect sizes, it is clear that the Year 2 sample was more educated and more likely to be female than the original Year 1 sample.

3.1.2. Sixteen-year follow-up—Although 711 participants were targeted for follow-up at Year 16, only 444 (62%) were re-interviewed. However, 146 of the targeted respondents were deceased and 15 were too ill to be interviewed, so that of those living and eligible to be interviewed, 81% were interviewed. Among those classified as non-responders, 14 were not found and 92 refused to be interviewed. Those respondents who completed the interview did not differ from non-completers in terms of sex or Year 1 substance use disorder (see Table 1, right panel). However, completers were more likely to be White and less likely to be Black than non-completers. In addition, completers tended to be younger, more educated, and had higher income than non-completers.

In sum, attrition analyses show that care must be exercised in generalizing findings from the Year 16 follow-up to older, less-educated individuals and to those with lower income. Although the parameters in this follow-up study were weighted to represent the original sample, our inferences are still based on a biased subset of data.

3.2. Alcohol–tobacco association

The number of respondents who met criteria for alcohol and tobacco use disorders at Years 1, 2, and 16 is shown in Table 2 (along with weighted descriptive information for sex, race, and age). All prospective analyses discussed below use past-year diagnoses and control for sex, race, and age, unless otherwise stated.

3.2.1. St. Louis full ECA: 1-year follow-up—About 6% of the sample were diagnosed with a past-year AUD at Year 1 and 2, and nearly 30% were diagnosed with past-year TD at

these years (see Table 2). At Year 1, the overall lifetime prevalence of AUDs was 16% and the lifetime prevalence of TD was 37%. Past-year alcohol and tobacco use disorders were cross-sectionally associated at Year 1 (OR = 2.47; 95% confidence intervals, CI: 1.67, 3.64) and at Year 2 (OR = 3.02; 95% CI: 1.99, 4.58). These associations were only slightly reduced when sex, race, and age were statistically controlled³. Cross-sectional associations between AUD and TD (controlling for sex, race, and age) are presented in Table 3, along with prospective associations for 1-year and long-term interval follow-up data.

Using logistic regression, we predicted Year 2 past-year AUD from Year 1 past-year TD, controlling for Year 1 past-year AUD. Year 1 TD prospectively predicted Year 2 AUD diagnosis (OR = 1.90; 95% CI: 1.16, 3.13). We tested the converse as well, controlling for Year 1 TD; Year 1 AUD did not prospectively predict Year 2 TD (OR = 1.17; 95% CI: 0.68, 2.01).

Next, we examined the extent to which the prospective association between TD and AUD differed by subgroup by testing the interaction of Year 1 TD with sex, with race, and with age, in the prediction of Year 2 AUD (controlling for Time 1 AUD). No interactions were significant, suggesting that this prospective effect was robust across subgroup. Likewise, no interactions with AUD were significant in the prediction of Year 2 TD by Year 1 AUD (controlling for Time 1 TD).

3.2.1.1. Onset and persistence: This set of prospective analyses, however, does not directly resolve the questions of onset or persistence. That is, individuals who are diagnosed with a given disorder at Year 1 may remit at Year 2 or may persistently be diagnosed with the disorder at Year 2. Likewise, those who fail to be diagnosed at Year 1 may be non-cases at Year 2 or may onset with the disorder at Year 2. In order to differentiate among these conditions, we conducted another set of analyses. Based on whether a respondent was diagnosed with AUD at Years 1 and 2, we created a categorical AUD variable with four levels: non-cases (no Year 1 AUD, no Year 2 AUD), onset (no Year 1 AUD, Year 2 AUD), remission (Year 1 AUD, no Year 2 AUD), and persistence (Year 1 AUD, Year 2 AUD). A similar variable was created for TD.

Table 4 shows the cross-tabulation of the four-level AUD variable with the four-level TD variable. The vast majority of the sample (91%) failed to be diagnosed with AUD at either Year 1 or 2⁴. The rest of the sample was equally divided into the newly onset group (4%), remission group (3%), and persistence group (3%). A greater proportion of the sample diagnosed with TD at some point. Although the majority of the sample still failed to be diagnosed (65%), a full fifth (22%) persistently diagnosed with TD at both Years 1 and 2. Five percent of the sample newly onsetted with TD, and 7% of the sample was diagnosed with TD at Year 1 but remitted by Year 2.

Using a multinomial logistic regression (Agresti, 1990), we predicted the four-level AUD variable from the four-level TD variable, creating three dummy codes for TD (new onset, remission, and persistence), with the non-diagnosing group as the reference group. Likewise, we predicted the four-level TD variable from the four-level AUD variable, creating three analogous dummy codes for AUD (new onset, remission, and persistence). Table 4 shows the

³Examination of the association between alcohol and tobacco use disorder with covariates was not a symmetric analysis. Consequently, we conducted two logistic regressions: AUD→TD (controlling for covariates), and TD→AUD (controlling for covariates).

⁴To examine the extent to which our “non-diagnosers” have actually been diagnosed with a lifetime disorder at some point (and hence were really diagnosers), we examined the prevalence of lifetime diagnosis among our non-diagnosers. For AUD, only 185 of 2239 AUD non-diagnosers (91.7%) had been diagnosed with AUD during their lifetime; a similar percentage of TD non-diagnosers had been diagnosed with lifetime TD (1485 of 1620; 91.7%). We conclude that a very high percentage of non-diagnosers were true non-diagnosers, and that our onset/persistence analyses are truly determining onset/ persistence.

relative risk (RR) ratios (and 95% CI) for the prediction of the four-level variable AUD by the four-level TD variable ($RR_{TD \rightarrow AUD}$) and the converse ($RR_{AUD \rightarrow TD}$). The table presents risk ratios for prediction in both directions; note that the values are very similar (in the absence of covariates, risk ratios would be identical). For all of the analyses discussed below, prediction of a given group (i.e. for the outcome variable) is relative to the stable non-diagnoser group. Also, given our interest in predicting onset and persistence, and the difficulty in how to interpret prediction of remission (which is analogous to retrospectively post-dicting a disorder, rather than prospectively predicting a disorder), we focus only on the prediction of onset and persistence (vs. non-diagnosers), although we present the parameters for predicting remission in Table 4 (third column/third row).

In terms of predicting new onset of an AUD at Year 2 (see Table 4, second column), having had TD at both Years 1 and 2 (persistent TD) was a robust predictor ($RR = 2.36$; 95% CI = 1.26, 4.41). Having had TD at only Year 1 (remission of TD) failed to predict new AUD onset, which may speak to these individuals as being less “severe” cases of TD or, more likely, may be a function of lower power due to the small expected cell frequency ($n = 4$; expected $n = 6$). New onset of TD failed to predict new onset of AUD; although the magnitude of the odds ratio suggested the presence of an effect ($RR = 2.45$), the association failed to reach significance, again perhaps due to the small expected cell frequency ($n = 7$; expected $n = 5$).

Diagnosing with AUD at both Years 1 and 2 (persistence of AUD; see Table 4, fourth column) was strongly predicted by being persistently diagnosed with TD at both waves ($RR = 3.73$; 95% CI = 1.98, 7.03). In addition, there was evidence that having TD at Year 1 but not Year 2 predicted persistent diagnosis with AUD ($RR = 3.34$; 95% CI = 1.38, 8.10).

New onset of TD at Year 2 (see Table 4, second row) was not predicted by any of the AUD dummy codes. However, being persistently diagnosed with TD at both Years 1 and 2 (see Table 4, fourth row) was strongly predicted by being persistently diagnosed with AUD at both waves ($RR = 3.45$; 95% CI = 1.82, 6.55). Also, having a newly onsetting AUD at Year 2 was predictive of persistent diagnosis with TD ($RR = 2.02$; 95% CI = 1.05, 3.86).

3.2.1.2. Testing for mediation through the concurrent diagnosis at Year 2: We sought to further resolve the mechanisms that underlie the prospective association between AUD and TD. Specifically, we examined the extent to which the association between Year 1 AUD and Year 2 TD could be accounted for, or mediated by, concurrent or synchronous diagnosis with Year 2 AUD, and vice versa. This can be viewed as a question of whether comorbidity is mediated through concurrent use of the co-occurring substance. That is, an individual might show a relation between Year 1 AUD and Year 2 TD simply because he or she is also diagnosing with AUD at Year 2 (which is associated with Year 2 TD). We specifically tested this hypothesis by examining the extent to which Year 1 AUD predicted Year 2 TD, controlling for Year 1 TD, as well as controlling for the potential mediator, Year 2 AUD (see Fig. 1, top panel, for illustrative purposes). In doing so, we examined whether the direct effect was still significant in the presence of the indirect (mediated) effect. We also tested the converse association (see Fig. 1, bottom panel). We found that the prospective effects that were evident in prior prospective analyses from Year 1 to 2 were reduced (from 1.90 to 1.08 for AUD and from 1.17 to .85 for TD; see Table 3) and were no longer significant, suggesting that prospective comorbidity might be partially mediated through concurrent use of the co-occurring substance.

3.2.1.3. Moderation of stability: Finally, we examined the extent to which TD moderated the stability of AUD diagnosis (e.g. are those with a Year 1 TD more likely to continue to diagnose with AUD) from Year 1 to 2 by examining the interaction of Year 1 TD with Year 1 AUD in the prediction of Year 2 AUD. TD did not moderate AUD stability, Wald χ^2 (1, $N = 2465$) = 0.001, ns. Likewise, we examined the extent to which AUD moderated the stability of TD

diagnosis by examining the interaction of Year 1 AUD with Year 1 TD in the prediction of Year 2 TD. The interaction was also non-significant, Wald χ^2 (1, $N = 2465$) = 1.72, ns. When sample sizes permitted, we also tested for interactions with sex, race, and age; none were found.

3.2.2. Sixteen-year follow-up—Alcohol and tobacco use disorders were cross-sectionally associated with the Year 16 subsample⁵, OR = 3.19; 95% CI: 1.05, 9.70. These parameters were virtually unchanged when sex, race, and age group were controlled for (see Table 3).

Using logistic regression, we tested the prediction of Year 1 past-year TD on Year 16 past-year AUD, controlling for Year 1 AUD. Year 1 TD failed to prospectively predict Year 16 AUD diagnosis, OR = 0.93; 95% CI: 0.36, 2.43. We also examined the prediction of Year 1 AUD on Year 16 TD, controlling for Year 1 TD. Year 1 AUD prospectively predicted Year 16 TD, OR = 2.60; 95% CI: 1.13, 5.99. No interactions were significant, suggesting these prospective effects were robust across subgroup.

3.2.2.1. Onset and persistence: Given the small sample size ($N = 444$) at the 16-year follow-up, we did not replicate the analyses using the four-level AUD and four-level TD variables. Instead, we examined onset and persistence by subsetting our sample. That is, for the question of onset, we considered only those participants who failed to diagnose with a given disorder at Year 1⁶, and we predicted the extent to which they diagnosed with that disorder at Year 16. Year 1 TD did not predict the onset of an AUD diagnosis (among the 365 respondents who did not have a Year 1 AUD diagnosis), OR = 0.85, 95% CI: 0.26, 2.81. Analogously, Year 1 AUD did not predict the onset of a TD diagnosis (among the 283 respondents who did not have a Year 1 TD diagnosis), OR = 3.26, 95% CI: 0.83, 12.87.

We also tested the question of whether persistence of diagnosing with an AUD varied as a function of a prior TD diagnosis, and conversely, whether TD persistence varied as a function of a prior AUD diagnosis. That is, we considered only those participants who were diagnosed with a given disorder at Year 1, and we predicted the extent to which they continued to diagnose with that disorder at Year 2. In terms of persistence, Year 1 TD did not predict the persistence of an AUD diagnosis (among the 78 respondents who had a Year 1 AUD diagnosis), OR = 0.79, 95% CI: 0.18, 3.36. Finally, Year 1 AUD did not predict the persistence of a TD diagnosis (among the 160 respondents who had a Year 1 TD diagnosis), OR = 2.01, 95% CI: 0.78, 5.19.) In sum, onset and persistence analyses failed to support comorbidity at this long-term follow-up.

3.2.2.2. Testing for mediation through the concurrent diagnosis at Year 16: We again tested whether comorbidity could be accounted for, or mediated by, use of the co-occurring substance at Year 16. Again, the prospective effect that was evident in previous analyses (i.e.

⁵In order to maintain comparability with current research findings, we also scored alcohol and tobacco use disorder diagnoses at the 16 year follow-up according to both DSM-III-R (American Psychiatric Association, 1987) and DSM-IV (American Psychiatric Association, 1994) criteria. Prevalence of past-year DSM-III-R AUD was 14%, as was past-year DSM-IV AUD. Prevalence estimates for past-year TD by DSM-III-R and DSM-IV criteria were both 26%. Findings using these classification systems tended to support the current findings. Cross-sectional analyses continued to show moderate, significant associations (with findings based on DSM-III-R criteria yielding higher magnitude than those using DSM-III, but those using DSM-IV showing lower magnitude than those using DSM-III). Likewise, prospective analyses continued to be significant (and of greater magnitude than those based on DSM-III criteria), in the direction of AUD predicting TD (but not the converse). For both onset and persistence analyses, TD continued to fail to predict AUD onset or persistence; however, using the new classification systems, DSM-III-R AUD predicted TD onset and DSM-IV AUD predicted TD persistence. Finally, analyses examining the extent to which one substance moderated the stability of the other continued to fail to show significance.

⁶To be consistent with the onset/persistence analyses for the Year 2 follow-up, these Year 16 onset/persistence analyses are based on past-year diagnoses (i.e. to examine onset and persistence, we subsetted the data based on whether respondents diagnosed with past-year AUD or TD). However, to resolve true onset and persistence, we re-ran the analyses based on lifetime diagnosis with AUD or TD. Examination of onset for AUD ($N = 256$) and TD ($N = 243$) showed similar results as the findings reported in text, with no significant effects, although the prediction of AUD onset yielded a larger parameter. Likewise, examination of persistence for AUD ($N = 187$) and TD ($N = 200$) continued to show no effects.

AUD→TD) was reduced and no longer significant (from 2.60 to 2.12; see Table 3), indicating that comorbidity might be an indirect effect through use of the co-occurring substance at the same time.

3.2.2.3. Moderation of stability: Year 1 AUD did not moderate the stability of a TD diagnosis from Year 1 to 16, Wald χ^2 (1, $N = 443$) = 0.41, ns; nor did Year 1 TD moderate the stability of an AUD diagnosis, Wald χ^2 (1, $N = 443$) = 0.001, ns. No interactions with sex, race, or age were found.

3.2.2.4. Influence of mortality on AUD and TD: We also examined whether mortality was significantly associated with a lifetime (DSM-III) AUD or TD diagnosis (or the interaction of the two) at Year 1 in this sample, in order to determine whether our findings were biased toward healthier individuals. A lifetime Year 1 AUD diagnosis (but not a Year 1 TD diagnosis) was associated with mortality, χ^2 (1, $N = 710$) = 3.88, $P < 0.05$; OR = 1.44 (1.002, 2.09). Among those who were deceased by Year 16, 23.9% had met criteria for lifetime AUD at Year 1 (vs. 17.8% of deceased participants who did not meet criteria for AUD at Year 1). This suggests that our estimates of the AUD–TD association at the 16 year follow-up were conservative estimates of comorbidity.

4. Conclusions

4.1. Alcohol–tobacco comorbidity

This study provides evidence of a bi-directional prospective association between alcohol and tobacco use disorders. Although the alcohol–tobacco association has repeatedly been demonstrated to be a robust one (e.g. Bien and Burge, 1990; Istvan and Matarazzo, 1984), most work has been limited to cross-sectional analyses and/or use of consumption measures, particularly among adolescents (e.g. Fleming et al., 1989; Jackson et al., 2002; Rohde et al., 1995; Simon et al., 1995; Torabi et al., 1993). Although these studies are informative with regard to identifying risk factors for substance use onset, they fail to inform us about the etiology of a substance use disorder. In studies where a prospective association has not been observed (e.g. Gordon and Doyle, 1986; Murray et al., 2002; Northwehr et al., 1995), many have examined consumption measures only, rather than syndromes of substance use disorders. Those studies that are based on substance use disorders have primarily been cross-sectional in nature and have used lifetime disorders (e.g. Batel et al., 1995; Breslau, 1995; Glassman et al., 1990; True et al., 1999; but see Sher et al., 1996; Jackson et al., 2000). It is questionable whether comorbidity truly exists if the criteria are based on a lifetime timeframe, as opposed to the same point in time.

Using a general population-based sample of adults, we found that past-year AUD and TD were associated not only cross-sectionally but also prospectively, using a combination of short-term (1 year) and long-term (15 year) follow-up intervals. These associations were present even after controlling for age, sex, and race. Year 1 TD prospectively predicted diagnosis with an AUD at Year 2, although the converse was not true in this middle-aged sample. Although consistent with research in younger samples supporting a prospective association from tobacco involvement to alcohol involvement (Fleming et al. 1989; Sher et al., 1996), this null finding for the prospective AUD to TD association is contrary to research showing prospective prediction from alcohol use to tobacco use over 1 year in 842 adolescents (Simon et al., 1995) and work showing a bi-directional association between alcohol and tobacco use disorders in a college sample (Sher et al., 1996) using a longer follow-up interval, and between alcohol and tobacco use in a nationally representative sample of adolescents and a community sample of adolescents/young adults (Jackson et al., 2002). However, we found that a baseline diagnosis of AUD did increase the likelihood of diagnosis with TD 15 years later. Evidence of alcohol–

tobacco use disorder associations over such a long time interval in older adults attests to the robust nature of this phenomenon. Unfortunately, these inconsistent findings between the Year 2 and 16 follow-ups do not resolve the extent to which the AUD–TD association is stable and trait-like versus a timebound process, and it is unclear why the direction of the effects would be opposite for short-versus long-term follow-up intervals.

4.1.1. Onset, persistence, and stability of a disorder—In addition to the overall prospective findings discussed above, we also performed a more fine-grained analysis of alcohol–tobacco comorbidity to determine the extent to which we could predict onset and persistence, as well as stability of each disorder. To examine onset and persistence for the short-term (Year 2) follow-up, we created four-level variables for both AUD and TD that took into account diagnosis at Year 1 and 2. This four-level categorization is similar to work in smoking research that characterizes smoking based on two time points (nonsmokers, stable smokers, adult-onset smokers/late adopters, and nonpersistent adolescent or former smokers; Juon et al., 2002; Chassin et al., 1991); neither of these studies, however, examined smoking’s association with alcohol involvement. Given the lower sample size, onset and persistence for the long-term (Year 16) follow-up were examined by subsetting the data.

Having been persistently diagnosed with TD at Years 1 and 2 predicted the onset of a new diagnosis with AUD; however, this analysis does not clearly resolve whether the prospective TD–AUD association is directional (i.e. Year 1 TD→Year 2 AUD) or whether it is due to (i.e. mediated by) concurrent use of TD Year 2 (discussed in Section 4.1.2). Conversely, we failed to observe short-term prediction of TD onset by AUD, suggesting that the directional association from AUD to TD is perhaps less strong than the converse. Fleming et al. (1989) found that among adolescents, onset of alcohol consumption 2 years later was higher for baseline smokers than non-smokers; there were too few drinkers at baseline to evaluate the converse relation. In our own work, we have found support for onset in both directions. Among college students, respondents were more likely to develop a TD either 3 or 6 years later if they had been diagnosed with AUD at baseline; likewise, respondents were more likely to develop a later AUD if they had been diagnosed with baseline TD (Sher et al., 1996). In a nationally representative sample of adolescents over 1 year and a community sample of adolescents/young adults over 5 years, onset of drinking was higher for baseline smokers and onset of smoking was higher for baseline drinkers, with similar magnitude across both directions (Jackson et al., 2002).

Having been diagnosed with TD at Year 1 (that is, those with persistent TD and remitted TD) predicted AUD persistence. We might consider having a persistent AUD diagnosis to be reflective of a more “severe” case than having a remitted AUD diagnosis; in fact, the risk ratios for TD’s prediction of these severe AUD cases were higher in magnitude than those for TD’s prediction of the less severe (remitted) AUD cases (see Table 4, third column), which supports prior research showing a dose-dependent association between smoking and drinking (Madden et al., 2000).

Having been diagnosed with an AUD (i.e. persistent AUD or new onset AUD) also predicted TD persistence. These findings again suggest the possibility that prospective comorbidity is mediated by having a concurrent diagnosis with the other disorder (discussed in Section 4.1.2). Previous work in our laboratory showed persistence effects for drinking and smoking in adolescents over both 1 and 5 year intervals (Jackson et al., 2002), although using a sample of college students, persistence effects for AUD and TD over 6 years were not evident (Sher et al., 1996). Moreover, in the current study, we failed to find any evidence that short-term stability of a disorder was moderated by the other disorder for either AUD or TD.

In terms of Year 16 results, long-term prediction of onset failed to show effects for either AUD or TD, as did moderation of either AUD or TD stability. Likewise, long-term prediction of persistence failed to show effects for either AUD or TD, although there was inconsistent support for an AUD effect on TD onset and persistence using alternate classification systems (DSM-III-R criteria for onset; DSM-IV criteria for persistence). We suspect that these findings may be in part due to the older age of the sample. By age 50 (average age for the Year 16 follow-up), existing cases are likely already somewhat chronic (and we are unlikely to see new onset as respondents move out of the age of risk) and are less likely to be predicted by (or moderated by) other substance related co-factors. There might be other risk factors for onset or persistence of substance use disorders (e.g. failure to negotiate role transitions such as career, marriage, or parenthood) that are already in place by early-to-mid adulthood and beyond, and these, rather than a diagnosis with the other substance use disorder, may tend to initiate or sustain the substance use disorder at this point in the life course. In addition, no other research to our knowledge has examined onset or persistence over such a long interval, although Gordon and Doyle (1986) found no prospective (overall) relationship between drinking and smoking over an 18 years follow-up period. It is unclear whether the inconsistency of persistence effects between the current study and other work in our laboratory might be due to the age of the sample, the long time-interval used here, or the severity of the outcome measures (i.e. drinking and smoking as opposed to AUD and TD). For example, it is possible that substance use diagnoses are more persistent than simple substance use, and are less easily predictable by other variables (including use of other substances/diagnosis with other substance use disorders). Data on consumption over time were not available at all time points in the ECA dataset, precluding prospective analyses of substance use variables.

4.1.2. Mediation of comorbidity through concurrent diagnosis with the other disorder—Our onset and persistence analyses raised the question that the prospective association between AUD and TD could be directional, or could be due to (i.e. mediated by) concurrent use of the other substance at the time of follow-up. We tested this hypothesis and found that the direct effect was diminished and no longer significant when the concurrent substance was included in the model. Note that although both mediation analyses and onset/persistence analyses reveal that there is a longitudinal association once you take into account the cross-sectional association, the current analyses indicate the extent to which the prospective association is mediated through Year 2, whereas the onset and persistence analyses reveal the extent to which there still a prospective association once the Year 1 cross-sectional association is controlled.

Work by Jessor et al. (1991) shows that the prospective (8-year) association between problem behavior proneness in adolescence and young adult problem behavior involvement is primarily a function of indirect associations via synchronous relations. Schulenberg et al. (in press) suggest that prospective associations between adolescent substance use and young adult functioning may be in part due to “a mutually reinforcing web of contemporaneous influences (p. 12)”. Our own findings showing mediation through concurrent substance use disorders speak to the high chronicity of alcohol and tobacco use disorders, particularly the latter, given the highly addictive nature of smoking (Department of Health and Human Services, 1988; Robinson and Pritchard, 1992).

4.1.3. Associations across sex, race, and age group—In general, findings did not vary by sex, race, or age group. Although men and Whites generally tended to drink and smoke more than women and ethnic minority groups, a common observation in the literature, the association between smoking and drinking remained constant across subgroup, similar to a finding that we reported based on data from the National Longitudinal Survey of Adolescent Health (Jackson et al., 2002). However, the mechanisms underlying the association may be different across subgroup; men may drink and smoke because they have a sensation-seeking

personality, whereas women may drink and smoke to relieve negative affectivity. Current work in our laboratory focuses on exploring dispositional and situational constructs that are common to both drinking and smoking, and determining the extent to which these multivariate associations differ across gender, race, and age.

4.2. Implications for treatment and prevention of alcohol and tobacco use disorders

Our own work and extant work on alcohol-tobacco comorbidity suggests that if an individual is diagnosed with an AUD, we might suspect that he/she would also be diagnosed with TD either concurrently or at some subsequent point in time (and vice versa). This suggests that if one disorder is treated, it would be valuable to assess for and potentially treat the other one as well, given the likelihood of co-occurring conditions. A number of studies reveal that quitting smoking does not adversely affect alcohol treatment outcomes (Bobo et al., 1987; Hurt et al., 1994; Northwehr et al., 1995), and studies have shown success in smoking cessation after alcohol treatment (Bobo et al., 1986; Zimmerman et al., 1990).

In addition, our finding that TD may lead to an AUD, and an AUD may lead to TD, is consistent with work showing a prospective association between alcohol and tobacco consumption (Fleming et al., 1989; Jackson et al., 2002; Rohde et al., 1995; Simon et al., 1995; Torabi et al., 1993). It is not unlikely, then, that desistence of use of one substance might lead to reduced use of the other substance, which has implications for prevention of substance use. Prevention programs that have targeted alcohol only have also shown effects on smoking (Perry et al., 1996) and vice versa (Perry et al., 1992). In addition, research has established that alcohol and tobacco tend to be “gateway” drugs to illicit drug use (Bailey, 1992; Kandel, 2002), with the highest rates of progression to illicit drug use for those who had engaged in both alcohol and tobacco use (Kandel and Yamaguchi, 2002). Relatively recent prevention efforts have capitalized on the idea that drug use occurs in an stage-sequential fashion, and have targeted earlier-stage drugs (i.e. alcohol and tobacco) as a means of reducing likelihood of advancing to later-stage drugs (i.e. illicit drugs; e.g. Graham et al., 1991; Pentz and Li, 2002; Scheier et al., 2002). However, these studies, like most work in substance use prevention, have primarily focused on adolescent populations; given the current findings that shows a prospective association between alcohol and tobacco use disorders during adulthood, future research might address the utility of prevention efforts during these later years. What is clear is that substances are not used in isolation, and issues of comorbidity and stage theory are on the forefront of current research in treatment and prevention of substance use/abuse.

4.3. Strengths and limitations

Our study benefits from a number of strengths, including a large sample size, two waves of data over a short interval and a long-term follow-up, and the use of structured diagnostic interviews. The data for this study were taken from the ECA study, which was drawn from the general population (of which the St. Louis site is relatively representative), and findings were back-weighted to adjust for the clustered nature of the data. Although the attrition bias and sampling design of the Year 16 follow-up precludes generalization to the US at large, our attempt to weight the sample back to the original ECA combined with our goal of characterizing different aspects of comorbidity, rather than simply describing national prevalence rates, increase our confidence in our findings. Our manuscript stands in contrast to much of the literature which has been focused on adolescent aged populations, or on adults from treatment facilities, and rarely on adults from a general population sample. In addition, our general population sample consists of a wide range of ages, racial groups, and approximately equal numbers of men and women at baseline.

However, as with many secondary data analyses, the dataset for the long-term follow-up was not designed to test prospective associations among AUD and TD; hence the sampling strategy

was not ideal, as it was a case-control study consisting primarily of stable alcoholics and heavy drinkers along with those who failed to diagnose with AUD. In addition, the follow-up population consisted primarily of men (79%), making it difficult to detect gender effects. We also found evidence of differential mortality; Year 1 AUD was associated with mortality at Year 16. This suggests that our Year 16 effects may be diluted due to the differential mortality, and are, in fact, conservative estimates of alcohol–tobacco comorbidity.

Also, ECA's sampling strategy may have overlooked transient populations (e.g. homeless persons) with high rates of alcoholism (Bucholz, 1992). We are reassured, however, that St. Louis ECA prevalence rates for Year 1 DSM-III lifetime AUD criteria (15.5%) were similar to those found at other ECA sites (e.g. New Haven, 12%; Baltimore, 14%) and to NCS data (14%; 7% for past-year alcohol dependence diagnosis), which used DSM-III-R criteria (Kessler et al., 1994)⁷. Regier et al. (1998) conducted an examination comparing prevalence rates in ECA and NCS data and found past-year alcohol dependence to be elevated in the NCS data, even when alcohol dependence was scored using DSM-III criteria and demographics were controlled. To our knowledge, no other studies have reported DSM-III prevalence data for TD⁸, and ECA is the only other study besides NCS (with a reported 24% TD rate using DSM-III-R criteria; Anthony et al., 1994; Breslau et al., 2001) to report prevalence data for TD across the life span with a general population-based sample.

In addition, given the nature of our constructs, our short-term prospective findings may be in part an assessment of measurement error of our constructs. Our DSM measures of alcohol and tobacco use disorders are based on meeting a certain threshold and thus some instability may be more apparent than real (Vandiver and Sher, 1991). For example, it is possible that a person who diagnoses with AUD at Year 1 but fails to diagnose at Year 2 is only one symptom short of an AUD diagnosis.

Additionally, although alcohol and tobacco use were ascertained using structured clinical interviews, these data are nonetheless self-report in nature and are prone to misreporting biases (e.g. underreporting to hide heavy alcohol consumption, overreporting to exaggerate drinking). No corroborative sources of information were obtained through biological assays or via a collateral source. Given these limitations, and the fact that this is an old sample (collected over a decade ago) with a now obsolete diagnostic classification system, it is important that our findings be replicated with a more recently ascertained sample and a current classification system.

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⁷Although Hasin et al. (1996) reported DSM-III prevalence for alcohol use disorder, their sample was screened for heavy past-year alcohol consumption and is not a comparable sample to this one.

⁸Although Hughes et al. (1987) documented prevalence rates for DSM-III tobacco dependence, their sample consisted only of smokers.

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Fig. 1. Theoretical model for prospective prediction of TD (top panel) and AUD (bottom panel), testing for mediation through the concurrent diagnosis at Year 2 (controlling for Year 1 autoregressivity).

Table 1
Respondent characteristics for non-completers and completers for each follow-up

Y1 respondent characteristic	Year 2				Year 16			
	Non-complete (N = 440)		Complete (N = 2564)		Non-complete (N = 267)		Complete (N = 444)	
	mean		mean	d ^a	mean		mean	Effect size
Age	44.8		44.1	0.09	50.0		33.2	1.17
Education	11.0		11.4	0.14	10.3		12.8	.81
Family income (in thousands)	5493.5		6237.6	0.06	4800.6		9173.6	.33
	%		%	h ^b	%		%	h ^b
Gender, % male	45		39	0.12	82		79	0.08
Race								
White	55		58	0.06	61		78	0.37
Black	41		38	0.06	34		20	0.32
Other	03		03	0.00	04		03	0.06
Past-year AUD	06		06	0.00	15		18	0.08
Lifetime AUD	15		16	0.03	45		42	0.06
Past-year TD	30		29	0.02	33		36	0.06
Lifetime TD	35		36	0.02	44		45	0.02

^a Cohen's (corrected) d (Hedges and Olkin, 1985).

^b Cohen's h (Cohen, 1977).

Table 2

(Weighted) prevalence of demographics and substance use disorders for Years 1, 2, and 16

Age in years	Full sample <i>N</i> = 3004	Young (<30) <i>N</i> = 882	Young adult (30–44) <i>N</i> = 823	Middle-aged (45–64) <i>N</i> = 721	Older (65+) <i>N</i> = 578
<i>Years 1 and 2</i>					
% Male	46.8	48.3	48.1	47.8	39.4
% White	78.6	72.5	73.4	82.8	86.2
% Black	19.0	22.9	22.8	14.4	12.7
Mean age at Year 1 (S.D.)	42.70 (13.49)	23.46 (2.56)	36.02 (3.03)	53.87 (4.55)	73.78 (4.31)
% Year 1 past-year AUD	6.0	9.3	7.3	3.4	1.7
% Year 1 past-year AUD ^a	6.0	8.5	7.5	3.3	2.0
% Year 2 past-year AUD	7.6	12.1	8.7	4.0	2.4
% Year 1 past-year TD	29.5	34.5	34.2	27.6	13.8
% Year 1 past-year TD ^a	29.5	34.8	34.3	27.1	10.9
% Year 2 past-year TD	28.0	34.8	32.2	23.2	12.5
% Year 1 lifetime AUD	15.7	18.9	20.8	11.6	7.2
% Year 1 lifetime TD	36.6	38.7	43.2	37.6	18.4
<i>Year 16</i>					
Full sample <i>N</i> = 444					
		Young (<30) <i>N</i> = 184	Young adult (30–44) <i>N</i> = 195	Middle-aged (45–64) <i>N</i> = 61	Older (65+) <i>N</i> = 4
% male	38.6	37.0	43.1	29.7	100.0
% white	50.7	55.1	55.8	30.7	70.3
% black	44.6	40.3	39.7	63.6	29.7
Mean age at Year 16 (S.D.)	51.54 (11.64)	41.37 (3.59)	52.21 (3.56)	69.23 (6.61)	84.38 (3.05)
% Year 1 past-year AUD	8.2	9.7	7.4	5.6	29.7
% Year 2 past-year AUD	13.3	13.0	17.3	7.2	0.0
% Year 16 past-year AUD	5.5	5.2	8.6	0.5	0.0
% Year 1 past-year TD	30.0	34.7	32.3	16.1	29.7
% Year 2 past-year TD	28.4	35.0	26.8	17.7	29.7
% Year 16 past-year TD	22.0	27.4	20.0	14.2	29.7

^aListwise deletion, *N* = 2564 (respondents were assessed at both Years 1 and 2).

Table 3
Summary table with odds ratios and 95% CI for AUD–TD comorbidity analyses, controlling for sex, race, and age

Analysis	AUD→TD			TD→AUD		
	N	OR	OR (95% CI)	N	OR	OR (95% CI)
Cross-sectional	Year 1	2950	2.11 (1.40, 3.18)	2950	2.32 (1.55, 3.47)	
	Year 2	2488	2.37 (1.53, 3.68)	2488	2.56 (1.67, 3.92)	
	Year 16	444	2.87 (0.99, 8.37)	444	2.89 (1.01, 8.29)	
Prospective	Year 2	2470	1.17 (0.68, 2.01)	2465	1.90 (1.16, 3.13)	
	Year 16	443	2.60 (1.13, 5.99)	443	0.93 (0.36, 2.43)	
Prospective, control for co-occurring disorder	Year 2	2470	0.85 (0.47, 1.53)	2465	1.08 (0.50, 2.36)	
	Year 16	443	2.12 (0.91, 4.94)	443	0.51 (0.19, 1.36)	

All prospective analyses control for autoregressivity. If the 95% CI contains 1.0, the association is not significant at $P < 0.05$.

Table 4

Cell frequencies, cell percentages, RR ratios, and 95% CI for four-level AUD by four-level TD

TD	AUD				
	Stable non-diagnoser	New onset	Remission	Persistence	Total
Stable non-diagnoser	1509 61.2%	113 4.6%	54 6.2%	457 18.5%	2223 90.6%
New onset	— 40 1.6%	— 7 0.3%	— 4 0.2%	— 36 1.5%	87 3.5%
Remission	— 33 1.3%	RR _{AUD→TD} = 2.22 (0.70, 7.07) RR _{TD→AUD} = 2.45 (0.80, 7.46)	RR _{AUD→TD} = 2.43 (0.61, 9.65) RR _{TD→AUD} = 2.60 (0.66, 10.23)	RR _{AUD→TD} = 2.25 (0.98, 6.26) RR _{TD→AUD} = 2.32 (0.72, 7.07)	65 2.6%
Persistence	28 1.1%	RR _{AUD→TD} = 0.54 (0.16, 1.82) RR _{TD→AUD} = 0.69 (0.21, 2.28)	RR _{AUD→TD} = 2.46 (0.92, 6.61) RR _{TD→AUD} = 2.92 (1.10, 7.74)	RR _{AUD→TD} = 2.98 (1.20, 7.35) RR _{TD→AUD} = 3.34 (1.38, 8.10)	80 3.2%
Total	1610 65.3%	130 5.3%	175 7.1%	550 22.3%	2465

The non-diagnosing group serves as the reference group for the predictor and for the outcome, and hence has no risk ratio associated with it.