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Genetic and Environmental Influences on Stages of Alcohol Use

Across Adolescence and Into Young Adulthood

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Introduction

The progression to alcohol dependence unfolds across multiple stages, including the decision to initiate use, the development of regular patterns of use, and (for some individuals) the subsequent development of problems associated with alcohol use. Several studies have examined the heritability of alcohol related behavior at each of these stages. Twin studies have found that the initiation of alcohol use is largely influenced by shared environmental factors (C), which account for 55-80% of the variance (1, 2, 3). Once initiation has occurred, genetic factors (A) explain a large amount of the variation in the frequency and amount of alcohol use (34-72%) and in later development of alcohol dependence in adulthood (50-70%), with much of the rest of the variance attributed to unique environmental factors (E; 2, 4, 5 6). Although genetic and environmental influences have been examined at each of these stages, these analyses were conducted with separate analyses across independent datasets. This traditional approach does not account for risk factors and influences of previous stages of initiation and use. In the present study, we apply multiple-stage genetic models (7) to progressive stages of alcohol use and misuse in two population-based, longitudinal twin samples, *FinnTwin16 (FT16)* and *FinnTwin12 (FT12)*. These multiple stage models allow us to more accurately assess the importance of genetic and environmental risk factors on patterns of use and misuse by making allowance for partial overlap with risk factors for initiation. With these models we can also examine the extent to which risk factors overlap between various stages of alcohol use and misuse.

Method

- Participants:** *FT16* and *FT12* are two independent, population-based longitudinal twin studies of health risk factors, each consisting of five consecutive birth cohorts of Finnish twins identified through Finland's Central Population Registry.
 - FT16* includes 2,280 twin pairs (born 1975-1979) who returned baseline questionnaires at age 16. Follow-up assessments conducted when twins were age 17, 18.5, and 25. Age 16 and follow-up data available for 1712 same-sex twin pairs.
 - FT12* includes 2,216 twin pairs (born 1983-1987) who returned baseline questionnaires at age 12. Follow-up assessments conducted at ages 14 and 17.5. Age 12 and follow-up data available for 1297 same-sex twin pairs.
 - ~ 90% retention for all data collection waves across samples
- Statistical Analyses:** We applied multiple-stage (bivariate and trivariate) Cholesky models to the data (7). All modeling was conducted using the raw ordinal data option in Mx (8). Model fitting was evaluated by the change in $-2 \log$ likelihood (chi-square distributed) between the initial model and the nested submodel. Significance was set at $p < .05$.
 - Bivariate Models (Figure 1):** Fit separately to initiation and frequency of alcohol use data from *FT16* and *FT12*:
 - Three-level *age of initiation* variable:
 - Never (by age 17)
 - Late (15-17)
 - Early (by age 14)
 - Six-level *frequency of use* outcome (at age 17)
 - Ranged from zero (once a year or less) to six (a few times per week or daily).
 - Those not initiating by 17 given a missing value on frequency of use outcome variable.
 - Trivariate Models (Figure 2):** Subsequently, we expanded the bivariate model to a trivariate model in the *FT16* dataset, studying
 - Four-level *age of initiation* variable (incorporating initiation after age 17)
 - Same six-level *frequency of use* outcome (at age 25)
 - Five-level *drinking problems* outcome (at age 25) measured using the Rutgers Alcohol Problem Index (RAPI; 9).
 - Those not initiating by 25 given a missing value on second and third stages.

Bivariate Model Fitting Results

- For both *FT16* and *FT12*, constraining the thresholds, but not standardized estimates of A, C, and E, to be equal across sex caused a significant decrease in fit.
- Constraining thresholds, but not A, C, and E estimates, on initiation and frequency of use to be equal across samples caused a significant decrease in fit.
- Thus, for all subsequent models, threshold estimates were allowed to vary across sex and sample, while A, C, and E standardized estimates were constrained equal across sex and sample.
- The bivariate genetic model that best fit the combined *FT16* and *FT12* alcohol initiation and frequency of use data was one in which A, C, and E estimates, but not thresholds, were constrained equal across gender with no shared (overlapping) unique environmental influences on the two stages of alcohol use.

Figure 1: Bivariate Cholesky Model

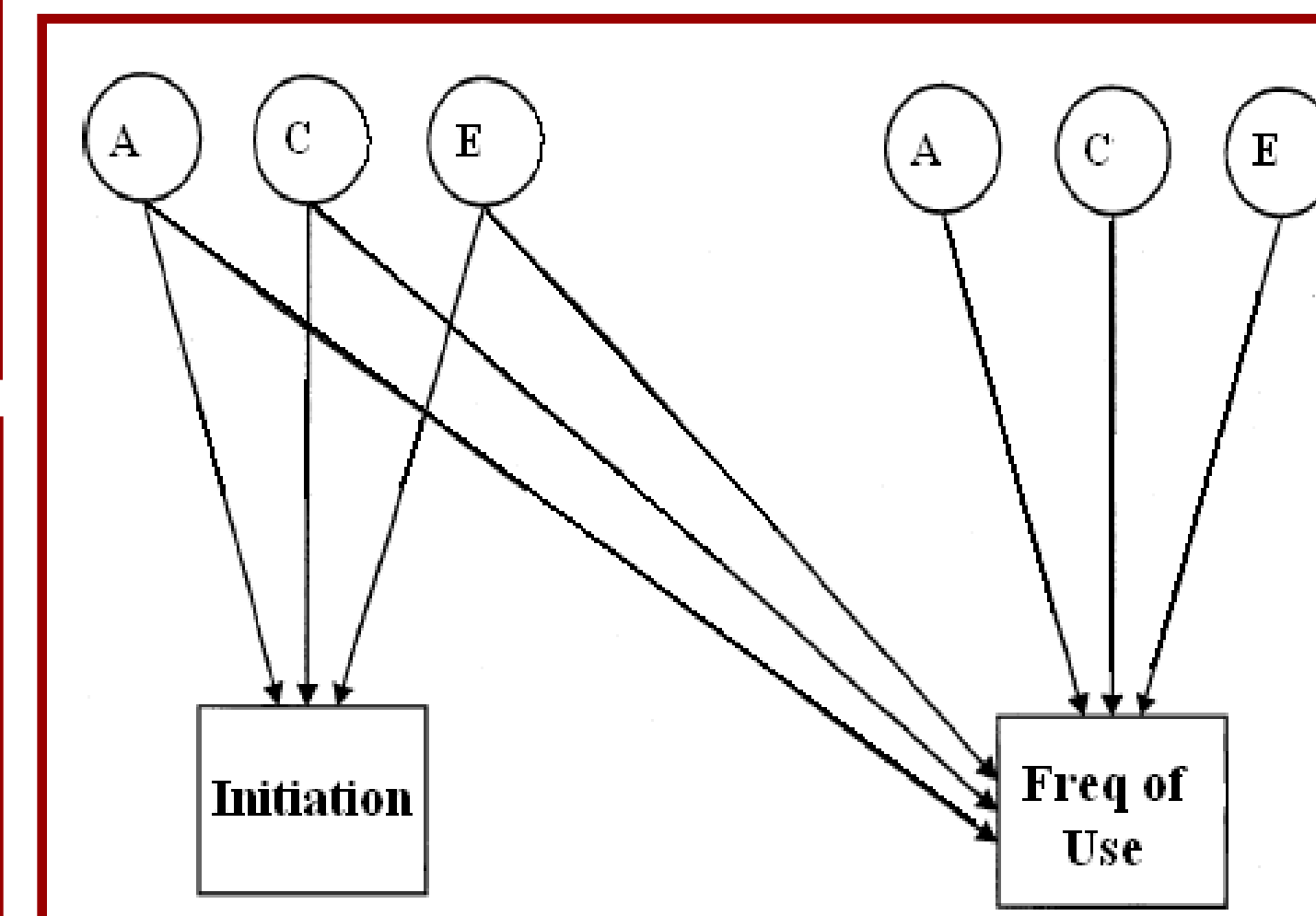
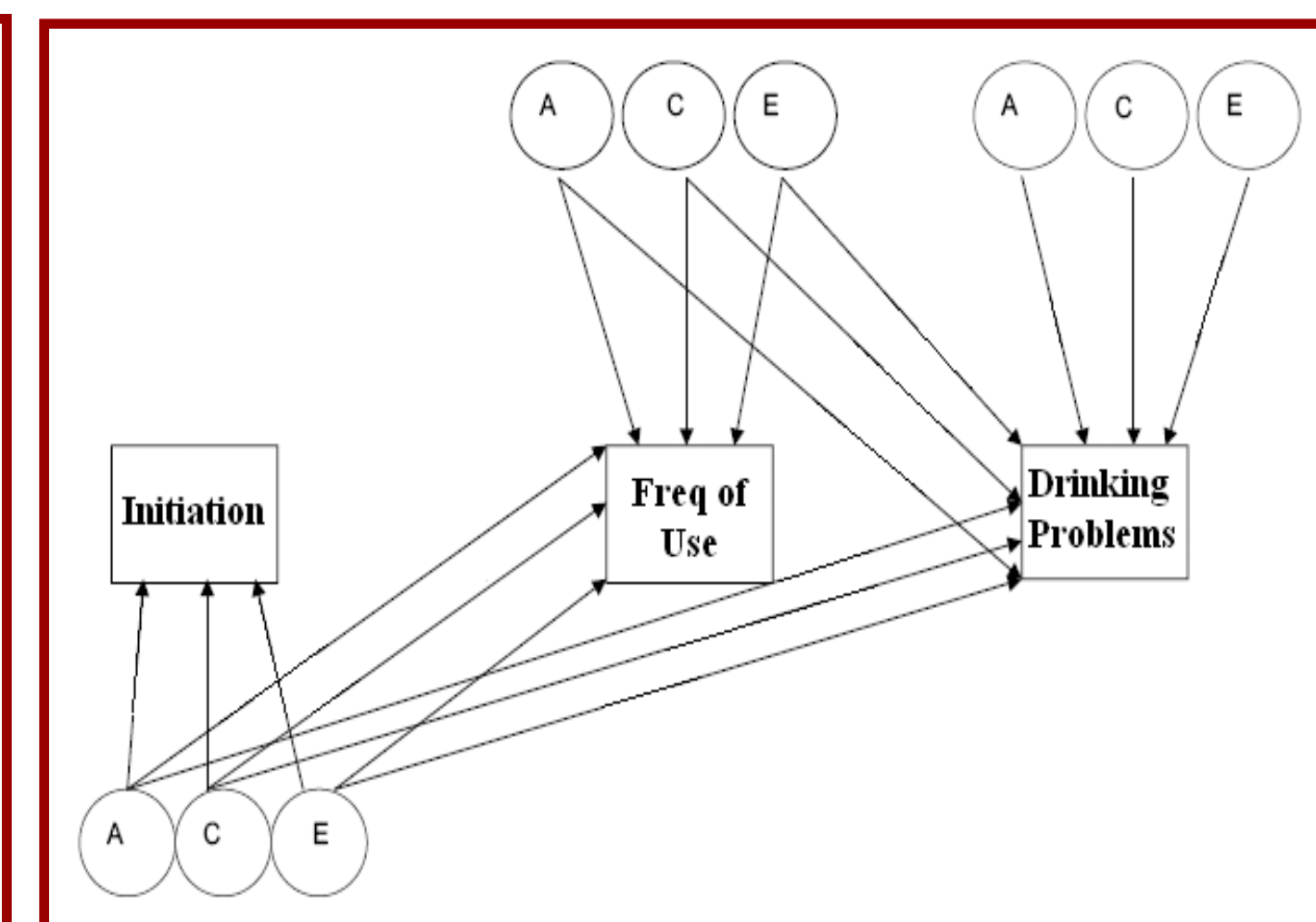


Figure 2: Trivariate Cholesky Model



Specific Factor Estimates (95% CI) Full Model

Combined	A	C	E
Initiation	.29 (.22-.37)	.59 (.51-.66)	.12 (.09-.13)
Frequency	.39 (.30-.49)	.34 (.25-.42)	.27 (.24-.30)

Common Factor Estimates (CI) Full Model

Combined	rA	rC	rE
Init-Freq	.51	.81	.02
Correlation	(.21-.81)	(.62-1.00)	(.00-.19)

Bivariate Model Fitting Conclusions

- Results are consistent with large shared environmental influences and small genetic influences on initiation of alcohol use.
- Results confirmed the consistent finding that genetic and unique environmental influences increase, while shared environmental influences decrease once initiation occurs.
- Most of the common environmental influences on initiation and a modest proportion of the genetic influences also impact frequency of use

Trivariate Model Fitting Results

- Constraining both the thresholds and standardized A, C, and E estimates across the three stages to be equal across sex caused a significant decrease in fit.
- For all subsequent models, thresholds and A, C, and E estimates at all three stages were allowed to vary across sex.
- For females, a model in which common A and E pathways between initiation and both frequency of use and alcohol problems were dropped fit the data best.
- The best-fitting model for males was one in which common A and E pathways between initiation and both frequency of use and alcohol problems were dropped as well as all C pathways from the frequency of use and problem drinking stages.

Specific Trivariate Factor Estimates (95% CI) Full Model

Females	A	C	E
Initiation	.44 (.31-.60)	.47 (.32-.60)	.09 (.06-.11)
Frequency	.19 (.01-.42)	.31 (.11-.47)	.50 (.43-.58)
Problem Drinking	.47 (.25-.65)	.15 (.00-.34)	.38 (.32-.45)
Males	A	C	E
Initiation	.22 (.06-.39)	.61 (.45-.74)	.17 (.13-.23)
Frequency	.48 (.29-.60)	.08 (.01-.23)	.44 (.36-.53)
Problem Drinking	.55 (.32-.69)	.08 (.00-.28)	.36 (.29-.44)

Common Trivariate Factor Estimates (95% CI) Full Model

Females	rA	rC	rE
Init-Freq	.23 (.00-.89)	.44 (.08-.86)	.06 (.00-.23)
Init-Prob	.15 (-.17-.47)	.55 (.23-1.00)	.08 (-.02-.25)
Freq-Prob	.78 (.29-1.00)	.23 (-.78-.92)	.46 (.35-.55)
Males	rA	rC	rE
Init-Freq	.23 (.00-.74)	1.00 (.43-1.00)	.16 (.00-.23)
Init-Prob	.29 (-.18-.84)	.61 (-1.00-1.00)	.01 (-.18-.22)
Freq-Prob	.63 (.39-.96)	.59 (-.62-1.00)	.30 (.15-.44)

Trivariate Model Fitting Conclusions

- Results demonstrate large genetic influences on problematic drinking, which is consistent with previous research finding large genetic influences on alcohol abuse/dependence in adulthood (50-70%; 4, 5).
- Given the large E influences on women's frequency of alcohol use at age 25, there appears to be some unique processes influencing women's drinking patterns in their early to mid-20s.
- Genetic influences on initiation appear independent from later stages, while genetic influences on drinking frequency and problem drinking overlap a great deal.

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