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## Supplementary Methods

***Participants***

HC participants in the EU-GEI High Risk study were recruited from four sites using the following means: through GP lists, national postal address file, and the website Gumtree in London; by online advertisement in Melbourne; through the website Proefbunny in Amsterdam and the Hague.

***Assessments and Measures***

Assessments were performed by trained raters, who were required to complete online training every 12 months in administering CAARMS (Yung et al., 2005) and the Global Assessment of Functioning (GAF) (Hall, 1995). Inter-rater reliability across centres was assessed using the online training as previously reported in Hedges et al. (2022). Assessments were administered in the local language and translated from English and back translated to ensure accuracy.

**Childhood Trauma.** Childhood trauma was measured using the total score from the Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 2003). Where participants were missing data for up to 3 items (out of a total of 25 items) in the CTQ questionnaire, the missing scores were imputed using the mean score across all participants for the relevant item. This imputation was applied to a total of 10 items across 5 participants.

**Stressful Life Events.** The independent LTE score was calculated using five items from the LTE questionnaire including: serious injury or illness to oneself or a close relative, death of a loved one, and having something valuable lost or stolen (Powers et al., 2013). The interpersonal LTE score was calculated based on three items from the LTE questionnaire which included separation from a partner they were living with, break-up of a steady relationship with a partner they were not living with, and a serious problem with a friend or relative (Park et al., 2015). The items for the full questionnaire are reported in Table S1, with superscripts indicating whether they were considered independent or interpersonal events.

**Positive symptoms.** We summed severity ratings for the Comprehensive Assessment of At-Risk Mental States (CAARMS) positive symptoms subscale (Yung et al., 2005) for items including unusual thought, non-bizarre ideas, perceptual abnormalities, and disorganised speech for a maximum total score of 24.

**Negative symptoms.** The Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1982; 1983) was used to measure negative symptoms scores. We summed ratings across 25-items for a maximum total score of 125. Where participants were missing data for up to two items in the SANS questionnaire, the missing scores was imputed using the median score for the relevant item. This imputation was applied to a total of 25 items for 19 participants. Where participants were missing data for more than two items in the SANS questionnaire, they were excluded from the analysis.

**Medication.** Antipsychotic and antidepressant medication use at baseline was dichotomised and coded as 0 = no current use and 1 = current use. Daily total dose and medication type was provided which allowed us to calculate the chlorpromazine (CPZ) equivalent dose for antipsychotic medication (Kroken et al., 2009; Leucht et al., 2014), and the fluoxetine equivalent dose for antidepressant medication (Hayasaka et al., 2015). In separate sensitivity analyses, we included the dichotomised medication use and the equivalent dose as covariates of no interest. 31 CHR individuals reported using antipsychotic medication at baseline, with a mean (SD) dosage of 137.10 (144.58) mg/day of CPZ equivalent (range: 6.67-666.67 mg/day), and mean (SD) length of use of 0.42 (0.58) years (range: 0.005-2.932 years), with four CHR missing dosage data. Antipsychotic medication types, in addition to CPZ, included aripiprazole, olanzapine, quetiapine, and risperidone. 91 CHR individuals reported using antidepressant medication at baseline, with a mean (SD) dosage of 27.99 (14.48) mg/day of fluoxetine equivalent (range: 6.09-81.22 mg/day), with a mean (SD) length of use of 0.50 (0.89) years (range: 0.003-6.159 years), with 14 CHR missing dosage data. Antidepressant medication types, in addition to fluoxetine, included citalopram, escitalopram, mirtazapine, sertraline, paroxetine, and venlafaxine.

## Figure S1. GAF disability scores against time over the course of the study for CHR participants.

A graph with black dots

Description automatically generated

*GAF = Global Assessment of Functioning; The regression line modelling GAF disability against time can be found in the main document in Fig. 1A.*

## Figure S2. CAARMS positive symptoms scores against time over the course of the study for CHR participants.

A graph with black dots

Description automatically generated

*CAARMS = Comprehensive Assessment for the At-Risk Mental State; The regression line modelling positive symptoms against time can be found in the main document in Fig. 1B.*

## Figure S3. SANS negative symptoms scores against time over the course of the study for CHR participants.

A graph of a number of dots

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*SANS = Scale for the Assessment of Negative Symptoms; The regression line modelling negative symptoms against time can be found in the main document in Fig. 1C.*

## Figure S4. Total LTE scores against time over the course of the study for CHR participants.

A graph showing a number of dots

Description automatically generated

*LTE = List of Threatening Experiences; Note: Due to overlapping data points, the scatter plot markers have been jittered to aid with visualisation. Total LTE score in this sample has a range from 0 to 8.*

## Table S1. The frequencies and percentages (%) of the List of Threatening Experiences (LTE) questionnaire items for CHR and HC participants at baseline.

|  |  |  |
| --- | --- | --- |
|  | **Frequencies (%)1** | |
| **Items** | **CHR**  (*n* = 331) | **HC**  (*n* = 67) |
| Serious injury or illness to yourself.\* | 57 (8.2) | 7 (9.1) |
| Serious injury or illness to a close relative.\* | 97 (13.9) | 15 (19.5) |
| Parent, child or your spouse (partner) died.\* | 15 (2.2) | < 5 |
| Close family friend or other relative died.\* | 63 (9.1) | 15 (19.5) |
| Separation from partner (living with) due to problems.† | 25 (3.6) | 4 (5.2) |
| Break-up of a steady relationship (not living together).† | 75 (10.8) | 5 (6.5) |
| A serious problem with a close friend, neighbour or relative.† | 107 (15.4) | 8 (10.4) |
| Became unemployed or were seeking work unsuccessfully. | 90 (12.9) | 9 (11.7) |
| Sacked or made redundant from your job. | 35 (5.0) | < 5 |
| A major financial crisis. | 61 (8.8) | < 5 |
| A problem with the police and/or court appearance. | 35 (5.0) | < 5 |
| Something you valued was lost or stolen.\* | 36 (5.2) | 9 (11.7) |

1 “*< 5*” denotes items that were reported by fewer than 5 participants and has been reported this way to preserve participant anonymity.

\* Independent events; † Interpersonal events.

CHR = Clinical High Risk; HC = Healthy Controls.

## Table S2a. Linear regression model coefficients and statistics comparing baseline LTE differences between CHR and HC.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  | ***95% CI*** | |  |
| **LTE Measure**1 | **Adjusted R2** | **Variable** | ***Estimate*** | ***SE*** | ***t*** | ***Lower*** | ***Upper*** | ***P*** |
| Total LTE | 0.179 | (Intercept) | 0.608 | 0.628 | 0.969 | -0.629 | 1.846 | .334 |
|  |  | **Group** | 1.441 | 0.248 | 5.812 | 0.952 | 1.929 | 1.98×10-8\*\* |
|  |  | Sex | -0.103 | 0.203 | -0.507 | -0.504 | 0.298 | .612 |
|  |  | Age | 0.020 | 0.024 | 0.839 | -0.027 | 0.066 | .402 |
|  |  | SES – Intermediate | 0.674 | 0.233 | 2.888 | 0.214 | 1.133 | .004\*\* |
|  |  | SES – Working Class | 0.494 | 0.262 | 1.890 | -0.021 | 1.010 | .060 |
|  |  | Site – Amsterdam | -1.468 | 0.392 | -3.747 | -2.240 | -0.696 | 2.25×10-4\*\* |
|  |  | Site – The Hague | -0.662 | 0.258 | -2.566 | -1.170 | -0.154 | .011 |
|  |  | Site – Melbourne | -0.186 | 0.292 | -0.636 | -0.762 | 0.390 | .526 |
| Independent LTE | 0.035 | (Intercept) | 0.557 | 0.392 | 1.419 | -0.216 | 1.329 | .157 |
|  |  | **Group** | 0.263 | 0.155 | 1.697 | -0.042 | 0.568 | .091 |
|  |  | Sex | 0.048 | 0.127 | 0.375 | -0.203 | 0.298 | .708 |
|  |  | Age | 0.002 | 0.015 | 0.120 | -0.027 | 0.031 | .905 |
|  |  | SES – Intermediate | 0.142 | 0.146 | 0.977 | -0.145 | 0.429 | .329 |
|  |  | SES – Working Class | 0.267 | 0.163 | 1.636 | -0.055 | 0.589 | .103 |
|  |  | Site – Amsterdam | -0.650 | 0.245 | -2.655 | -1.132 | -0.168 | .008\*\* |
|  |  | Site – The Hague | 0.013 | 0.161 | 0.081 | -0.304 | 0.331 | .935 |
|  |  | Site – Melbourne | 0.000 | 0.183 | -0.002 | -0.360 | 0.359 | .998 |
| Interpersonal LTE | 0.122 | (Intercept) | 0.256 | 0.264 | 0.968 | -0.265 | 0.777 | .334 |
|  |  | **Group** | 0.550 | 0.104 | 5.274 | 0.345 | 0.756 | 2.99×10-7\*\* |
|  |  | Sex | 0.017 | 0.086 | 0.194 | -0.152 | 0.185 | .846 |
|  |  | Age | -0.004 | 0.010 | -0.369 | -0.023 | 0.016 | .713 |
|  |  | SES – Intermediate | 0.201 | 0.098 | 2.052 | 0.008 | 0.395 | .041 |
|  |  | SES – Working Class | 0.073 | 0.110 | 0.661 | -0.144 | 0.290 | .509 |
|  |  | Site – Amsterdam | -0.439 | 0.165 | -2.659 | -0.764 | -0.114 | .008\*\* |
|  |  | Site – The Hague | -0.225 | 0.109 | -2.071 | -0.439 | -0.011 | .039\* |
|  |  | Site – Melbourne | 0.039 | 0.123 | 0.320 | -0.203 | 0.282 | .750 |

\*p < .05; \*\*p < .01; All main findings survived FDR correction for multiple comparisons. The p-values reported are uncorrected.

LTE = List of Threatening Experiences; CHR = Clinical High Risk; HC = Healthy Controls; SES = Socioeconomic status (based on father’s socioeconomic status at participant’s birth).

1 All models were controlled for age, sex, socioeconomic status, and site. LTE score is the dependent variable.

Categorical Variables: Group: 0 = HC, 1 = CHR; Sex: 0 = Male, 1 = Female; SES: 0 = Salariat; Site: 0 = London.

## Table S2b. Linear regression model coefficients and statistics comparing baseline LTE differences between CHR and HC adjusting for childhood trauma and cannabis use.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  | ***95% CI*** | |  |
| **LTE Measure**1 | **Adjusted R2** | **Variable** | ***Estimate*** | ***SE*** | ***t*** | ***Lower*** | ***Upper*** | ***P*** |
| Total LTE | 0.211 | (Intercept) | 0.298 | 0.642 | 0.464 | -0.967 | 1.563 | .643 |
|  |  | **Group** | 1.191 | 0.270 | 4.403 | 0.658 | 1.724 | 1.63×10-5\*\* |
|  |  | **Childhood trauma**2 | 0.018 | 0.007 | 2.538 | 0.004 | 0.032 | .012\* |
|  |  | Sex | -0.171 | 0.204 | -0.837 | -0.573 | 0.231 | .403 |
|  |  | Age | 0.011 | 0.023 | 0.454 | -0.035 | 0.057 | .650 |
|  |  | SES – Intermediate | 0.664 | 0.236 | 2.815 | 0.199 | 1.129 | .005\*\* |
|  |  | SES – Working Class | 0.364 | 0.264 | 1.381 | -0.155 | 0.883 | .169 |
|  |  | Site – Amsterdam | -1.356 | 0.394 | -3.447 | -2.132 | -0.581 | .001\*\* |
|  |  | Site – The Hague | -0.696 | 0.255 | -2.728 | -1.198 | -0.193 | .007\*\* |
|  |  | Site – Melbourne | -0.327 | 0.296 | -1.106 | -0.911 | 0.256 | .270 |
| Total LTE | 0.252 | (Intercept) | 1.422 | 0.722 | 1.970 | -0.003 | 2.846 | .050 |
|  |  | **Group** | 1.345 | 0.298 | 4.514 | 0.757 | 1.933 | 1.17×10-5\*\* |
|  |  | **Current cannabis use** | 0.419 | 0.234 | 1.795 | -0.042 | 0.880 | .074 |
|  |  | Sex | -0.147 | 0.235 | -0.625 | -0.610 | 0.316 | .533 |
|  |  | Age | -0.019 | 0.026 | -0.713 | -0.071 | 0.033 | .477 |
|  |  | SES – Intermediate | 0.923 | 0.259 | 3.568 | 0.412 | 1.433 | 4.64×10-4\*\* |
|  |  | SES – Working Class | 0.737 | 0.301 | 2.446 | 0.142 | 1.331 | .015\* |
|  |  | Site – Amsterdam | -1.628 | 0.432 | -3.771 | -2.480 | -0.776 | 2.22×10-4\*\* |
|  |  | Site – The Hague | -0.703 | 0.287 | -2.452 | -1.269 | -0.137 | .015\* |
|  |  | Site – Melbourne | -0.288 | 0.364 | -0.793 | -1.007 | 0.430 | .429 |

\*p < .05; \*\*p < .01. All main findings survived FDR correction for multiple comparisons. The p-values reported are uncorrected.

LTE = List of Threatening Experiences; CHR = Clinical High Risk; HC = Healthy Controls; CHR-T = CHR transitioned; CHR-NT = CHR non-transitioned; SES = Socioeconomic status (based on father’s socioeconomic status at participant’s birth).

1 All models were controlled for age, sex, socioeconomic status, and site. LTE score is the dependent variable.; 2 Childhood Trauma Questionnaire total score.

Categorical Variables: Group: 0 = HC, 1 = CHR; Sex: 0 = Male, 1 = Female; SES: 0 = Salariat; Site: 0 = London; Current cannabis use: 0 = No use, 1 = Current use.

## Table S3a. Linear regression model coefficients and statistics comparing baseline LTE differences between CHR-T and CHR-NT.

|  |  |  |  |  |  | ***95% CI*** | |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **LTE Measure1** | **Adjusted R2** | **Variable** | ***Estimate*** | ***SE*** | ***t*** | ***Lower*** | ***Upper*** | ***P*** |
| Total LTE | 0.222 | (Intercept) | 1.071 | 0.543 | 1.973 | 0.003 | 2.139 | .049\* |
|  |  | **Transition Status** | -0.247 | 0.236 | -1.043 | -0.712 | 0.219 | .298 |
|  |  | Sex | -0.192 | 0.195 | -0.987 | -0.576 | 0.191 | .325 |
|  |  | Age | 0.069 | 0.021 | 3.298 | 0.028 | 0.110 | .001\*\* |
|  |  | SES – Intermediate | 0.549 | 0.223 | 2.470 | 0.111 | 0.988 | .014\* |
|  |  | SES – Working Class | 0.450 | 0.236 | 1.905 | -0.015 | 0.916 | .058 |
|  |  | Site – Amsterdam | -1.614 | 0.449 | -3.598 | -2.497 | -0.731 | 3.80×10-4\*\* |
|  |  | Site – Den Haag | -0.823 | 0.276 | -2.981 | -1.367 | -0.280 | .003\*\* |
|  |  | Site – Vienna | -1.933 | 0.492 | -3.927 | -2.901 | -0.964 | 1.09×10-4\*\* |
|  |  | Site – Basel | -0.551 | 0.470 | -1.173 | -1.476 | 0.373 | .242 |
|  |  | Site – Cologne | -1.220 | 0.430 | -2.836 | -2.067 | -0.373 | .005\*\* |
|  |  | Site – Melbourne | 0.192 | 0.355 | 0.541 | -0.507 | 0.892 | .589 |
|  |  | Site – Copenhagen | -0.780 | 0.577 | -1.352 | -1.915 | 0.356 | .177 |
|  |  | Site – Paris | -1.918 | 0.408 | -4.698 | -2.721 | -1.114 | 4.16×10-6\*\* |
|  |  | Site – Barcelona | -1.647 | 0.366 | -4.502 | -2.367 | -0.927 | 9.92×10-6\*\* |
|  |  | Site – Sao Paulo | -1.738 | 0.466 | -3.733 | -2.655 | -0.822 | 2.30×10-4\*\* |
| Independent LTE | 0.094 | (Intercept) | 0.394 | 0.325 | 1.210 | -0.247 | 1.034 | .227 |
|  |  | **Transition Status** | -0.156 | 0.142 | -1.098 | -0.435 | 0.123 | .273 |
|  |  | Sex | -0.050 | 0.117 | -0.430 | -0.280 | 0.180 | .668 |
|  |  | Age | 0.025 | 0.013 | 2.036 | 0.001 | 0.050 | .043\* |
|  |  | SES – Intermediate | 0.067 | 0.133 | 0.500 | -0.196 | 0.329 | .618 |
|  |  | SES – Working Class | 0.178 | 0.142 | 1.254 | -0.101 | 0.457 | .211 |
|  |  | Site – Amsterdam | -0.716 | 0.269 | -2.661 | -1.245 | -0.186 | .008\*\* |
|  |  | Site – Den Haag | -0.005 | 0.166 | -0.033 | -0.331 | 0.320 | .974 |
|  |  | Site – Vienna | -0.605 | 0.295 | -2.050 | -1.186 | -0.024 | .041\* |
|  |  | Site – Basel | -0.101 | 0.282 | -0.360 | -0.656 | 0.453 | .719 |
|  |  | Site – Cologne | -0.450 | 0.258 | -1.745 | -0.958 | 0.058 | .082 |
|  |  | Site – Melbourne | 0.159 | 0.213 | 0.747 | -0.260 | 0.579 | .456 |
|  |  | Site – Copenhagen | -0.461 | 0.346 | -1.334 | -1.142 | 0.219 | .183 |
|  |  | Site – Paris | -0.682 | 0.245 | -2.788 | -1.164 | -0.200 | .006\*\* |
|  |  | Site – Barcelona | -0.597 | 0.219 | -2.722 | -1.029 | -0.165 | .007\*\* |
|  |  | Site – Sao Paulo | -0.506 | 0.279 | -1.812 | -1.056 | 0.044 | .071 |
|  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| Interpersonal LTE | 0.106 | (Intercept) | 0.738 | 0.236 | 3.124 | 0.273 | 1.203 | .002\*\* |
|  |  | **Transition Status** | -0.100 | 0.103 | -0.971 | -0.302 | 0.103 | .332 |
|  |  | Sex | -0.059 | 0.085 | -0.701 | -0.226 | 0.107 | .484 |
|  |  | Age | 0.003 | 0.009 | 0.337 | -0.015 | 0.021 | .737 |
|  |  | SES – Intermediate | 0.120 | 0.097 | 1.236 | -0.071 | 0.310 | .217 |
|  |  | SES – Working Class | 0.070 | 0.103 | 0.684 | -0.132 | 0.273 | .495 |
|  |  | Site – Amsterdam | -0.571 | 0.195 | -2.924 | -0.955 | -0.187 | .004\*\* |
|  |  | Site – Den Haag | -0.269 | 0.120 | -2.240 | -0.506 | -0.033 | .026\* |
|  |  | Site – Vienna | -0.544 | 0.214 | -2.541 | -0.966 | -0.123 | .012\* |
|  |  | Site – Basel | -0.205 | 0.204 | -1.003 | -0.607 | 0.197 | .317 |
|  |  | Site – Cologne | -0.159 | 0.187 | -0.851 | -0.528 | 0.209 | .395 |
|  |  | Site – Melbourne | 0.195 | 0.155 | 1.262 | -0.109 | 0.500 | .208 |
|  |  | Site – Copenhagen | 0.220 | 0.251 | 0.876 | -0.274 | 0.714 | .382 |
|  |  | Site – Paris | -0.537 | 0.178 | -3.020 | -0.886 | -0.187 | .003\*\* |
|  |  | Site – Barcelona | -0.620 | 0.159 | -3.892 | -0.933 | -0.306 | 1.25×10-4\*\* |
|  |  | Site – Sao Paulo | -0.623 | 0.203 | -3.074 | -1.022 | -0.224 | .002\*\* |

\*p < .05; \*\*p < .01. All main findings survived FDR correction for multiple comparisons. The p-values reported are uncorrected.

LTE = List of Threatening Experiences; CHR = Clinical High Risk; HC = Healthy Controls; CHR-T = CHR who transitioned to psychosis; CHR-NT = CHR who did not transition to psychosis; SES = Socioeconomic status (based on father’s socioeconomic class at participant’s birth).

1 All models were controlled for age, sex, socioeconomic status, and site. LTE score is the dependent variable.

Categorical Variables: Transition Status: 0 = CHR-NT, 1 = CHR-T; Sex: 0 = Male, 1 = Female; SES: 0 = Salariat; Site: 0 = London.

## Table S3b. Linear regression model coefficients and statistics comparing baseline LTE differences between CHR-T and CHR-NT adjusting for childhood trauma and cannabis use.

|  |  |  |  |  |  | ***95% CI*** | |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **LTE Measure**1 | **Adjusted R2** | **Variable** | ***Estimate*** | ***SE*** | ***t*** | ***Lower*** | ***Upper*** | ***P*** |
| Total LTE | 0.244 | (Intercept) | 0.433 | 0.600 | 0.721 | -0.749 | 1.615 | .471 |
|  |  | **Transition Status** | -0.289 | 0.238 | -1.216 | -0.758 | 0.179 | .225 |
|  |  | **Childhood trauma**2 | 0.019 | 0.007 | 2.911 | 0.006 | 0.032 | .004\*\* |
|  |  | Sex | -0.233 | 0.199 | -1.169 | -0.625 | 0.159 | .244 |
|  |  | Age | 0.061 | 0.021 | 2.918 | 0.020 | 0.102 | .004\*\* |
|  |  | SES – Intermediate | 0.514 | 0.227 | 2.264 | 0.067 | 0.961 | .024\* |
|  |  | SES – Working Class | 0.358 | 0.241 | 1.482 | -0.118 | 0.833 | .140 |
|  |  | Site – Amsterdam | -1.471 | 0.452 | -3.258 | -2.361 | -0.582 | .001\*\* |
|  |  | Site – Den Haag | -0.888 | 0.276 | -3.220 | -1.431 | -0.345 | .001\*\* |
|  |  | Site – Vienna | -1.900 | 0.489 | -3.883 | -2.863 | -0.936 | 1.30×10-4\*\* |
|  |  | Site – Basel | -0.450 | 0.470 | -0.956 | -1.376 | 0.476 | .340 |
|  |  | Site – Cologne | -0.800 | 0.474 | -1.689 | -1.733 | 0.133 | .092 |
|  |  | Site – Melbourne | -0.027 | 0.362 | -0.075 | -0.740 | 0.686 | .940 |
|  |  | Site – Copenhagen | -0.774 | 0.607 | -1.275 | -1.970 | 0.421 | .203 |
|  |  | Site – Paris | -1.885 | 0.417 | -4.525 | -2.705 | -1.065 | 9.15×10-6\*\* |
|  |  | Site – Barcelona | -1.512 | 0.371 | -4.080 | -2.242 | -0.782 | 5.97×10-5\*\* |
|  |  | Site – Sao Paulo | -1.634 | 0.491 | -3.330 | -2.601 | -0.668 | .001\*\* |
| Total LTE | 0.217 | (Intercept) | 1.523 | 0.617 | 2.467 | 0.306 | 2.740 | .014\* |
|  |  | **Transition Status** | -0.156 | 0.271 | -0.574 | -0.690 | 0.379 | .566 |
|  |  | **Current cannabis use** | 0.528 | 0.230 | 2.298 | 0.075 | 0.982 | .023\* |
|  |  | Sex | -0.131 | 0.224 | -0.585 | -0.572 | 0.310 | .559 |
|  |  | Age | 0.037 | 0.024 | 1.560 | -0.010 | 0.083 | .120 |
|  |  | SES – Intermediate | 0.763 | 0.255 | 2.991 | 0.260 | 1.266 | .003\*\* |
|  |  | SES – Working Class | 0.683 | 0.284 | 2.407 | 0.123 | 1.242 | .017\* |
|  |  | Site – Amsterdam | -1.538 | 0.486 | -3.167 | -2.495 | -0.580 | .002\*\* |
|  |  | Site – Den Haag | -0.861 | 0.306 | -2.813 | -1.465 | -0.257 | .005\*\* |
|  |  | Site – Vienna | -2.005 | 0.576 | -3.482 | -3.140 | -0.869 | .001\*\* |
|  |  | Site – Basel | -0.647 | 0.512 | -1.264 | -1.656 | 0.363 | .208 |
|  |  | Site – Cologne | -1.068 | 0.471 | -2.268 | -1.997 | -0.139 | .024\* |
|  |  | Site – Melbourne | 0.009 | 0.449 | 0.019 | -0.877 | 0.894 | .985 |
|  |  | Site – Copenhagen | -0.976 | 0.666 | -1.465 | -2.290 | 0.338 | .145 |
|  |  | Site – Paris | -2.048 | 0.495 | -4.141 | -3.024 | -1.073 | 5.12×10-5\*\* |
|  |  | Site – Barcelona | -1.707 | 0.466 | -3.666 | -2.625 | -0.789 | 3.16×10-4\*\* |
|  |  | Site – Sao Paulo | -1.645 | 0.731 | -2.251 | -3.087 | -0.204 | .025\* |

\*p < .05; \*\*p < .01. All main findings survived FDR correction for multiple comparisons. The p-values reported are uncorrected.

LTE = List of Threatening Experiences; CHR = Clinical High Risk; HC = Healthy Controls; CHR-T = CHR who transitioned to psychosis; CHR-NT = CHR who did not transition to psychosis; SES = Socioeconomic status (based on father’s socioeconomic status at participant’s birth).

1 All models were controlled for age, sex, socioeconomic status, and site. LTE score is the dependent variable.; 2 Childhood Trauma Questionnaire total score.

Categorical Variables: Transition Status: 0 = CHR-NT, 1 = CHR-T; Sex: 0 = Male, 1 = Female; SES: 0 = Salariat; Site: 0 = London; Current cannabis use: 0 = No use, 1 = Current use.

## Table S4a. Model estimates from the linear mixed models investigating the association between LTE score and functioning (GAF disability) for the CHR sample.

|  |  |  |  |  |  |  |  |  |  | ***95% CI*** | |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Model**1 | **LTE Measure** | **Model Fit** |  | **Random Effects** |  | **Fixed Effects** | ***Estimate*** | ***SE*** | ***t*** | ***Lower*** | ***Upper*** | ***P*** |
| GAF Base Model | Total LTE | R2 (conditional) | 0.50 | Site, *SD* | 3.20 | (Intercept) | 65.458 | 3.420 | 19.141 | 58.866 | 72.070 | 2.30×10-39\*\* |
|  |  | R2 (marginal) | 0.14 | Participants | Site, *SD* | 7.32 | Total LTE score | -1.269 | 0.339 | -3.740 | -1.931 | -0.574 | 2.05×10-4\*\* |
|  |  |  |  | ICC, *%* | 42.2 | Time (years from baseline) | 4.558 | 0.541 | 8.426 | 3.510 | 5.655 | 1.08×10-15\*\* |
|  |  |  |  |  |  | Sex | 0.352 | 1.304 | 0.270 | -2.267 | 2.866 | .787 |
|  |  |  |  |  |  | Age (at baseline) | -0.293 | 0.135 | -2.171 | -0.553 | -0.030 | .031\* |
|  |  |  |  |  |  | SES - Intermediate | -2.080 | 1.513 | -1.375 | -5.001 | 0.925 | .170 |
|  |  |  |  |  |  | SES - Working class | -2.295 | 1.570 | -1.462 | -5.335 | 0.820 | .145 |
| Interaction Model | Total LTE | R2 (conditional) | 0.50 | Site, *SD* | 2.49 | (Intercept) | 65.287 | 3.420 | 19.092 | 58.696 | 71.895 | 2.33×10-39\*\* |
|  |  | R2 (marginal) | 0.14 | Participants | Site, *SD* | 7.61 | Total LTE score | -1.097 | 0.389 | -2.819 | -1.854 | -0.305 | .005\*\* |
|  |  |  |  | ICC, *%* | 42.0 | Time (years from baseline) | 5.159 | 0.862 | 5.987 | 3.495 | 6.889 | 4.95×10-9\*\* |
|  |  |  |  |  |  | LTE score × Time | -0.368 | 0.412 | -0.893 | -1.179 | 0.432 | .372 |
|  |  |  |  |  |  | Sex | 0.347 | 1.303 | 0.267 | -2.272 | 2.858 | .790 |
|  |  |  |  |  |  | Age (at baseline) | -0.298 | 0.135 | -2.211 | -0.559 | -0.036 | .028\* |
|  |  |  |  |  |  | SES - Intermediate | -2.108 | 1.514 | -1.392 | -5.028 | 0.894 | .165 |
|  |  |  |  |  |  | SES - Working class | -2.332 | 1.571 | -1.485 | -5.374 | 0.778 | .139 |
| Independent Events | Independent LTE | R2 (conditional) | 0.49 | Site, *SD* | 2.49 | (Intercept) | 64.890 | 3.388 | 19.155 | 58.390 | 71.422 | 5.69×10-38\*\* |
| R2 (marginal) | 0.13 | Participants | Site, *SD* | 7.61 | Independent LTE score | -0.718 | 0.578 | -1.243 | -1.828 | 0.456 | .214 |
|  |  | ICC, *%* | 42.1 | Time (years from baseline) | 4.960 | 0.533 | 9.301 | 3.934 | 6.053 | 2.09×10-18\*\* |
|  |  |  |  | Sex | 0.328 | 1.323 | 0.248 | -2.409 | 2.868 | .804 |
|  |  |  |  | Age (at baseline) | -0.328 | 0.135 | -2.428 | -0.588 | -0.065 | .016\* |
|  |  |  |  | SES - Intermediate | -2.441 | 1.538 | -1.588 | -5.391 | 0.655 | .114 |
|  |  |  |  | SES - Working class | -2.599 | 1.598 | -1.627 | -5.674 | 0.602 | .105 |
| Interpersonal Events | Interpersonal LTE | R2 (conditional) | 0.49 | Site, *SD* | 2.35 | (Intercept) | 65.158 | 3.386 | 19.243 | 58.669 | 71.682 | 3.74×10-38\*\* |
| R2 (marginal) | 0.13 | Participants | Site, *SD* | 7.58 | Interpersonal LTE score | -0.777 | 0.782 | -0.993 | -2.296 | 0.769 | .321 |
|  |  | ICC, *%* | 41.4 | Time (years from baseline) | 4.925 | 0.541 | 9.103 | 3.885 | 6.038 | 8.19×10-18\*\* |
|  |  |  |  | Sex | 0.230 | 1.319 | 0.175 | -2.525 | 2.757 | .862 |
|  |  |  |  | Age (at baseline) | -0.341 | 0.134 | -2.544 | -0.599 | -0.080 | .012\* |
|  |  |  |  | SES - Intermediate | -2.425 | 1.535 | -1.579 | -5.365 | 0.676 | .115 |
|  |  |  |  | SES - Working class | -2.567 | 1.596 | -1.609 | -5.634 | 0.637 | .109 |

\*p < .05; \*\*p < .01. All main findings survived FDR correction for multiple comparisons. The p-values reported are uncorrected.

GAF = Global Assessment of Functioning; LTE = List of Threatening Experiences; CHR = Clinical High Risk; SES = Socioeconomic Status (based on father’s socioeconomic status at participant’s birth); ICC = Intra-Class Correlation.

1 All models were controlled for sex, age at baseline, and SES. Models were fitted with participants (*n* = 286) nested in sites (*n* = 11) as a random intercept. The number of participants was dependent on available data across covariates. GAF Disability is the dependent variable.

Categorical Variables: Sex: 0 = Male, 1 = Female; SES: 0 = Salariat.

## Table S4b. Model estimates from the linear mixed models investigating the association between LTE score and functioning (GAF disability) for the CHR sample adjusting for childhood trauma and cannabis use.

|  |  |  |  |  |  |  |  |  |  | ***95% CI*** | |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Model**1 | **LTE Measure** | **Model Fit** |  | **Random Effects** |  | **Fixed Effects** | ***Estimate*** | ***SE*** | ***t*** | ***Lower*** | ***Upper*** | ***P*** |
| Childhood trauma | Total LTE | R2 (conditional) | 0.50 | Site, *SD* | 3.13 | (Intercept) | 67.955 | 3.724 | 18.248 | 60.802 | 75.172 | 2.49×10-40\*\* |
|  |  | R2 (marginal) | 0.15 | Participants | Site, *SD* | 7.21 | Total LTE score | -1.127 | 0.346 | -3.257 | -1.800 | -0.409 | .001\*\* |
|  |  |  |  | ICC, *%* | 41.1 | Time (years from baseline) | 4.622 | 0.548 | 8.427 | 3.562 | 5.739 | 1.13×10-15\*\* |
|  |  |  |  |  |  | Childhood trauma2 | -0.089 | 0.046 | -1.919 | -0.178 | 0.001 | .056 |
|  |  |  |  |  |  | Sex | 0.821 | 1.331 | 0.617 | -1.831 | 3.383 | .538 |
|  |  |  |  |  |  | Age (at baseline) | -0.266 | 0.136 | -1.952 | -0.529 | -0.003 | .052 |
|  |  |  |  |  |  | SES - Intermediate | -1.675 | 1.547 | -1.083 | -4.654 | 1.378 | .280 |
|  |  |  |  |  |  | SES - Working class | -1.459 | 1.616 | -0.903 | -4.572 | 1.759 | .367 |
| Cannabis use | Total LTE | R2 (conditional) | 0.47 | Site, *SD* | 2.51 | (Intercept) | 66.411 | 3.698 | 17.958 | 59.351 | 73.556 | 5.04×10-38\*\* |
|  |  | R2 (marginal) | 0.16 | Participants | Site, *SD* | 6.71 | Total LTE score | -1.152 | 0.390 | -2.956 | -1.905 | -0.288 | .003\*\* |
|  |  |  |  | ICC, *%* | 36.7 | Time (years from baseline) | 4.720 | 0.620 | 7.617 | 3.532 | 6.062 | 4.11×10-13\*\* |
|  |  |  |  |  |  | Current cannabis use | -1.506 | 1.468 | -1.026 | -4.506 | 1.288 | .306 |
|  |  |  |  |  |  | Sex | 0.265 | 1.412 | 0.188 | -2.515 | 2.974 | .851 |
|  |  |  |  |  |  | Age (at baseline) | -0.303 | 0.145 | -2.095 | -0.580 | -0.022 | .038\* |
|  |  |  |  |  |  | SES - Intermediate | -2.211 | 1.626 | -1.360 | -5.349 | 0.956 | .175 |
|  |  |  |  |  |  | SES - Working class | -1.812 | 1.778 | -1.020 | -5.227 | 1.705 | .309 |

\*p < .05; \*\*p < .01. All main findings survived FDR correction for multiple comparisons. The p-values reported are uncorrected.

GAF = Global Assessment of Functioning; LTE = List of Threatening Experiences; CHR = Clinical High Risk; SES = Socioeconomic status (based on father’s socioeconomic status at participant’s birth); ICC = Intra-Class Correlation.

1 All models were controlled for sex, age at baseline, and SES. Models were fitted with participants nested in sites (*n* = 11) as a random intercept. The number of participants was dependent on available data across covariates (Childhood trauma, *n* = 276; Cannabis use, *n* = 213). GAF Disability is the dependent variable. 2 Childhood trauma was measured using the total score from the Childhood Trauma Questionnaire.

Categorical Variables: Sex: 0 = Male, 1 = Female; SES: 0 = Salariat; Current cannabis use: 0 = No use, 1 = Current use.

## Table S5a. Model estimates from the linear mixed models investigating the association between LTE score and positive psychotic symptoms (CAARMS positive symptom subscale) for the CHR sample.

|  |  |  |  |  |  |  |  |  |  | ***95% CI*** | |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Model1** | **LTE Measure** | **Model Fit** |  | **Random Effects** |  | **Fixed Effects** | ***Estimate*** | ***SE*** | ***t*** | ***Lower*** | ***Upper*** | ***P*** |
| CAARMS Base Model | Total LTE | R2 (conditional) | 0.47 | Site, *SD* | 1.33 | (Intercept) | 7.912 | 1.083 | 7.306 | 5.791 | 10.069 | 2.59×10-11\*\* |
|  | R2 (marginal) | 0.21 | Participants | Site, *SD* | 1.89 | Total LTE score | 0.290 | 0.111 | 2.622 | 0.076 | 0.510 | .009\* |
|  |  |  |  | ICC, *%* | 33.0 | Time (years from baseline) | -2.266 | 0.181 | -12.526 | -2.625 | -1.915 | 1.88×10-30\*\* |
|  |  |  |  |  |  | Sex | 0.158 | 0.397 | 0.398 | -0.615 | 0.929 | .691 |
|  |  |  |  |  |  | Age (at baseline) | 0.062 | 0.041 | 1.494 | -0.024 | 0.142 | .136 |
|  |  |  |  |  |  | SES - Intermediate | 0.079 | 0.459 | 0.173 | -0.820 | 0.972 | .863 |
|  |  |  |  |  |  | SES - Working class | 0.163 | 0.475 | 0.343 | -0.761 | 1.091 | .732 |
| Interaction Model | Total LTE | R2 (conditional) | 0.48 | Site, *SD* | 1.33 | (Intercept) | 8.031 | 1.086 | 7.393 | 5.906 | 10.189 | 1.62×10-11\*\* |
|  |  | R2 (marginal) | 0.21 | Participants | Site, *SD* | 1.90 | Total LTE score | 0.181 | 0.128 | 1.412 | -0.067 | 0.434 | .158 |
|  |  |  |  | ICC, *%* | 33.4 | Time (years from baseline) | -2.643 | 0.287 | -9.214 | -3.206 | -2.085 | 1.35×10-18\*\* |
|  |  |  |  |  |  | LTE score × Time | 0.224 | 0.132 | 1.694 | -0.035 | 0.482 | .091 |
|  |  |  |  |  |  | Sex | 0.158 | 0.397 | 0.398 | -0.615 | 0.929 | .691 |
|  |  |  |  |  |  | Age (at baseline) | 0.065 | 0.041 | 1.577 | -0.020 | 0.146 | .116 |
|  |  |  |  |  |  | SES - Intermediate | 0.102 | 0.459 | 0.221 | -0.797 | 0.994 | .825 |
|  |  |  |  |  |  | SES - Working class | 0.190 | 0.476 | 0.399 | -0.734 | 1.119 | .690 |
| Independent Events | Independent LTE | R2 (conditional) | 0.47 | Site, *SD* | 1.37 | (Intercept) | 8.011 | 1.090 | 7.351 | 5.876 | 10.176 | 2.18×10-11\*\* |
| R2 (marginal) | 0.20 | Participants | Site, *SD* | 1.89 | Independent LTE score | 0.299 | 0.188 | 1.584 | -0.068 | 0.675 | .114 |
|  |  | ICC, *%* | 33.3 | Time (years from baseline) | -2.337 | 0.179 | -13.073 | -2.693 | -1.990 | 1.73×10-32\*\* |
|  |  |  |  | Sex | 0.118 | 0.398 | 0.296 | -0.658 | 0.892 | .767 |
|  |  |  |  | Age (at baseline) | 0.069 | 0.041 | 1.676 | -0.016 | 0.150 | .095 |
|  |  |  |  | SES - Intermediate | 0.171 | 0.458 | 0.374 | -0.726 | 1.063 | .709 |
|  |  |  |  | SES - Working class | 0.221 | 0.476 | 0.465 | -0.703 | 1.151 | .642 |
| Interpersonal Events | Interpersonal LTE | R2 (conditional) | 0.48 | Site, *SD* | 1.39 | (Intercept) | 8.056 | 1.108 | 7.269 | 5.888 | 10.253 | 3.11×10-11\*\* |
| R2 (marginal) | 0.20 | Participants | Site, *SD* | 1.95 | Interpersonal LTE score | 0.009 | 0.255 | 0.036 | -0.486 | 0.514 | .971 |
|  |  | ICC, *%* | 34.5 | Time (years from baseline) | -2.350 | 0.181 | -12.998 | -2.709 | -1.999 | 2.63×10-32\*\* |
|  |  |  |  | Sex | 0.131 | 0.402 | 0.327 | -0.651 | 0.913 | .744 |
|  |  |  |  | Age (at baseline) | 0.075 | 0.042 | 1.797 | -0.010 | 0.156 | .074 |
|  |  |  |  | SES - Intermediate | 0.204 | 0.463 | 0.441 | -0.702 | 1.104 | .660 |
|  |  |  |  | SES - Working class | 0.250 | 0.480 | 0.520 | -0.684 | 1.190 | .603 |

\*p < .05; \*\*p < .01. All main findings survived FDR correction for multiple comparisons. The p-values reported are uncorrected.

CAARMS = Comprehensive Assessment for the At-Risk Mental State; LTE = List of Threatening Experiences; CHR = Clinical High Risk; SES = Socioeconomic Status (based on father’s socioeconomic status at participant’s birth); ICC = Intra-Class Correlation.

1 All models were controlled for sex, age at baseline, and SES. Models were fitted with participants (*n* = 289) nested in sites (*n* = 11) as a random intercept. The number of participants was dependent on available data across covariates. CAARMS positive symptom score is the dependent variable.

Categorical Variables: Sex: 0 = Male, 1 = Female; SES: 0 = Salariat.

## Table S5b. Model estimates from the linear mixed models investigating the association between LTE score and positive psychotic symptoms (CAARMS positive symptom subscale) for the CHR sample adjusting for childhood trauma and cannabis use.

|  |  |  |  |  |  |  |  |  |  | ***95% CI*** | |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Model1** | **LTE Measure** | **Model Fit** |  | **Random Effects** |  | **Fixed Effects** | ***Estimate*** | ***SE*** | ***t*** | ***Lower*** | ***Upper*** | ***P*** |
| Childhood trauma | Total LTE | R2 (conditional) | 0.49 | Site, *SD* | 1.45 | (Intercept) | 7.990 | 1.180 | 6.772 | 5.704 | 10.304 | 3.35×10-10\*\* |
|  |  | R2 (marginal) | 0.21 | Participants | Site, *SD* | 1.88 | Total LTE score | 0.270 | 0.111 | 2.423 | 0.054 | 0.489 | .016\* |
|  |  |  |  | ICC, *%* | 34.9 | Time (years from baseline) | -2.259 | 0.180 | -12.518 | -2.618 | -1.910 | 2.43×10-30\*\* |
|  |  |  |  |  |  | Childhood trauma2 | 0.003 | 0.014 | 0.182 | -0.025 | 0.031 | .855 |
|  |  |  |  |  |  | Sex | 0.137 | 0.403 | 0.340 | -0.648 | 0.918 | .734 |
|  |  |  |  |  |  | Age (at baseline) | 0.054 | 0.042 | 1.289 | -0.032 | 0.135 | .199 |
|  |  |  |  |  |  | SES - Intermediate | 0.176 | 0.465 | 0.379 | -0.740 | 1.075 | .705 |
|  |  |  |  |  |  | SES - Working class | 0.221 | 0.486 | 0.456 | -0.725 | 1.166 | .649 |
| Cannabis use | Total LTE | R2 (conditional) | 0.49 | Site, *SD* | 1.27 | (Intercept) | 7.721 | 1.258 | 6.139 | 5.282 | 10.204 | 7.45×10-9\*\* |
|  |  | R2 (marginal) | 0.21 | Participants | Site, *SD* | 2.05 | Total LTE score | 0.252 | 0.131 | 1.930 | 0.001 | 0.514 | .054 |
|  |  |  |  | ICC, *%* | 35.1 | Time (years from baseline) | -2.277 | 0.209 | -10.892 | -2.690 | -1.871 | 1.86×10-23\*\* |
|  |  |  |  |  |  | Current cannabis use | -0.107 | 0.482 | -0.223 | -1.045 | 0.824 | .824 |
|  |  |  |  |  |  | Sex | 0.458 | 0.463 | 0.989 | -0.444 | 1.353 | .324 |
|  |  |  |  |  |  | Age (at baseline) | 0.064 | 0.048 | 1.342 | -0.033 | 0.158 | .181 |
|  |  |  |  |  |  | SES - Intermediate | 0.240 | 0.534 | 0.449 | -0.805 | 1.273 | .654 |
|  |  |  |  |  |  | SES - Working class | 0.602 | 0.583 | 1.032 | -0.529 | 1.733 | .303 |

\*p < .05; \*\*p < .01. All main findings survived FDR correction for multiple comparisons. The p-values reported are uncorrected.

CAARMS = Comprehensive Assessment for the At-Risk Mental State; LTE = List of Threatening Experiences; CHR = Clinical High Risk; SES = Socioeconomic Status (based on father’s socioeconomic status at participant’s birth).

1 All models were controlled for sex, age at baseline, and SES. Models were fitted with participants nested in sites (*n* = 11) as a random intercept. The number of participants was dependent on available data across covariates (Childhood trauma, *n* = 278; Cannabis use, *n* = 214). CAARMS positive symptom score is the dependent variable. 2Childhood Trauma Questionnaire total score.

Categorical Variables: Sex: 0 = Male, 1 = Female; SES: 0 = Salariat; Current cannabis use: 0 = No use, 1 = Current use.

## Table S6a. Model estimates from the linear mixed models investigating the association between LTE score and negative psychotic symptoms (SANS total severity score) for the CHR sample.

|  |  |  |  |  |  |  |  |  |  | ***95% CI*** | |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Model**1 | **LTE Measure** | **Model Fit** |  | **Random Effects** |  | ***Fixed Effects*** | ***Estimate*** | ***SE*** | ***t*** | ***Lower*** | ***Upper*** | ***P*** |
| SANS Base Model | Total LTE | R2 (conditional) | 0.62 | Site, *SD* | 5.45 | (Intercept) | 16.545 | 4.262 | 3.882 | 8.300 | 24.804 | 1.72×10-4\*\* |
|  | R2 (marginal) | 0.06 | Participants | Site, *SD* | 9.69 | Total LTE score | 0.961 | 0.365 | 2.635 | 0.239 | 1.668 | .009\*\* |
|  |  |  |  | ICC, *%* | 59.2 | Time (years from baseline) | -3.343 | 0.547 | -6.114 | -4.430 | -2.281 | 3.22×10-9\*\* |
|  |  |  |  |  |  | Sex | -1.319 | 1.541 | -0.856 | -4.359 | 1.664 | .393 |
|  |  |  |  |  |  | Age (at baseline) | 0.163 | 0.162 | 1.006 | -0.156 | 0.476 | .315 |
|  |  |  |  |  |  | SES - Intermediate | 1.773 | 1.783 | 0.994 | -1.700 | 5.252 | .321 |
|  |  |  |  |  |  | SES - Working class | 0.530 | 1.860 | 0.285 | -3.085 | 4.178 | .776 |
| Interaction Model | Total LTE | R2 (conditional) | 0.62 | Site, *SD* | 5.44 | (Intercept) | 16.569 | 4.269 | 3.881 | 8.313 | 24.842 | 1.72×10-4\*\* |
|  |  | R2 (marginal) | 0.0 | Participants | Site, *SD* | 9.67 | Total LTE score | 0.940 | 0.419 | 2.241 | 0.107 | 1.752 | .025\* |
|  |  |  |  | ICC, *%* | 59.1 | Time (years from baseline) | -3.411 | 0.877 | -3.887 | -5.162 | -1.711 | 1.24×10-4\*\* |
|  |  |  |  |  |  | LTE score × Time | 0.041 | 0.417 | 0.097 | -0.768 | 0.867 | .923 |
|  |  |  |  |  |  | Sex | -1.322 | 1.541 | -0.858 | -4.361 | 1.661 | .392 |
|  |  |  |  |  |  | Age (at baseline) | 0.163 | 0.162 | 1.010 | -0.156 | 0.476 | .314 |
|  |  |  |  |  |  | SES - Intermediate | 1.773 | 1.783 | 0.994 | -1.698 | 5.253 | .321 |
|  |  |  |  |  |  | SES - Working class | 0.529 | 1.860 | 0.285 | -3.082 | 4.180 | .776 |
| Independent Events | Independent LTE | R2 (conditional) | 0.61 | Site, *SD* | 5.31 | (Intercept) | 16.933 | 4.248 | 3.986 | 8.714 | 25.168 | 1.16×10-4\*\* |
| R2 (marginal) | 0.06 | Participants | Site, *SD* | 9.68 | Independent LTE score | 0.836 | 0.627 | 1.332 | -0.407 | 2.055 | .184 |
|  |  | ICC, *%* | 58.5 | Time (years from baseline) | -3.598 | 0.540 | -6.661 | -4.669 | -2.547 | 1.46×10-10\*\* |
|  |  |  |  | Sex | -1.447 | 1.544 | -0.937 | -4.492 | 1.541 | .349 |
|  |  |  |  | Age (at baseline) | 0.187 | 0.162 | 1.159 | -0.132 | 0.500 | .248 |
|  |  |  |  | SES - Intermediate | 2.118 | 1.780 | 1.189 | -1.350 | 5.591 | .235 |
|  |  |  |  | SES - Working class | 0.750 | 1.860 | 0.403 | -2.866 | 4.402 | .687 |
| Interpersonal Events | Interpersonal LTE | R2 (conditional) | 0.60 | Site, *SD* | 5.27 | (Intercept) | 17.014 | 4.252 | 4.001 | 8.787 | 25.259 | 1.08×10-4\*\* |
| R2 (marginal) | 0.06 | Participants | Site, *SD* | 9.60 | Interpersonal LTE score | 0.087 | 0.832 | 0.105 | -1.543 | 1.709 | .916 |
|  |  | ICC, *%* | 57.8 | Time (years from baseline) | -3.645 | 0.552 | -6.606 | -4.738 | -2.572 | 1.91×10-10\*\* |
|  |  |  |  | Sex | -1.412 | 1.540 | -0.917 | -4.449 | 1.569 | .360 |
|  |  |  |  | Age (at baseline) | 0.203 | 0.161 | 1.265 | -0.114 | 0.514 | .207 |
|  |  |  |  | SES - Intermediate | 2.195 | 1.776 | 1.236 | -1.264 | 5.661 | .218 |
|  |  |  |  | SES - Working class | 0.790 | 1.856 | 0.426 | -2.816 | 4.437 | .671 |

\*p < .05; \*\*p < .01. All main findings survived FDR correction for multiple comparisons. The p-values reported are uncorrected.

SANS = Scale for the Assessment of Negative Symptoms; LTE = List of Threatening Experiences; CHR = Clinical High Risk; SES = Socioeconomic Status (based on father’s socioeconomic status at participant’s birth); ICC = Intra-Class Correlation.

1 All models were controlled for sex, age at baseline, and SES. Models were fitted with participant (*n* = 287 nested in site (*n* = 11) as a random intercept. The number of participants was dependent on available data across covariates. SANS negative symptom score is the dependent variable.

Categorical Variables: Sex: 0 = Male, 1 = Female; SES: 0 = Salariat.

## Table S6b. Model estimates from the linear mixed models investigating the association between LTE score and negative psychotic symptoms (SANS total severity score) for the CHR sample adjusting for childhood trauma and cannabis use.

|  |  |  |  |  |  |  |  |  |  | **95% CI** | |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Model**1 | **LTE Measure** | **Model Fit** |  | **Random Effects** |  | **Fixed Effects** | **Estimate** | **SE** | **t** | **Lower** | **Upper** | **P** |
| Childhood trauma | Total LTE | R2 (conditional) | 0.61 | Site, *SD* | 5.56 | (Intercept) | 17.316 | 4.633 | 3.737 | 8.361 | 26.334 | 2.72×10-04\*\* |
|  |  | R2 (marginal) | 0.06 | Participants | Site, *SD* | 9.53 | Total LTE score | 0.906 | 0.370 | 2.447 | 0.172 | 1.623 | .015\* |
|  |  |  |  | ICC, *%* | 58.7 | Time (years from baseline) | -3.387 | 0.553 | -6.119 | -4.487 | -2.312 | 3.17×10-9\*\* |
|  |  |  |  |  |  | Childhood trauma2 | 0.012 | 0.055 | 0.213 | -0.097 | 0.117 | .832 |
|  |  |  |  |  |  | Sex | -1.429 | 1.573 | -0.908 | -4.516 | 1.611 | .365 |
|  |  |  |  |  |  | Age (at baseline) | 0.115 | 0.163 | 0.706 | -0.205 | 0.430 | .481 |
|  |  |  |  |  |  | SES - Intermediate | 1.558 | 1.817 | 0.858 | -1.970 | 5.099 | .392 |
|  |  |  |  |  |  | SES - Working class | 0.470 | 1.908 | 0.246 | -3.232 | 4.214 | .806 |
| Cannabis use | Total LTE | R2 (conditional) | 0.60 | Site, *SD* | 4.92 | (Intercept) | 19.016 | 4.758 | 3.996 | 9.835 | 28.207 | 1.05×10-04\*\* |
|  |  | R2 (marginal) | 0.07 | Participants | Site, *SD* | 9.57 | Total LTE score | 0.704 | 0.438 | 1.607 | -0.164 | 1.548 | .109 |
|  |  |  |  | ICC, *%* | 56.4 | Time (years from baseline) | -3.743 | 0.645 | -5.805 | -5.028 | -2.493 | 2.13×10-8\*\* |
|  |  |  |  |  |  | Current cannabis use | -3.449 | 1.823 | -1.893 | -6.987 | 0.101 | .060 |
|  |  |  |  |  |  | Sex | -1.179 | 1.756 | -0.672 | -4.626 | 2.207 | .503 |
|  |  |  |  |  |  | Age (at baseline) | 0.135 | 0.182 | 0.743 | -0.223 | 0.486 | .458 |
|  |  |  |  |  |  | SES - Intermediate | 0.433 | 2.021 | 0.214 | -3.474 | 4.368 | .830 |
|  |  |  |  |  |  | SES - Working class | 0.041 | 2.211 | 0.019 | -4.238 | 4.348 | .985 |

\*p < .05; \*\*p < .01. All main findings survived FDR correction for multiple comparisons. The p-values reported are uncorrected.

SANS = Scale for the Assessment of Negative Symptoms; LTE = List of Threatening Experiences; CHR = Clinical High Risk; SES = Socioeconomic Status (based on father’s socioeconomic status at participant’s birth); ICC = Intra-Class Correlation.

1 All models were controlled for sex, age at baseline, and SES. Models were fitted with participant nested in site as a random intercept. The number of participants was dependent on available data across covariates (Childhood trauma, *n* = 276; Cannabis use, *n* = 212). SANS negative symptom score is the dependent variable.; 2 Childhood Trauma Questionnaire total score.

Categorical Variables: Sex: 0 = Male, 1 = Female; SES: 0 = Salariat; Current cannabis use: 0 = No use, 1 = Current use.

## Table S7. Baseline and clinical characteristics for CHR participants grouped by the number of completed assessments to test for attrition bias.

To examine attrition bias over the study follow-up period, we compared baseline characteristics and clinical measures for the CHR participants (*n* = 331) grouped by their number of completed assessments. As an example, participants in group 2 included participants who completed assessments at Baseline and 6-months, or Baseline and 24-months, and were compared against participants who completed 1, 3, or 4 assessments.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | ***CHR participants (n = 331) grouped by the number of***  ***completed assessments*** | | | | ***Group comparisons of baseline characteristics*** | |
| **Variable** |  | ***1***  *(n = 152)* | ***2***  *(n = 82)* | ***3***  *(n = 86)* | ***4***  *(n = 11)* | *Test Statistic*  *F / χ2* | *p-value* |
| Age (years), *mean (SD)* |  | 21.94 (4.89) | 22.02 (4.57) | 23.66 (5.39) | 22.55 (4.74) | 2.456 | .062 |
| Sex, *n (%)* | Female | 72 (47.4) | 37 (45.1) | 43 (50.0) | 3 (27.3) | 2.203 | .542 |
| Ethnicity, *n (%)* | White | 100 (65.8) | 61 (74.4) | 66 (76.7) | 7 (63.6) | *Fisher's exact* | .020\* |
|  | Black | 18 (11.8) | 9 (11.0) | 5 (5.8) | 2 (18.2) |  |  |
|  | Mixed | 14 (9.2) | 4 (4.9) | 8 (9.3) | 2 (18.2) |  |  |
|  | Asian | 3 (2.0) | 7 (8.5) | 1 (1.2) | 0 (0.0) |  |  |
|  | Other1 | 17 (11.2) | 1 (1.2) | 6 (7.0) | 0 (0.0) |  |  |
| Socioeconomic Status2, *n (%)* | Salariat | 45 (29.6) | 19 (23.2) | 31 (36.1) | 2 (18.2) | *Fisher's exact* | .471 |
|  | Intermediate | 51 (33.6) | 27 (32.9) | 24 (27.9) | 3 (27.3) |  |  |
|  | Working Class | 35 (23.0) | 24 (29.3) | 26 (30.2) | 5 (45.5) |  |  |
| Years in education, *mean (SD)* |  | 13.78 (3.13) | 13.99 (3.02) | 15.62 (2.55) | 16.00 (3.00) | 8.30 | 2.55×10-5\*\*,a |
| Antipsychotic medication, *n (%)* |  | 21 (13.8) | 7 (8.5) | 2 (2.3) | 1 (9.1) | *Fisher's exact* | .011\* |
| Antidepressant medication, *n (%)* |  | 34 (22.4) | 23 (28.1) | 31 (36.1) | 3 (27.3) | *Fisher's exact* | .303 |
| Current cannabis use, *n (%)* |  | 38 (25) | 22 (26.8) | 22 (25.6) | 5 (45.5) | *Fisher's exact* | .803 |
| Childhood trauma3, *mean (SD)* |  | 49.36 (17.20) | 45.05 (14.74) | 47.98 (13.53) | 49.73 (16.64) | 1.326 | .266 |
| Total LTE Score, *mean (SD)* |  | 2.09 (1.71) | 2.07 (1.73) | 2.05 (1.81) | 3 (1.55) | 1.021 | .384 |
| GAF disability, *mean (SD)* |  | 55.77 (13.10) | 53.93 (12.30) | 56.17 (10.81) | 55.18 (13.91) | 0.547 | .651 |
| CAARMS positive symptom severity, *mean (SD)* |  | 10.47 (3.96) | 10.76 (3.63) | 8.7 (4.12) | 12.82 (1.89) | 6.782 | 1.90×10-4\*\*,b |
| SANS negative symptom score, *mean (SD)* |  | 21.66 (15.90) | 23.63 (15.00) | 17.79 (12.81) | 17.64 (13.17) | 2.463 | .063 |

\*p < .05; \*\*p < .01

a Post-hoc Tukey’s HSD (Honestly Significant Difference) test revealed CHR participants who returned for 3 assessments had spent more time in education compared to those who returned for 1 or 2 assessments.

b Post-hoc Tukey’s HSD test revealed CHR participants who returned for 3 assessments had less severe positive symptoms as compared to participants who completed 1, 2, or 4 assessments.

1 Other includes those of North African and other ethnic backgrounds; 2 Socioeconomic status is based on the father’s socioeconomic class at participant’s birth; 3 Childhood Trauma Questionnaire total score.

CHR = Clinical High Risk; LTE = List of Threatening Experiences; GAF = Global Assessment of Functioning; CAARMS = Comprehensive Assessment for the At-Risk Mental State; SANS = Scale for the Assessment of Negative Symptoms.

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