Supplementary tables for Latvala et al. *Association of parental substance misuse with offspring substance misuse and criminality: A genetically informed register-based study*

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | One offspring | Full sibling offspring | Half sibling offspring | One offspring in both parents | Full sibling offspring for both parents | Half sibling offspring for both parents | One offspring for one parent, full siblings for other | One offspring in one parent, half siblings in other | Full siblings in one parent, half siblings in other parent | Sum |
| Parent no sibling | 162,277 | 351,145 | 37,589 | 0 | 0 | 0 | 0 | 0 | 0 | 551,011 |
| Parents full siblings | 0 | 0 | 0 | 22,596 | 162,908 | 3,084 | 101,836 | 12,330 | 32,618 | 335,372 |
| Parents maternal half siblings | 0 | 0 | 0 | 2,636 | 9,238 | 472 | 8,852 | 1,766 | 3,548 | 26,512 |
| Parents paternal half siblings | 0 | 0 | 0 | 2,286 | 7,248 | 246 | 7,454 | 1,404 | 2,686 | 21,324 |
| Parents MZ twins | 0 | 0 | 0 | 96 | 1,018 | 22 | 470 | 36 | 188 | 1,830 |
| Parents DZ twins | 0 | 0 | 0 | 114 | 1,288 | 22 | 616 | 72 | 186 | 2,298 |
| Sum | 162,277 | 351,145 | 37,589 | 27,728 | 181,700 | 3,846 | 119,228 | 15,608 | 39,226 | 938,347 |

**Supplementary Table 1.** Number of parents used for quantitative genetic models based on fathers

**Supplementary Table 2.** Number of offspring used for quantitative genetic models based on fathers

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | One offspring | Full sibling offspring | Half sibling offspring | One offspring in both parents | Full sibling offspring for both parents | Half sibling offspring for both parents | One offspring for one parent, full siblings for other | One offspring in one parent, half siblings in other | Full siblings in one parent, half siblings in other parent | Sum |
| Parent no sibling | 162,277 | 702,290 | 75,178 | 0 | 0 | 0 | 0 | 0 | 0 | 939,745 |
| Parents full siblings | 0 | 0 | 0 | 22,596 | 325,816 | 6,168 | 152,754 | 18,495 | 65,236 | 591,065 |
| Parents maternal half siblings | 0 | 0 | 0 | 2,636 | 18,476 | 944 | 13,278 | 2,649 | 7,096 | 45,079 |
| Parents paternal half siblings | 0 | 0 | 0 | 2,286 | 14,496 | 492 | 11,181 | 2,106 | 5,372 | 35,933 |
| Parents MZ twins | 0 | 0 | 0 | 96 | 2,036 | 44 | 705 | 54 | 376 | 3,311 |
| Parents DZ twins | 0 | 0 | 0 | 114 | 2,576 | 44 | 924 | 108 | 372 | 4,138 |
| Sum | 162,277 | 702,290 | 75,178 | 27,728 | 363,400 | 7,692 | 178,842 | 23,412 | 78,452 | 1,619,271 |

**Supplementary Table 3.** Number of parents used for quantitative genetic models based on mothers

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | One offspring | Full sibling offspring | Half sibling offspring | One offspring in both parents | Full sibling offspring for both parents | Half sibling offspring for both parents | One offspring for one parent, full siblings for other | One offspring in one parent, half siblings in other | Full siblings in one parent, half siblings in other parent | Sum |
| Parent no sibling | 160,098 | 361,513 | 37,750 | 0 | 0 | 0 | 0 | 0 | 0 | 559,361 |
| Parents full siblings | 0 | 0 | 0 | 21,914 | 168,100 | 3,818 | 98,894 | 12,820 | 33,464 | 339,010 |
| Parents maternal half siblings | 0 | 0 | 0 | 2,754 | 10,830 | 894 | 9,828 | 2,782 | 4,890 | 31,978 |
| Parents paternal half siblings | 0 | 0 | 0 | 2,212 | 8,162 | 406 | 7,640 | 1,824 | 3,066 | 23,310 |
| Parents MZ twins | 0 | 0 | 0 | 222 | 1,342 | 46 | 564 | 56 | 214 | 2,444 |
| Parents DZ twins | 0 | 0 | 0 | 174 | 1,446 | 24 | 698 | 90 | 238 | 2,670 |
| Sum | 160,098 | 361,513 | 37,750 | 27,276 | 189,880 | 5,188 | 117,624 | 17,572 | 41,872 | 958,773 |

**Supplementary Table 4.** Number of offspring used for quantitative genetic models based on mothers

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | One offspring | Full sibling offspring | Half sibling offspring | One offspring in both parents | Full sibling offspring for both parents | Half sibling offspring for both parents | One offspring for one parent, full siblings for other | One offspring in one parent, half siblings in other | Full siblings in one parent, half siblings in other parent | Sum |
| Parent no sibling | 160,098 | 723,026 | 75,500 | 0 | 0 | 0 | 0 | 0 | 0 | 958,624 |
| Parents full siblings | 0 | 0 | 0 | 21,914 | 336,200 | 7,636 | 148,341 | 19,230 | 66,928 | 600,249 |
| Parents maternal half siblings | 0 | 0 | 0 | 2,754 | 21,660 | 1,788 | 14,742 | 4,173 | 9,780 | 54,897 |
| Parents paternal half siblings | 0 | 0 | 0 | 2,212 | 16,324 | 812 | 11,460 | 2,736 | 6,132 | 39,676 |
| Parents MZ twins | 0 | 0 | 0 | 222 | 2,684 | 92 | 846 | 84 | 428 | 4,356 |
| Parents DZ twins | 0 | 0 | 0 | 174 | 2,892 | 48 | 1,047 | 135 | 476 | 4,772 |
| Sum | 160,098 | 723,026 | 75,500 | 27,276 | 379,760 | 10,376 | 176,436 | 26,358 | 83,744 | 1,662,574 |

**Supplementary Table 5.** Person-years at risk and rates (95% confidence intervals) of substance misuse events and criminal convictions in the offspring by paternal and maternal substance misuse

|  |  |  |  |
| --- | --- | --- | --- |
|  | Paternal substance misuse | Maternal substance misuse | Total |
|  | Yes | No | Yes | No |  |
| Offspring substance misuse |  |  |  |  |  |
| Person-years at risk | 10,242,027 | 59,674,854 | 3,139,629 | 66,777,252 | 69,916,881 |
| Rate (95% CI) per 10,000 person-years | 54.9 (54.4; 55.3) | 22.1 (22.0; 22.3) | 70.3 (69.4; 71.2) | 24.9 (24.8; 25.0) | 26.9 (26.8; 27.1) |
| Offspring criminal convictions |  |  |  |  |  |
| Person-years at risk | 9,724,777 | 57,866,098 | 2,971,651 | 64,619,224 | 67,590,874 |
| Rate (95% CI) per 10,000 person-years | 81.9 (81.4; 82.5) | 39.7 (39.5; 39.8) | 97.3 (96.2) | 43.4 (43.2; 43.5) | 45.7 (45.6; 45.9) |

**Supplementary Table 6.** Observed correlations, father’s substance misuse (SM) and offspring’s substance misuse, estimate (standard error)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | Unadjusted |  |  | Adjusted\* |  |
|  | SM parent | SM offspring | SM parent - SM offspring | SM parent | SM offspring | SM parent - SM offspring |
| Within nuclear family | NA | NA | 0.284 (0.002) | NA | NA | 0.263 (0.002) |
| Within nuclear family, Full siblings | NA | 0.282 (0.004) | NA | NA | 0.275 (0.004) | NA |
| Within nuclear family, Half siblings | NA | 0.153 (0.008) | NA | NA | 0.103 (0.010) | NA |
| Between nuclear families, Parents MZ twins | 0.620 (0.055) | 0.134 (0.066) | 0.333 (0.047) | 0.507 (0.077) | 0.080 (0.076) | 0.254 (0.055) |
| Between nuclear families, Parents DZ twins | 0.546 (0.018) | 0.169 (0.035) | 0.143 (0.044) | 0.457 (0.066) | 0.157 (0.101) | 0.105 (0.052) |
| Between nuclear families, Parents full siblings | 0.332 (0.005) | 0.079 (0.005) | 0.143 (0.004) | 0.303 (0.005) | 0.070 (0.005) | 0.124 (0.004) |
| Between nuclear families, Parents maternal half siblings | 0.245 (0.013) | 0.074 (0.014) | 0.123 (0.010) | 0.159 (0.016) | 0.046 (0.016) | 0.076 (0.011) |
| Between nuclear families, Parents paternal half siblings | 0.148 (0.016) | 0.041 (0.017) | 0.066 (0.012) | 0.080 (0.019) | 0.020 (0.019) | 0.027 (0.014) |
|  |  |  |  |

\* Both parental and offspring expected prevalence adjusted for extended family type (parents being: without sibling, full siblings, maternal half siblings, paternal half siblings, MZ twin, or DZ twins), nuclear family type (offspring being: without sibling, full siblings, half siblings), parental phenotype additionally adjusted for parent's birth year, and offspring phenotype additionally adjusted for offspring sex and birth year.

**Supplementary Table 7.** Observed correlations, father’s substance misuse (SM) and offspring’s crime, estimate (standard error)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | Unadjusted |  |  | Adjusted\* |  |
|  | SM parent | Crime offspring | SM parent - Crime offspring | SM parent | Crime offspring | SM parent - Crime offspring |
| Within nuclear family | NA | NA | 0.247 (0.002) | NA | NA | 0.233 (0.002) |
| Within nuclear family, Full siblings | NA | 0.272 (0.003) | NA | NA | 0.262 (0.003) | NA |
| Within nuclear family, Half siblings | NA | 0.140 (0.006) | NA | NA | 0.122 (0.008) | NA |
| Between nuclear families, Parents MZ twins | 0.621 (0.061) | 0.083 (0.057) | 0.188 (0.047) | 0.504 (0.068) | 0.054 (0.064) | 0.131 (0.051) |
| Between nuclear families, Parents DZ twins | 0.551 (0.061) | 0.077 (0.050) | 0.158 (0.040) | 0.462 (0.066) | 0.049 (0.049) | 0.131 (0.044) |
| Between nuclear families, Parents full siblings | 0.332 (0.005) | 0.096 (0.004) | 0.134 (0.003) | 0.302 (0.005) | 0.082 (0.004) | 0.119 (0.003) |
| Between nuclear families, Parents maternal half siblings | 0.246 (0.013) | 0.063 (0.011) | 0.081 (0.009) | 0.159 (0.016) | 0.045 (0.014) | 0.044 (0.011) |
| Between nuclear families, Parents paternal half siblings | 0.149 (0.016) | 0.034 (0.014) | 0.058 (0.011) | 0.082 (0.019) | 0.025 (0.016) | 0.031 (0.012) |
|  |  |  |  |

\* Both parental and offspring expected prevalence adjusted for extended family type (parents being: without sibling, full siblings, maternal half siblings, paternal half siblings, MZ twin, or DZ twins), nuclear family type (offspring being: without sibling, full siblings, half siblings), parental phenotype additionally adjusted for parent's birth year, and offspring phenotype additionally adjusted for offspring sex and birth year.

**Supplementary Table 8.** Observed correlations, mother’s substance misuse (SM) and offspring’s substance misuse, estimate (standard error)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | Unadjusted |  |  | Adjusted\* |  |
|  | SM parent | SM offspring | SM parent - SM offspring | SM parent | SM offspring | SM parent - SM offspring |
| Within nuclear family | NA | NA | 0.287 (0.003) | NA | NA | 0.262 (0.003) |
| Within nuclear family, Full siblings | NA | 0.290 (0.004) | NA | NA | 0.279 (0.004) | NA |
| Within nuclear family, Half siblings | NA | 0.208 (0.008) | NA | NA | 0.185 (0.009) | NA |
| Between nuclear families, Parents MZ twins | 0.670 (0.099) | 0.195 (0.059) | 0.221 (0.061) | 0.571 (0.095) | 0.160 (0.059) | 0.171 (0.065) |
| Between nuclear families, Parents DZ twins | 0.297 (0.118) | 0.113 (0.059) | 0.140 (0.065) | 0.233 (0.118) | 0.101 (0.059) | 0.093 (0.063) |
| Between nuclear families, Parents full siblings | 0.303 (0.009) | 0.101 (0.004) | 0.143 (0.005) | 0.267 (0.009) | 0.089 (0.005) | 0.116 (0.005) |
| Between nuclear families, Parents maternal half siblings | 0.226 (0.021) | 0.072 (0.012) | 0.120 (0.015) | 0.163 (0.023) | 0.040 (0.014) | 0.074 (0.013) |
| Between nuclear families, Parents paternal half siblings | 0.134 (0.026) | 0.066 (0.016) | 0.071 (0.015) | 0.089 (0.030) | 0.046 (0.017) | 0.037 (0.017) |
|  |  |  |  |

\* Both parental and offspring expected prevalence adjusted for extended family type (parents being: without sibling, full siblings, maternal half siblings, paternal half siblings, MZ twin, or DZ twins), nuclear family type (offspring being: without sibling, full siblings, half siblings), parental phenotype additionally adjusted for parent's birth year, and offspring phenotype additionally adjusted for offspring sex and birth year.

**Supplementary Table 9.** Observed correlations, mother’s substance misuse (SM) and offspring’s crime, estimate (standard error)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | Unadjusted |  |  | Adjusted\* |  |
|  | SM parent | Crime offspring | SM parent - Crime offspring | SM parent | Crime offspring | SM parent - Crime offspring |
| Within nuclear family | NA | NA | 0.243 (0.003) | NA | NA | 0.225 (0.003) |
| Within nuclear family, Full siblings | NA | 0.276 (0.003) | NA | NA | 0.265 (0.003) | NA |
| Within nuclear family, Half siblings | NA | 0.193 (0.006) | NA | NA | 0.179 (0.008) | NA |
| Between nuclear families, Parents MZ twins | 0.666 (0.085) | 0.162 (0.044) | 0.249 (0.053) | 0.571 (0.095) | 0.127 (0.048) | 0.236 (0.057) |
| Between nuclear families, Parents DZ twins | 0.288 (0.121) | 0.130 (0.041) | 0.146 (0.051) | 0.227 (0.120) | 0.096 (0.047) | 0.101 (0.056) |
| Between nuclear families, Parents full siblings | 0.303 (0.008) | 0.108 (0.004) | 0.129 (0.004) | 0.266 (0.009) | 0.094 (0.004) | 0.106 (0.005) |
| Between nuclear families, Parents maternal half siblings | 0.229 (0.019) | 0.054 (0.010) | 0.092 (0.010) | 0.164 (0.023) | 0.031 (0.012) | 0.048 (0.012) |
| Between nuclear families, Parents paternal half siblings | 0.130 (0.025) | 0.057 (0.013) | 0.061 (0.013) | 0.087 (0.031) | 0.051 (0.015) | 0.041 (0.015) |
|  |  |  |  |

\* Both parental and offspring expected prevalence adjusted for extended family type (parents being: without sibling, full siblings, maternal half siblings, paternal half siblings, MZ twin, or DZ twins), nuclear family type (offspring being: without sibling, full siblings, half siblings), parental phenotype additionally adjusted for parent's birth year, and offspring phenotype additionally adjusted for offspring sex and birth year.

**Supplementary Table 10.** Cox proportional hazard ratios (95% confidence intervals) for substance misuse and criminal convictions associated with paternal and maternal substance misuse as time varying covariates

|  |  |  |
| --- | --- | --- |
|  | Individual-level analysis | Within-family analysis1 |
|  | Minimally adjusted model2 | Fully adjusted model3 | Minimally adjusted model2 | Fully adjusted model3 |
| **Paternal substance misuse**  |  |  |  |  |
| Offspring substance misuse: Lifetime | 2.62 (2.59; 2.65) | 2.00 (1.98; 2.02) | 1.79 (1.69; 1.90) | 1.55 (1.45; 1.65) |
| Offspring substance misuse: By age 18 | 2.79 (2.73; 2.85) | 2.04 (2.00; 2.09) | 1.86 (1.67; 2.07) | 1.56 (1.40; 1.75) |
| Offspring criminality: Lifetime | 2.23 (2.21; 2.25) | 1.72 (1.71; 1.74) | 1.64 (1.56; 1.72) | 1.46 (1.39; 1.54) |
| Offspring criminality: By age 18 | 2.42 (2.40; 2.45) | 1.81 (1.79; 1.84) | 1.66 (1.56; 1.77) | 1.46 (1.37; 1.56) |
| **Maternal substance misuse**  |  |  |  |  |
| Offspring substance misuse: Lifetime | 2.98 (2.94; 3.03) | 1.80 (1.77; 1.83) | 1.89 (1.71; 2.08) | 1.45 (1.31; 1.61) |
| Offspring substance misuse: By age 18 | 3.38 (3.28; 3.49) | 1.83 (1.77; 1.90) | 2.14 (1.80; 2.54) | 1.61 (1.34; 1.94) |
| Offspring criminality: Lifetime | 2.45 (2.41; 2.49) | 1.59 (1.56; 1.61) | 1.83 (1.68; 2.00) | 1.45 (1.32; 1.58) |
| Offspring criminality: By age 18 | 2.67 (2.61; 2.72) | 1.60 (1.57; 1.64) | 1.88 (1.68; 2.10) | 1.47 (1.31; 1.65) |

1 Stratified Cox regression in pairs of paternal/maternal full cousins

2 Adjusted for parental and offspring birth years and offspring sex

3 Further adjusted for birth year and substance misuse of the co-parent, and immigrant status, educational level and psychiatric disorders of both parents

**Supplementary Table 11.** Cox proportional hazard ratios (95% confidence intervals) for substance misuse and criminal convictions associated with paternal and maternal substance misuse of parents born after 1957

|  |  |  |
| --- | --- | --- |
|  | Individual-level analysis | Within-family analysis1 |
|  | Minimally adjusted model2 | Fully adjusted model3 | Minimally adjusted model2 | Fully adjusted model3 |
| **Paternal substance misuse**  |  |  |  |  |
| Offspring substance misuse | 2.43 (2.39; 2.48) | 1.90 (1.87; 1.95) | 1.80 (1.59; 2.02) | 1.63 (1.44; 1.85) |
| Offspring criminality | 2.15 (2.12; 2.18) | 1.67 (1.64; 1.70) | 1.60 (1.44; 1.78) | 1.46 (1.31; 1.63) |
| **Maternal substance misuse**  |  |  |  |  |
| Offspring substance misuse | 2.74 (2.67; 2.81) | 1.77 (1.72; 1.82) | 1.83 (1.53; 2.18) | 1.53 (1.27; 1.85) |
| Offspring criminality | 2.25 (2.21; 2.31) | 1.53 (1.49; 1.57) | 1.91 (1.64; 2.24) | 1.66 (1.41; 1.96) |

1 Stratified Cox regression in pairs of paternal/maternal full cousins

2 Adjusted for parental and offspring birth years and offspring sex

3 Further adjusted for birth year and substance misuse of the co-parent, and immigrant status, educational level and psychiatric disorders of both parents

**Supplementary Table 12.** Cox proportional hazard ratios (95% confidence intervals) for substance misuse and criminal convictions associated with paternal and maternal substance misuse in male and female offspring

|  |  |  |
| --- | --- | --- |
|  | Male offspring | Female offspring |
|  | Minimally adjusted model1 | Fully adjusted model2 | Minimally adjusted model1 | Fully adjusted model2 |
| **Paternal substance misuse**  |  |  |  |  |
| Offspring substance misuse | 2.52 (2.49; 2.56) | 1.98 (1.95; 2.00) | 2.50 (2.45; 2.54) | 1.91 (1.88; 1.95) |
| Offspring criminality | 2.05 (2.03; 2.07) | 1.64 (1.62; 1.66) | 2.16 (2.13; 2.20) | 1.71 (1.68; 1.74) |
| **Maternal substance misuse**  |  |  |  |  |
| Offspring substance misuse | 2.68 (2.63; 2.73) | 1.78 (1.74; 1.81) | 3.12 (3.05; 3.20) | 1.96 (1.90; 2.02) |
| Offspring criminality | 2.12 (2.09; 2.15) | 1.52 (1.50; 1.55) | 2.43 (2.37; 2.49) | 1.67 (1.62; 1.71) |

1 Adjusted for parental and offspring birth years and offspring sex

2 Further adjusted for birth year and substance misuse of the co-parent, and immigrant status, educational level and psychiatric disorders of both parents

**Supplementary Table 13.** Cox proportional hazard ratios (95% confidence intervals) for offspring outcomes from within-family Cox models stratified by the birth order of sibling parents. Fully adjusted results.

|  |  |  |
| --- | --- | --- |
|  | Substance misuse in older sibling parent | Substance misuse in younger sibling parent |
| **Paternal substance misuse**  |  |  |
| Offspring substance misuse | 1.52 (1.36-1.70) | 1.65 (1.47-1.84) |
| Offspring criminality | 1.43 (1.30-1.56) | 1.40 (1.28-1.53) |
| **Maternal substance misuse**  |  |  |
| Offspring substance misuse | 1.65 (1.36-2.01) | 1.35 (1.12-1.61) |
| Offspring criminality | 1.70 (1.44-2.01) | 1.52 (1.30-1.77) |