**SUPPLEMENTARY MATERIAL**

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**This supplementary material has been provided by the authors to give readers additional information about their work.**

**eTable 1: PRISMA statement and checklist**

|  |  |  |  |
| --- | --- | --- | --- |
| **Section/topic** | **#** | **Checklist item** | **Page** |
| **TITLE** | | |  |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | |  |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2-3 |
| **INTRODUCTION** | | |  |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 4 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 4-5 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 5 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 5-6 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 5 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 5 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 5-6 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 6 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 6 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at study or outcome level), and how this information is to be used in any data synthesis. | 7 |
| Summary measures | 13 | State the principal summary measures. | 7 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias (i.e. Newcastle-Ottawa Scale (NOS), that may affect the cumulative evidence. | e7 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 7-8 |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 8,  figure 1 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 24-25 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 10, 24-25 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study a summary data for each intervention group. | 8-9,  24-25 |
| Results synthesis | 21 | Present results of study analyzed. | 8-10, e8-10 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 10 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 9-10 |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 11-14 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 14 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 14 |
| **FUNDING** |  |  |  |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 15 |

**eTable 2: MOOSE checklist**

|  |  |  |
| --- | --- | --- |
| **Criteria** | | **Brief description of how the criteria were handled in the meta-analysis** |
| **Reporting of background should include** | | |
| √ | Problem definition | No meta-analysis has comprehensively assessed the progression of outcomes in non-transitioned CHR-P individuals. |
| √ | Hypothesis statement | We hypothesized that outcomes would be significant in non-transitioned CHR-P individuals. |
| √ | Description of study outcomes | The outcomes are defined in eTable 3. |
| √ | Type of exposure or intervention used | We included original studies reporting outcomes after a certain follow-up period. |
| √ | Type of study designs used | Longitudinal studies only. |
| √ | Study population | CHR-P individuals according to established psychometric instruments. |
| **Reporting of search strategy should include** | | |
| √ | Qualifications of searchers | The credentials of the investigators are detailed in the manuscript. |
| √ | Search strategy, including time period included in the synthesis and keywords | Multi-step literature search detailed in methods section. |
| √ | Databases and registries searched | Pubmed and Web of Science databases. |
| √ | Use of hand searching | We carried out a manual search as specified in the manuscript. |
| √ | List of citations located and those excluded, including justifications | A PRISMA flowchart was added to the main text, including reasons for exclusion. |
| √ | Method of addressing articles published in languages other than English | Only articles in English language were included. |
| √ | Method of handling abstracts and unpublished studies | This point is detailed in the methods section. |
| √ | Description of any contact with authors | We contacted corresponding authors to request additional data when this was needed. |
| **Reporting of methods should include** | | |
| √ | Description of relevance or appropriateness of studies assembled for assessing the hypothesis  to be tested | Detailed inclusion and exclusion criteria were described in the methods section. |
| √ | Rationale for the selection and coding of data | Data was selected and extracted to answer our research questions. |
| √ | Assessment of confounding | Meta-regressions were carried out when at least 7 studies were available per outcome. |
| √ | Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results | This is detailed in the methods section and supplementary. We adapted the Newcastle-Ottawa Scale for the evaluation of cohort studies to assess the study quality. |
| √ | Assessment of heterogeneity | Heterogeneity was assessed with the I2 index. |
| √ | Description of statistical methods in sufficient detail to be replicated | This is detailed in the methods section. |
| √ | Provision of appropriate tables and graphics | We included several tables and graphics in the main text and supplementary section to give readers additional information about our work. |
| **Reporting of results should include** | | |
| √ | Graph summarizing individual study estimates and overall estimate | We have appended several graphs summarizing our meta-analytical estimations. |
| √ | Table giving descriptive information for each study included | We have presented descriptive information for each study in the tables and as supplementary material. |
| √ | Results of sensitivity testing | Sensitivity testing results are provided. |
| √ | Indication of statistical uncertainty of findings | We reported the 95% CI for all our estimations. |
| **Reporting of discussion should include** | | |
| √ | Quantitative assessment of bias | Quantitative assessment of bias is reported and discussed in the text. |
| √ | Justification for exclusion | Our inclusion and exclusion criteria aim to obtain the highest quality evidence possible as detailed in the manuscript. |
| √ | Assessment of quality of included studies | The quality of our studies is summarized and discussed. |
| **Reporting of conclusions should include** | | |
| √ | Consideration of alternative explanations for observed results | We discussed other explanations for our findings, specifically considering potential methodological shortcomings. |
| √ | Generalization of the conclusions | We have addressed the generalization of the conclusions in the discussion section. |
| √ | Guidelines for future research | We have suggested possible streams of future development and research in the discussion. |
| √ | Disclosure of funding source | Funding sources are detailed. No separate funding was required for this meta-analysis. |

**eTable 3:** **Definitions and instruments employed to define outcomes.**

|  |  |
| --- | --- |
| **Outcome** | **Definition/ Instruments Used** |
| Attenuated psychotic symptoms (change from baseline to follow-up) | Positive and Negative Syndrome Scale (PANSS) (Kay *et al.*, 1987)  Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984)  Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1988) |
| Negative psychotic symptoms (change from baseline to follow-up) | Positive and Negative Syndrome Scale (PANSS) (Kay *et al.*, 1987)  Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1983)  Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1988)  Montgomery–Åsberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979) |
| Depressive symptoms (change from baseline to follow-up) | Hamilton Rating Scale for Depression (HAM-D) (Hamilton, 1960)  Calgary Depression Scale for Schizophrenia (CDSS) (Addington *et al.*, 1992)  Beck Depression Inventory (BDI) (Beck *et al.*, 1996) |
| Functioning (change from baseline to follow-up) | Global Assessment of Functioning (GAF) (Piersma and Boes, 1997)  Social and Occupational Functioning Assessment Scale (SOFAS ) (Morosini *et al.*, 2000)  Global Functioning: Role (GFR); Global Functioning: Social (GFS) (Niendam *et al.*, 2006; Cornblatt *et al.*, 2007) |
| Remission (% at follow-up) | Symptoms remission as defined by the psychometric instruments (e.g., SIPS/SOPS, CAARMSa) or CHR-P criteria remission (i.e. individuals not meeting CHR-P criteria at follow-up according to established instruments) |

aDefinitions employed by the included individual studies: SIPS/SOPS severity <3 or ≤2 for all the attenuated positive symptoms; CAARMS total positive subscale score <5.

**eTable 4: Risk of bias (quality) assessment using the modified Newcastle Ottawa Scale for cohort studies.**

|  |  |
| --- | --- |
| **Criteria** | **Maximum Score** |
| Representativeness of exposed cohort (e.g. total population or random sample, selected group) | 1 |
| Method used to ascertain exposure is robust? | 1 |
| Exposed and unexposed are matched or there is an adjustment for confounding factors? | 2 |
| Assessment of outcome was blind to exposure status or used record linkage, were robust tools used? | 2 |
| Follow-up period was sufficiently long for outcomes to occur? | 1 |
| Loss to follow-up rate is reported, low (<30%), and same in exposed and non-exposed? | 1 |

**eTable 5: Other characteristics of the included studies**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **First author, year** | **CHR-P sample size baseline** | **CHR-P sample size end of the study** | **% loss to follow-up** | **Remission definition** | **Outcomes assessed**a | **% on psychotherapy** | **% on medication** |
| (Addington *et al.*, 2011) | 303 | 111 | 63.4 | Remission of attenuated symptoms used to index clinical high-risk status. | APS, FX, NEG | 0 | 18.1 AP |
| (Addington *et al.*, 2019) | 278 | 278 | 0 | Remission from CHR-P syndrome (i.e. scores of 2 or less on all five positive symptoms on the SIPS) | APS, FX, NEG, REM | N.a. | N.a. |
| (Armando *et al.*, 2015) | 35 | 35 | 0 | Remission from UHR status. | REM | N.a. | 0 AP; 2.9 AD; 2.9 BZ |
| (Beck *et al.*, 2019) | 255 | 72 | 71.8 | Absence of APS or BLIPS (i.e., sub-threshold severity on all positive symptom items for at least 12 consecutive months preceding latest follow-up). | FX, REM | 0 | 0 |
| (Cannon *et al.*, 2015) | 274 | 274 | 0 | N.a. | POS | N.a. | 34.7 AP |
| (Chen *et al.*, 2016) | 63 | 47 | 25.4 | N.a. | DEP, FX | N.a. | N.a. |
| (Cotter *et al.*, 2017) | 268 | 268 | 0 | N.a. | DEP | N.a. | N.a. |
| (de Wit *et al.*, 2014) | 44 | 44 | 0 | No longer exhibited positive prodromal symptoms at the sub-psychotic level. | REM, FX | N.a. | Baseline: 43.2 Any  Follow-up: 20.4 AP |
| (Falkenberg *et al.*, 2017) | 34 | 23 | 32.4 | Not fulfilling the UHR criteria. | REM | N.a. | Baseline: 8.8 AP; 20.6 AD |
| (Guo *et al.*, 2019) | 117 | 117 | 0 | All SIPS positive symptoms scores below 3. | REM | N.a. | N.a. |
| (Kline *et al.*, 2016) | 21 | 21 | 0 | Symptoms remission. | REM | N.a. | N.a. |
| (Landa *et al.*, 2016) | 6 | 6 | 0 | Significant decrease in CAARMS positive symptoms and CAARMS total global and frequency scales. | APS, DEP, FX, NEG, REM | 100 CBT | Baseline: 16.6 AP  33.3 AP+MS  16.6 AP+ANX+AD  Follow-up: 50 AP |
| (Lemos-Giráldez *et al.*, 2009) | 61 | 61 | 0 | N.a. | APS, FX, NEG | 82 CBT | 79 AP |
| (Lin *et al.*, 2013) | 325 | 325 | 0 | N.a. | DEP, FX | 8 CBT; 23.4 CT | 19.4 AP + CBT or AP + CT; 7.4 Lithium |
| (Michel *et al.*, 2018) | 246 | 246 | 0 | Remission of CHR-P according to symptomatic ultra-high risk or cognitive disturbances criteria. | FX | N.a. | Baseline: 13.8 AP; 13 AD; 0.8 MS |
| (Mittal *et al.*, 2010) | 90 | 90 | 0 | N.a. | APS, NEG | N.a. | 14.4 AP; 37.8 AD; 20 Stimulants |
| (Mongan *et al.*, 2020) | 133 | 133 | 0 | N.a. | FX | N.a. | Baseline: 27.8 AD; 11.3 AP;6.0 Hypnotics; 10.5 Other |
| (Pelizza *et al.*, 2019) | 55 | 41 | 25.5 | Not satisfying inclusion criteria for CHR-P. | REM | 4.9 | N.a. |
| (Phillips *et al.*, 2007) | 17 | 17 | 0 | N.a. | DEP, FX, NEG | N.a. | 0 |
| (Rüsch *et al.*, 2015) | 172 | 101 | 41.3 | N.a. | APS, FX, NEG | N.a. | Baseline: 19.2 AP |
| (Rutigliano *et al.*, 2016) | 154 | 74 | 51.9 | No longer presenting with APS meeting CAARMS threshold, and GAF < 60. | DEP, REM | 77.1 CBT | 4.1 APS; 25.7 APS + CBT |
| (Ryan *et al.*, 2017) | 180 | 173 | 3.9 | N.a. | APS, NEG | N.a. | N.a. |
| (Sawada *et al.*, 2017) | 47 | 39 | 17 | N.a. | APS, FX, NEG | N.a. | N.a. |
| (Shi *et al.*, 2016) | 32 | 27 | 15.6 | Remission from CHR-P. status. | DEP, REM | N.a. | N.a. |
| (Velthorst *et al.*, 2011) | 77 | 70 | 9.1 | Remission from CHR-P. status. | APS, FX, NEG | N.a. | 12.3 AP; 15.6 AD; 6.5 ANX; 6.5 MET |
| (Yee *et al.*, 2018) | 105 | 71 | 32.4 | A change in CAARMS status from positive at baseline to not meeting CHR-P. criteria at follow-up. | DEP, REM | N.a. | 0 AP; 43.8 AD; 0 MS |
| (Zhang *et al.*, 2017) | 117 | 86 | 26.5 | Positive symptoms scores of 2 or less, or the return of GAF to 90% of the previous best GAF for GRD. | REM | N.a. | 49.6 AP; 41 AD /MD; 23.9 AD/MD+APS |
| (Ziermans *et al.*, 2011) | 42 | 42 | 0 | N.a. | REM | N.a. | Baseline: 36 Any; 17 AP; 14 MS; 7 PS  2 Other; Follow-up: 38 Any; 5 AP; 14 MS; 12 PS; 0 ANX; 4 other |

AD: antidepressants; ANX: anxiolytics; AP: antipsychotics APS: attenuated psychotic symptoms; BLIPS: brief limited intermittent psychotic symptoms BZ: benzodiazepines; CAARMS: Comprehensive Assessment of At-Risk Mental States CBT: cognitive behavioural therapy; CHR-P: clinical high risk for psychosis; CT: cognitive therapy: DEP: depressive symptoms; GAF: global assessment of functioning; GRD: genetic risk and deterioration FX: functioning; MET: Methylphenidate; MS: mood stabilizers; PS: psychostimulants; NEG: negative symptoms; REM: remission SIPS: Structured Interview for Psychosis-risk Syndromes.

aDue to overlap some all the outcomes were not meta-analyzed.

**eTable 6: Outcomes in non-transitioned CHR-P individuals**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Symptom**, follow-up period | **No. of**  **Studies**a | **Sample size** | **Hedges’ g** | | | **z Score** | **P** | **Test for Heterogeneity** | | | **Funnel plot assymetry** | **Egger´s test**  **p** |
| **Mean** | **95 CI** | | **Q** | **I2** | **P** |
| **Attenuated psychotic symptoms** | | | | | | | | | | | | |
| **Last follow-up/total** | **10** | **872** | **1.410** | **1.002** | **1.818** | **6.768** | **<0.001** | **118.376** | **93.242** | **<0.001** | **N** | **0.785** |
| 12 months follow-up | 7 | 511 | 1.069 | 0.772 | 1.367 | 7.042 | <0.001 | 24.470 | 79.567 | <0.001 | N | 0.396 |
| 24 months follow-up | 4 | 455 | 1.479 | 1.197 | 1.761 | 10.287 | <0.001 | 7.085 | 71.772 | 0.029 | N | 0.779 |
| ≥36 months follow-up | 4 | 341 | 1.243 | 0.120 | 2.366 | 2.169 | 0.029 | 76.146 | 97.373 | <0.001 | N | 0.937 |
| **Negative symptoms** | | | | | | | | | | | | |
| **Last follow-up/total** | **10** | **872** | **0.683** | **0.371** | **0.995** | **4.291** | **<0.001** | **137.111** | **93.436** | **<0.001** | **N** | **0.947** |
| 12 months follow-up | 7 | 459 | 0.679 | 0.481 | 0.878 | 6.711 | <0.001 | 17.643 | 60.324 | 0.014 | N | 0.979 |
| 24 months follow-up | 4 | 503 | 0.771 | 0.633 | 0.908 | 11.003 | <0.001 | 5.749 | 30.419 | 0.219 | Y | 0.313 |
| ≥36 months follow-up | 4 | 377 | 0.920 | 0.797 | 1.043 | 14.657 | <0.001 | 31.048 | 90.337 | <0.001 | N | 0.340 |
| **Depressive symptoms** | | | | | | | | | | | | |
| **Last follow-up/total** | **4** | **301** | **0.844** | **0.371** | **1.317** | **3.495** | **<0.001** | **14.626** | **79.488** | **0.002** | **N** | **0.201** |
| **Functioning** | | | | | | | | | | | | |
| **Last follow-up/total** | **12** | **1,095** | **0.776** | **0.463** | **1.089** | **4.858** | **<0.001** | **206.805** | **94.681** | **<0.001** | **Y** | **0.134** |
| 12 months follow-up | 8 | 386 | 0.647 | 0.303 | 0.991 | 3.686 | <0.001 | 56.074 | 87.516 | <0.001 | N | 0.465 |
| 24 months follow-up | 5 | 514 | 0.572 | 0.086 | 1.058 | 2.308 | 0.021 | 74.884 | 94.658 | <0.001 | N | 0.533 |
| ≥36 months follow-up | 5 | 434 | 0.896 | 0.779 | 1.012 | 15.077 | <0.001 | 74.289 | 94.616 | <0.001 | N | 0.232 |
|  | | | | | | | | | | | | |
| **Symptom**, follow-up period | **No. of**  **Studies**a | **Sample size** | **Proportion** | | | **z Score** | **P** | **Test for Heterogeneity** | | | **Publication bias asessmentb** | |
| **%** | **95 CI** | | **Q** | **I2** | **P** |
| **Remission** | | | | | | | | | | | | |
| **Last follow-up/total** | **15** | **1,219** | **0.487** | **0.393** | **0.582** | **-0.260** | **0.795** | **117.236** | **88.058** | **<0.001** | β=-0.003, p=0.253 | |
| 12 months follow-up | 6 | 240 | 0.480 | 0.345 | 0.618 | -0.285 | 0.776 | 15.643 | 68.037 | 0.008 |
| 24 months follow-up | 5 | 534 | 0.506 | 0.389 | 0.624 | 0.105 | 0.916 | 22.229 | 82.006 | <0.001 |
| ≥36 months follow-up | 5 | 464 | 0.519 | 0.265 | 0.764 | 0.137 | 0.891 | 81.484 | 95.091 | <0.001 |

aOverlapping samples can contribute with different outcomes; bMetaregression of the effect size on study’s sample size.

**eTable 7: Comparison transitioned vs non-transitioned CHR-P individuals**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | | | | | | | | |
| **Symptom**, follow-up period | **No. of**  **Studies**a | **Sample size no transition** | **Sample size transition** | **Hedges’ g** | | | **z Score** | **P** | **Test for Heterogeneity** | | | **Funnel plot assymetry** | **Egger´s**  **test**  **p** |
| **%** | **95 CI** | | **Q** | **I2** | **P** |
| **Attenuated psychotic symptoms** | 5 | 405 | 165 | 0.706 | 0.091 | 1.322 | 2.249 | 0.025 | 38.178 | 92.142 | <0.001 | N | 0.762 |
| **Negative symptoms** | 5 | 405 | 165 | 0.246 | -0.097 | 0.589 | 1.407 | 0.159 | 15.163 | 73.619 | 0.004 | N | 0.202 |
| **Depressive symptoms** | 3 | 295 | 96 | 0.785 | -0.062 | 1.632 | 1.817 | 0.069 | 9.800 | 79.591 | 0.007 | N | 0.363 |
| **Functioning** | 6 | 545 | 214 | 0.623 | 0.375 | 0.871 | 4.925 | <0.001 | 68.400 | 15.823 | 0.007 | N | 0.465 |
|  | | | | | | | | | | | | | |
| **Symptom**, follow-up period | **No. of**  **Studies**a | **Sample size no transition** | **Sample size transition** | **Proportion** | | | **z Score** | **P** | **Test for Heterogeneity** | | | **Publication bias asessmentb** | |
| **OR** | **95 CI** | | **Q** | **I2** | **P** |
| **Remission** | 3 | 148 | 73 | 16.110 | 0.473 | 549.02 | 1.544 | 0.123 | 15.836 | 87.371 | <0.001 | β=0.037, p=0.252 | |

\*Trim and fill method was applied and small effect bias was not identified.

aOverlapping samples can contribute with different outcomes; bMetaregression of the effect size on study’s sample size.

**eTable 8: Moderating factors**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **Meta-regressor**a | **No. of Studies** | **β Coefficient** | **SE** | **95% CI** | | | **Z-Value** | **P value** |
| **Attenuated psychotic symptoms** | Continent | 10 | 0.542 | 0.765 | -0.957 | 2.042 | 0.709 | | 0.478 |
| Psychometric instrument | 10 | -0.529 | 0.663 | -1.829 | 0.770 | -0.798 | | 0.425 |
| Quality of the study | 10 | -0.029 | 0.421 | -0.855 | 0.797 | -0.068 | | 0.946 |
| Mean age | 10 | 0.225 | 0.090 | 0.048 | 0.402 | 2.499 | | **0.012** |
| Sex | 10 | -0.021 | 0.020 | -0.060 | 0.018 | -1.057 | | 0.290 |
| Year of publication | 10 | -0.0959 | 0.071 | -0.236 | 0.044 | -1.344 | | 0.179 |
| Follow-up period | 10 | -0.0043 | 0.005 | -0.014 | 0.0057 | -0.838 | | 0.402 |
| **Negative symptoms** | Continent | 10 | 0.553 | 0.956 | -1.322 | 2.427 | 0.578 | | 0.563 |
| Psychometric instrument | 10 | -0.120 | 0.465 | -1.031 | 0.791 | -0.259 | | 0.796 |
| Quality of the study | 10 | 0.261 | 0.192 | -0.115 | 0.064 | 1.359 | | 0.174 |
| Mean age | 10 | 0.072 | 0.092 | -0.109 | 0.253 | 0.780 | | 0.435 |
| Sex | 10 | -0.0046 | 0.018 | -0.040 | 0.031 | -0.250 | | 0.803 |
| Year of publication | 10 | -0.092 | 0.053 | -0.196 | 0.012 | -1.738 | | 0.082 |
| Follow-up period | 10 | 0.00037 | 0.0035 | -0.0065 | 0.0073 | 0.105 | | 0.916 |
| **Functioning** | Continent | 12 | 0.259 | 0.920 | -1.545 | 2.062 | 0.281 | | 0.779 |
| Psychometric instrument | 12 | 0.397 | 0.422 | -0.430 | 1.223 | 0.941 | | 0.347 |
| Quality of the study | 12 | -0.028 | 0.188 | -0.396 | 0.340 | -0.150 | | 0.881 |
| Mean age | 12 | 0.058 | 0.071 | -0.081 | 0.197 | 0.815 | | 0.415 |
| Sex | 12 | -0.019 | 0.021 | -0.059 | 0.022 | -0.911 | | 0.362 |
| Year of publication | 12 | -0.124 | 0.041 | -0.204 | -0.043 | -3.013 | | **0.0026** |
| Follow-up period | 12 | 0.0029 | 0.0027 | -0.0023 | 0.0081 | 1.097 | | 0.273 |
| **Remission** | Continent | 15 | -0.714 | 1.110 | -2.888 | 1.460 | -0.643 | | 0.520 |
| Psychometric instrument | 15 | 0.889 | 0.581 | -0.248 | 2.027 | 1.532 | | 0.126 |
| Quality of the study | 15 | -0.144 | 0.437 | -1.000 | 0.711 | -0.331 | | 0.741 |
| APS | 7 | -0.009 | 0.005 | -0.019 | 0.0015 | -1.67 | | 0.094 |
| BLIPS | 7 | -0.054 | 0.021 | -0.094 | -0.014 | -2.633 | | **0.0085** |
| GRD | 7 | -0.0034 | 0.016 | -0.034 | 0.027 | -0.217 | | 0.828 |
| Mean age | 15 | 0.027 | 0.086 | -0.142 | 0.195 | 0.312 | | 0.755 |
| Sex | 15 | 0.087 | 0.051 | -0.012 | 0.187 | 1.719 | | 0.086 |
| Year of publication | 15 | -0.014 | 0.140 | -0.288 | 0.260 | -0.098 | | 0.922 |
| Follow-up period | 15 | 0.00045 | 0.0033 | -0.0061 | 0.0070 | 0.134 | | 0.893 |

aSome meta-regressors could not be analysed due to limited amount of studies.

APS: Attenuated Psychosis Symptoms; BLIPS: Brief and Limited Intermittent Psychotic Symptoms; GRD: Genetic Risk and Deterioration.

**eMethods 1** Types of CHR-P assessments included (modified from (Fusar-Poli *et al.*, 2020))

The CHR-P state comprises the Ultra High Risk state and/or the Basic Symptoms (Fusar-Poli *et al.*, 2020).

* The following UHR instruments were considered to define the UHR state: Comprehensive Assessment of At-Risk Mental States (CAARMS) (Yung *et al.*, 2005) and Structured Interview for Psychosis-risk Syndromes (SIPS) (Fusar-Poli *et al.*, 2016; McGlashan T, 2010) and Early Recognition Inventory (ERIraos) (Haefner *et al.*, 2011). Furthermore, before the development of these instruments, the CHR-P state was defined through the Positive and Negative Syndrome Scale (PANSS) (Kay *et al.*, 1987), Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1988).
* The following UHR instruments were considered to define the BS (Fusar-Poli *et al.*, 2020): Bonn Scale for the Assessment of Basic Symptoms (BSABS) (Vollmer-Larsen *et al.*, 2007), Basel Screening Instrument for Psychosis (BSIP) (Riecher-Rössler *et al.*, 2008), and Schizophrenia Proneness Instrument (Fux *et al.*, 2013) - Adult (SPI-A) and Child and Youth (SPI-CY) version -.
* Transition to psychosis was operationalised as defined by each CHR-P instruments or according to ICD/DSM criteria.
* Basic symptoms are subjectively experienced disturbances in thought, affect, motor functioning, bodily sensation, perception and tolerance of stress (Schultze-Lutter and Theodoridou, 2017).

**eMethods 2: Data extraction details**

1. **Main characteristics of the included studies:**

* First author and year of publication
* Country
* Design (longitudinal cohort, non-randomized clinical trial, randomized clinical trial)
* CHR-P sample size
* CHR-P subgroups (% Attenuated Psychosis Symptoms -APS-, % Brief Limited Intermittent Psychotic Symptoms -BLIPS-,% Genetic risk and deterioration syndrome -GRD- and % Basic symptoms -BS-);
* Age (mean, SD, range)
* Sex (% female);
* CHR-P assessment tools (as listed in eMethods 1);
* Follow up period (in months);

1. **Main outcomes:**

* Attenuated psychotic symptoms: PANSS, SAPS, BPRS (mean±SD); at baseline and follow-up
* Negative symptoms: PANSS, SANS, BPRS (mean±SD); at baseline and follow-up
* Depressive symptoms: MADRS, HAM-D, CDSS, BDI (mean±SD); at baseline and follow-up
* Functioning GAF, SOFAS, GFS (mean±SD); at baseline and follow-up
* Remission %; at follow-up

1. **Information to detect overlapping studies:**
   * Study program, recruitment period (if applicable)
   * City, country
2. **Meta-regression analyses**

* Continent (Europe vs North America vs Other)
* Psychometric instrument (CAARMS, vs SIPS vs other)
* Quality of the study
* Proportion of Attenuated Psychosis Symptoms -APS-
* Proportion of Brief Limited Intermittent Psychotic Symptoms -BLIPS-
* Proportion of Genetic risk and deterioration syndrome -GRD-
* Proportion of Basic symptoms -BS-
* Age (mean age)
* Sex (% female)
* Year of publication
* Follow-up period
* Duration of untreated attenuated psychotic symptoms – in months- (as per (Fusar-Poli *et al.*, 2012))
* ICD or DSM-defined comorbidity: a) any non-psychotic mental disorder; b) any mood disorder c) major depressive disorder; d) depressive disorders; e) bipolar disorder type I; f) other bipolar disorders; g) personality disorders; h) borderline personality disorder; i) neurodevelopmental disorders; j) autism spectrum disorders; k) anxiety disorders; l) ADHD; m) cannabis use disorder; n) alcohol use disorder; o) stimulant use disorder; p) other substance use disorder; q) PTSD; r) OCD
* Exposure to baseline interventions:a) antipsychotics b) antidepressants c) other psychotropics d) psychotherapy [including CBT, IPT and other psychotherapeutic interventions].

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