**Genetic and environmental correlations contribute to associations between substance use disorders and suicidal behavior**

**Supplemental Material**

Supplemental Methods

Suicide attempts and deaths were identified using the following ICD codes: ICD-8 codes E950-E959, E980-987, ICD-9 codes E950-E959, E980-987, ICD-10 codes X60-X84, Y10-Y34. Distinctions between attempt and death were made by cross-referencing the Swedish mortality register.

Alcohol use disorder was identified using the following ICD codes: ICD9: V79B, 305A, 357F, 571A-D, 425F, 535D, 291, 303, 980; ICD 10: E244, G312, G621, G721, I426, K292, K70, K852, K860, O354, T51, F10). In the Prescribed Drug Register, AUD was identified by the drugs disulfiram (Anatomical Therapeutic Chemical (ATC) Classification System N07BB01), acamprosate (N07BB03), and naltrexone (N07BB04). In the Crime Register, AUD was identified by codes 3005, 3201, which reflect crimes related to alcohol abuse; and in the Suspicion Register by codes 0004, 0005 (Only those individuals with at least two alcohol-related crimes or suspicion of crimes from both Crime Register and Suspicion Register were included).

Drug use disorder was identified using the following ICD codes: ICD8: Drug dependence (304); ICD9: Drug psychoses (292) and Drug dependence (304); ICD10: Mental and behavioral disorders due to psychoactive substance use (F10-F19), except those due to alcohol (F10) or tobacco (F17). In the Prescribed Drug Register, DUD was identified in individuals who had retrieved (in average) more than four defined daily doses a day for 12 months from either of Hypnotics and Sedatives (Anatomical Therapeutic Chemical (ATC) Classification System N05C and N05BA) or Opioids (ATC: N02A), excluding those suffering from cancer. In the Crime Register, DUD was identified by references to laws covering narcotics (law 1968:64, paragraph 1, point 6) and drug-related driving offences (law 1951:649, paragraph 4, subsection 2 and paragraph 4A, subsection 2), and in the Suspicion Register by codes 3070, 5010, 5011, and 5012, which reflect crimes related to DUD.

**Supplemental Table 1.** Tetrachoric correlations (95% confidence intervals) within individuals and across sibling pairs, within and across outcomes, by sex.

*SA=suicide attempt; AUD=alcohol use disorder; DUD=drug use disorder; S1=sibling 1; S2=sibling 2*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Sibling pair type** |  |  |  |  |
|  | Monozygotic twins | Dizygotic twins | Full siblings | Half siblings reared together | Half siblings reared apart |
| **Females** |  |  |  |  |  |
| S1 SA \* S1 AUD | 0.75 (0.69; 0.82) | 0.73 (0.65; 0.80) | 0.66 (0.65; 0.66) | 0.68 (0.65; 0.71) | 0.65 (0.62; 0.67) |
| S1 SA \* S1 DUD | 0.73 (0.65; 0.81) | 0.68 (0.59; 0.78) | 0.67 (0.66; 0.68) | 0.64 (0.60; 0.68) | 0.64 (0.61; 0.66) |
| S1 AUD \* S1 DUD DUD | 0.78 (0.70; 0.85) | 0.68 (0.59; 0.78) | 0.70 (0.69; 0.71) | 0.68 (0.65; 0.72) | 0.71 (0.68; 0.73) |
| S1 SA \* S2 SA | 0.52 (0.41; 0.62) | 0.30 (0.17; 0.43) | 0.27 (0.25; 0.28) | 0.18 (0.12; 0.24) | 0.10 (0.06; 0.14) |
| S1 AUD \* S2 AUD | 0.67 (0.59; 0.76) | 0.57 (0.46; 0.67) | 0.28 (0.26; 0.30) | 0.23 (0.17; 0.29) | 0.16 (0.12; 0.20) |
| S1 DUD \* S2 DUD | 0.63 (0.52; 0.74) | 0.25 (0.03; 0.46) | 0.36 (0.35; 0.38) | 0.29 (0.22; 0.35) | 0.09 (0.04; 0.13) |
| S1 SA \* S2 AUD | 0.46 (0.35; 0.58) | 0.33 (0.20; 0.47) | 0.21 (0.19; 0.23) | 0.18 (0.12; 0.25) | 0.07 (0.03; 0.11) |
| S1 SA \* S2 DUD | 0.48 (0.36; 0.61) | 0.30 (0.14; 0.47) | 0.23 (0.22; 0.25) | 0.09 (0.02; 0.16) | 0.07 (0.02; 0.11) |
| S1 AUD \* S2 DUD | 0.55 (0.43; 0.66) | 0.46 (0.31; 0.60) | 0.29 (0.27; 0.31) | 0.19 (0.12; 0.26) | 0.11 (0.06; 0.16) |
| S1 SD \* S1 AUD | 0.49 (0.24; 0.74) | 0.55 (0.29; 0.81) | 0.45 (0.42; 0.48) | 0.24 (0.11; 0.38) | 0.41 (0.33; 0.48) |
| S1 SD \* S1 DUD | 0.45 (0.16; 0.74) | 0.51 (0.21; 0.80) | 0.45 (0.42; 0.48) | 0.30 (0.16; 0.43) | 0.42 (0.34, 0.50) |
| S1 SD \* S2 SD | - | - | 0.22 (0.14; 0.31) | - | 0.19 (-0.02; 0.40) |
| S1 SD \* S2 AUD | 0.24 (-0.13; 0.60) | 0.28 (-0.10; 0.65) | 0.18 (0.14; 0.22) | 0.16 (0.01; 0.31) | 0.10 (-0.01; 0.21) |
| S1 SD \* S2 DUD | 0.55 (0.30; 0.80) | - | 0.15 (0.10; 0.20) | 0.18 (0.02; 0.34) | 0.06 (-0.06; 0.18) |
|  |  |  |  |  |  |
| **Males** |  |  |  |  |  |
| S1 SA \* S1 AUD | 0.61 (0.52; 0.70) | 0.57 (0.47; 0.66) | 0.61 (0.60; 0.61) | 0.61 (0.58; 0.64) | 0.60 (0.58; 0.62) |
| S1 SA \* S1 DUD | 0.61 (0.50; 0.71) | 0.54 (0.41; 0.66) | 0.60 (0.59; 0.61) | 0.63 (0.59; 0.66) | 0.58 (0.56; 0.61) |
| S1 AUD \* S1 DUD DUD | 0.71 (0.63; 0.78) | 0.65 (0.56; 0.74) | 0.73 (0.73; 0.74) | 0.73 (0.70; 0.75) | 0.74 (0.73; 0.76) |
| S1 SA \* S2 SA | 0.36 (0.22; 0.50) | 0.29 (0.13; 0.45) | 0.28 (0.27; 0.29) | 0.20 (0.14; 0.25) | 0.11 (0.07; 0.15) |
| S1 AUD \* S2 AUD | 0.67 (0.60; 0.74) | 0.37 (0.27; 0.47) | 0.35 (0.34; 0.36) | 0.22 (0.18; 0.26) | 0.13 (0.11; 0.16) |
| S1 DUD \* S2 DUD | 0.87 (0.82; 0.92) | 0.52 (0.38; 0.65) | 0.47 (0.46; 0.48) | 0.34 (0.29; 0.38) | 0.14 (0.11; 0.17) |
| S1 SA \* S2 AUD | 0.39 (0.27; 0.51) | 0.23 (0.09; 0.37) | 0.22 (0.21; 0.23) | 0.14 (0.10; 0.19) | 0.07 (0.04; 0.11) |
| S1 SA \* S2 DUD | 0.40 (0.26; 0.53) | 0.26 (0.08; 0.43) | 0.23 (0.22; 0.25) | 0.18 (0.12; 0.23) | 0.06 (0.02; 0.09) |
| S1 AUD \* S2 DUD | 0.57 (0.47; 0.66) | 0.25 (0.10; 0.40) | 0.34 (0.32; 0.35) | 0.25 (0.21; 0.29) | 0.11 (0.09; 0.14) |
| S1 SD \* S1 AUD | 0.66 (0.49; 0.83) | 0.49 (0.26; 0.71) | 0.37 (0.35; 0.39) | 0.37 (0.29; 0.44) | 0.35 (0.31; 0.40) |
| S1 SD \* S1 DUD | 0.58 (0.37; 0.78) | 0.57 (0.34; 0.79) | 0.38 (0.36; 0.40) | 0.36 (0.28; 0.44) | 0.37 (0.31; 0.42) |
| S1 SD \* S2 SD | 0.81 (0.65; 0.98) | - | 0.20 (0.16; 0.25) | - | 0.13 (0.02; 0.25) |
| S1 SD \* S2 AUD | 0.55 (0.35; 0.75) | - | 0.19 (0.17; 0.22) | 0.08 (-0.01; 0.17) | 0.06 (0.00; 0.12) |
| S1 SD \* S2 DUD | 0.51 (0.28; 0.74) | - | 0.19 (0.17; 0.22) | 0.17 (0.08; 0.27) | 0.06 (-0.01; 0.12) |

**Supplemental Table 2.** Variance component estimates and 95% confidence intervals from univariate models.

|  |  |  |
| --- | --- | --- |
|  | FEMALES | MALES |
|  | Estimate | 95% Confidence Intervals | Estimate | 95% Confidence Intervals |
| Suicide Attempt |
| A | 0.41  | 0.30; 0.53 | 0.36  | 0.24; 0.48 |
| C | 0.06  | 0.01; 0.12 | 0.10  | 0.04; 0.16 |
| E | 0.52  | 0.47; 0.58 | 0.54  | 0.48; 0.60 |
|  |  |  |  |  |
| Alcohol Use Disorder |
| A | 0.59  | 0.55; 0.62 | 0.55  | 0.47; 0.62 |
| C | 0.00  | 0.00; 0.00 | 0.08  | 0.04; 0.11 |
| E | 0.41  | 0.38; 0.45 | 0.38  | 0.34; 0.42 |
|  |  |  |  |  |
| Drug Use Disorder |
| A | 0.39  | 0.25; 0.52 | 0.65  | 0.57; 0.74 |
| C | 0.17  | 0.10; 0.24 | 0.15  | 0.10; 0.19 |
| E | 0.44  | 0.37; 0.51 | 0.20  | 0.16; 0.24 |
|  |  |  |  |  |
| Suicide Death |
| A | 0.43  | 0.00; 0.58 | 0.44  | 0.31; 0.52 |
| C | 0.00  | 0.00; 0.26 | 0.00  | 0.00; 0.00 |
| E | 0.57  | 0.42; 0.74 | 0.56  | 0.48; 0.65 |

**Supplemental Table 3.** Genetic, shared environmental, and unique environmental correlations and 95% confidence intervals. Estimates for women are below the diagonal and estimates for men are above the diagonal. Correlations between AUD and DUD were estimated in two trivariate models, one with SA and one with SD. Given superior power in the former, results from that model are presented below.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Suicide Attempt** | **Alcohol Use Disorder** | **Drug Use Disorder** | **Suicide Death** |
| **Genetic Correlations (rA)** |
| Suicide Attempt |  | 0.60 (0.51; 1.00) | 0.62 (0.49; 0.68) | n/a |
| Alcohol Use Disorder | 0.72 (0.54; 1.00) |  | 0.67 (0.63; 0.71) | 0.72 (0.62; 1.00) |
| Drug Use Disorder | 0.88 (0.69; 0.88) | 0.90 (0.81; 0.96) |  | 0.48 (0.21; 0.66) |
| Suicide Death | n/a | 0.71 (0.59; 1.00) | 0.59 (0.57; 0.92) |  |
| **Shared Environmental Correlations (rC)** |
| Suicide Attempt |  | 0.76 (0.43; 1.00) | 0.59 (0.46; 1.00) | n/a |
| Alcohol Use Disorder | 0.89 (0.81; 1.00) |  | 0.87 (0.73; 1.00) | 1.00 (-0.55; 1.00) |
| Drug Use Disorder | 0.42 (0.30; 0.47) | 0.66 (-1.00; 1.00) |  | 0.94 (-1.00; 1.00) |
| Suicide Death | n/a | 0.92 (-1.00; 1.00) | 0.92 (-0.86; 1.00) |  |
| **Unique Environmental Correlations (rE)** |
| Suicide Attempt |  | 0.56 (0.39; 0.57) | 0.47 (0.39; 0.54) | n/a |
| Alcohol Use Disorder | 0.57 (0.53; 0.70) |  | 0.67 (0.63; 0.75) | -0.01 (-0.09; 0.08) |
| Drug Use Disorder | 0.42 (0.25; 0.48) | 0.43 (0.43; 0.49) |  | 0.17 (0.01; 0.57) |
| Suicide Death | n/a | 0.19 (0.09; 0.30) | 0.31 (0.16; 0.48) |  |

**Supplemental Table 4.** Bivariate variance decomposition estimates, which reflect the proportion of the phenotypic correlation that is accounted for by genetic (A), shared environmental (C), and unique environmental (E) factors shared across phenotypes. *SA=suicide attempt; SD=suicide death; AUD=alcohol use disorder; DUD=drug use disorder*

|  |  |  |  |
| --- | --- | --- | --- |
| *Women* | Bivariate A | Bivariate C | Bivariate E |
| SA-AUD | 55% | 4% | 41% |
| SA-DUD | 67% | 4% | 29% |
| SD-AUD | 73% | 3% | 24% |
| SD-DUD | 59% | 6% | 34% |
|  |  |  |  |
| *Men* |  |  |  |
| SA-AUD | 49% | 11% | 41% |
| SA-DUD | 61% | 14% | 25% |
| SD-AUD | 94% | 6% | 0% |
| SD-DUD | 73% | 11% | 16% |

**Supplemental Figure**. Variance component estimates and 95% confidence intervals for each outcome, stratified by sex, from univariate models. *SA=suicide attempt; SD=suicide death; AUD=alcohol use disorder; DUD=drug use disorder; A=genetic variance; C=shared environmental variance; E=unique environmental variance*

