www.AUSTRALIANACADEMICPRESS.com.au

ARTICLE AVAILABLE ONLINE
Twin Research and Human Genetics
Volume 14 ▮ Number 1 ▮ pp. 1–15

Toward a Comprehensive Developmental Model for Alcohol Use Disorders in Men

Kenneth S. Kendler,[1,2] Charles O. Gardner[1] and Carol A. Prescott[3]

[1] *Department of Psychiatry, Virginia Commonwealth University School of Medicine, United States of America*
[2] *Department of Human and Molecular Genetics, Virginia Commonwealth University School of Medicine, United States of America*
[3] *Department of Psychology, University of Southern California, United States of America*

The multiple risk factors for alcohol use (AU) and alcohol use disorders (AUDs) are interrelated through poorly understood pathways, many of which begin in childhood. In this report, the authors seek to develop an empirical, broad-based developmental model for the etiology of AU and AUDs in men. We assessed 15 risk factors in four developmental tiers in 1,794 adult male twins from the Virginia population based twin registry. The best fitting model explained 39% of the variance in late adolescent AU, and 30% of the liability to lifetime symptoms of AUD. AU and AUDs can be best understood as arising from the action and interaction of two pathways reflecting externalizing genetic/temperamental and familial/social factors. Peer group deviance was important in each pathway. Internalizing symptoms played a more minor role. Familial/social factors were especially important influences on AU, while genetic/temperamental factors were more critical for AUDs. We conclude that AU and AUDs in men are complex traits influenced by genetic, family, temperamental, and social factors, acting and interacting over developmental time.

■ **Keywords:** alcoholism, genetics, development, peer deviance

> To chart the manner in which the causal structures [of alcohol use disorders] interact requires model building that will cross-multiple levels of analysis and multiple disciplines, operating over social, individual, and biological time … To capture such a multilevel structure, a developmental systems framework is essential … (Zucker, 2006, p. 625)

Alcohol use (AU) and alcohol use disorders (AUDs) are prototypical complex traits, influenced by a wide range of variables, including genetic factors that impact on AU (Heath et al., 1991; Hettema et al., 1999; Kaprio et al., 1991; Prescott et al., 1994) and which substantially alter risk for AUDs (Goodwin et al., 1973; Heath et al., 1997; Sigvardsson et al., 1996; Pickens et al., 1991; Prescott & Kendler, 1999b; Sigvardsson et al., 1996) and for broader externalizing traits (Kendler et al., 2003b; Sher et al., 2005), as well as religiosity (Kendler et al., 1997a; Kendler et al., 2003a; Koenig et al., 2001), parental attitudes to and use of alcohol (Tucker et al., 2008), childhood sexual and physical abuse (Kendler et al., 2000; Fergusson & Mullen, 1999), internalizing symptoms and personality traits (Kessler et al., 1997; Sher et al., 2005), parental monitoring (Dielman et al., 1990; Tucker et al., 2008) and peer group deviancy (Coie & Miller-Johnson, 2001; Farrington, 2005; Fergusson et al., 1995; Hawkins et al., 1998; Patterson et al., 2000). Levels of AU and risk for AUDs in adulthood can be predicted by risk factors measured in early to mid-childhood (Caspi et al., 1996; Dubow et al., 2008; Englund et al., 2008; Manzardo et al., 2005; Maggs et al., 2008; Pitkanen et al., 2008) suggesting that a complete understanding of the etiology of AUDs will require a developmental perspective (Windle, 1999; Zucker, 2006).

Several prior attempts have been made to develop empirical broad-based models for the etiology of AUDs (e.g., (Fergusson et al., 1995; Dubow et al., 2008; Guo et al., 2001; Ohannessian & Hesselbrock, 2008)) some of which have been particularly comprehensive (Dubow et al., 2008; Guo et al., 2001). However, we are unaware of

RECEIVED 26 October, 2010; ACCEPTED 03 December, 2010.

ADDRESS FOR CORRESPONDENCE: Kenneth S. Kendler, MD, Virginia Institute for Psychiatric and Behavioral Genetics of VCU, Box 980126, Richmond, VA 23298-0126. E-mail: kendler@vcu.edu

any such effort that has included all the above factors and, particularly, measures of genetic risk which, given heritability estimates for AUDs in the range of 50–60% (Heath et al., 1997; Kendler et al., 1997b; Pickens et al., 1991; Prescott & Kendler, 1999b), are critical to include in any model-building. To develop a more complete understanding of the etiology of high levels of AU and AUDs, we need to develop a broad, inclusive model that would begin to integrate, over developmental time, these diverse risk factors. The aim of this study is to present such an effort in male twins from the Virginia Adult Twin Study of Psychiatric and Substance Use Disorders (VATSPSUD) (Kendler & Prescott, 2006).

Methods

SAMPLE

This report utilizes data collected in first (MM1), second (MM2) and third wave (MM3) interviews with Caucasian adult male twins born between 1940 and 1974 from VATSPSUD (Kendler & Prescott, 2006). All subjects were ascertained from the Virginia Twin Registry — a population-based register formed from a systematic review of birth certificates in the Commonwealth of Virginia. Response rates for the MM1 (1993–1996) and MM2 (1994–1998) interviews were 72.4% and 82.6%, respectively. The MM3 interview, restricted to male–male twins, was completed in 1998–2004 by 1,796 (75%) of the male twins who had participated in the second interview. There were two sets of complete triplets from which we excluded one member each to give us a final sample of 1,794, including both members of 469 monozygotic (MZ) and 287 dizygotic (DZ) pairs. MM3 subjects were 24–62 years old (mean age = 40.3 years, *SD* = 9.0). Most subjects were interviewed by telephone by clinically trained interviewers. Signed informed consent was obtained for face-to-face interviews and verbal consent for telephone interviews. This project was approved by the Office of Research Subjects Protection at Virginia Commonwealth University. Members of a twin pair were always interviewed by different interviewers. Zygosity was assigned by a combination of self-report measures, photographs and DNA polymorphisms (Kendler & Prescott, 2006). Short-term test–retest reliability was available on variables assessed at the MM2 (195 subjects interviewed an average of 31 days apart) and MM3 interviews (141 subjects interviewed an average of 29 days apart), but not for variables entirely or partially assessed at the MM1 interview.

OUTCOME VARIABLES

Our model had two key outcome variables: (1) average monthly AU for the ages of 15–17 and, (2) lifetime history of symptoms of AUDs, here defined as symptoms of DSM-IV alcohol abuse or dependence (American Psychiatric Association, 1994). Both of these traits were treated as ordinal variables, assuming an underlying normal liability distribution.

MODEL VARIABLES

We examined 15 risk factors conceptualized as four developmental 'tiers' reflecting: (1) *genetic risk* (and year of birth), (2) relevant aspects of the *childhood environment*, (3) critical *temperamental* and *symptom* variables, and (4) key personal, social and environmental risk factors in *late adolescence*.

GENETIC RISK

Genetic risk for AUDs. This factor was indexed from the history of alcohol abuse and dependence in the subject's parents and co-twin, based on interviews with the co-twin and family history reports about parents and co-twins obtained from the index twin (Muffler et al., 1991). Information from the MZ co-twin was weighted twice as high as that for the siblings and parents to reflect the greater genetic similarity of MZ twins compared to first-degree relatives.

Genetic risk for externalizing disorders. For genetic risk for externalizing disorders, we used a composite measure of the co-twin self-report symptoms of DSM-IV (American Psychiatric Association, 1994) conduct disorder (obtained at MM1 and MM2), antisocial personality disorder (MM2) and twin report of antisocial personality disorder in their co-twin and father using FH-RDC criteria (Muffler et al., 1991) (MM2). Scores from MZ co-twins were weighted twice as strongly as reports from DZ co-twins or parents.

Birth year. This factor was included as a covariate because of prior evidence that individuals across this age span differ in the prevalence of AUDs (Prescott & Kendler, 1999a).

CHILDHOOD ENVIRONMENT

Low church attendance. This factor was a continuously scored measure, reflecting the sum of responses to the item 'When you were between the ages of x and y, how often would you attend religious services?' asked in our MM3 interview for ages 8–11, 12–14 and 15–17. Response options were *More than once a week*, *Once a week*, *A few times a month*, *Once a month*, *Less than once a month*, and *Never*. Reliability for this variable (intraclass correlation [ICC]) equaled +0.88.

Household alcohol use was the sum of two items (MM3) about how often, when he was between the ages of 8 and 17, did people in the twin's household (other than the co-twin) 'drink alcohol' or 'get drunk.' Response options were *Nearly every day*, *Once or twice a week*, *A few times a month*, *Once or twice a year*, or *Never*. Reliability — weighted kappa (Fleiss, 1973) — equaled +0.78.

https://doi.org/10.1375/twin.14.1.1 Published online by Cambridge University Press

Parental attitude toward AU in their children. Response to one item (MM3) asking, during the time they were growing up, what the attitude of the parents would be to the statement 'It is OK for a teenager to drink alcohol.' Response options were: *Strongly agree*, *Agree, Disagree*, or *Strongly disagree.* Reliability (weighted kappa) equaled +0.43.

Childhood physical and sexual abuse. This factor was assessed with two items (MM1) inquiring from the twin whether he had ever been 'sexually abused or molested' before the age of 16, or 'physically abused as a child.'

CRITICAL TEMPERAMENTAL AND SYMPTOM VARIABLES

Attention deficit hyperactive disorder (ADHD). A continuous measure was obtained from 14 items reflecting DSM-IV symptoms for Attention Deficit Hyperactive Disorder (11 items) and Oppositional Defiant Disorder (3 items) (MM3) asked about for when the twins were 'growing up' (defined as before age 18) (American Psychiatric Association, 1994). Reliability (ICC) equaled +0.81.

Neuroticism. This factor was assessed by the Short-Scale (12-item) version from the EPQ-R (Eysenck et al., 1985) (MM1) scored as a 5 level ordinal measure.

Sensation-seeking was a continuous measure based on 11 items selected from the Sensation Seeking Scale (MM3)(Zuckerman & Neeb, 1979). Reliability for this variable (ICC) equaled +0.81.

Early onset anxiety disorder was a binary variable scored 1 for subjects with an onset, prior to age 18, of panic disorder, generalized anxiety disorder (MM1) or any form of phobia (MM2) using diagnostic criteria outlined previously (Kendler & Prescott, 2006).

KEY PERSONAL, FAMILY AND SOCIAL RISK FACTORS IN LATE ADOLESCENCE

Conduct disorder. This factor was assessed by items based on the symptomatic criteria in DSM-IV (American Psychiatric Association, 1994) conduct disorder scored on a 4-point frequency scale asked for ages 15–17 (MM3). Reliability (weighted kappa) equaled +0.59.

Low parental monitoring was assessed as the sum of 4 items asked (MM3) for ages 15–17 based on previous work examining parental effects on risk of drug use and delinquency (Kerr & Stattin, 2000; Steinberg et al., 1994): how much parents really knew about: who the twin's friends were, how the twin spent his money, what he did with his free time, and where he was at night. Response options were they 'didn't know,' 'knew a little,' or 'knew a lot.' Reliability (weighted kappa) equaled +0.69.

Peer group deviance was assessed by two validated instruments (Johnston et al., 1982; Tarter & Hegedus, 1991) that evaluated the proportion of the respondent's friends, at ages 15–18, who engaged in specific deviant behaviors (MM3; see Kendler et al., 2007, for details). Reliability (ICC) equaled +0.81.

Alcohol availability. This was assessed by a single item from the Monitoring the Future study (Johnston et al., 1982) which asked subjects at ages 15–17, on a 4-point scale, how easy it would have been to get alcohol if they wanted to use it. Reliability (weighted kappa) equaled +0.58.

OUTCOME VARIABLES

AU was assessed using a life history calendar (MM3) (Freedman et al., 1988). Following methods of Cohen et al. (2003), the calendar contained columns for each year of the subject's life. The first rows, completed early in the interview, documented key changes in living situation as well as major educational, employment and interpersonal milestones. If necessary, the interviewers would use other memory prompts from the information previously recorded on the calendar to 'cue' the respondent into the relevant 'memory files'. For alcohol, we inquired separately about the average number of days per month on which the subject consumed alcoholic beverages and the average number of drinks consumed per day when drinking. We defined a drink as 'one bottle of beer, one glass of wine or one shot of liquor'. Drinking quantity and frequency were multiplied to give a weighted monthly consumption and this value was averaged for ages 15 through 17. Because this variable was positively skewed, the data were grouped into 5 values ranging from 0 to > 15 drinks per month. Reliability (weighted kappa (Fleiss, 1973)) equaled +0.59.

AUD reflected a count of the lifetime DSM-IV alcohol abuse or dependence criteria met (MM2). Reliability (weighted kappa (Fleiss, 1973)) equaled +0.68.

We examined social-environmental risk factors for the age period 15–17 because the age at onset of AUD syndromes in this sample began to increase sharply at the age of 18. Consequently, for the vast majority of the sample, environmental variables and drinking behaviors for age 15–17 represent risk factors that predate the onset of AUD symptoms.

STATISTICAL METHODS

Model fitting was done using Mplus version 5.1 (Muthen & Muthen, 2007) because of its ability to combine categorical, ordinal and continuous data. Since the path model contained categorical and ordinal intermediate variables, the theta parameterization was used with weighted least squares as the fit function. We began with a fully saturated model and then fixed paths to zero sequentially, choosing the path with the smallest z-score (in absolute value) at each step until all paths with an associated p value of > .05 had been set to zero. Next, because of our large sample size, some paths remained statistically significant, which

https://doi.org/10.1375/twin.14.1.1 Published online by Cambridge University Press

were too small to be meaningful. Therefore, our second step was to set all paths to zero with an absolute value of < 0.05, regardless of z value. All remaining paths in the model were statistically significant. This approach does result in the inclusion of paths in the model with modest explanatory power.

We utilized three fit-indices, which reflect the model's balance of explanatory power and parsimony: the Tucker-Lewis Index (TLI) (Tucker & Lewis, 1973), the Comparative Fit Index (CFI) (Bentler, 1990), and the root mean square error of approximation (RMSEA) (Steiger, 1990). For the TLI and CFI, values between 0.90 and 0.95 are considered acceptable, and ≥ 0.95 as good. For the RMSEA, good models have values ≤ 0.05.

Results

MODEL FITTING

Of the 1,794 male twins who participated in the third interview wave, the mean (± *SD*) monthly consumption of drinks of alcohol at ages 15–17 was 7.3 (23.4) while the mean (± *SD*) number of symptoms of AUD was 1.8 (2.8). 39.6% of the sample reported consuming no alcohol at ages 15–17 and 57.6% reported no lifetime symptoms of AUDs. The fit of our best model was very good (CFI = 0.98, TLI = 0.96 and RMSEA=0.02) and it explained 39% of the variance in late adolescent AU and 30% of the liability to lifetime symptoms of AUD.

PREDICTED CORRELATIONS

Table 1 depicts the correlations between the 17 variables predicted from this best fit model.

PARAMETER ESTIMATES

Tier 1: Genetic Risk and Year of Birth

As seen in Figure 1, the genetic risk for AUD had a moderate correlation with the genetic risk for externalizing disorders and significantly predicted three downstream variables: household alcohol use, neuroticism, and AUDs.

The genetic risk for externalizing disorders predicted nine variables: low church attendance, household alcohol use, childhood abuse, ADHD, conduct disorder, low parental monitoring, peer group deviance, AU, and AUDs.

A more recent birth year was modestly correlated with genetic risk for externalizing disorders and was associated with six other variables: low church attendance, sensation seeking, conduct disorder, peer group deviance, alcohol availability, and AU. Adjusting for its impact on these intermediate variables, year of birth had no direct effect on risk for symptoms of AUDs.

Tier 2: Early Familial Factors

Low church attendance in childhood had significant associations with household alcohol use and parental alcohol attitudes, and significantly predicted neuroticism, conduct disorder, parental monitoring, peer group deviance, and alcohol availability. When adjusting for this widespread set of effects, church attendance had no direct impact on either AU or AUDs.

Household alcohol use significantly predicts seven downstream variables: alcohol attitudes, childhood abuse, ADHD, sensation seeking, conduct disorder, alcohol availability, and AU.

Parental attitudes toward AU significantly predicted five variables: low neuroticism, low parental monitoring, peer group deviance, alcohol availability, and AU.

Childhood abuse also predicted five downstream variables: neuroticism, sensation seeking, early onset anxiety disorder, low parental monitoring, and alcohol availability.

Tier 3: Temperamental and Symptom Variables

Remarkably, symptoms of ADHD were significantly related to all nine downstream variables in the model: neuroticism, sensation seeking, early onset anxiety disorder, conduct disorder, low parental monitoring, peer-group deviance, alcohol availability, AU, and AUDs. In the context of all the other paths, the path between ADHD and AU is modest but negative. Given the overall positive correlation between ADHD and AU (+0.17), this result is more likely artifactual than substantive.

Neuroticism predicts significantly six other variables, three positive (early onset anxiety, low parental monitoring and peer group deviance), and three negative (sensation seeking, alcohol availability and AU). This suggests that after accounting for the other paths, high levels of negative emotionality reduce levels of sensation seeking, the chances of selecting social environments where alcohol is easily available, and reduce the probability of consuming high levels of alcohol in late adolescence.

Sensation-seeking predicted only conduct disorder and low parental monitoring. Early onset anxiety disorder predicted only symptoms of AUD. Of note, while neuroticism reduces the risk for high AU and strongly predicts early onset anxiety disorders, anxiety disorders themselves increase the risk for AUDs.

Tier 4: Conduct Disorder and Social-Environmental Risk Factors in Late Adolescence

Conduct disorder symptoms at age 15–17 predicted 4 of the 5 remaining variables in the model: low parental monitoring, peer group deviance, AU, and symptoms of AUD.

Low parental monitoring at age 15–17 predicted 3 of the 4 down-stream variables: peer group deviance, AU and symptoms of AUD. Peer group deviancy predicted alcohol availability and AU. Alcohol availability predicted only AU. AU at ages 15–17 strongly predicted symptoms of AUD.

Direct Influences on Alcohol Consumption and Symptoms of Alcohol Use Disorders

Ten variables in the model significantly and directly predicted AU at ages 15–17. In order of their *direct* impact, the five most important were: peer deviance, alcohol avail-

https://doi.org/10.1375/twin.14.1.1 Published online by Cambridge University Press

TABLE 1

Correlations Among Variables as Predicted by Our Best Fit Model

	Estimated Correlation Matrix for the Latent Variables																
	Genetic Risk Alcoholism	Genetic Risk Ext Disorders	Birth Year	Low Church Attendance	Alcohol Household Use	Alcohol Attitude	Childhood Phys Sexual Abuse	ADHD	Neuroticism	Sensation Seeking	Early Onset Anxiety Disorder	Conduct Disorder 15–17	Parental Monitoring 15–17	Peer Group Deviance 15–17	Alcohol Availability 15–17	Alcohol Intake 18–21	Symptoms of Alcohol Abuse/ Dependence
Genetic risk ext disorders	0.37																
Birth year	0	0.10															
Low church attendance	0.07	0.19	0.19														
Alcohol household use	0.23	0.20	0.06	0.30													
Alcohol attitude	0.09	0.09	0.04	0.22	0.38												
Childhood physical sexual abuse	0.14	0.31	0.03	0.10	0.23	0.09											
ADHD	0.11	0.24	0.02	0.08	0.17	0.07	0.09										
Neuroticism	0.11	0.14	0.02	0.08	0.08	-0.04	0.22	0.26									
Sensation seeking	0.05	0.10	0.24	0.09	0.13	0.06	0.11	0.24	0.03								
Early onset anxiety disorder	0.07	0.12	0.01	0.05	0.08	0.01	0.22	0.23	0.38	0.06							
Conduct disorder 15–17	0.14	0.33	0.12	0.17	0.19	0.09	0.13	0.40	0.13	0.22	0.11						
Parental monitoring 15–17	0.12	0.28	0.09	0.25	0.20	0.16	0.24	0.28	0.18	0.18	0.13	0.40					
Peer group deviance 15–17	0.13	0.30	0.02	0.22	0.19	0.16	0.16	0.33	0.18	0.14	0.12	0.53	0.46				
Alcohol Availability 15-17	0.11	0.20	0.11	0.23	0.32	0.28	0.22	0.22	0.06	0.13	0.08	0.26	0.25	0.40			
Alcohol Intake 18-21	0.12	0.26	0.21	0.23	0.28	0.26	0.16	0.17	0.04	0.15	0.06	0.39	0.38	0.50	0.40		
Symptoms of Alcohol Abuse/Dependence	0.33	0.31	0.08	0.14	0.20	0.12	0.16	0.24	0.14	0.12	0.20	0.33	0.30	0.31	0.22	0.40	

https://doi.org/10.1375/twin.14.1.1 Published online by Cambridge University Press

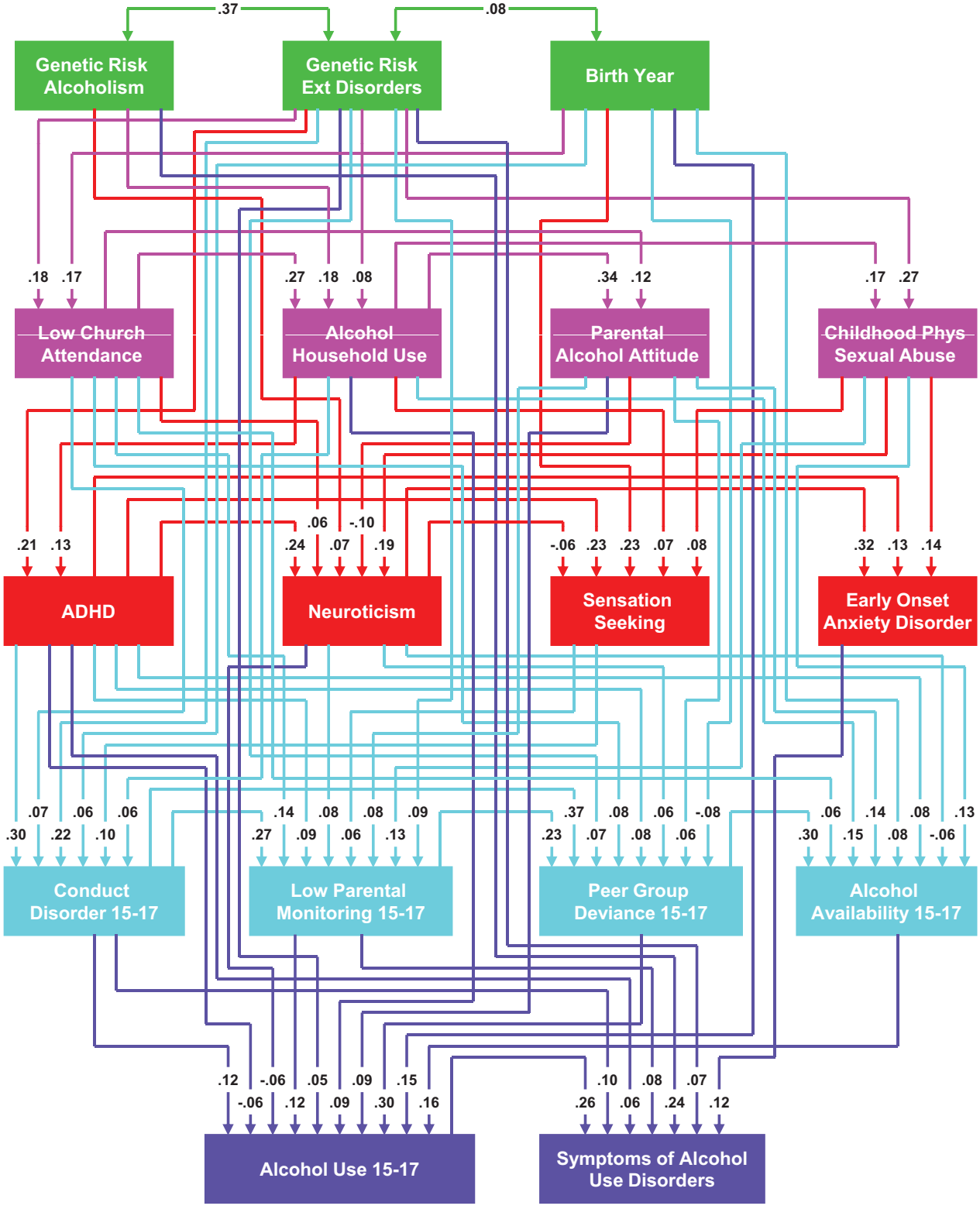

FIGURE 1

Results of our best fit model for the prediction of level of alcohol use at ages 15–17 and lifetime symptoms of Alcohol Use Disorders (DSM-IV Alcohol Abuse and Dependence).

Note: Two-headed arrows represent correlation coefficients while one-headed arrows represent path coefficients or standardized partial regression coefficients. 'ADHD' stands for symptoms of attention deficit hyperactivity disorder. 'Ext Disorders' stands for externalizing disorders. All variables have estimated residual variance that is not depicted in the figure. See text for a description of each variable. The variables are chosen and positioned to approximate a developmental process.

https://doi.org/10.1375/twin.14.1.1 Published online by Cambridge University Press

ability, birth year, low parental monitoring, and conduct disorder. While significant, the direct effect of genetic risk factors on AU was modest, reflecting the mediation of genetic risk through other variables in the model.

Seven variables impacted significantly on AUD symptoms. In order of the magnitude of their *direct* impact, the four most important were: AU, genetic risk for AUDs, early onset anxiety disorder, and conduct disorder. Of note, social environmental factors were consistently stronger influences on AU than on AUDs.

DIRECT VERSUS INDIRECT ASSOCIATIONS

The correlations depicted in Table 1 reflect both the direct path between the variables plus all the indirect paths mediated by other variables in the model. By contrast, the path estimates in figure 1 reflect only the direct relationship adjusting for all the other variables in the model. Therefore, a comparison between the values in the table and figure gives us an estimate of the proportion of the total correlation between any two variables in the model that results from direct effects versus total indirect effects. For example, from table 1, the total correlation between Genetic Risk for Alcoholism and symptoms of AUD is +0.33 while the direct path between these two variables from Figure 1 is +0.24. This suggests that 73% (.24/.33) of effect of alcohol risk genes on AUD in our model is direct and 27% indirect, mediated by factors such as household alcohol use and neuroticism. These results can be usefully contrasted with those obtained for alcohol household use and AU where the total correlation is 0.31 and the direct path .09. Our model predicts that 29% of the association between alcohol household use and AU is direct and 71% indirect, mediated largely by conduct disorder, alcohol availability and genetic risk for externalizing disorders.

PATHWAYS TO ALCOHOL CONSUMPTION AND SYMPTOMS OF ALCOHOL USE DISORDERS

Our best-fit model suggests two major pathways to AU and AUDs in men. The first, depicted in figure 2, is characterized by externalizing genetic/temperamental factors and includes, as major variables, genetic risk for AUDs and externalizing disorders, ADHD, sensation seeking, conduct disorder, and peer group deviance. Of note, the social trait of peer deviance was clearly part of this network given important input from conduct disorder, genetic risk for alcoholism and ADHD. As seen in Figure 2, this pathway had a greater relative impact on AUDs than on AU.

The second major pathway, seen in Figure 3, is dominated by familial and social factors, and includes all four tier 2 familial environmental exposures as well as low parental monitoring, peer group deviance and alcohol availability. This pathway had a greater relative impact on AU than on AUDs.

These two pathways intersect in three important ways. First, genetic risk factors impact both on early familial factors (e.g., paths from genetic risk for externalizing disorders to alcohol household use and childhood physical and sexual abuse) and later social-environmental factors (the path for externalizing disorders to peer-group deviance). Second, adjusting for these genetic effects, familial factors impact on temperamental variables (e.g., pathways from alcohol household use to ADHD and low church attendance to conduct disorder). Third, temperamental variables contribute, sometimes quite strongly, to social–environmental factors (e.g., paths from ADHD to alcohol availability and from conduct disorder to low parental monitoring and peer group deviance.)

In addition to these two major pathways, a third minor internalizing pathway is detectable focused on two variables: neuroticism and early onset anxiety disorders (Figure 4). The impact of these variables on AU and AUDs was complex. The overall correlation of neuroticism with AU and AUDs is weakly *positive*. However, accounting for other variables in the model, neuroticism directly predicts reduced levels of AU and has no direct relationship with AUDs. Early onset anxiety disorder by contrast has stronger and more positive overall relationships with AU and AUDs, and has the third strongest direct impact on risk for symptoms of AUDs. Overall, this internalizing pathway has weak and mixed effects on AU but given high levels of AU significantly predicts risk for subsequent symptoms of AUDs.

Discussion

This report describes our effort to construct a broad-based etiologic model for AU and AUDs that would integrate, over developmental time, a diverse range of relevant risk factors including genetic susceptibility. While many in psychiatry have advocated the development of bio-psychosocial (Engel, 1977), multi-level (Schaffner, 1994) or integrative (Kendler, 2005) etiological models, the empirical implementation of such approaches is challenging. Indeed, our efforts suffer from a number of important limitations outlined below. However, models in science do not need to be complete or entirely true to be useful (Wimsatt, 2007). Indeed, our results provide a range of useful insights into the etiology of AU and AUDs six of which are noteworthy.

First, our results are consistent with a recent review of the major developmental studies of AU and AUD (Zucker, 2008) that found the most robust risk factor to be 'an externalizing pathway.' Our model is also congruent with prior reviews (Sher et al., 2005; Windle, 1999) that AU and AUDs are positively associated with several externalizing-like personality traits including extraversion/sociability, impulsivity/disinhibition and novelty or sensation seeking (Grucza et al., 2006; Verdejo-Garcia et al., 2008; Zuckerman, 1972). Finally, our results are consistent with twin studies from the Virginia (Kendler et al., 2003b), Australian (Slutske et al., 2002) and Minnesota Twin Registries (McGue & Iacono, 2008) in suggesting a sharing

https://doi.org/10.1375/twin.14.1.1 Published online by Cambridge University Press

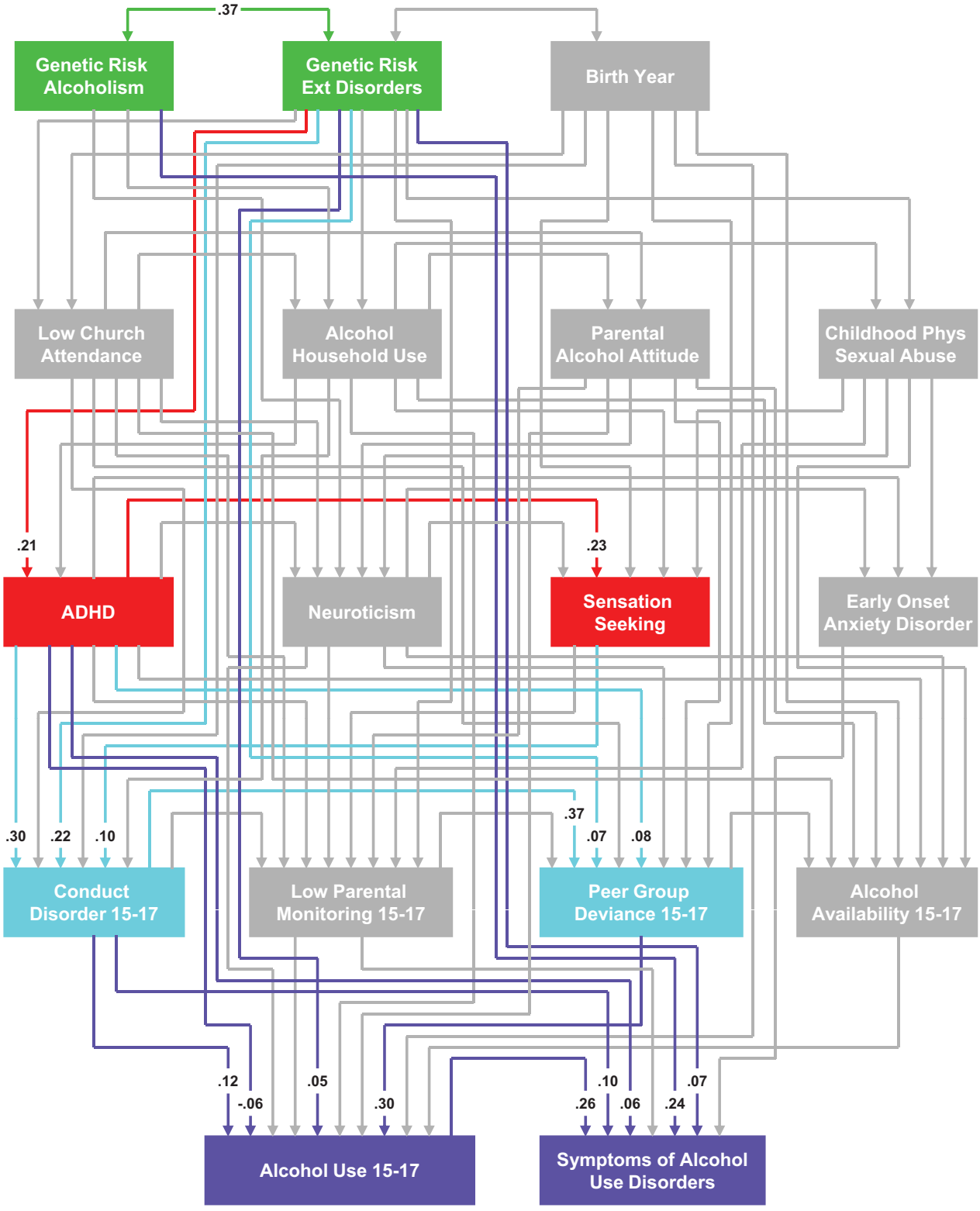

FIGURE 2

A broad pathway to alcohol use and abuse/dependence characterized by genetic and temperamental factors including symptoms of ADHD and conduct disorder.

https://doi.org/10.1375/twin.14.1.1 Published online by Cambridge University Press

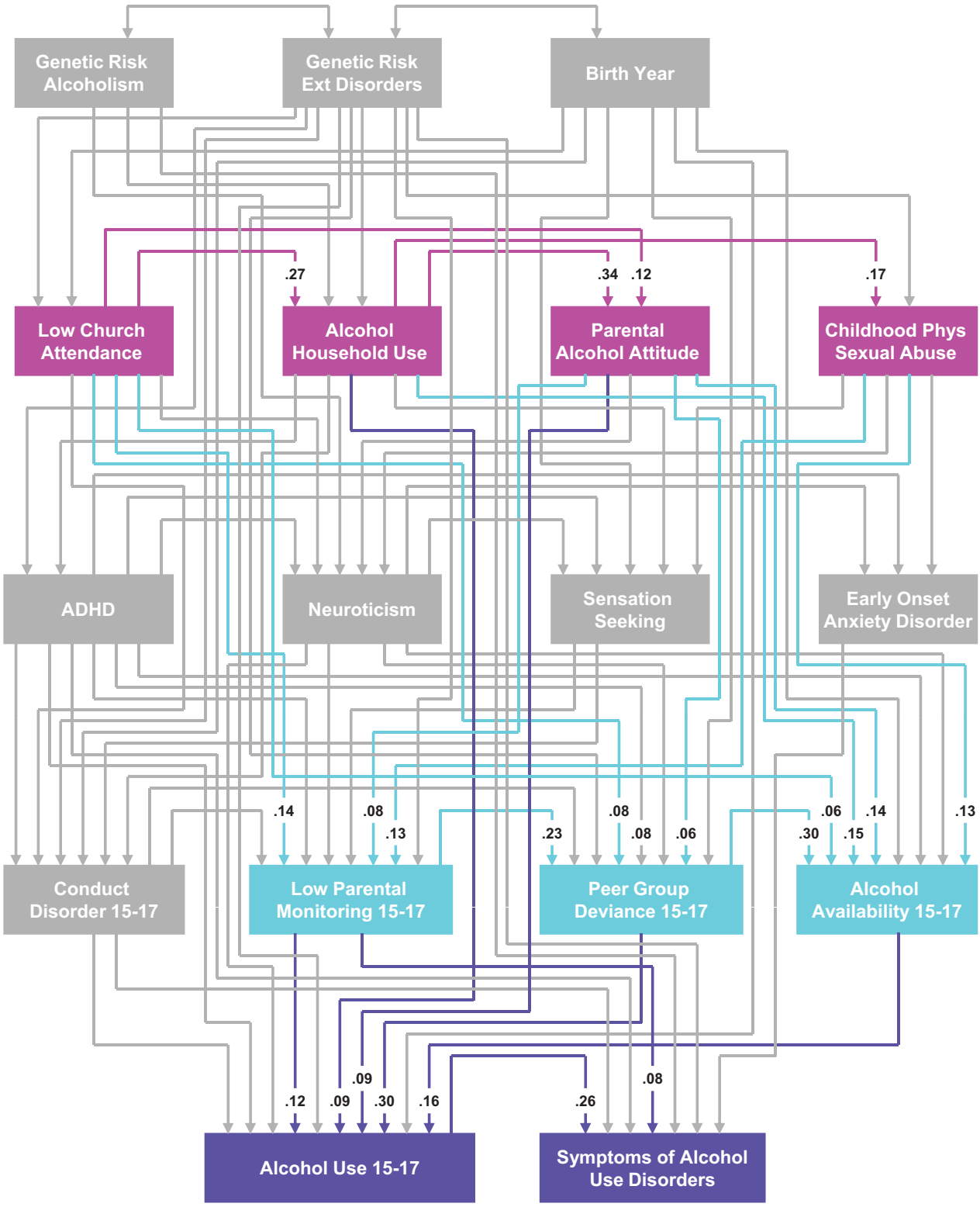

FIGURE 3
A broad pathway to alcohol use and abuse/dependence dominated by familial and social factors.

https://doi.org/10.1375/twin.14.1.1 Published online by Cambridge University Press

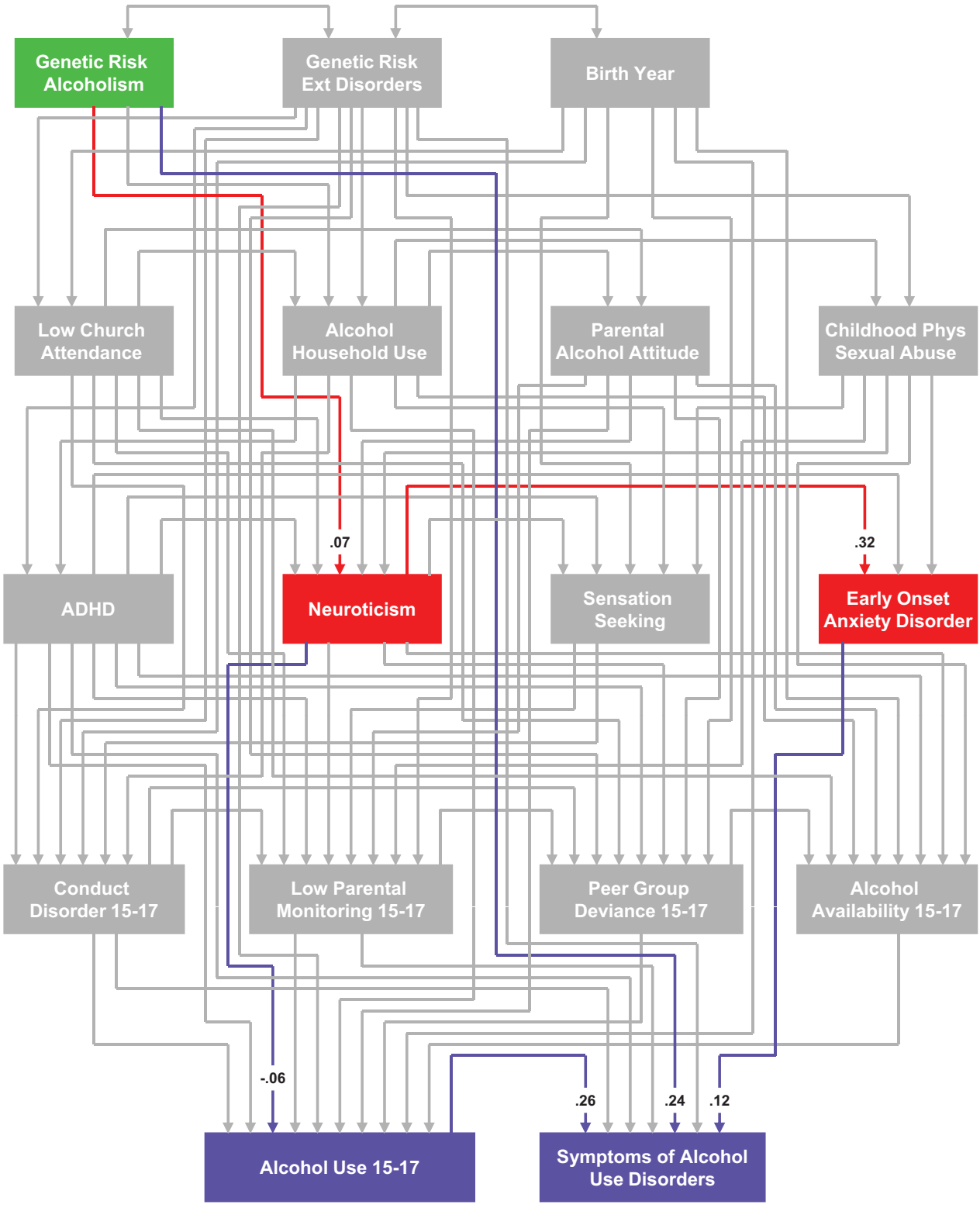

FIGURE 4
A pathway to alcohol use and abuse/dependence characterized by internalizing personality traits and symptoms.

https://doi.org/10.1375/twin.14.1.1 Published online by Cambridge University Press

of genetic risk factors for AU and AUDs with externalizing disorders and traits. Our model also illustrates the breadth of the 'externalizing' construct associated with AU/AUDs, which includes personality traits (sensation seeking), deviant behaviors (conduct symptoms) and symptoms of undercontrol and impulsivity (ADHD).

Second, our findings support prior results that risk for AU and AUDs is influenced by a relatively wide range of familial and social–environmental factors, including childhood sexual and physical abuse (Kendler et al., 2000; Fergusson & Mullen, 1999), parental monitoring (Dielman et al., 1990; Tucker et al., 2008), religiosity (Kendler et al., 1997a; Koenig et al., 2001; Larson, 1993), parental attitudes toward alcohol and exposure to drinking in the home (Hops et al., 2000; Tucker et al., 2008; Nash et al., 2005), and peer deviancy (Coie & Miller-Johnson, 2001; Fergusson et al., 1995; Farrington, 2005; Hawkins et al., 1998; Patterson et al., 2000). Our model shows that these exposures are substantially intercorrelated and can produce a developmental trajectory of high-risk environmental exposures that in aggregate strongly predict future alcohol consumption and AUDs.

Third, while earlier studies focusing on clinical alcoholism generally support an internalizing pathway to AUDs (Hawkins et al., 1992), our findings are more congruent with recent longitudinal studies which have produced much less consistent results (Zucker, 2008). In some studies (e.g., Maggs et al., 2008; Dubow et al., 2008) internalizing symptoms predict *reduced* AU while in others (e.g., Pitkanen et al., 2008; Caspi et al., 1996) they predict heavy AU and/or symptoms of AUD. Showing the potential subtly of the relationships involved, in one longitudinal US sample, symptoms of generalized anxiety at age 9 predicted increased risk of alcohol use over the next four years while symptoms of separation anxiety predicted a decreased risk (Kaplow et al., 2001)! We agree with Sher's conclusion that 'Additional prospective … studies are needed to clarify the relationship between negative emotionality and the development of alcoholism.' (Sher et al., 2005).

Fourth, in addition to clarifying the roles of externalizing, social and internalizing pathways in the etiology of AU and AUDs, our model begins to clarify the intricate developmental interactions that occur between these pathways. To oversimplify, genetic risk is often associated with early environmental risk which together impact on temperament. These three processes — genetics, environment and temperament — together substantially shape the adolescent environment which, in combination with these earlier risk factors, critically influences the probability of heavy AU, which in turn strongly predicts symptoms of AUDs.

Fifth, our findings well illustrate the complexity of the pathway from genes to phenotypes. We know that some specific genetic variants impact on risk for AU and AUDs via classical 'inside the skin' pathways (Kendler, 2001) such as alterations in liver alcohol metabolism, or interactions between ethanol and specific brain receptor systems (Mayfield et al., 2008). However, our model provides strong evidence that 'outside the skin' pathways (Kendler, 2001) for gene action are also important in the etiology of AUDs and include 'classical' environmental variables such as household alcohol use, childhood abuse, church attendance, and peer group deviance. Our results are also consistent with studies of the children of alcoholics that suggest the risk for future AUDs is partly mediated by temperament (Sher, 1993).

Sixth, environmental factors were more potent influences on AU in late adolescence than on AUDs and the opposite was seen for genetic effects. These results are congruent with prior studies showing that genetic influences on substance use generally increase during development while the impact of the shared environment — reflecting social and familial factors — declines (Bergen et al., 2007; Kendler et al., 2008; Koopmans et al., 1997; Viken et al., 1999).

Finally, it is useful to note some consistency in results from our study and those obtained from the two most comparable prior reports of which we are aware. Guo et al. studied 808 students and found that AUDs at age 21 were positively predicted by a wide range of traits measured at ages 10 to 16 including alcohol use, internalizing and externalizing behaviors, delinquency, parental and peer alcohol use, peer deviance, school misbehaviors, and negatively predicted by family monitoring and school involvement (Guo et al., 2001). Unfortunately, these variables were analyzed one at a time and their developmental interrelationships were not examined.

Dubow et al. developed, in 856 individuals from an epidemiological sample, a path analytic model predicting AU and AUD at ages 30 and 48 from assessments of 6 key variables at ages 8 and 19 (Dubow et al., 2008). Their single externalizing measure — aggression — robustly predicted AU and AUD while their single internalizing measure — behavioral inhibition — was protective against both outcomes. Neither negative family interactions at age 8 nor depression at age 19 were predictive of alcohol outcomes. Educational attainment directly and IQ indirectly were predictive of AU at age 48 but not AUDs.

LIMITATIONS

These results should be interpreted in the context of six potentially important methodologic limitations. First, our results are dependent upon decisions we made about what variables to include, how to arrange them into developmental tiers, and whether to conceptualize relations between variables as correlated, mediating, or causal. The validity of the causal assumptions varies across our model. Some of the intervariable relationships that we assume take the form of A→B may be truly either A←B or, more likely,

https://doi.org/10.1375/twin.14.1.1 Published online by Cambridge University Press

A↔B, i.e., processes influencing each other over time. Others — for example, the relationship between abuse in childhood and low parental monitoring in adolescence — are not likely to be causal but rather to result from other variables, in this case level of parental care and attention.

Second, a number of variables were assessed by long-term retrospective recall and may be subject to bias. However, we did use a life-history method to collect most of this data and an accumulating body of evidence indicates that such methods, which reflect the structure of autobiographical memory and promote sequential retrieval within memory networks, improve the completeness and accuracy of retrospective reports (Belli, 1998; Cook et al., 2003; Freedman et al., 1988; Yoshihama et al., 2002). Furthermore, we demonstrated good-to-excellent reliability for many of our variables. Finally, our use of information from three different interviews completed over an 11-year interval may further reduce the impact of correlated errors of recall.

Third, our model assumes that multiple independent variables act additively and linearly in their impact on risk for high levels of AU and AUDs. This is unlikely to be true. For example, high levels of parental monitoring may modify the impact of peer group deviance on alcohol intake (Fletcher et al., 1995; Steinberg et al., 1994). However, the possible interactions among our 17 variables are too numerous to permit us to evaluate them systematically with any degree of statistical power.

Fourth, this sample consisted of adult white male twins born in Virginia. With respect to the rates of alcohol use and symptoms of AUDs, these twins are probably representative of the general population (Kendler & Prescott, 2006). However, our results might differ in females or males from other ethnic groups.

Fifth, our model probably underestimates the total impact of genetic factors on the etiology of AUDs. Our measure of genetic risk was indirect and we did not include in our model the well known genetic influences on key risk factors for AUD such as ADHD (Thapar et al., 2005) and neuroticism (Loehlin, 1992).

Sixth, while extensive, the risk factors considered for AU and symptoms of AUD were far from complete and did not, for example, include specific genetic polymorphisms (Mayfield et al., 2008), intra-uterine alcohol exposure (Spear & Molina, 2005), alcohol expectancies (Sher et al., 2005), pro-social behaviors, (Guo et al., 2001) or drinking motives (Cooper, 1994; Prescott et al., 2004).

Acknowledgments

This work was supported in part by grants RO1-011408 and P20-017828 from the NIAAA.

References

American Psychiatric Association (1994). *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.* Washington, DC: American Psychiatric Association.

Belli, R. F. (1998). The structure of autobiographical memory and the event history calendar: Potential improvements in the quality of retrospective reports in surveys. *Memory, 6,* 383–406.

Bentler, P. M. (1990). Comparative fit indexes in structural models. *Psychological Bulletin, 107,* 238–246.

Bergen, S. E., Gardner, C. O., & Kendler, K. S. (2007). Age related changes in heritability of behavioral phenotypes over adolescence and young adulthood: A meta-analysis. *Twin Research, 10,* 423–433.

Caspi, A., Moffitt, T. E., Newman, D. L., & Silva, P. A. (1996). Behavioral observations at age 3 years predict adult psychiatric disorders. Longitudinal evidence from a birth cohort. *Archives of General Psychiatry, 53,* 1033–1039.

Cohen, P., Kasen, S., Chen, H., Hartmark, C., & Gordon, K. (2003). Variations in patterns of developmental transitions in the emerging adulthood period. *Developmental Psychology, 39,* 657–669.

Coie, J. D., & Miller-Johnson, S. (2001). Peer factors and interventions. In R. Loeber & D. P. Farrington (Eds.), *Child Delinquents: Development, Intervention, and Service Needs* (pp. 191–209). London: Sage Publications,Inc.

Cook, L. S., White, J. L., Stuart, G. C., & Magliocco, A. M. (2003). The reliability of telephone interviews compared with in-person interviews using memory aids. *Annual Epidemiology, 13,* 495–501.

Cooper, M. L. (1994). Motivations for alcohol use among adolescents: Development and validation of a four-factor model. *Psychological Assessment, 6,* 117–128.

Dielman, T. E., Butchart, A. T., Shope, J. T., & Miller, M. (1990). Environmental correlates of adolescent substance use and misuse: Implications for prevention programs. *International Journal of Addiction, 25,* 855–880.

Dubow, E. F., Boxer, P., & Huesmann, L. R. (2008). Childhood and adolescent predictors of early and middle adulthood alcohol use and problem drinking: The Columbia County Longitudinal Study. *Addiction, 103 Suppl 1,* 36–47.

Engel, G. L. (1977). The need for a new medical model: A challenge for biomedicine. *Science, 196,* 129–136.

Englund, M. M., Egeland, B., Oliva, E. M., & Collins, W. A. (2008). Childhood and adolescent predictors of heavy drinking and alcohol use disorders in early adulthood: A longitudinal developmental analysis. *Addiction, 103 Suppl 1,* 23–35.

Eysenck, S. B. G., Eysenck, H. J., & Barrett, P. (1985). A revised version of the psychoticism scale. *Personality and Individual Differences, 6,* 21–29.

Farrington, D. (2005). Childhood origins of antisocial behavior. *Clinical Psychology and Psychotherapy, 12,* 177–190.

Fergusson, D. M., Horwood, L. J., & Lynskey, M. T. (1995). The prevalence and risk factors associated with abusive or

hazardous alcohol consumption in 16-year-olds. *Addiction, 90,* 935–946.

Fergusson, D. M., & Mullen, P. E. (1999). *Childhood sexual abuse: An evidence based perspective.* Thousand Oaks, CA: Sage Publications.

Fleiss, J. (1973). The equivalence of weighted kappa and the intraclass correlation coefficient as measures of reliability. *Educational and Psychological Measurement, 33,* 613–619.

Fletcher, A., Darling, N., & Steinberg, L. (1995). Parental monitoring and peer influences on adolescent substance use. In J. McCord (Ed.), *Coercion and Punishment in Long-Term Perspectives* (pp. 259–271). Cambridge, New York, Melbourne: Cambridge University Press.

Freedman, D., Thornton, A., Camburn, D., Alwin, D., & Young-DeMarco, L. (1988). The life history calendar: A technique for collecting retrospective data. *Sociological Methodology, 18,* 37–68.

Goodwin, D. W., Schulsinger, F., Hermansen, L., Guze, S. B., & Winokur, G. (1973). Alcohol problems in adoptees raised apart from alcoholic biological parents. *Archives of General Psychiatry, 28,* 238–243.

Grucza, R. A., Robert, C. C., Bucholz, K. K., Constantino, J. N., Schuckit, M. I., Dick, D. M. & Beirut, L. J. (2006). Novelty seeking as a moderator of familial risk for alcohol dependence. *Alcoholism: Clinical and Experimental Research, 30,* 1176–1183.

Guo, J., Hawkins, J. D., Hill, K. G., & Abbott, R. D. (2001). Childhood and adolescent predictors of alcohol abuse and dependence in young adulthood. *Journal of Studies on Alcohol, 62,* 754–762.

Hawkins, J. D., Catalano, R. F., & Miller, J. Y. (1992). Risk and protective factors for alcohol and other drug problems in adolescence and early adulthood: Implications for substance abuse prevention. *Psychological Bulletin, 112,* 64–105.

Hawkins, J. D., Herrenkohl, T., Farrington, D. P., Brewer, D., Catalano, R. F., & Harachi, T. W. (1998). A Review of Predictors of Youth Violence. In R. Loeber & D. P. Farrington (Eds.), *Serious & violent juvenile offenders: Risk factors and successful interventions* (pp. 106–146). London: Sage Publications,Inc.

Heath, A. C., Bucholz, K. K., Madden, P. A., Dinwiddie, S. H., Slutske, W. S., Bierut, L. J., Statham, D. J., Dunne, M. P., Whitfield, J. B., & Martin, N. G. (1997). Genetic and environmental contributions to alcohol dependence risk in a national twin sample: consistency of findings in women and men. *Psychological Medicine, 27,* 1381–1396.

Heath, A. C., Meyer, J., Jardine, R., & Martin, N. G. (1991). The inheritance of alcohol consumption patterns in a general population twin sample: II. Determinants of consumption frequency and quantity consumed. *Journal of Studies on Alcohol, 52,* 425–433.

Hettema, J. M., Corey, L. A., & Kendler, K. S. (1999). A multivariate genetic analysis of the use of tobacco, alcohol, and caffeine in a population based sample of male and female twins. *Drug and Alcohol Dependence, 57,* 69–78.

Hops, H., Andrews, J. A., Duncan, S. C., Tildesley, E., & Tildesley, T. E. (2000). Adolescent drug use development: A social interactional and contextual perspective. In A. J.Sameroff, M. Lewis, & S. M. Miller (Eds.), *Handbook of developmental psychopathology* (pp. 589–605). New York: Kluwer Academic/Plenum Publishers.

Johnston, L. D., Bachman, J. G., & O'Malley, P. M. (1982). *Monitoring the future: Questionnaire responses from the nation's high school seniors, 1981.* Ann Arbor, MI: Institute for Social Research.

Kaplow, J. B., Curran, P. J., Angold, A., & Costello, E. J. (2001). The prospective relation between dimensions of anxiety and the initiation of adolescent alcohol use. *Journal of Clinical Child Psychiatry, 30,* 316–326.

Kaprio, J., Rose, R. J., Romanov, K., & Koskenvuo, M. (1991). Genetic and environmental determinants of use and abuse of alcohol: The Finnish Twin Cohort studies. *Alcohol and Alcoholism Supplement, 1,* 131–136.

Kendler, K. S. (2001). Twin studies of psychiatric illness: An update. *Archives of General Psychiatry, 58,* 1005–1014.

Kendler, K. S. (2005). Toward a philosophical Structure for psychiatry. *American Journal of Psychiatry, 163,* 433–440.

Kendler, K. S., Bulik, C. M., Silberg, J., Hettema, J. M., Myers, J., & Prescott, C. A. (2000). Childhood sexual abuse and adult psychiatric and substance use disorders in women: An epidemiological and cotwin control analysis. *Archives of General Psychiatry, 57,* 953–959.

Kendler, K. S., Gardner, C. O., & Prescott, C. A. (1997a). Religion, psychopathology, and substance use and abuse; a multimeasure, genetic-epidemiologic study. *American Journal of Psychiatry, 154,* 322–329.

Kendler, K. S., Jacobson, K. C., Gardner, C. O., Gillespie, N. A., Aggen, S. H., & Prescott, C. A. (2007). Creating a Social World: A developmental study of peer deviance. *Archives of General Psychiatry, 64,* 958–965.

Kendler, K. S., Liu, X. Q., Gardner, C. O., McCullough, M. E., Larson, D., & Prescott, C. A. (2003a). Dimensions of religiosity and their relationship to lifetime psychiatric and substance use disorders. *American Journal of Psychiatry, 160,* 496–503.

Kendler, K. S. & Prescott, C. A. (2006). *Genes, environment, and psychopathology: Understanding the causes of psychiatric and substance use disorders* (1st ed.) New York: Guilford Press (July 26, 2006).

Kendler, K. S., Prescott, C. A., Myers, J., & Neale, M. C. (2003b). The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. *Archives of General Psychiatry, 60,* 929–937.

Kendler, K. S., Prescott, C. A., Neale, M. C., & Pedersen, N. L. (1997b). Temperance board registration for alcohol abuse in a national sample of Swedish male twins, born 1902 to 1949. *Archives of General Psychiatry, 54,* 178–184.

Kendler, K. S., Schmitt, E., Aggen, S. H., & Prescott, C. A. (2008). Genetic and environmental influences on alcohol, caffeine, cannabis, and nicotine use from early adolescence to middle adulthood. *Archives of General Psychiatry, 65,* 674–682.

Kerr, M. & Stattin, H. (2000). What parents know, how they know it, and several forms of adolescent adjustment:

https://doi.org/10.1375/twin.14.1.1 Published online by Cambridge University Press

further support for a reinterpretation of monitoring. *Developmental Psychology, 36,* 366–380.

Kessler, R. C., Crum, R. M., Warner, L. A., Nelson, C. B., Schulenberg, J., & Anthony, J. C. (1997). Lifetime co-occurrence of DSM-III-R alcohol abuse and dependence with other psychiatric disorders in the National Comorbidity Survey. *Archives of General Psychiatry, 54,* 313–321.

Koenig, H., McCullough, M. E., & Larson, D. B. (2001). *Handbook of religion and health.* New York: Oxford University Press.

Koopmans, J. R., van Doornen, L. J., & Boomsma, D. I. (1997). Association between alcohol use and smoking in adolescent and young adult twins: A bivariate genetic analysis. *Alcoholism: Clinical and Experimental Research, 21,* 537–546.

Larson, D. B. (1993). *The faith factor, Volume 2: An annotated bibliography of systematic reviews and clinical research on spiritual subjects.* Rockville, MD: National Institute for Healthcare Research.

Loehlin, J. C. (1992). *Genes and environment in personality development.* Newbury Park, CA: Sage Publications.

Maggs, J. L., Patrick, M. E., & Feinstein, L. (2008). Childhood and adolescent predictors of alcohol use and problems in adolescence and adulthood in the National Child Development Study. *Addiction, 103 Suppl 1,* 7–22.

Manzardo, A. M., Penick, E. C., Knop, J., Nickel, E. J., Hall, S., Jensen, P., & Gabrielli, W. F., Jr. (2005). Developmental differences in childhood motor coordination predict adult alcohol dependence: Proposed role for the cerebellum in alcoholism. *Alcoholism: Clinical Experimental Research, 29,* 353–357.

Mayfield, R. D., Harris, R. A., & Schuckit, M. A. (2008). Genetic factors influencing alcohol dependence. *British Journal of Pharmacology, 154,* 275–287.

McGue, M., & Iacono, W. G. (2008). The adolescent origins of substance use disorders. *International Journal of Methods in Psychiatric Research, 17,* S30-S38.

Muffler, J., Langrod, J., & Larson, D. B. (1991). 'There is a balm in Gilead': Religion and substance abuse rehabilitation. In J. Lowinson & P. Ruiz (Eds.), *Comprehensive textbook of substance abuse.* Baltimore, MD: Williams and Wilkins.

Muthen, L. K., & Muthen, B. O. (2007). *Mplus user's guide: Fifth edition.* Los Angeles, CA: Muthen & Muthen.

Nash, S. G., McQueen, A., & Bray, J. H. (2005). Pathways to adolescent alcohol use: family environment, peer influence, and parental expectations. *Journal of Adolescent Health, 37,* 19–28.

Ohannessian, C. M., & Hesselbrock, V. M. (2008). A comparison of three vulnerability models for the onset of substance use in a high-risk sample. *Journal of Studies on Alcohol and Drugs, 69,* 75–84.

Patterson, G. R., Dishion, T. J., & Yoerger, K. (2000). Adolescent growth in new forms of problem behavior: macro- and micro-peer dynamics. *Previews of Science, 1,* 3–13.

Pickens, R. W., Svikis, D. S., McGue, M., Lykken, D. T., Heston, L. L., & Clayton, P. J. (1991). Heterogeneity in the inheritance of alcoholism. A study of male and female twins. *Archives of General Psychiatry, 48,* 19–28.

Pitkanen, T., Kokko, K., Lyyra, A. L., & Pulkkinen, L. (2008). A developmental approach to alcohol drinking behaviour in adulthood: A follow-up study from age 8 to age 42. *Addiction, 103 Suppl 1* , 48–68.

Prescott, C. A., Cross, R. J., Kuhn, J. W., Horn, J. L., & Kendler, K. S. (2004). Is risk for alcoholism mediated by individual differences in drinking motivations? *Alcoholism: Clinical and Experimental Research, 28,* 29–39.

Prescott, C. A., Hewitt, J. K., Heath, A. C., Truett, K. R., Neale, M. C., & Eaves, L. J. (1994). Environmental and genetic influences on alcohol use in a volunteer sample of older twins. *Journal of Studies on Alcohol, 55,* 18–33.

Prescott, C. A. & Kendler, K. S. (1999a). Age at first drink and risk for alcoholism: A noncausal association. *Alcoholism: Clinical and Experimental Research, 23,* 101–107.

Prescott, C. A., & Kendler, K. S. (1999b). Genetic and environmental contributions to alcohol abuse and dependence in a population-based sample of male twins. *American Journal of Psychiatry, 156,* 34–40.

Schaffner, K. F. (1994). *Psychiatry and molecular biology: Reductionistic approaches to schizophrenia in philosophical perspectives on psychiatric diagnostic classification.* Baltimore: Johns Hopkins University Press.

Sher, K. J. (1993). Children of alcoholics and the intergenerational transmission of alcoholism: A biopsychosocial perspective. In J. Baer, G. Marlatt & J. McMahon (Eds.), *Addictive behaviors across the lifespan* (pp. 3–33). Newbury Park, CA: Sage Publications.

Sher, K. J., Grekin, E. R., & Williams, N. A. (2005). The development of alcohol use disorders. *Annual Review of Clinical Psychology, 1,* 493–523.

Sigvardsson, S., Bohman, M., & Cloninger, C. R. (1996). Replication of the Stockholm Adoption Study of alcoholism. Confirmatory cross-fostering analysis. *Archives of General Psychiatry, 53,* 681–687.

Slutske, W. S., Heath, A. C., Madden, P. A., Bucholz, K. K., Statham, D. J., & Martin, N. G. (2002). Personality and the genetic risk for alcohol dependence. *Journal of Abnormal Psychology, 111,* 124–133.

Spear, N. E. & Molina, J. C. (2005). Fetal or infantile exposure to ethanol promotes ethanol ingestion in adolescence and adulthood: A theoretical review. *Alcoholism: Clinical and Experimental Research, 29,* 909–929.

Steiger, J. H. (1990). Structural model evaluation and modification: An interval estimation approach. *Multivariate Behavior Research, 25,* 173–180.

Steinberg, L., Fletcher, A., & Darling, N. (1994). Parental monitoring and peer influences on adolescent substance use. *Pediatrics, 93,* 1060–1064.

Tarter, R. E. & Hegedus, A. (1991). The drug use screening inventory: Its application in the evaluation and treatment of alcohol and drug abuse. *Alcohol Health & Research World, 15,* 65–75.

https://doi.org/10.1375/twin.14.1.1 Published online by Cambridge University Press

Thapar, A., O'Donovan, M., & Owen, M. J. (2005). The genetics of attention deficit hyperactivity disorder. *Human Molecular Genetics, 14,* R275-R282.

Tucker, J. S., Ellickson, P. L., & Klein, D. J. (2008). Growing up in a permissive household: What deters at-risk adolescents from heavy drinking? *Journal of Studies on Alcohol and Drugs, 69,* 528–534.

Tucker, L. R. & Lewis, C. (1973). A reliability coefficient for maximum likelihood factor analysis. *Psychometrika, 38,* 1–10.

Verdejo-Garcia, A., Lawrence, A. J., & Clark, L. (2008). Impulsivity as a vulnerability marker for substance-use disorders: Review of findings from high-risk research, problem gamblers and genetic association studies. *Neuroscience and Biobehavioral Reviews, 32,* 777–810.

Viken, R. J., Kaprio, J., Koskenvuo, M., & Rose, R. J. (1999). Longitudinal analyses of the determinants of drinking and of drinking to intoxication in adolescent twins. *Behavior Genetics, 29,* 455–461.

Wimsatt, W. C. (2007). False models as means to truer theories. In *Re-engineering philosophy for limited beings: Piecewise approximations to reality* (1st ed., pp. 94–132). Cambridge, MA: Harvard University Press.

Windle, M. (1999). *Alcohol use among adolescents* (1st ed.) London: Sage Publications.

Yoshihama, M., Clum, K., Crampton, A., & Gillespie, B. (2002). Measuring the lifetime experience of domestic violence: Application of the life history calendar method. *Violence Victims, 17,* 297–317.

Zucker, R. A. (2006). Alcohol Use and the Alcohol Use Disorders: A developmental-biopsychosocial systems formulation covering the life course. In D. Cicchetti & D. J. Cohen (Eds.), *Developmental psychopathology, Vol. 3: Risk, Disorder, and adaptation* (2nd ed., pp. 620–656). Hoboken, NJ: John Wiley & Sons Inc.

Zucker, R. A. (2008). Anticipating problem alcohol use developmentally from childhood into middle adulthood: what have we learned? *Addiction, 103 Suppl 1*, 100–108.

Zuckerman, M. (1972). Drug use as one manifestation of a 'sensation-seeking trait'. In W. Keup (Ed.), *Drug abuse: Current concepts and research* (pp. 154–163). Springfield, IL: Charles C. Thomas.

Zuckerman, M. & Neeb, M. (1979). Sensation seeking and psychopathology. *Psychiatry Research, 1,* 255–264.

https://doi.org/10.1375/twin.14.1.1 Published online by Cambridge University Press