Supplementary Notes

Genetic and Environmental Influences on Alcohol Consumption in Middle to Late Life

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Additional Description of Twin Samples

All studies were of twins and not selected based on any clinical diagnoses or health characteristics. Screening Across the Lifespan Twin study (SALT) participants who were included in other Swedish studies were removed prior to analysis to avoid having duplicates in the pooled data (*n*=13,940). Similarly, participants in the Australian Over 50s study (OVER50) who had alcohol data as a part of the Older Australian Twin Study (OATS) were removed prior to analysis (*n*=352). No other studies had overlapping participants. For all studies in the pooled analysis, we used data from the first assessment of alcohol use. Participants under age 40 were excluded because they represented only a small fraction of the available data (*n*=460 aged 26 to 39; 0.6% of the available data) from 3 samples and 2 countries (Sweden and the USA). We therefore did not have power to examine moderation of genetic and environmental influences in these individuals and wanted to ensure their inclusion did not bias other parameter estimates.

Histograms of age (Figure S1 and S2) and harmonized educational attainment (Figure S3 and S4) by sample are displayed below. Information about race and ethnicity for each sample are provided below, which should closely reflect the sample analyzed here (i.e., individuals with data at the first assessment of alcohol use).

Australia. OATS is a longitudinal study of Australian twins born between 1919 and 1946 (Sachdev et al., 2009). OVER50 is based on a questionnaire mailed between 1993 and 1995 to Australian twins aged 50–95 (Hopper, 2002; Hopper et al., 2013). All individuals in both samples are White and non-Hispanic.

Denmark. LSADT is a study of 70+ year-old, mostly same-sex Danish twins born prior to 1920 (McGue and Christensen, 2007, PMID:17564515. MADT and MIDT are studies of

middle-aged Danish twins born between 1931-1952 (MADT) or 1931-1969 (MIDT; Osler et al., 2008). The three studies all consist of participants recruited from the Danish Twin Registry (Pedersen et al., 2019). All individuals in all three samples are White and non-Hispanic.

Sweden. Five samples were drawn from the Swedish Twin Register of twins born in Sweden since 1886 (Lichtenstein et al., 2006). They include GENDER (Ageing in Women and Men: A Longitudinal Study of Gender Differences in Health Behavior and Health among Elderly) (Gold et al., 2002), HARMONY (the Study of Dementia in Swedish Twins) (Gatz et al., 2005), OCTO-Twin (Origins of Variance in the Oldest-Old) (McClearn et al., 1997), SATSA (the Swedish Adoption/Twin Study of Aging) (Pedersen et al., 1991), and SALT (the Screening Across the Lifespan Twin study) (Lichtenstein et al., 2002). All individuals in these samples are White and non-Hispanic.

USA. MIDUS is a national telephone/mail survey carried out in 1995-1996 that included middle-aged twins (Kendler et al., 2000; Radler, 2014). 90.5% of participants are White and 1.9% are Hispanic. The Minnesota Twin Study of Adult Development and Aging (MTSADA) is a population-based sample drawn from state birth records (McGue et al., 1993). 98.5% of participants are White and all are non-Hispanic. The National Academy of Sciences-National Research Council (NAS-NRC) Twin Registry consists of white non-Hispanic male twin pairs born in the years 1917–1927, both of whom served in the armed forces, mostly during World War II (Gatz et al., 2015). VETSA is a study of middle-aged male twins who both served in the US military at some point between 1965 and 1975 (Kremen et al., 2013). 91.2% of participants are White and 3.1% are Hispanic.

Finland. Data from the data from the 3rd (collected in 1990-1991) and 4th (collected in 2011-2012) waves of the Finnish Twin Cohort (FTC) were analyzed here, which was most like

the age range of other IGEMS cohorts (Kaprio et al., 2019). Specifically, we used all individuals with alcohol data from the 4th wave (age range 53 to 67 years) and included some additional individuals from the 3rd wave who were older than 53 (i.e., the minimum age of subjects in the 4th wave). The total sample size was 10,037 individuals and included 1,174 full monozygotic (MZ) twin pairs and 2,120 opposite-sex dizygotic (DZ) twin pairs. FTC data was only included in the meta-analyses presented in the supplement because subjects did not provide consent to share data externally. For this dataset only, summary data was shared with the primary study investigators in the US, and meta-analyzed alongside other studies. All individuals are White and non-Hispanic.

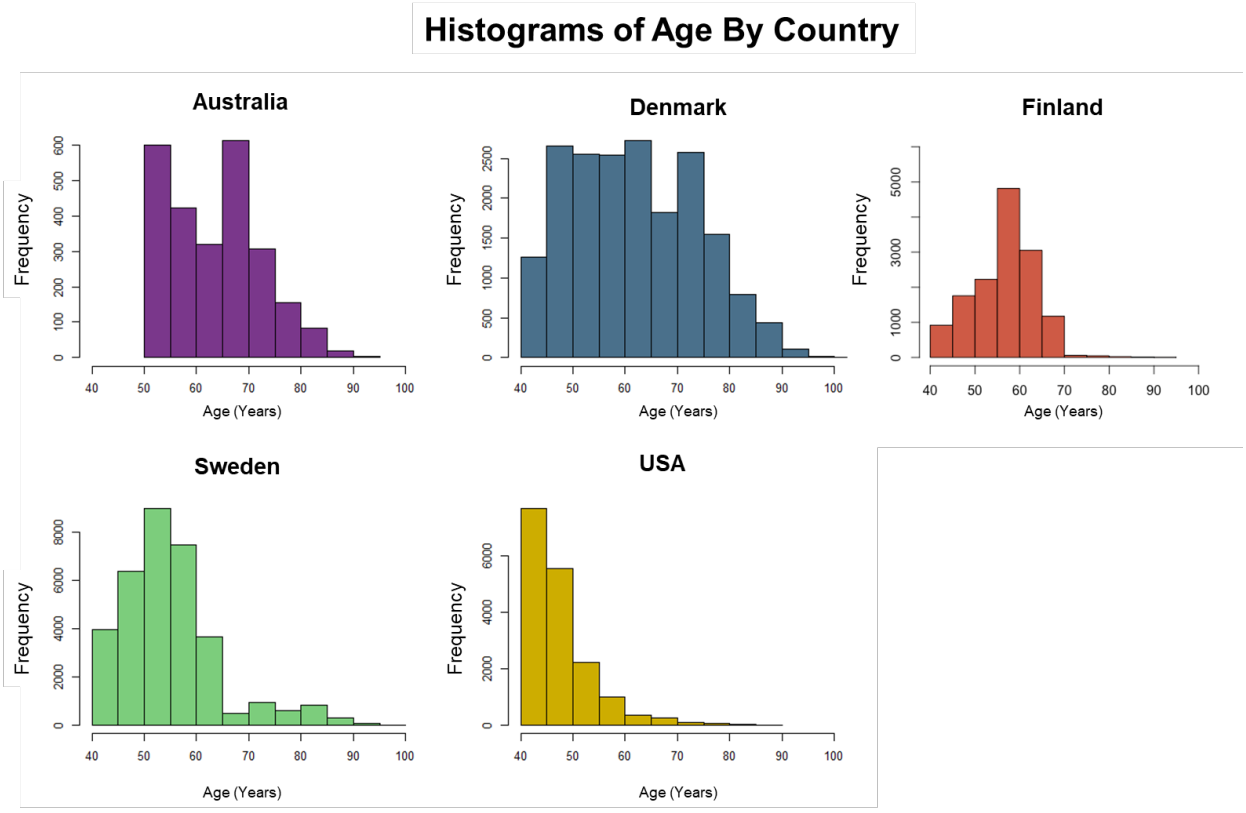

Figure S1. Histograms of age by country.

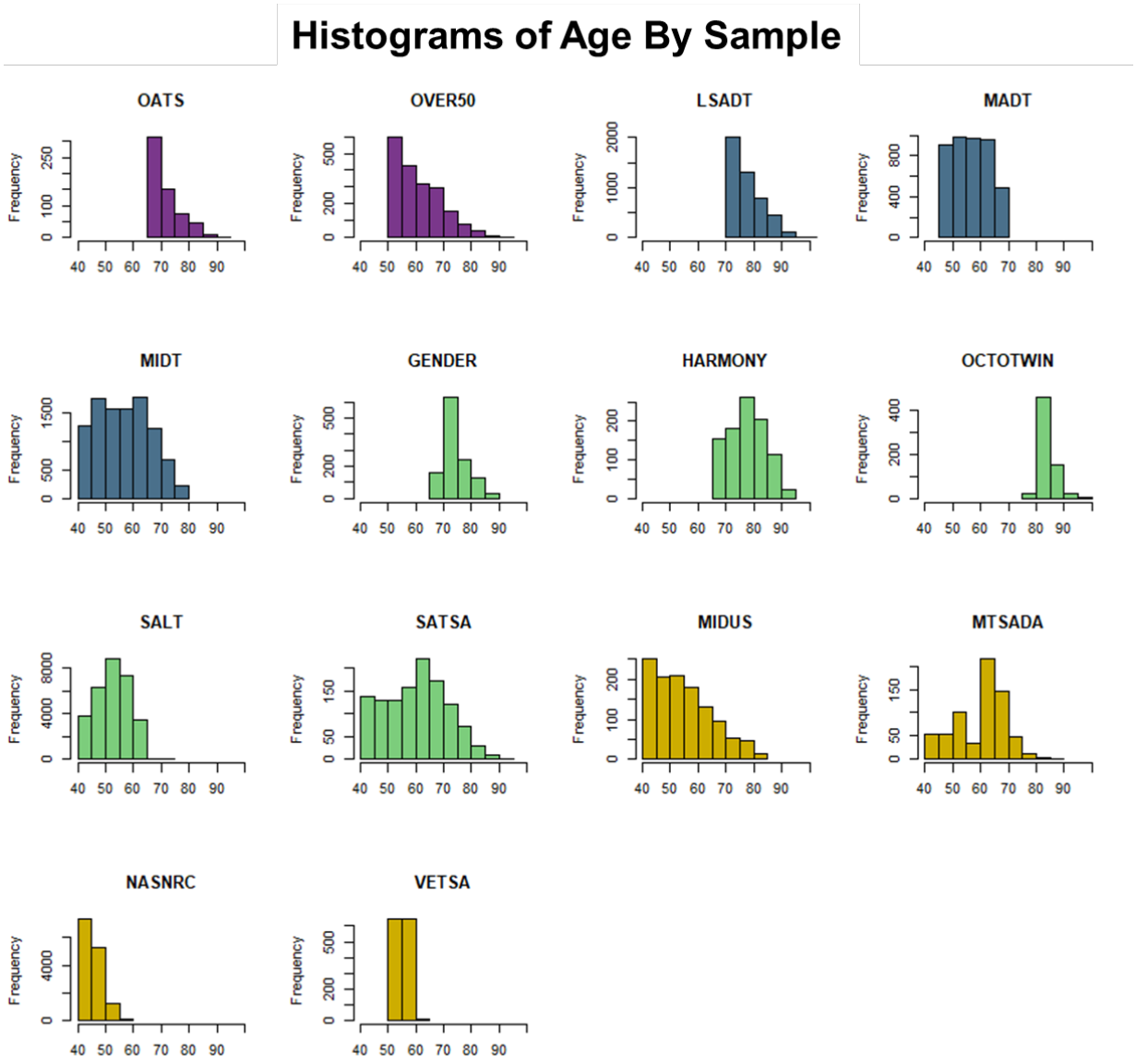

Figure S2. Histograms of age by sample. Australian Studies (purple): OATS = Older Australian Twins Study; Danish Studies (blue): OVER50 = Australian Over 50 study, LSADT = Longitudinal Study of Aging Danish Twins, MIDT/MADT = Middle Age Danish Twin Studies; Swedish Studies (green): GENDER = Ageing in Women and Men: A Longitudinal Study of Gender Differences in Health Behavior and Health among Elderly, HARMONY = Study of Dementia in Swedish Twins, OCTO-Twin = Octogenarian Twins, SALT = Screening Across the Lifespan Twin Study, SATSA = Swedish Adoption/Twin Study on Aging; USA Studies (yellow): NAS-NRC = National Academy of Sciences-National Research Council, MIDUS = Midlife in the United States, VETSA = Vietnam Era Twin Study of Aging. See Figure S1 for the Finnish Twin Cohort (FTC), the only sample from Finland.

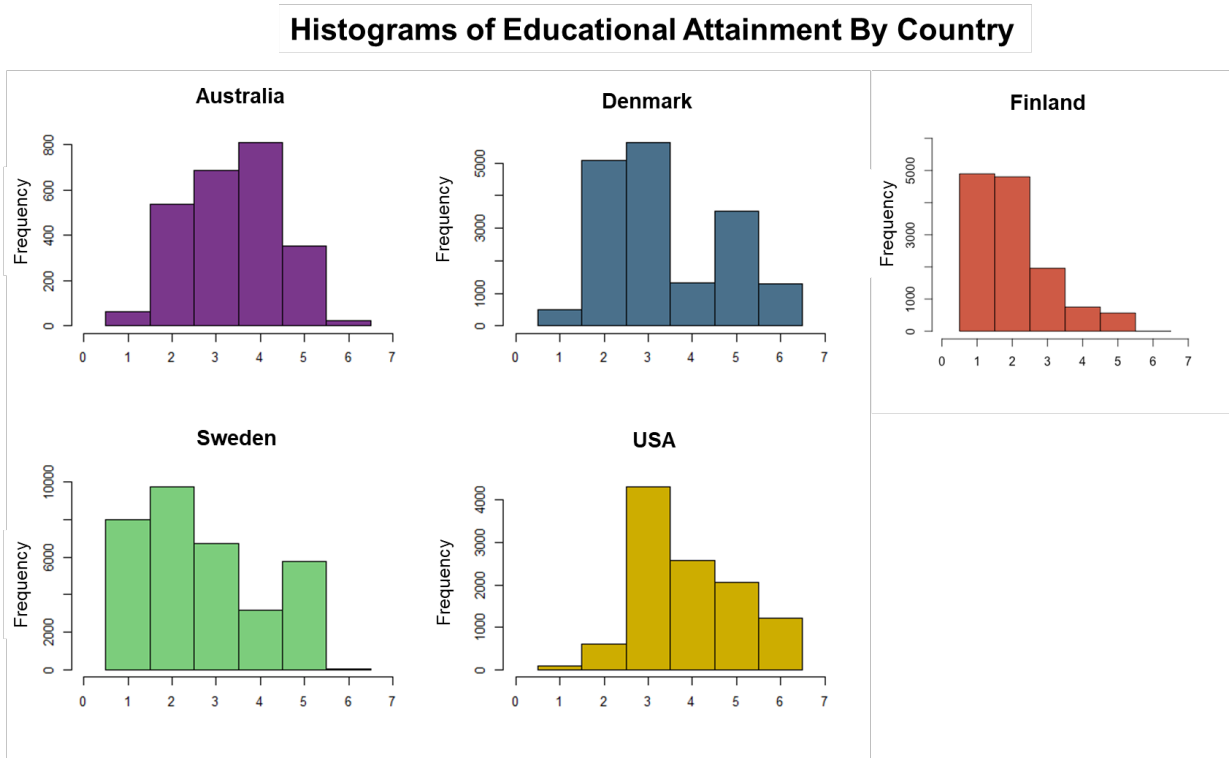

Figure S3. Histograms of binned educational attainment by country. 1 = completion of primary school or less; 2 = completion of a lower secondary school, 3 = completion of upper secondary school, 4 = completion of some post-secondary education, 5 = completion of a 4-year degree, 6 = completion of a graduate degree.

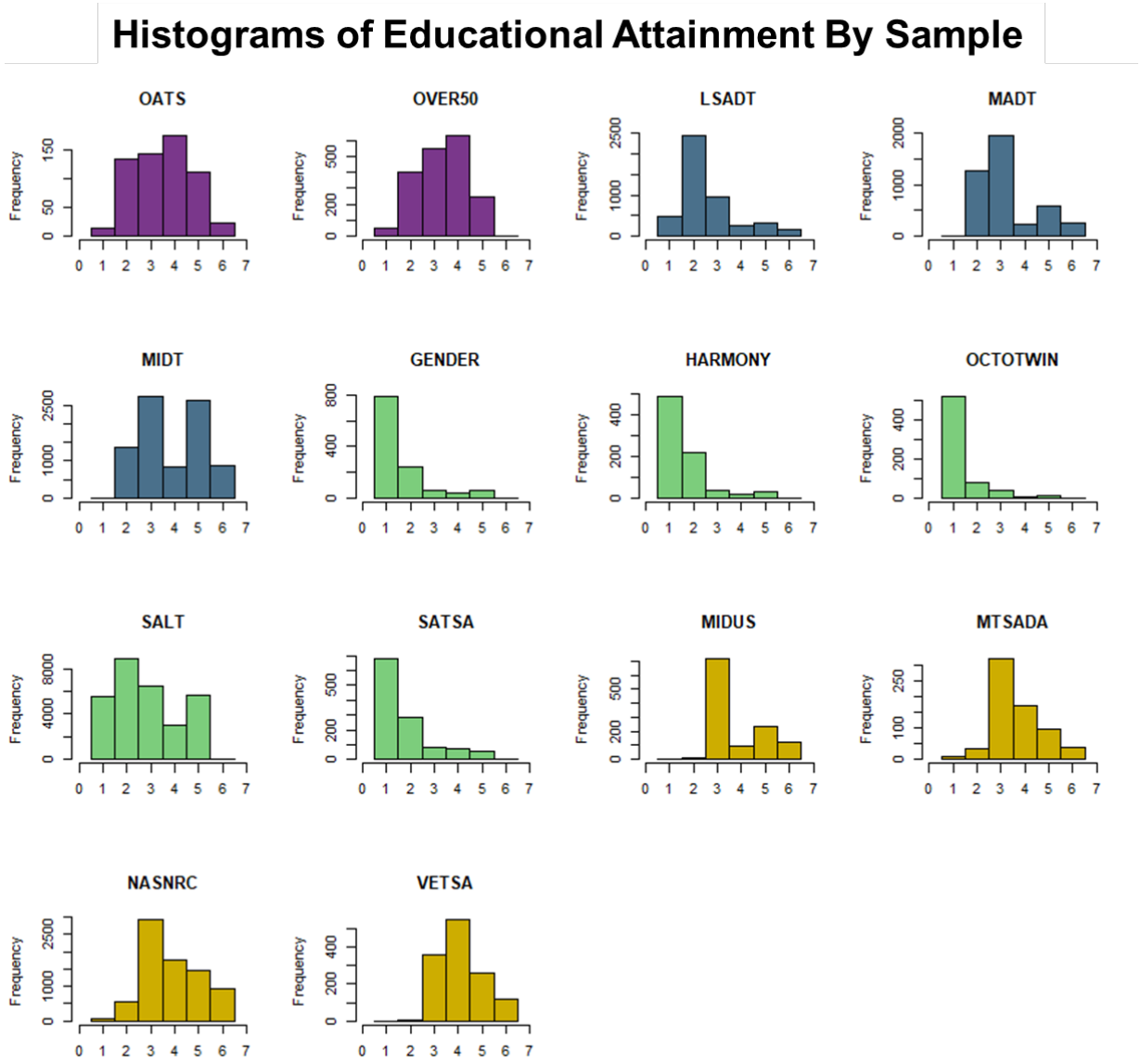

Figure S4. Histograms of binned educational attainment by sample. 1 = completion of primary school or less; 2 = completion of a lower secondary school, 3 = completion of upper secondary school, 4 = completion of some post-secondary education, 5 = completion of a 4-year degree, 6 = completion of a graduate degree. Australian Studies (purple): OATS = Older Australian Twins Study; Danish Studies (blue): OVER50 = Australian Over 50 study, LSADT = Longitudinal Study of Aging Danish Twins, MIDT/MADT = Middle Age Danish Twin Studies; Swedish Studies (green): GENDER = Ageing in Women and Men: A Longitudinal Study of Gender Differences in Health Behavior and Health among Elderly, HARMONY = Study of Dementia in Swedish Twins, OCTO-Twin = Octogenarian Twins, SALT = Screening Across the Lifespan Twin Study, SATSA = Swedish Adoption/Twin Study on Aging; USA Studies (yellow): NAS-NRC = National Academy of Sciences-National Research Council, MIDUS = Midlife in the United States, VETSA = Vietnam Era Twin Study of Aging. See Figure S3 for the Finnish Twin Cohort (FTC), the only sample from Finland.

Table S1: Additional Descriptive Statistics for Sample Characteristics

	Year of Assessment		Year of Birth		Proportion of Sample in Each Education Bin					
Variable	Mean	Range	Mean		1	2	3	4	5	6
Full Sample	1995	[1966, 2012]	1939	[1892, 1969]	0.13	0.25	0.27	0.12	0.18	0.04
By Country										
Australia	1997	[1993, 2012]	1934	[1903, 1946]	0.02	0.22	0.28	0.33	0.14	0.01
Denmark	2004	[1995, 2012]	1942	[1892, 1969]	0.03	0.29	0.32	0.08	0.20	0.07
Sweden	2000	[1984, 2003]	1944	[1892, 1958]	0.24	0.29	0.20	0.09	0.17	0.00
USA	1974	[1966, 2010]	1927	[1904, 1965]	0.01	0.06	0.40	0.24	0.19	0.11
By Study										
OATS	2009	[2006, 2012]	1937	[1919, 1946]	0.02	0.22	0.24	0.29	0.18	0.04
OVER50	1994	[1993, 1996]	1933	[1903, 1945]	0.03	0.22	0.29	0.34	0.13	0.00
LSADT	1997	[1995, 2001]	1919	[1892, 1930]	0.11	0.53	0.20	0.05	0.07	0.03
MADT	1999	[1998, 1999]	1942	[1931, 1952]	0.00	0.29	0.46	0.06	0.14	0.06
MIDT	2010	[2009, 2012]	1953	[1931, 1969]	0.00	0.16	0.32	0.10	0.31	0.10
GENDER	1994	[1994, 1994]	1920	[1905, 1925]	0.66	0.21	0.05	0.03	0.05	0.00
HARMONY	1999	[1988, 2002]	1921	[1903, 1934]	0.62	0.27	0.05	0.03	0.04	0.00
OCTOTWIN	1992	[1991, 1994]	1909	[1893, 1914]	0.79	0.12	0.06	0.00	0.02	0.00
SALT	2001	[1998, 2003]	1947	[1927, 1958]	0.19	0.30	0.22	0.10	0.19	0.00
SATSA	1984	[1984, 1984]	1924	[1892, 1944]	0.58	0.24	0.07	0.06	0.05	0.00
MIDUS	2004	[2004, 2005]	1949	[1921, 1965]	0.00	0.01	0.61	0.08	0.20	0.10
MTSADA	1991	[1986, 1996]	1930	[1904, 1952]	0.01	0.05	0.48	0.25	0.15	0.06
NAS-NRC	1968	[1966, 1995]	1923	[1917, 1927]	0.01	0.07	0.38	0.23	0.19	0.12
VETSA	2005	[2002, 2010]	1949	[1943, 1954]	0.00	0.01	0.28	0.42	0.20	0.09

Note: Australian Studies: OATS=Older Australian Twins Study, OVER50=Australian Over 50 study; Danish Studies: LSADT=Longitudinal Study of Aging Danish Twins, MIDT/MADT=Middle Age Danish Twin Studies; Swedish Studies: GENDER=Ageing in Women and Men, HARMONY=Study of Dementia in Swedish Twins, OCTO-Twin=Octogenarian Twins, SALT=Screening Across the Lifespan Twin Study, SATSA=Swedish Adoption/Twin Study on Aging; USA Studies: NAS-NRC=National Academy of Sciences-National Research Council. MIDUS=Midlife in the United States, VETSA=Vietnam Era Twin Study of Aging; Finnish Study: FTC=Finnish Twin Cohort (* this sample was only included in the supplementary meta-analysis).

Additional Description of Quantity of Alcohol Consumption Harmonization

Unless otherwise specified, we assumed 5% alcohol by volume (ABV) for beer, 12% ABV for wine, and 40% ABV for liquor. We assumed a standard 75 cl bottle of wine contains 5 glasses (15 cl or about 5 oz for USA) and a standard drink of liquor was 4 cl (or 1.5 oz for USA). We also assumed a standard beer was 33 cl (or 12 oz for USA).

Nine studies asked about alcohol consumption using multiple choice items rather than asking participants directly about the average number of alcoholic drinks per week. In these cases, we generally took the middle observation for multiple choice questions (e.g., 2.5 beers for the response "1-4 beers per week"). For responses indicating <1 drink per week, unless otherwise specified, we assigned a number that would sum to 0.5 drinks per week after collapsing across other types of alcohol (e.g., "<1 beer per week" corresponded so that .166 beers + .166 wine + .166 liquor = 0.5 total drinks per week). These scores were then transformed into grams of ethanol (as described above). When the final response option indicated a non-bounded range (e.g., ">48 bottles") we extrapolated a value based on the other available response options so that the final few response options were relatively evenly spaced. Additionally, some participants were assigned a value of 0 grams of ethanol per week when they responded no to questions related to whether they currently drink any alcohol (which usually resulted in their missing weekly consumption data for each beverage type).

Australia. In OATS, participants were asked about their drinking from the prior year from multiple categories of alcohol (light beer, regular beer, wine, spirits, fortified wine, and 'other') using the following questions: "In the past year, approximately how often have you had a drink containing alcohol?" (6 response options) and "How many standard drinks do you have on a typical day when you are drinking?" (5 response options). In OVER50, participants filled

out a table in which they reported the number of alcoholic drinks they had each day in the past week for the following categories: light beer, regular beer, wine, spirits, fortified wine, and other alcohol.

Denmark. In LSADT, participants were asked to report their average number of drinks per week (with no duration or type of alcohol specified). Alcohol consumption was reported for most subjects using 6-item multiple choice questions for beer, red wine, white wine, and strong alcohol. A small subset of participants were asked a 5-item multiple choice question about their weekly alcohol consumption in total. In MADT/MIDT, participants were asked to directly report their average drinks per week (over the past 6 months) from four categories (beer, strong alcoholic drinks, red wine, and white wine). In MIDT only, participants also reported on consumption of dessert wine separately.

Sweden. In GENDER and SATSA, weekly alcohol consumption was based on responses to two sets of items: “How often do you drink (beer/wine/ hard liquor)?” and “How much (beer/wine/hard liquor) do you drink at a time?”. The first question had 9 response options and the second question had 7 response options (with a fill-in-the blank for the final category capturing high consumption for SATSA). In OCTO-Twin, frequency of alcohol consumption was asked with a similar 9-item question (for beer, light wine, strong wine, and hard liquor), but the participant directly reported how many cl of each beverage they drink at a time. In HARMONY and SALT, participants were asked “How often do you usually drink beer/wine/spirits?” (9 response options) and “How much beer/wine/spirits do you usually drink at any given time?” (value specified).

USA. In MIDUS, if participants reported ever having a drink, they were asked up to 2 subsequent multiple-choice questions regarding the number of days they typically drank (in the

past month), and one free response (i.e., the number of drinks consumed on days they drank). In MTSADA, participants were asked the frequency of the days of drinking of beer, wine, and 'other alcoholic beverages' (7 response options) and how many glasses (or ounces) they drink on these days (value specified). For NAS-NRC, participants were asked "How often do you usually drink beer/wine/liquor?" (9 response options) and "On a day when you drink beer/wine/liquor, how much do you usually drink? (4 response options). In VETSA, participants were interviewed about consumption of beer, wine, and hard liquor and asked, for each: "During the past 2 weeks, on how many days did you drink any beer/wine/hard liquor?" and "On the day(s) when you drank beer/wine/hard liquor, about how many glasses of beer/wine/hard liquor did you drink a day?" (numeric value provided for both questions).

Finland. For FTC, participants were asked the quantity they typically drink of different types of alcohol in a given time frame with multiple choice items that had seven (liquor, asked monthly use) or eight (beer, wine both weekly) options. The number of drinks per week/month were converted into grams based on guidelines given to subjects during data collection (e.g., one beer = .33 liters, one bottle of wine = .75 liters, one bottle of liquor = .5 liters). Consumption was computed as grams of ethanol per week over all types (Virtanen et al., 2019).

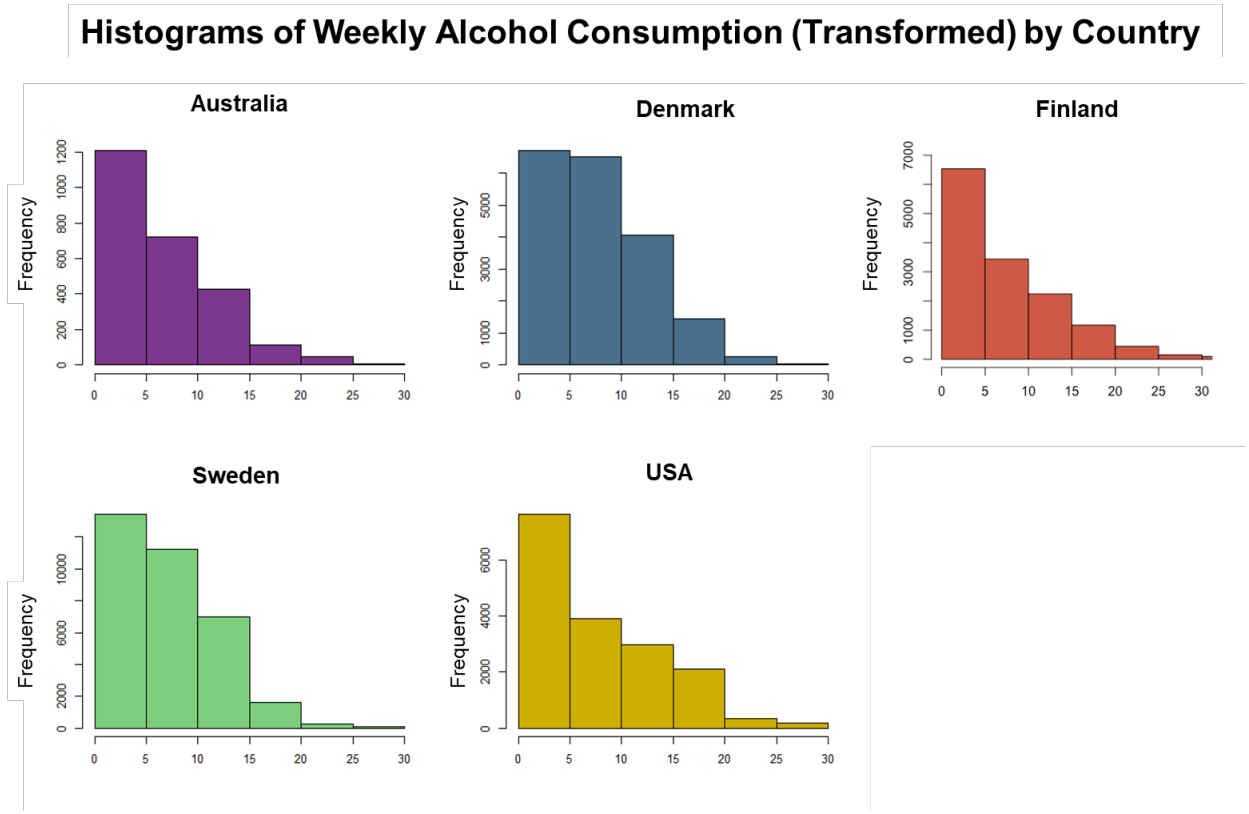

Figure S5. Histograms of harmonized weekly alcohol consumption (grams of ethanol consumed, square-root transformed and winsorized based on 4 SD) by country. A standard drink contains about 10-14 grams of ethanol, so the overall mean (M=81.59) corresponds to about 6-7 standard drinks per week.

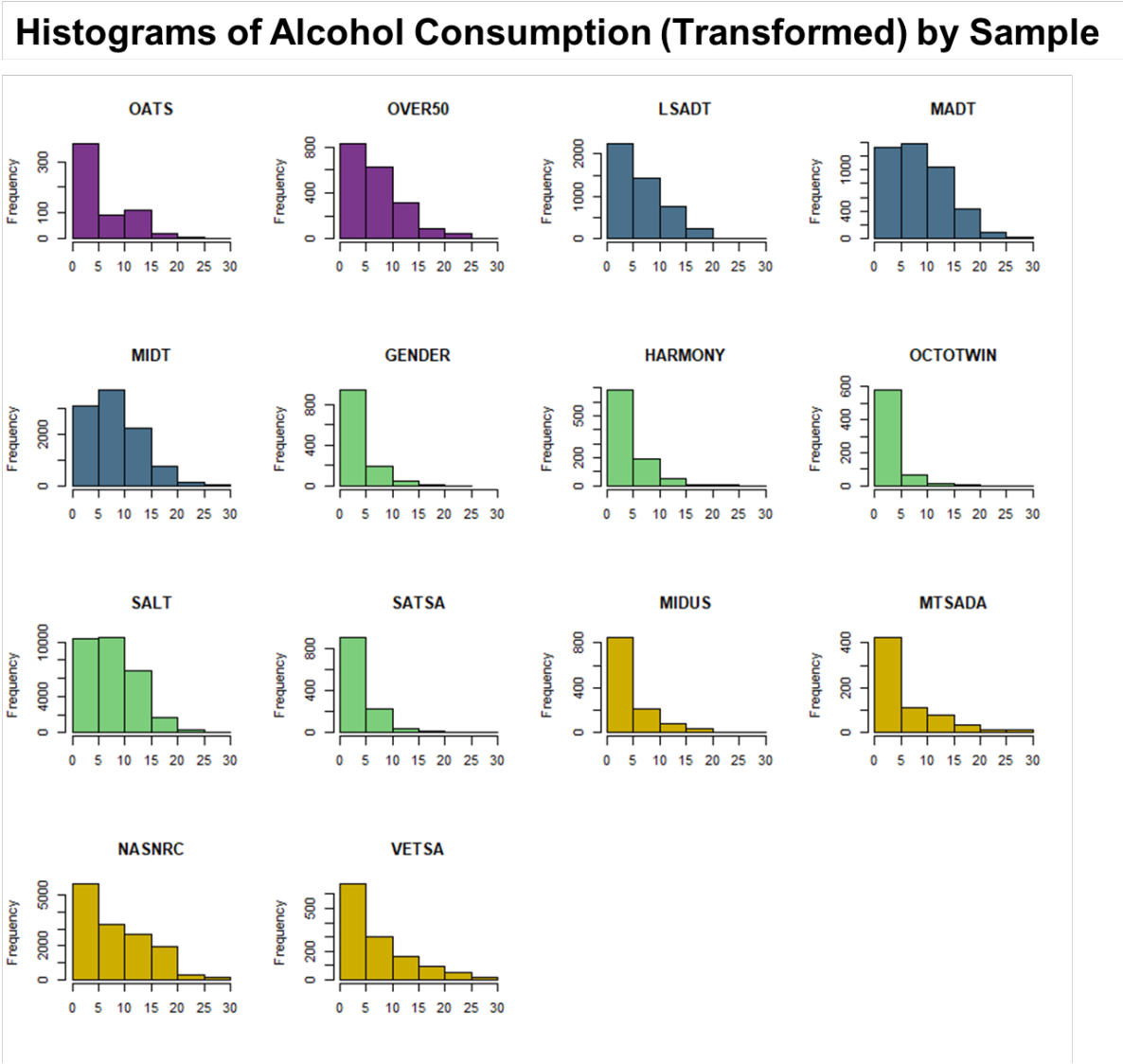

Figure S6. Histograms of harmonized weekly alcohol consumption (grams of ethanol consumed, square-root transformed and winsorized based on 4 SD) by country. A standard drink contains about 10-14 grams of ethanol, so the overall mean (M=81.59) corresponds to about 6-7 standard drinks per week. Australian Studies: OATS = Older Australian Twins Study; Danish Studies: OVER50 = Australian Over 50 study, LSADT = Longitudinal Study of Aging Danish Twins, MIDT/MADT = Middle Age Danish Twin Studies; Swedish Studies: GENDER = Ageing in Women and Men: A Longitudinal Study of Gender Differences in Health Behavior and Health among Elderly, HARMONY = Study of Dementia in Swedish Twins, OCTO-Twin = Octogenarian Twins, SALT = Screening Across the Lifespan Twin Study, SATSA = Swedish Adoption/Twin Study on Aging; USA Studies: NAS-NRC = National Academy of Sciences-National Research Council, MIDUS = Midlife in the United States, VETSA = Vietnam Era Twin Study of Aging. See Figure S5 for the Finnish Twin Cohort (FTC), the only sample from Finland.

Table S2: Final Harmonized Measure of Alcohol Consumption Means By Sex, Educational Attainment, and Age

Sample	Full Sample		By Sex		By Education						By Age	
	M	*SD*	Females	Males	1	2	3	4	5	6	Below 75	Above 75
Full Sample	7.00	5.68	5.26	8.24	4.66	6.38	7.46	7.17	7.72	8.31	7.22	4.34
By Country												
Australia	6.27	5.60	5.29	8.34	5.26	5.34	6.17	6.52	7.32	6.85	6.44	4.91
Denmark	7.57	5.34	5.94	9.45	4.60	5.91	8.31	7.78	8.16	9.83	8.06	5.36
Finland	6.96	6.54	4.89	9.26	6.25	6.96	8.00	8.26	8.04	-	6.98	2.57
Sweden	6.52	5.35	4.97	8.15	4.66	6.64	7.36	7.26	7.61	8.91	6.76	2.37
USA	7.40	6.53	3.39	7.66	4.89	6.90	6.73	6.96	7.35	6.72	7.42	3.69

Note: Our final harmonized measures of alcohol consumption was based on the square-root transformed grams of ethanol consumed per week (and winsorized based on 4 SD). The standard deviation is provided for the full sample, and all other columns display means. Data for Finland is not included in the full sample due to restrictions on data sharing.

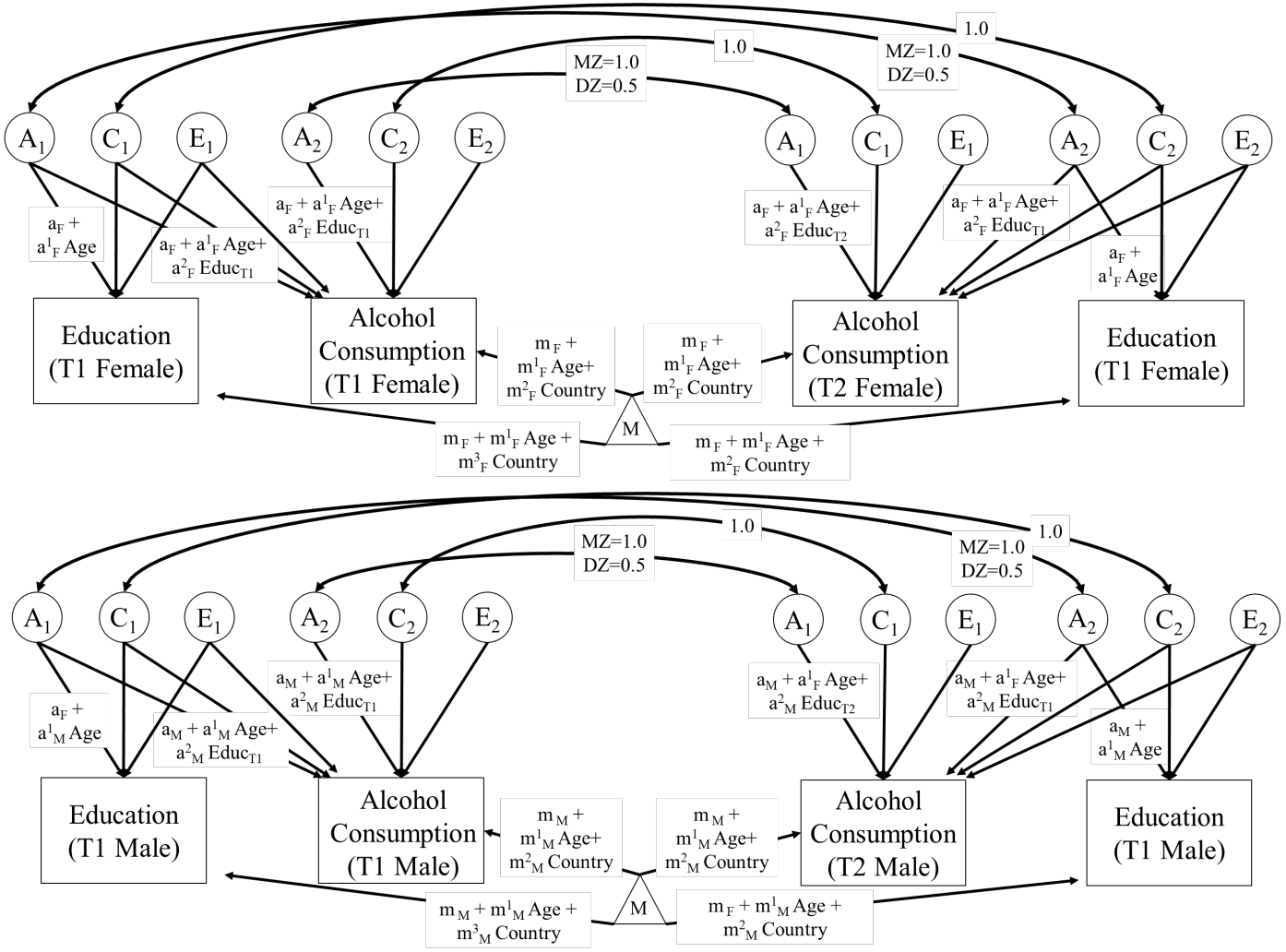

Figure S7: Path diagram of the biometric model involving moderation of genetic (A), shared environment (C), and nonshared environmental variance (E) by age, educational attainment, and sex. This model was adapted from the univariate moderation model from Purcell (2002) and van der Sluis et al. (2012). Parameters denoting genetic variance (a) are displayed, with a^1 representing the moderation of genetic variance by age of the twin and a^2 representing moderation of genetic variance by educational attainment.

Similar paths were estimated for shared environment (c) and nonshared environment (e) but were omitted from this diagram for ease of viewing. Age was included as a family-level variable (i.e., the mean age for that twin pair) whereas educational attainment was included separately for each twin. Fixed-effects of country on the mean were estimated using three separate variables (Code 1: Sweden = 1, Other Countries = –0.333; Code 2: Denmark = 1, Sweden = 0, Australia/USA = –0.5; Code 3: USA=1, Australia = –1, Sweden/Denmark = 0). Opposite sex twins were included in this analysis, with twin 1 always coded as male (with the same estimates as the male same-sex twins) and twin 2 always coded as female (with the same estimates as the female same-sex twins). The m parameter corresponds to the intercept (i.e., at the mean age of 56 years and educational attainment score of 3.1) and the m^1 and m^2 parameters reflect the regression coefficients on the mean. T1 = Twin 1; T2 = Twin 2; MZ = monozygotic; DZ = dizygotic.

Supplemental Results

Regression Spline Results

Table S3 displays the different regression spline models evaluated, and the unstandardized parameter estimates from that model. Education was centered in all models. A single cut-point (for age) was included in each model, but the cut-point varied by 5-year intervals. We also evaluated a cut-point at the mean. The best-fitting model had separate linear effects of age before and after age 75. The choice of spline cut point had little impact on the other regression coefficients, including interaction terms. This final model (AIC=389749**)** also fit better than a model with only a single linear slope for age (e.g., AIC=389820) or a model with linear and quadratic terms (e.g., AIC=389803).

Figure S8 displays phenotypic associations between alcohol use and age by country (Figure S8a) and by sample (Figure S8b) using age 75 as a cutoff point. These scatterplots only display associations with age before and after the age 75 cut-point, and do not control for other covariates used in the primary analyses.

Figure S9 displays tests of non-normality of residuals from the final model from the main text (Table 3), including the QQ plot, plot of fitted vs. residuals, and a density plot. These plots indicate some evidence for non-normality.

Table S3: Comparison of Regression Spline Cut Points in Phenotypic Analyses

Spline Cut Point	AIC	BIC	loglikelihood	Intercept	Age (low)	Age (high)	Sex	Education	Age (low) * Sex	Age (high) * Sex	Age (low) * Educ	Age (high) * Educ	Sex * Educ	3 way (Age low)	3 way (Age high)
45	389866	390011	-194917	8.20	0.02	-0.04	-3.36	-0.09	0.00	0.01	-0.03	0.04	0.43	0.24	-0.02
50	389841	389986	-194904	8.15	0.02	-0.05	-3.37	0.10	-0.04	0.02	0.02	0.04	0.39	0.08	-0.03
55	389838	389983	-194903	7.97	-0.01	-0.06	-3.38	0.30	-0.03	0.02	0.03	0.03	0.29	0.03	-0.03
Mean	389837	389982	-194903	7.94	-0.01	-0.06	-3.38	0.33	-0.03	0.03	0.03	0.03	0.28	0.03	-0.03
60	389833	389978	-194900	7.73	-0.02	-0.07	-3.34	0.52	-0.01	0.03	0.04	0.02	0.21	0.01	-0.03
65	389804	389949	-194886	7.69	-0.02	-0.11	-3.28	0.73	0.00	0.04	0.04	0.01	0.12	0.00	-0.03
70	389757	389903	-194863	7.52	-0.02	-0.18	-3.13	0.92	0.01	0.04	0.04	-0.01	0.00	-0.01	-0.03
75	**389749**	**389894**	**-194858**	**7.20**	**-0.03**	**-0.25**	**-2.96**	**1.07**	**0.01**	**0.05**	**0.04**	**-0.05**	**-0.13**	**-0.01**	**-0.03**
80	389792	389937	-194880	6.87	-0.04	-0.35	-2.81	1.21	0.02	0.06	0.04	-0.11	-0.24	-0.01	-0.02

Note: Unstandardized parameter estimates are displayed. The best-fitting model (based on all fit indices) is highlighted in bold. AIC = Akaike information criterion; BIC = Bayesian information criterion.

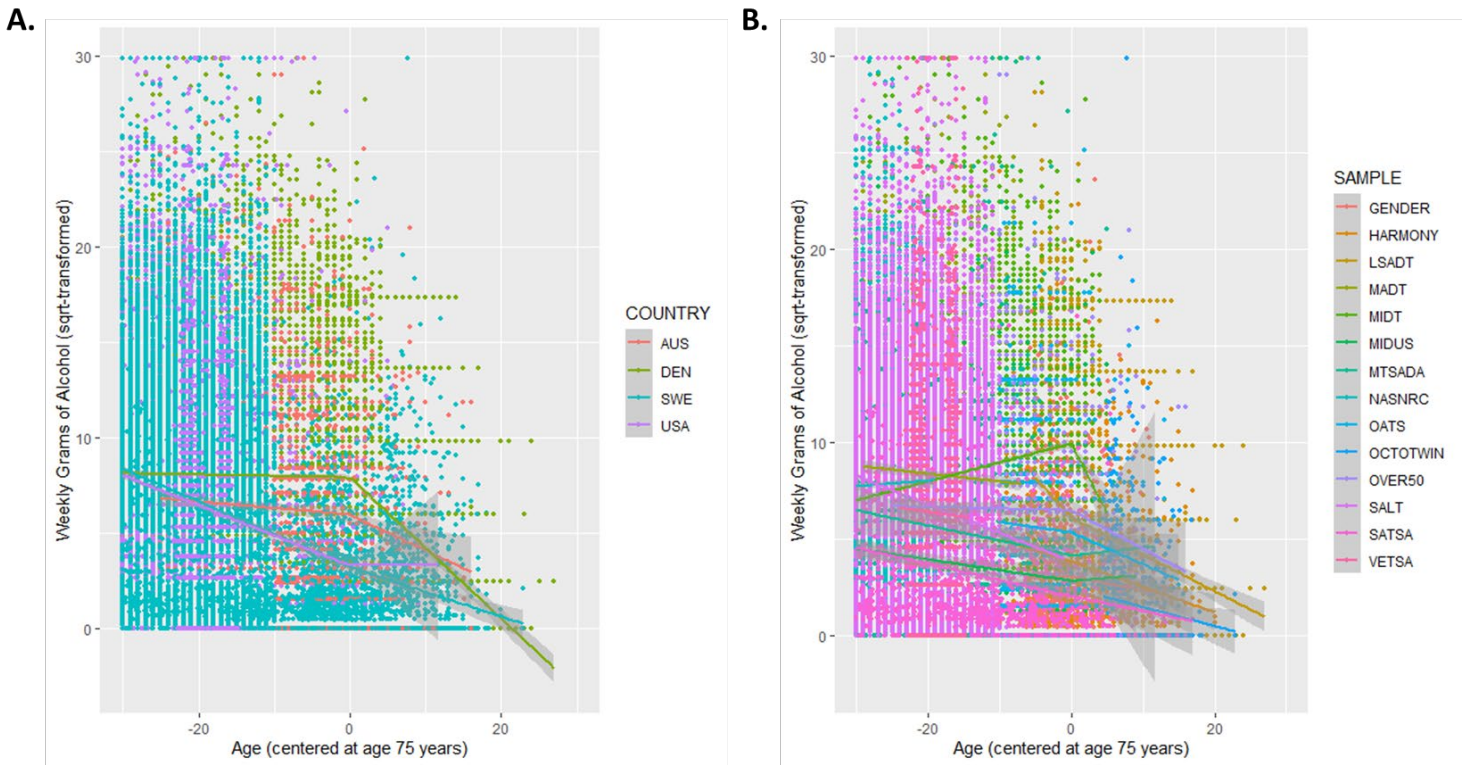

Figure S8: Associations between alcohol consumption and age by country (A) and sample (B). All models included a regression spline at age 75. Trend lines displayed here do not control for other covariates in the final model. AUS = Australia; DEN = Denmark; SWE = Sweden; USA = United States of America; OATS = Older Australian Twins Study; Danish Studies: OVER50 = Australian Over 50 study, LSADT = Longitudinal Study of Aging Danish Twins, MIDT/MADT = Middle Age Danish Twin Studies; Swedish Studies: GENDER = Ageing in Women and Men: A Longitudinal Study of Gender Differences in Health Behavior and Health among Elderly, HARMONY = Study of Dementia in Swedish Twins, OCTO-Twin = Octogenarian Twins, SALT = Screening Across the Lifespan Twin Study, SATSA = Swedish Adoption/Twin Study on Aging; USA Studies: NAS-NRC = National Academy of Sciences-National Research Council, MIDUS = Midlife in the United States, VETSA = Vietnam Era Twin Study of Aging.

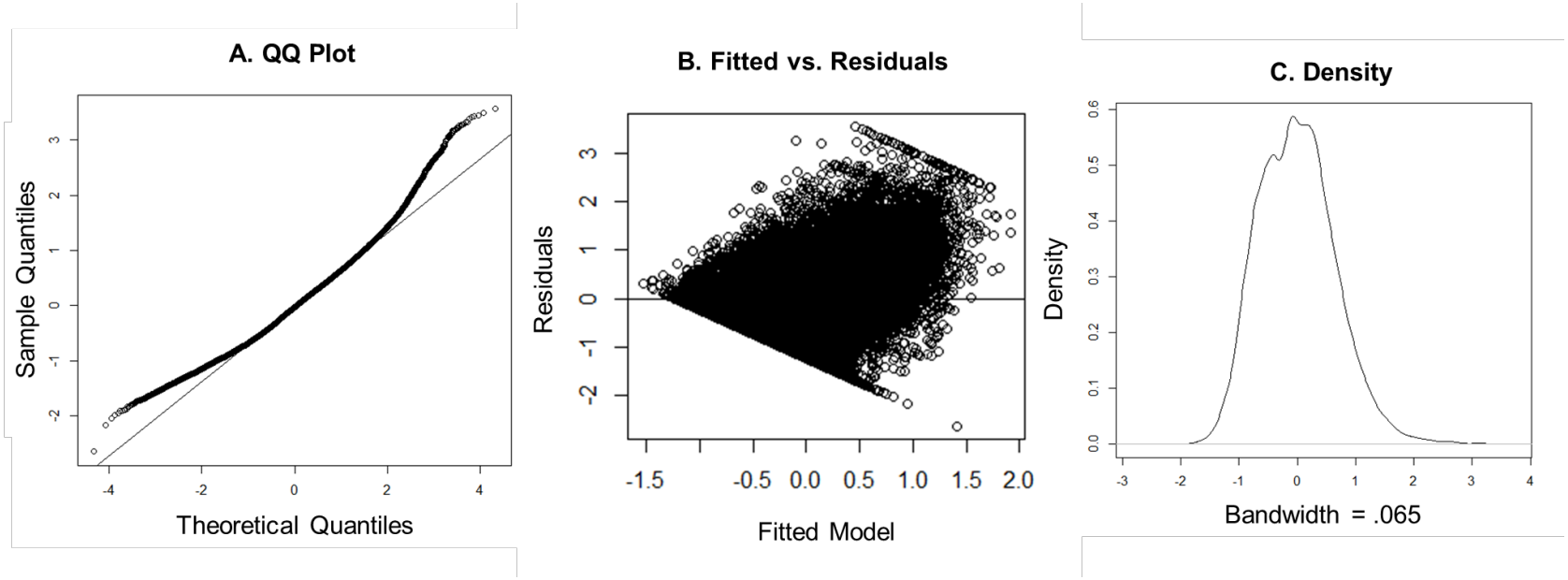

Figure S9: Plots to test assumptions of normality based on the final phenotypic model (from Table 3).

Sensitivity Analysis for Birth Cohort Effects

Figure S10 displays a histogram of the birth year for all participants in the combined sample. A dichotomous variable for earlier born vs. later born birth cohort was created based on the cutoff year of 1931, which appeared to be in the center of the bimodal age distribution for the full sample. The descriptive statistics table in the main text (Table 1) displays the proportion of subjects in each country/sample that were in the later born birth cohort (i.e., born after 1931).

The regression model including birth cohort is displayed in Table S4. This model was identical to Table 3 in the main text, but also included a main effect of cohort and interaction terms between cohort and age, sex, and educational attainment. Cohort was only allowed to interact with the younger age effect (i.e., age below 75) because there were very few individuals who were in the later born birth cohort and above age 75 at the time of assessment (n=213, 0.29% of the sample). Thus, age and cohort represent distinct predictors, but these sensitivity analyses primarily examined cohort effects within individuals under age 75 at the time of assessment.

Model results are briefly summarized in the main text and corresponded well to those in Table 3. Namely, all significant associations (based on an α=.01) in the original model remained statistically significant except for the two-way interactions between sex * age (before the regression spline) and sex * education, and the three-way interaction between sex * age (before the regression spline) * education, which were nonsignificant in this model. There was no main effect of cohort on alcohol consumption. Additionally, there was only one significant interaction term: the three-way interaction between cohort * education * age (below 75). One interpretation of this interaction is that the two-way interaction for education * age (i.e., that the positive association between education and alcohol assumption is stronger in older middle-aged individuals than younger middle-aged individuals) is even more pronounced in individuals from

the earlier born birth cohort. However, even this three-way interaction term was not large in magnitude, with the two-way interaction between education * age (below 75) being estimated at *b*=.07 for the later-born cohort and *b*=.10 for the earlier-born cohort.

Figure S10: Histogram of year of birth for all subjects in the combined sample. The vertical line corresponds to 1931, where we dichotomized this variable for analysis.

Table S4: Phenotypic Regression Model Including Effect of Birth Cohort (Born Before or After 1931)

Independent Variable	*β*	*SE*	*p*	95% CI
Intercept	0.11	0.12	0.403	[-.12, .33]
Age (Below 75)	-0.08	0.02	1.14E-03	[-.13, -.03]
Age (Above 75)	-0.08	0.01	5.10E-18	[-.09, -.06]
Sex	-0.51	0.08	6.12E-10	[-.68, -.35]
Education	0.08	0.01	3.12E-17	[.06, .10]
Sex * Age (Below 75)	0.02	0.05	0.675	[-.08, .12]
Sex * Age (Above 75)	0.01	0.01	0.488	[-.02, .03]
Education * Age (Below 75)	0.07	0.01	2.27E-21	[.06, .09]
Education * Age (Above 75)	-0.02	0.01	0.009	[-.04, -.01]
Sex * Education	-0.07	0.07	0.270	[-.21, .06]
Sex * Education * Age (Below 75)	0.01	0.04	0.799	[-.07, .09]
Sex * Education * Age (Above 75)	-0.01	0.01	0.409	[-.03, .01]
Cohort	0.03	0.05	0.524	[-.06, .12]
Cohort * Age (Below 75)	0.05	0.03	0.067	[.00, .10]
Cohort * Sex	-0.06	0.08	0.448	[-.23, .10]
Cohort * Education	-0.01	0.01	0.343	[-.04, .01]
Cohort * Sex * Age (Below 75)	-0.03	0.05	0.526	[-.13, .07]
Cohort * Education * Age (Below 75)	0.03	0.01	0.006	[.01, .06]
Cohort * Sex * Education	0.12	0.07	0.082	[-.01, .25]
Cohort * Sex * Education * Age (Below 75)	-0.03	0.04	0.546	[-.11, .06]

Note: All effect sizes are standardized. Sex was treated as a factor (with the estimate displaying the effect for females) and cohort was treated as a factor (with the estimate displaying the effect for individuals born after 1931). Educational attainment was standardized. Age was standardized and centered at the regression spline of 75.

Sensitivity Analysis for Year of Data Collection

Similar to the prior analysis, we repeated the primary phenotypic analysis (from Table 3) after including a main effect of year of data collection and interaction terms between year of data collection and all other model parameters. Year of data collection was *z*-scored such that all parameters should be interpreted at the mean (1994), but note that the maximum observation (2012) is only about 1.2 *SD* above the mean (see Figure S11 for histogram).

Results are displayed in Table S5. Importantly, all parameters from the original model remained significant except the two sex * age interactions (though one of them was still significant at the p=.05 threshold). Additionally, year of data collection had a strong main effect, suggesting alcohol use was considerably higher in more contemporary studies (β=.50). Moreover, two-way interaction terms indicated this trend was slightly stronger for individuals with lower education (β= -.04) or those in late middle age (compared to early middle age; β=.11). Finally, there was a 4-way interaction between year assessed * sex * education * age (below 75). Although difficult to interpret, this suggests the 3-way interaction from the primary analysis (sex * education * age below 75) was primarily observed for studies that collected data before the late-90s. However, it is important to remember that this original 3-way interaction was no longer significant after controlling for cohort in the prior analysis, so this 4-way interaction may be capturing the cohort effect (i.e., considering that older-born cohorts are more likely to have been assessed earlier).

To aid in base-level interpretation, a final combined sensitivity analysis is displayed in Table S6 which includes only the main effects of age (before and after age 75), sex, education, cohort, and year of data collection. This model includes no interaction terms, but still includes random intercepts for country, sample, and family (as in all other models).

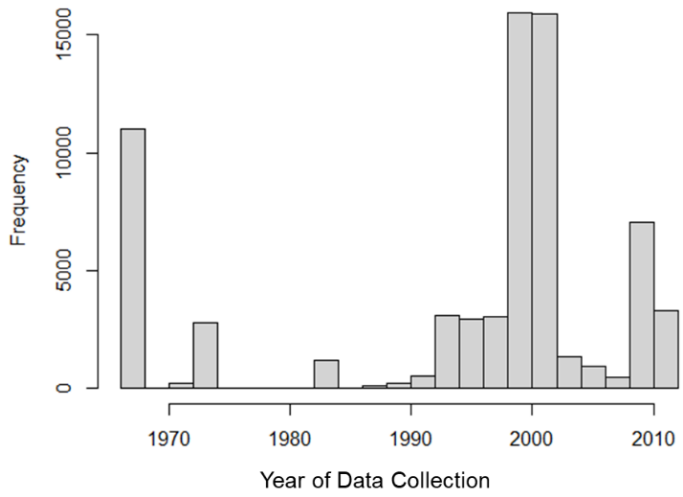

Figure S11: Histogram of year of data collection for all subjects in the combined sample. Despite the large number of observations at some of the tails, the overall measure was analyzed continuously given that it showed acceptable distributional characteristics (skew = -1.09, kurtosis = -0.20).

Table S5: Phenotypic Regression Model Including Effect of Year of Data Collection

Independent Variable	*β*	*SE*	*p*	95% CI
Intercept	0.01	0.10	0.897	[-.18, .21]
Age (Below 75)	-0.08	0.01	1.09E-19	[-.10, -.06]
Age (Above 75)	-0.06	0.01	3.27E-12	[-.08, -.05]
Sex	-0.56	0.01	1.99E-319	[-.59, -.54]
Education	0.07	0.01	1.68E-27	[.06, .08]
Sex * Age (Below 75)	0.00	0.01	0.908	[-.02, .03]
Sex * Age (Above 75)	0.03	0.01	0.014	[.01, .05]
Education * Age (Below 75)	0.10	0.01	1.71E-45	[.08, .11]
Education * Age (Above 75)	-0.03	0.01	0.001	[-.04, -.01]
Sex * Education	0.05	0.01	6.37E-05	[.02, .07]
Sex * Education * Age (Below 75)	-0.09	0.01	1.30E-13	[-.11, -.07]
Sex * Education * Age (Above 75)	0.01	0.01	0.469	[-.01, .03]
Year Assessed	0.50	0.04	0.000	[.42, .59]
Year Assessed * Age (Below 75)	0.11	0.01	8.09E-24	[.09, .13]
Year Assessed * Age (Above 75)	-0.05	0.03	0.085	[-.10, .01]
Year Assessed * Sex	-0.06	0.03	0.021	[-.11, -.01]
Year Assessed * Education	-0.04	0.01	7.11E-05	[-.06, -.02]
Year Assessed * Sex * Age (Below 75)	0.02	0.02	0.311	[-.02, .06]
Year Assessed * Sex * Age (Above 75)	-0.01	0.04	0.722	[-.09, .06]
Year Assessed * Education * Age (Below 75)	-0.01	0.01	0.200	[-.03, .01]
Year Assessed * Education * Age (Above 75)	-0.01	0.02	0.791	[-.05, .04]
Year Assessed * Sex * Education	0.02	0.02	0.261	[-.02, .06]
Year Assessed * Sex * Education * Age (Below 75)	0.08	0.02	1.87E-06	[.05, .12]
Year Assessed * Sex * Education * Age (Above 75)	-0.03	0.03	0.296	[-.09, .03]

Note: All effect sizes are standardized. Sex was treated as a factor (with the estimate displaying the effect for females) and year of data collection and educational attainment were standardized. Age is standardized but centered at the regression spline of 75.

Table S6: Phenotypic Regression Model Including Only Main Effects

Independent Variable	*β*	*SE*	*p*	95% CI
Intercept	-0.05	0.13	0.798	[-.31, .22]
Age (Below 75)	-0.01	0.01	0.365	[-.02, .01]
Age (Above 75)	-0.05	0.00	1.70E-21	[-.06, -.04]
Sex	-0.58	0.01	0.00E+00	[-.60, -.56]
Education	0.09	0.00	6.54E-105	[.08, .10]
Year Assessed	0.44	0.04	1.4E-23	[.35, .52]
Cohort	0.07	0.03	0.009	[.02, .13]

Note: Sex and cohort were treated as factors (with estimates displaying effects for females and individuals born after 1931). Year of data collection and educational attainment were standardized. Age is standardized and centered at the regression spline of 75. The *p*-value for sex could not be computed.

Sensitivity Analysis Excluding Current Abstainers or Heavier Users

We repeated the final phenotypic regression model after excluding individuals who report currently abstaining from alcohol (i.e., 0 grams of ethanol per week; remaining sample *n*=60,649; *n*=53,858 with complete data). This model is displayed in Table S7. Importantly, compared to the analyses described in the main text (Table 3), all the parameters remained statistically significant and were estimated in the same direction. Moreover, almost all associations were also observed to be the same magnitude (i.e., overlapping 95% confidence intervals). The only exception was that the main effect of educational attainment was slightly weaker after excluding abstainers (β= .04; β= .08 in the full model).

We also repeated the final phenotypic regression model after excluding heavier drinkers (>1.5 *SD* above the mean for alcohol consumption; remaining sample *n*=66,579; *n*=59,737 with complete data), corresponding to greater than about 20 drinks per week (i.e., about 3 drinks per day). This model is displayed in Table S8. Again, all parameters from the original model remained statistically significant and with similar magnitude. The only exception was the weak 3-way interaction between sex * education * age (below 75) was no longer significant in the model excluding heavier drinkers (β= -.03 vs .00).

Table S7: Phenotypic Regression Model After Excluding Individuals Who Abstain from Alcohol (i.e. reporting consuming zero grams per week of ethanol)

Independent Variable	*β*	*SE*	*p*	95% CI
(Intercept)	0.16	0.11	2.14E-01	[-.06, .38]
Age (Below 75)	-0.02	0.01	5.18E-03	[-.04, -.01]
Age (Above 75)	-0.07	0.01	1.44E-19	[-.09, -.06]
Sex	-0.58	0.01	0.00E+00	[-.60, -.56]
Education	0.03	0.01	8.35E-10	[.02, .05]
Sex * Age (Below 75)	0.03	0.01	5.93E-04	[.01, .05]
Sex * Age (Above 75)	0.01	0.01	2.49E-01	[-.01, .03]
Education * Age (Below 75)	0.09	0.01	2.15E-50	[.08, .10]
Education * Age (Above 75)	-0.02	0.01	4.05E-03	[-.03, -.01]
Sex * Education	0.05	0.01	3.84E-09	[.03, .07]
Sex * Education * Age (Below 75)	-0.03	0.01	1.52E-03	[-.05, -.01]
Sex * Education * Age (Above 75)	-0.01	0.01	1.44E-01	[-.03, .00]

Note: All effect sizes are standardized. Sex was treated as a factor (with the estimate displaying the effect for females) and cohort was treated as a factor (with the estimate displaying the effect for individuals born after 1931). The exact *p* value for the main effect of sex could not be computed.

Table S8: Phenotypic Regression Model After Excluding Individuals Who Reported Heavier Drinking (>1.5 SD Above the Mean)

Independent Variable	*β*	*SE*	*p*	95% CI
(Intercept)	0.09	0.14	5.64E-01	[-.19, .36]
Age (Below 75)	-0.08	0.01	4.18E-22	[-.10, -.06]
Age (Above 75)	-0.08	0.01	2.60E-17	[-.10, -.06]
Sex	-0.49	0.01	0.00E+00	[-.50, -.47]
Education	0.10	0.01	1.70E-70	[.09, .12]
Sex * Age (Below 75)	0.04	0.01	3.36E-05	[.02, .06]
Sex * Age (Above 75)	0.00	0.01	7.49E-01	[-.03, .02]
Education * Age (Below 75)	0.07	0.01	4.05E-26	[.05, .08]
Education * Age (Above 75)	-0.03	0.01	1.61E-03	[-.04, -.01]
Sex * Education	0.03	0.01	3.02E-04	[.01, .05]
Sex * Education * Age (Below 75)	0.00	0.01	7.35E-01	[-.01, .02]
Sex * Education * Age (Above 75)	-0.02	0.01	4.49E-02	[-.04, .00]

Note: All effect sizes are standardized. Sex was treated as a factor (with the estimate displayingthe effect for females) and cohort was treated as a factor (with the estimate displaying the effect for individuals born after 1931). The exact *p* value for the main effect of sex could not be computed.

Parameter Estimates from the Genetic Model (Pooled Analyses)

Table S9: Parameter Estimates for the Genetic Model

Parameter	Estimate	95% CI	Parameter	Estimate	95% CI
ACE Paths - Females			*ACE Paths - Males*		
a11 Education	0.52	[.47, .57]	a11 Education	0.68	[.66, .70]
a12 Alcohol	0.11	[.05, .17]	a12 Alcohol	0.04	[.00, .07]
a22 Alcohol	0.43	[.37, .48]	a22 Alcohol	0.66	[.63, .68]
c11 Education	0.49	[.44, .53]	c11 Education	0.31	[.27, .35]
c12 Alcohol	0.09	[.03, .15]	c12 Alcohol	0.20	[.16, .25]
c22 Alcohol	0.24	[.17, .31]	c22 Alcohol	0.03	[-.08, .08]
e11 Education	0.53	[.52, .55]	e11 Education	0.51	[.50, .52]
e12 Alcohol	0.01	[-01, .03]	e12 Alcohol	0.02	[.00, .04]
e22 Alcohol	0.56	[.55, .58]	e22 Alcohol	0.74	[.73, .76]
ACE Moderation for Education - Females			*ACE Moderation for Education - Males*		
a12 Education Moderation	-0.07	[-.10, -.02]	a12 Education Moderation	0.00	[-.03, .03]
a22 Education Moderation	0.01	[-.04, .09]	a22 Education Moderation	-0.01	[-.04, .02]
c12 Education Moderation	0.06	[.01, .08]	c12 Education Moderation	-0.03	[-.06, .00]
c22 Education Moderation	0.03	[-.02, .09]	c22 Education Moderation	0.06	[-.01, .12]
e12 Education Moderation	-0.01	[-.03, .01]	e12 Education Moderation	-0.04	[-.06, -.01]
e22 Education Moderation	0.02	[.00, .02]	e22 Education Moderation	-0.02	[-.03, .00]
ACE Moderation for Age - Females			*ACE Moderation for Age - Males*		
a11 Age Moderation	-0.02	[-.04, .00]	a11 Age Moderation	0.01	[-.01, .03]
a12 Age Moderation	-0.02	[-.06, .03]	a12 Age Moderation	0.08	[.05, .12]
a22 Age Moderation	-0.03	[-.08, .03]	a22 Age Moderation	-0.07	[-.10, -.04]
c11 Age Moderation	-0.02	[-.04, .00]	c11 Age Moderation	0.01	[-.02, .05]
c12 Age Moderation	0.10	[-.05, .14]	c12 Age Moderation	0.01	[-.04, .05]
c22 Age Moderation	0.01	[-.11, .11]	c22 Age Moderation	0.07	[.00, .13]
e11 Age Moderation	-0.02	[-.03, -.01]	e11 Age Moderation	0.05	[.03, .06]
e12 Age Moderation	0.02	[.00, .04]	e12 Age Moderation	-0.03	[-.05, .00]
e22 Age Moderation	-0.03	[-.04, -.01]	e22 Age Moderation	0.00	[-.02, .01]
Mean Effects - Females			*Mean Effects - Males*		
Education Intercept	0.23	[.21, .26]	Education Intercept	0.26	[.23, .28]
Alcohol Intercept	-0.27	[-.30, -.25]	Alcohol Intercept	0.30	[.27, .33]
Age on Education	-0.20	[-.22, -.19]	Age on Education	-0.03	[-.05, .00]
Age on Alcohol	-0.20	[-.22, -.19]	Age on Alcohol	-0.23	[-.25, -.21]
Sweden vs Other (on Education)	-0.43	[-.46, -.39]	Sweden vs Other (on Education)	-0.54	[-.57, -.50]
Sweden vs Other (on Alcohol)	-0.07	[-.10, -.05]	Sweden vs Other (on Alcohol)	-0.04	[-.07, -.01]
Denmark vs. Aus/USA (on Education)	-0.25	[-.29, -.21]	Denmark vs. Aus/USA (on Education)	-0.42	[-.47, -.37]
Denmark vs. Aus/USA (on Alcohol)	0.21	[.18, .24]	Denmark vs. Aus/USA (on Alcohol)	0.30	[.26, .34]
USA vs Australia (on Education)	0.22	[.17, .27]	USA vs Australia (on Education)	0.15	[.09, .21]
USA vs Australia (on Alcohol)	-0.24	[-.28, -.20]	USA vs Australia (on Alcohol)	-0.26	[-.31, -.21]

Note: Parameter estimates from the primary genetic model described in the main text. Genetic (A), shared environment (C), and nonshared environment (E) paths were estimated on educational attainment (a11, c11, e11), the covariance between education and alcohol consumption (a12, c12, e12), and the unique variance on alcohol consumption (a22, c22, e22).

Table S10: Model Estimates for Proportion of Variance Explained by Genetic and Environmental Influences by Age

Age		Females			Males		
SD	Years	A	C	E	A	C	E
-1.5	39.1	0.38	0.09	0.54	0.49	0.04	0.48
-1.25	42.0	0.37	0.09	0.54	0.48	0.04	0.49
-1	44.8	0.37	0.09	0.54	0.47	0.04	0.50
-0.75	47.6	0.36	0.09	0.55	0.46	0.04	0.51
-0.5	50.4	0.36	0.10	0.55	0.44	0.04	0.52
-0.25	53.2	0.35	0.10	0.55	0.43	0.04	0.53
0	56.1	0.34	0.12	0.54	0.42	0.04	0.54
0.25	58.9	0.33	0.13	0.54	0.41	0.04	0.55
0.5	61.7	0.32	0.14	0.53	0.40	0.05	0.56
0.75	64.5	0.31	0.16	0.53	0.39	0.05	0.56
1	67.4	0.30	0.18	0.52	0.38	0.05	0.57
1.25	70.2	0.29	0.20	0.51	0.37	0.06	0.57
1.5	73.0	0.28	0.23	0.50	0.36	0.07	0.58
1.75	75.8	0.26	0.25	0.49	0.35	0.07	0.58
2	78.7	0.25	0.28	0.48	0.34	0.08	0.58
2.25	81.5	0.23	0.31	0.46	0.33	0.09	0.58

Note: Model estimates for proportion of variance explained by genetic (A), shared environmental (C), and nonshared environmental influences (E) displayed for *z*-scored age and age in years. All estimates also assume individuals are at the mean level of education and should be interpreted in light of moderation effects for education.

Table S11: Model Estimates for Proportion of Variance Explained by Genetic and Environmental Influences by Educational Attainment

Education		Females			Males		
SD	Bin	A	C	E	A	C	E
-1.1	1.5	0.39	0.08	0.54	0.41	0.05	0.54
-0.7	2.1	0.37	0.09	0.54	0.42	0.05	0.54
-0.3	2.6	0.35	0.10	0.54	0.42	0.04	0.54
0.1	3.2	0.34	0.12	0.54	0.42	0.04	0.54
0.5	3.8	0.33	0.14	0.54	0.42	0.04	0.54
0.9	4.3	0.31	0.15	0.53	0.43	0.04	0.54
1.3	4.9	0.30	0.17	0.53	0.43	0.04	0.53
1.7	5.5	0.30	0.19	0.52	0.43	0.04	0.53
2.1	6.1	0.29	0.21	0.51	0.43	0.05	0.53

Note: Model estimates for proportion of variance explained by genetic (A), shared environmental (C), and nonshared environmental influences (E) at different levels of education (displayed for both *z*-scored education and binned educational attainment). All estimates also assume individuals are at the mean age (56.07 years) and should be interpreted in light of moderation effects for age.

Complementary Meta-Analysis for the Genetic Model (9 Samples)

Table S12 displays results from an alternate approach where the genetic model was fit separately within each sample, then the parameter estimates were meta-analyzed across sample. The fixed-effects meta-analysis was conducted using the metafor package in R (Viechtbauer, 2010). This model only included 9 studies total (n= 67,125 with phenotypic data) including 8 of the studies in the original analysis and the Finnish Twin Cohort (FTC) sample (which we could not include in the primary analysis due to data sharing restrictions). Of the remaining 6studies, GENDER was excluded because it only contains opposite-sex DZ twins, 4 of the studies were excluded because the sample size was too small (n<1,000; most of which did not converge when attempting to run the genetic model), and SATSA was excluded because it also did not converge (and was only just over the n>1,000 threshold). The genetic model within each study was identical to that of the pooled analysis, but it did not include country-level effects on the means (because all samples were collected within a given country). Parameter estimates for females were based on only 7 of the 9 studies (because NAS-NRC and VETSA did not have females in their samples).

Importantly, parameter estimates from the meta-analysis were like those from the pooled analysis (see Table S9 vs. Table S12). Visual inspection of the forest plots suggests results were generally consistent across the 9 samples, but some differences are described in the main text. Forest plots for the most relevant parameter estimates are displayed in Figures S12 to S16.

Table S12: Parameter Estimates from the Meta-Analysis (9 studies)

Parameter	Estimate	95% CI	Parameter	Estimate	95% CI
ACE Paths - Females			*ACE Paths - Males*		
a11 Education	0.59	[.37, .82]	a11 Education	0.55	[.38, .73]
a12 Alcohol	0.10	[-.16, .35]	a12 Alcohol	0.01	[-.21, .23]
a22 Alcohol	0.44	[.19, .69]	a22 Alcohol	0.61	[.41, .82]
c11 Education	0.47	[.25, .69]	c11 Education	0.17	[-.04, .38]
c12 Alcohol	0.12	[-.13, .36]	c12 Alcohol	0.10	[-.12, .32]
c22 Alcohol	-0.15	[-.47, .16]	c22 Alcohol	0.06	[-.28, .39]
e11 Education	0.54	[.41, .67]	e11 Education	0.53	[.41, .66]
e12 Alcohol	0.02	[-.13, .17]	e12 Alcohol	0.03	[-.14, .21]
e22 Alcohol	0.57	[.44, .70]	e22 Alcohol	0.76	[.62, .91]
ACE Moderation for Education - Females			*ACE Moderation for Education - Males*		
a12 Education Moderation	-0.05	[-.23, .13]	a12 Education Moderation	0.00	[-.18, .18]
a22 Education Moderation	0.00	[-.20, .19]	a22 Education Moderation	-0.01	[-.19, .17]
c12 Education Moderation	0.04	[-.13, .21]	c12 Education Moderation	-0.01	[-.20, .18]
c22 Education Moderation	0.00	[-.23, .23]	c22 Education Moderation	-0.04	[-.34, .26]
e12 Education Moderation	-0.01	[-.16, .14]	e12 Education Moderation	-0.03	[-.21, .14]
e22 Education Moderation	0.00	[-.12, .11]	e22 Education Moderation	-0.04	[-.17, .10]
ACE Moderation for Age - Females			*ACE Moderation for Age - Males*		
a11 Age Moderation	0.07	[-.15, .30]	a11 Age Moderation	0.10	[-.09, .29]
a12 Age Moderation	-0.14	[-.44, .16]	a12 Age Moderation	-0.07	[-.33, .19]
a22 Age Moderation	-0.04	[-.34, .26]	a22 Age Moderation	0.01	[-.22, .24]
c11 Age Moderation	0.03	[-.20, .25]	c11 Age Moderation	0.00	[-.24, .23]
c12 Age Moderation	0.10	[-.19, .38]	c12 Age Moderation	0.02	[-.27, .30]
c22 Age Moderation	-0.10	[-.43, .24]	c22 Age Moderation	-0.07	[-.45, .31]
e11 Age Moderation	0.04	[-.11, .19]	e11 Age Moderation	0.05	[-.09, .20]
e12 Age Moderation	-0.04	[-.24, .16]	e12 Age Moderation	-0.03	[-.25, .19]
e22 Age Moderation	-0.02	[-.18, .13]	e22 Age Moderation	0.01	[-16, .18]
Mean Effects - Females			*Mean Effects - Males*		
Education Intercept	-0.07	[-.20, .07]	Education Intercept	-0.02	[-.15, .11]
Alcohol Intercept	-0.25	[-.40, -.11]	Alcohol Intercept	0.34	[.19, .50]
Age on Education	-0.22	[-.41, -.04]	Age on Education	-0.14	[-.32, .04]
Age on Alcohol	-0.15	[-.30, .01]	Age on Alcohol	-0.11	[-.27, .05]

Note: Parameter estimates from the primary genetic model described in the main text. Genetic (A), shared environment (C), and nonshared environment (E) paths were estimated on educational attainment (a11, c11, e11), the covariance between educational attainment and alcohol consumption (a12, c12, e12), and the unique variance on alcohol consumption (a22, c22, e22).

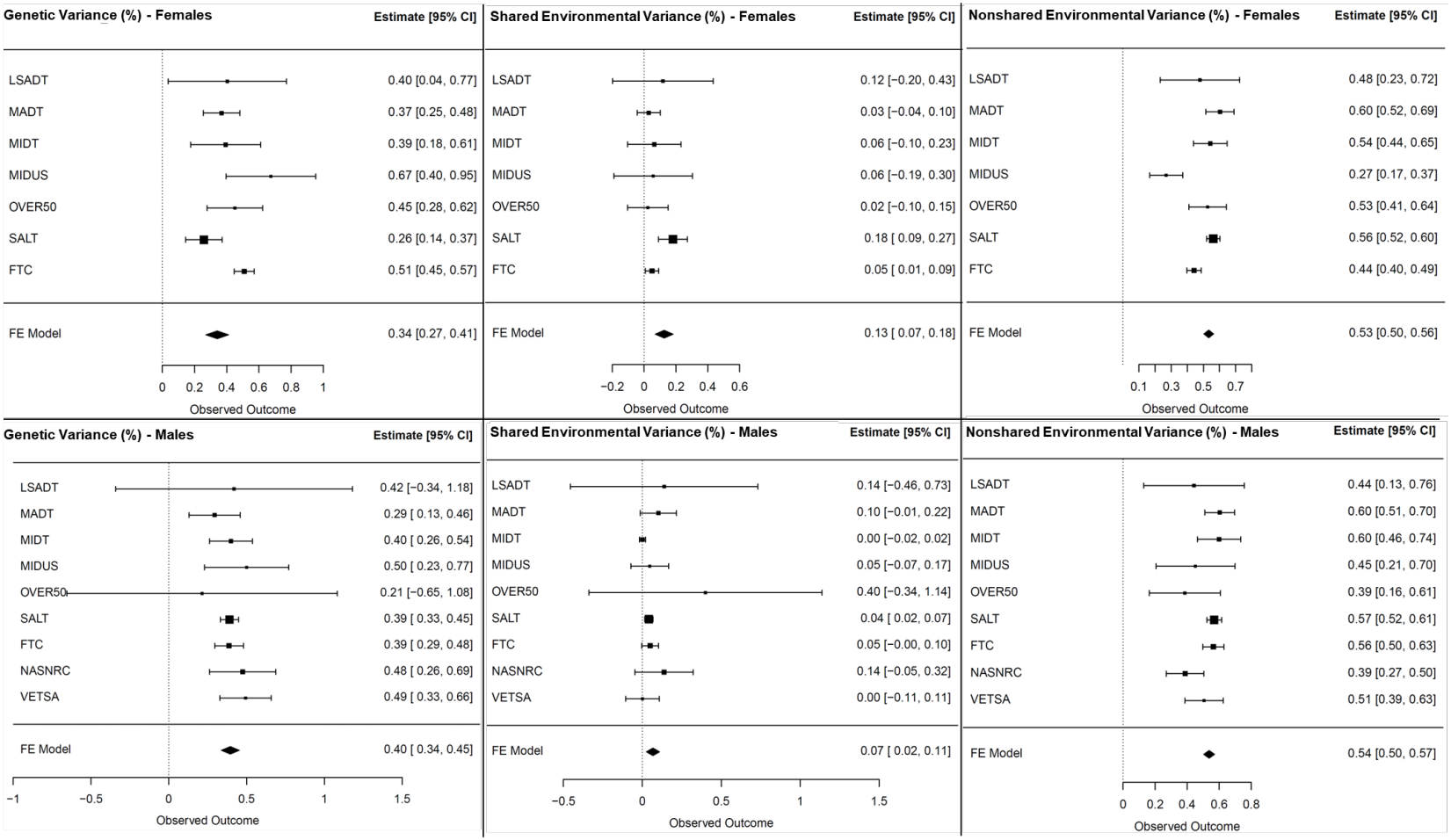

Figure S12: Forest plots from the meta-analysis displaying the proportion of genetic (A), shared environmental (C), or nonshared environmental (E) influences. Note that these estimates are based on the grand mean from the full pooled analysis (55.6 years). This was close to the mean of each individual cohort, except for LSADT which did not have any subjects in this age range (which is why the standard errors are much larger for this study compared to its large sample size). FTC = Finnish Twin Cohort; LSADT = Longitudinal Study of Aging Danish Twins; MIDT/MADT = Middle Age Danish Twin Studies; MIDUS = Midlife in the United States; NAS-NRC = National Academy of Sciences-National Research Council, OVER50 = Australian Over 50 study; SALT = Screening Across the Lifespan Twin Study; VETSA = Vietnam Era Twin Study of Aging.

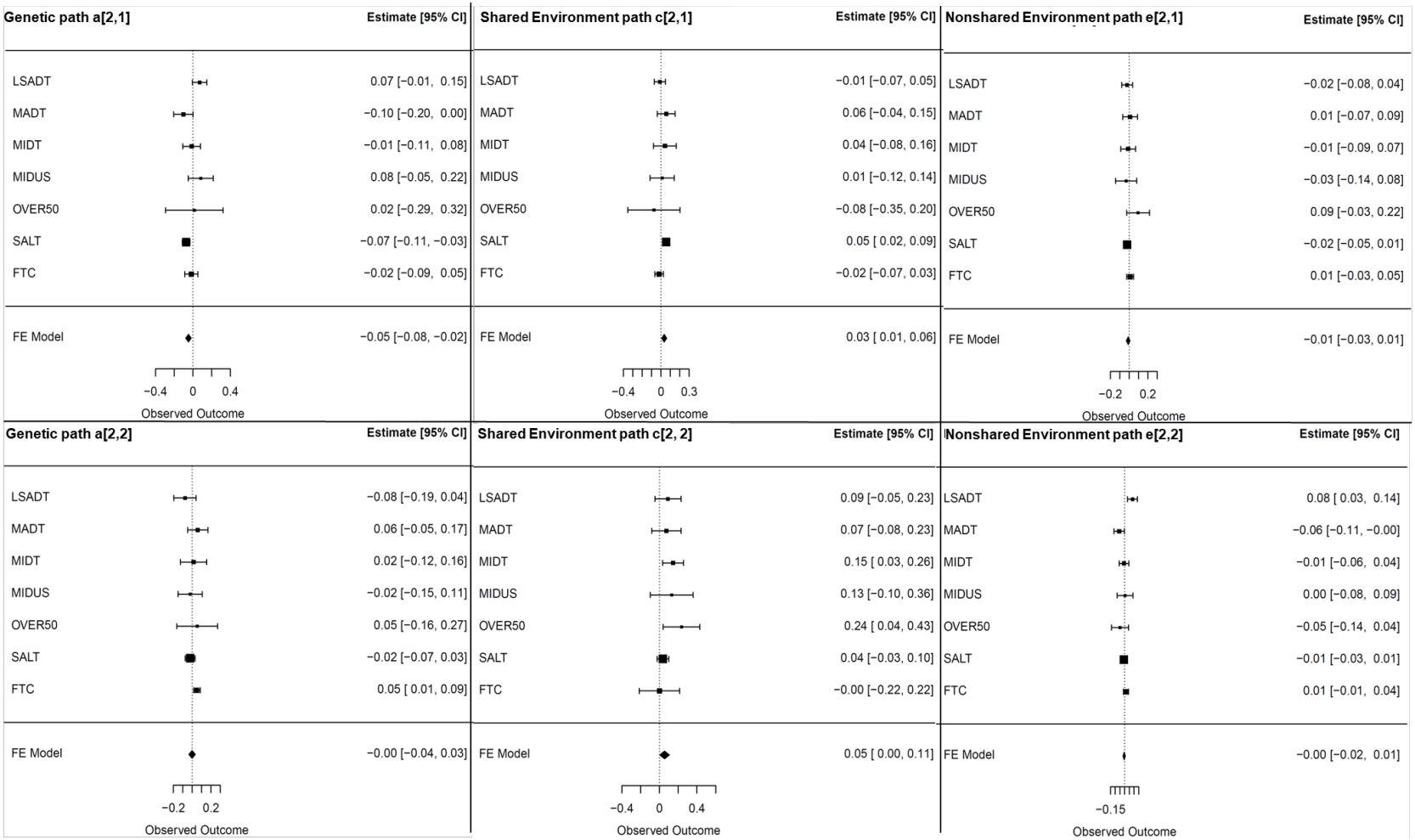

Figure S13: Forest plots from the meta-analysis focusing on whether educational attainment moderated the genetic (A), shared environmental (C), or nonshared environmental (E) influences for females. Parameters with the suffix [2,1] reflect moderation of paths capturing the genetic/environmental influences on educational attainment that predict alcohol use (top row). Parameters with the suffix [2,2] reflect moderation of the unique genetic/environmental influences on alcohol use (bottom row). FTC = Finnish Twin Cohort; LSADT = Longitudinal Study of Aging Danish Twins; MIDT/MADT = Middle Age Danish Twin Studies; MIDUS = Midlife in the United States; OVER50 = Australian Over 50 study; SALT = Screening Across the Lifespan Twin Study.

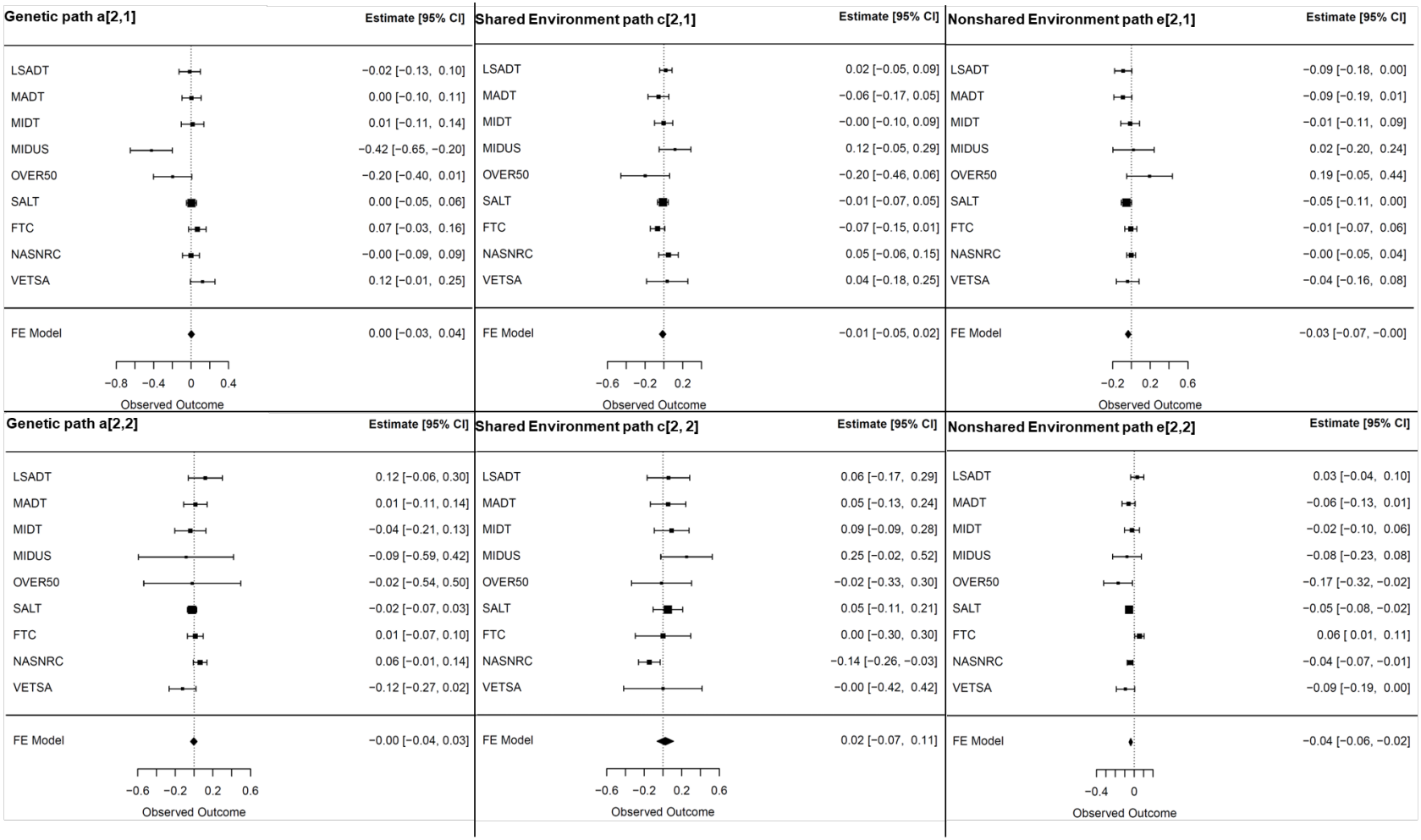

Figure S14: Forest plots from the meta-analysis focusing on whether educational attainment moderated the genetic (A), shared environmental (C), or nonshared environmental (E) influences for males. Parameters with the suffix [2,1] reflect moderation of paths capturing the genetic/environmental influences on educational attainment that predict alcohol use (top row). Parameters with the suffix [2,2] reflect moderation of the unique genetic/environmental influences on alcohol use (bottom row). FTC = Finnish Twin Cohort; LSADT = Longitudinal Study of Aging Danish Twins; MIDT/MADT = Middle Age Danish Twin Studies; MIDUS = Midlife in the United States; NAS-NRC = National Academy of Sciences-National Research Council, OVER50 = Australian Over 50 study; SALT = Screening Across the Lifespan Twin Study; VETSA = Vietnam Era Twin Study of Aging.

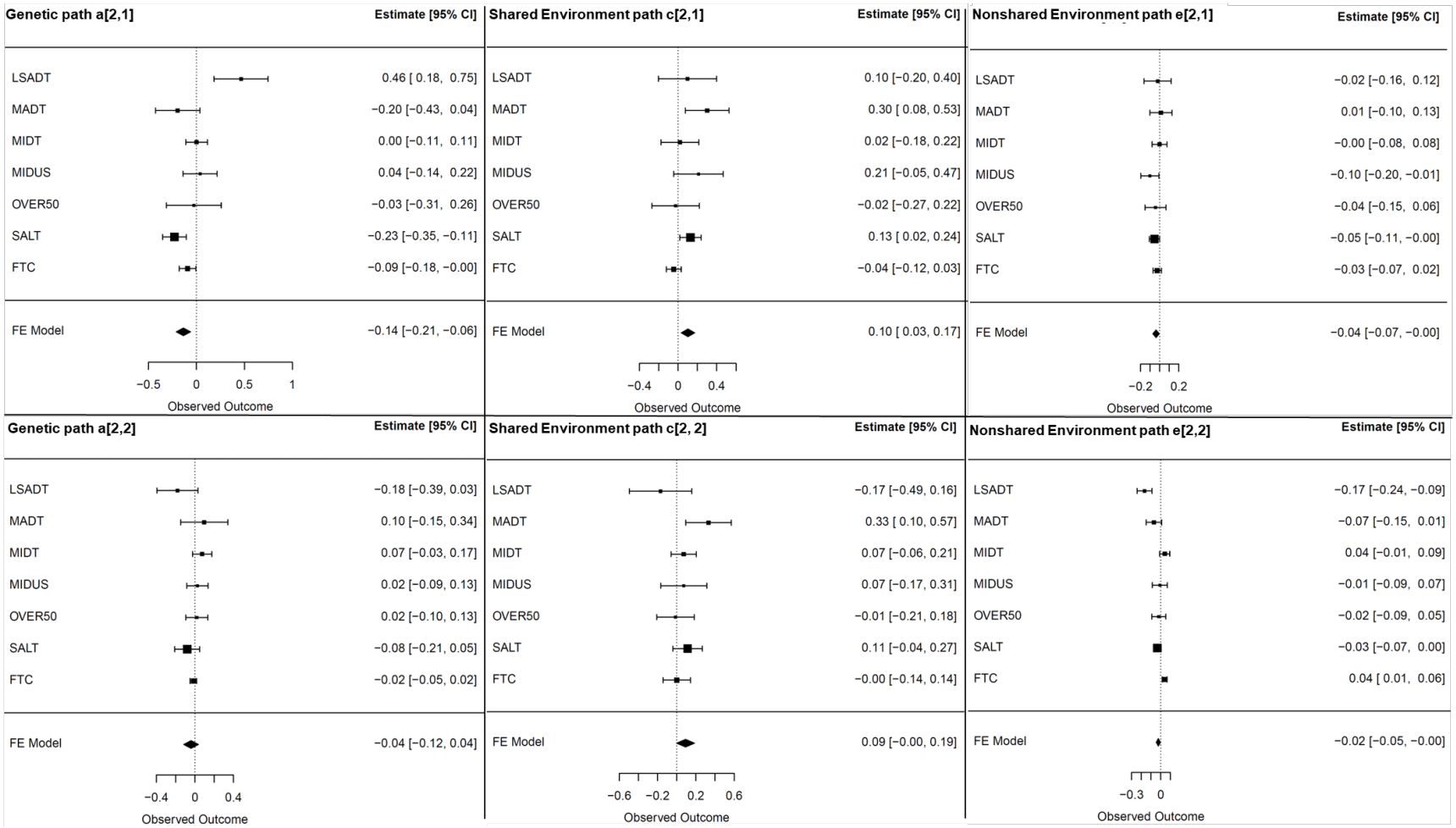

Figure S15: Forest plots from the meta-analysis focusing on whether age moderated the genetic (A), shared environmental (C), or nonshared environmental (E) influences for females. Parameters with the suffix [2,1] reflect moderation of paths capturing the genetic/environmental influences on educational attainment that predict alcohol use (top row). Parameters with the suffix [2,2] reflect moderation of the unique genetic/environmental influences on alcohol use (bottom row). FTC = Finnish Twin Cohort; LSADT = Longitudinal Study of Aging Danish Twins; MIDT/MADT = Middle Age Danish Twin Studies; MIDUS = Midlife in the United States; OVER50 = Australian Over 50 study; SALT = Screening Across the Lifespan Twin Study.

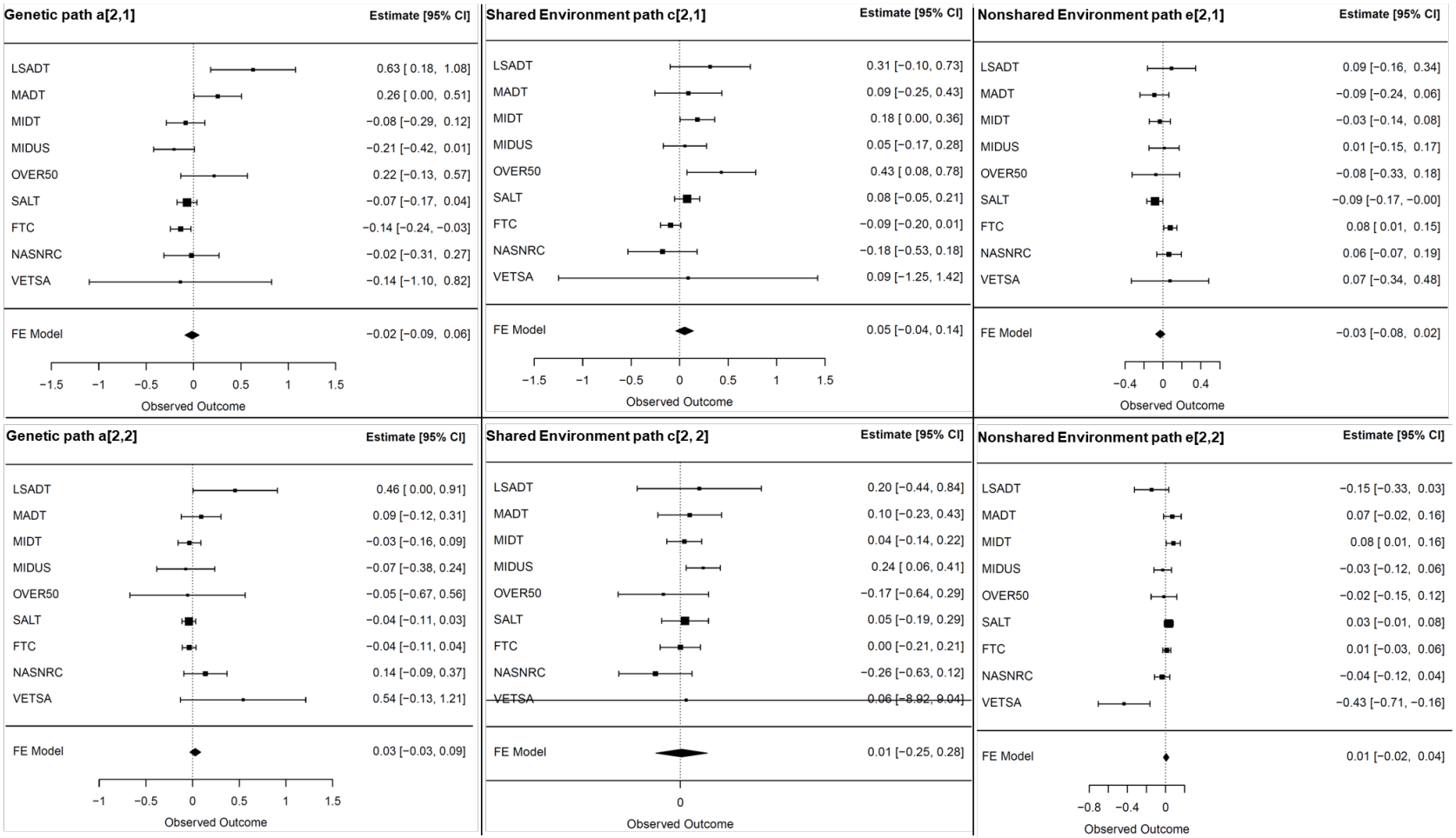

Figure S16: Forest plots from the meta-analysis focusing on whether age moderated the genetic (A), shared environmental (C), or nonshared environmental (E) influences for males. Parameters with the suffix [2,1] reflect moderation of paths capturing the genetic/environmental influences on educational attainment that predict alcohol use (top row). Parameters with the suffix [2,2] reflect moderation of the unique genetic/environmental influences on alcohol use (bottom row). FTC = Finnish Twin Cohort; LSADT = Longitudinal Study of Aging Danish Twins; MIDT/MADT = Middle Age Danish Twin Studies; MIDUS = Midlife in the United States; NAS-NRC = National Academy of Sciences-National Research Council, OVER50 = Australian Over 50 study; SALT = Screening Across the Lifespan Twin Study; VETSA = Vietnam Era Twin Study of Aging.

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