Supplemental Online Content

Salazar de Pablo G, Radua J, Pereira J, et al. Probability of transition to psychosis in individuals at clinical high risk: an updated meta-analysis. *JAMA Psychiatry*. Published online July 14, 2021. doi:10.1001/jamapsychiatry.2021.0830

This supplemental 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.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	2
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.	2
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.	2, e28
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.	2
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	2, e27
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).	2
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.	2

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	2, e29-30
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 the study or outcome level), and how this information is to be used in any data synthesis.	2
Summary	13	State the principal summary measures.	2-3
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.	2, e8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	2-3, e32
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.	3
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.	e9-16
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).	e9-16
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study a summary data for each intervention group	e9-16
Synthesis of results	21	Present results of study analyzed.	3-4
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	4
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	4
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).	4-6
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).	7
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	7
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.	7

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 updated meta-analysis has evaluated the transition to psychosis in individuals at CHR-P.
√	Hypothesis statement	We hypothesized transition to psychosis would be significant in CHR-P and increase during the follow-up.
√	Description of study outcomes	Detailed in methods section and in eMethods 2-3.
√	Type of exposure or intervention	We included original articles that reported the risk of transition in individuals at CHR-P.
√	Type of study designs used	Longitudinal studies only, including clinical trials.
√	Study population	Individuals at CHR-P defined according to established instruments, see eMethods 2.
Reporting of search strategy should include		
√	Qualifications of searchers	The credentials of the investigators are indicated in the author list.
√	Search strategy, including time period included and keywords	Multi-step literature search detailed in the methods section, until 1st November 2020.
√	Databases and registries searched	Pubmed and Web of Science database (Clarivate Analytics), including the Web of Science Core Collection, BIOSIS Citation Index, KCI-Korean Journal Database, MEDLINE, Russian Science Citation Index, SciELO Citation, Cochrane Central Register of Reviews, and Ovid/PsychINFO databases.
√	Use of hand searching	We hand-searched bibliographies of retrieved papers and published reviews for additional references.
√	List of citations located and those excluded, including justifications	Details of the literature search process are outlined in the results section and in the PRISMA flowchart (figure 1).
√	Method of addressing articles in languages other than English	Only articles in English language were selected.
√	Method of handling abstracts and unpublished studies	This point and the steps carried out are detailed in the methods section.
√	Description of any contact with authors	We contacted corresponding authors to request additional data about the transition to psychosis in individuals at CHR-P when needed.
Reporting of methods should include		
√	Description of relevance or appropriateness of studies assembled for assessing the hypothesis	Detailed inclusion/ exclusion criteria are detailed in the methods section.
√	Rationale for the selection and coding of data	Data extraction is in accordance with the population characteristics, study design, exposure, outcome, and possible effect of confounders.

√	Assessment of confounding	Meta-regressions were carried out as detailed in the methods section.
√	Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors	This is detailed in the methods section as well as in the supplementary. We used a modified version of the Newcastle-Ottawa Scale, previously used in the CHR-P field. We also evaluated the influence of other factors through meta-regressions.
√	Assessment of heterogeneity	Heterogeneity was assessed with the I^2 index and the Q statistic.
√	Description of statistical methods in sufficient detail to be replicated	Statistical methods are detailed in the methods section, including details on sensitivity analysis.
√	Provision of appropriate tables and graphics	Tables and graphics in the main text and supplementary provide methodological details and results about the work carried out.
Reporting of results should include		
√	Graph summarizing individual study estimates and overall estimate	Graphs with the overall estimates are appended in the main text.
√	Table giving descriptive information for each study included	We have presented descriptive information for each study included in the supplementary material (eTable_IV)
√	Results of sensitivity testing	Sensitivity analysis are reported in the results section.
√	Indication of statistical uncertainty of findings	We reported mean estimates and 95% CI.
Reporting of discussion should include		
√	Quantitative assessment of bias	We tested for publication biases by conducting a Cox regression in which the dependent variable was the time to transition and the independent variable was the sample size.
√	Justification for exclusion	We excluded studies about other conditions because the purpose of our review was to see the transition of individuals at CHR-P. Our exclusion criteria aim to obtain the highest quality evidence possible.
√	Assessment of quality of included studies	We used a modified version of the Newcastle-Ottawa Scale, previously used in the CHR-P field.
Reporting of conclusions should include		
√	Consideration of alternative explanations for observed results	We discussed other explanations for our findings, specifically considering methodological limitations.
√	Generalization of the conclusions	We have addressed the generalization of the conclusions in the discussion of the manuscript.
√	Guidelines for future research	We have suggested possible streams of future development and research in our manuscript.
√	Disclosure of funding source	Funding source was detailed. No separate funding was necessary for the undertaking of this meta-analysis.

eTable 3: 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
Groups are matched or is there an adjustment for confounding factor?	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 all the groups?	1

eTable 4: Characteristics of the included studies.

First author and year of publication[a]	Country	Study design	CHR-P subgroups	CHR-P sample size	Age: mean, SD (range)	% of female	CHR-P assessment tools	Follow-up period	NOS or RoB
Addington 2012[1]	Multi	Longitudinal cohort	98.2% APS, 2.3% GRD	171	19.8 (4.5)	43.2	SIPS/SOPS	24	4
Amminger 2015[2]	Austria	Randomized clinical trial	90.1% APS, 43.2% BLIPS, 7.4% GRD	40	16.4 (2.1), 13-25	67.0	PANSS	3	Low risk of bias
Atkinson 2017[3]	Australia	Longitudinal cohort	N.a.	102	18.6 (2.7), 13-25	53.9	CAARMS	12	5
Bang 2019[4]	Korea	Longitudinal cohort	97.4% APS, 15.6% BIPS, 15.6% GRD	77	19.9 (3.4), 15-32	40.3	SIPS/SOPS	25.8[b]	4
Barbato 2013[5]	Multi	Longitudinal cohort	98.7% APS, 2% GRD	151	19.7 (4.7), 12-21	43.7	SIPS/SOPS	6	4
Barbato 2014[6]	Multi	Longitudinal cohort	97.4% APS, 1.3% GRD	153	19.7 (4.2)	42.1	SIPS/SOPS	6	3
Bechdolf 2012[7]	Germany	Randomized clinical trial	N.a.	65	26.8 (6.2)	35.4	ERIraos	24	High risk of bias
Beck 2019[8]	Switzerland	Longitudinal cohort	N.a.	255	24.1 (8.2), 14-57	59.0	SIPS/SOPS	192	3
Berger 2017[9]	Australia	Longitudinal cohort	N.a.	69	16.3 (1.8), 13-25	68.1	CAARMS	84	6
Bolt 2019[10]	Multi	Longitudinal cohort	N.a.	294	19.1 (4.5)	54.4	CAARMS	40.8[b]	5
Bourgin 2020[11]	France	Longitudinal cohort	N.a.	27	17.6 (3.7), 15-25	14.8	CAARMS	22.4[b]	3
Brewer 2012[12]	Australia	Longitudinal cohort	N.a.	219	25.8 (5.1), 15-30	N.a.	CAARMS	24	4
Brucato 2018[13]	USA	Longitudinal cohort	N.a.	200	20.1 (3.9), 13-30	28.0	SIPS/SOPS	24	5
Bruene 2011[14]	Germany	Longitudinal cohort	N.a.	10	25.5 (5.3)	30.0	SIPS/SOPS	12	4
Buchy 2014[15]	Multi	Longitudinal cohort	98.2% APS, 3.5% GRD	170	19.8 (4.5), 12-31	43.5	SIPS/SOPS	48	4

Carrion 2017[16]	USA	Longitudinal cohort	N.a.	92	15.9 (2.1), 12-22	37.0	SIPS/SOPS	12	5
Catalan 2020[17]	Multi	Longitudinal cohort	83.2% APS, 6.9% BLIPS, 16.2% GRD	303	22.5 (4.6),15-35	48.2	CAARMS	24	4
Chan 2019[18]	Singapore	Longitudinal cohort	60% APS, 2.7% BLIPS, 21.2% GRD, 16.1% Combined	255	20.8 (3.3), 16-30	32.2	CAARMS	24	5
Chen 2016[19]	China	Longitudinal cohort	100% APS	63	21.9 (4.5), 14-30	47.6	SIPS/SOPS	6	4
Chung 2018[20]	Australia	Longitudinal cohort	N.a.	275	17.3 (3.1)	38.5	SIPS/SOPS	12	4
Colibazzi 2017[21]	USA	Longitudinal cohort	N.a.	51	21.0 (3.8)	27.4	SIPS/SOPS	48	6
Conrad 2017[22]	Australia	Longitudinal cohort	69.1% APS, 16.2%, BLIPS, 26.2% GRD	191	17.5 (3.0), 12-25	42.9	CAARMS	120	5
Corcoran 2011[23]	USA	Longitudinal cohort	98.2% APS, 1.8% BIPS, 28.6% GRD	56	19.6 (3.6), 13-27	23.0	SIPS/SOPS	36	5
Cornblatt 2015[24]	USA	Longitudinal cohort	100% APS	101	15.9 (2.2), 12-22	30.8	SIPS/SOPS	60	6
Damme 2019[25]	USA	Longitudinal cohort	N.a.	73	18.6 (1.8), 13-22	39.7	SIPS/SOPS	12	4
de Wit 2014[26]	Netherlands	Longitudinal cohort	N.a.	44	14.9 (2.2), 12-18	47.1	SIPS/SOPS	72	4
DeVylder 2013[27]	USA	Longitudinal cohort	100% APS, 1.5% BIPS, 4.6% GRD	65	19.5 (3.7), 12-30	23.1	SIPS/SOPS	48	5
Dragt 2011[28]	Holland	Longitudinal cohort	95.8% APS, 15.3% BIPS, 13.9% GRD, 70.8% BS	72	19.3 (4.0), 12-35	34.7	SIPS/SOPS, BSABS-P	36	4
Francesconi 2017[29]	Italy	Longitudinal cohort	N.a.	67	24.5 (3.4), 17-31	42.2	CAARMS	36	5
Fuijoka 2020[30]	Japan	Longitudinal cohort	87.5% APS, 8.3% BIPS, 25.0% GRD	24	20.4 (3.7),14-28	50.0	SIPS/SOPS	37.8	5
Fusar-Poli 2020[31]	UK	Longitudinal cohort	80.4% APS, 18.1% BLIPS, 1.5% GRD	598	22.6 (4.9), 14-35	44.7	CAARMS	120	5
Gaspar 2019[32]	Chile	Longitudinal cohort	92.6% APS, 7.4% GRD	27	17.6 (2.9), 12-28	29.7	SIPS/SOPS	24	4
Geros 2020[33]	Australia	Longitudinal cohort	N.a.	467	18.7 (2.8), 15-24	55.7	CAARMS	12	4

Glenthøj 2020[34]	Denmark	Longitudinal cohort	98.6% APS, 2.1% BLIPS, 21.9% GRD	146	23.9 (4.2), 18-40	58.2	CAARMS	12	4
Grent-'t-Jong 2020[35]	Scotland	Longitudinal cohort	73.1% APS, 1.7% GRD, 25.2% BS	119	22.0 (4.4)	73.1	CAARMS	36	4
Guo 2019[36]	USA	Longitudinal cohort	N.a.	117	16.6 (3.5), 12-25	42.7	SIPS/SOPS	12	4
Hamilton 2019[37]	USA	Longitudinal cohort	100% APS, 2.3% BIPS, 2.3% GRD	43	16.9 (3.5), 12.0-26.6	37.2	SIPS/SOPS	28	5
Healey 2013[38]	Multi	Longitudinal cohort	98.6% APS, 2% GRD	147	19.8 (4.7)	42.2	SIPS/SOPS	24	4
Heinze 2018[39]	UK	Longitudinal cohort	N.a.	14	20.8 (3.1)	64.3	CAARMS	12	3
Hengartner 2017[40]	Switzerland	Longitudinal cohort	53.2% APS, 3.2% BIPS, 92.0% BS	188	20.5 (5.8), 13-35	39.8	SIPS/SOPS, SPI-A, SPI-CY	36	4
Hormozpour 2016[41]	Iran	Longitudinal cohort	N.a.	50	27.5 (5.0), 15-35	47.8	SIPS/SOPS	12	5
Howes 2011[42]	UK	Longitudinal cohort	N.a.	24	24.2 (3.5), 14-35	37.0	CAARMS	36	5
Howes 2019[43]	UK	Longitudinal cohort	N.a.	51	23.0 (4.0), 14-35	43.0	CAARMS	15	7
Hui 2013[44]	UK	Longitudinal cohort	100% APS, 11.7% GRD	60	20.2 (2.9), 16-35	48.3	CAARMS	12	5
Hur 2012[45]	Korea	Longitudinal cohort	92.3% APS, 10.8% GRD	65	20.9 (3.9)	38.5	CAARMS	12	5
Iftimovici 2020[46]	France	Longitudinal cohort	N.a.	133	21.0 (4.0), 16-30	N.a.	CAARMS	12	5
Jang 2011[47]	Korea	Longitudinal cohort	N.a.	57	21.2 (4.0)	35.1	CAARMS	62.4	4
Kambeitz-Ilankovic 2019[48]	Germany	Longitudinal cohort	N.a.	48	24.7 (5.8)	33.3	CAARMS	48	6
Kantrowitz 2015[49]	USA	Randomized clinical trial	N.a.	20	19.0 (3.5), 13-35	25.0	SIPS/SOPS	4	Unclear risk of bias
Katsura 2014[50]	Japan	Longitudinal cohort	95.3% APS, 3.8% BIPS, 14.2% GRD	106	20.0 (4.3), 14-35	62.3	CAARMS	36	4
Kayser 2013[51]	USA	Longitudinal cohort	100% APS	21	21.4 (3.8), 13-27	38.1	SIPS/SOPS	48	4
Keri 2009[52]	Hungary	Longitudinal cohort	100% APS, 100% BLIPS, 55.2% GRD	67	21.2 (3.6)	46.3	CAARMS	12	6

Kim 2012[53]	Korea	Longitudinal Cohort	91% APS, 1.3% BLIPS, 16.7% GRD	78	21.5 (4.2)	34.3	CAARMS	60	5
Kleineidam 2019[54]	Germany	Longitudinal cohort	N.a.	160	25.7 (6.7)	32.5	ERIraos	24	6
Kline 2015[55]	USA	Longitudinal cohort	N.a.	21	16.2 (3.1), 12-22	65.0	SIPS/SOPS	6	5
Kollias 2018[56]	Greece	Longitudinal cohort	76.9% APS, 11.5% BLIPS, 11.5% GRD	26	25.3 (4.3)	46.2	CAARMS	36	4
Konishi 2018[57]	USA	Longitudinal cohort	N.a.	19	20.9 (4.3)	31.6	SIPS/SOPS	12	3
Korkeila 2013[58]	Multi	Longitudinal cohort	84% APS, 0.8% BIPS, 16.4% GRD, 70.1% BS	244	22.6 (5.1), 16-36	44.0	SIPS/SOPS, BSABS–P	48	5
Kotlicka-Antczak 2017[59]	Poland	Longitudinal cohort	76.5% APS, 4.9% BLIPS, 38.3% GRD	81	18.7 (3.5), 15-32	51.9	CAARMS	62	6
Kotlicka-Antczak 2018[60]	Poland	Longitudinal cohort	N.a.	82	18.6; 3.4, 14-29	51.2	CAARMS	42	6
Kraan 2015[61]	Netherlands	Longitudinal cohort	82.4% APS, 8.8% BIPS, 15.2% GRD, 64.0% BS	125	17.7 (3.9), 12-35	32.0	SIPS/SOPS	24	6
Kraan 2017[62]	Netherlands	longitudinal cohort	85.8% APS, 0.9% BLIPS, 13.3% GRD	113	23.5 (5.4), 14-35	55.8	CAARMS	48	4
Kraan 2018[63]	Multi	Longitudinal cohort	85.7% APS, 5.8% BLIPS, 15.8% GRD	259	22.7 (4.5), 15-35	46.1	CAARMS	24	4
Kristensen 2020[64]	Denmark	Randomized clinical trial	N.a.	57	24.1 (3.6),18-40	54.4	CAARMS	6.5	Low risk of bias
Labad 2015[65]	Spain	Longitudinal cohort	61.5% APS, 17.9% BLIPS, 20.5% GRD	39	22.3 (4.6)	30.8	CAARMS	12	5
Lam 2018[66]	Singapore	Longitudinal cohort	N.a.	173	21.3 (3.5), 14-29	32.4	CAARMS	24	4
Landa 2016[67]	USA	Longitudinal cohort	66.7% APS, 16.7% BLIPS, 16.7% GRD	6	19.5 (1.5), 16-21	66.7	CAARMS	6.7	3
Lee 2013[68]	Singapore	Longitudinal cohort	83.2% APS, 3.5% BLIPS, 28.3% GRD	173	21.3 (3.5), 14-29	32.4	CAARMS	24	5
Lee 2014[69]	Korea	Longitudinal cohort	92.5% APS, 0.7% BIPS, 18.7% GRD	134	19.7 (3.2)	27.6	SIPS/SOPS	24	4
Lemos-Giraldez 2009[70]	Spain	Longitudinal cohort	85.2% APS, 4.9% BIPS, 9.8% GRD	61	21.7 (3.8), 15-31	34.4	SIPS/SOPS	36	5

Lencz 2006[71]	USA	Longitudinal cohort	100% APS	38	16.5 (2.2)	42.0	SIPS/SOPS	72	5
Leon-Ortiz 2017[72]	Mexico	Longitudinal cohort	N.a.	33	19.6 (4.1)	21.2	SIPS/SOPS	24	6
Lindgren 2014[73]	Finland	Longitudinal cohort	98.1% APS, 5.5% GRD	54	16.7 (0.8), 15.2-18.1	81.5	SIPS/SOPS	12	5
Lindgren 2017[74]	Finland	Longitudinal cohort	N.a.	152	16.6 (0.8), 15-18	79.1	SIPS/SOPS	108	4
Liu 2011[75]	Taiwan	Longitudinal cohort	N.a.	59	21.5 (4.0), 16-32	44.1	SIPS/SOPS	52.8	6
Mamah 2016[76]	Kenya	Longitudinal cohort	N.a.	135	17.4 (1.3), 14-20	61.5	SIPS/SOPS	20	4
Manninen 2014[77]	Finland	Longitudinal cohort	100% APS	7	n.a., 15-18	28.6	SIPS/SOPS	60	3
Matsumoto 2019[78]	Japan	Longitudinal cohort	95.1% APS, 11% BLIPS/BIPS, 20.4% GRD	309	21.4 (5.5), 14-40	61.5	CAARMS, SIPS/SOPS	60	5
Morcillo 2015[79]	UK	Longitudinal cohort	100% APS, 11.7% GRD	60	19.9 (2.4), 16-35	48.3	CAARMS	24	7
Morrison 2007[80]	Australia	Randomized clinical trial	N.a.	23	N.a., 16-36	N.a.	PANSS	36	High risk of bias
Morrison 2012[81]	UK	Randomized clinical trial	N.a.	144	20.7 (4.5), 14-35	36,9	CAARMS	24	High risk of bias
Nelson 2011[82]	Australia	Longitudinal cohort	81.3% APS, 4.4% BLIPS, 25.6% Trait	817	N.a. (median: 14), 14-29	59.0	CAARMS	6	5
Nelson 2016[83]	Australia	Longitudinal cohort	N.a.	416	N.a., 15-30	N.a.	CAARMS	90	4
Niles 2019[84]	USA	Longitudinal cohort	100% APS	223	16.7 (4.1), 12-35	40.2	SIPS/SOPS	24	5
Nussbaum 2014[85]	Romania	Longitudinal cohort	N.a.	105	13.8 (4.0), 9-18	41.0	SIPS/SOPS	36	5
Ohmuro 2016[86]	Japan	Longitudinal cohort	97.2% APS, 19.4% GRD	36	20.9 (4.7), 14-35	61.1	CAARMS	25.6[b]	4
Osborne 2019[87]	USA	Longitudinal cohort	N.a.	68	18.6 (1.8), 13-21	41.2	SIPS/SOPS	24	4
Pelizza 2020[88]	Italy	Longitudinal cohort	89.6% APS, 5.2% BLIPS, 5.2% GRD	97	18.8 (4.3),13-35	54.6	CAARMS	24	4

Pelletier-Baldelli 2017[89]	USA	Longitudinal cohort	N.a.	53	18.8 (1.6), 12-21	39.6	SIPS/SOPS	12	3
Perkins 2019[90]	Multi	Longitudinal cohort	N.a.	764	18.6 (4.2), 12-35	42.7	SIPS/SOPS	48	4
Poletti, 2019[91]	Italy	Longitudinal cohort	70.6% APS, 3.9% BLIPS, 2% GRD, 84.3% BS	51	15.4 (1.6), 13-18	58.8	CAARMS, SPI-CY	24	5
Pontillo 2019[92]	Italy	Longitudinal cohort	N.a.	75	14.6 (5.1), 6-27	41.3	SIPS/SOPS	12	5
Pozza 2020[93]	Italy	Randomized clinical trial	100% APS, 3.4% BLIPS, 17.2% GRD	29	26.0 (6.0), 16-35	31.0	CAARMS	14	Low risk of bias
Provenzano 2020[94]	USA	Longitudinal cohort	100% APS	75	21.2 (3.9), 15-30	30.7	SIPS/SOPS	30	6
Pruessner 2012[95]	Canada	Longitudinal cohort	83.3% APS, 3.3% BLIPS, 13.3% vulnerable	30	20.3 (3.2)	46.7	CAARMS	12	4
Pruessner 2017[96]	Canada	Longitudinal cohort	80.8% APS, 5.1% BLIPS, 14.1% GRD	177	19.3 (4.0), 14-35	38.9	CAARMS	24	4
Quijada 2015[97]	Spain	Longitudinal cohort	N.a.	38	16.7 (5.9), 12-39	23,7	SIPS/SOPS	12	4
Rehki 2019[98]	Singapore	Longitudinal cohort	96.5% APS	173	21.3 (3.5), 14-29	32.4	CAARMS	24	4
Roalf 2019[99]	USA	Longitudinal cohort	N.a.	38	15.5 (2.5), 8-21	52.6	SIPS/SOPS	40	4
Rosen 2019[100]	Germany	Longitudinal cohort	73.7% APS, 20.7% BIPS, 94.8% BS	213	24.9, 14-40	35.7	SIPS/SOPS, SPI-A	125.5	5
Ryan 2018[101]	Multi	Longitudinal cohort	92.8% APS, 3% BIPS, 11% GRD, 6% Schizotypal	1093	18.4 (4.4)	N.a.	SIPS/SOPS	24	4
Sakuma 2018[102]	Japan	Longitudinal cohort	93.3% APS, 6.7% BLIPS, 11.1% GRD	45	21.0 (5.0), 14-35	60.0	CAARMS	12	5
Salokangas 2016[103]	Multi	Longitudinal cohort	N.a.	245	22.4, 14-35	44.1	SIPS/SOPS, SPI-A	18	4
Sasabayashi 2020[104]	Japan	Longitudinal cohort	N.a.	107	21.3 (5.4)	54.2	CAARMS, SIPS/SOPS	90	4
Sawada 2017[105]	Japan	Longitudinal cohort	N.a.	47	19.9, 3.5, 12-30	52.9	SIPS/SOPS	54	5

Schlosser 2012[106]	USA	Longitudinal cohort	77.5% APS, 20.2% BIPS, 2.4% GRD	84	16.9 (3.5)	38.0	SIPS/SOPS	24	4
Schneider 2016[107]	Multi	Longitudinal cohort	72.7% APS, 9.1% BIPS, 31.8% GRD	22	16.6 (6.4), 9-24	45.4	SIPS/SOPS	85	4
Schultze-lutter 2014[108]	Germany	Longitudinal cohort	N.a.	246	25.3, (6.6)	38.2	SIPS/SOPS, BSABS, SPI-A	48	4
Sevilla-Llewellyn-Jones 2018[109]	UK	Longitudinal cohort	100% APS, 7.5% GRD	40	21.6 (2.6), 18-35	52.5	CAARMS	36	5
Simon 2012[110]	Switzerland	Longitudinal cohort	93.2% APS, 4.1% LIPS, 2.7% GRD, 35.6% BS	73	20.4 (5.2), 14-40	39,7	SIPS/SOPS	24	4
Takahashi 2013[111]	Japan	Longitudinal cohort	95.5% APS, 9.1% BLIPS, 4.5% GRD	22	19.1 (4.1), 15-30	50.0	CAARMS	15.6[b]	5
Takahashi 2018[112]	Japan	Longitudinal cohort	100% APS	38	18.4 (3.9), 15-30	36.8	CAARMS	29.9[b]	4
Takahashi 2019[113]	Japan	Longitudinal cohort	N.a.	38	18.4 (3.9)	36.8	CAARMS	126.8[b]	4
van der Gaag 2012[114]	Netherlands	Randomized clinical trial	N.a.	103	22.6 (5.5), 14-35	51.5	CAARMS	18	High risk of bias
van Tricht 2015[115]	Netherlands	Longitudinal cohort	N.a.	61	20.3 (4.0), 15-35	25.6	SIPS/SOPS	36	6
Velthorst 2011[116]	Netherlands	Longitudinal cohort	N.a.	77	19.2 (3.8), 12-35	33.8	SIPS/SOPS	36	5
Velthorst 2013[117]	Netherlands	Longitudinal cohort	89.9% APS, 6.8% BIPS, 4.1% GRD, 25% BS	148	17.2 (3.8)	35.8	SIPS/SOPS, BSABS-P	51	4
Velthorst 2018[118]	Multi	Longitudinal cohort	95.8% APS, 3.9% BIPS, 0.6% GRD	358	17.1 (2.8), 12-23	34.6	SIPS/SOPS	30	6
von Hohenberg 2014[119]	USA	Longitudinal cohort	89.3% APS, 14.3% GRD	28	20.6 (3.9), 13-35	36.0	SIPS/SOPS	12.3	5
Wang 2020[120]	China	Longitudinal cohort	N.a.	18	24.6 (5.8)	33.3	SIPS/SOPS	48	3
Welsh 2014[121]	UK	Longitudinal cohort	100% APS, 13.3% GRD	30	15.8 (1.4), 12-18	53.0	CAARMS	24	4
Woodberry 2013[122]	USA	Longitudinal cohort	94% APS, 17% GRD	53	16.0 (2.4), 12-25	51.0	SIPS/SOPS	23[b]	4
Woods 2009[123]	Multi	Longitudinal cohort	91.2% APS, 3.2% BIPS, 23.6% GRD	377	18.2	37.9	SIPS/SOPS	36	4

Youn 2019[124]	Multi	Longitudinal cohort	90.1% APS, 43.1% BS	304	19.1 (4.6), 13-39	54.3	CAARMS, SPI-A	60	5
Yoviene Sykes 2019[125]	USA	Longitudinal cohort	N.a.	432	19.1 (4.3), 12-35	41.9	SIPS/SOPS	12	5
Yung 2004[126]	Australia	Longitudinal cohort	66.3% APS, 27.9% BLIPS, 37.5% GRD	104	19.4 (3.5), 14-28	51.0	CAAMRS	28	4
Zhang 2018[127]	China	Longitudinal cohort	N.a.	511	20.6 (6.2), 14-45	52.8	SIPS/SOPS	24	4
Zhang 2019[128]	China	Longitudinal cohort	91.8% APS, 3.4% BIPS, 12.5% GRD	417	20.9 (6.4), 14-45	52.0	SIPS/SOPS	78	5
Zhang 2020[129]	China	Longitudinal cohort	N.a.	517	20.5 (6.2), 13-45	52.8	SIPS/SOPS	36	4
Ziermans 2011[130]	Netherlands	Longitudinal cohort	N.a.	72	15.3 (1.9), 12-18	38.0	SIPS/SOPS	24	4

[a] Two or more studies from the same sample could be included in the meta-analysis if they provided independent data at different time points; [b] Mean duration of follow-up.
APS: Attenuated Psychosis Symptoms; BIPS: Brief Intermittent Psychosis Syndrome; BLIPS: Brief Limited Intermittent Psychotic Symptoms; BS: Basic symptoms; BSABS: Bonn Scale for the Assessment of Basic Symptoms; BSIP: Basel Screening Instrument for Psychosis; CAARMS: Comprehensive Assessment of At-Risk Mental States; ERIraos: Early Recognition Inventory; GRD: Genetic risk and deterioration syndrome; NOS: Newcastle-Ottawa Scale; PANSS: Positive and Negative Syndrome Scale; RoB: Risk of Bias Tool; SIPS: Structured Interview for Prodromal Syndromes; SPI-A: Schizophrenia Proneness Instrument–Adult; SPI-CY: Schizophrenia Proneness Instrument–Child and Youth.

eTable 5: Sensitivity analyses.

Sensitivity analyses estimated the cumulative risk of psychosis under different assumptions relating to individuals at CHR-P lost at follow-up (dropouts). See also eFigure 1.

Follow-up	k	Sample size	Cumulative risk of psychosis	95%CI	Q	df	I^2
0.5 years							
Dropouts no transition	37	6.485	0.076	0.061-0.09	169.622	36	78.776
Equal risk of transition in dropouts and non-dropouts	37	6.485	0.085	0.069-0.101	174.649	36	79.387
Dropouts all transition	37	6.485	0.143	0.117-0.169	377.680	36	90.468
1 year							
Dropouts no transition	53	7.907	0.130	0.114-0.147	239.386	52	78.278
Equal risk of transition in dropouts and non-dropouts	53	7.907	0.145	0.128-0.163	235.363	52	77.906
Dropouts all transition	53	7.907	0.229	0.200-0.258	535.193	52	90.284
1.5 years							
Dropouts no transition	30	5.488	0.158	0.134-0.182	165.249	29	82.451
Equal risk of transition in dropouts and non-dropouts	30	5.488	0.195	0.166-0.223	195.342	29	85.154
Dropouts all transition	30	5.488	0.352	0.283-0.422	910.026	29	96.813
2 years							
Dropouts no transition	44	7.351	0.165	0.148-0.181	142.784	43	69.885
Equal risk of transition in dropouts and non-dropouts	44	7.351	0.194	0.174-0.215	197.557	43	78.234
Dropouts all transition	44	7.351	0.322	0.273-0.372	1074.378	43	95.998

2.5 years							
Dropouts no transition	19	3.114	0.203	0.168-0.238	111.599	18	83.871
Equal risk of transition in dropouts and non-dropouts	19	3.114	0.247	0.209-0.285	107.809	18	83.304
Dropouts all transition	19	3.114	0.431	0.350-0.512	421.421	18	95.729
3 years							
Dropouts no transition	29	4.029	0.208	0.179-0.238	143.734	28	80.520
Equal risk of transition in dropouts and non-dropouts	29	4.029	0.250	0.215-0.285	183.238	28	84.719
Dropouts all transition	29	4.029	0.387	0.313-0.461	740.537	28	96.219
4 years							
Dropouts no transition	16	2.926	0.216	0.185-0.246	56.390	15	73.400
Equal risk of transition in dropouts and non-dropouts	16	2.926	0.265	0.227-0.303	79.118	15	81.041
Dropouts all transition	16	2.926	0.439	0.322-0.556	756.624	15	98.018
>4 years							
Dropouts no transition	14	2.301	0.221	0.167-0.275	124.215	13	89.534
Equal risk of transition in dropouts and non-dropouts	14	2.301	0.283	0.198-0.369	304.356	13	95.729
Dropouts all transition	14	2.301	0.431	0.203-0.659	3180.00	13	99.59

eTable 6: Meta-analytical estimates of the hazard rate of transition to psychosis in individuals at CHR-P.

Follow-up time	Sample size	N of transitions to psychosis	Hazard rate of transition to psychosis	95% CI
0.5	4860	451	0.143	0.131-0.153
1	3408	677	0.121	0.115-0.134
1.5	2892	819	0.100	0.094-0.113
2	2357	905	0.083	0.073-0.094
2.5	1444	1013	0.086	0.077-0.112
3	1029	1040	0.047	0.035-0.058
3.5	808	1053	0.030	0.020-0.041
4	737	1062	0.022	0.016-0.035
4.5	662	1069	0.016	0.011-0.027
5	628	1073	0.014	0.009-0.025
5.5	420	1076	0.014	0.010-0.032
6	397	1079	0.015	0.009-0.026
6.5	373	1081	0.012	0.007-0.020
7	323	1087	0.012	0.007-0.018
7.5	323	1087	0.012	0.008-0.021
8	323	1087	0.014	0.008-0.029
8.5	250	1088	0.015	0.008-0.042
9	250	1088	0.020	0.010-0.102
9.5	132	1089	0.027	0.012-0.389
10	114	1092	0.028	0.011-(Inf)

eTable 7: Meta-analytical estimates of the Kaplan-Meier failure function (1 − survival) of transition to psychosis in individuals at CHR-P, re-estimated 1 year after the start of the follow-up.

Follow-up time	N of individuals at CHR-P at risk	N of transitions to psychosis	Cumulative risk of transition to psychosis	95%CI	
0.5	2892	142	0.044	0.051	0.037
1	2357	228	0.076	0.085	0.066
1.5	1444	336	0.130	0.143	0.116
2	1029	363	0.150	0.166	0.135
2.5	808	376	0.163	0.180	0.147
3	737	385	0.173	0.190	0.155
3.5	662	392	0.182	0.200	0.163
4	628	396	0.187	0.205	0.167
4.5	420	399	0.192	0.211	0.172
5	397	402	0.198	0.218	0.177
5.5	373	404	0.202	0.223	0.180
6	323	410	0.216	0.239	0.192
6.5	323	410	0.216	0.239	0.192
7	323	410	0.216	0.239	0.192
7.5	250	411	0.219	0.243	0.194
8	250	411	0.219	0.243	0.194
8.5	132	412	0.225	0.251	0.198
9	114	415	0.245	0.279	0.210
9.5	111	417	0.259	0.296	0.219
10	111	417	0.259	0.296	0.219

eTable 8: Meta-analytical estimates of the Kaplan-Meier failure function (1 − survival) of transition to psychosis in individuals at CHR-P, re-estimated 2 years after the start of the follow-up.

Follow-up time	N of individuals at CHR-P at risk	N of transitions to psychosis	Cumulative risk of transition to psychosis	95%CI	
0.5	1444	108	0.058	0.069	0.048
1	1029	135	0.081	0.094	0.067
1.5	808	148	0.095	0.110	0.079
2	737	157	0.105	0.122	0.089
2.5	662	164	0.115	0.132	0.097
3	628	168	0.120	0.138	0.101
3.5	420	171	0.126	0.145	0.106
4	397	174	0.132	0.153	0.111
4.5	373	176	0.137	0.158	0.115
5	323	182	0.152	0.176	0.127
5.5	323	182	0.152	0.176	0.127
6	323	182	0.152	0.176	0.127
6.5	250	183	0.155	0.180	0.130
7	250	183	0.155	0.180	0.130
7.5	132	184	0.162	0.189	0.133
8	114	187	0.183	0.219	0.146
8.5	111	189	0.198	0.238	0.156
9	111	189	0.198	0.238	0.156

eTable 9: Meta-analytical estimates of the Kaplan-Meier failure function (1 − survival) of transition to psychosis in individuals at CHR-P, re-estimated 3 years after the start of the follow-up.

Follow-up time	N of individuals at CHR-P at risk	N of transitions to psychosis	Cumulative risk of transition to psychosis	95%CI	
0.5	808	13	0.015	0.023	0.007
1	737	22	0.027	0.038	0.016
1.5	662	29	0.037	0.050	0.023
2	628	33	0.043	0.057	0.028
2.5	420	36	0.049	0.064	0.033
3	397	39	0.056	0.073	0.038
3.5	373	41	0.061	0.079	0.042
4	323	47	0.077	0.099	0.054
4.5	323	47	0.077	0.099	0.054
5	323	47	0.077	0.099	0.054
5.5	250	48	0.081	0.104	0.057
6	250	48	0.081	0.104	0.057
6.5	132	49	0.088	0.114	0.060
7	114	52	0.111	0.148	0.073
7.5	111	54	0.127	0.169	0.084
8	111	54	0.127	0.169	0.084

eTable 10: Meta-analytical estimates of the Kaplan-Meier failure function (1 − survival) of transition to psychosis in individuals at CHR-P, re-estimated 4 years after the start of the follow-up.

Follow-up time	N of individuals at CHR-P at risk	N of transitions to psychosis	Cumulative risk of transition to psychosis	95%CI	
0.5	662	7	0.010	0.018	0.003
1	628	11	0.016	0.026	0.007
1.5	420	14	0.023	0.034	0.011
2	397	17	0.030	0.044	0.015
2.5	373	19	0.035	0.051	0.019
3	323	25	0.052	0.072	0.031
3.5	323	25	0.052	0.072	0.031
4	323	25	0.052	0.072	0.031
4.5	250	26	0.056	0.077	0.033
5	250	26	0.056	0.077	0.033
5.5	132	27	0.063	0.088	0.037
6	114	30	0.087	0.123	0.049
6.5	111	32	0.103	0.145	0.060
7	111	32	0.103	0.145	0.060

eTable 11: Meta-analytical estimates of the Kaplan-Meier failure function (1 − survival) of transition to psychosis in individuals at CHR-P, re-estimated 5 years after the start of the follow-up.

Follow-up time	N of individuals at CHR-P at risk	N of transitions to psychosis	Cumulative risk of transition to psychosis	95%CI	
0.5	420	3	0.006	0.014	0.000
1	397	6	0.014	0.025	0.003
1.5	373	8	0.019	0.032	0.006
2	323	14	0.036	0.055	0.017
2.5	323	14	0.036	0.055	0.017
3	323	14	0.036	0.055	0.017
3.5	250	15	0.040	0.060	0.020
4	250	15	0.040	0.060	0.020
4.5	132	16	0.047	0.071	0.022
5	114	19	0.072	0.107	0.035
5.5	111	21	0.089	0.130	0.045
6	111	21	0.089	0.130	0.045

eTable 12: Meta-regressions transition to psychosis, duration and moderating factors.
All studies were pooled together across any timepoints. In case of overlapping studies, the ones with the longest follow-up time were selected. The final database thus included only non-overlapping studies. To control for the variable duration of follow-up, the latter factor was used as fixed covariate in multiple meta-regressions.

Factor (reference)		No. of Studies	β Coefficient	SE	95% CI		Z-Value	P value
Fixed covariate: Duration of follow-up		74	0.002	0.001	0.001	0.003	3.930	<**0.001**
Year of publication		74	-0.014	0.026	-0.065	0.037	-0.530	0.596
Study design: *(Cohort)* *RCT*		74	 0.038	 0.377	 -0.701	 0.776	 0.100	 0.920
% of APS		38	0.012	0.014	-0.015	0.041	0.877	0.380
% of BLIPS/BIPS		33	0.020	0.007	0.005	0.034	2.706	**0.007**
% of GRD		34	-0.014	0.013	-0.041	0.012	-1.087	0.277
% of Basic symptoms		5	D.n.a. [a]					
Mean age		73	0.016	0.027	-0.036	0.069	0.615	0.538
% of females		73	-0.021	0.007	-0.035	-0.006	-2.827	**0.005**
CHR-P assessment instrument: *(CAARMS)* *SIPS* *Others*		74	 0.135 0.359	 0.175 0.332	 -0.209 -0.291	 0.479 1.010	 0.768 1.082	 0.442 0.279
Quality of the study: NOS scores [b]		69	0.086	0.061	-0.034	0.205	1.41	0.160
Continent: *(Europe)* *Asia* *North America* *Australia* *Other*		74	 -0.163 0.044 0.188 -0.342	 0.253 0.215 0.377 0.525	 -0.660 -0.377 -0.841 -1.081	 0.333 0.464 1.217 0.396	 -0.644 0.204 0.358 -0.909	 0.519 0.838 0.720 0.364
Duration of untreated attenuated psychotic symptoms		3	D.n.a.[a]					
Baseline ICD/ DSM comorbid disorders	% any non-psychotic mental disorder	5	D.n.a.[a]					
	% of any mood disorder	14	0.016	0.0157	-0.015	0.047	1.022	0.306
	% of major depressive disorder	7	D.n.a.[a]					

	% of bipolar disorders	6	D.n.a.[a]					
	% of personality disorders	4	D.n.a.[a]					
	% of neurodevelopmental disorders	4	D.n.a.[a]					
	% of anxiety disorders	20	0.010	0.011	-0.011	0.031	0.943	0.346
	% of ADHD	4	D.n.a.[a]					
	% of cannabis use disorder	4	D.n.a.[a]					
	% of alcohol use disorder	3	D.n.a.[a]					
	% of other substance use disorder[c]	6	D.n.a.[a]					
	% of PTSD	5	D.n.a.[a]					
	% of OCD	7	D.n.a.[a]					
Interventions	% of antipsychotics baseline	30	0.009	0.005	-0.001	0.020	1.728	0.084
	% of antipsychotics at follow-up	9	D.n.a.[a]					
	% of antidepressants at baseline	16	-0.001	0.008	-0.018	0.015	-0.126	0.900
	% of antidepressants at follow-up	6	D.n.a.[a]					
	% of any other psychotropics at baseline	14	0.004	0.010	-0.015	0.023	0.405	0.685
	% of any other psychotropics at follow-up	4	D.n.a.[a]					
	% of psychotherapy at baseline	6	D.n.a.[a]					
	% of psychotherapy at follow-p	3	D.n.a.[a]					

[a]D.n.a: does not apply due to lack of enough studies (<10 studies) providing this data to evaluate its influence; [b] Within the RoB2, 50% RCT had a high risk of bias, 37.5% unclear risk of bias and 12.5% low risk of bias; however these data were not used in the meta-regression analyses; [c]Excluding alcohol use disorders and cannabis use disorder.
ADHD: Attention Deficit and Hyperactivity Disorder; APS: Attenuated Psychosis Symptoms; BLIPS: Brief Limited Intermittent Psychotic Symptoms; BS: Basic symptoms; CAARMS: Comprehensive Assessment of At Risk Mental States; GRD: Genetic risk and deterioration syndrome; DSM: Diagnostic and Statistical Manual of Mental Disorders; ICD: International classification of diseases; OCD: obsessive-compulsive disorder; PTSD: Posttraumatic stress disorder; RCT: randomized controlled trial; SIPS: Structured Interview for Prodromal Syndromes.

eMethods 1: Search terms used for the literature search.

The following search terms were applied:

("risk" OR "prodrom*" OR "prediction" OR "onset" OR "ultra-high risk" OR "clinical high risk" OR "attenuat*" OR "APS" OR "high risk" OR "BLIPS" OR "brief limited" OR "brief intermittent" OR "genetic high risk" OR "GRD" OR "at-risk mental state" OR "risk of progression" OR "progression to first-episode" OR "basic symptoms")

AND

("psychosis" OR "schizophrenia" OR "schizoaffective").

eMethods 2: CHR-P instruments included (modified from[131]).

The CHR-P state comprises the Ultra High Risk state and/or the Basic Symptoms[131].

- The following UHR instruments were considered to define the UHR state: Comprehensive Assessment of At Risk Mental States (CAARMS[132]) and Structured Interview for Psychosis-risk Syndromes (SIPS[133,134]) and Early Recognition Inventory (ERIraos[135]). Furthermore, before the development of these instruments, the CHR-P state was defined through the Positive and Negative Syndrome Scale (PANSS[136]), Brief Psychiatric Rating Scale (BPRS[137]).
- The following UHR instruments were considered to define the BS[131]: Bonn Scale for the Assessment of Basic Symptoms (BSABS[138]), Basel Screening Instrument for Psychosis (BSIP[139]), and Schizophrenia Proneness Instrument[140] - Adult (SPI-A) and Child and Youth (SPI-CY) version -.
- Transition to psychosis was operationalised as defined by each CHR-P instrument or according to ICD/DSM-any version.

Individuals not formally assessed with these instruments were not included in the current systematic review and meta-analysis. For example, those at genetic risk for psychosis (twins, first or second-degree relatives) or with a schizotypal personality disorder but without functional impairments were not included.

Current meta-analytic estimates of psychosis onset are closely related to the way the psychosis threshold is operationalised in the CHR-P field. Addressing validity of this threshold is outside the scope of the current review of existing cohort studies and meta-analysis. However, we have recently demonstrated that psychosis onset in this population is associated with meaningful real-world outcomes[141] that deserve clinical attention. Notably, psychotic experiences[142], measured through self-administered questionnaires[143], are relatively frequent at the population-level (prevalence about 8% in young adults aged 24[144]) and poorly predictive of psychosis onset (risk of psychosis: 0.5-1% per year[144]). However, these manifestations cannot be conflated with the CHR-P, which requires detection by an experienced and trained clinician to distinguish pathological from non-pathological phenomena[145], and it is not common in the general population (only 0.3% of individuals[146]), being highly predictive of psychosis onset (risk of psychosis: 20% at 2 years[131,147].

eMethods 3: Study measures.

A) Measures describing the main characteristics of the studies included:

- First author and year of publication.
- Country.
- Study design (Longitudinal cohort, Randomized clinical trial, Other trials [e.g. non-randomised trial, non-blinded (e.g. open-label), non-controlled (e.g. naturalistic 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-.
- CHR-P sample size.
- Mean age (SD or range).
- Proportion of females.
- CHR-P assessment instrument (as listed in eMethods 2).
- Duration of follow-up (in months).
- Study quality: total NOS scores.

B) Planned meta-regressor factors that may affect transition risk:

- Duration of follow-up (fixed covariate for meta-regressions).
- Year of publication, study design, proportion of APS, BLIPS, GRD, BS, mean age, proportion of females, CHR-P assessment tools, study quality (**see A**).
- Continent: Europe, Asia, North America, Australia, Other.
- Duration of untreated attenuated psychotic symptoms – in months- (as per Fusar-Poli 2012[148]).
- Proportion of baseline comorbid mental disorders (al ICD or DSM-defined): a) any non-psychotic mental disorder; b) any mood disorder c) major depressive disorder; d) bipolar disorders; e) personality disorders; f) neurodevelopmental disorders; g) anxiety disorders; h) ADHD; i) cannabis use disorder; j) alcohol use disorder; k) other substance use disorder; l) PTSD; m) OCD.
- Proportion of interventions at baseline and follow-up: a) antipsychotics, b) antidepressants, c) other psychotropics, d) psychotherapy [including CBT, IPT and other psychotherapeutic interventions], e) needs-based-intervention (as previously defined i.e. encompassing: supportive psychotherapy primarily focusing on pertinent

issues such as social relationships and vocational or family problems; case management, providing psychosocial assistance with accommodation, education or employment; brief family psychoeducation and support).

eMethods 4: Quality assessment.

All the included studies were evaluated using a modified version of the Newcastle-Ottawa Scale (NOS) for cohort studies. This modified version has been repeatedly used for systematic reviews and meta-analysis in the CHR-P field[147,149-151] (see eTable_3). Studies were awarded a maximum of eight points on six items: a) Representativeness of exposed cohort: the sample should be representative and not focus on a selected group with particular socio-demographic characteristics; sample size should be adequate; b) Robustness of the method used to ascertain exposure: comprehensive UHR state and BS instruments that have been validated should be used to characterize the CHR-P state (see eMethods 2); c) Comparability between the groups: studies matching the groups or adjusting for confounding factors or moderators are associated with higher quality; the influence of sociodemographic and clinical factors in the results should be analysed and discussed; d) Assessment of outcome: robust tools should be used to determine the outcome of interest (i.e. transition to psychosis); blinding of the researchers is associated with higher study quality; e) Follow-up duration: follow-up should be sufficiently long for outcomes to occur. In studies with short follow-up durations (<6 months), there is an increased risk of transition to psychosis being found as a result of a better characterization and more comprehensive reporting of symptoms by patients after a longer interaction with the researchers; f) Loss to follow-up: loss to follow-up rate should be reported, and this should be low (<30%), and similar in all the included groups.

We additionally used the Cochrane Risk of Bias tool (RoB2)[152] to assess the risk of bias within Randomized Controlled Trials only (i.e. this tool was not applied to observational studies). For RoB2, a judgment was made about whether each study had a high, low or unclear risk of bias in each of the following six domains: random sequence generation, allocation concealment, blinding of participants and study personnel, blinding of outcome assessments, incomplete outcome data, and selective outcome reporting. The overall risk of bias was classified as low if none of the domains was rated as high risk and three or less were rated as unclear risk; as unclear if one domain was rated as high risk, or none rated as high risk but four or more rated as unclear risk; as high risk of bias if more domains were rated as high or unclear risk[153].

eMethods 5: Recreation of individual data from Kaplan-Meier plots.

We digitalized the Kaplan-Meier plots associating each angle or censor mark of the curve with a pixel coordinate, and we scaled the coordinates so that the plot's width corresponded to the maximum follow-up time and the plot's height to 100% individuals. We used the GNU Image Manipulation Program (GIMP)[154], but many other programs could be used at this regard. Afterward, the script[155] recreated the survival plot starting from time zero and 100% individuals.

The script understands every censor mark as a patient lost to follow-up at that time, and every curve descent as one or more transitions at that time. Note that the magnitude of each drop depends on the number of transitions at that time. When the number of transitions is inexact (e.g., 2.2-2.8 could correspond to either 2 or 3 transitions), the script rounds the number of transitions randomly up or down, and it repeats the recreation process many times (5000) to find the best recreation according to the root mean square error (RMSE) criterion.

The reader may find the script at:
https://karger.figshare.com/ndownloader/files/7546831.

eMethods 6: Script used to conduct the primary analyses.

Note: we estimated the hazard rate with the “muhaz” package for R[156].

```
library(survival)
library(muhaz)

# Read individual data (estimated as in eMethods 4)
X = read.csv("individual_data.csv")

# Cumulative incidence of psychosis
m = survfit(Surv(X$time, X$status) ~ 1)
plot(0, 0, type = "n", xlim = c(0, 10), ylim = c(0, 0.4),
    xlab = "Follow-up (years)", ylab = "Cumulative incidence")
lines(m$time, 1 - m$lower, col = "#aabbcc")
lines(m$time, 1 - m$upper, col = "#aabbcc")
lines(m$time, 1 - m$surv, col = "#333399")

# Add hazard rate
m = muhaz(X$time, X$status, max.time = 10)
par(new = TRUE)
plot(0, 0, type = "n", xlim = c(0, 10), ylim = c(0, 0.2),
    xlab = "", ylab = "", xaxt = "n", yaxt = "n", frame.plot = FALSE)
axis(4, at = 0:8 / 40, labels = c(0, sub("0.", ".", 1:8 / 40)))
mtext("Hazard rate", side = 4, col = "#993333", line = 2.1)
lines(m$est.grid, m$haz.est, col = "#993333")

# Survival estimates after k years (e.g., k = 1)
k = 1
Xk = X
Xk$time = Xk$time - 1
Xk = Xk[which(Xk$time > 0),]
m = summary(survfit(Surv(Xk$time, Xk$status) ~ 1))
m = data.frame(stime = m$time, n.risk = m$n.risk, n.event = cumsum(m$n.event),
            surv=m$surv, lower=m$lower, upper=m$upper)
SURV= NULL
for(time in 1:20 / 2) {
  SURV = rbind(SURV, cbind(time, m[which(m$stime > time)[1] - 1,]))
}
SURV$stime = NULL
SURV
```

eResults. Prediction interval analyses and assessment of publication bias.

Prediction interval analyses

Prediction intervals were estimated for all the evaluated time points.

At 0.5 years follow-up prediction interval was 0.015-0.368; at 1 year follow-up prediction interval was 0.068-0.281; at 1.5 years follow-up prediction interval was 0.097-0.354; at 2 years follow-up prediction interval was 0.108-0.325; at 2.5 years follow-up prediction interval was 0.119-0.442; at 3 years follow-up prediction interval was 0.129-0.429; at 4 years follow-up prediction interval was 0.146-0.433; at >4 years follow-up prediction interval was 0.092-0.607.

Assessment of publication bias

We conducted a Cox regression in which the dependent variable was the time to transition and the independent variable was the sample size, and the regression did not detect any relationship between sample size and transition hazard (HR=1, z=-0.3, p=0.77).

eDiscussion: Potential implications of attrition in the current study.

Study drop out is a frequent phenomenon in prospective cohort studies. The exact factors that may lead to study dropout are not well established in CHR-P research and there is limited evidence investigating the hazard rate of transition to psychosis in individuals at CHR-P who drop out compared to those who complete the follow-up. However, there is converging evidence suggesting that attrition occurs at random.

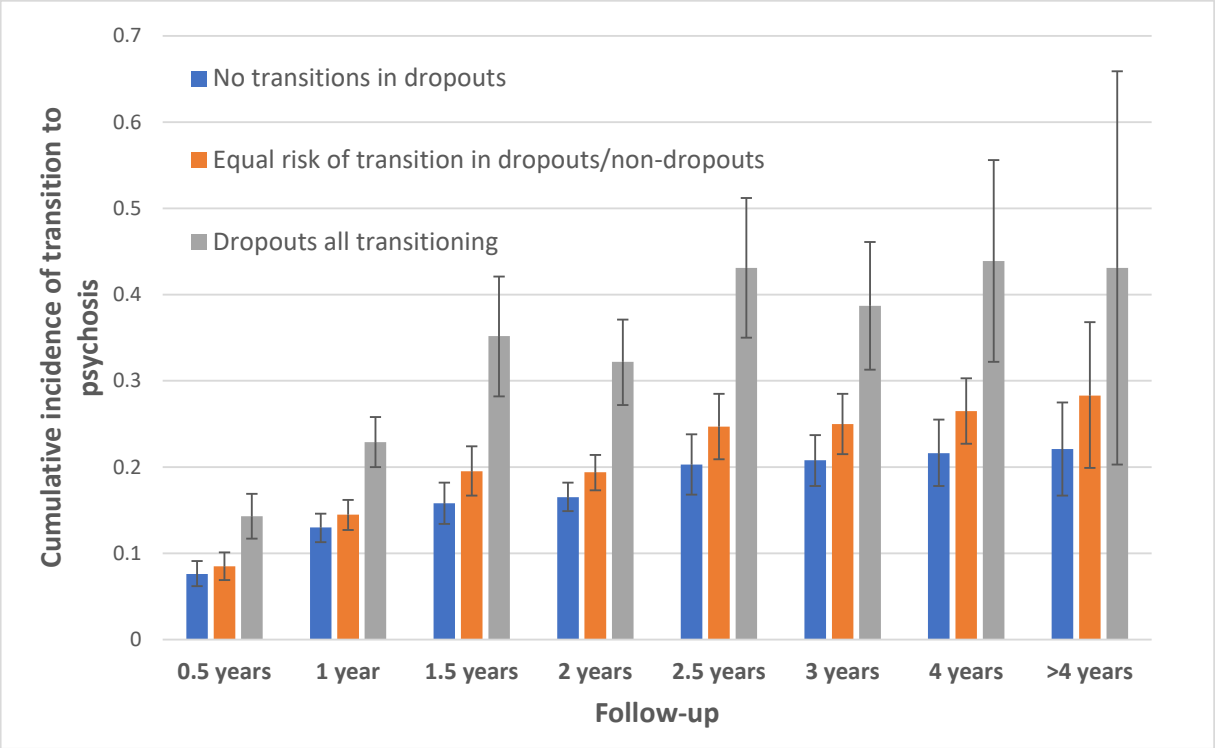
First, recent large-scale, real-world cohort studies that leverage Electronic Health Records (EHRs) demonstrated that transition risk is similar among individuals at CHR-P followed and not followed-up (see[157] and eFigure 6 published in[158]). There is additional independent evidence indicating that individuals at CHR-P who drop out share similar demographic characteristics with those who are followed-up and are similarly impaired with respect to functional status, severity of attenuated psychotic symptoms and baseline to follow-up changes in severity of symptoms[159]. Furthermore, there is evidence that individuals at CHR-P who drop out have greater severity of disorganised symptoms[160], which are a strong predictor of transition to psychosis[161]. Based on this evidence, we thus assumed an equal transition risk across the two groups. To further test our assumption, we conducted sensitivity analyses assuming a best-case (i.e. none of the dropouts would transition to psychosis) and worst-case scenario (i.e. all the dropouts would transition to psychosis) regarding transition risks in individuals at CHR-P. These sensitivity analyses confirmed that our assumption of a similar transition risk between those followed up or not is reasonable. Furthermore, our meta-analytic estimate aligns with the meta-analytic Kaplan-Meier transition estimate.

Finally, we note that similar assumptions are made in any survival analysis which is being conducted in prospective research in the medical field, and therefore do not represent intrinsic limitations of the CHR-P field.

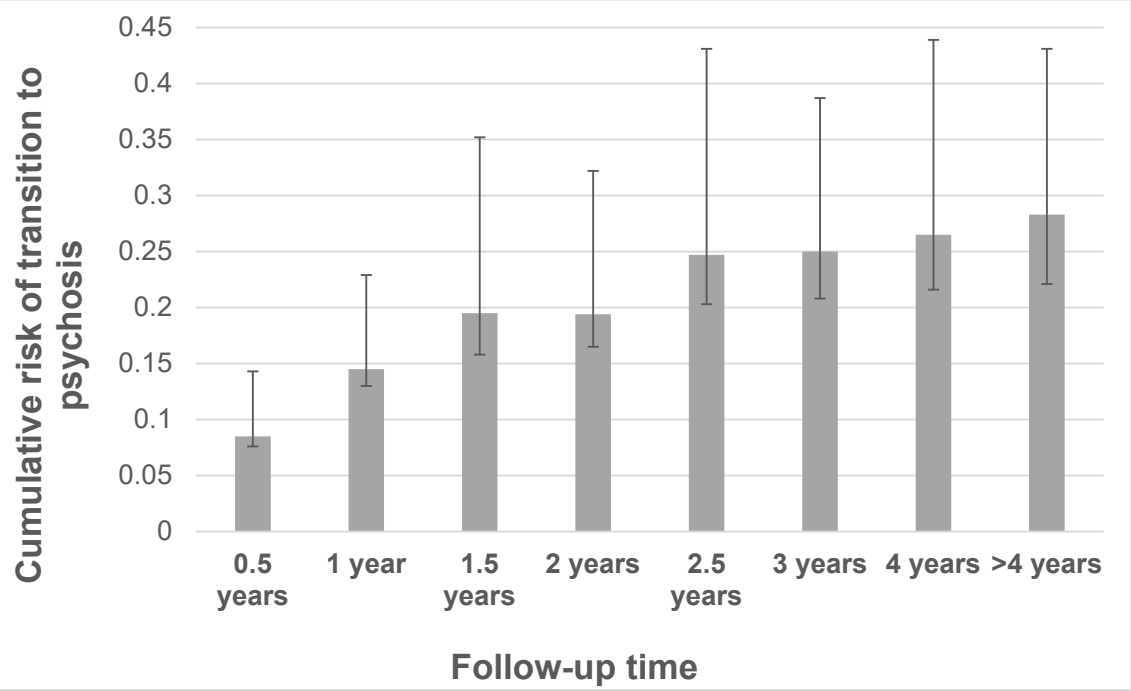
eFigure 1: Sensitivity analyses.

Sensitivity analyses estimated the cumulative risk of psychosis under different assumptions relating to Individuals at CHR-P lost at follow-up (dropouts).

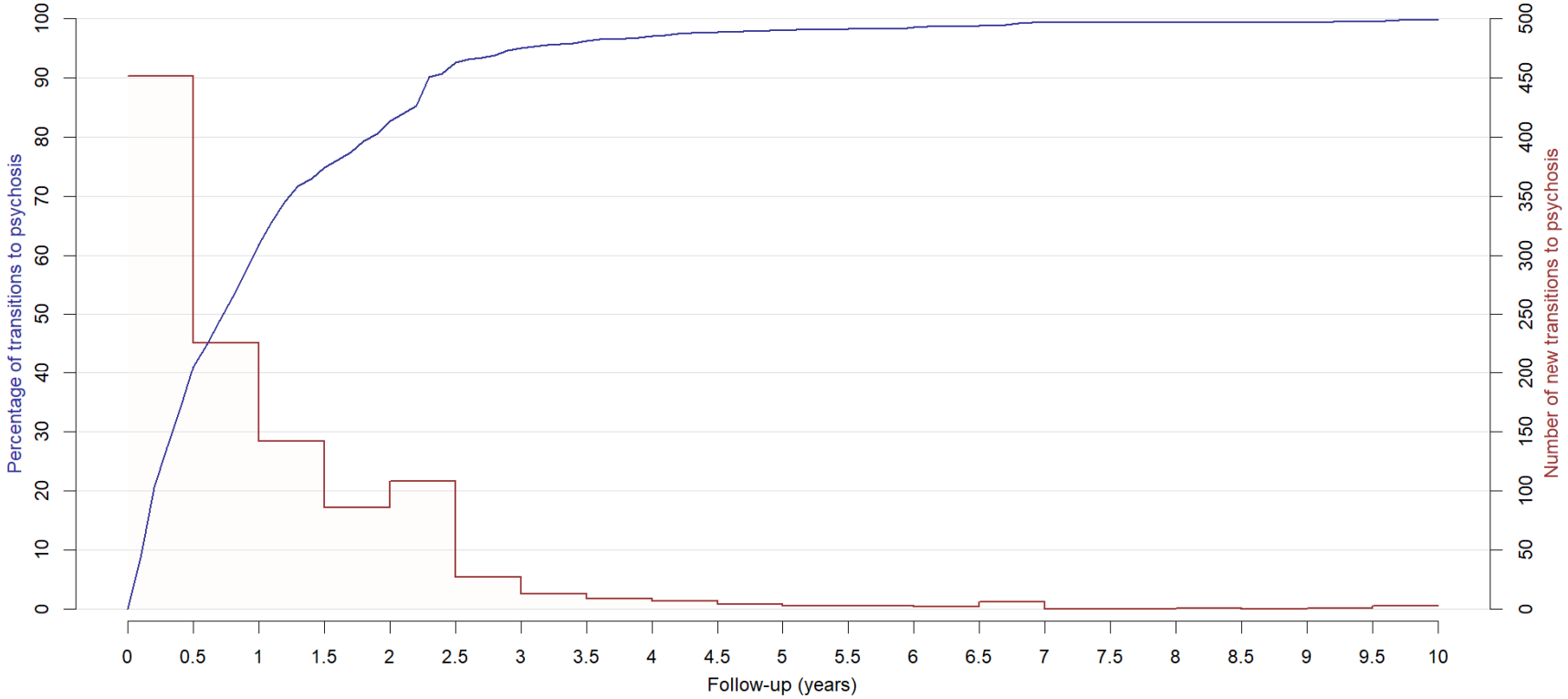
The main analysis (grey histogram in eFigure1) assumed that transition risk is similar among CHR-P followed and not followed-up (see[157] and eFigure 6 published in[158] and [159]). Accordingly, we used the study-specific transition risk to compute the raw number of transitions among those not followed-up. Two sensitivity analyses estimated the impact of such an assumption. A first analysis was conducted assuming that none of the Individuals at CHR-P lost at followed transitioned to psychosis (green histograms in eFigure 1). A second analysis was conduct assuming that all Individuals at CHR-P lost to follow-up transitioned to psychosis (violet histograms in eFigure 1). eTable_5 reports the corresponding estimates along with their 95%CIs. B)



A second version of the same eFigure 1 illustrated above is represented, which superimposes the highest and lowest 95%CIs emerging from the sensitivity analyses (for each timepoint) on the main analysis (equal risk of transition in dropouts/non-dropouts).



eFigure 2: Frequency and percentage of transitions over time.
Frequency (numbers) of transition to psychosis from a CHR-P stage (red line, y axis on the right) and percentage of transition to psychosis from a CHR-P stage (blue line, y axis on the left)



Bibliografia

1. Addington J, Piskulic D, Perkins D, Woods SW, Liu L, Penn DL. Affect recognition in people at clinical high risk of psychosis. *Schizophrenia Research.* 2012;140(1-3):87-92.
2. Amminger GP, Mechelli A, Rice S, et al. Predictors of treatment response in young people at ultra-high risk for psychosis who received long-chain omega-3 fatty acids. *Translational Psychiatry.* 2015;5.
3. Atkinson RJ, Fulham WR, Michie PT, et al. Electrophysiological, cognitive and clinical profiles of at-risk mental state: The longitudinal Minds in Transition (MinT) study. *Plos One.* 2017;12(2).
4. Bang M, Park JY, Kim KR, et al. Psychotic conversion of individuals at ultra-high risk for psychosis: The potential roles of schizotypy and basic symptoms. *Early Intervention in Psychiatry.* 2019;13(3):546-554.
5. Barbato M, Colijn MA, Keefe RSE, et al. The course of cognitive functioning over six months in individuals at clinical high risk for psychosis. *Psychiatry Research.* 2013;206(2-3):195-199.
6. Barbato M, Penn DL, Perkins DO, Woods SW, Liu L, Addington J. Metacognitive Functioning in Individuals at Clinical High Risk for Psychosis. *Behavioural and Cognitive Psychotherapy.* 2014;42(5):526-534.
7. Bechdolf A, Wagner M, Ruhrmann S, et al. Preventing progression to first-episode psychosis in early initial prodromal states. *British Journal of Psychiatry.* 2012;200(1):22-29.
8. Beck K, Studerus E, Andreou C, et al. Clinical and functional ultra-long-term outcome of patients with a clinical high risk (CHR) for psychosis. *European Psychiatry.* 2019;62:30-37.
9. Berger ME, Smesny S, Kim SW, et al. Omega-6 to omega-3 polyunsaturated fatty acid ratio and subsequent mood disorders in young people with at-risk mental states: a 7-year longitudinal study. *Translational Psychiatry.* 2017;7.
10. Bolt LK, Amminger GP, Farhall J, et al. Neurocognition as a predictor of transition to psychotic disorder and functional outcomes in ultra-high risk participants: Findings from the NEURAPRO randomized clinical trial. *Schizophrenia Research.* 2019;206:67-74.
11. Bourgin J, Duchesnay E, Magaud E, Gaillard R, Kazes M, Krebs MO. Predicting the individual risk of psychosis conversion in at-risk mental state (ARMS): a multivariate model reveals the influence of nonpsychotic prodromal symptoms. *Eur Child Adolesc Psychiatry.* 2020;29(11):1525-1535.
12. Brewer WJ, Lin A, Moberg PJ, et al. Phenylthiocarbamide (PTC) perception in ultra-high risk for psychosis participants who develop schizophrenia: Testing the evidence for an endophenotypic marker. *Psychiatry Research.* 2012;199(1):8-11.
13. Brucato G, Appelbaum PS, Lieberman JA, et al. A Longitudinal Study of Violent Behavior in a Psychosis-Risk Cohort. *Neuropsychopharmacology.* 2018;43(2):264-271.
14. Bruene M, Oezguerdal S, Ansorge N, et al. An fMRI study of "theory of mind" in at-risk states of psychosis: Comparison with manifest schizophrenia and healthy controls. *Neuroimage.* 2011;55(1):329-337.
15. Buchy L, Perkins D, Woods SW, Liu L, Addington J. Impact of substance use on conversion to psychosis in youth at clinical high risk of psychosis. *Schizophrenia Research.* 2014;156(2-3):277-280.

16. Carrion RE, Correll CU, Auther AM, Cornblatt BA. A Severity-Based Clinical Staging Model for the Psychosis Prodrome: Longitudinal Findings From the New York Recognition and Prevention Program. *Schizophrenia Bulletin.* 2017;43(1):64-74.
17. Catalan A, Tognin S, Kempton MJ, et al. Relationship between jumping to conclusions and clinical outcomes in people at clinical high-risk for psychosis. *Psychol Med.* 2020:1-9.
18. Chan CT, Abdin E, Subramaniam M, Tay SA, Lim LK, Verma S. Two-Year Clinical and Functional Outcomes of an Asian Cohort at Ultra-High Risk of Psychosis. *Frontiers in Psychiatry.* 2019;9.
19. Chen FZ, Wang Y, Sun XR, et al. Emotional Experiences Predict the Conversion of Individuals with Attenuated Psychosis Syndrome to Psychosis: A 6-Month Follow up Study. *Frontiers in Psychology.* 2016;7.
20. Chung Y, Addington J, Bearden CE, et al. Use of Machine Learning to Determine Deviance in Neuroanatomical Maturity Associated With Future Psychosis in Youths at Clinically High Risk. *Jama Psychiatry.* 2018;75(9):960-968.
21. Colibazzi T, Yang Z, Horga G, et al. Aberrant Temporal Connectivity in Persons at Clinical High Risk for Psychosis. *Biological Psychiatry-Cognitive Neuroscience and Neuroimaging.* 2017;2(8):696-705.
22. Conrad AM, Lewin TJ, Sly KA, et al. Utility of risk-status for predicting psychosis and related outcomes: evaluation of a 10-year cohort of presenters to a specialised early psychosis community mental health service. *Psychiatry Research.* 2017;247:336-344.
23. Corcoran CM, Kimhy D, Parrilla-Escobar MA, et al. The relationship of social function to depressive and negative symptoms in individuals at clinical high risk for psychosis. *Psychological Medicine.* 2011;41(2):251-261.
24. Cornblatt BA, Carrion RE, Auther A, et al. Psychosis Prevention: A Modified Clinical High Risk Perspective From the Recognition and Prevention (RAP) Program. *American Journal of Psychiatry.* 2015;172(10):986-994.
25. Damme KSF, Vargas T, Calhoun V, Turner J, Mittal VA. Global and Specific Cortical Volume Asymmetries in Individuals With Psychosis Risk Syndrome and Schizophrenia: A Mixed Cross-sectional and Longitudinal Perspective. *Schizophrenia bulletin.* 2019.
26. de Wit S, Schothorst PF, Oranje B, Ziermans TB, Durston S, Kahn RS. Adolescents at ultra-high risk for psychosis: Long-term outcome of individuals who recover from their at-risk state. *European Neuropsychopharmacology.* 2014;24(6):865-873.
27. DeVylder JE, Ben-David S, Schobel SA, Kimhy D, Malaspina D, Corcoran CM. Temporal association of stress sensitivity and symptoms in individuals at clinical high risk for psychosis. *Psychological Medicine.* 2013;43(2):259-268.
28. Dragt S, Nieman DH, Veltman D, et al. Environmental factors and social adjustment as predictors of a first psychosis in subjects at ultra high risk. *Schizophrenia Research.* 2011;125(1):69-76.
29. Francesconi M, Minichino A, Carrion RE, et al. Psychosis prediction in secondary mental health services. A broad, comprehensive approach to the "at risk mental state" syndrome. *European Psychiatry.* 2017;40:96-104.
30. Fujioka M, Kirihara K, Koshiyama D, et al. Mismatch Negativity Predicts Remission and Neurocognitive Function in Individuals at Ultra-High Risk for Psychosis. *Front Psychiatry.* 2020;11:770.

31. Fusar-Poli P, De Micheli A, Signorini L, Baldwin H, Salazar de Pablo G, McGuire P. Real-world long-term outcomes in individuals at clinical risk for psychosis: The case for extending duration of care. *EClinicalMedicine.* 2020.
32. Gaspar PA, Castillo RI, Maturana A, et al. Early psychosis detection program in Chile: A first step for the South American challenge in psychosis research. *Early Intervention in Psychiatry.* 2019;13(2):328-334.
33. Geros H, Sizer H, Mifsud N, et al. Migrant status and identification as ultra-high risk for psychosis and transitioning to a psychotic disorder. *Acta Psychiatrica Scandinavica.* 2020;141(1):52-59.
34. Glenthøj LB, Kristensen TD, Wenneberg C, Hjorthøj C, Nordentoft M. Experiential negative symptoms are more predictive of real-life functional outcome than expressive negative symptoms in clinical high-risk states. *Schizophr Res.* 2020;218:151-156.
35. Grent-'t-Jong T, Gajwani R, Gross J, et al. Association of Magnetoencephalographically Measured High-Frequency Oscillations in Visual Cortex With Circuit Dysfunctions in Local and Large-scale Networks During Emerging Psychosis. *JAMA Psychiatry.* 2020.
36. Guo JY, Niendam TA, Auther AM, et al. Predicting psychosis risk using a specific measure of cognitive control: a 12-month longitudinal study. *Psychological medicine.* 2019:1-10.
37. Hamilton HK, Woods SW, Roach BJ, et al. Auditory and Visual Oddball Stimulus Processing Deficits in Schizophrenia and the Psychosis Risk Syndrome: Forecasting Psychosis Risk With P300. *Schizophrenia Bulletin.* 2019;45(5):1068-1080.
38. Healey KM, Penn DL, Perkins D, Woods SW, Addington J. Theory of mind and social judgments in people at clinical high risk of psychosis. *Schizophrenia Research.* 2013;150(2-3):498-504.
39. Heinze K, Lin A, Nelson B, et al. The impact of psychotic experiences in the early stages of mental health problems in young people. *Bmc Psychiatry.* 2018;18.
40. Hengartner MP, Heekeren K, Dvorsky D, Walitza S, Roessler W, Theodoridou A. Checking the predictive accuracy of basic symptoms against ultra high-risk criteria and testing of a multivariable prediction model: Evidence from a prospective three-year observational study of persons at clinical high-risk for psychosis. *European Psychiatry.* 2017;45:27-35.
41. Hormozpour M, Amini H, Pajouhanfar S, Faghankhani M, Rahmani A, Sharifi V. Transition to Psychosis: Evaluation of the First-Degree Relatives of Patients with Schizophrenia. *Iranian journal of psychiatry.* 2016;11(1):15-23.
42. Howes OD, Bose SK, Turkheimer F, et al. Dopamine Synthesis Capacity Before Onset of Psychosis: A Prospective F-18 -DOPA PET Imaging Study. *American Journal of Psychiatry.* 2011;168(12):1311-1317.
43. Howes OD, Bonoldi I, McCutcheon RA, et al. Glutamatergic and dopaminergic function and the relationship to outcome in people at clinical high risk of psychosis: a multi-modal PET-magnetic resonance brain imaging study. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology.* 2019.
44. Hui C, Morcillo C, Russo DA, et al. Psychiatric morbidity, functioning and quality of life in young people at clinical high risk for psychosis. *Schizophrenia Research.* 2013;148(1-3):175-180.
45. Hur J-W, Shin NY, Jang JH, et al. Clinical and neurocognitive profiles of subjects at high risk for psychosis with and without obsessive-compulsive symptoms. *Australian and New Zealand Journal of Psychiatry.* 2012;46(2):161-169.

46. Iftimovici A, Kebir O, He Q, et al. Stress, Cortisol and NR3C1 in At-Risk Individuals for Psychosis: A Mendelian Randomization Study. *Front Psychiatry.* 2020;11:680.
47. Jang JH, Shin NY, Shim G, et al. Longitudinal patterns of social functioning and conversion to psychosis in subjects at ultra-high risk. *Australian and New Zealand Journal of Psychiatry.* 2011;45(9):763-770.
48. Kambeitz-Ilankovic L, Haas SS, Meisenzahl E, et al. Neurocognitive and neuroanatomical maturation in the clinical high-risk states for psychosis: A pattern recognition study. *Neuroimage-Clinical.* 2019;21.
49. Kantrowitz JT, Woods SW, Petkova E, et al. D-serine for the treatment of negative symptoms in individuals at clinical high risk of schizophrenia: a pilot, double-blind, placebo-controlled, randomised parallel group mechanistic proof-of-concept trial. *Lancet Psychiatry.* 2015;2(5):403-412.
50. Katsura M, Ohmuro N, Obara C, et al. A naturalistic longitudinal study of at-risk mental state with a 2.4 year follow-up at a specialized clinic setting in Japan. *Schizophrenia Research.* 2014;158(1-3):32-38.
51. Kayser J, Tenke CE, Kroppmann CJ, et al. Olfaction in the psychosis prodrome: Electrophysiological and behavioral measures of odor detection. *International Journal of Psychophysiology.* 2013;90(2):190-206.
52. Kéri S, Kiss I, Kelemen O. Effects of a neuregulin 1 variant on conversion to schizophrenia and schizophreniform disorder in people at high risk for psychosis. *Mol Psychiatry.* 2009;14(2):118-119.
53. Kim E, Jang JH, Park H-Y, et al. Pharmacotherapy and clinical characteristics of ultra-high-risk for psychosis according to conversion status: a naturalistic observational study. *Early Intervention in Psychiatry.* 2012;6(1):30-37.
54. Kleineidam L, Frommann I, Ruhrmann S, et al. Antisaccade and prosaccade eye movements in individuals clinically at risk for psychosis: comparison with first-episode schizophrenia and prediction of conversion. *Eur Arch Psychiatry Clin Neurosci.* 2019;269(8):921-930.
55. Kline E, Thompson E, Demro C, Bussell K, Reeves G, Schiffman J. Longitudinal validation of psychosis risk screening tools. *Schizophrenia Research.* 2015;165(2-3):116-122.
56. Kollias C, Xenaki L-A, Dimitrakopoulos S, et al. Early psychosis intervention outpatient service of the 1st Psychiatric University Clinic in Athens: 3 Years of experience. *Early Intervention in Psychiatry.* 2018;12(3):491-496.
57. Konishi J, del Re EC, Bouix S, et al. Abnormal relationships between local and global brain measures in subjects at clinical high risk for psychosis: a pilot study. *Brain Imaging and Behavior.* 2018;12(4):974-988.
58. Korkeila J, Salokangas RKR, Heinimaaa M, et al. Physical illnesses, developmental risk factors and psychiatric diagnoses among subjects at risk of psychosis. *European Psychiatry.* 2013;28(3):135-140.
59. Kotlicka-Antczak M, Pawelczyk A, Karbownik MS, et al. Deficits in the identification of pleasant odors predict the transition of an at-risk mental state to psychosis. *Schizophrenia Research.* 2017;181:49-54.
60. Kotlicka-Antczak M, Pawelczyk A, Pawelczyk T, Strzelecki D, Zurner N, Karbownik MS. A history of obstetric complications is associated with the risk of progression from an at risk mental state to psychosis. *Schizophrenia Research.* 2018;197:498-503.
61. Kraan T, van Dam DS, Velthorst E, et al. Childhood trauma and clinical outcome in patients at ultra-high risk of transition to psychosis. *Schizophrenia Research.* 2015;169(1-3):193-198.

62. Kraan TC, Ising HK, Fokkema M, et al. The effect of childhood adversity on 4-year outcome in individuals at ultra high risk for psychosis in the Dutch Early Detection Intervention Evaluation (EDIE-NL) Trial. *Psychiatry Research.* 2017;247:55-62.
63. Kraan TC, Velthorst E, Themmen M, et al. Child Maltreatment and Clinical Outcome in Individuals at Ultra-High Risk for Psychosis in the EU-GEI High Risk Study. *Schizophrenia Bulletin.* 2018;44(3):584-592.
64. Kristensen TD, Ebdrup BH, Hjorthøj C, et al. No Effects of Cognitive Remediation on Cerebral White Matter in Individuals at Ultra-High Risk for Psychosis-A Randomized Clinical Trial. *Front Psychiatry.* 2020;11:873.
65. Labad J, Stojanovic-Perez A, Montalvo I, et al. Stress biomarkers as predictors of transition to psychosis in at-risk mental states: Roles for cortisol, prolactin and albumin (vol 60, pg 163, 2015). *Journal of Psychiatric Research.* 2015;62:138-138.
66. Lam M, Lee J, Rapisarda A. Longitudinal Cognitive Changes in Young Individuals at Ultrahigh Risk for Psychosis (vol 75, pg 929, 2018). *Jama Psychiatry.* 2018;75(9):974-974.
67. Landa Y, Mueser KT, Wyka KE, et al. Development of a group and family-based cognitive behavioural therapy program for youth at risk for psychosis. *Early Intervention in Psychiatry.* 2016;10(6):511-521.
68. Lee J, Rekhi G, Mitter N, et al. The Longitudinal Youth at Risk Study (LYRIKS) - An Asian UHR perspective. *Schizophrenia Research.* 2013;151(1-3):279-283.
69. Lee TY, Kim SN, Correll CU, et al. Symptomatic and functional remission of subjects at clinical high risk for psychosis: A 2-year naturalistic observational study. *Schizophrenia Research.* 2014;156(2-3):266-271.
70. Lemos-Giráldez S, Vallina-Fernández O, Fernández-Iglesias P, et al. Symptomatic and functional outcome in youth at ultra-high risk for psychosis: a longitudinal study. *Schizophr Res.* 2009;115(2-3):121-129.
71. Lencz T, Smith CW, McLaughlin D, et al. Generalized and specific neurocognitive deficits in prodromal schizophrenia. *Biol Psychiatry.* 2006;59(9):863-871.
72. Leon-Ortiz P, Reyes-Madrigal F, Kochunov P, Rowland L, de la Fuente-Sandoval C. White Matter Alterations and the Conversion to Psychosis: A Combined Diffusion Tensor Imaging and Magnetic Resonance Spectroscopy Study. *Neuropsychopharmacology.* 2017;42:S217-S218.
73. Lindgren M, Manninen M, Kalska H, et al. Predicting psychosis in a general adolescent psychiatric sample. *Schizophrenia Research.* 2014;158(1-3):1-6.
74. Lindgren M, Manninen M, Kalska H, et al. Evaluation of verbal list learning as a predictor of psychosis. *Early Intervention in Psychiatry.* 2017;11(2):171-176.
75. Liu C-C, Lai M-C, Liu C-M, et al. Follow-up of subjects with suspected pre-psychotic state in Taiwan. *Schizophrenia Research.* 2011;126(1-3):65-70.
76. Mamah D, Musau A, Mutiso VN, et al. Characterizing psychosis risk traits in Africa: A longitudinal study of Kenyan adolescents. *Schizophrenia Research.* 2016;176(2-3):340-348.
77. Manninen M, Lindgren M, Therman S, et al. Clinical high-risk state does not predict later psychosis in a delinquent adolescent population. *Early Intervention in Psychiatry.* 2014;8(1):87-90.
78. Matsumoto K, Katsura M, Tsujino N, et al. Federated multi-site longitudinal study of at-risk mental state for psychosis in Japan. *Schizophrenia Research.* 2019;204:343-352.
79. Morcillo C, Stochl J, Russo DA, et al. First-Rank Symptoms and Premorbid Adjustment in Young Individuals at Increased Risk of Developing Psychosis. *Psychopathology.* 2015;48(2):120-126.

80. Morrison AP, French P, Parker S, et al. Three-year follow-up of a randomized controlled trial of cognitive therapy for the prevention of psychosis in people at ultrahigh risk. *Schizophr Bull.* 2007;33(3):682-687.
81. Morrison A, Grp E-T. Early detection and intervention evaluation for people at risk of psychosis (EDIE-2): a multisite randomized controlled trial of cognitive therapy for at-risk mental states. *Early Intervention in Psychiatry.* 2012;6:11-11.
82. Nelson B, Yuen K, Yung AR. Ultra high risk (UHR) for psychosis criteria: Are there different levels of risk for transition to psychosis? *Schizophrenia Research.* 2011;125(1):62-68.
83. Nelson B, Yuen HP, Lin A, et al. Further examination of the reducing transition rate in ultra high risk for psychosis samples: The possible role of earlier intervention. *Schizophrenia Research.* 2016;174(1-3):43-49.
84. Niles HF, Walsh BC, Woods SW, Powers AR, III. Does hallucination perceptual modality impact psychosis risk? *Acta Psychiatrica Scandinavica.* 2019;140(4):360-370.
85. Nussbaum LA, Andreescu N, Nussbaum L, Gradinaru R, Puiu M. ETHICAL ISSUES RELATED TO EARLY INTERVENTION IN CHILDREN AND ADOLESCENTS WITH ULTRA HIGH RISK FOR PSYCHOSIS: CLINICAL IMPLICATIONS AND FUTURE PERSPECTIVES. *Revista Romana De Bioetica.* 2014;12(3):64-81.
86. Ohmuro N, Katsura M, Obara C, et al. Deficits of cognitive theory of mind and its relationship with functioning in individuals with an at-risk mental state and first-episode psychosis. *Psychiatry Research.* 2016;243:318-325.
87. Osborne KJ, Mittal VA. External validation and extension of the NAPLS-2 and SIPS-RC personalized risk calculators in an independent clinical high-risk sample. *Psychiatry Research.* 2019;279:9-14.
88. Pelizza L, Poletti M, Azzali S, et al. Subjective experience of social cognition in young people at Ultra-High Risk of psychosis: a 2-year longitudinal study. *Nord J Psychiatry.* 2020:1-12.
89. Pelletier-Baldelli A, Strauss GP, Visser KH, Mittal VA. Initial development and preliminary psychometric properties of the Prodromal Inventory of Negative Symptoms (PINS). *Schizophrenia Research.* 2017;189:43-49.
90. Perkins DO, Olde Loohuis L, Barbee J, et al. Polygenic Risk Score Contribution to Psychosis Prediction in a Target Population of Persons at Clinical High Risk. *Am J Psychiatry.* 2020;177(2):155-163.
91. Poletti M, Pelizza L, Azzali S, et al. Clinical high risk for psychosis in childhood and adolescence: findings from the 2-year follow-up of the ReARMS project. *European Child & Adolescent Psychiatry.* 2019;28(7):957-971.
92. Pontillo M, Menghini D, Vicari S. Neurocognitive profile and onset of psychosis symptoms in children, adolescents and young adults with 22q11 deletion syndrome: A longitudinal study. *Schizophrenia Research.* 2019;208:76-81.
93. Pozza A, Dèttore D. Modular cognitive-behavioral therapy for affective symptoms in young individuals at ultra-high risk of first episode of psychosis: Randomized controlled trial. *J Clin Psychol.* 2020;76(3):392-405.
94. Provenzano FA, Guo J, Wall MM, et al. Hippocampal Pathology in Clinical High-Risk Patients and the Onset of Schizophrenia. *Biol Psychiatry.* 2020;87(3):234-242.
95. Pruessner M, Iyer SN, Faridi K, Joober R, Malla AK. Stress and protective factors in individuals at ultra-high risk for psychosis and patients with first episode psychosIS. *Early Intervention in Psychiatry.* 2012;6:117-117.

96. Pruessner M, Faridi K, Shah J, et al. The Clinic for Assessment of Youth at Risk (CAYR): 10 years of service delivery and research targeting the prevention of psychosis in Montreal, Canada. *Early Intervention in Psychiatry.* 2017;11(2):177-184.
97. Quijada Y, Kwapil TR, Tizon J, Sheinbaum T, Barrantes-Vidal N. Impact of attachment style on the 1-year outcome of persons with an at-risk mental state for psychosis. *Psychiatry Research.* 2015;228(3):849-856.
98. Rekhi G, Rapisarda A, Lee J. Impact of distress related to attenuated psychotic symptoms in individuals at ultra high risk of psychosis: Findings from the Longitudinal Youth at Risk Study. *Early Intervention in Psychiatry.* 2019;13(1):73-78.
99. Roalf DR, de la Garza AG, Rosen A, et al. Alterations in white matter microstructure in individuals at persistent risk for psychosis. *Molecular psychiatry.* 2019.
100. Rosen M, Haidl TK, Ruhrmann S, Vogeley K, Schultze-Lutter F. Sex differences in symptomatology of psychosis-risk patients and in prediction of psychosis. *Archives of women's mental health.* 2019.
101. Ryan AT, Addington J, Bearden CE, et al. Latent class cluster analysis of symptom ratings identifies distinct subgroups within the clinical high risk for psychosis syndrome. *Schizophrenia Research.* 2018;197:522-530.
102. Sakuma A, Obara C, Katsura M, et al. No regional gray matter volume reduction observed in young Japanese people at ultra-high risk for psychosis: A voxel-based morphometry study. *Asian Journal of Psychiatry.* 2018;37:167-171.
103. Salokangas RKR, Schultze-Lutter F, Hietala J, et al. Depression predicts persistence of paranoia in clinical high-risk patients to psychosis: results of the EPOS project. *Social Psychiatry and Psychiatric Epidemiology.* 2016;51(2):247-257.
104. Sasabayashi D, Takayanagi Y, Takahashi T, et al. Subcortical Brain Volume Abnormalities in Individuals With an At-risk Mental State. *Schizophr Bull.* 2020;46(4):834-845.
105. Sawada K, Kanehara A, Sakakibara E, et al. Identifying neurocognitive markers for outcome prediction of global functioning in individuals with first-episode and ultra-high-risk for psychosis. *Psychiatry and Clinical Neurosciences.* 2017;71(5):318-327.
106. Schlosser DA, Jacobson S, Chen Q, et al. Recovery From an At-Risk State: Clinical and Functional Outcomes of Putatively Prodromal Youth Who Do Not Develop Psychosis. *Schizophrenia Bulletin.* 2012;38(6):1225-1233.
107. Schneider M, Armando M, Pontillo M, et al. Ultra high risk status and transition to psychosis in 22q11.2 deletion syndrome. *World Psychiatry.* 2016;15(3):259-265.
108. Schultze-Lutter F, Klosterkoetter J, Ruhrmann S. Improving the clinical prediction of psychosis by combining ultra-high risk criteria and cognitive basic symptoms. *Schizophrenia Research.* 2014;154(1-3):100-106.
109. Sevilla-Llewellyn-Jones J, Camino G, Russo DA, et al. Clinically significant personality traits in individuals at high risk of developing psychosis. *Psychiatry Research.* 2018;261:498-503.
110. Simon AE, Grädel M, Cattapan-Ludewig K, et al. Cognitive functioning in at-risk mental states for psychosis and 2-year clinical outcome. *Schizophr Res.* 2012;142(1-3):108-115.
111. Takahashi T, Nakamura K, Nishiyama S, et al. Increased pituitary volume in subjects at risk for psychosis and patients with first-episode schizophrenia. *Psychiatry and Clinical Neurosciences.* 2013;67(7):540-548.
112. Takahashi T, Higuchi Y, Komori Y, et al. Pituitary Volume and Socio-Cognitive Functions in Individuals at Risk of Psychosis and Patients With Schizophrenia. *Frontiers in Psychiatry.* 2018;9.

113. Takahashi T, Nakamura M, Nishikawa Y, et al. Potential role of orbitofrontal surface morphology on social and cognitive functions in high-risk subjects for psychosis and schizophrenia patients. *Psychiatry Research-Neuroimaging.* 2019;283:92-95.
114. van der Gaag M, Nieman DH, Rietdijk J, et al. Cognitive Behavioral Therapy for Subjects at Ultrahigh Risk for Developing Psychosis: A Randomized Controlled Clinical Trial. *Schizophrenia Bulletin.* 2012;38(6):1180-1188.
115. van Tricht MJ, Bour LJ, Koelman JHTM, et al. Qualitative and quantitative aspects of information processing in first psychosis: Latent class analyses in patients, at-risk subjects, and controls. *Psychophysiology.* 2015;52(4):585-593.
116. Velthorst E, Nieman DH, Klaassen RMC, et al. Three-year course of clinical symptomatology in young people at ultra high risk for transition to psychosis. *Acta Psychiatrica Scandinavica.* 2011;123(1):36-42.
117. Velthorst E, Derks EM, Schothorst P, et al. Quantitative and qualitative symptomatic differences in individuals at Ultra-High Risk for psychosis and healthy controls. *Psychiatry Research.* 2013;210(2):432-437.
118. Velthorst E, Zinberg J, Addington J, et al. Potentially important periods of change in the development of social and role functioning in youth at clinical high risk for psychosis. *Development and Psychopathology.* 2018;30(1):39-47.
119. von Hohenberg CC, Pasternak O, Kubicki M, et al. White Matter Microstructure in Individuals at Clinical High Risk of Psychosis: A Whole-Brain Diffusion Tensor Imaging Study. *Schizophrenia Bulletin.* 2014;40(4):895-903.
120. Wang L, Li X, Zhu Y, et al. Discriminative Analysis of Symptom Severity and Ultra-High Risk of Schizophrenia Using Intrinsic Functional Connectivity. *Int J Neural Syst.* 2020;30(9):2050047.
121. Welsh P, Tiffin PA. The 'At-Risk Mental State' for Psychosis in Adolescents: Clinical Presentation, Transition and Remission. *Child Psychiatry & Human Development.* 2014;45(1):90-98.
122. Woodberry KA, McFarlane WR, Giuliano AJ, et al. Change in neuropsychological functioning over one year in youth at clinical high risk for psychosis. *Schizophrenia Research.* 2013;146(1-3):87-94.
123. Woods SW, Addington J, Cadenhead KS, et al. Validity of the prodromal risk syndrome for first psychosis: findings from the North American Prodrome Longitudinal Study. *Schizophr Bull.* 2009;35(5):894-908.
124. Youn S, Phillips LJ, Amminger GP, et al. Basic symptoms in young people at ultra-high risk of psychosis: Association with clinical characteristics and outcomes. *Schizophr Res.* 2020;216:255-261.
125. Yoviene Sykes LA, Ferrara M, Addington J, et al. Predictive validity of conversion from the clinical high risk syndrome to frank psychosis. *Schizophr Res.* 2020;216:184-191.
126. Yung AR, Phillips LJ, Yuen HP, McGorry PD. Risk factors for psychosis in an ultra high-risk group: psychopathology and clinical features. *Schizophr Res.* 2004;67(2-3):131-142.
127. Zhang T, Xu L, Tang Y, et al. Isolated hallucination is less predictive than thought disorder in psychosis: Insight from a longitudinal study in a clinical population at high risk for psychosis. *Scientific Reports.* 2018;8.
128. Zhang T, Xu L, Tang Y, et al. Prediction of psychosis in prodrome: development and validation of a simple, personalized risk calculator. *Psychological Medicine.* 2019;49(12):1990-1998.
129. Zhang T, Xu L, Tang X, et al. Real-world effectiveness of antipsychotic treatment in psychosis prevention in a 3-year cohort of 517 individuals at clinical high risk from

the SHARP (ShangHai At Risk for Psychosis). *Aust N Z J Psychiatry.* 2020;54(7):696-706.
130. Ziermans TB, Schothorst PF, Sprong M, van Engeland H. Transition and remission in adolescents at ultra-high risk for psychosis. *Schizophrenia Research.* 2011;126(1-3):58-64.
131. Fusar-Poli P, Salazar de Pablo G, Correll CU, et al. Prevention of Psychosis: Advances in Detection, Prognosis, and Intervention. *JAMA Psychiatry.* 2020.
132. Yung AR, Yuen HP, McGorry PD, et al. Mapping the onset of psychosis: the Comprehensive Assessment of At-Risk Mental States. *Aust N Z J Psychiatry.* 2005;39(11-12):964-971.
133. Fusar-Poli P, Cappucciati M, Rutigliano G, et al. Towards a Standard Psychometric Diagnostic Interview for Subjects at Ultra High Risk of Psychosis: CAARMS versus SIPS. *Psychiatry J.* 2016;2016:7146341.
134. McGlashan T WB, Woods S. *The psychosis-risk syndrome: handbook for diagnosis and follow-up.*: Oxford: Oxford University 2010.
135. Haefner H, Bechdolf A, Klosterkotter J, Maurer K. Early detection and intervention in psychosis. A practice handbook. In: Stuttgart: Schattauer; 2011.
136. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull.* 1987;13(2):261-276.
137. Overall J, Gorham D. The Brief Psychiatric Rating Scale (BPRS): recent developments in ascertainment and scaling. *Psychopharmacol Bull.* 1988;24:97-99.
138. Vollmer-Larsen A, Handest P, Parnas J. Reliability of measuring anomalous experience: the Bonn Scale for the Assessment of Basic Symptoms. *Psychopathology.* 2007;40(5):345-348.
139. Riecher-Rössler A, Aston J, Ventura J, et al. [The Basel Screening Instrument for Psychosis (BSIP): development, structure, reliability and validity]. *Fortschr Neurol Psychiatr.* 2008;76(4):207-216.
140. Fux L, Walger P, Schimmelmann BG, Schultze-Lutter F. The Schizophrenia Proneness Instrument, Child and Youth version (SPI-CY): practicability and discriminative validity. *Schizophr Res.* 2013;146(1-3):69-78.
141. Fusar-Poli P, De Micheli A, Patel R, et al. Real-World Clinical Outcomes Two Years After Transition to Psychosis in Individuals at Clinical High Risk: Electronic Health Record Cohort Study. *Schizophr Bull.* 2020.
142. van Os J, Reininghaus U. Psychosis as a transdiagnostic and extended phenotype in the general population. *World Psychiatry.* 2016;15(2):118-124.
143. Karcher NR, Barch DM, Avenevoli S, et al. Assessment of the Prodromal Questionnaire-Brief Child Version for Measurement of Self-reported Psychoticlike Experiences in Childhood. *JAMA Psychiatry.* 2018;75(8):853-861.
144. Sullivan SA, Kounali D, Cannon M, et al. A Population-Based Cohort Study Examining the Incidence and Impact of Psychotic Experiences From Childhood to Adulthood, and Prediction of Psychotic Disorder. *Am J Psychiatry.* 2020;177(4):308-317.
145. Fusar-Poli P, Raballo A, Parnas J. What Is an Attenuated Psychotic Symptom? On the Importance of the Context. *Schizophr Bull.* 2017;43(4):687-692.
146. Schultze-Lutter F, Michel C, Ruhrmann S, Schimmelmann BG. Prevalence and clinical significance of DSM-5-attenuated psychosis syndrome in adolescents and young adults in the general population: the Bern Epidemiological At-Risk (BEAR) study. *Schizophr Bull.* 2014;40(6):1499-1508.

147. Catalan A, Salazar de Pablo G, Vaquerizo Serrano J, et al. Annual Research Review: Prevention of psychosis in adolescents - systematic review and meta-analysis of advances in detection, prognosis and intervention. *J Child Psychol Psychiatry.* 2020.
148. Fusar-Poli P, Bonoldi I, Yung AR, et al. Predicting psychosis: meta-analysis of transition outcomes in individuals at high clinical risk. *Arch Gen Psychiatry.* 2012;69(3):220-229.
149. Salazar de Pablo G, Catalan A, Fusar-Poli P. Clinical Validity of DSM-5 Attenuated Psychosis Syndrome: Advances in Diagnosis, Prognosis, and Treatment. *JAMA Psychiatry.* 2019.
150. Fusar-Poli P, Tantardini M, De Simone S, et al. Deconstructing vulnerability for psychosis: Meta-analysis of environmental risk factors for psychosis in subjects at ultra high-risk. *Eur Psychiatry.* 2017;40:65-75.
151. Fusar-Poli P, Rocchetti M, Sardella A, et al. Disorder, not just state of risk: meta-analysis of functioning and quality of life in people at high risk of psychosis. *British Journal of Psychiatry.* 2015;207(3):198-206.
152. Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ.* 2011;343:d5928.
153. Davies C, Cipriani A, Ioannidis JPA, et al. Lack of evidence to favor specific preventive interventions in psychosis: a network meta-analysis. *World Psychiatry.* 2018;17(2):196-209.
154. The GIMP Development Team. GIMP. In: Retrieved from https://www.gimp.org; 2020.
155. Radua J, Grunze H, Amann BL. Meta-Analysis of the Risk of Subsequent Mood Episodes in Bipolar Disorder. *Psychother Psychosom.* 2017;86(2):90-98.
156. Hess K, Gentleman R. muhaz: Hazard Function Estimation in Survival Analysis. R package version 1.2.6.1. URL: https://CRAN.R-project.org/package=muhaz. In:2019.
157. Green CEL, McGuire PK, Ashworth M, Valmaggia LR. Outreach and Support in South London (OASIS). Outcomes of non-attenders to a service for people at high risk of psychosis: the case for a more assertive approach to assessment. *Psychological Medicine.* 2011;41(2):243-250.
158. Fusar-Poli P, Rutigliano G, Stahl D, et al. Deconstructing Pretest Risk Enrichment to Optimize Prediction of Psychosis in Individuals at Clinical High Risk. *JAMA Psychiatry.* 2016;73(12):1260-1267.
159. Stowkowy J, Liu L, Cadenhead KS, et al. Exploration of clinical high-risk dropouts. *Schizophr Res.* 2018;195:579-580.
160. Leanza L, Studerus E, Mackintosh AJ, et al. Predictors of study drop-out and service disengagement in patients at clinical high risk for psychosis. *Soc Psychiatry Psychiatr Epidemiol.* 2020;55(5):539-548.
161. Fusar-Poli P, Cappucciati M, De Micheli A, et al. Diagnostic and Prognostic Significance of Brief Limited Intermittent Psychotic Symptoms (BLIPS) in Individuals at Ultra High Risk. *Schizophr Bull.* 2017;43(1):48-56.