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Supplementary Material

Article Title: Interventions and Transition in Youth at Risk of Psychosis: A Systematic Review and Meta-Analyses

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Supplementary Search 1. Transition Search Strategies Examples

Database: Ovid MEDLINE(R)

1 exp psychotic disorders/ (47422)
2 deficit syndrome.ti,ab. (347)
3 exp schizophrenia/ (96189)
4 ((chronic$ or serious or persistent or severe$) adj (mental$ or psychological$) adj (disorder$ or ill$)).mp. (9524)
5 (delusion$ or hebephreni$ or psychosis or psychoses or psychotic$ or schizo$).mp. (208786)
6 or/1-5 (214816)
7 risk factors/ (683418)
8 symptom$.sh. or (prodrom$ or risk$).hw. (987343)
9 (blips or brief limited intermittent psychotic symptom$ or ((attenuat$ or early or pre?monitory) adj2 (sign$ or symptom$)) or pre?delusion$ or pre?hallucin$ or pre?psychos$ or pre?psychotic$ or pre?schizo$ or (pre adj (delusion$ or hallucin$ or psychos$ or psychotic$ or schizo$)) or prodrom$ or sub?clinical$ or sub?threshold$ or at risk$ or ((high$ or incipient or increas$) adj3 risk$)).ti,ab,kw. (796772)
10 or/8-9 (1523318)
11 (conversion$ or ((develop$ or progress$) adj2 (psychos$ or psychotic$ or schiz$)) or first episode$ or fullthreshold$ or full threshold$ or onset$ or progression or transition$ or transitory).ti,ab. (1272434)
12 10 and 11 (124494)
13 clinical high risk.ti,ab. (456)
14 ultra high risk.ti,ab. (700)
15 basic symptoms.ti,ab. (246)
16 attenuated psychosis syndrome.ti,ab. (60)
17 at risk mental state.ti,ab. (269)
18 ((at risk or ((high or increase$) adj2 risk) or blips or brief limited intermittent psychotic symptom$ or ((attenuat$ or early or premonitory) adj2 (sign$ or symptom$)) or prodrom$ or subclinical$ or sub$ clinical$ or subthreshold or sub$ threshold) and (psychos$ or psychotic$ or schiz$)).ti. or ((at risk or ((high or increase$) adj2 risk) or blips or brief limited intermittent psychotic symptom$ or ((attenuat$ or earlyor premonitory) adj2 (sign$ or symptom$)) or prodrom$ or subclinical$ or sub$ clinical$ or subthreshold or sub$ threshold) adj3 (psychos$ or psychotic$ or schiz$)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (4992)
19 or/13-18 (5497)
20 (Experimental or interventional or experiment$ or multiple arm trial$ or clinical trial$ or double blind or randomization or random sample or placebo or RCT$ or randomized control trial or doubleblind$ or singleblind$ or tripleblind or block design$ or cluster randomized trial$ or two-arm trial$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol

supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (3078666)
21 (treatment or case-crossover or ecological or naturalistic or case-control or non-randomized controlled trial or controlled before after study or interrupted time series study or historically controlled study or cohort study or cross-sectional study or quasi-design or quasi-experimental designs or quasi or factorial designs or time series designs or uncontrolled before after studies or open label or openlabel).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (4552593)
22 20 and 21 (849367)
23 6 and (7 or 12 or 19) and 22 (579)

Database: Embase
1 exp psychotic disorders/ (262725)
2 deficit syndrome.ti,ab. (482)
3 exp schizophrenia/ (173439)
4 ((chronic$ or serious or persistent or severe$) adj (mental$ or psychological$) adj (disorder$ or ill$)).mp. (11717)
5 (delusion$ or hebephreni$ or psychosis or psychoses or psychotic$ or schizo$).mp. (289781)
6 or/1-5 (317140)
7 risk factors/ (429596)
8 symptom$.sh. or (prodrom$ or risk$).hw. (2677408)
9 (blips or brief limited intermittent psychotic symptom$ or ((attenuat$ or early or pre?monitory) adj2 (sign$ or symptom$)) or pre?delusion$ or pre?hallucin$ or pre?psychos$ or pre?psychotic$ or pre?schizo$ or (pre adj (delusion$ or hallucin$ or psychos$ or psychotic$ or schizo$)) or prodrom$ or sub?clinical$ or sub?threshold$ or at risk$ or ((high$ or incipient or increas$) adj3 risk$)).ti,ab,kw. (1123392)
10 or/8-9 (3005604)
11 (conversion$ or ((develop$ or progress$) adj2 (psychos$ or psychotic$ or schiz$)) or first episode$ or fullthreshold$ or full threshold$ or onset$ or progression or transition$ or transitory).ti,ab. (1610550)
12 10 and 11 (277648)
13 clinical high risk.ti,ab. (854)
14 ultra high risk.ti,ab. (1436)
15 basic symptoms.ti,ab. (466)
16 attenuated psychosis syndrome.ti,ab. (99)
17 at risk mental state.ti,ab. (627)
18 ((at risk or ((high or increase$) adj2 risk) or blips or brief limited intermittent psychotic symptom$ or ((attenuat$ or early or premonitory) adj2 (sign$ or symptom$)) or prodrom$ or subclinical$ or sub$ clinical$ or subthreshold or sub$ threshold) and (psychos$ or psychotic$ or schiz$)).ti. or ((at risk or ((high or increase$) adj2 risk) or blips

or brief limited intermittent psychotic symptom$ or ((attenuat$ or earlyor premonitory) adj2 (sign$ or symptom$)) or prodrom$ or subclinical$ or sub$ clinical$ or subthreshold or sub$ threshold) adj3 (psychos$ or psychotic$ or schiz$)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading] (8067)
19 or/13-18 (9060)
20 (Experimental or interventional or experiment$ or multiple arm trial$ or clinical trial$ or double blind or randomization or random sample or placebo or RCT$ or randomized control trial or doubleblind$ or singleblind$ or tripleblind or block design$ or cluster randomized trial$ or two-arm trial$).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading] (5780300)
21 (treatment or case-crossover or ecological or naturalistic or case-control or non-randomized controlled trial or controlled before after study or interrupted time series study or historically controlled study or cohort study or cross-sectional study or quasi-design or quasi-experimental designs or quasi or factorial designs or time series designs or uncontrolled before after studies or open label or openlabel).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading] (6190361)
22 20 and 21 (1682879)
23 6 and (7 or 12 or 19) and 22 (2189)

Database: EMB Reviews
1 psychotic disorders.mp. (114)
2 deficit syndrome.mp. (0)
3 schizophrenia.mp. (402)
4 ((chronic* or serious or persistent or severe*) adj (mental* or psychological*) adj (disorder* or ill*)).mp. (70)
5 (delusion* or hebephreni* or psychosis or psychoses or psychotic* or schizo*).mp. (554)
6 1 or 2 or 3 or 4 or 5 (598)
7 risk factors.mp. (2761)
8 (symptom* or (prodrom* or risk*)).mp. (12470)
9 (blips or brief limited intermittent psychotic symptom* or ((attenuat* or early or pre?monitory) adj2 (sign* or symptom*)) or pre?delusion* or pre?hallucin* or pre?psychos* or pre?psychotic* or pre?schizo* or (pre adj (delusion* or hallucin* or psychos* or psychotic* or schizo*)) or prodrom* or sub?clinical* or sub?threshold* or at risk* or ((high* or incipient or increas*) adj3 risk*)).mp. (10903)
10 or/8-9 (12479)
11 (conversion* or ((develop* or progress*) adj2 (psychos* or psychotic* or schiz*)) or first episode* or fullthreshold* or full threshold* or onset* or progression or transition* or transitory).mp. (1768)

12 10 and 11 (1167)
13 clinical high risk.mp. (0)
14 ultra high risk.mp. (3)
15 basic symptoms.mp. (1)
16 attenuated psychosis syndrome.mp. (0)
17 at risk mental state.mp. (0)
18 ((at risk or ((high or increase*) adj2 risk) or blips or brief limited intermittent psychotic symptom* or ((attenuat* or early or premonitory) adj2 (sign* or symptom*)) or prodrom* or subclinical* or sub* clinical* or subthreshold or sub* threshold) and (psychos* or psychotic* or schiz*)).ti. or ((at risk or ((high or increase*) adj2 risk) or blips or brief limited intermittent psychotic symptom* or ((attenuat* or earlyor premonitory) adj2 (sign* or symptom*)) or prodrom* or subclinical* or sub* clinical* or subthreshold or sub* threshold) adj3 (psychos* or psychotic* or schiz*)).mp. (33)
19 or/13-18 (33)
20 (Experimental or interventional or experiment* or multiple arm trial* or clinical trial* or double blind or randomization or random sample or placebo or RCT* or randomized control trial or doubleblind* or singleblind* or tripleblind or block design* or cluster randomized trial* or two-arm trial*).mp. [mp=title, full text, keywords] (11903)
21 (treatment or case-crossover or ecological or naturalistic or case-control or non-randomized controlled trial or controlled before after study or interrupted time series study or historically controlled study or cohort study or cross-sectional study or quasi-design or quasi-experimental designs or quasi or factorial designs or time series designs or uncontrolled before after studies or open label or openlabel).mp. [mp=title, full text, keywords] (17024)
22 20 and 21 (9620)
23 6 and (7 or 12 or 19) and 22 (62)

Database: PsychINFO
1 exp psychosis/ (103886)
2 deficit syndrome.ti,ab. (289)
3 exp schizophrenia/ (81402)
4 ((chronic* or serious or persistent or severe*) adj (mental* or psychological*) adj (disorder* or ill*)).mp. (13290)
5 (delusion* or hebephreni* or psychosis or psychoses or psychotic* or schizo*).mp. (174521)
6 or/1-5 (184458)
7 risk factors/ (64138)
8 symptom*.sh. or (prodrom* or risk*).hw. (180124)
9 (blips or brief limited intermittent psychotic symptom* or ((attenuat* or early or pre?monitory) adj2 (sign* or symptom*)) or pre?delusion* or pre?hallucin* or pre?psychos* or pre?psychotic* or pre?schizo* or (pre adj (delusion* or hallucin* or

psychos* or psychotic* or schizo*)) or prodrom* or sub?clinical* or sub?threshold* or at risk* or ((high* or incipient or increas*) adj3 risk*)).ti,ab,kw. (137684)
10 or/8-9 (264103)
11 (conversion* or ((develop* or progress*) adj2 (psychos* or psychotic* or schiz*)) or first episode* or fullthreshold* or full threshold* or onset* or progression or transition* or transitory).ti,ab. (182961)
12 10 and 11 (24934)
13 clinical high risk.ti,ab. (380)
14 ultra high risk.ti,ab. (608)
15 basic symptoms.ti,ab. (211)
16 attenuated psychosis syndrome.ti,ab. (68)
17 ((at risk or ((high or increase*) adj2 risk) or blips or brief limited intermittent psychotic symptom* or ((attenuat* or early or premonitory) adj2 (sign* or symptom*)) or prodrom* or subclinical* or sub* clinical* or subthreshold or sub* threshold) and (psychos* or psychotic* or schiz*)).ti. or ((at risk or ((high or increase*) adj2 risk) or blips or brief limited intermittent psychotic symptom* or ((attenuat* or earlyor premonitory) adj2 (sign* or symptom*)) or prodrom* or subclinical* or sub* clinical* or subthreshold or sub* threshold) adj3 (psychos* or psychotic* or schiz*)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (4874)
18 exp at risk populations/ (34452)
19 or/13-18 (37901)
20 (Experimental or interventional or experiment* or multiple arm trial* or clinical trial* or double blind or randomization or random sample or placebo or RCT* or randomized control trial or doubleblind* or singleblind* or tripleblind or block design* or cluster randomized trial* or two-arm trial*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (521516)
21 (treatment or case-crossover or ecological or naturalistic or case-control or non-randomized controlled trial or controlled before after study or interrupted time series study or historically controlled study or cohort study or cross-sectional study or quasi-design or quasi-experimental designs or quasi or factorial designs or time series designs or uncontrolled before after studies or open label or openlabel).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (658596)
22 20 or 21 (1083370)
23 6 and (7 or 12 or 19) and 22 (4695)

Database: CINAHL

S1 (MH "Psychotic Disorders+") OR "psychotic disorders" OR (MH "Schizophrenia+") OR "schizophrenia"

S2 "ultra high risk" OR "clinical high risk" OR "basic symptoms" OR "attenuated psychosis syndrome" or "conversion" OR "transition" or (MH "Risk Factors") OR "risk factors"

S3 "experimental" OR "interventional" OR "experiment*" OR "multiple arm trial*" OR "clinical trial*" OR "double blind" OR "randomization" OR "random sample" OR "placebo" OR "RCT*" OR "randomized control trial" OR "doubleblind*" OR "singleblind*" OR "tripleblind" OR "block design*" OR "cluster randomized trial*" OR "two-arm trial*"

S4 S1 AND S2 AND S3

Supplementary Table 1. PRISMA Checklists for Both Transition Pairwise and Network Meta-Analysis

A. Transition Pairwise Checklist

Section/topic	#	Checklist item	Reported on 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
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3-4
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.	4
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
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.	3
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	3, Supplementary Material 2
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).	3
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.	5-6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-6

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 the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6-7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I_2) for each meta-analysis.	6-8

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6-8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	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.	9
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.	9-10
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
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10-15, Supplementary 5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-15
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10, Figure 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
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).	15-16
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).	16-18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18-19

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.	19

*** page numbers correspond to the original word document and do not reflect the page numbers in the published manuscript for both A and B.**

B. Transition NMA Checklist. Checklist of Items to Include When Reporting A Systematic Review Involving a Network Meta-analysis

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review *incorporating a network meta-analysis (or related form of meta-analysis).*	***1***
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: **Background:** main objectives **Methods:** data sources; study eligibility criteria, participants, and interventions; study appraisal; and *synthesis methods, such as network meta-analysis.* **Results:** number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; *treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity.* **Discussion/Conclusions:** limitations; conclusions and implications of findings. **Other:** primary source of funding; systematic review registration number with registry name.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known, *including mention of why a network meta-analysis has been conducted.*	***3***
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	***3-4***
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number.	4

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. *Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).*	***5***
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.	***3***
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	***3, SM 2***
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).	3
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.	***5-6***
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	***5-6***
Geometry of the network	**S1**	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	***6-7, 10, Figure 3***
Risk of bias within 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.	***6, Figure 3***
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). *Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.*	***6-8***
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: • *Handling of multi-arm trials;* • *Selection of variance structure;* • *Selection of prior distributions in Bayesian analyses; and* • *Assessment of model fit.*	***6-8***
Assessment of Inconsistency	**S2**	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	***6-8***
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	***6-8***
Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: • Sensitivity or subgroup analyses; • Meta-regression analyses; • *Alternative formulations of the treatment network; and* • *Use of alternative prior distributions for Bayesian analyses (if applicable).*	***6-8***

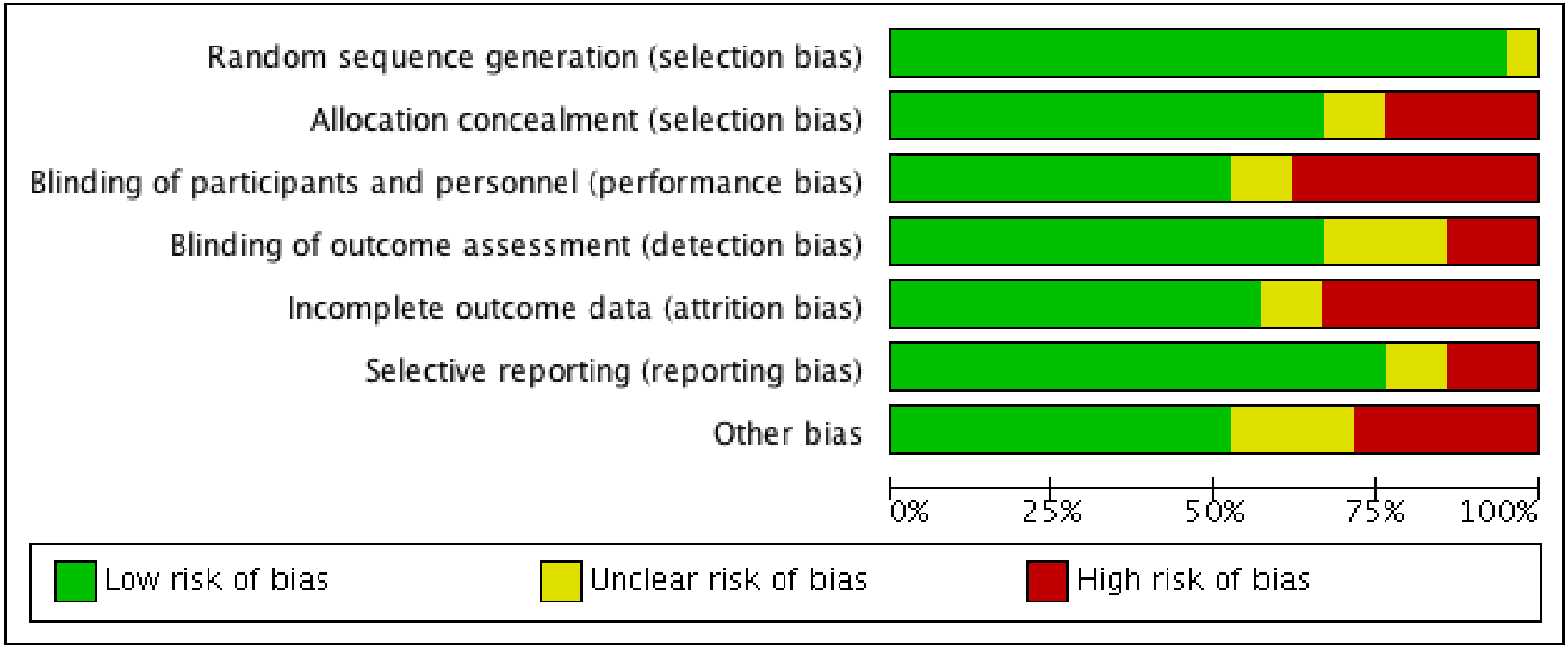
RESULTS†			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	***9***
Presentation of network structure	**S3**	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	***10-11, Figure 3***
Summary of network geometry	**S4**	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	***10-11***
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.	***Table 1***
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	***10, Figure 2, Figure 3***
Results of individual studies	20	*For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. Modified approaches may be needed to deal with information from larger networks.*	***11-15***
Synthesis of results	21	*Present results of each meta-analysis done, including confidence/credible intervals. In larger networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons. If additional summary measures were explored (such as treatment rankings), these should also be presented.*	***11-15, Figure 4***
Exploration for inconsistency	**S5**	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, *P* values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	***11***
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	***10, Figure 2, Figure 3***
Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses, *alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses,* and so forth).	***NA***
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).	***15-16***

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). *Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).*	***17-18***
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	***18-19***
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. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	***19***

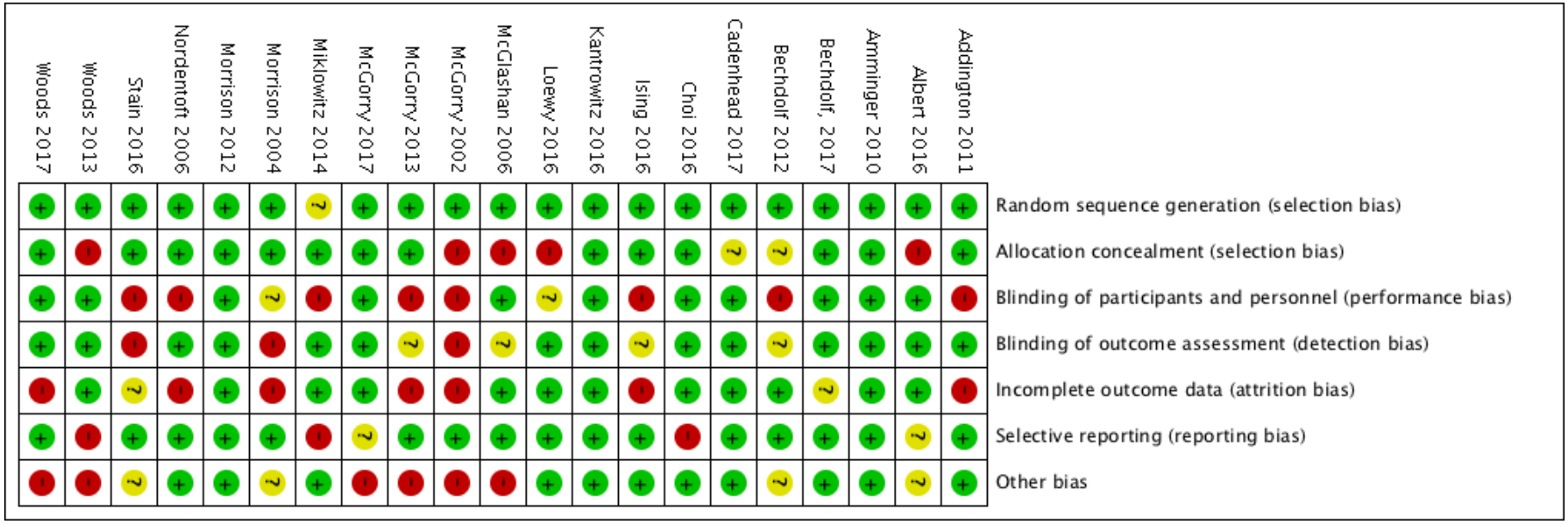
PICOS = population, intervention, comparators, outcomes, study design.

Supplementary Figure 1. Risk-of-Bias Assessments

A. Cochrane Risk-of-Bias Assessment for RCTs: Graph



B. Cochrane Risk-of-Bias Assessment for RCTs: Summary



A. Risk of bias graph for RCTs: review authors' judgements about each risk of bias item presented as percentages across all included studies.

B. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Supplementary Table 2. ROBINS-I Risk-of-Bias Assessment for Nonrandomized Studies

Author, Year	Biases							
	Confounding	Selection of participants	Classification of interventions	Deviations from intended interventions	Missing data	Measurement of outcomes	Selection of reported result	Overall Bias
Berger, 2012	Low	NI	Low	NI	NI	NI	NI	NI
Cornblatt, 2007	Moderate	Serious	Moderate	Low	Moderate	Moderate	Low	Serious
Fusar-Poli, 2015	Serious	Moderate	Serious	Low	NI	Low	Low	Serious
Kerri, 2006	Low	Low	Low	Moderate	Low	Moderate	Low	Moderate
Kim, 2011	Moderate	Low	Low	Low	Low	Moderate	Low	Moderate
Kim, 2012	Serious	Low	Serious	Moderate	Low	Moderate	Moderate	Serious
Kobayashi, 2009	Low	Low	Moderate	Low	Low	Moderate	Low	Moderate
Liu, 2010	Low	Low	Low	NI	Low	Moderate	Moderate	Moderate
McFarlane, 2015	Low	Serious	Low	Moderate	Moderate	Low	Moderate	Serious
Morita, 2014	Moderate	Low	Moderate	Serious	Moderate	Moderate	Moderate	Serious
O'Brien, 2007	Low	Low	Low	Low	Moderate	Moderate	Moderate	Moderate
Rybakowski, 2003	Low	Low	Low	Low	Low	Moderate	Low	Moderate
Shim, 2008	Moderate	Low	Moderate	Serious	Moderate	NI	Low	Serious
Tsujino, 2013	Low	Low	Moderate	NI	Low	Moderate	Low	Moderate
Walker, 2009	Serious	Serious	Moderate	Moderate	NI	Moderate	Serious	Serious
Woods, 2007	Low	Low	Low	Low	Low	Moderate	Low	Moderate
Woods, 2013	Low	Low	Low	Low	Low	Moderate	Moderate	Moderate

Supplementary Table 3. GRADE Risk-of-Bias Assessment

Intervention	Comparator	# of trials for direct comparison	NMA RR (95% CI)	Risk of bias ‡	Inconsistency §	Indirectness ¥	Imprecision χ	Publication bias Ψ	Overall Quality
6-months									
RIS	PLA	0	0.36 (0.07, 2.00)			*	**		Very low
OLA	PLA	1	0.42 (0.12, 1.49)	*			*		Low
OME	PLA	3	0.74 (0.30, 1.85)				*		Moderate
NBI	PLA	0	1.33 (0.22, 7.93)			*	**		Very low
CBT	PLA	1	0.62 (0.08, 5.08)	*			**		Very low
SUP	PLA	0	1.10 (0.20, 6.01)			*	**		Very low
IPT	PLA	0	0.09 (0.00, 2.60)			*	**		Very low
FAM	PLA	0	0.19 (0.01, 3.88)			*	**		Very low
OLA	RIS	0	1.15 (0.14, 9.65)			*	**		Very low
OME	RIS	0	4.43 (0.60, 32.98)			*	**		Very low
NBI	RIS	1	2.70 (0.71, 10.20)	*			**		Very low
CBT	RIS	1	1.71 (0.39, 7.38)	*			**		Very low
SUP	RIS	1	3.03 (0.53, 17.29)	*			**		Very low
IPT	RIS	0	0.24 (0.01, 7.33)			*	**		Very low
FAM	RIS	0	0.52 (0.04, 6.92)			*	**		Very low
OME	OLA	0	3.87 (0.74, 20.16)			*	**		Very low
NBI	OLA	0	2.36 (0.21, 26.39)			*	**		Very low
CBT	OLA	0	1.49 (0.13, 17.42)			*	**		Very low
SUP	OLA	0	2.64 (0.32, 22.08)			*	**		Very low
IPT	OLA	0	0.21 (0.01, 7.88)			*	**		Very low
FAM	OLA	0	0.45 (0.02, 12.06)			*	**		Very low
NBI	OME	0	0.61 (0.06, 6.16)			*	**		Very low
CBT	OME	1	0.38 (0.04, 4.07)				**		Low
SUP	OME	0	0.68 (0.09, 5.02)			*	**		Very low
IPT	OME	0	0.05 (0.00, 1.89)			*	**		Very low
FAM	OME	0	0.12 (0.00, 2.89)			*	**		Very low
CBT	NBI	4	0.63 (0.30, 1.34)	*			*		Low
SUP	NBI	0	1.12 (0.16, 8.04)			*	**		Very low
IPT	NBI	0	0.09 (0.00, 3.06)			*	**		Very low
FAM	NBI	1	0.19 (0.02, 1.78)	*			*		Low
SUP	CBT	1	1.78 (0.24, 12.88)				**		Low
IPT	CBT	0	0.14 (0.00, 4.88)			*	**		Very low
FAM	CBT	0	0.30 (0.03, 3.19)			*	**		Very low
IPT	SUP	1	0.08 (0.00, 1.50)	*			*		Low
FAM	SUP	0	0.17 (0.01, 3.34)			*	**		Very low

FAM	IPT	0	2.14 (0.03, 140.72)			*	**		Very low
12-month									
RIS	PLA	0	0.90 (0.24, 3.43)			*	**		Very low
OLA	PLA	1	0.43 (0.11, 1.60)	*			*		Low
OME	PLA	3	0.74 (0.30, 1.85)				*		Moderate
NBI	PLA	0	1.33 (0.22, 7.93)			*	**		Very low
CBT	PLA	1	0.70 (0.11, 4.54)	*			**		Very low
SUP	PLA	0	1.53 (0.40, 5.88)			*	**		Very low
IPT	PLA	0	0.29 (0.03, 2.60)			*	**		Very low
ZIP	PLA	1	0.56 (0.05, 6.99)			*	**		Very low
OLA	RIS	0	0.47 (0.07, 3.07)			*	**		Very low
OME	RIS	0	0.82 (0.17, 4.00)			*	**		Very low
NBI	RIS	1	1.47 (0.42, 5.11)	*			**		Very low
CBT	RIS	1	0.78 (0.19, 3.13)	*			**		Very low
SUP	RIS	1	1.69 (0.46, 6.20)	*			**		Very low
IPT	RIS	0	0.32 (0.04, 2.79)			*	**		Very low
ZIP	RIS	0	0.62 (0.04, 10.76)			*	**		Very low
OME	OLA	0	1.74 (0.35, 8.70)			*	**		Very low
NBI	OLA	0	3.13 (0.34, 28.90)			*	**		Very low
CBT	OLA	0	1.65 (0.17, 16.28)			*	**		Very low
SUP	OLA	0	3.60 (0.55, 23.81)			*	**		Very low
IPT	OLA	0	0.68 (0.05, 8.84)			*	**		Very low
ZIP	OLA	0	1.32 (0.08, 22.80)			*	**		Very low
NBI	OME	0	1.80 (0.26, 12.49)			*	**		Very low
CBT	OME	1	0.95 (0.13, 7.16)				**		Low
SUP	OME	0	2.08 (0.40, 10.86)			*	**		Very low
IPT	OME	0	0.39 (0.04, 4.31)			*	**		Very low
ZIP	OME	0	0.76 (0.05, 11.13)			*	**		Very low
CBT	NBI	4	0.53 (0.25, 1.12)	*			*		Low
SUP	NBI	0	1.15 (0.21, 6.40)			*	**		Very low
IPT	NBI	0	0.22 (0.02, 2.49)			*	**		Very low
ZIP	NBI	0	0.42 (0.02, 9.26)				**		Low
SUP	CBT	1	2.18 (0.37, 12.88)				**		Low
IPT	CBT	0	0.41 (0.03, 4.93)			*	**		Very low
ZIP	CBT	0	0.80 (0.03, 18.46)			*	**		Very low
IPT	SUP	1	0.19 (0.03, 1.07)	*			*		Low
ZIP	SUP	0	0.37 (0.02, 6.39)			*	**		Very low
ZIP	IPT	0	1.96 (0.07, 55.61)			*	**		Very low
Long-term									
NBI	RIS	1	1.33 (0.68, 2.59)	*			**		Very low
CBT	RIS	1	0.87 (0.38, 1.99)	*			*		Low
CBT	NBI	0	0.65 (0.40, 1.08)			*	**		Very low

Abbreviations: PLA= Placebo; RIS= Risperidone; OLA= Olanzapine; OME= Omega-3; NBI= Needs-based interventions; CBT= Cognitive behavioral therapy; SUP= Supportive therapy; IPI= Integrated psychological interventions; FAM= Family therapy (6-months); ZIP= Ziprasidone (12-months)

‡ Risk-of-bias assessment based on rating from the Cochrane Risk-of-bias tool assessments.

§ Inconsistency was only assessed in intervention comparisons with >1 study.

¥ Indirectness was based on if there was an actual study with that intervention comparison. All comparisons were considered direct as all of this research was performed within the last 20 years and was restricted to CHR study populations.

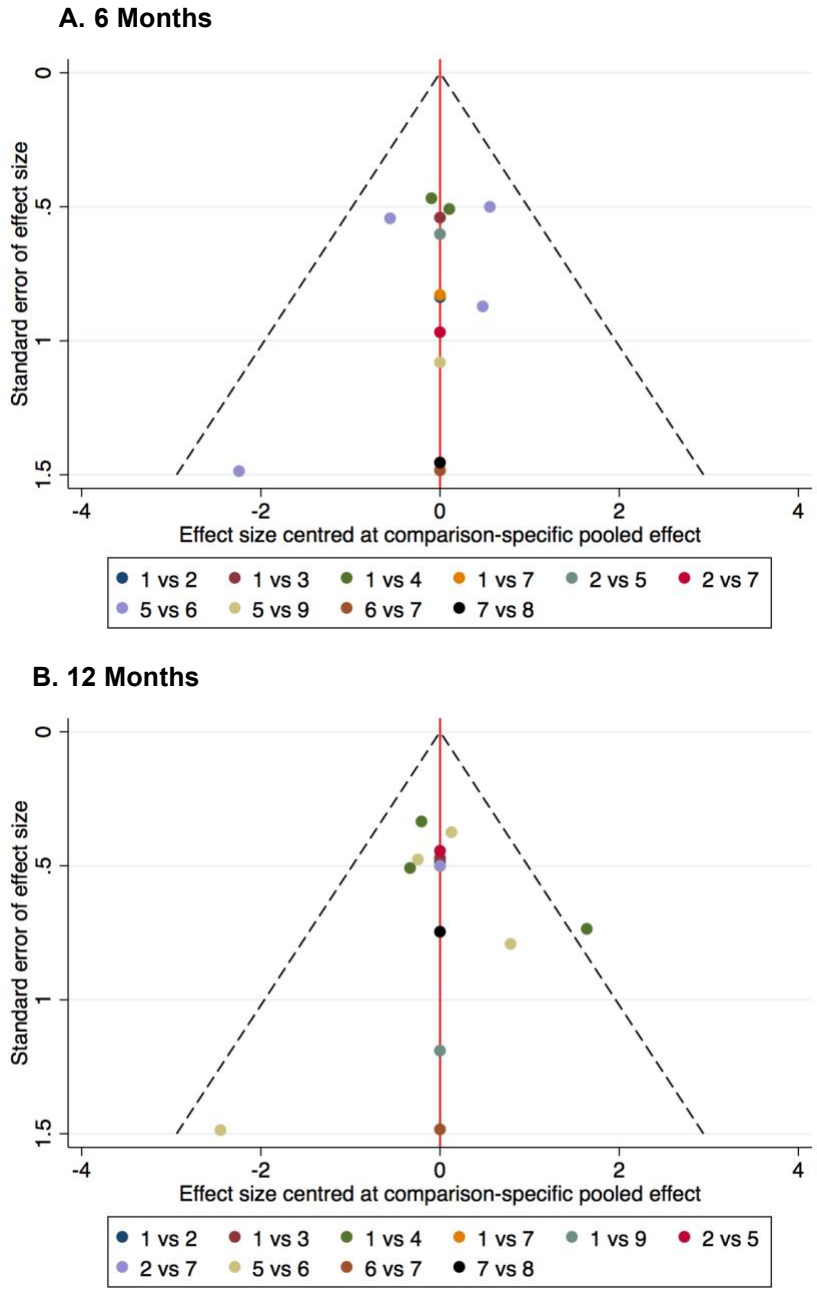
χ Imprecision was observed in all estimates, both direct and indirect for 6-, 12- months and long-term networks and therefore all estimates were downgraded by one point.

Ψ Publication bias was assessed based on the funnel plots. Since a comprehensive systematic literature review was concerned, publication bias is less of a concern.

* Downgraded by one point.

** Downgraded by two points.

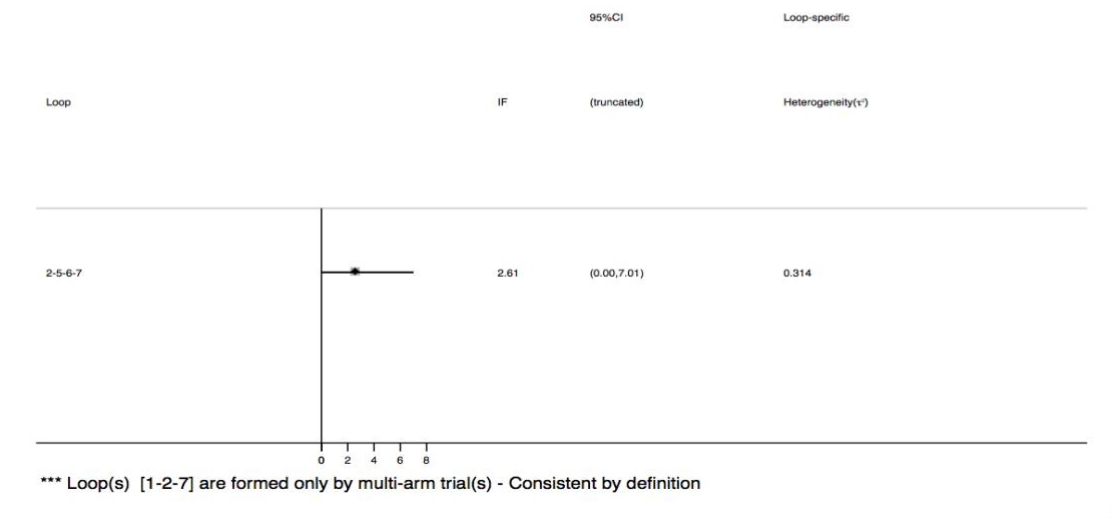
Supplementary Figure 2. Network Comparison-Adjusted Funnel Plots



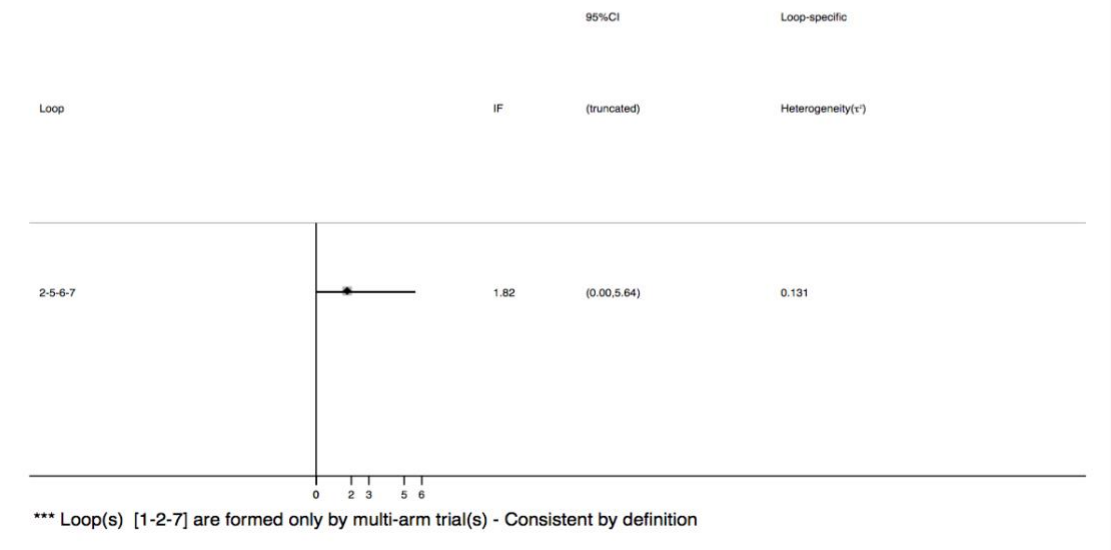
Comparison-adjusted funnel plot for the transition network at 6- and 12-months. Zero represents the null hypothesis that the study-specific effect sizes do not differ from the respective comparison-specific pooled effect estimates. Different colours correspond to different comparisons. Abbreviations: 1= Placebo; 2= Risperidone; 3= Olanzapine; 4= Omega-3; 5= Needs-based interventions; 6= Cognitive behavioral therapy; 7= Supportive therapy; 8= Integrated psychological therapy; 9= Family therapy (6-months); 9= Ziprasidone (12-months)

Supplementary Figure 3. Inconsistency Plot

A. 6 Months



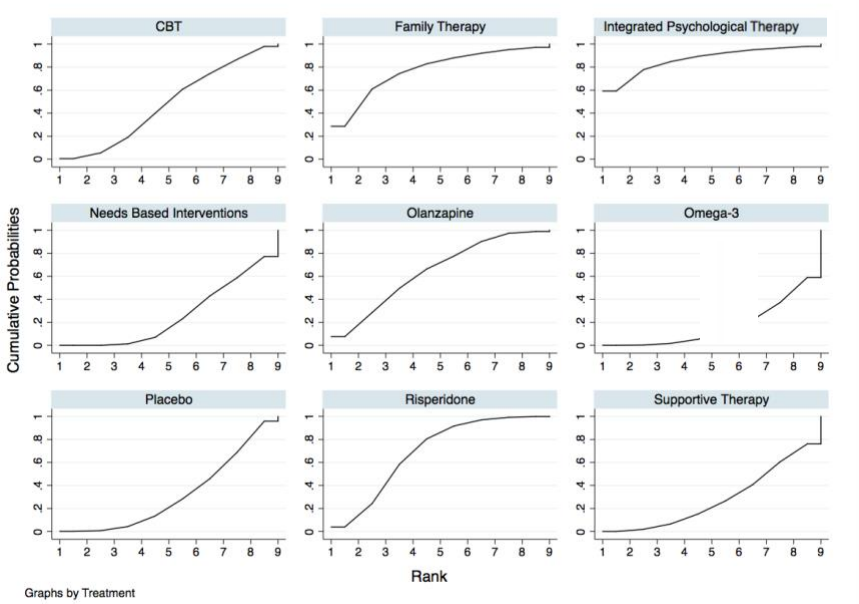
B. 12 Months



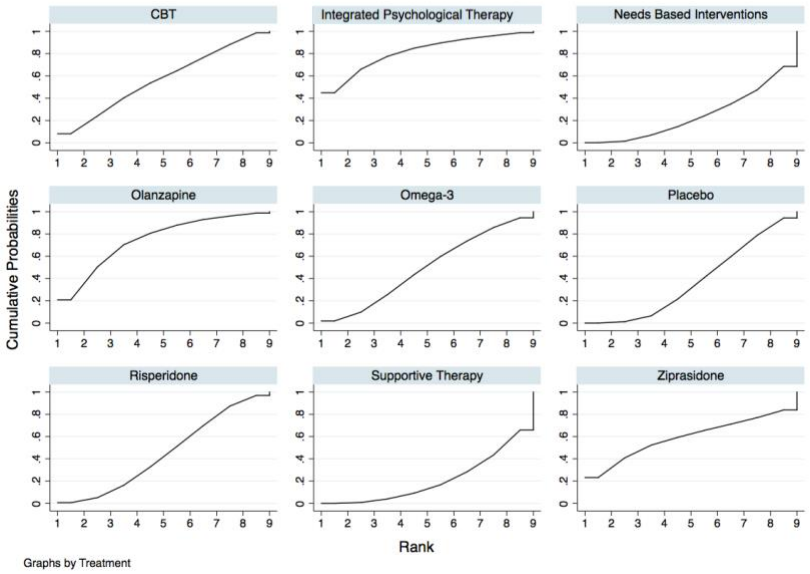
Inconsistency plot produced of one quadratic loop for both 6- and 12-months. Abbreviations: 01= Placebo; 02= Risperidone; 05= Needs-based interventions; 6= Cognitive behavioral therapy; 7= Supportive therapy

Supplementary Figure 4. Surface Under the Cumulative Ranking Curve (SUCRA)

A. 6 Months



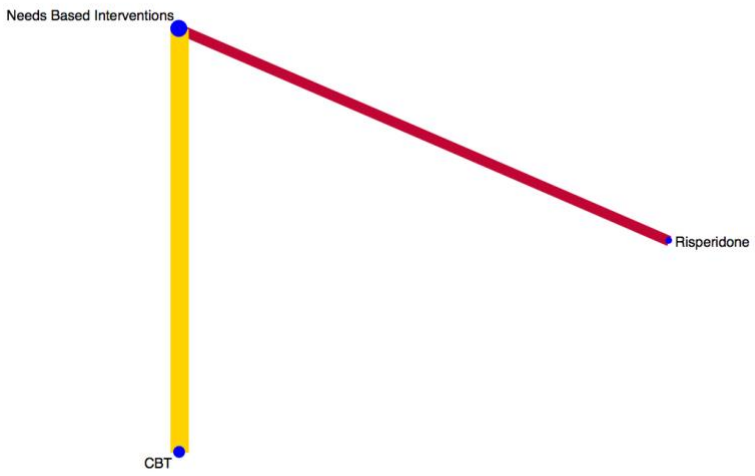
B. 12 Months



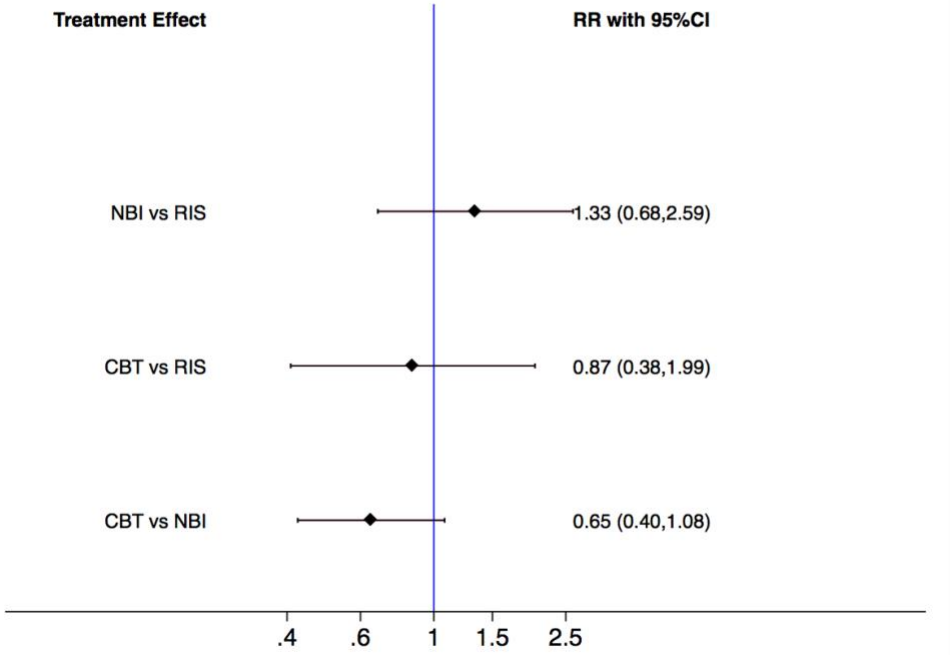
Plots of the surface under the cumulative ranking curves for all treatments in the transition network at 6- and 12-months. Black solid lines correspond to the unadjusted model. Abbreviations: CBT= Cognitive behavioral therapy

Supplementary Figure 5. Long-Term Follow-up Network

A. Long-Term Network Plot



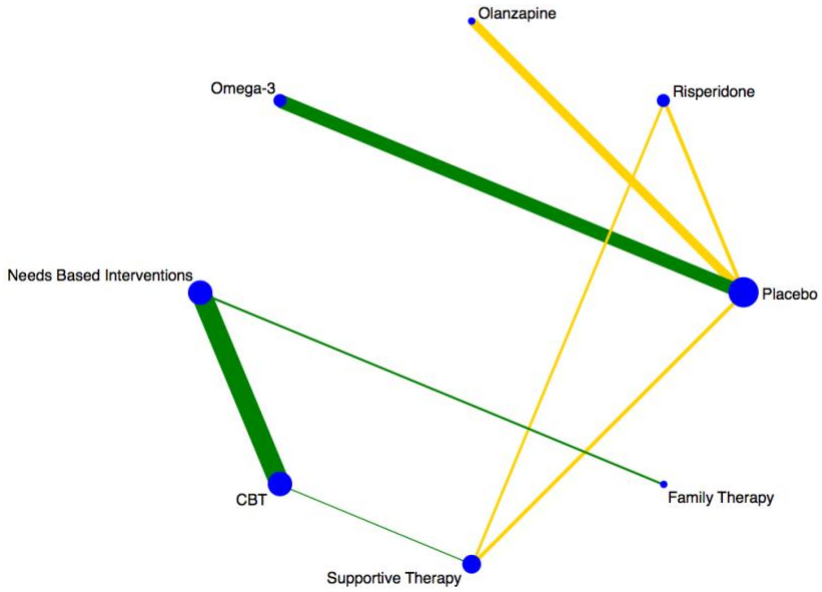
B. Long-Term Network Forest Plot



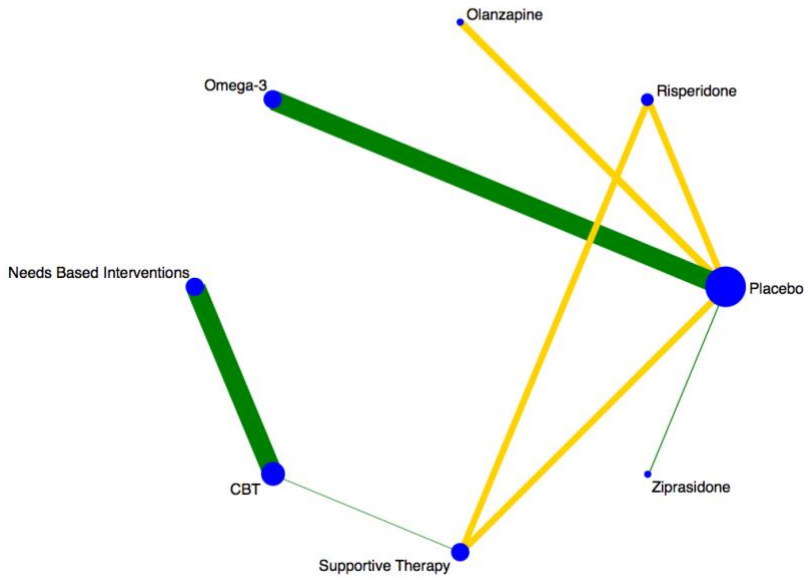
Abbreviations: CBT= Cognitive behavioral therapy; NBI= Needs-based interventions; RIS= Risperidone

Supplementary Figure 6. Sensitivity Analyses

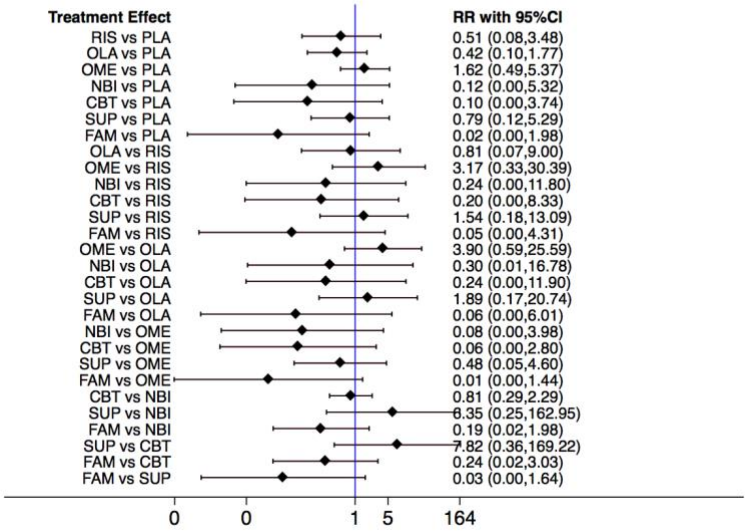
A. 6 Months



B. 12 Months

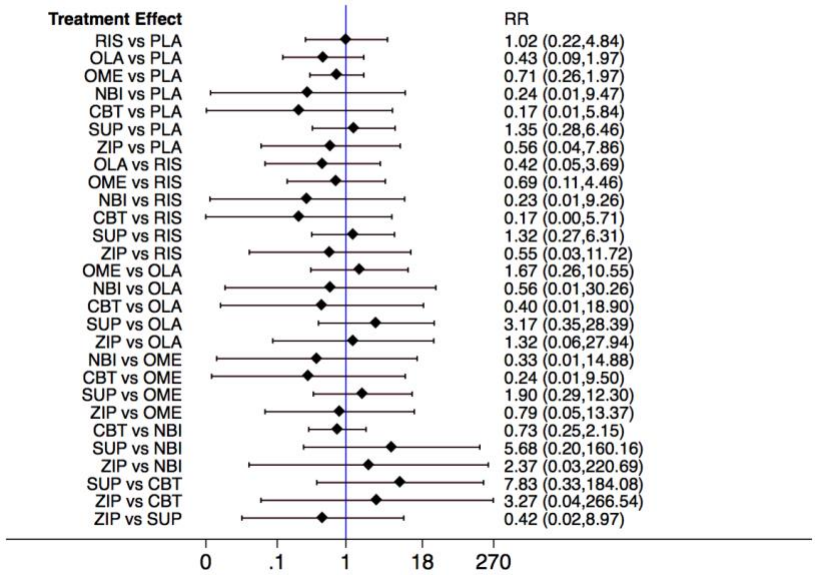


C. Sensitivity Analyses Forest Plot 6-Months



Favors First Intervention **Favors Second Intervention**

D. Sensitivity Analyses Forest Plot 12-Months



Favors First Intervention **Favors Second Intervention**

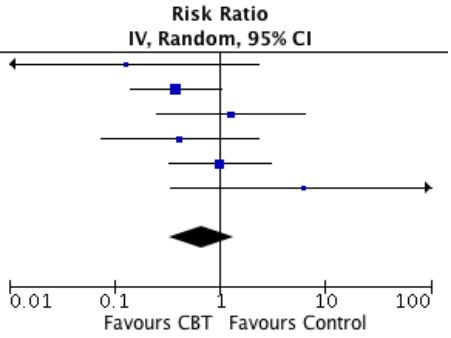
Sensitivity analysis of 6- and 12-month forest plots of the transition network meta-analysis (1=null line). Abbreviations: PLA = Placebo; RIS = Risperidone; OLA = Olanzapine; OME = Omega-3; NBI = Needs Based Interventions; CBT = Cognitive Behavioral Therapy; SUP= Supportive-Therapy; IPI = Integrated Psychological Interventions; FAM = Family-Therapy (6-months); ZIP = Ziprasidone (12-months)

Supplementary Figure 7. Pairwise Forest Plots CBT

A. 6 Months

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
Addington 2011	0	27	3	24	5.4%	0.13 [0.01, 2.35]
Ising 2016	5	97	14	104	32.3%	0.38 [0.14, 1.02]
McGorry 2013z	4	44	2	28	15.3%	1.27 [0.25, 6.50]
Morrison 2004	2	37	3	23	14.1%	0.41 [0.07, 2.30]
Morrison 2012	6	144	6	144	27.6%	1.00 [0.33, 3.03]
Stain 2016	3	30	0	27	5.4%	6.32 [0.34, 117.09]
Total (95% CI)		**379**		**350**	**100.0%**	**0.66 [0.33, 1.34]**
Total events	20		28			

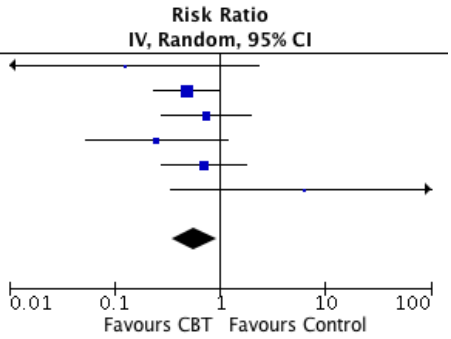
Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 6.15$, df = 5 (P = 0.29); $I^2 = 19\%$
Test for overall effect: Z = 1.15 (P = 0.25)



B. 12 Months

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
Addington 2011	0	27	3	24	2.8%	0.13 [0.01, 2.35]
Ising 2016	9	97	20	104	37.4%	0.48 [0.23, 1.01]
McGorry 2013z	7	44	6	28	22.7%	0.74 [0.28, 1.98]
Morrison 2004	2	37	5	23	9.7%	0.25 [0.05, 1.18]
Morrison 2012	7	144	10	144	24.6%	0.70 [0.27, 1.79]
Stain 2016	3	30	0	27	2.8%	6.32 [0.34, 117.09]
Total (95% CI)		**379**		**350**	**100.0%**	**0.57 [0.35, 0.93]**
Total events	28		44			

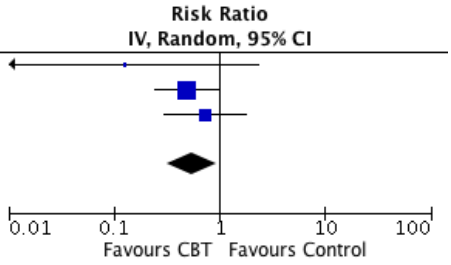
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 5.38$, df = 5 (P = 0.37); $I^2 = 7\%$
Test for overall effect: Z = 2.25 (P = 0.02)



C. 18 Months

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
Addington 2011	0	27	3	24	3.4%	0.13 [0.01, 2.35]
Ising 2016	10	97	22	104	59.6%	0.49 [0.24, 0.98]
Morrison 2012	8	144	11	144	37.0%	0.73 [0.30, 1.76]
Total (95% CI)		**268**		**272**	**100.0%**	**0.54 [0.32, 0.92]**
Total events	18		36			

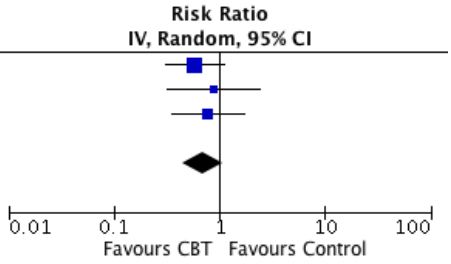
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.46$, df = 2 (P = 0.48); $I^2 = 0\%$
Test for overall effect: Z = 2.25 (P = 0.02)



D. Long-Term (24 to 48 Months)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
Ising 2016	12	97	22	104	48.4%	0.58 [0.31, 1.12]
Morrison 2004	7	37	5	23	19.3%	0.87 [0.31, 2.42]
Morrison 2012	10	144	13	144	32.3%	0.77 [0.35, 1.70]
Total (95% CI)		**278**		**271**	**100.0%**	**0.69 [0.44, 1.08]**
Total events	29		40			

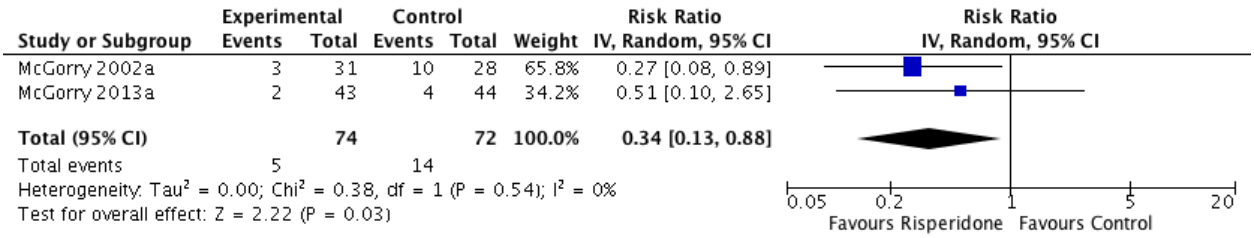
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.52$, df = 2 (P = 0.77); $I^2 = 0\%$
Test for overall effect: Z = 1.62 (P = 0.11)



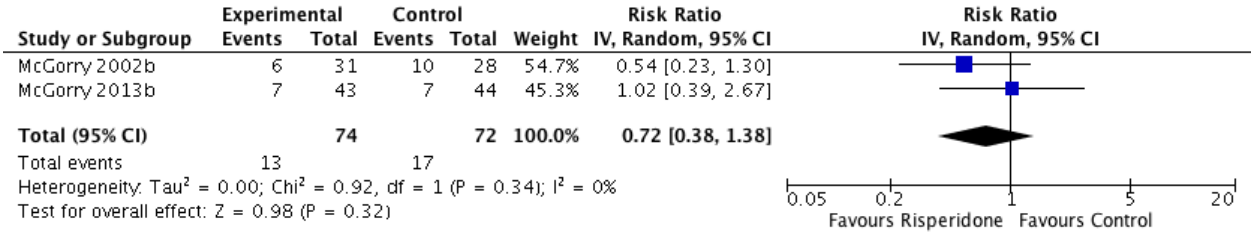
NOTES: Ising 2016 – randomized numbers reported in original van der Gaag et al., 2012 paper used for each time-point; z = CBT + placebo versus supportive + placebo; Morrison 2004 utilizing PANSS transition criteria & Morrison 2004 long-term follow-up as reported in Morrison et al., 2007 paper utilizing PANSS transition criteria.

Supplementary Figure 8. Pairwise Forest Plots Risperidone + CBT

A. 6 Months



B. 12 Months



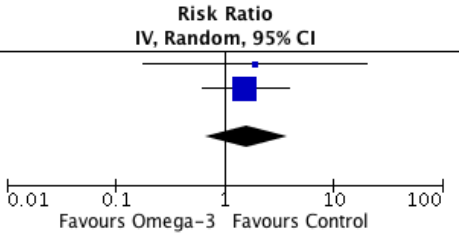
Risperidone + CBT versus controls impact on transition in CHR.

Supplementary Figure 9. Pairwise Forest Plots Omega-3

A. 6 Months

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
Cadenhead 2017	2	65	1	62	13.1%	1.91 [0.18, 20.51]
McGorry 2016	11	153	7	151	86.9%	1.55 [0.62, 3.89]
Total (95% CI)		**218**		**213**	**100.0%**	**1.59 [0.68, 3.76]**
Total events	13		8			

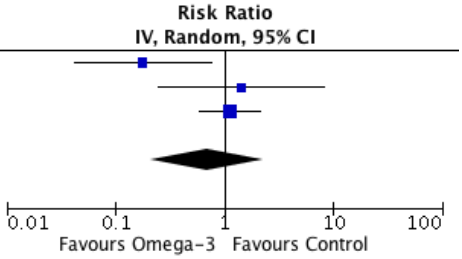
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.87); I² = 0%
Test for overall effect: Z = 1.06 (P = 0.29)



B. 12 Months

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
Amminger 2010	2	41	11	40	29.9%	0.18 [0.04, 0.75]
Cadenhead 2017	3	65	2	62	24.7%	1.43 [0.25, 8.28]
McGorry 2016	17	153	15	151	45.4%	1.12 [0.58, 2.16]
Total (95% CI)		**259**		**253**	**100.0%**	**0.69 [0.21, 2.27]**
Total events	22		28			

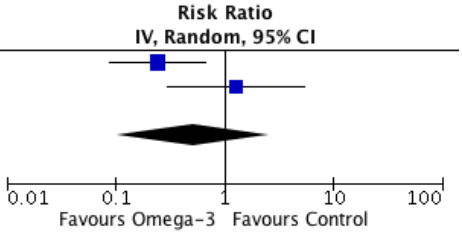
Heterogeneity: Tau² = 0.71; Chi² = 5.54, df = 2 (P = 0.06); I² = 64%
Test for overall effect: Z = 0.62 (P = 0.54)



C. Long-Term (post one-year)

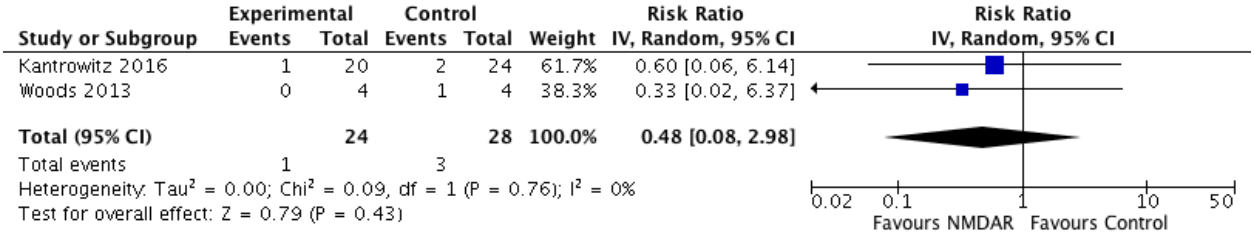
Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
Amminger 2010	4	41	16	40	55.3%	0.24 [0.09, 0.67]
Cadenhead 2017	4	65	3	62	44.7%	1.27 [0.30, 5.45]
Total (95% CI)		**106**		**102**	**100.0%**	**0.51 [0.10, 2.55]**
Total events	8		19			

Heterogeneity: Tau² = 0.96; Chi² = 3.35, df = 1 (P = 0.07); I² = 70%
Test for overall effect: Z = 0.82 (P = 0.41)



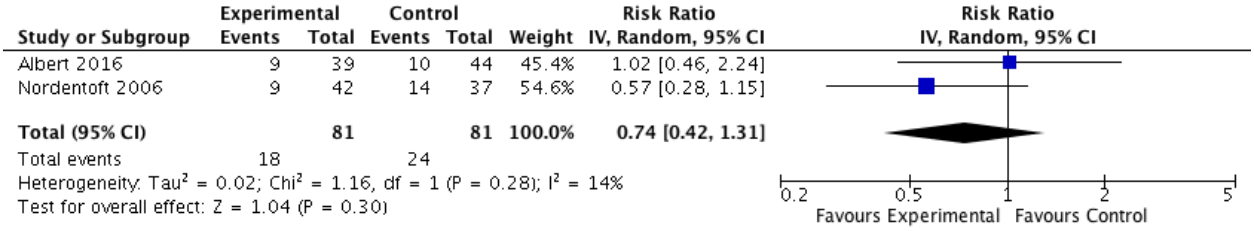
Notes: Amminger 2010 long-term outcome from Amminger et al., 2014

Supplementary Figure 10. Pairwise Forest Plots NMDAR Modulators



NMDAR impact on transition in CHR at 12- to 16-week follow-up. Kantrowitz 2016 includes 1 participant who transitioned at week 16.

Supplementary Figure 11. Pairwise Forest Plots Integrated Treatment (Schizotypal)



Note: Integrated treatment impact on transition in schizotypal participants at long-term follow-up using allocation n values for both experimental and control groups in both studies.