**Supplementary Materials**

1. **Supplementary Methods**

The childhood and adolescent tier included family history of AUD or DUD of the biological parents or siblings, any sexual abuse, vulnerable family environment (assessed using the childhood emotional neglect scale of the Childhood Trauma Questionnaire)1 and parental loss (parent’s divorce or death of at least one parent before the participant was 18 years old), impulsivity (dichotomous, scored 1 if the respondents considered that they had often done things impulsively), low self-esteem (dichotomous, scored 1 if respondents stated they had often been very critical of themselves), early onset of SUD (AUD, DUD or TUD with onset before age 18), and social deviance (assessed as the number of conduct disorder or antisocial personality disorder (ASPD) behaviors before age 15, range 0 to 33).

The late adolescence tier included educational attainment (in years), number of axis I disorders with onset before age 21, and number of personality disorders.

The adulthood tier included any history of trauma out of the list of 23 traumatic events that measure post-traumatic stress disorder (PTSD), history of divorce, lifetime history of SUD, lifetime history of mood or anxiety disorders, lifetime history of eating disorders and social deviance (assessed as the number of conduct disorder or antisocial personality disorder (ASPD) behaviors after age 15, range 0 to 33).

The past year tier included lack of social support (assessed with the Interpersonal Social Support Evaluation List)2 past year AUD, TUD, comorbidity with psychiatric disorders other than SUD, religious service attendance, marital problems (whether the respondent got separated, divorced or broke off a steady relationship in the last 12 months), and number of stressful life events in the past year (range 0-14), and social deviance (measured as the number of ASPD behaviors in which the respondent engaged after age 15).

References

1. Bernstein DP, Fink L, Handelsman L, Foote J, Lovejoy M, Wenzel K, et al. Initial reliability and validity of a new retrospective measure of child abuse and neglect. Am J Psychiatry. 1994;151:1132–1136
2. Cohen S MR, Kamarck T, Hoberman HM: Measuring the functional components of social support. Social support: theory, research, and applications ed. In: Sarason IG SB, editors, editor. The Hague, Holland 1985.

**2. Supplementary Tables**

**Supplemental Table 1: SEM direct effects between risk factors in each tier and past year psychopathology**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|   | **Late Adolescence** |   | **Adulthood** |   | **Past Year**  |   | **Past year psychopathology**  |
|   | Edu | PD | Axis1 |   | Hx Trma | Divor | Hx SUD | Hx MA | Hx ED | Soc Dev |   | Lack socsup | Religion | Marital prob | SLE |   | General psychopathology | Internaliz-ing-Fear factor | Externaliz-ing factor |
| **Childhood/Early Adolescence** |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Family history (FH) of AUD/DUD | **-0.061** | 0.013 | **0.036** |   | **0.049** | **0.039** | **0.076** | **0.027** | 0.006 | **0.047** |   | -0.008 | -0.011 | 0.011 | **0.054** |   | 0.013 | -0.001 | **0.042** |
| FH of MDD | **0.095** | **0.067** | **0.054** |   | **0.086** | 0.001 | **0.042** | **0.153** | **0.030** | **0.016** |   | -0.013 | 0.010 | 0.006 | **0.050** |   | **0.019** | -0.006 | -0.020 |
| Sexual abuse | 0.017 | **0.064** | **0.031** |   | **0.174** | **0.046** | 0.021 | **0.074** | 0.027 | **0.027** |   | 0.020 | 0.018 | 0.017 | **0.047** |   | **0.026** | -0.014 | 0.003 |
| Vulnerable family environment | **-0.137** | **0.054** | -0.011 |   | 0.000 | 0.027 | -0.002 | **0.029** | 0.007 | 0.012 |   | **0.260** | **-0.071** | -0.009 | -0.004 |   | 0.004 | -0.005 | **-0.040** |
| Parental loss | **-0.058** | -0.001 | 0.012 |   | **0.031** | **0.042** | **0.030** | 0.009 | -0.012 | **0.032** |   | -0.018 | **-0.038** | 0.014 | **0.029** |   | 0.005 | -0.004 | 0.003 |
| Impulsivity | **-0.046** | **0.224** | **0.083** |   | **0.044** | **0.034** | **0.068** | **0.031** | -0.008 | **0.185** |   | -0.010 | 0.003 | 0.016 | 0.013 |   | 0.020 | -0.016 | 0.043 |
| Low self-esteem | **0.084** | **0.152** | **0.078** |   | **0.099** | **0.032** | **0.070** | **0.176** | **0.051** | **0.065** |   | **0.058** | -0.009 | 0.017 | **0.036** |   | **0.043** | **0.038** | 0.001 |
| Childhood-onset SUD | **-0.065** | 0.026 | **0.040** |   | **0.033** | **0.034** | **0.283** | **0.036** | 0.011 | **0.083** |   | -0.007 | 0.009 | 0.012 | 0.014 |   | **0.029** | 0.007 | **0.040** |
| Social deviance (before 15) | **-0.033** | **0.392** | **0.068** |   | **0.071** | -0.017 | **0.042** | 0.001 | 0.009 | **0.513** |   | **-0.043** | 0.012 | -0.027 | -0.023 |   | **-0.046** | -0.009 | -0.006 |
| **Late Adolescence** |   |   |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |
| Education years |   |   |   |   | 0.024 | -0.028 | -0.003 | 0.012 | **0.022** | **-0.031** |   | **-0.061** | **0.053** | -0.001 | -0.016 |   | **-0.054** | **-0.023** | **-0.065** |
| Number of personality disorders |   |   |   |   | **0.048** | **0.033** | 0.024 | **0.172** | **0.085** | **0.126** |   | **0.115** | 0.016 | **0.041** | **0.083** |   | **0.178** | **0.121** | **-0.044** |
| Number of Axis I disorders (before 21) |   |   |   |   | **0.039** | 0.007 | **0.304** | **0.157** | **0.076** | **0.067** |   | 0.007 | 0.007 | 0.012 | 0.010 |   | **0.048** | 0.021 | **0.037** |
| **Adulthood** |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| History of trauma |   |   |   |   |   |   |   |   |   |   |   | **-0.029** | 0.010 | 0.017 | **0.056** |   | **0.019** | -0.015 | -0.016 |
| Ever divorced |   |   |   |   |   |   |   |   |   |   |   | 0.002 | **-0.075** | **0.084** | **0.041** |   | 0.005 | -0.016 | 0.011 |
| History of SUD |   |   |   |   |   |   |   |   |   |   |   | 0.011 | **-0.095** | 0.009 | **0.077** |   | **0.070** | -0.004 | **0.279** |
| History of Mood or Anxiety Disorder |   |   |   |   |   |   |   |   |   |   |   | **0.058** | -0.002 | 0.018 | **0.073** |   | **0.471** | **0.353** | **-0.109** |
| History of Eating Disorder |   |   |   |   |   |   |   |   |   |   |   | -0.009 | 0.014 | -0.002 | 0.001 |   | **0.092** | -0.009 | **-0.034** |
| Social deviance |   |   |   |   |   |   |   |   |   |   |   | 0.038 | **-0.092** | **0.079** | **0.183** |   | **0.050** | -0.046 | **0.169** |
| **Past year** |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |   |   |
| Lack of social support |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | **0.055** | 0.007 | 0.005 |
| Religious service attendance |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | **-0.038** | -0.008 | **-0.087** |
| Marital problems |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | **0.029** | **-0.030** | **0.037** |
| Stressful life events |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | **0.091** | -0.010 | **0.122** |
| \*All values represent standardized path coefficients. Values > 0.05 highlighted in red; Values < -0.05 highlighted in green. All bolded values are statistically significant after Bonferroni correction p<0.0002 (.05/237 paths tested) |

**Supplemental Table 1: SEM direct effects between risk factors in each tier and past year psychopathology**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|   | **Late Adolescence** |   | **Adulthood** |   | **Past Year**  |   | **Past year psychopathology**  |
|   | Edu | PD | Axis1 |   | Hx Trma | Divor | Hx SUD | Hx MA | Hx ED | Soc Dev |   | Lack socsup | Religion | Marital prob | SLE |   | General psychopathology | Fear | Externaliz-ing factor |
| **Childhood/Early Adolescence** |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Family history (FH) of AUD/DUD | **-0.061** | 0.013 | **0.036** |   | **0.049** | **0.039** | **0.076** | **0.027** | 0.006 | **0.047** |   | -0.008 | -0.011 | 0.011 | **0.054** |   | 0.013 | -0.001 | **0.042** |
| FH of MDD | **0.095** | **0.067** | **0.054** |   | **0.086** | 0.001 | **0.042** | **0.153** | **0.030** | **0.016** |   | -0.013 | 0.010 | 0.006 | **0.050** |   | **0.019** | -0.006 | -0.020 |
| Sexual abuse | 0.017 | **0.064** | **0.031** |   | **0.174** | **0.046** | 0.021 | **0.074** | 0.027 | **0.027** |   | 0.020 | 0.018 | 0.017 | **0.047** |   | **0.026** | -0.014 | 0.003 |
| Vulnerable family environment | **-0.137** | **0.054** | -0.011 |   | 0.000 | 0.027 | -0.002 | **0.029** | 0.007 | 0.012 |   | **0.260** | **-0.071** | -0.009 | -0.004 |   | 0.004 | -0.005 | **-0.040** |
| Parental loss | **-0.058** | -0.001 | 0.012 |   | **0.031** | **0.042** | **0.030** | 0.009 | -0.012 | **0.032** |   | -0.018 | **-0.038** | 0.014 | **0.029** |   | 0.005 | -0.004 | 0.003 |
| Impulsivity | **-0.046** | **0.224** | **0.083** |   | **0.044** | **0.034** | **0.068** | **0.031** | -0.008 | **0.185** |   | -0.010 | 0.003 | 0.016 | 0.013 |   | 0.020 | -0.016 | 0.043 |
| Low self-esteem | **0.084** | **0.152** | **0.078** |   | **0.099** | **0.032** | **0.070** | **0.176** | **0.051** | **0.065** |   | **0.058** | -0.009 | 0.017 | **0.036** |   | **0.043** | **0.038** | 0.001 |
| Childhood-onset SUD | **-0.065** | 0.026 | **0.040** |   | **0.033** | **0.034** | **0.283** | **0.036** | 0.011 | **0.083** |   | -0.007 | 0.009 | 0.012 | 0.014 |   | **0.029** | 0.007 | **0.040** |
| Social deviance | **-0.033** | **0.392** | **0.068** |   | **0.071** | -0.017 | **0.042** | 0.001 | 0.009 | **0.513** |   | **-0.043** | 0.012 | -0.027 | -0.023 |   | **-0.046** | -0.009 | -0.006 |
| **Late Adolescence** |   |   |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |
| Education years |   |   |   |   | 0.024 | -0.028 | -0.003 | 0.012 | **0.022** | **-0.031** |   | **-0.061** | **0.053** | -0.001 | -0.016 |   | **-0.054** | **-0.023** | **-0.065** |
| Number of personality disorders (PD) |   |   |   |   | **0.048** | **0.033** | 0.024 | **0.172** | **0.085** | **0.126** |   | **0.115** | 0.016 | **0.041** | **0.083** |   | **0.178** | **0.121** | **-0.044** |
| Number of Axis I disorders before age 21 (Axis1) |   |   |   |   | **0.039** | 0.007 | **0.304** | **0.157** | **0.076** | **0.067** |   | 0.007 | 0.007 | 0.012 | 0.010 |   | **0.048** | 0.021 | **0.037** |
| **Adulthood** |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| History of trauma |   |   |   |   |   |   |   |   |   |   |   | **-0.029** | 0.010 | 0.017 | **0.056** |   | **0.019** | -0.015 | -0.016 |
| Ever divorced |   |   |   |   |   |   |   |   |   |   |   | 0.002 | **-0.075** | **0.084** | **0.041** |   | 0.005 | -0.016 | 0.011 |
| History of SUD |   |   |   |   |   |   |   |   |   |   |   | 0.011 | **-0.095** | 0.009 | **0.077** |   | **0.070** | -0.004 | **0.279** |
| History of Mood or Anxiety Disorder |   |   |   |   |   |   |   |   |   |   |   | **0.058** | -0.002 | 0.018 | **0.073** |   | **0.471** | **0.353** | **-0.109** |
| History of Eating Disorder |   |   |   |   |   |   |   |   |   |   |   | -0.009 | 0.014 | -0.002 | 0.001 |   | **0.092** | -0.009 | **-0.034** |
| Social deviance |   |   |   |   |   |   |   |   |   |   |   | 0.038 | **-0.092** | **0.079** | **0.183** |   | **0.050** | -0.046 | **0.169** |
| **Past year** |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |   |   |
| Lack of social support |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | **0.055** | 0.007 | 0.005 |
| Religious service attendance |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | **-0.038** | -0.008 | **-0.087** |
| Marital problems |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | **0.029** | **-0.030** | **0.037** |
| Stressful life events |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | **0.091** | -0.010 | **0.122** |
| \*All values represent standardized path coefficients. Values > 0.05 highlighted in red; Values < -0.05 highlighted in green. All highlighted paths are statistically significant after Bonferroni correction. |

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| --- |
| **Supplemental Table 2. Statistically significant direct effects of risk factors on individual psychiatric disordersa** |
| Disorder | Risk Factors | Modification Index | Standardized Direct Effect |  |  |  |  |
| Generalized Anxiety Disorder | History of mood or anxiety disorders | 21.5 | 0.525 |  |  |  |  |
| Tobacco Use Disorder | Family history of substance use disorders | 49.1 | 0.499 |  |  |  |  |
| PTSD | Family history of substance use disorders | 35.5 | 0.401 |  |  |  |  |
| Tobacco Use Disorder | History of trauma | 46.8 | 0.375 |  |  |  |  |
| PTSD | History of trauma | 37.3 | 0.371 |  |  |  |  |
| Eating Disorders | History of Eating Disorders | 555.8 | 0.308 |  |  |  |  |
| PTSD | History of mood or anxiety disorders | 24.1 | 0.307 |  |  |  |  |
| PTSD | Low self-esteem | 31.0 | 0.303 |  |  |  |  |
| Tobacco Use Disorder | History of substance use disorders | 39.4 | 0.272 |  |  |  |  |
| Alcohol Use Disorder | Educational attainment | 129.1 | 0.246 |  |  |  |  |
| Tobacco Use Disorder | Childhood onset substance use disorder | 71.0 | 0.224 |  |  |  |  |
| Alcohol Use Disorder | Ages 21-29 | 92.9 | 0.210 |  |  |  |  |
| Bipolar Disorder | History of substance use disorders | 35.6 | 0.208 |  |  |  |  |
| Eating Disorders | Educational attainment | 37.3 | 0.206 |  |  |  |  |
| Tobacco Use Disorder | Ages 21-29 | 100.2 | -0.200 |  |  |  |  |
| Tobacco Use Disorder | Educational attainment | 107.3 | -0.201 |  |  |  |  |
| Major Depressive Disorder | Low self-esteem | 25.9 | -0.250 |  |  |  |  |
| Major Depressive Disorder | History of trauma | 23.4 | -0.257 |  |  |  |  |
| Alcohol Use Disorder | History of trauma | 26.2 | -0.305 |  |  |  |  |
| Eating Disorders | History of trauma | 33.6 | -0.471 |  |  |  |  |
| Eating Disorders | Family history of substance use disorders | 40.1 | -0.483 |  |  |  |  |
| Alcohol Use Disorder | Family history of substance use disorders | 48.2 | -0.527 |  |  |  |  |
| Eating Disorders | History of mood or anxiety disorders | 114.4 | -0.801 |  |  |  |  |
| 1. All standardized direct effects with absolute value > 0.20 are shown and presented sorted from largest to smallest
 |
| Estimates in italics indicate direct effects in the opposite direction as the total effect |  |