Published in final edited form as:

Addiction. 2017 August ; 112(8): 1378–1385. doi:10.1111/add.13833.

A National Swedish Longitudinal Twin-Sibling Study of Alcohol Use Disorders

E.C. Long, MS^{1,*}, S.L. Lönner, PhD², J. Sundquist, MD, PhD², K. Sundquist, MD, PhD^{2,**}, and K.S. Kendler, MD^{**},^{1,3,4}

¹Virginia Institute for Psychiatric and Behavioral Genetics, Richmond, VA, USA

²Center for Primary Health Care Research, Lund University, Malmö, Sweden

³Department of Psychiatry, Virginia Commonwealth University, Richmond, VA, USA

⁴Department of Human and Molecular Genetics, Virginia Commonwealth University, Richmond, VA, USA

Abstract

Aims—To examine whether genetic influences on the development of AUD during emerging adulthood through mid-adulthood are stable or dynamic.

Design—A twin study modeling developmental changes in the genetic and environmental influences on AUD over three age periods (18–25, 26–33, and 33–41) as a Cholesky decomposition.

Setting—Sweden.

Participants—Swedish male twin pairs (1,532 monozygotic and 1,940 dizygotic) and 66,033 full male sibling pairs born less than two years apart.

Measurements—AUD was identified based on Swedish medical and legal registries.

Findings—The best fitting model included additive genetic and unique environmental factors, with no evidence for shared environmental factors. Although the total heritability was stable across time, there were two major genetic factors contributing to AUD risk, one beginning at ages 18–25 with a modest decline in importance over time, and another of less impact beginning at ages 26–33 with a modest increase in importance by ages 33–41.

Conclusions—The heritability of AUD was stable across the three age periods. Two sets of genetic risk factors contributed to AUD risk, with one originating during the ages 18–25 and another coming online at ages 26–33, providing support for the developmentally dynamic hypothesis.

*Corresponding author: Elizabeth Long, Virginia Commonwealth University, Virginia Institute for Psychiatric and Behavioral Genetics, Box 980126, Richmond, VA 23298-0126 (USA); longe@vcu.edu.

**These authors jointly supervised this work.

Conflicts of interest: None

Keywords

alcohol use disorders; twin modeling; longitudinal modeling; genetic influences; developmentally dynamic hypothesis; general population

Introduction

Alcohol use disorders (AUDs) are common in both the United States and Sweden, affecting 12.5% of the U.S. population (1) and 6–11% of the Swedish population (2, 3). AUDs are a significant public health burden and a leading cause of premature death in both countries (3–7). Therefore, understanding the etiologic mechanisms contributing to AUDs is important.

It has been well established that the development of AUDs are influenced by both genetic and environmental contributions, with consistent heritability estimates of 50% – 60% (8, 9). The majority of research to date has suggested that genetic influences on alcohol consumption become stronger with age, while shared environmental influences attenuate (10–13). However, these studies did not use developmentally informative models (see below) to explore the continuity of the underlying genetic factors influencing consumption. Even less is understood about the nature of genetic factors influencing the development of AUD specifically. Accordingly, it is unclear whether the genetic contributions to the development of AUD are the same or different across different age periods.

Two competing hypotheses are relevant to help clarify this question. The developmentally stable hypothesis predicts that a single set of genetic influences contribute to AUD across time, while the developmentally dynamic hypothesis predicts that new genetic influences on AUD come online at certain ages, referred to as genetic innovations. One study has supported the developmentally stable hypothesis and showed that risks for AUD in male and female Dutch twins between the ages of 15 to 32 are attributable to a single, stable set of risk genes of increasing magnitude across time (14). Conversely, another study supported the developmentally dynamic hypothesis and showed that two genetic factors accounted for the variance in alcohol consumption among male twins in the United States ages 12 to 33 (13). One factor was most influential during adolescence through age 21, when the influence of the other factor became pronounced. This discrepancy may be explained by different phenotypes – van Beek et al (2012) used symptoms of alcohol abuse and dependence while Edwards and Kendler (2013) used alcohol consumption. However, high levels of consumption are often a significant predictor of AUD symptoms (15, 16) and thus, may serve as a rough proxy for AUD.

Due to the limited, conflicting extant literature, more research is needed to distinguish between the two hypotheses and clarify the underlying mechanisms of genetic influences on AUD across time. Examining these influences within a developmental framework can narrow the time frames where genetic influences are most important, leading to a better understanding of the etiologic mechanisms contributing to AUDs over time. Therefore, the aim of the present study is to examine whether genetic influences on the development of AUD from emerging adulthood through mid-adulthood are stable or dynamic.

Methods

Sample

We linked nationwide Swedish registers via the unique 10-digit identification number assigned at birth or immigration to all Swedish residents. The identification number was replaced by a serial number to ensure anonymity.

To create an analysis dataset we used the following sources: the Total Population Register, containing data such as year of birth, sex, and annual data on place of residences; the Swedish National Census; the Swedish Mortality Register, containing dates of death; the Multi-generation register, linking children born after 1932 to their parents; The Swedish Twin Register, containing information about known zygosity; the Swedish Inpatient Register, containing hospitalizations from 1964 to 2010; and the Swedish Crime Register, which include national data on all convictions in lower court from 1973 to 2011.

We included male-male twin and full sibling pairs born between 1955 and 1971 with both individuals alive at least until age 20. Twins with known zygosity were identified from the Twin Register and full siblings were identified from the Multigenerational Register. We require that the siblings are born within two years of each other and reared together, defined as living together for at least 80% of the possible years until age 18. Females were not included in this analysis because the prevalence of AUD was too low. Specifically, the prevalence of AUD among females in this sample is less than half than what is in males (17).

As detailed elsewhere (18), zygosity in the same-sex pairs from the twin registry was assigned using standard self-report items from mailed questionnaires which, when validated against biological markers, were 95–99% accurate. We have previously noted that the prevalence of externalizing behavior, including AUD, is lower in same-sex monozygotic (MZ) and dizygotic (DZ) twin pairs than in opposite sex twin pairs (17, 19). This is almost surely because the former but not the latter were screened for level of cooperation because at least one of the pair had to return a questionnaire to the twin registry and cooperation was lower in subjects with AUD.

Measures

Our longitudinal measure of AUD requires sources covering the whole follow-up period. AUD was identified from the Inpatient Register by the following medical diagnoses: ICD-8 codes: 571.0, 291, 303, 980, ICD-9 codes: V79B, 305A, 357F, 571A, 571B, 571C, 571D, 425F, 535D, 291, 303, 980 and ICD-10 codes: E244, G312, G621, G721, I426, K292, K700, K701, K702, K703, K704, K709, K852, K860, O354, T510, T511, T512, T513, T518, T519, F101, F102, F103, F104, F105, F106, F107, F108, and F109. From the Crime Register, we defined AUD if individuals were convicted for at least two records of drunk driving (suspicion code: 3005 and law 1951:649 and Paragraph 4 and 4A) or drunk in charge of maritime vessel (suspicion code: 3201 and law 1994:1009 and Paragraph 4 and 5 and Chapter 20). The date of the second crime was chosen as the timing of the first AUD event while each following crime was counted as an event. The data was measured during three age ranges meant to correspond to meaningful developmental periods: 18–25 (emerging adulthood); 26–33 (early adulthood); and 33–41 (mid-adulthood). Individuals were defined

to have an AUD during an age period if they had at least one hospitalization or conviction during that period.

Statistical analyses

We utilized an extension of a classical twin model assuming three sources of liability to AUD: additive genetic (A), shared environment (C), and unique environment (E). The exception arose because the number of DZ twin pairs concordant for AUD in these age periods was insufficient to produce stable estimates. Therefore, we added full sibling pairs born within two years of each other and reared together to the sample of DZ pairs. The model assumes that MZ twins share all their genes while DZ twins and siblings share half of their genes identical by descent, and that the shared environment, reflecting family and community experiences, is the same within each twin or sibling pair. Unique environment includes stochastic developmental effects, environmental experiences not shared by siblings, and random error.

We assumed the same thresholds for AUD for MZ and DZ twins – given they both were weakly screened for cooperation by returning zygosity questionnaires – and permitted a separate threshold for full siblings who did not undergo a parallel screening.

Developmental changes in the genetic and environmental influences on AUD over the three age periods (18–25, 26–33, and 33–41) were modeled as a Cholesky decomposition. This developmentally informative approach divides genetic risk into three factors (A1 through A3), the first of which begins during the first period (ages 18–25) and is continually active over the entire developmental period. The strength of its effect at each age is reflected in the path coefficients from this factor to AUD at ages 18–25, 26–33, and 33–41. The second factor begins in the second period (ages 26–33) and impacts on AUD at ages 26–33 and 33–41. The third and final factor begins at ages 33–41 and acts only during this period. A developmentally stable hypothesis for AUD predicts that genetic liability to AUD originates solely in the first factor with no later genetic innovation. The developmentally dynamic hypothesis predicts both genetic innovation (new genetic variation impacting on AUD emerging later in development) and genetic attenuation (declining impact over time of the genetic factors acting earlier in development). To account for possible cohort effects, we allow each threshold to linearly depend on birth year by including the corresponding regression parameters (referred to as age regression).

The objective is to quantify the nature and magnitude of developmental changes in genetic and environmental risk factors for AUD. Although our sample size is considerable, the prevalence of AUD is low resulting in limited statistical power and a model with many parameters might result in unstable estimates. We therefore choose to also fit submodels and compare with the larger baseline model utilizing Akaike's Information Criterion (AIC; (20). Models were fit with the OpenMx software (21).

Results

Descriptive Statistics

The total prevalences of AUD and prevalences by registration type for MZ twins, DZ twins, and full siblings born less than two years apart across the three age periods are shown in Table 1. The patterns of results across the years show a slight increase in prevalence from age 18 through age 41. Rates of AUD are similar in MZ and DZ twins, but are slightly higher in the full siblings.

The tetrachoric twin and sibling correlations for AUD by age period are displayed in Table 2. The within-pair twin/sibling correlations are shown along the diagonal for each age period. The within-pair MZ twin correlations are greater than both the within-pair DZ twin and within-pair sibling correlations, suggesting that genetic influences are playing an important role. Of note is the increasing MZ correlation across the years, while the correlations for DZ twins and full siblings remain similar, suggesting that genetic factors increase in importance. Additionally, at ages 18–25 and 34–41, the within-pair DZ twin correlations are just slightly greater than half than of the within-pair MZ twin correlations, suggesting that shared environmental effects are also important during these two age periods, although these effects may be minimal. Both the within-DZ twin and within-sibling correlations were fairly stable across time. The DZ twin correlations are also quite similar to the full siblings, indicating that there is no evidence for the special twin environment. The cross-twin/sibling cross-time correlations are shown on the off-diagonals.

The cross-temporal genetic and unique environmental correlations are shown in Supplementary Table 2. The genetic correlations across the age groups are high, ranging from 0.84 to 0.98. The unique environmental correlations are low to moderate, ranging from –0.03 to 0.34.

Multivariate Twin Modeling

Model fit statistics for the four models we ran are shown in Table 3. The best-fitting model as per the AIC was Model 4, which included the age regression and eliminated the C component (i.e., an AE model), indicating there is no evidence for shared environmental influences on the development of AUD across the ages of 18–41. The parameter estimates and 95% confidence intervals for the genetic and individual-specific environmental risk factors from our AE Cholesky model are depicted in Figure 1. As illustrated in Figure 2, the first genetic factor (A_1) is robust and strongly impacts the liability to AUD at ages 18–25. The influence of this factor is sustained at ages 26–33 and 34–41, although its relative importance declines modestly. A second genetic factor (A_2) of much less impact begins at ages 26–33 and increases modestly at ages 34–41. The third genetic factor (A_3) has virtually no influence on the liability to AUD at ages 34–41.

The first unique environmental factor (E_1) also has a strong influence on AUD at ages 18–25 but decreases substantially with time. A second unique environmental factor (E_2) begins at ages 26–33 but also shows a declining influence over time. Finally, the third unique environmental factor (E_3) has the same effect at ages 34–41 as E_2 did at ages 26–33.

The parameters from the full ACE model (Model 3) are shown in Supplementary Table 1. As shown, the C parameters are not statistically significant and could be dropped from the model without a significant deterioration of fit. Thus, the AE model was chosen on the basis of parsimony. Importantly, both the full ACE model and AE model support the developmentally dynamic hypothesis, as the A_2 parameter in the full model is 0.17. This is evidence for a second genetic factor coming online, although the impact of the second genetic factor is stronger in the AE model.

The estimates and 95% confidence intervals for the heritability and unique environmental effects from the AE Cholesky model for each of the three time periods are displayed in Table 4. Both the heritability and individual-specific effects are stable across the three age periods.

Discussion

The goal of the present study was to determine whether genetic influences on the development of AUD are developmentally stable or dynamic. Our results showed evidence for both genetic innovation and attenuation, providing support for the developmentally dynamic hypothesis. Although the total heritability was stable across the ages of 18–41, we showed evidence for two major sets of genetic influences on AUD, one originating in emerging adulthood (ages 18–25) and another set with less impact coming online during early adulthood (ages 26–33). However, by mid-adulthood (ages 34–41), there was no evidence for any additional genetic innovation.

These results are inconsistent with those of van Beek et al. (2012), who showed that risks for AUD are attributable to a single, stable set of risk genes. They are, however, broadly consistent with those of Edwards and Kendler (2013), who showed that two genetic factors influenced risk for alcohol consumption, with one factor most influential during adolescence through age 21 and the second factor becoming more pronounced thereafter. This is somewhat surprising, given that our phenotype was similar to the phenotype used in the van Beek et al. (2012) study. Similar age ranges were also used in all three studies, and, importantly, captured the important developmental period of emerging adulthood. However, one possible explanation for the inconsistency in results may be due to different prevalences of AUD in the three countries the samples were drawn from. Van Beek et al. (2012) used a sample from the Netherlands, where the past 12-month prevalence of alcohol dependence is the lowest (0.7%) (22). We used a Swedish sample and Edwards and Kendler (2013) used a U.S. sample, where the past-12 month prevalences were more similar (6.3% and 3.8%, respectively) (1, 3). Thus, an important area for future research is to further examine how cultural influences may impact genetic influences across time.

Another possible explanation may be due to the different modeling approaches used. The present study and Edwards and Kendler (2013) used Cholesky decompositions, whereas van Beek et al. (2012) used both Cholesky decomposition and simplex models. Future research should use more comprehensive modeling approaches that test competing developmental hypotheses for a deeper understanding of how genetic processes influence AUD risk over time.

Congruent with the findings of Grant et al. (2006)(23), we showed no evidence for shared environmental influences in the development of AUD. Because our first age group started at age 18, our results are also consistent with previous studies suggesting that shared environmental influences are more pronounced risks for alcohol consumption during adolescence and genetic risks are more pronounced during adulthood. This effect is likely due to relaxing social constraints during adulthood (10–12).

In terms of heritability estimates, our estimates are higher than those that are typically reported (50% - 60%; (8, 9). One possible explanation for this may be that we restricted our sample to ages 18 through 41, which further adds to the research showing that genetic factors become more important with increasing age. However, we are not able to make any conclusions regarding the role of genes after age 41. Another possible explanation is that our use of registries detected more severe cases where genes may play a more important role, thereby increasing our heritability estimates. We also were only able to include males. One recent study, which was the largest of its kind, found a substantial sex difference, with the heritability of AUD estimated to be 22% for females, but 57% for males (17). This study also showed that shared environmental influences and twin-specific environmental effects were more important in females than males.

Our finding that there are two major sets of genetic risk factors for AUD is broadly consistent with other developmental twin studies of externalizing behaviors and disorders. For example, genetic factors for antisocial behavior are more influential after the age of 15, and the heritability increases from childhood to adulthood (24, 25). There is also evidence that the genetic influences on childhood and adolescent conduct disorder (before age 18) overlap with those of adult antisocial behavior (after age 18) (26).

Likewise, the development of externalizing behavior is influenced by genetic continuity, but with some genetic innovation during early and late adolescence (27). The genetic variation in externalizing disorders has also been shown to increase from ages 17 to 24 (28). Relatedly, Kendler et al. (29) found evidence for two genetic factors influencing risk for criminal behavior. One began during the ages 15–19 and declined over time, while the other came online at ages 20–24 and showed stability over time. Taken together, these results suggest that genetic risk for AUD and the associated phenotypes (e.g., externalizing disorders) are developmentally dynamic from early adolescence through middle adulthood.

Our findings can help to inform gene-finding efforts. Recent genome-wide association studies have had limited success in identifying the genetic variants that increase the risk for developing AUD (30, 31). Our results suggest that this may be because these studies used a sample with too wide of an age range, thus increasing the amount of genetic heterogeneity. By restricting the sample to early adulthood (ages 18–25) or more likely, mature adults (age 26 or older), gene-finding efforts may be improved.

Limitations

These results should be considered within the context of three potential limitations. First, our analyses were limited to Swedish males between the ages of 18 and 41. It is therefore uncertain if our results generalize to women as well as other populations. However, it is

likely that the results are generalizable to other industrialized countries. Additionally, although we had a large sample size, prevalence for AUD before age 18 and in females was too low to be able to obtain stable statistical results, and thus were not included in this analysis.

Second, we relied on medical and legal records for our measure of AUD. This method has the advantage of not being subject to recall or reporting biases, but it can produce false negatives and false positives. Although the extent to which this occurred could not be estimated, we suspect that registries detect more severe cases of AUD than population-based interview studies, due to a recent report using the same sample that found the prevalence of AUD to be lower than estimates from most epidemiologic surveys (2, 3), including the nearby country of Norway (32, 33). However, a previous study using the same registry data showed high concordance rates for registration across the different methods, providing support for our AUD measure (2). In addition, those cases that require hospital care are more clinically relevant than those who are based on population-based interviews.

Third, individuals who were assigned a diagnosis based on inpatient registrations entered treatment for both voluntary and involuntary reasons. Accordingly, it is possible that including treatment-seeking individuals rather than using a population-based sample only may have resulted in different conclusions about the genetic and environmental influences on AUD risk across time (34, 35). For example, Prescott and Kendler (1999) found evidence for shared environmental influences on AUD risk when using a treatment-seeking population, but not a population-based sample. However, it should be noted that we also diagnosed AUD cases from the criminal registry, which required no treatment seeking.

Conclusion

Using a nationwide sample of Swedish male twins and full siblings born less than two years apart, we provided support for the developmentally dynamic hypothesis regarding the nature of genetic influences contributing to the development of AUD during emerging adulthood through mid-adulthood. We showed stable heritability over time with two sets of genetic risk factors, one originating during the ages 18–25 and another coming online at ages 26–33. These results contribute to our understanding of the etiologic mechanisms contributing to AUDs by elucidating the nature of genetic influences across time.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This project was supported by the National Institute of Alcohol Abuse and Alcoholism grant AA023534 and the Swedish Research Council to K.S., the Swedish Research Council for Health, Working Life and Welfare (in Swedish: Forte; registration no: 2013–1836) to K.S., the Swedish Research Council to J.S. as well as ALF funding from Region Skåne awarded to J.S. and K.S.

References

1. Hasin DS, Stinson FS, Ogburn E, Grant BF. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Archives of General Psychiatry*. 2007; 64(7):830–42. [PubMed: 17606817]
2. Kendler KS, Ji J, Edwards AC, Ohlsson H, Sundquist J, Sundquist K. An Extended Swedish National Adoption Study of Alcohol Use Disorder. *JAMA psychiatry*. 2015; 72(3):211–8. [PubMed: 25565339]
3. Lundin A, Hallgren M, Forsman M, Forsell Y. Comparison of DSM-5 Classifications of Alcohol Use Disorders With Those of DSM-IV, DSM-III-R, and ICD-10 in a General Population Sample in Sweden. *Journal of Studies on Alcohol and Drugs*. 2015; 76(5):773–80. [PubMed: 26402358]
4. Campbell, KE., Zobeck, T., Bertolucci, D. Surveillance Report# 38: Trends in Alcohol-Related Fatal Traffic Crashes, United States: 1977–94. Rockville, MD: National Institute on Alcohol Abuse and Alcoholism, Division of Biometry and Epidemiology; 1995.
5. Cases, M., Stinson, FS., Dufour, MC. Surveillance Report# 36: Trends in alcohol-related morbidity among short stay community hospital discharges, United States 1979–93. Bethesda (MD): National Institute on Alcoholism; 1995.
6. Rehm J, Room R, Van Den Brink W, Jacobi F. Alcohol use disorders in EU countries and Norway: An overview of the epidemiology. *European Neuropsychopharmacology*. 2005; 15(4):377–88. [PubMed: 15925491]
7. Kendler KS, Ohlsson H, Sundquist J, Sundquist K. Alcohol Use Disorder and Mortality Across the Lifespan: A Longitudinal Cohort and Co-relative Analysis. *JAMA psychiatry*. 2016; 73(6):575–81. [PubMed: 27097014]
8. Kendler KS, Neale MC, Heath AC, Kessler RC, Eaves LJ. A twin-family study of alcoholism in women. *American Journal of Psychiatry*. 1994; 151(5):707–15. [PubMed: 8166312]
9. Verhulst B, Neale MC, Kendler KS. The heritability of alcohol use disorders: a meta-analysis of twin and adoption studies. *Psychological Medicine*. 2015; 45:1061–72. [PubMed: 25171596]
10. Edwards AC, Maes HH, Prescott CA, Kendler KS. Multiple mechanisms influencing the relationship between alcohol consumption and peer alcohol use. *Alcoholism: Clinical and Experimental Research*. 2015; 39:324–32.
11. Kendler KS, Gardner C, Dick DM. Predicting alcohol consumption in adolescence from alcohol-specific and general externalizing genetic risk factors, key environmental exposures and their interaction. *Psychological Medicine*. 2011; 41(7):1507–16. [PubMed: 20942993]
12. Kendler KS, Schmitt E, Aggen SH, Prescott CA. Genetic and environmental influences on alcohol, caffeine, cannabis, and nicotine use from early adolescence to middle adulthood. *Archives of General Psychiatry*. 2008; 65:674–82. [PubMed: 18519825]
13. Edwards AC, Kendler KS. Alcohol consumption in men is influenced by qualitatively different genetic factors in adolescence and adulthood. *Psychological Medicine*. 2013; 43(9):1857–68. [PubMed: 23282961]
14. van Beek JH, Kendler KS, de Moor MH, Geels LM, Bartels M, Vink JM, et al. Stable genetic effects on symptoms of alcohol abuse and dependence from adolescence into early adulthood. *Behavior Genetics*. 2012; 42(1):40–56. [PubMed: 21818662]
15. Dawson DA, Grant BF, Li TK. Quantifying the risks associated with exceeding recommended drinking limits. *Alcohol Clin Exp Res*. 2005; 29(5):902–8. [PubMed: 15897737]
16. Whitfield JB, Zhu G, Madden PA, Neale MC, Heath AC, Martin NG. The genetics of alcohol intake and of alcohol dependence. *Alcohol Clin Exp Res*. 2004; 28(8):1153–60. [PubMed: 15318113]
17. Kendler KS, PirouziFard M, Lonn S, Edwards AC, Maes HH, Lichtenstein P, et al. A National Swedish Twin-Sibling Study of Alcohol Use Disorders. *Twin Research and Human Genetics*. 2016; 19(5):430–7. [PubMed: 27515133]
18. Lichtenstein P, De Faire U, Floderus B, Svartengren M, Svedberg P, Pedersen NL. The Swedish Twin Registry: a unique resource for clinical, epidemiological and genetic studies. *J Intern Med*. 2002; 252(3):184–205. [PubMed: 12270000]

19. Kendler KS, Maes HH, Lonn SL, Morris NA, Lichtenstein P, Sundquist J, et al. A Swedish national twin study of criminal behavior and its violent, white-collar and property subtypes. *Psychol Med*. 2015; 45(11):2253–62. [PubMed: 25936380]
20. Akaike H. Factor analysis and AIC. *Psychometrika*. 1987; 52(3):317–32.
21. Boker S, Neale M, Maes H, Wilde M, Spiegel M, Brick T, et al. OpenMx: An Open Source Extended Structural Equation Modeling Framework. *Psychometrika*. 2011; 76(2):306–17. [PubMed: 23258944]
22. de Graaf R, ten Have M, van Gool C, van Dorsselaer S. Prevalence of mental disorders and trends from 1996 to 2009. Results from the Netherlands Mental Health Survey and Incidence Study-2. *Soc Psychiatry Psychiatr Epidemiol*. 2012; 47(2):203–13. [PubMed: 21197531]
23. Grant JD, Scherrer JF, Lynskey MT, Lyons MJ, Eisen SA, Tsuang MT, et al. Adolescent alcohol use is a risk factor for adult alcohol and drug dependence: evidence from a twin design. *Psychological Medicine*. 2006; 36(1):109–18. [PubMed: 16194286]
24. Jacobson KC, Prescott CA, Kendler KS. Sex differences in the genetic and environmental influences on the development of antisocial behavior. *Dev Psychopathol*. 2002; 14(2):395–416. [PubMed: 12030698]
25. Lyons MJ, True WR, Eisen SA, Goldberg J, Meyer JM, Faraone SV, et al. Differential heritability of adult and juvenile antisocial traits. *Arch Gen Psychiatry*. 1995; 52(11):906–15. [PubMed: 7487339]
26. Meier MH, Slutske WS, Heath AC, Martin NG. Sex differences in the genetic and environmental influences on childhood conduct disorder and adult antisocial behavior. *J Abnorm Psychol*. 2011; 120(2):377–88. [PubMed: 21319923]
27. Wichers M, Gardner C, Maes HH, Lichtenstein P, Larsson H, Kendler KS. Genetic innovation and stability in externalizing problem behavior across development: a multi-informant twin study. *Behav Genet*. 2013; 43(3):191–201. [PubMed: 23377846]
28. Hicks BM, Blonigen DM, Kramer MD, Krueger RF, Patrick CJ, Iacono WG, et al. Gender differences and developmental change in externalizing disorders from late adolescence to early adulthood: A longitudinal twin study. *J Abnorm Psychol*. 2007; 116(3):433–47. [PubMed: 17696699]
29. Kendler KS, Lonn SL, Maes HH, Morris NA, Lichtenstein P, Sundquist J, et al. A National Swedish Longitudinal Twin-Sibling Study of Criminal Convictions From Adolescence Through Early Adulthood. *Twin Research and Human Genetics*. 2015; 18(03):227–33. [PubMed: 25917500]
30. Gelernter J, Kranzler HR, Sherva R, Almasy L, Koesterer R, Smith AH, et al. Genome-wide association study of alcohol dependence: significant findings in African- and European-Americans including novel risk loci. *Mol Psychiatry*. 2014; 19(1):41–9. [PubMed: 24166409]
31. Zuo L, Lu L, Tan Y, Pan X, Cai Y, Wang X, et al. Genome-wide association discoveries of alcohol dependence. *Am J Addict*. 2014; 23(6):526–39. [PubMed: 25278008]
32. Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. *Results from the National Comorbidity Survey*. *Arch Gen Psychiatry*. 1994; 51(1):8–19. [PubMed: 8279933]
33. Kringlen E, Torgersen S, Cramer V. A Norwegian psychiatric epidemiological study. *Am J Psychiatry*. 2001; 158(7):1091–8. [PubMed: 11431231]
34. Prescott CA, Kendler KS. Genetic and environmental contributions to alcohol abuse and dependence in a population-based sample of male twins. *Am J Psychiatry*. 1999; 156(1):34–40. [PubMed: 9892295]
35. True WR, Heath AC, Bucholz K, Slutske W, Romeis JC, Scherrer JF, et al. Models of treatment seeking for alcoholism: the role of genes and environment. *Alcohol Clin Exp Res*. 1996; 20(9):1577–81. [PubMed: 8986206]

Figure 1.

Parameter estimates (and SEs) for the genetic and unique environmental effects from the AE Cholesky Model for alcohol use disorders at ages 18–25, 26–33, and 34–41 in Swedish male–male twin and male sibling pairs born less than two years apart. ‘A’ refers to additive genetic factors and ‘E’ refers to unique environmental factors. The subscripts 1, 2, and 3 indicate that the respective effects come online at ages 18–25, 26–33, and 34–41, respectively.

Figure 2.

The proportion of total variance in alcohol use disorders accounted for by genetic factors from ages 18 to 41. The y-axis represents the cumulative proportion of variance. The first genetic factor, which starts at ages 18–25, is represented in dark grey. Light grey represents the second genetic factor, starting at ages 26–33.

Table 1

Sample size and prevalence of AUD

Relationship	Number of Pairs	Prevalence of AUD		
		Ages 18–25	Ages 26–33	Ages 34–41
MZ twins	1,532	37 (1.2%)	39 (1.3%)	56 (1.8%)
Registration type				
Hospitalization		20 (0.7%)	23 (0.8%)	35 (1.1%)
Crime		21 (0.7%)	25 (0.8%)	29 (0.9%)
DZ twins	1,940	55 (1.4%)	53 (1.4%)	77 (2.0%)
Registration type				
Hospitalization		31 (0.8%)	33 (0.9%)	54 (1.4%)
Crime		27 (0.7%)	28 (0.7%)	33 (0.9%)
Full siblings, born 0–2 years apart	66,033	3,001 (2.3%)	3,176 (2.4%)	3,451 (2.6%)
Registration type				
Hospitalization		1,290 (1.0%)	1,671 (1.3%)	2,119 (1.6%)
Crime		2,086 (1.6%)	1,986 (1.5%)	1,835 (1.4%)

Table 2

Tetrachoric twin correlations (SE) for AUD by age period

Twin 1	Twin 2		
	Ages 18–25	Ages 26–33	Ages 34–41
Monozygotic Twins			
Ages 18–25	0.546 (0.138)	0.695 (0.103)	0.706 (0.089)
Ages 26–33	0.421 (0.164)	0.679 (0.105)	0.688 (0.091)
Ages 34–41	0.211 (0.202)	0.564 (0.123)	0.716 (0.080)
Dizygotic Twins			
Ages 18–25	0.317 (0.156)	0.419 (0.137)	0.284 (0.155)
Ages 26–33	0.181 (0.192)	0.333 (0.157)	0.150 (0.190)
Ages 34–41	0.399 (0.123)	0.399 (0.123)	0.477 (0.105)
Full siblings, born 0–2 years apart			
Ages 18–25	0.385 (0.019)	0.362 (0.019)	0.318 (0.020)
Ages 26–33	0.358 (0.019)	0.379 (0.019)	0.386 (0.018)
Ages 34–41	0.320 (0.020)	0.352 (0.019)	0.365 (0.018)

Table 3

Model fit statistics

Model	-2LL	# Parameters	AIC	Compared to model	p-value
1. No age regression	79,483.22	21	-754,534.80		–
2. With age regression	79,303.11	27	-754,702.90	1	3.6·10 ⁻³⁶
3. With age regression, common C	79,303.14	24	-754,708.90	2	0.999
4. With age regression, no C	79,304.08	21	-754,713.90	2	0.990

Table 4Estimates of additive genetic (a^2) and individual-specific environmental (e^2) effects by age

	a^2 (95% CI)	e^2 (95% CI)
Ages 18–25	70.6% (68.9, 77.4)	29.2% (25.0, 34.8)
Ages 26–33	70.5% (55.0, 89.3)	28.2% (26.9, 36.0)
Ages 34–41	71.6% (52.5, 99.1)	27.3% (24.5, 41.7)

Note. Totals may not equal 100% due to rounding.