**Supplementary Methods**

*Registry descriptions*

National Patient Register

In the 1960's the National Board of Health and Welfare started to collect information regarding in-patients at public hospitals, the National Patient Register (NPR). Initially it contained information about all patients treated in psychiatric care and approximately 16 percent of patients in somatic care. The register at that time covered six of the 26 county councils in Sweden. In 1984, the Ministry of Health and Welfare together with the Federation of County Councils decided a mandatory participation for all county councils. From 1987, NPR includes all in-patient care in Sweden. Since 2001, the register also covers outpatient doctor visits including day surgery and psychiatric care from both private and public caregivers. For more information, see https://www.socialstyrelsen.se/en/statistics-and-data/registers/register-information/the-national-patient-register/

Primary Care Registry

We also used information from our new Primary Care Registry (PCR), a research dataset including individual-level information on clinical diagnoses from primary health care centers from the following 15 of the 21 Swedish counties: Blekinge (2009-2016), Värmland (2005-2015), Kalmar (2007-2016), Sörmland (1997-2017), Uppsala (2005-2015), Västernorrland (2008-2015), Norrbotten (2009-2016), Gävleborg (2010-2016), Halland (2007-2014), Jönköping (2008-2014), Kronoberg (2006-2016), Skåne (1998-2013), Östergötland (1997-2014), Stockholm (2003-2016), and Västergötland (2000-2013). In 2016, these counties included 87% of the Swedish population. For more information see Sundquist, J., Ohlsson, H., Sundquist, K. et al. Common adult psychiatric disorders in Swedish primary care where most mental health patients are treated (Sundquist, Ohlsson, Sundquist, & Kendler, 2017).

*ICD codes*

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|  | Registers Used | Definition |
| Suicide Attempt (SA) | National Patient Register and Primary Care Registry | IC10: X60-X84 and Y10-Y34  For registrations prior to 1997  ICD9: E950-E959 and E980-E989 |
| Suicide death (SD) | The Swedish mortality register | IC10: X60-X84 and Y10-Y34  For registrations prior to 1997  ICD9: E950-E959 and E980-E989 |
| Alcohol Use Disorder (AUD) | National Patient Register and Primary Care Registry and the Swedish Drug Register (2005-2017); the Swedish Mortality Register, and the Swedish Criminal Register (1973-2017) and the Swedish Suspicion Register (1998-2017) | Alcohol Use Disorder (AUD) was identified in the Swedish medical and mortality registries by 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 Crime Register by codes 3005, 3201, which reflect crimes related to alcohol abuse; 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); in the Prescribed Drug Register by the drugs disulfiram (Anatomical Therapeutic Chemical (ATC) Classification System N07BB01), acamprosate (N07BB03), and naltrexone (N07BB04). |
| Cannabis | National Patient Register and Primary Care Registry | ICD-9: 304D ICD-10: F12 |
| Cocaine/Stimulants | National Patient Register and Primary Care Registry | ICD-9: 304C, 304E; ICD-10: F14, F15 |
| Hallucinogens | National Patient Register and Primary Care Registry | ICD-9: 304F ICD-10: F16 |
| Opiates | National Patient Register and Primary Care Registry | ICD-9: 304A ICD-10: F11 |
| Sedatives | National Patient Register and Primary Care Registry | ICD-9: 305E, 304B ICD-10: F13 |
| Multiple substance abuse | National Patient Register and Primary Care Registry | ICD-9: 304H; ICD-10: F19 |

*Family Genetic Risk Score derivation*

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| The dataset for the calculations includes:  Column1 = Identification number of the proband (Born 1932-1995)  Column2 = Identification number of the relative (1st to 5th degree relatives)  Column3 = Proportion of shared additive genetic effects (0.03125 to 0.50) with the proband  Column4 = Year of Birth of relative  Column5 = Sex of relative  Column6 = Age at registration for trait  Column7 = Age at end of follow-up (2017-12-31 or age at death, or age at emigration whichever came first) |
| **Step 1:** Using all unique relatives with a registration for the disorder, we non-parametrically estimated the distribution of *Age at first registration*. The empirical distribution is used to obtain weights for relatives without a registration for the disorder, in order to account for the proportion of the time-at-risk period they had completed at the end of follow-up. For example, for relatives at age x at end of follow-up, the weight corresponds to the proportion of relatives registered for the trait that had been registration at age x. For relatives born prior to 1958 we subtracted age at the end of follow-up with the following formula: 1958 - Year of birth of relative. This modification was done in order to control for registration effects (i.e., most registers in Sweden start in 1973 suggesting that relatives from early birth cohorts do not have the possibility to be registered at younger ages). Note that all relatives with the disorder are weighted one. |
| **Step 2:** Transform the binary variable (trait yes/no) into a z-score based on the threshold for each trait. The underlying liability of the individual is not assessable. Instead, we estimated the mean of the underlying liability to obtain sex and birth decade specific Z-scores for relatives with the trait registration and relatives without the trait. We generate n random numbers from a N (0, 1) distribution and estimate the mean for relatives registered with the disorder (i.e., mean of the observations above the threshold) and for relatives without a registration (i.e., mean of all observation below the threshold). The thresholds are calculated for each decade of birth and sex. |
| **Step 3**: Correct for cohabitation effects. To estimate the cohabitation effect (i.e., “shared environment”), we created a database with all individuals in the Swedish population born in Sweden 1955-1990. We also included the number of years, during ages 0-15, that individuals resided in the same household as their biological father. We thereby were able to define two kinds of families: i) “not-lived-with” father families (offspring never resided for more than 1 year in the same household or in the same community as their biological father); ii) “lived-with” father (offspring resided a minimum of 13 year in the same household as their biological father. We performed a logistic regression model with the binary trait in offspring as outcome and the binary trait in father, type of father, and their interaction as predictors. We used the interaction term as the difference of effect between genes only and genes + environment. The same approach was performed for half-siblings where we compared those who were reared together versus reared apart. The following interaction terms were used in the calculations for each of our 7 main disorders:   |  |  |  | | --- | --- | --- | |  | Parent/Children | Siblings | | SA | .66 | .76 | | SD | .70 | .98 | |
| **Step 4:** Calculate the product for each relative using the four components:   1. Z-score (reflecting sex and year of birth adjusted rates) 2. Weight (reflecting the proportion of risk period they had completed) 3. Cohabitation effects 4. Proportion of shared genetic effects (0.03125 – 0.5) with the proband |
| **Step 5:** Average the product calculated in step 4 across all relatives to a proband |
| **Step 6**: Correct for the number of relatives. We multiplied the results from step 5 with a shrinkage factor. Shrinkage factor (SF): B/(B+A/C). It produces more shrinkage if B and C are small and A is large.   1. the variance of the z-score of the disorder across all relatives, 2. the variance in the mean z-score across all probands, 3. the weighted number of relatives for each proband (sum of Column 3 across each proband). |
| **Step 7:** Correct for difference by year of birth and county differences. There are 21 counties in Sweden. For each proband we used the county they had resided in during the maximum number of years (measured from 1969 and onwards) We standardized the risk score by year of birth and county of the proband into a z-score with mean 0 and SD 1. This was then used as the FGRS in the analyses. |

**Supplementary Table 1.** Main effects of, and interaction effects with, family genetic risk scores for suicide attempt (FGRSSA). In each model, the predictors of interest were substance use disorder registration, FGRSSA, and the corresponding interaction term; covariates were sex, year of birth, and age at index suicide attempt. Results are presented as hazard ratios and 95% confidence intervals.

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|  | Main effect | | Interaction effect | |
|  | SUD registration | FGRSSA | Additive Scale (RERI) | Multiplicative Scale |
| AUD | 2.70 (2.49; 2.94) | 1.04 (0.98; 1.11) | 0.10 (-0.06; 0.26) | 1.01 (0.93; 1.10) |
| Cannabis | 2.95 (2.46; 3.53) | 1.08 (1.03; 1.12) | 0.01 (-0.43; 0.45) | 0.96 (0.82; 1.12) |
| Cocaine/Stimulants | 2.67 (2.32; 3.08) | 1.07 (1.03; 1.12) | -0.01 (-0.33; 0.30) | 0.95 (0.84; 1.08) |
| Hallucinogens | 3.31 (2.42; 4.54) | 1.08 (1.04; 1.12) | 0.40 (-0.51; 1.30) | 1.06 (0.83; 1.35) |
| Opiates | 3.79 (3.36; 4.27) | 1.05 (1.00; 1.10) | 0.27 (-0.08; 0.62) | 1.03 (0.94; 1.14) |
| Sedatives | 3.52 (3.17; 3.90) | 1.06 (1.01; 1.11) | 0.25 (-0.05; 0.55) | 1.03 (0.94; 1.13) |
| Multiple substance abuse | 3.70 (3.39; 4.03) | 1.02 (0.97; 1.08) | 0.14 (-0.09; 0.37) | 1.02 (0.94; 1.11) |

**Supplementary Table 2.** Results from a model testing the interaction between age at index suicide attempt and substance use disorder registration.

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|  | Main effect | | Interaction effect | |
|  | SUD registration | Age at SA | Additive Scale (RERI)1 | Multiplicative Scale |
| AUD | 3.53 (2.62; 4.75) | 0.995 (0.985; 1.005) | 0.03 (0.01; 0.05) | 0.992 (0.983; 1.001) |
| Cannabis | 3.05 (1.61; 5.78) | 0.996 (0.987; 1.005) | 0.01 (-0.05; 0.07) | 0.999 (0.979; 1.019) |
| Cocaine/Stimulants | 8.13 (4.78; 13.83) | 0.997 (0.988; 1.006) | 0.09 (0.05; 0.14) | 0.966 (0.950; 0.982) |
| Hallucinogens | 12.83 (3.89; 42.43) | 0.997 (0.988; 1.007) | 0.14 (0.04; 0.24) | 0.955 (0.916; 0.996) |
| Opiates | 7.18 (4.60; 11.20) | 0.994 (0.984; 1.003) | 0.09 (0.04; 0.15) | 0.981 (0.968; 0.994) |
| Sedatives | 5.38 (3.60; 7.86) | 0.998 (0.988; 1.007) | 0.05 (0.01; 0.10) | 0.987 (0.976; 0.999) |
| Multiple substance abuse | 7.16 (5.21; 9.84) | 0.996 (0.987; 1.006) | 0.09 (0.05; 0.12) | 0.980 (0.971; 0.989) |

1This is the RERI for one year decrease from the mean value of age at attempt (33 years).

RERI=relative excess risk due to interaction

**Supplementary Table 3.** Results from a multivariate Cox proportional hazards model in which a suicide attempt subsequent to the index attempt is included as a time-varying covariate (Model 3). Models 1 and 2, which do not include that covariate, are duplicated from the main text (Table 3) for reference.

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| --- | --- | --- | --- | --- | --- | --- |
|  | Model 1 | | Model 2 | | Model 3 | |
|  | Hazard Ratio | 95% CI | Hazard Ratio | 95% CI | Hazard Ratio | 95% CI |
| AUD | 2.72 | 2.50; 2.95 | 1.86 | 1.68; 2.05 | 1.76 | 1.60; 1.95 |
| Cannabis | 2.96 | 2.48; 3.53 | 1.18 | 0.97; 1.43 | 1.22 | 1.00; 1.48 |
| Cocaine/Stimulants | 2.68 | 2.33; 3.08 | 0.94 | 0.80; 1.11 | 0.94 | 0.80; 1.10 |
| Hallucinogens | 3.40 | 2.50; 4.62 | 1.35 | 0.98; 1.86 | 1.26 | 0.91; 1.73 |
| Opiates | 3.86 | 3.44; 4.34 | 1.58 | 1.37; 1.82 | 1.57 | 1.37; 1.81 |
| Sedatives | 3.56 | 3.22; 3.94 | 1.93 | 1.70; 2.18 | 1.69 | 1.49; 1.91 |
| Multiple substance abuse | 3.72 | 3.72; 4.05 | 2.09 | 1.86; 2.35 | 1.87 | 1.66; 2.11 |
| Subsequent suicide attempt | *n/a* | *n/a* | *n/a* | *n/a* | 2.63 | 2.40; 2.88 |

AUD – alcohol use disorder; CI – confidence interval

**Supplementary Figure 1.** Prevalence of suicide death (with 95% confidence intervals) among individuals with a previous non-fatal suicide attempt, as a function of registration status for substance use disorders.



**Supplementary Figure 2.** Inverse survival curves for the transition from suicide attempt to suicide death as a function of substance use disorder (SUD) registration. The blue line represents the prevalence of suicide death (y-axis) among individuals with a registration for the specific SUD; red line represents individuals without the SUD registration. Estimates are presented as a function of time elapsed in months since index suicide attempt (x-axis).

AUD – alcohol use disorder; MSA – multiple substance abuse.

Chart

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**Supplementary Figure 3.** Tetrachoric correlation matrix for suicide death and registration for each substance use disorder.



SD – suicide death; AUD – alcohol use disorder; CAN – cannabis; CO – cocaine/stimulants; HAL – hallucinogens; OP – opiates; SED – sedative; MSA – multiple substance abuse

**References**

Sundquist, J., Ohlsson, H., Sundquist, K., & Kendler, K. S. (2017). Common adult psychiatric disorders in Swedish primary care where most mental health patients are treated. *BMC Psychiatry, 17*(1), 235. doi:10.1186/s12888-017-1381-4