TRANSITION OF SUBSTANCE-INDUCED, BRIEF, AND ATYPICAL PSYCHOSES TO SCHIZOPHRENIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

SUPPLEMENTARY MATERIAL

PROTOCOL

Transition of substance-induced psychosis to schizophrenia: a systematic review and meta-analysis

Benjamin Murrie, Julia Lappin, Matthew Large, Grant Sara

Citation

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Review question

(i) What proportion of people with a diagnosis of drug-induced or other brief psychoses progress to a later diagnosis of schizophrenia?

(ii) What factors are associated with a greater likelihood of progression from drug-induced or other brief psychoses to schizophrenia?

Searches

We will search the following electronic bibliographic databases: MEDLINE, EMBASE, PsycINFO. The search strategy includes terms describing the psychosis and outcome. Searches will be limited to English language studies, published in peer reviewed journals, excluding individual case studies. Studies published between January 1980 and the date the searches are run will be sought.

Search strategy:
"first episode" or "drug induced" or "substance induced" or "cannabis induced" or "marijuana induced" or "amphetamine induced" or "cocaine induced" or "stimulant induced" or "first-episode" or "drug-induced" or "substance-induced" or "cannabis-induced" or "marijuana-induced" or "amphetamine-induced" or "cocaine-induced" or "stimulant-induced"
AND
Psychosis OR psychotic
AND
"diagnostic stability" OR "diagnostic-stability" OR outcome OR "follow up" OR follow-up OR course OR prognosis OR transition OR conversion OR longitudinal

Types of study to be included

Studies describing follow-up of a group of persons with drug-induced or other brief psychoses diagnosed according to standardised diagnostic criteria. Includes: cohort studies, case-control studies, randomised controlled trials and case series.

Inclusion criteria:
(1) Study in English
(2) Publication in peer-reviewed journal article
(3) Human participants
(4) Target condition
- Any diagnosed psychotic syndrome: drug induced, brief, atypical/NOS, first episode or schizophreniform psychoses, diagnosed according to DSM or ICD criteria.

(5) Outcome:

- Study reports on rate of subsequent diagnosis of schizophrenia, diagnosis made according to recognised/standardised criteria.

(6) Study design:
- Case-control studies, cohort studies, randomised controlled trials, case series.
- Follow up period at least 6 months

(7) Results report usable empirical data, specifically
- Index diagnosis quantified
- Outcome (Schizophrenia and/or other psychoses) quantified

Exclusion criteria
(1) Study not in English
(2) Study in other formats: Book chapters, conference papers/abstracts
(3) Study does not report empirical data: Commentary, editorial, review, single case study, qualitative studies.
(4) Animal and non-human primate studies
(5) Target condition not defined using standard diagnostic framework. Exclude psychosis purely defined by symptom measures or scales, self-report.
(6) Outcome not defined using standardised criteria. Exclude psychosis purely defined by symptom measures or scales, self-report.
(7) Studies where no empirical data can be extracted

Condition or domain being studied

Drug-induced and other brief psychoses, and schizophrenia.

Participants/population

Persons with a diagnosis of drug-induced, or brief psychoses (or equivalent DSM or ICD diagnostic terms)

Intervention(s), exposure(s)

This is a descriptive review summarizing rate of progression from drug induced and other brief psychoses to a later diagnosis of schizophrenia, and factors associated with heterogeneity in that rate of progression. No specific intervention will be examined.

Comparator(s)/control

Not applicable.

Context

Studies are expected to be primarily drawn from outpatient and inpatient clinical treatment settings, primarily those involved in care of people with substance use or psychiatric conditions.

Main outcome(s)

Progression to a clinical diagnosis of schizophrenia over a follow up period of at least 6 months. Establishing the rate and factors that influence the progression from drug-induced or brief psychoses to schizophrenia.

Timing and effect measures

-

Additional outcome(s)

None.

Timing and effect measures

Not applicable

Data extraction (selection and coding)

Search strategy and inclusion / exclusion criteria will be agreed on in advance by all investigators. Search will be run by one investigator (BM). Abstract screening and full text screening will be conducted independently by two investigators (BM, GS). Discrepancies will be resolved by discussion with a third investigator (JL). Investigators will not be blinded. Authors of eligible studies will not be contacted to provide missing or additional data.

Data to be extracted
1 - Study Identification
2 - Study details: author; year; country (urban/rural); study design; study aim
3 - Recruitment characteristics: N in total sample; years of recruitment; setting for recruitment; relevant exclusion criteria
4 - Total sample characteristics: age; sex; other psychiatric comorbidities; education or employment
5 - Index episode definition: type of drug induced/brief psychosis; method of diagnosis; diagnostic system; duration; first or any episode; subtopic
6 - Follow up: how many follow up periods reported; duration of follow up; number followed up/drop out rate
7 - Outcome: schizophrenia (type of measure, method of diagnosis, scope of definition, subtype); other conditions reported; adjusted vs unadjusted effects; significant covariates
8 - Study quality

Risk of bias (quality) assessment

Risk of bias will be assessed by two investigators (BM, GS). Studies will be rated using Joanna Briggs Institute Critical Appraisal tools for the relevant study designs. Quality assessments will be used to define a threshold for inclusion of studies. Impact of quality ratings on findings will be examined by meta-regression. Sensitivity analyses will be conducted examining the impact of exclusion of studies with lower quality ratings.

Strategy for data synthesis

Analysis will be conducted using Stata. An a priori choice of a random effects model was made for all analyses because of significant variation in study design and populations. A pooled estimate of rate of progression to schizophrenia will be calculated. Potential factors associated with heterogeneity in this outcome will be treated as subgroups and be examined separately. To investigate possible publication bias, a funnel (Egger's) plot of the main effect will be examined for interaction between progression to schizophrenia and standard error. Duval and Tweedie's 'trim and fill' method will be used to examine the effect on the pooled effect rate of hypothetical missing studies.

Analysis of subgroups or subsets

The contribution of categorical study characteristics (e.g. type of drug) to between-study heterogeneity will be assessed using Q-value statistics. The contribution of continuous variables (e.g. age, sex, year of publication, drug rate) to between-study heterogeneity will be examined using a

random effects (restricted maximum likelihood) meta-regression model. Continuous and categorical variables with univariate significance will be examined together using a random effects (restricted maximum likelihood) meta-regression model, with Knapp-Hartung distribution. Categorical variables will be examined and, where required, collapsed into fewer categories to ensure that no variable has a Variance Inflation Factor (VIF) greater than 3.

Contact details for further information

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Organisational affiliation of the review

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Review team members and their organisational affiliations

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Dr Grant Sara. Northern Clinical School, Sydney Medical School, University of Sydney, Australia

Type and method of review

Meta-analysis, Qualitative synthesis, Systematic review

Anticipated or actual start date

23 January 2018

Anticipated completion date

31 December 2018

Funding sources/sponsors

No external funding

Conflicts of interest

None

Language

(there is not an English language summary)

Country

Australia

Stage of review

Review Completed not published

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

Disease Progressio; Humans; Psychotic Disorders; Schizophrenia

Date of registration in PROSPERO

29 January 2018

Date of publication of this version

05 August 2019

Revision note for this version

Updated authors; Updated level of completion

Details of any existing review of the same topic by the same authors

-

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	Yes
Risk of bias (quality) assessment	Yes	Yes
Data analysis	Yes	Yes

Revision note

Updated authors; Updated level of completion

Versions

29 January 2018

21 February 2018

27 November 2018

05 August 2019

PROSPERO
This information has been provided by the named contact for this review. CRD has accepted this

information in good faith and registered the review in PROSPERO. The registrant confirms that the information supplied for this submission is accurate and complete. CRD bears no responsibility or liability for the content of this registration record, any associated files or external websites.

TABLE 1S: SUMMARY OF DEVIATIONS FROM PROTOCOL

Section	**Deviation**	**Rationale**	**Potential impact on findings**
Search strategy	The original planned search terms were extended to include terms for psychoses induced by lysergic acid/LSD, hallucinogens, psilocybin, phencyclidine, PCP, angel dust and alcohol.	The original search terms included generic terms for substance-induced psychosis but may have failed to detect some studies examining specific substances.	Nil. The two search strategies were compared. Compared to the original strategy, the broader strategy identified 38 additional abstracts, of which two were screened in full text and none included in analysis.
Types of study to be included	The selection criteria required initial measurement of a group with known exposure (substance induced psychosis) and follow up to assess rate of outcome (transition). Therefore while criteria indicated that case-control and other designs would be included, in effect case control studies were excluded.	Case-control designs would measure prior exposure (substance use or prior substance-induced psychosis) in people with a diagnosis of schizophrenia. This would not allow calculation of the risk of transition following exposure.	Nil
Risk of bias (quality) assessment	Quality assessment tool was changed to use the Newcastle Ottawa Scale (NOS) for cohort studies	Selection criteria limited the included studies to cohort studies. NOS provides more specific and relevant criteria for this study type	Improved ability to assess potential impact of study quality
Strategy for data synthesis	Data analysis was conducted with Comprehensive Meta- Analysis (CMA) rather than Stata as planned	Availability of expertise in CMA use	Different applications may produce minor differences in results but no known systematic difference between the two applications
Data extraction	Additional potential covariates were extracted for analysis: PANSS total score, BPRS, GAF, use of toxicology, rate of comorbid substance use	Reviewer request	Improved ability to examine relevant covariates
Data analysis	Bonferroni correction was applied for subgroup analysis	Additional subgroup comparisons were included, increasing the number of comparisons to 10	Reduced risk of false positive associations, but possible reduced sensitivity

SEARCH SYNTAX USED

(("first episode" or "drug induced" or "substance induced" or "cannabis induced" or "marijuana induced" or "amphetamine induced" or "cocaine induced" or "stimulant induced" or "first-episode" or "drug-induced" or "substance-induced" or "cannabis-induced" or "marijuana-induced" or "amphetamine-induced" or "cocaine-induced" or "stimulant-induced" or "LSD induced" or "LSD-induced" or "lysergic acid induced" or "lysergic-acid-induced" or "hallucinogen induced" or "hallucinogen-induced" or "PCP induced" or "PCP-induced" or "angel dust induced" or "angel-dust-induced" or "phencyclidine induced" or "phencyclidine-induced" or "psilocybin induced" or "psilocybin-induced" or "alcohol induced" or "alcohol-induced" or "opioid induced" or "opioid-induced" or "benzodiazepine induced" or "benzodiazepine-induced") and (Psychosis or psychotic) and ("diagnostic stability" or "diagnostic-stability" or outcome or "follow up" or follow-up or course or prognosis or transition or conversion or longitudinal)).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, an, ui, sy, tc, id, tm, mh]

Limit to

- English
- Human studies
- Publication year between 1980 and 2018

PRISMA 2009 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.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	1
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
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
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.	3
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	3
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.	3
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	3
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.	3

PRISMA 2009 Checklist

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).	3
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	3
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.	Table 1
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).	Supplementary material
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.	Supplementary material
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Table 2
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Table 3
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Table 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).	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).	9
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	9
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.	10

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

MOOSE (Meta-analyses Of Observational Studies in Epidemiology) Checklist

A reporting checklist for Authors, Editors, and Reviewers of Meta-analyses of Observational Studies. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Reporting Criteria	Reported (Yes/No)	Reported on Page No.
Reporting of Background		
Problem definition	Yes	2
Hypothesis statement	Yes	2
Description of Study Outcome(s)	Yes	2
Type of exposure or intervention used	Yes	2
Type of study design used	Yes	2
Study population	Yes	2
Reporting of Search Strategy		
Qualifications of searchers (eg, librarians and investigators)	Yes	2
Search strategy, including time period included in the synthesis and keywords	Yes	2
Effort to include all available studies, including contact with authors	Yes	2
Databases and registries searched	Yes	2
Search software used, name and version, including special features used (eg, explosion)	Yes	2
Use of hand searching (eg, reference lists of obtained articles)	Yes	2
List of citations located and those excluded, including justification	Yes	Fig 1
Method for addressing articles published in languages other than English	Yes	3
Method of handling abstracts and unpublished studies	Yes	3
Description of any contact with authors	Yes	3
Reporting of Methods		
Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Yes	2
Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	Yes	3
Documentation of how data were classified and coded (eg, multiple raters, blinding, and interrater reliability)	Yes	3
Assessment of confounding (eg, comparability of cases and controls in studies where appropriate	Yes	3

Reporting Criteria	Reported (Yes/No)	Reported on Page No.
Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	Yes	6
Assessment of heterogeneity	Yes	4
Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	Yes	3
Provision of appropriate tables and graphics	Yes	Throughout
Reporting of Results		
Table giving descriptive information for each study included	Yes	5-6
Results of sensitivity testing (eg, subgroup analysis)	Yes	Table 3
Indication of statistical uncertainty of findings	Yes	All tables
Reporting of Discussion		
Quantitative assessment of bias (eg, publication bias)	Yes	6
Justification for exclusion (eg, exclusion of non–English-language citations)	Yes	9
Assessment of quality of included studies	Yes	6
Reporting of Conclusions		
Consideration of alternative explanations for observed results	Yes	8
Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	Yes	9
Guidelines for future research	No	
Disclosure of funding source	Yes	10

FIGURE 1S: FORREST PLOT, OVERALL COMPARISON

Fig 1s: Forrest plot, random effects meta-analysis, proportion of people transitioning to a diagnosis of schizophrenia, comparing (i) substance-induced psychosis, (ii) brief and atypical psychosis or psychosis not otherwise specified (NOS), and (iii) schizophreniform psychosis.

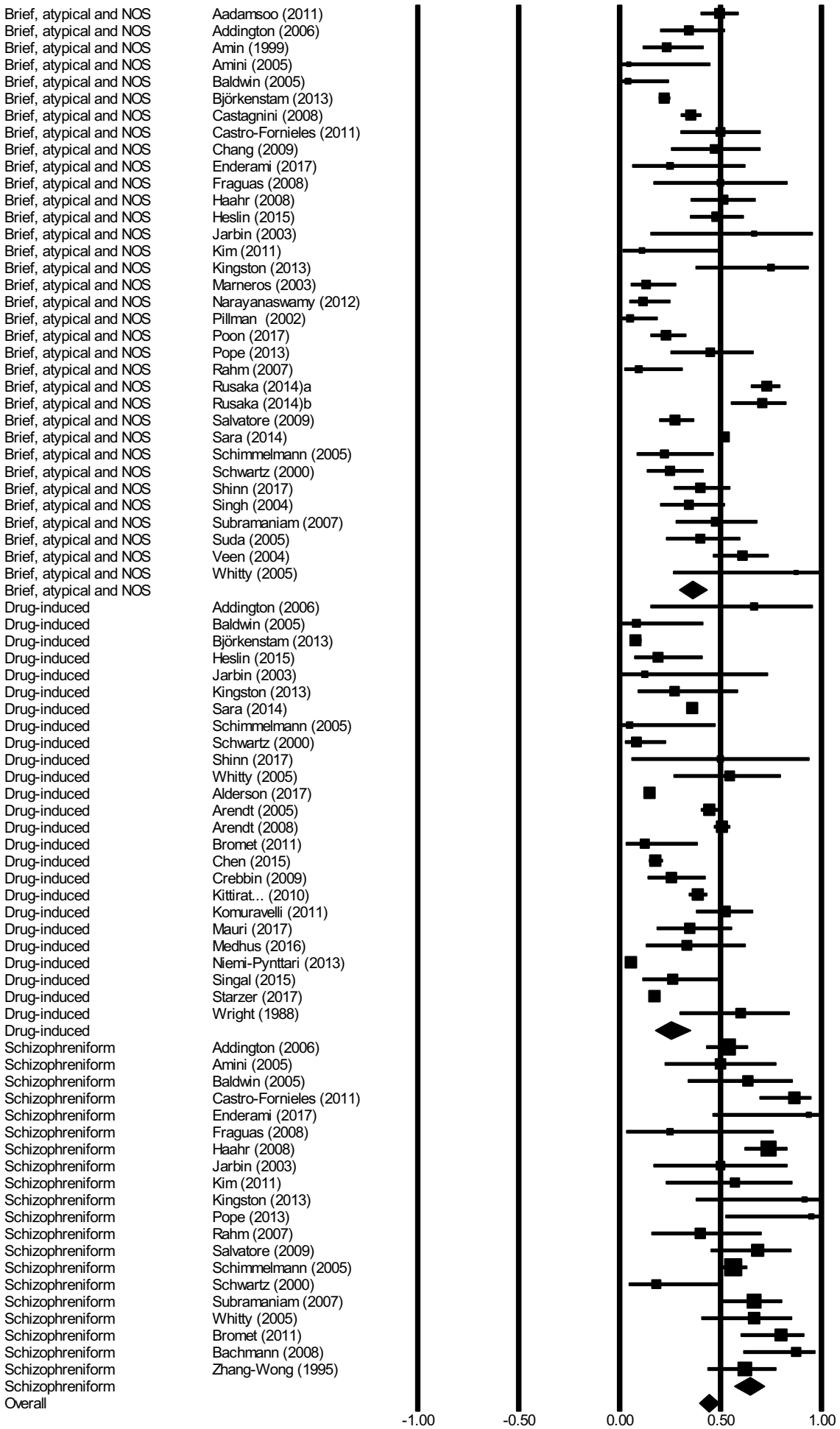
Group by
Subgroup within study
Study name
Brief, atypical and NOS
Aadamsoo (2011)
Addington (2006)
Amin (1999)
Amini (2005)
Baldwin (2005)
Björkenstam (2013)
Castagnini (2008)
Castro-Fornieles (2011)
Chang (2009)
Enderami (2017)
Fraguas (2008)
Haahr (2008)
Heslin (2015)
Jarbin (2003)
Kim (2011)
Kingston (2013)
Marneros (2003)
Narayanaswamy (2012)
Pillman (2002)
Poon (2017)
Pope (2013)
Rahm (2007)
Rusaka (2014)a
Rusaka (2014)b
Salvatore (2009)
Sara (2014)
Schimmelmann (2005)
Schwartz (2000)
Shinn (2017)
Singh (2004)
Subramaniam (2007)
Suda (2005)
Veen (2004)
Whitty (2005)
Drug-induced
Addington (2006)
Baldwin (2005)
Björkenstam (2013)
Heslin (2015)
Jarbin (2003)
Kingston (2013)
Sara (2014)
Schimmelmann (2005)
Schwartz (2000)
Shinn (2017)
Whitty (2005)
Alderson (2017)
Arendt (2005)
Arendt (2008)
Bromet (2011)
Chen (2015)
Crebbin (2009)
Kittirat... (2010)
Komuravelli (2011)
Mauri (2017)
Medhus (2016)
Niemi-Pynttari (2013)
Singal (2015)
Starzer (2017)
Wright (1988)
Schizophreniform
Addington (2006)
Amini (2005)
Baldwin (2005)
Castro-Fornieles (2011)
Enderami (2017)
Fraguas (2008)
Haahr (2008)
Jarbin (2003)
Kim (2011)
Kingston (2013)
Pope (2013)
Rahm (2007)
Salvatore (2009)
Schimmelmann (2005)
Schwartz (2000)
Subramaniam (2007)
Whitty (2005)
Bromet (2011)
Bachmann (2008)
Zhang-Wong (1995)
Overall
-1.00
-0.50
0.00
0.50
1.00

FIGURE 2S: FUNNEL PLOT, OVERALL COMPARISON

Fig 2s: Funnel plot, proportion of people transitioning to a diagnosis of schizophrenia , comparing (i) substance0induced psychosis, (ii) brief and atypical psychosis and psychosis not otherwise specified (NOS), and (iii) schizophreniform psychosis.

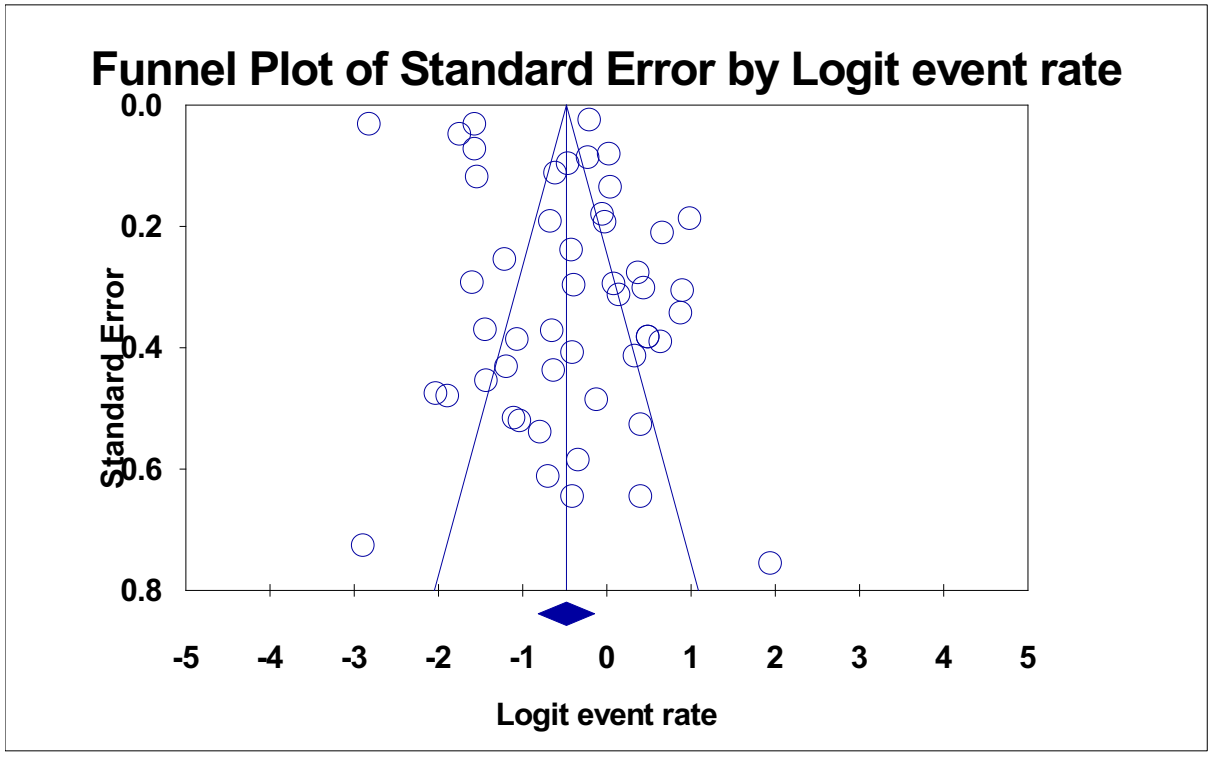

FIGURE 3S: FUNNEL PLOT, SUBSTANCE-INDUCED ONLY

Fig 3s: Funnel plot, proportion of people transitioning to a diagnosis of schizophrenia: substance-induced psychosis only.

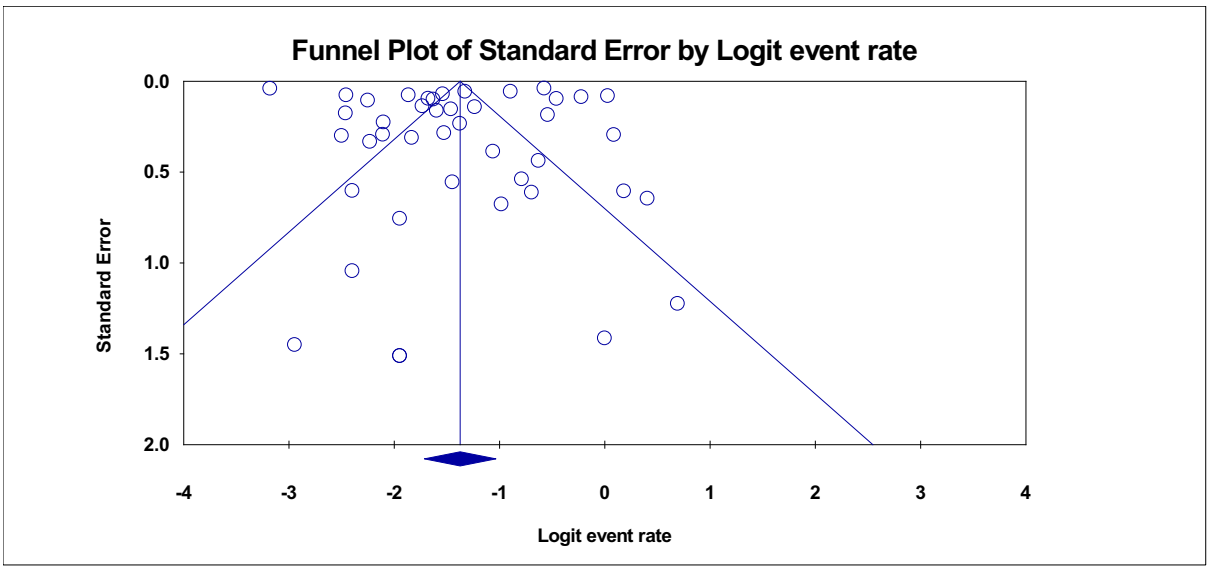

FIGURE 4S: FUNNEL PLOT, BRIEF AND ATYPICAL PSYCHOSIS AND PSYCHOSIS NOT OTHERWISE SPECIFIED (NOS) ONLY

Fig 4s: Funnel plot, proportion of people transitioning to a diagnosis of schizophrenia: brief and atypical psychosis and psychosis not otherwise specified (NOS) only.

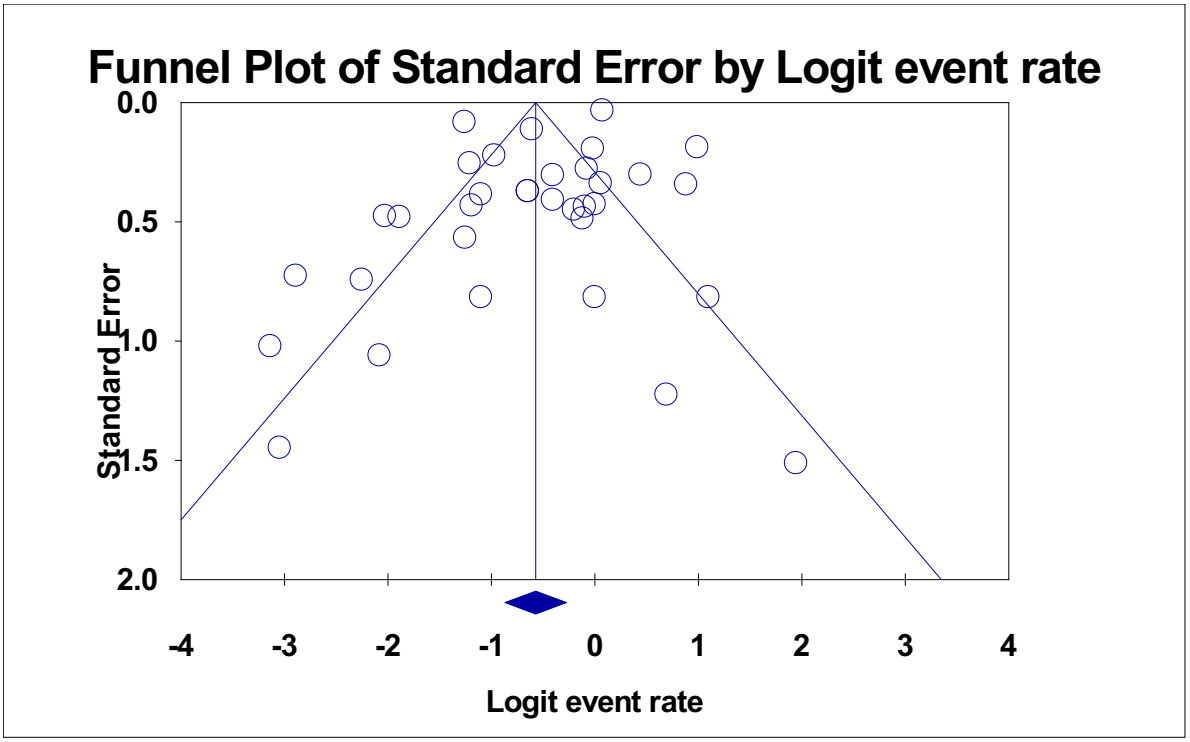

FIGURE 5S: FUNNEL PLOT, SCHIZOPHRENIFORM PSYCHOSIS ONLY

Fig 5s: Funnel plot, proportion of people transitioning to a diagnosis of schizophrenia: schizophreniform psychosis only.

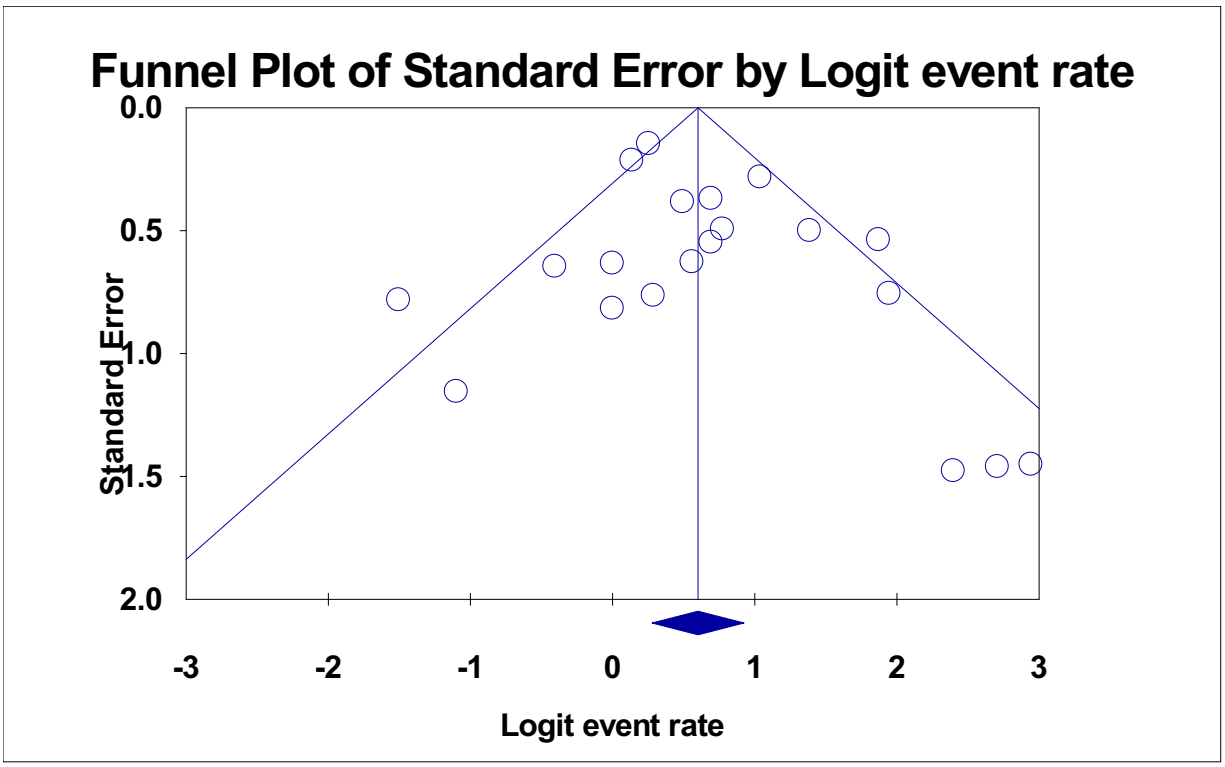

FIGURE 6S: FORREST PLOT, SUBSTANCE-INDUCED PSYCHOSIS, BETWEEN SUBSTANCE COMPARISONS

Fig 6s: Forrest plot, random effects meta-analysis, proportion of people with an initial diagnosis of substance-induced psychosis transitioning to a diagnosis of schizophrenia, comparing different substance types.

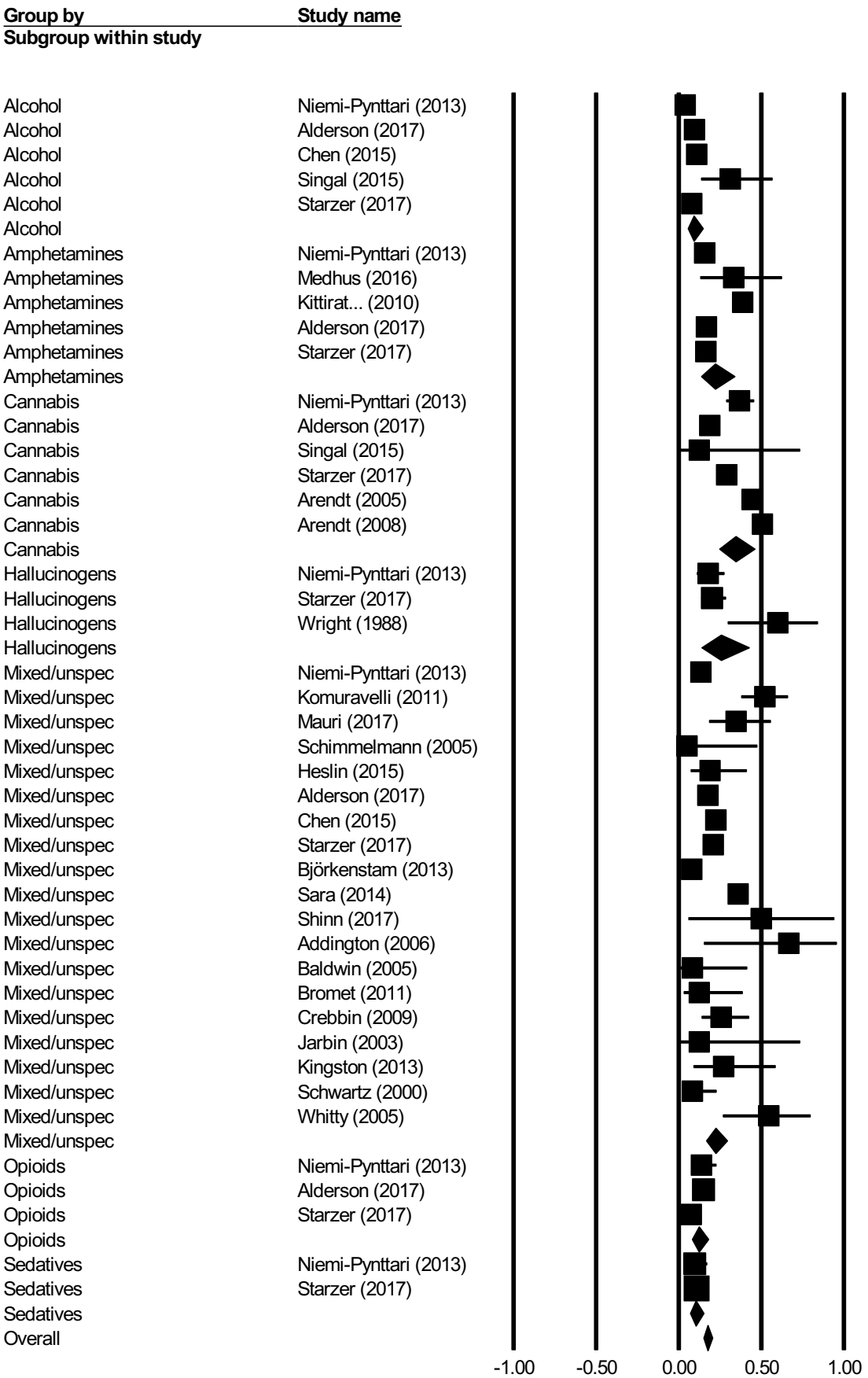

FIGURE 7S: FUNNEL PLOT, SUBSTANCE-INDUCED PSYCHOSIS, BETWEEN SUBSTANCE COMPARISONS

Fig 7s: Funnel plot, proportion of people with an initial diagnosis of substance-induced psychosis transitioning to a diagnosis of schizophrenia.

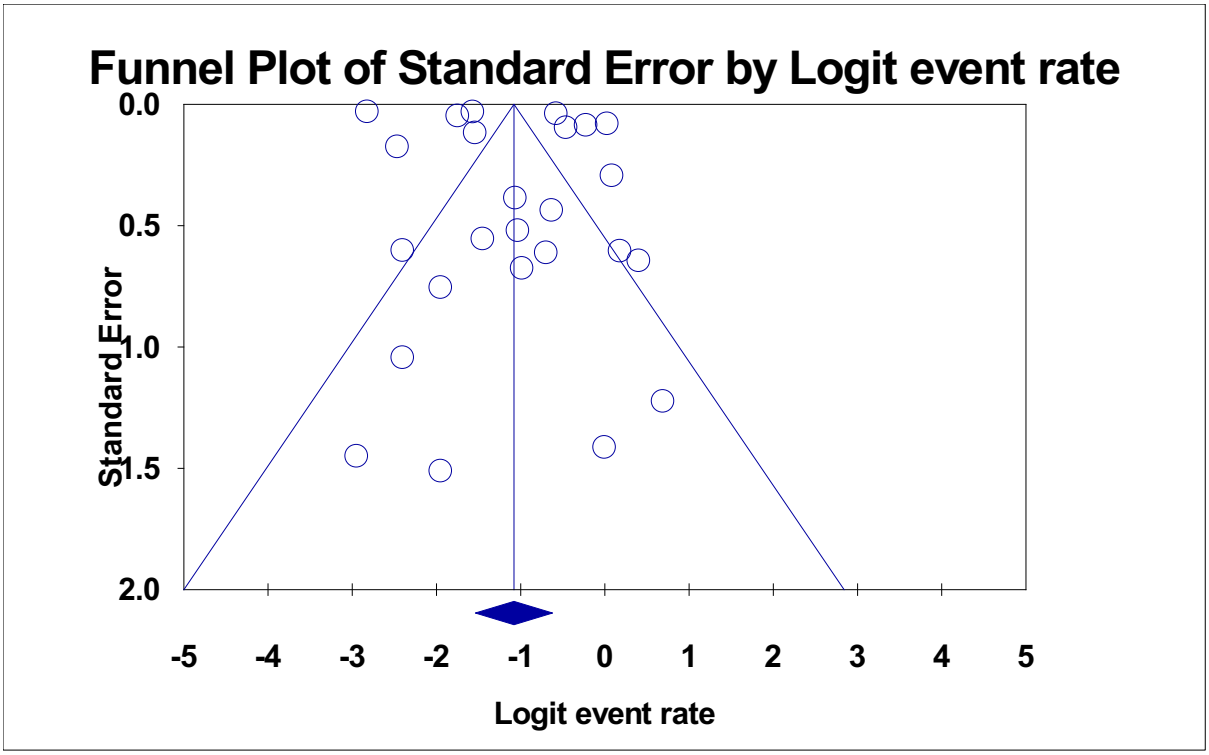

FIGURE 8S: SCATTER PLOT, META-REGRESSION, YEAR OF DATA COLLECTION

Fig 8s: Scatter plot, meta-regression of proportion of people with substance-induced psychosis transitioning to a diagnosis of schizophrenia, by year of data collection.

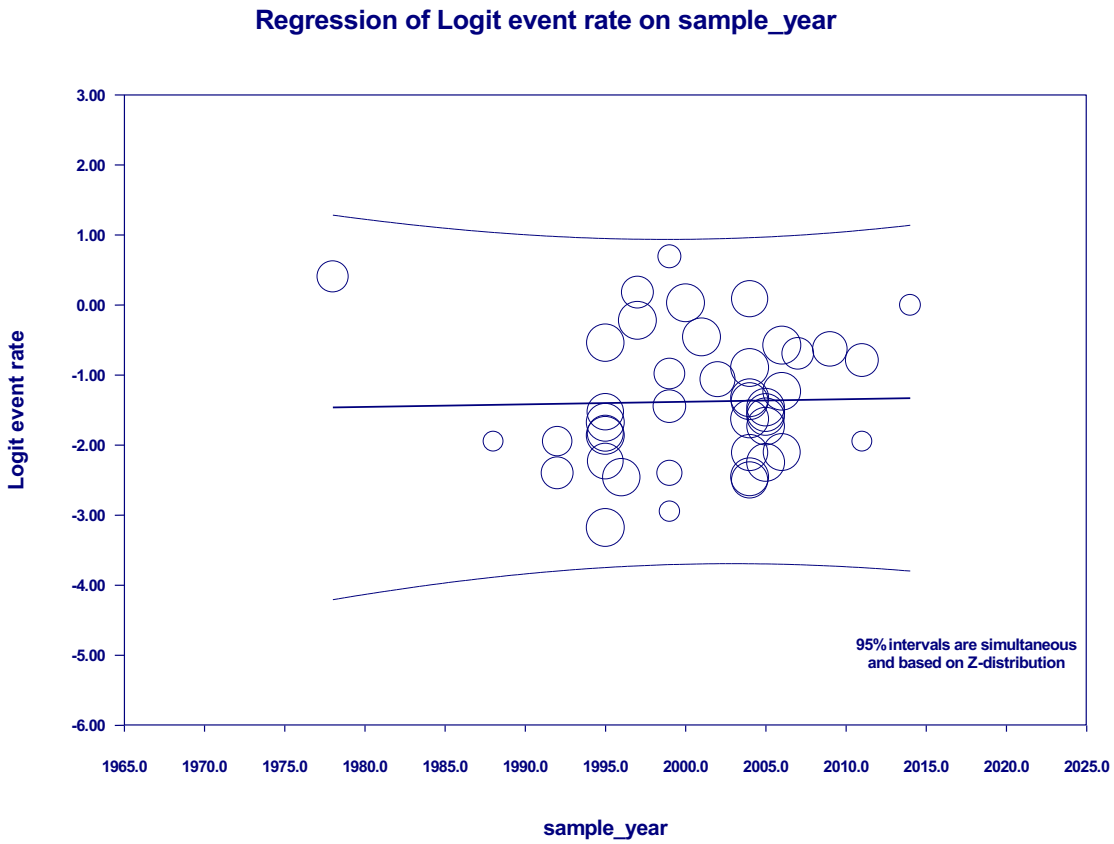

FIGURE 9S: SCATTER PLOT, META-REGRESSION, AVERAGE AGE

Fig 9s: Scatter plot, meta-regression of proportion of people with substance-induced psychosis transitioning to a diagnosis of schizophrenia, by average age of study participants.

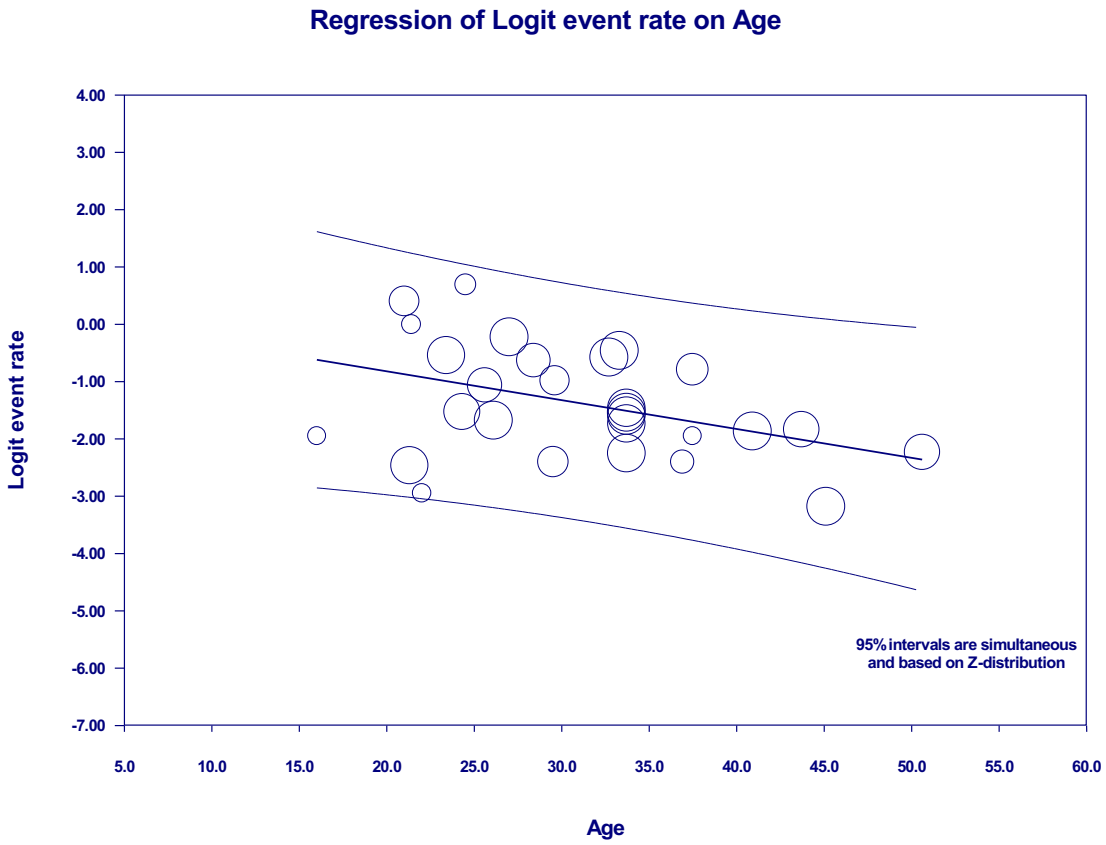

FIGURE 10S: SCATTER PLOT, META-REGRESSION, PROPORTION MALE

Fig 10s: Scatter plot, meta-regression of proportion of people with substance-induced psychosis transitioning to a diagnosis of schizophrenia, by percent of study population who were male

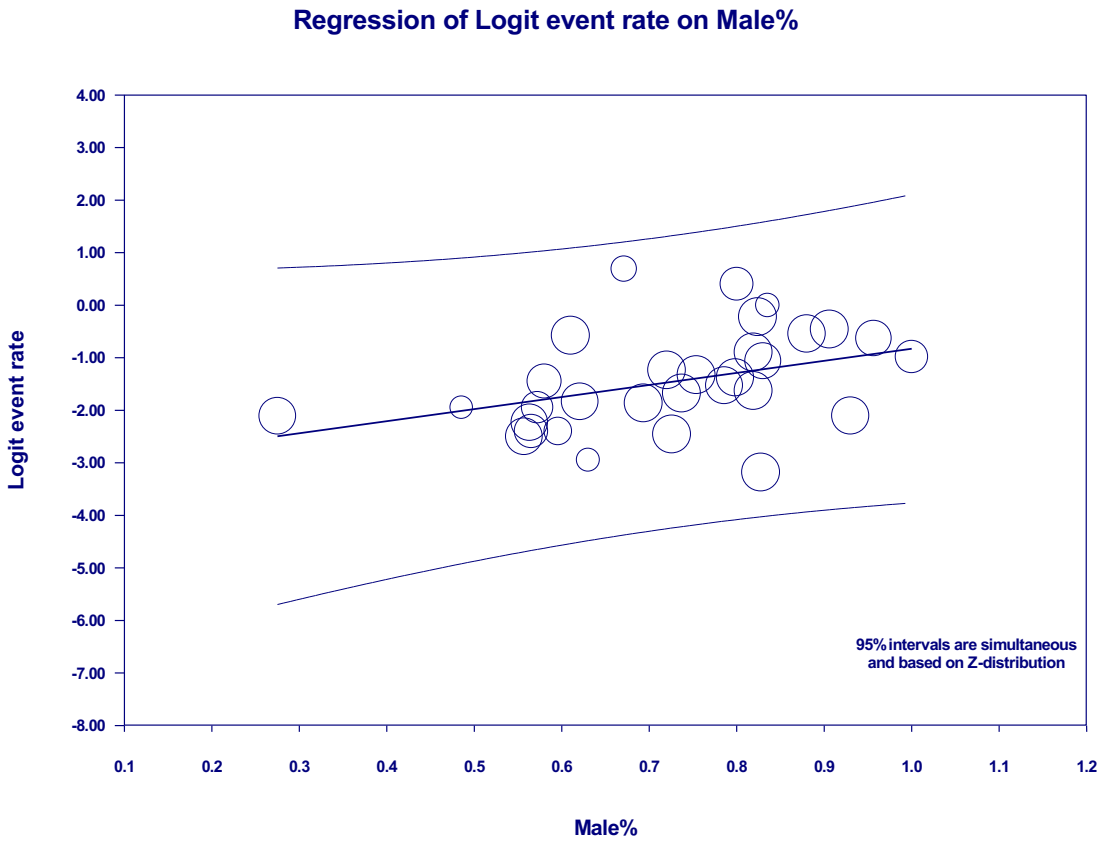

FIGURE 11S: SCATTER PLOT, META-REGRESSION, FOLLOW-UP PERIOD

Fig 11s: Scatter plot, meta-regression of proportion with substance-induced psychosis transitioning to a diagnosis of schizophrenia, by length of follow up period (years).

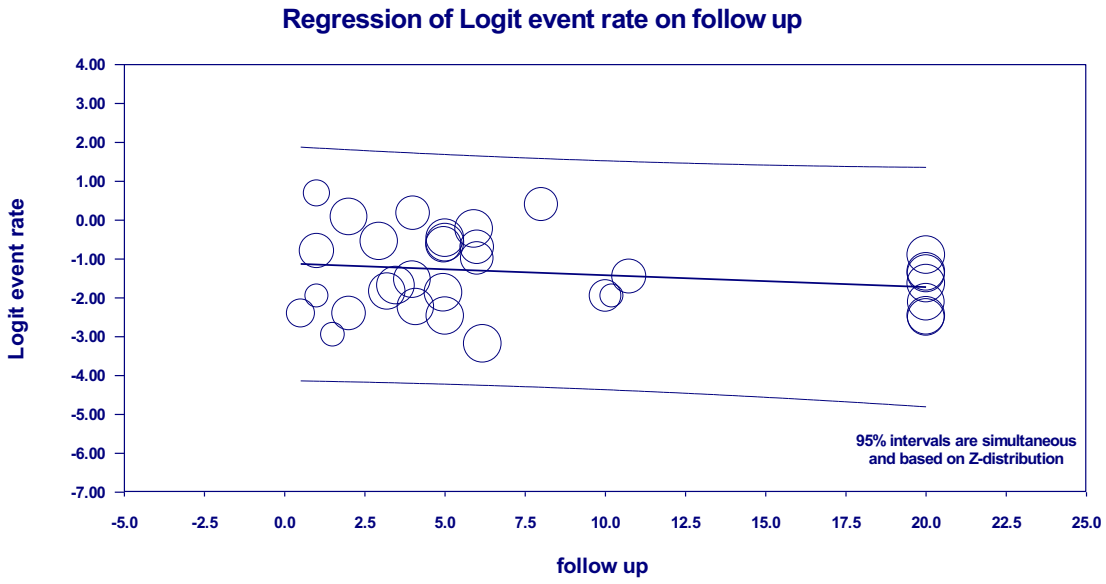

FIGURE 12S: SCATTER PLOT, META-REGRESSION, PROPORTION WITH FOLLOW-UP DIAGNOSIS

Fig 12s: Scatter plot, meta-regression of proportion of people with substance-induced psychosis transitioning to a diagnosis of schizophrenia, by proportion of baseline sample who had a follow-up diagnosis for analysis.

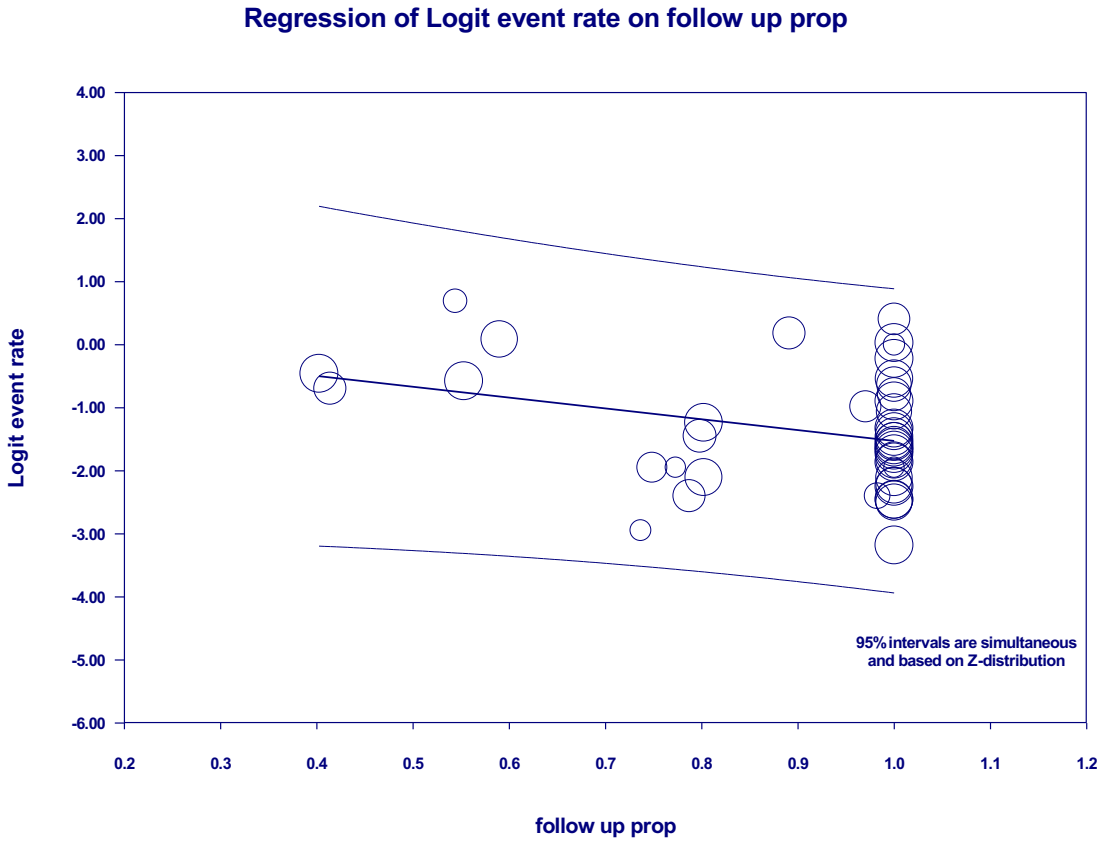

FIGURE 13S: SCATTER PLOT, META-REGRESSION, QUALITY SCORE

Fig 13s: Scatter plot, meta-regression of proportion of people with substance-induced psychosis transitioning to a diagnosis of schizophrenia, by quality score (Newcastle-Ottawa Scale for cohort studies).

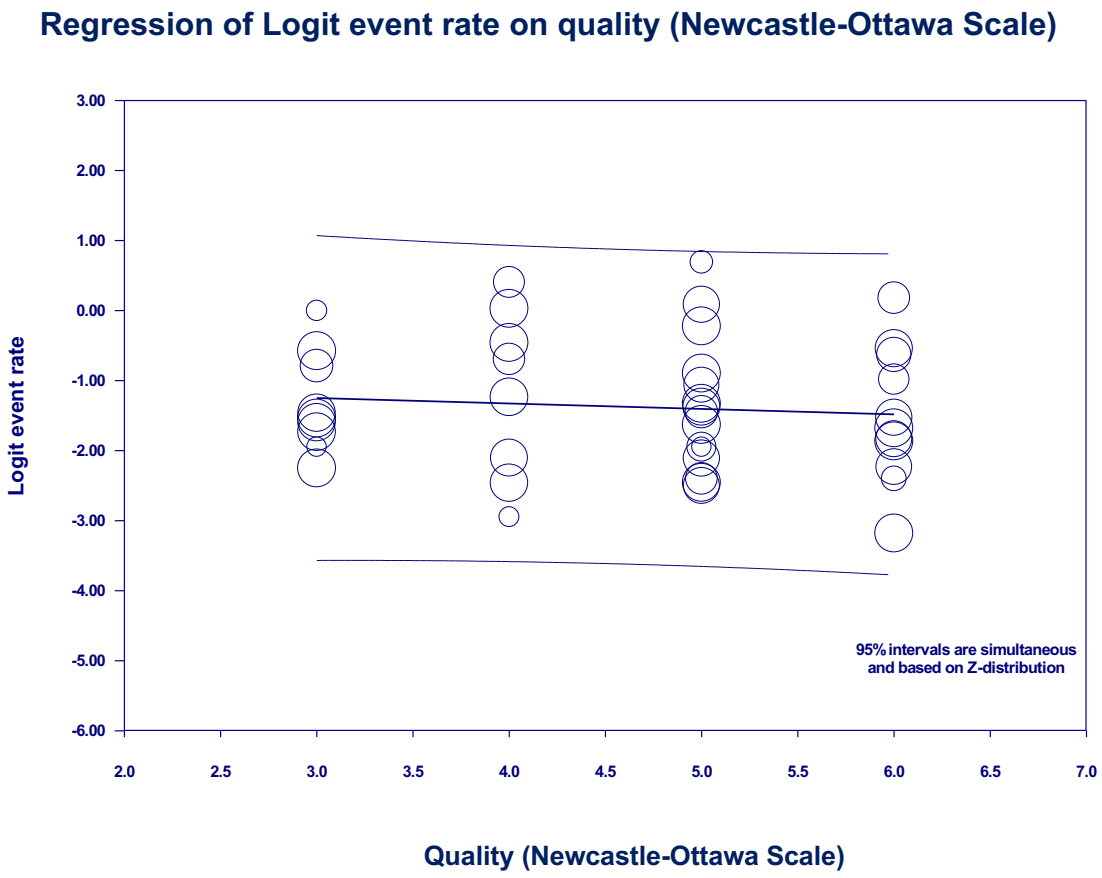

Table 2s: Additional variables, studies reporting psychosis groups

Study	Psychosis group	Sample year	Country	Population coverage	Urban or rural	Quality score	Toxicology	Sample size	Transition to Sza	Transition rate	Logit event rate	SE	Variance
Aadamsoo (2011)	Brief, atypical and NOS	2005	Europe	Subnational	Mixed/ unspecified	3	No/ unspec	107	53	0.4953	-0.0187	0.1934	0.0374
Addington (2006)	Brief, atypical and NOS	1999	North America	Subnational	Urban	5	No/ unspec	32	11	0.3438	-0.6466	0.3722	0.1385
Addington (2006)	Drug-induced	1999	North America	Subnational	Urban	5	No/ unspec	3	2	0.6667	0.6931	1.2247	1.5000
Addington (2006)	Schizophreniform	1999	North America	Subnational	Urban	5	No/ unspec	88	47	0.5341	0.1366	0.2137	0.0457
Alderson (2017)	Drug-induced	2005	UK and Ireland	National	Mixed/ unspecified	3	No/ unspec	3375	502	0.1487	-1.7445	0.0484	0.0023
Amin (1999)	Brief, atypical and NOS	1993	UK and Ireland	Subnational	Mixed/ unspecified	6	No/ unspec	30	7	0.2333	-1.1896	0.4317	0.1863
Amini (2005)	Brief, atypical and NOS	1993	S&E Asia	Subnational	Mixed/ unspecified	3	No/ unspec	10	0	0.0455	-3.0445	1.4475	2.0952
Amini (2005)	Schizophreniform	1993	S&E Asia	Subnational	Mixed/ unspecified	3	No/ unspec	10	5	0.5000	0.0000	0.6325	0.4000
Arendt (2005)	Drug-induced	1997	Scandinavia	National	Mixed/ unspecified	5	No/ unspec	535	238	0.4449	-0.2215	0.0870	0.0076
Arendt (2008)	Drug-induced	2000	Scandinavia	National	Mixed/ unspecified	4	No/ unspec	609	309	0.5074	0.0296	0.0811	0.0066
Bachmann (2008)	Schizophreniform	2000	Europe	Subnational	Urban	4	No/ unspec	16	14	0.8750	1.9459	0.7559	0.5714
Baldwin (2005)	Brief, atypical and NOS	1999	UK and Ireland	Subnational	Rural	6	No/ unspec	24	1	0.0417	-3.1355	1.0215	1.0435
Baldwin (2005)	Drug-induced	1999	UK and Ireland	Subnational	Rural	6	No/ unspec	12	1	0.0833	-2.3979	1.0445	1.0909
Baldwin (2005)	Schizophreniform	1999	UK and Ireland	Subnational	Rural	6	No/ unspec	11	7	0.6364	0.5596	0.6268	0.3929
Björkenstam (2013)	Brief, atypical and NOS	1996	Scandinavia	National	Mixed/ unspecified	4	No/ unspec	868	192	0.2212	-1.2587	0.0818	0.0067
Björkenstam (2013)	Drug-induced	1996	Scandinavia	National	Mixed/ unspecified	4	No/ unspec	445	35	0.0787	-2.4608	0.1761	0.0310
Bromet (2011)	Drug-induced	1992	North America	Subnational	Mixed/ unspecified	5	No/ unspec	16	2	0.1250	-1.9459	0.7559	0.5714
Bromet (2011)	Schizophreniform	1992	North America	Subnational	Mixed/ unspecified	5	No/ unspec	25	20	0.8000	1.3863	0.5000	0.2500
Castagnini (2008)	Brief, atypical and NOS	1996	Scandinavia	National	Mixed/ unspecified	4	No/ unspec	346	122	0.3526	-0.6076	0.1125	0.0127
Castro-Fornieles (2011)	Brief, atypical and NOS	1996	Europe	Subnational	Mixed/ unspecified	5	No/ unspec	22	11	0.5000	0.0000	0.4264	0.1818
Castro-Fornieles (2011)	Schizophreniform	1996	Europe	Subnational	Mixed/ unspecified	5	No/ unspec	30	26	0.8667	1.8718	0.5371	0.2885
Chang (2009)	Brief, atypical and NOS	2002	S&E Asia	Subnational	Urban	0	No/ unspec	17	8	0.4706	-0.1178	0.4859	0.2361
Chen (2015)	Drug-induced	2006	S&E Asia	National	Mixed/ unspecified	4	No/ unspec	486	86	0.1770	-1.5371	0.1189	0.0141
Crebbin (2009)	Drug-induced	2002	UK and Ireland	Subnational	Mixed/ unspecified	5	No/ unspec	35	9	0.2571	-1.0609	0.3867	0.1496
Enderami (2017)	Brief, atypical and NOS	2013	S&E Asia	Subnational	Mixed/ unspecified	5	No/ unspec	8	2	0.2500	-1.0986	0.8165	0.6667
Enderami (2017)	Schizophreniform	2013	S&E Asia	Subnational	Mixed/ unspecified	5	No/ unspec	7	7	0.9375	2.7081	1.4606	2.1333
Fraguas (2008)	Brief, atypical and NOS	2003	Europe	Subnational	Mixed/ unspecified	6	No/ unspec	6	3	0.5000	0.0000	0.8165	0.6667

Table 2s: Additional variables, studies reporting psychosis groups

Study	Psychosis group	Sample year	Country	Population coverage	Urban or rural	Quality score	Toxicology	Sample size	Transition to Sza	Transition rate	Logit event rate	SE	Variance
Fraguas (2008)	Schizophreniform	2003	Europe	Subnational	Mixed/ unspecified	6	No/ unspec	4	1	0.2500	-1.0986	1.1547	1.3333
Haahr (2008)	Brief, atypical and NOS	1999	Scandinavia	Subnational	Mixed/ unspecified	7	No/ unspec	35	18	0.5143	0.0572	0.3382	0.1144
Haahr (2008)	Schizophreniform	1999	Scandinavia	Subnational	Mixed/ unspecified	7	No/ unspec	65	48	0.7385	1.0380	0.2822	0.0797
Heslin (2015)	Brief, atypical and NOS	1999	UK and Ireland	Subnational	Urban	5	No/ unspec	52	25	0.4808	-0.0770	0.2776	0.0770
Heslin (2015)	Drug-induced	1999	UK and Ireland	Subnational	Urban	5	No/ unspec	21	4	0.1905	-1.4469	0.5557	0.3088
Jarbin (2003)	Brief, atypical and NOS	1988	Scandinavia	Subnational	Mixed/ unspecified	5	No/ unspec	3	2	0.6667	0.6931	1.2247	1.5000
Jarbin (2003)	Drug-induced	1988	Scandinavia	Subnational	Mixed/ unspecified	5	No/ unspec	3	0	0.1250	-1.9459	1.5119	2.2857
Jarbin (2003)	Schizophreniform	1988	Scandinavia	Subnational	Mixed/ unspecified	5	No/ unspec	6	3	0.5000	0.0000	0.8165	0.6667
Kim (2011)	Brief, atypical and NOS	2002	S&E Asia	Subnational	Mixed/ unspecified	5	No/ unspec	9	1	0.1111	-2.0794	1.0607	1.1250
Kim (2011)	Schizophreniform	2002	S&E Asia	Subnational	Mixed/ unspecified	5	No/ unspec	7	4	0.5714	0.2877	0.7638	0.5833
Kingston (2013)	Brief, atypical and NOS	1999	UK and Ireland	Subnational	Rural	6	No/ unspec	8	6	0.7500	1.0986	0.8165	0.6667
Kingston (2013)	Drug-induced	1999	UK and Ireland	Subnational	Rural	6	No/ unspec	11	3	0.2727	-0.9808	0.6770	0.4583
Kingston (2013)	Schizophreniform	1999	UK and Ireland	Subnational	Rural	6	No/ unspec	5	5	0.9167	2.3979	1.4771	2.1818
Kittirattanapaiboon (2010)	Drug-induced	2001	S&E Asia	Subnational	Urban	4	No/ unspec	449	174	0.3875	-0.4577	0.0969	0.0094
Komuravelli (2011)	Drug-induced	2004	UK and Ireland	Subnational	Urban	5	No/ unspec	46	24	0.5217	0.0870	0.2952	0.0871
Marneros (2003)	Brief, atypical and NOS	1995	Europe	Subnational	Mixed/ unspecified	6	No/ unspec	38	5	0.1316	-1.8871	0.4799	0.2303
Mauri (2017)	Drug-induced	2009	Europe	Subnational	Urban	6	Yes	23	8	0.3478	-0.6286	0.4378	0.1917
Medhus (2016)	Drug-induced	2007	Europe	National	Mixed/ unspecified	4	No/ unspec	12	4	0.3333	-0.6931	0.6124	0.3750
Narayanaswamy (2012)	Brief, atypical and NOS	2004	S&E Asia	Subnational	Mixed/ unspecified	2	No/ unspec	43	5	0.1163	-2.0281	0.4757	0.2263
Niemi-Pynttari (2013)	Drug-induced	1995	Scandinavia	National	Mixed/ unspecified	6	No/ unspec	18478	1041	0.0563	-2.8184	0.0319	0.0010
Pillman (2002)	Brief, atypical and NOS	1995	Europe	Subnational	Mixed/ unspecified	5	No/ unspec	38	2	0.0526	-2.8904	0.7265	0.5278
Poon (2017)	Brief, atypical and NOS	1995	S&E Asia	Subnational	Urban	5	No/ unspec	87	20	0.2299	-1.2090	0.2548	0.0649
Pope (2013)	Brief, atypical and NOS	2007	S&E Asia	Subnational	Mixed/ unspecified	4	No/ unspec	20	9	0.4500	-0.2007	0.4495	0.2020
Pope (2013)	Schizophreniform	2007	S&E Asia	Subnational	Mixed/ unspecified	4	No/ unspec	9	9	0.9500	2.9444	1.4510	2.1053
Rahm (2007)	Brief, atypical and NOS	1997	Scandinavia	Subnational	Mixed/ unspecified	5	No/ unspec	21	2	0.0952	-2.2513	0.7434	0.5526
Rahm (2007)	Schizophreniform	1997	Scandinavia	Subnational	Mixed/ unspecified	5	No/ unspec	10	4	0.4000	-0.4055	0.6455	0.4167
Rusaka (2014)a	Brief, atypical and NOS	2005	Europe	Subnational	Mixed/ unspecified	5	No/ unspec	144	105	0.7292	0.9904	0.1875	0.0352

Table 2s: Additional variables, studies reporting psychosis groups

Study	Psychosis group	Sample year	Country	Population coverage	Urban or rural	Quality score	Toxicology	Sample size	Transition to Sza	Transition rate	Logit event rate	SE	Variance
Rusaka (2014)b	Brief, atypical and NOS	2011	Europe	Subnational	Mixed/ unspecified	5	No/ unspec	41	29	0.7073	0.8824	0.3432	0.1178
Salvatore (2009)	Brief, atypical and NOS	1996	S&E Asia	Subnational	Mixed/ unspecified	6	No/ unspec	102	28	0.2745	-0.9719	0.2219	0.0492
Salvatore (2009)	Schizophreniform	1996	S&E Asia	Subnational	Mixed/ unspecified	6	No/ unspec	19	13	0.6842	0.7732	0.4935	0.2436
Sara (2014)	Brief, atypical and NOS	2006	Australia	Subnational	Mixed/ unspecified	3	No/ unspec	3632	1883	0.5184	0.0738	0.0332	0.0011
Sara (2014)	Drug-induced	2006	Australia	Subnational	Mixed/ unspecified	3	No/ unspec	2790	1005	0.3602	-0.5744	0.0394	0.0016
Schimmelmann (2005)	Brief, atypical and NOS	1999	Australia	Subnational	Urban	4	No/ unspec	18	4	0.2222	-1.2528	0.5669	0.3214
Schimmelmann (2005)	Drug-induced	1999	Australia	Subnational	Urban	4	No/ unspec	9	0	0.0500	-2.9444	1.4510	2.1053
Schimmelmann (2005)	Schizophreniform	1999	Australia	Subnational	Urban	4	No/ unspec	190	107	0.5632	0.2540	0.1463	0.0214
Schwartz (2000)	Brief, atypical and NOS	1992	North America	Subnational	Mixed/ unspecified	5	No/ unspec	36	9	0.2500	-1.0986	0.3849	0.1481
Schwartz (2000)	Drug-induced	1992	North America	Subnational	Mixed/ unspecified	5	No/ unspec	36	3	0.0833	-2.3979	0.6030	0.3636
Schwartz (2000)	Schizophreniform	1992	North America	Subnational	Mixed/ unspecified	5	No/ unspec	11	2	0.1818	-1.5041	0.7817	0.6111
Shinn (2017)	Brief, atypical and NOS	2014	North America	Subnational	Mixed/ unspecified	3	No/ unspec	45	18	0.4000	-0.4055	0.3043	0.0926
Shinn (2017)	Drug-induced	2014	North America	Subnational	Mixed/ unspecified	3	No/ unspec	2	1	0.5000	0.0000	1.4142	2.0000
Singal (2015)	Drug-induced	2011	S&E Asia	Subnational	Mixed/ unspecified	3	Yes	19	5	0.2632	-1.0296	0.5210	0.2714
Singh (2004)	Brief, atypical and NOS	1993	UK and Ireland	Subnational	Mixed/ unspecified	4	No/ unspec	32	11	0.3438	-0.6466	0.3722	0.1385
Starzer (2017)	Drug-induced	2004	Scandinavia	National	Mixed/ unspecified	5	No/ unspec	6788	1174	0.1730	-1.5648	0.0321	0.0010
Subramaniam (2007)	Brief, atypical and NOS	2004	S&E Asia	National	Mixed/ unspecified	5	No/ unspec	21	10	0.4762	-0.0953	0.4369	0.1909
Subramaniam (2007)	Schizophreniform	2004	S&E Asia	National	Mixed/ unspecified	5	No/ unspec	33	22	0.6667	0.6931	0.3693	0.1364
Suda (2005)	Brief, atypical and NOS	1992	S&E Asia	Subnational	Urban	4	No/ unspec	25	10	0.4000	-0.4055	0.4082	0.1667
Veen (2004)	Brief, atypical and NOS	1998	Europe	Subnational	Urban	7	No/ unspec	46	28	0.6087	0.4418	0.3021	0.0913
Whitty (2005)	Brief, atypical and NOS	1997	UK and Ireland	Subnational	Urban	6	No/ unspec	3	3	0.8750	1.9459	1.5119	2.2857
Whitty (2005)	Drug-induced	1997	UK and Ireland	Subnational	Urban	6	No/ unspec	11	6	0.5455	0.1823	0.6055	0.3667
Whitty (2005)	Schizophreniform	1997	UK and Ireland	Subnational	Urban	6	No/ unspec	15	10	0.6667	0.6931	0.5477	0.3000
Wright (1988)	Drug-induced	1978	North America	Subnational	Mixed/ unspecified	4	Yes	10	6	0.6000	0.4055	0.6455	0.4167
Zhang-Wong (1995)	Schizophreniform	1978	North America	Subnational	Mixed/ unspecified	6	No/ unspec	29	18	0.6207	0.4925	0.3827	0.1465

Table 3s: Additional variables, studies reporting substance-induced psychosis

Study	Psychosis group	Substance	PANSS score	Substance use %	GAF score	Sample size	Transition to Sza	Event rate	Logit event rate	Std Err	Variance
Addington (2006)	Mixed/unspec	Mixed/unspec	-	43%	-	3	2	0.6667	0.6931	1.2247	1.5000
Alderson (2017)	Alcohol	Alcohol	-	-	-	1038	99	0.0954	-2.2497	0.1057	0.0112
Alderson (2017)	Amphetamines	Amphetamines	-	-	-	273	46	0.1685	-1.5963	0.1617	0.0261
Alderson (2017)	Cannabis	Cannabis	-	-	-	276	52	0.1884	-1.4604	0.1539	0.0237
Alderson (2017)	Mixed/unspec	Mixed/unspec	-	-	-	1369	242	0.1768	-1.5384	0.0708	0.0050
Alderson (2017)	Opioids	Opioids	-	-	-	419	63	0.1504	-1.7318	0.1367	0.0187
Arendt (2005)	Cannabis	Cannabis	-	-	-	535	238	0.4449	-0.2215	0.0870	0.0076
Arendt (2008)	Cannabis	Cannabis	-	-	-	609	309	0.5074	0.0296	0.0811	0.0066
Baldwin (2005)	Mixed/unspec	Mixed/unspec	-	19%	-	12	1	0.0833	-2.3979	1.0445	1.0909
Björkenstam (2013)	Mixed/unspec	Mixed/unspec	-	-	-	445	35	0.0787	-2.4608	0.1761	0.0310
Bromet (2011)	Mixed/unspec	Mixed/unspec	-	-	58	16	2	0.1250	-1.9459	0.7559	0.5714
Chen (2015)	Alcohol	Alcohol	-	-	-	202	22	0.1089	-2.1019	0.2259	0.0510
Chen (2015)	Mixed/unspec	Mixed/unspec	-	-	-	284	64	0.2254	-1.2347	0.1420	0.0202
Crebbin (2009)	Mixed/unspec	Mixed/unspec	-	-	-	35	9	0.2571	-1.0609	0.3867	0.1496
Heslin (2015)	Mixed/unspec	Mixed/unspec	-	-	-	21	4	0.1905	-1.4469	0.5557	0.3088
Jarbin (2003)	Mixed/unspec	Mixed/unspec	22	-	70	3	0	0.1250	-1.9459	1.5119	2.2857
Kingston (2013)	Mixed/unspec	Mixed/unspec	-	-	-	11	3	0.2727	-0.9808	0.6770	0.4583
Kittirattanapaiboon (2010)	Amphetamines	Amphetamines	-	-	-	449	174	0.3875	-0.4577	0.0969	0.0094
Komuravelli (2011)	Mixed/unspec	Mixed/unspec	-	-	-	46	24	0.5217	0.0870	0.2952	0.0871
Mauri (2017)	Mixed/unspec	Mixed/unspec	-	-	-	23	8	0.3478	-0.6286	0.4378	0.1917
Medhus (2016)	Amphetamines	Amphetamines	-	-	28	12	4	0.3333	-0.6931	0.6124	0.3750
Niemi-Pynttari (2013)	Alcohol	Alcohol	-	-	-	15787	631	0.0400	-3.1788	0.0406	0.0017
Niemi-Pynttari (2013)	Amphetamines	Amphetamines	-	-	-	825	130	0.1576	-1.6764	0.0956	0.0091
Niemi-Pynttari (2013)	Cannabis	Cannabis	-	-	-	125	46	0.3680	-0.5408	0.1855	0.0344
Niemi-Pynttari (2013)	Hallucinogens	Hallucinogens	-	-	-	84	15	0.1786	-1.5261	0.2849	0.0812
Niemi-Pynttari (2013)	Mixed/unspec	Mixed/unspec	-	-	-	1467	197	0.1343	-1.8636	0.0766	0.0059
Niemi-Pynttari (2013)	Opioids	Opioids	-	-	-	87	12	0.1379	-1.8326	0.3109	0.0967
Niemi-Pynttari (2013)	Sedatives	Sedatives	-	-	-	103	10	0.0971	-2.2300	0.3328	0.1108
Sara (2014)	Mixed/unspec	Mixed/unspec	-	-	-	2790	1005	0.3602	-0.5744	0.0394	0.0016
Schimmelmann (2005)	Mixed/unspec	Mixed/unspec	-	51%	70	9	0	0.0500	-2.9444	1.4510	2.1053
Schwartz (2000)	Mixed/unspec	Mixed/unspec	-	-	-	36	3	0.0833	-2.3979	0.6030	0.3636
Shinn (2017)	Mixed/unspec	Mixed/unspec	-	63%	-	2	1	0.5000	0.0000	1.4142	2.0000
Singal (2015)	Alcohol	Alcohol	83	-	-	16	5	0.3125	-0.7885	0.5394	0.2909
Singal (2015)	Cannabis	Cannabis	83	-	-	3	0	0.1250	-1.9459	1.5119	2.2857
Starzer (2017)	Alcohol	Alcohol	-	-	-	2315	183	0.0790	-2.4553	0.0770	0.0059
Starzer (2017)	Amphetamines	Amphetamines	-	-	-	725	119	0.1641	-1.6278	0.1003	0.0101
Starzer (2017)	Cannabis	Cannabis	-	-	-	1492	433	0.2902	-0.8943	0.0570	0.0033
Starzer (2017)	Hallucinogens	Hallucinogens	-	-	-	114	23	0.2018	-1.3754	0.2334	0.0545
Starzer (2017)	Mixed/unspec	Mixed/unspec	-	-	-	1864	391	0.2098	-1.3263	0.0569	0.0032
Starzer (2017)	Opioids	Opioids	-	-	-	158	12	0.0759	-2.4987	0.3003	0.0902
Starzer (2017)	Sedatives	Sedatives	-	-	-	120	13	0.1083	-2.1079	0.2937	0.0863
Whitty (2005)	Mixed/unspec	Mixed/unspec	-	-	-	11	6	0.5455	0.1823	0.6055	0.3667
Wright (1988)	Hallucinogens	Hallucinogens	-	-	-	10	6	0.6000	0.4055	0.6455	0.4167

NEWCASTLE-OTTAWA SCALE FOR COHORT STUDIES, AS APPLIED

Selection
1. Representativeness of the exposed cohort a) truly representative of the average person with psychosis (e.g. population-wide registers) ★ b) somewhat representative of the person with psychosis e.g. large clinical cohorts drawn from catchment-wide services likely to access a high proportion or representative group of people with brief psychoses in that community, without likely exclusion of people with likely higher or lower risk of developing schizophrenia ★ c) selected group of patients, e.g. follow up studies of clinical samples with significant exclusions, small specialized clinical units, samples that are solely hospital or community based d) no description of the derivation of the cohort
2. Selection of the non exposed cohort a) drawn from the same community as the exposed cohort ★ b) drawn from a different source c) no description of the derivation of the non exposed cohort
3. Ascertainment of exposure a) secure record (e.g. health care record) ★ b) structured interview ★ c) written self report or routine clinical diagnosis only d) other / no description
4. Demonstration that outcome of interest (i.e. diagnosis of schizophrenia/schizoaffective disorder) was not present at start of study a) yes ★ b) no
Comparability (tick one or both boxes, as appropriate)
1. Comparability of cohorts on the basis of the design or analysis a) study controls for age, sex, marital status ★ b) study controls for any additional factors (e.g. socio-economic status, education) ★
Outcome (tick one box in each section)
1. Assessment of outcome a) independent blind assessment ★ b) record linkage ★ c) self report or routine clinical diagnosis d) other / no description
2. Was follow up long enough for outcomes to occur a) yes, if median duration of follow-up >= 6 month ★ b) no, if median duration of follow-up < 6 months
3. Adequacy of follow up of cohorts a) complete follow up: all subjects accounted for ★ b) subjects lost to follow up unlikely to introduce bias: number lost <= 20%, or description of those lost suggesting no different from those followed ★ c) follow up rate < 80% and no description of those lost d) no statement

NEWCASTLE-OTTAWA SCALE – CODING MANUAL FOR COHORT STUDIES

SELECTION

1) Representativeness of the Exposed Cohort (NB exposure = intervention)

Item is assessing the representativeness of exposed individuals in the community, not the representativeness of the study sample from some general population. For example, subjects derived from groups likely to contain exposed people are likely to be representative of exposed individuals, while they are not representative of all people the community.

Allocation of stars as per rating sheet.

2) Selection of the Non-Exposed Cohort

Allocation of stars as per rating sheet.

3) Ascertainment of Exposure

Allocation of stars as per rating sheet.

4) Demonstration That Outcome of Interest Was Not Present at Start of Study

In the case of mortality studies, outcome of interest is still the presence of a disease/ incident, rather than death. That is to say that a statement of no history of disease or incident earns a star.

COMPARABILITY

1) Comparability of Cohorts on the Basis of the Design or Analysis

Either exposed and non-exposed individuals must be matched in the design and/or confounders must be adjusted for in the analysis. Statements of no differences between groups or that differences were not statistically significant are not sufficient for establishing comparability. Note: If the relative risk for the exposure of interest is adjusted for the confounders listed, then the groups will be considered to be comparable on each variable used in the adjustment.

A maximum of 2 stars can be allotted in this category.

OUTCOME

1) Assessment of Outcome

For some outcomes, reference to the medical record is sufficient to satisfy the requirement for confirmation. This may not be adequate for other outcomes where reference to specific tests or measures would be required.

2) Was Follow-Up Long Enough for Outcomes to Occur

An acceptable length of time should be decided before quality assessment begins.

3) Adequacy of Follow Up of Cohorts

This item assesses the follow-up of the exposed and non-exposed cohorts to ensure that losses are not related to either the exposure or the outcome.

Allocation of stars as per rating sheet.

TABLE 4S: QUALITY ASSESSMENT RATINGS – NEWCASTLE-OTTAWA SCALE

Author (Year)	1. REPRESENTATIVENESS OF EXPOSED	2. SELECTION OF NON-EXPOSED	3. ASCERTAINMENT OF EXPOSURE	4. PRIOR EXPOSURE	5. COMPARABILITY	6. ASSESSMENT OF OUTCOME	7. FOLLOW UP LENGTH	8. FOLLOW UP OF COHORT	TOTAL SCORE
Aadamsoo (2011)	-	⁎	-	⁎	-	-	⁎	-	3
Addington (2006)	⁎	⁎	⁎	⁎	-	⁎	-	-	5
Alderson (2017)	-	⁎	-	⁎	-	-	-	⁎	3
Amin (1999)	-	⁎	⁎	⁎	-	⁎	⁎	⁎	6
Amini (2005)	-	⁎	-	⁎	-	-	-	⁎	3
Arendt (2005)	⁎	⁎	-	⁎	-	-	⁎	⁎	5
Arendt (2008)	⁎	⁎	-	⁎	-	-	-	⁎	4
Bachmann (2008)	-	⁎	⁎	⁎	-	⁎	-	-	4
Baldwin (2005)	⁎	⁎	⁎	⁎	-	⁎	-	⁎	6
Björkenstam (2013)	-	⁎	-	⁎	-	-	⁎	⁎	4
Bromet (2011)	-	⁎	⁎	⁎	-	⁎	⁎	-	5
Castagnini (2008)	⁎	⁎	-	⁎	-	-	⁎	-	4
Castro-Fornieles (2011)	-	⁎	⁎	⁎	-	⁎	⁎	-	5
Chang (2009)	⁎	⁎	-	⁎	-	-	⁎	⁎	5
Chen (2015)	⁎	⁎	-	⁎	-	-	-	⁎	4
Crebbin (2009)	-	⁎	⁎	⁎	-	⁎	-	⁎	5
Enderami (2017)	-	⁎	⁎	⁎	-	⁎	-	⁎	5
Fraguas (2008)	-	⁎	⁎	⁎	-	⁎	⁎	⁎	6
Haahr (2008)	⁎	⁎	⁎	⁎	-	⁎	⁎	⁎	7
Heslin (2015)	⁎	⁎	⁎	⁎	-	⁎	⁎	-	6
Jarbin (2003)	-	⁎	⁎	⁎	-	⁎	⁎	-	5
Kim (2011)	-	⁎	⁎	⁎	-	⁎	⁎	-	5
Kingston (2013)	-	⁎	⁎	⁎	-	⁎	⁎	⁎	6
Kittirattanapaiboon (2010)	-	⁎	⁎	-	-	⁎	⁎	-	4
Komuravelli (2011)	-	⁎	⁎	⁎	-	⁎	⁎	-	5
Marneros (2003)	-	⁎	⁎	⁎	-	⁎	⁎	⁎	6
Mauri (2017)	-	⁎	⁎	⁎	-	⁎	⁎	⁎	6
Medhus (2016)	-	⁎	⁎	-	-	⁎	⁎	-	4
Narayanaswamy (2012)	-	⁎	-	-	-	-	⁎	-	2
Niemi-Pynttari (2013)	-	⁎	⁎	⁎	-	⁎	⁎	⁎	6
Pillman (2002)	-	⁎	⁎	-	-	⁎	⁎	⁎	5

Author (Year)	1. REPRESENTATIVENESS OF EXPOSED	2. SELECTION OF NON-EXPOSED	3. ASCERTAINMENT OF EXPOSURE	4. PRIOR EXPOSURE	5. COMPARABILITY	6. ASSESSMENT OF OUTCOME	7. FOLLOW UP LENGTH	8. FOLLOW UP OF COHORT	TOTAL SCORE
Poon (2017)	-	✻	✻	✻	-	✻	✻	-	5
Pope (2013)	✻	✻	✻	✻	-	✻	-	-	5
Rahm (2007)	-	✻	✻	✻	-	✻	-	✻	5
Rusaka (2014)	-	✻	✻	✻	-	✻	✻	-	5
Rusaka (2014)	-	✻	✻	✻	-	✻	✻	-	5
Salvatore (2009)	-	✻	✻	✻	-	✻	✻	✻	6
Sara (2014)	-	✻	-	✻	-	-	✻	-	3
Schimmelmann (2005)	✻	✻	✻	✻	-	✻	-	-	5
Schwartz (2000)	-	✻	✻	✻	-	✻	✻	-	5
Shinn (2017)	-	✻	-	✻	-	-	-	✻	3
Singal (2015)	-	✻	-	✻	-	-	-	✻	3
Singh (2004)	✻	✻	-	✻	-	-	✻	-	4
Starzer (2017)	✻	✻	-	✻	-	-	✻	✻	5
Subramaniam (2007)	-	✻	✻	✻	-	✻	✻	-	5
Suda (2005)	-	✻	✻	-	-	✻	✻	-	4
Veen (2004)	✻	✻	✻	✻	-	✻	✻	✻	7
Whitty (2005)	✻	✻	✻	✻	-	✻	✻	✻	7
Wright (1988)	-	✻	-	✻	-	-	✻	✻	4
Zhang-Wong (1995)	✻	✻	✻	✻	-	✻	-	✻	6