Transition of Substance-Induced, Brief, and Atypical Psychoses to Schizophrenia: A Systematic Review and Meta-analysis

Benjamin Murrie1, Julia Lappin2,3, Matthew Large2, and Grant Sara4,5

1St George Hospital and Sutherland Hospital, South Eastern Sydney Local Health District, Kogarah, Australia; 2School of Psychiatry, University of NSW, Sydney, Australia; 3National Drug and Alcohol Research Centre, University of NSW, Sydney, Australia; 4InforMH, System Information and Analytics Branch, NSW Ministry of Health, North Ryde, Australia; 5Northern Clinical School, Sydney Medical School, University of Sydney, St Leonards, Australia

*To whom correspondence should be addressed; PO Box 169, North Ryde NSW 1670, Australia; tel: 61-2-88775132, fax: 61-2-98875722, e-mail: grant.sara@health.nsw.gov.au

Some people who experience substance-induced psychosis later develop an enduring psychotic disorder such as schizophrenia. This study examines the proportion of people with substance-induced psychoses who transition to schizophrenia, compares this to other brief and atypical psychoses, and examines moderators of this risk. A search of MEDLINE, PsychINFO, and Embase identified 50 eligible studies, providing 79 estimates of transition to schizophrenia among 40,783 people, including 25 studies providing 43 substance-specific estimates in 34,244 people. The pooled proportion of transition from substance-induced psychosis to schizophrenia was 25% (95% CI 18%–35%), compared with 36% (95% CI 30%–43%) for brief, atypical and not otherwise specified psychoses. Type of substance was the primary predictor of transition from drug-induced psychosis to schizophrenia, with highest rates associated with cannabis (6 studies, 34%, CI 25%–46%), hallucinogens (3 studies, 26%, CI 14%–43%) and amphetamines (5 studies, 22%, CI 14%–34%). Lower rates were reported for opioid (12%), alcohol (10%) and sedative (9%) induced psychoses. Transition rates were slightly lower in older cohorts but were not affected by sex, country of the study, hospital or community location, urban or rural setting, diagnostic methods, or duration of follow-up. Substance-induced psychoses associated with cannabis, hallucinogens, and amphetamines have a substantial risk of transition to schizophrenia and should be a focus for assertive psychiatric intervention.

Key words: early psychosis/drug-induced psychosis/diagnostic stability/schizophrenia/course/prognosis/cannabis/amphetamine

Introduction

Substance-induced psychotic disorders, sometimes called drug-induced psychoses, are brief psychotic syndromes triggered by substance use and persisting for days or weeks after substance intoxication has resolved.1 They are common disorders: estimates of their incidence range from 1.52 to 6.53 per 100,000 person-years, similar to estimated incidence rates for affective psychoses and bipolar disorder (4.6 and 6.1 episodes per 100,000, respectively).4 Up to 25% of first hospital admissions for psychosis may include a diagnosis of substance-induced psychosis.5 In high-risk populations, such as amphetamine users, their prevalence may exceed 40%.6 Despite this, debate continues about the overlap of substance-induced psychoses with other brief and atypical psychoses, and the validity and reliability of their diagnostic criteria.7,8 People with substance-induced psychoses are often excluded from studies of early psychosis,9 limiting the evidence on prevalence, course, and outcomes that is required to guide the management and treatment of these conditions.10

A significant proportion of people with substance-induced psychosis later transition to a diagnosis of schizophrenia. Estimates of this proportion vary widely. Studies of treatment cohorts from early psychosis services have reported probabilities of transition as high as 44%11 and 66%.12 Some of these studies found that the probability of transition to schizophrenia was highest in people with cannabis-12 or amphetamine-induced psychoses.13 However, estimates derived from treatment cohorts may be increased because people with enduring disorders may be more likely to remain in contact with

© The Author(s) 2019. Published by Oxford University Press on behalf of the Maryland Psychiatric Research Center. This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com
services. Early psychosis services may also be more likely to see young people who have high rates of substance use, increasing the rate of apparent transition by chance.14

Population-based registers may provide a more accurate estimate of the probability of transition than studies of treatment cohorts because of better follow-up and more representative sampling. Studies of national register data from Sweden, Denmark, and Finland have reported proportions of transition from substance-induced psychosis to schizophrenia ranging from 6% to 17%.15-17 However, these lower proportions may also reflect the different diagnostic mix captured by registry data compared to clinical cohorts. In several registry studies alcohol-induced psychosis was the most common subtype of substance-induced psychosis, and had a lower probability of transition to schizophrenia.16,17 Estimates of transition might also vary for other reasons including differences in study design, patient populations, and health care settings.

A meta-analytically derived estimate of transition from substance-induced psychosis to schizophrenia has been provided by a recent review of transition in first-episode psychosis.18 This study found that 21% of people with first-episode substance-induced psychosis received a later diagnosis of schizophrenia or schizoaffective disorder, based on 10 studies and 164 subjects. The broader focus of that review meant that it could not examine whether substance type or other factors predicted transition to schizophrenia in substance-induced psychoses.

The primary aim of the current study was to synthesize the results of longitudinal observational studies of transition from substance-induced psychosis to schizophrenia. Studies of transition from other brief and atypical psychoses were also examined as a comparison group. These were included to reflect the complex and heterogeneous nature of presentations to early psychosis and other clinical services, and because many people with these diagnoses also transition to later diagnosis of schizophrenia.10,18 We hypothesized that substance-induced psychosis would be associated with the same risk for transition to a later diagnosis of schizophrenia as is observed in other brief and atypical psychoses, based on the findings of the clinical follow-up and register studies described above.

The secondary aim of the study was to examine potential moderators of the risk for transition to schizophrenia. Several studies have found that cannabis-associated psychoses have a greater risk of transition to schizophrenia than other substance-related psychoses.16,17,19 Other potential moderators of prognosis in early psychosis include male gender,20,21 urban location,21-23 age at onset,24 duration of untreated psychosis,25,26 symptom profile27 and the ongoing use of cannabis or other substances following the index psychosis episode.28 Methodological issues such as diagnostic criteria,29 diagnostic methods, follow-up periods, or completeness of follow-up could also potentially influence study findings.

Methods

The study was registered with PROSPERO (CRD42018086734) and conducted in accordance with PRISMA and MOOSE guidelines. We aimed to examine rates of transition to schizophrenia associated with cannabis, hallucinogens, amphetamines, opioids, alcohol, sedatives, and multiple or not specified substance-induced psychosis and to compare rates of transition among those with brief and atypical psychosis, psychosis NOS, and schizophreniform psychosis. The term substance-induced was used because of convention and not because of a presumed causal link between the substance use and the psychosis.

Search Strategy

PsychINFO, MEDLINE, and Embase were searched via Ovid for peer-reviewed, English-language publications reporting follow-up diagnoses in people with substance-induced psychoses, brief psychosis, atypical psychosis, schizophreniform psychosis, and psychosis not otherwise specified from 1980 to 2018. A broad search strategy was used because substance-induced psychoses are often reported as a subgroup in multi-diagnostic psychosis cohorts where they are not the primary focus. Titles, abstracts, and keywords were searched for: (first episode OR drug induced OR substance induced OR stimulant induced OR hallucinogen induced OR cannabis induced OR marijuana induced OR amphetamine induced OR cocaine induced OR LSD induced OR lysergic acid induced OR angel dust induced OR PCP induced OR phencyclidine OR psilocybin induced OR alcohol induced OR opioid induced OR benzodiazepine induced) AND (psychosis OR psychotic) AND (diagnostic stability OR outcome OR follow up OR course OR prognosis OR transition OR conversion OR longitudinal). The reference lists of identified studies were hand-searched for further relevant studies. The literature search was conducted by 1 author (B.M.) and hand searching of reference lists by 2 authors (B.M. and G.S.).

Inclusion and Exclusion Criteria

Studies were included which reported (1) a baseline diagnosis of substance-induced, brief, atypical, not otherwise specified (NOS) or schizophreniform psychoses, (2) a follow-up diagnosis in the same subjects with a minimum follow-up period of 6 months, and (3) the number of persons with a diagnosis of schizophrenia at the follow-up assessment. Case-series, case-control studies, cohort studies, and randomized-controlled trials were included. Commentaries, book chapters, conference abstracts, editorials, reviews, single case studies, gray literature, and qualitative studies were excluded. Two authors (B.M. and G.S.) selected the studies independently and resolved differences on inclusion and exclusion by consensus.
Psychoses were defined using syndromal diagnoses made according to DSM, ICD, or other recognized diagnostic criteria: studies which defined psychosis by symptom scales or self-report were excluded. The specific psychosis subtype or grouping used by the study authors was recorded. Where specified, the type of substance was recorded for subgroup analysis. Schizoaffective disorders were typically grouped with schizophrenia by authors: where schizophrenia and schizoaffective disorder follow-up diagnoses were reported separately these were combined into a single estimate by the addition of the numbers in each subsample. Substance-induced psychoses associated with methamphetamine, amphetamine, or cocaine were recorded as stimulant-induced psychoses, and those associated with methylene-dioxymethamphetamine (MDMA), lysergic acid diethylamide (LSD), phencyclidine (PCP) or psilocybin as hallucinogen-induced psychoses. Estimates for delusional disorder were excluded from analysis.

If several publications reported on the same cohort, only the largest was included. On full-text review a number of studies appeared likely to have collected relevant information but reported it in an aggregated form, preventing extraction of data for the specific psychosis subgroup or specific substances. For example, some studies identified the proportion with different psychosis types at baseline (substance-induced, brief, affective etc.) but reported a pooled rate of transition to a later schizophrenia diagnosis. The corresponding author of these studies was e-mailed to seek supplementary data. The authors of 16 studies were contacted for supplementary information and additional data were provided for 3, 19, 41, 42

Outcome and Moderator Variables

The primary outcome measure was the proportion of the original cohort with a follow-up diagnosis of schizophrenia. Potential moderator variables examined included: (1) service setting (inpatient, community, or mixed); (2) country; (3) location within country (urban, rural, or mixed); (4) average age of cohort; (5) percent of cohort who were male; (6) diagnostic system used (DSM, ICD, or other); (7) diagnostic method (file review, routine clinical diagnoses, or structured interview); (8) duration of follow-up period; (9) drop-out rate between baseline and follow-up assessment; (10) Positive and Negative Symptom Scale (PANSS) positive, negative, and total symptom scores; (11) Brief Psychiatric Rating Scale (BPRS) scores; (12) Global Assessment of Function (GAF) ratings; (13) whether cohort was limited to first-episode/incident episodes; (14) year of follow-up, using median year for multi-year studies, and publication year when data collection year was not specified, and (15) whether toxicity (blood, urine, or hair assays) were used in establishing diagnoses of substance-induced
conditions. Where studies reported BPRS but not PANSS, Leucht's equipercentile method was used to estimate a PANSS total score.

Two authors (B.M. and G.S.) extracted all data independently: differences were resolved by joint examination of papers by a third author (J.L.). Subgroup characteristics were extracted separately for each diagnostic subgroup where these were reported. Study quality was rated by the same authors using the Newcastle-Ottawa Scale for cohort studies. Studies were rated as more representative if drawn from mixed hospital and community cohorts. Diagnostic quality (at baseline and outcome) was rated as higher when based on structured diagnostic interview or detailed file review, and lower when based on routine clinical diagnosis.

Meta-analysis

Meta-analysis was conducted using CMA. Analysis was conducted in 2 stages. First, substance-induced psychoses were compared to other brief and atypical psychoses, using a single estimate per study. Second, to examine differences between types of substance, meta-analysis was conducted only for studies of substance-induced psychosis, analyzing each substance type as a separate subgroup. All analyses employed mixed-effects models (random effects within-subgroup and fixed effects between-subgroup), logit-transformed event rates and z-distribution confidence intervals.

For studies of substance-induced psychosis, subgroup analysis was used to examine potential moderators of the primary outcome. These were conducted using study-level data because substance-specific estimates within studies were considered not to be independent observations. Between-subgroup heterogeneity was assessed using the q-value. Because of the number of planned subgroup analyses, a Bonferroni correction was applied: a threshold of P < .01 was used for defining significant subgroup differences. Continuous variables, such as average age and follow-up period, were analyzed via metaregression. Publication bias was assessed using Egger's test, and if significant bias existed a revised estimate was calculated using Duval and Tweedie's trim and fill test.

Results

Search Results

The search strategy identified 6097 potentially relevant publications, of which 5906 were excluded following abstract review, and a further 141 excluded after review of full text (figure 1). Four additional papers were identified through hand searching, resulting in 50 eligible studies included.

The 50 eligible studies provided 79 estimates of transition to a diagnosis of schizophrenia among 40 783 people, including 25 studies of
substance-induced psychosis (34 244 people). The mean follow-up period was 4.0 years (range 1–20 y) or 8.4 years when weighted by the number of participants in each study. Study samples included more males than females (mean study proportion male 61%, weighted mean 72%). The mean study age was 28 years (weighted mean 29 y). Studies were from 25 countries including England (5 studies), Denmark (4), United States (4), Ireland, Sweden, Germany, and India (3 each): these were aggregated into regional groupings for subgroup analysis. Diagnoses were most often made by structured interview (22) or by extraction of routine clinical diagnoses from medical records or registers (16). For most studies, the index diagnosis was made in hospital (27) or in mixed hospital and community (13) settings. All but 8 studies examined first-episode cohorts. All eligible studies used a cohort design.

**Pooled Rate of Transition to Schizophrenia**

Overall one-quarter (25%, 95% CI 18%–35%) of people with substance-induced psychosis had a follow-up diagnosis of schizophrenia (table 2). This pooled estimate was lower than that for brief, atypical, NOS psychoses, and schizophreniform psychosis (between-group $Q = 5,830$, df 3, $P < .0001$). There was substantial heterogeneity between studies with non-substance-induced psychosis (table 2). Amongst the brief, atypical, and NOS group, transition rates were lower in those with brief and atypical psychoses (26 estimates, 30% transition, 95% CI 23%–38%) than in psychosis NOS (18 estimates, 46% transition, 95% CI 40%–52%).

The 25 studies of substance-induced psychosis provided 43 substance-specific estimates (table 2). Substance-specific estimates differed significantly ($Q = 137$, df 6, $P < .0001$). Pooled estimates of transition to schizophrenia were highest (34%, 95% CI 25%–46%) for cannabis-induced psychoses, intermediate for amphetamines and hallucinogens, and lowest for alcohol-, sedative- and opioid-induced psychoses. Within-group heterogeneity ($F$) exceeded 90% for all substance types where it could be meaningfully estimated on the basis of more than 3 samples.
Table 1. Studies Included in Summary Analysis

| Study                | Country                | Psychosis Groups Reported | Transition to Szp (%) | Sample Number | Age (y) | Male (%) | Follow-up | Setting       | Diagnosis System | Diagnosis Method |
|----------------------|------------------------|---------------------------|-----------------------|---------------|---------|----------|-----------|---------------|------------------|------------------|
| Aadamsoo (2011)      | Estonia                | Brief                     | 50%                   | 153           | 28      | 40%      | 2.0       | 70%           | Hospital          | ICD Clinical Dx  |
| Addington (2006)     | Canada                 | Brief, SIP, NOS, Szp      | 53%                   | 228           | 25      | 67%      | 1.0       | 54%           | Mixed             | DSM Structured IV |
| Alderson (2017)      | Scotland               | SIP                       | 15%                   | 3486          | 34      | 76%      | 3.0       | 100%          | Hospital          | ICD Clinical Dx  |
| Amin (1999)          | England                | Brief                     | 23%                   | 161           | 24      | 54%      | 1.0       | 80%           | Hospital          | ICD Structured IV |
| Arendt (2005)        | Denmark                | SIP                       | 44%                   | 535           | 27      | 82%      | 5.9       | 100%          | Mixed             | DSM Clinical Dx  |
| Arendt (2008)        | Denmark                | SIP                       | 51%                   | 609           |         |          |           |               | Mixed             | DSM Clinical Dx  |
| Bachmann (2008)      | Germany                | Szp                       | 88%                   | 62            | 29      | 45%      | 1.2       | 65%           | Hospital          | DSM Structured IV |
| Baldwin (2005)       | Ireland                | Brief, SIP, NOS, Szp      | 64%                   | 57            | 37      | 60%      | 0.5       | 98%           | Mixed             | DSM Structured IV |
| Björkenstam (2013)   | Sweden                 | Brief, SIP                | 8%                    | 1840          | 21      |          | 5.0       | 100%          | Hospital          | ICD Clinical Dx  |
| Bromet (2011)        | United States          | SIP, Szp                  | 80%                   | 628           |         |          |           |               | Hospital          | DSM Structured IV |
| Castagnini (2008)    | Denmark                | Brief                     | 35%                   | 503           | 42      | 58%      | 6.0       | 69%           | Mixed             | ICD Clinical Dx  |
| Castro-Fornieles (2011) | Spain             | Brief, NOS, Szp           | 87%                   | 110           | 16      | 68%      | 2.0       | 75%           | Unspecified       | DSM Structured IV |
| Chang (2009)         | China                  | Brief                     | 50%                   | 166           | 20      | 54%      | 4.5       | 100%          | Mixed             | DSM Clinical Dx  |
| Chen (2015)          | Taiwan                 | SIP                       | 18%                   | 606           |         |          |           |               | Mixed             | ICD Clinical Dx  |
| Crebbin (2009)       | England                | SIP                       | 26%                   | 35            | 26      | 83%      | 100%      | Mixed          | DSM Structured IV |
| Enderami (2017)      | Iran                   | NOS, Szp                  | 100%                  | 38            | 29      | 78%      | 1.0       | 84%           | Hospital          | DSM Structured IV |
| Fragauss (2008)      | Spain                  | NOS, Szp                  | 25%                   | 24            | 16      | 75%      | 2.0       | 96%           | Hospital          | DSM Structured IV |
| Haahr (2008)         | Norway and Denmark     | NOS, Szp                  | 74%                   | 301           | 28      | 59%      | 2.0       | 93%           | Mixed             | DSM Structured IV |
| Hasslin (2015)       | England                | Brief, SIP, NOS           | 64%                   | 505           |         |          | 10.7      | 80%           | Community         | ICD File Review  |
| Jarbin (2003)        | Sweden                 | SIP, NOS, Szp             | 50%                   | 88            | 16      | 49%      | 10.5      | 77%           | Hospital          | DSM Structured IV |
| Kim (2011)           | South Korea            | Brief                     | 57%                   | 637           | 28      | 60%      | 2.3       | 24%           | Hospital          | DSM File Review   |
| Kingston (2013)      | Ireland                | SIP, NOS, Szp             | 100%                  | 202           | 46      | 45%      | 6.0       | 97%           | Hospital          | DSM File Review   |
| Kittirattanaipiaiboon (2010) | Thailand   | SIP                       | 39%                   | 1116          | 33      | 91%      | 5.0       | 40%           | Hospital          | Other File Review |
| Komuravelli (2003)   | England                | SIP                       | 52%                   | 78            |         |          |           |               | Hospital          | DSM Structured IV |
| Marneros (2003)      | Germany                | Brief                     | 13%                   | 42            | 36      | 21%      | 8.2       | 90%           | Hospital          | File Review       |
| Mauri (2017)         | Italy                  | SIP                       | 35%                   | 48            | 28      | 96%      | 5.0       | 100%          | Hospital          | DSM Structured IV |
| Medhus (2016)        | India                  | Brief                     | 12%                   | 54            | 31      | 35%      | 2.0       | 80%           | Hospital          | ICD Clinical Dx  |
| Narayanaswamy (2012) | India                  | Brief                     | 12%                   | 54            | 31      | 35%      | 2.0       | 80%           | Hospital          | ICD Clinical Dx  |
| Niemi-Pynttari (2013) | Finland               | SIP                       | 6%                    | 18 478        | 45      | 83%      | 6.2       | 100%          | Hospital          | ICD File Review   |
| Pillman (2002)       | Germany                | Brief                     | 5%                    | 42            | 40      | 21%      | 2.2       | 90%           | Hospital          | ICD Structured IV |
| Poon (2017)          | Hong Kong              | Brief                     | 23%                   | 179           |         |          | 14%       | 20%           | Hospital          | ICD File Review   |
| Pope (2013)          | Hong Kong              | NOS, Szp                  | 100%                  | 333           | 23      | 70%      | 1.0       | 64%           | Community         | DSM Structured IV |
| Rahni (2007)         | Sweden                 | Brief, Szp                | 40%                   | 175           | 0       | 0%       | 0.0       | 83%           | Unspecified       | DSM Structured IV |
| Russa (2014)         | Latvia                 | Brief                     | 71%                   | 102           | 36      | 39%      | 2.2       | 40%           | Hospital          | ICD Structured IV |
| Russa (2014)         | Latvia                 | Brief                     | 73%                   | 294           | 33      | 46%      | 5.6       | 40%           | Hospital          | File Review       |
| Salvatore (2009)     | India                  | Brief, NOS, Szp           | 68%                   | 517           | 32      | 55%      | 2.0       | 97%           | Unspecified       | DSM Structured IV |
| Sara (2014)          | Australia              | Brief, SIP, NOS           | 50%                   | 43 968        | 33      | 61%      | 5.0       | 55%           | Hospital          | ICD Clinical Dx  |
| Schimmelmann (2005)  | Australia              | Brief, SIP                | 56%                   | 668           | 22      | 63%      | 1.5       | 74%           | Community         | DSM File Review   |
| Schwartz (2000)      | United States          | Brief, SIP, NOS, Szp      | 18%                   | 695           | 30      | 57%      | 2.0       | 79%           | Hospital          | DSM Structured IV |

Schizophrenia Risk in Substance-Induced Psychosis
Subgroup Analysis

Subgroups of the studies examining substance-induced psychosis were compared (table 3). After correction for multiple comparisons, study design characteristics did not predict significant between-group differences. Continuous moderators were examined using meta-regression (table 4). Studies of older cohorts reported lower rates of transition to schizophrenia. There was no association between transition rate and sex, duration of follow-up, proportion of sample followed up or year of publication. There were insufficient studies for meta-regression of PANSS positive, negative, or total scores (reported by 3 studies), percent with comorbid substance use (4 studies) or GAF scores (4 studies).

Study Quality

Study quality did not predict significant between-group differences: studies scoring above and below the median (5 or more on the Newcastle-Ottawa Scale) did not differ in estimates (table 3). Potential impact of study quality was also examined by subgroup analysis for each integer value of the quality scale, and by meta-regression on quality scores as a continuous variable (supplementary material): no significant effects of study quality were observed using any method.

Publication Bias

There was no apparent impact of publication bias on pooled estimates for psychosis subtypes (table 5). Egger's test was not significant for any psychosis subgroup, and Duval and Tweedie's trim and fill test was therefore not conducted. Funnel plots for psychosis subgroups are provided as supplementary material.

Discussion

This meta-analysis of transition from substance-induced psychosis to a diagnosis of schizophrenia identified 25 studies of substance-induced psychosis, which provided 43 substance-specific estimates in 34,244 individuals. The overall proportion transitioning to schizophrenia was 25%. The strongest predictor of transition was the type of substance: one-third (34%) of people with cannabis-induced psychosis transitioned to a later diagnosis of schizophrenia, based on estimates from 6 studies and 3,040 people. Rates were intermediate for hallucinogens and amphetamines, and below 10% for alcohol and sedative-induced psychoses. There was significant heterogeneity of estimates, and the likelihood of transition to schizophrenia was not predicted by sex, country, study setting, urban or rural location, diagnostic system, diagnostic methods or completeness or duration of follow-up. Studies of older cohorts reported a reduced proportion transitioning to schizophrenia. This may, however, be an
Table 2. Meta-analysis of Rate of Transition to a Later Diagnosis of Schizophrenia in People With Substance-Induced, Brief, and Atypical Psychoses

| Estimates | Subjects | Transition Rate % (95% CI) | Heterogeneity |
|-----------|----------|----------------------------|--------------|
|           |          | Q  | P      | F (%) | |
| Type of psychosis | | | | | | |
| Substance-induced | 25 | 34,224 | 25 (18–35) | 3,034 | <.0001 | 99 |
| Brief, atypical and NOS | 34 | 3,969 | 36 (30–43) | 420 | <.0001 | 92 |
| Schizophreniform | 20 | 390 | 65 (57–72) | 42 | .0020 | 54 |
| Overall | 79 | 40,783 | 44 (39–49) | 5,830 | <.0001 | 99 |
| Substance | | | | | | |
| Alcohol | 5 | 1,935 | 9 (6–15) | 146 | <.0001 | 97 |
| Sedatives | 2 | 223 | 10 (7–15) | 0.1 | .7832 | 0 |
| Opioids | 3 | 664 | 12 (8–18) | 5 | .0668 | 63 |
| Amphetamines | 5 | 2,284 | 22 (14–34) | 16 | <.0001 | 96 |
| Mixed or not specified | 19 | 8,447 | 22 (17–29) | 426 | <.0001 | 96 |
| Hallucinogens | 3 | 208 | 26 (14–43) | 8 | .0211 | 74 |
| Cannabis | 6 | 3,040 | 34 (25–46) | 137 | <.0001 | 96 |

Note: NOS, psychosis not otherwise specified. Subgroup analysis showing specific substances in studies of drug-induced psychosis (25 studies, providing 43 substance-specific estimates).

Table 3. Predictors of Rate of Transition From Substance-Induced Psychosis to Schizophrenia: Subgroup Analyses of Categorical Variables

| Moderator | Details | Studies | Subjects | Transition to Schizophrenia % (95% CI) | Within Group | Between Group |
|-----------|---------|---------|----------|----------------------------------------|--------------|---------------|
| Study aim | Diagnostic stability | 22 | 34,200 | 25 (17–34) | 99 | 99 | .5910 |
| | Coincidental | 3 | 24 | 35 (8–77) | 62 | \[\text{I}^2\] | 0 |
| Target population | First episode | 21 | 26,489 | 25 (16–38) | 99 | 99 | .9366 |
| | Mixed | 4 | 7,735 | 25 (15–38) | 97 | \[\text{I}^2\] | 0 |
| Service setting | Community | 3 | 41 | 25 (7–61) | 67 | 99 | .7698 |
| | Hospital | 14 | 25,713 | 23 (13–37) | 97 | \[\text{I}^2\] | 0 |
| | Mixed/unspecified | 8 | 8,470 | 30 (17–47) | 99 | \[\text{I}^2\] | 0 |
| Region | Australia | 2 | 2,799 | 21 (3–70) | 62 | 99 | .8700 |
| | Europe | 2 | 35 | 34 (21–51) | 0 | \[\text{I}^2\] | 0 |
| | North America | 5 | 67 | 31 (10–64) | 72 | \[\text{I}^2\] | 0 |
| | S&E Asia | 3 | 9,54 | 27 (13–47) | 96 | \[\text{I}^2\] | 0 |
| | Scandinavia | 6 | 26,858 | 19 (8–39) | 100 | \[\text{I}^2\] | 0 |
| | United Kingdom and Ireland | 7 | 3,511 | 27 (14–45) | 88 | \[\text{I}^2\] | 0 |
| Population coverage | National | 8 | 30,728 | 20 (11–33) | 100 | 99 | .0559 |
| | Subnational | 17 | 3,496 | 34 (28–40) | 55 | \[\text{I}^2\] | 0 |
| Urban or rural location | Urban | 7 | 562 | 39 (30–50) | 48 | 99 | .0432 |
| | Rural | 2 | 23 | 19 (6–46) | 23 | \[\text{I}^2\] | 0 |
| | Mixed/unspecified | 16 | 33,639 | 22 (14–33) | 99 | \[\text{I}^2\] | 0 |
| Diagnostic method | File review | 7 | 19,038 | 24 (8–53) | 99 | 99 | .8829 |
| | Clinical diagnosis | 10 | 15,059 | 27 (18–37) | 99 | \[\text{I}^2\] | 0 |
| | Research interview | 8 | 1,27 | 23 (13–38) | 51 | \[\text{I}^2\] | 0 |
| Diagnostic system | DSM | 10 | 126 | 24 (13–39) | 49 | 99 | .1069 |
| | ICD | 13 | 33,639 | 24 (15–36) | 100 | \[\text{I}^2\] | 0 |
| | Other | 2 | 459 | 43 (27–61) | 43 | \[\text{I}^2\] | 0 |
| Toxicology used | Yes | 3 | 52 | 38 (22–56) | 35 | 99 | .1423 |
| | No or unspecified | 22 | 34,172 | 24 (16–34) | 99 | \[\text{I}^2\] | 0 |
| Study quality | Median or above | 14 | 26,018 | 24 (14–37) | 99 | 99 | .6683 |
| | Below median | 11 | 8,206 | 27 (18–39) | 98 | \[\text{I}^2\] | 0 |

Note: DSM, Diagnostic and Statistical Manual of Mental Disorders, any edition; ICD, International Classification of Diseases, any edition.
Table 4. Predictors of Rate of Transition From Drug-Induced Psychosis to Schizophrenia: Meta-regression of Continuous Variables

| Variable                      | Coefficient β | 95% CI     | P     |
|-------------------------------|---------------|-----------|-------|
| Year of publication           | 0.004         | −0.048    | 0.055 | .8892 |
| Average age                   | −0.050        | −0.095    | −0.005| .0286 |
| Percent of sample male        | 2.298         | −0.492    | 5.087 | .1065 |
| Length of follow-up period    | −0.030        | −0.093    | 0.033 | .3433 |
| Percent of sample followed up | −1.716        | −3.628    | 0.196 | .0785 |

Table 5. Tests of Publication Bias

|                          | Intercept | t      | P       |
|--------------------------|-----------|--------|---------|
| Substance-induced        | 3.02      | 1.07   | .2966   |
| Brief, atypical and NOS  | −1.41     | 1.94   | .0581   |
| Schizophreniform         | 0.77      | 1.38   | .1854   |
| Overall                  | 3.16      | 1.70   | .0963   |

Note: NOS = psychosis not otherwise specified.

The estimate of a 25% probability of transition in substance-induced psychoses is slightly higher than the previously reported meta-analytic estimate of 21%,18 There are several likely reasons for this difference. The current study included additional studies published since July 2015.17,56,71,72,81 It employed a larger search strategy, restricting in the inclusion of several large population-based studies which used first hospital admission to define incident episodes.16,19,56 The current study also included 4 studies of substance-induced psychosis which were not limited to incident episodes,13,17,61,72 though this group did not have significantly higher rates of transition.

Consistent with other reviews,18 we found that around two-thirds (65%) of people with a diagnosis of schizophreniform psychoses received a later diagnosis of schizophrenia. This is likely to reflect the significant overlap in diagnostic criteria, with the 2 conditions being mainly distinguished on the basis of duration of illness. However, a significant subgroup of people with these diagnoses do not receive a later diagnosis of schizophrenia,90 emphasizing the need for a recovery-focused approach in early psychosis, regardless of diagnosis.

Clinical and Service Implications

These findings have important implications for mental health care and services. Substance-induced psychoses are common reasons for seeking mental health care: in younger Australians more than one-fifth of first hospital admissions for psychosis are due to substance-induced psychosis.91 This study has found that substance-induced psychoses (particularly cannabis-, hallucinogen- and amphetamine-induced psychoses) are associated with a significant risk of receiving a later diagnosis of schizophrenia, and that this risk is only slightly less than that observed for some other brief psychotic disorders. Yet despite this, people with substance-induced psychoses are often excluded from early psychosis services or assertive mental health care due to a perception that these are benign or self-limiting conditions.9 This perception may be reinforced by the frequent exclusion of substance-induced psychosis from both primary research studies9,92 and reviews93 of psychosis outcomes. The findings of this study suggest that decisions about the care of people with substance-induced psychoses should consider the different level of risk associated with different types of substances, rather than seeing all substance-induced psychoses as equivalent.

In particular, the treatment of psychoses induced by cannabis, amphetamines, and hallucinogens should be considered within the same framework of assertive early psychosis intervention as for other brief psychotic disorders. All persons with these disorders should ideally receive a comprehensive psychiatric assessment which considers their individual risk factors and the potential need for assertive monitoring and support.94 The importance of assertive intervention in this group is underlined by evidence that integrated care which addresses substance use disorders and psychosis can have a significant impact on course. Such care can double the likelihood of remission in early psychosis,92,95 reduce the risk for hospital re-admission96 and lead to better symptomatic, drug use and functional outcomes at 10-year follow-up.97,98

Clinical care should always consider factors potentially associated with higher risk in some individuals. The current study found few meta-analytically derived demographic predictors of transition to schizophrenia in substance-induced psychosis. However, predictors of greater rates of transition are likely to be similar to those reported in other first episode psychoses, including younger age of first psychosis,16,17,49,75,90 longer duration of untreated psychosis90,80,84 and impaired premorbid social function.17,49,79,80,84
Cannabis and Transition to Schizophrenia
The rate of transition to schizophrenia was higher following cannabis-induced psychosis (34%) than other substance-induced psychoses, including those associated with amphetamines and hallucinogens. Three studies provided separate estimates for cannabis and other substances. All found that cannabis-induced psychoses had the highest rate of transition to schizophrenia, although in one of these studies the difference from stimulants was not significant. These consistent within-study findings suggest that the higher transition rate in cannabis-induced psychosis is unlikely to merely reflect methodological differences between studies. They are also consistent with findings that among young people with brief and atypical psychoses, comorbid cannabis use disorders were associated with a greater risk for transition to schizophrenia than comorbid amphetamine disorders.

A study by Kendler and colleagues, published after the inclusion period for the current review, examined the interaction between substance type and other risk factors in the transition from substance-induced psychosis to schizophrenia. Kendler found that cannabis-induced psychoses were associated with the highest risk of later schizophrenia, and that this was not due to younger age of onset, or differences in gender or service setting. They found that amongst people with substance-induced psychosis, familial risk scores for psychosis were twice as high in those with a later diagnosis of schizophrenia. This study adds evidence that cannabis interacts with other risk factors to double the risk for schizophrenia in vulnerable individuals. Reduced engagement in treatment and follow-up also contributes to this association, further underlining the importance of assertive engagement and care in this group.

While finding the same gradient of risk when comparing individual substance types, Kendler's study reported lower proportions of transition to schizophrenia than some other comparable studies. The cumulative hazard was 11.3% for all substance-induced psychoses and 18.0% for cannabis-induced psychoses. They suggest that this may reflect a narrower definition of schizophrenia than some comparable studies. Their study also included a higher proportion of subjects from community settings, who they found had lower risk of transition to schizophrenia than people admitted to hospital.

Limitations
The current study has a number of limitations. First, variability in study design and the substantial heterogeneity of estimates are likely to have contributed to the lack of demonstrable associations with some known or likely risk factors for schizophrenia, including gender, urban setting, hospital setting, or longer duration of follow-up. Many subgroup analyses included small numbers of studies, resulting in significant uncertainty in subgroup estimates.

Second, and likely to contribute to these negative findings of studies reporting different subgroups of psychosis, almost none reported age, sex, or other demographics separately for each subgroup. Therefore, the pooled demographic characteristics for all subgroups were used for those studies.

Third, the studies reviewed include insufficient data to allow meta-analytic comparison of several important potential confounders. In particular, very few studies provided detailed information on the amount or duration of substance use prior to the episode of psychosis, the rate and type of comorbid substance use disorder at the index diagnosis, or the rate of ongoing substance use during follow-up. All these factors are likely to moderate the risk of transition to schizophrenia in people with substance-induced and other brief and atypical psychoses. In particular, there is evidence that ongoing substance use is a critical risk factor, with reduced likelihood of further admissions or transition to schizophrenia in people who cease substance use after a substance-related psychoses but increased risks in people with ongoing use.

Fourth, the estimates reported here rely on the accuracy of diagnoses in the studies included. Most used diagnoses recorded in registers from routine clinical care (10 studies, 15,059 persons) or from file review (7 studies 19,038 persons). Only 8 studies (127 persons) used research diagnostic interviews. Routine diagnoses of substance-induced, atypical, and brief psychoses are often imprecise due to overlap in diagnostic constructs and variation in clinical practice. Subgroup analysis did not suggest any systematic difference in estimates associated with these different sources of diagnosis, but the small number of studies using research diagnostic interviews may have prevented identification of possible differences.

Fifth, too few studies reported values for relevant moderators, such as duration of psychosis, symptom scores, global functioning, and rates of ongoing substance use, to allow completion of the planned meta-regression analyses.

Finally, the research team did not have the resources or expertise to review studies in languages other than English, which may bias findings. However, nearly half of the included studies of substance-induced psychosis (11 of 25) came from European, Scandinavian, and southern and eastern Asian countries.

Conclusions
Substance-induced psychoses are common and serious conditions. They are associated with a substantial risk for transition to schizophrenia. The risk of transition to schizophrenia is particularly increased following cannabis-induced psychosis, which should be responded to with assertive attempts at engagement, assessment, and care.
Supplementary Material

Supplementary material is available at Schizophrenia Bulletin online.

Funding

This study received no source of external funding.

Acknowledgments

We would like to thank Dr Christoffer Rahm and Dr Paola Salvatore for providing additional data for this article. The authors have declared that there are no conflicts of interest in relation to the subject of this study.

References

1. World Health Organization. The ICD-10 Classification of Mental and Behavioural Disorders - Diagnostic Criteria for Research. Geneva, Switzerland: World Health Organization; 1993.

2. Kirkbride JB, Hameed Y, Ankireddypalli G, et al. The epidemiology of first-episode psychosis in early intervention in psychosis services: findings from the social epidemiology of psychoses in East Anglia [SEPEA] study. Am J Psychiatry. 2017;174(2):143–153.

3. Weibell MA, Joa I, Bramness J, et al. Treated incidence and baseline characteristics of substance induced psychosis in a Norwegian catchment area. BMC Psychiatry. 2013;13:319.

4. Jongsma HE, Turner C, Kirkbride JB, Jones PB. International incidence of psychotic disorders, 2002-17: a systematic review and meta-analysis. Lancet Public Health. 2019;4(5):e229–e244.

5. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.

6. Lecomte T, Dumais A, Dugré JR, Potvin S. The prevalence of substance-induced psychotic disorder in methamphetamine misusers: a meta-analysis. Psychiatry Res. 2018;268:189–192.

7. Mathias S, Lubman DI, Hides L. Substance-induced psychosis: a diagnostic conundrum. J Clin Psychiatry. 2008;69(3):358–367.

8. Wilson L, Szigi G, Kearney A, Clarke M. Clinical characteristics of primary psychotic disorders with concurrent substance abuse and substance-induced psychotic disorders: a systematic review. Schizophr Res. 2018;197:78–86.

9. Weibell MA, ten Velden Hegelstad W, Johannessen JO. Chapter 5 - substance-induced psychosis: conceptual and diagnostic challenges in clinical practice. In: Preedy VR, ed. Neuropathology of Drug Addictions and Substance Misuse. San Diego, CA: Academic Press; 2016:50–57.

10. Fusar-Poli P, Cappucciani M, Bonoldi I, et al. Prognosis of brief psychotic episodes: a meta-analysis. JAMA Psychiatry. 2016;73(3):211–220.

11. Arendt M, Rosenberg R, Foldager L, Perto G, Munk-Jørgensen P. Cannabis-induced psychosis and subsequent schizophrenia-spectrum disorders: follow-up study of 535 incident cases. Br J Psychiatry. 2005;187:510–515.

12. Addington J, Chaves A, Addington D. Diagnostic stability over one year in first-episode psychosis. Schizophr Res. 2006;86(1-3):71–75.

13. Kittirattanapaiboon P, Mahatnirunkul S, Booncharoen H, Thumnawong P, Dumrongchai U, Chutha W. Long-term outcomes in methamphetamine psychosis patients after first hospitalisation. Drug Alcohol Rev. 2010;29(4):456–461.

14. Morgan C, Lappin J, Helin M, et al. Reappraising the long-term course and outcome of psychotic disorders: the AESOP-10 study. Psychol Med. 2014;44(13):2713–2726.

15. Björkenstam E, Björkenstam C, Hjern A, Reutfors J, Bodén R. A five year diagnostic follow-up of 1840 patients after a first episode non-schizophrenia and non-ffective psychosis. Schizophr Res. 2013;150(1):205–210.

16. Niemi-Pynttäri JA, Sund R, Putkonen H, Vorma H, Wahlbeck K, Pirkola SP. Substance-induced psychoses converting into schizophrenia: a register-based study of 18,478 Finnish inpatient cases. J Clin Psychiatry. 2013;74(1):e94–e99.

17. Starzer MSK, Nordentoft M, Hjorthøj C. Rates and predictors of conversion to schizophrenia or bipolar disorder following substance-induced psychosis. Am J Psychiatry. 2018;175(4):343–350.

18. Fusar-Poli P, Cappucciani M, Rutigliano G, et al. Diagnostic stability of ICD/DSM first episode psychosis diagnoses: meta-analysis. Schizophr Bull. 2016;42(6):1395–1406.

19. Sara GE, Burgess PM, Malhi GS, Whiteford HA, Hall WC. The impact of cannabis and stimulant disorders on diagnostic stability in psychosis. J Clin Psychiatry. 2014;75(4):349–356.

20. McGrath J, Saha S, Chant D, Welham J. Schizophrenia: a concise overview of incidence, prevalence, and mortality. Epidemiol Rev. 2008;30:67–76.

21. McGrath JJ. The surprisingly rich contours of schizophrenia epidemiology. Arch Gen Psychiatry. 2007;64(1):14–16.

22. McGrath J, Saha S, Welham J, El Saadi O, MacCauley C, Chant D. A systematic review of the incidence of schizophrenia: the distribution of rates and the influence of sex, urbanicity, migrant status and methodology. BMC Med. 2004;2:13.

23. van Os J, Kapur S. Schizophrenia. Lancet. 2009;374(9690):635–645.

24. Immonen J, Jääskeläinen E, Korpela H, Miettunen J. Age at onset and the outcomes of schizophrenia: a systematic review and meta-analysis. Early Interv Psychiatry. 2017;11(6):453–460.

25. Penttilä M, Jääskeläinen E, Hirvonen N, Isohanni M, Miettunen J. Duration of untreated psychosis as predictor of long-term outcome in schizophrenia: systematic review and meta-analysis. Br J Psychiatry. 2014;205(2):88–94.

26. Perkins DO, Gu H, Boteva K, Lieberman JA. Relationship between duration of untreated psychosis and outcome in first-episode schizophrenia: a critical review and meta-analysis. Am J Psychiatry. 2005;162(10):1785–1804.

27. Diaz-Caneja CM, Pina-Camacho L, Rodríguez-Quiroga A, Fraguas D, Parellada M, Arango C. Predictors of outcome in early-onset psychosis: a systematic review. npj Schizophr. 2015;1:14005.

28. Di Forti M, Quattrone D, Freeman TP, et al.; EU-GEI WP2 Group. The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study. Lancet Psychiatry. 2019;6(5):427–436.

29. Jablensky A. Psychiatric classifications: validity and utility. World Psychiatry. 2016;15(1):26–31.

30. Amminger GP, Henry LP, Harrigan SM, et al. Outcome in early-onset schizophrenia revisited: findings from the early psychosis prevention and intervention centre long-term follow-up study. Schizophr Res. 2011;131(1-3):112–119.
31. Bergé D, Mané A, Salgado P, et al. Predictors of relapse and functioning in first-episode psychosis: a two-year follow-up study. *Psychiatr Serv.* 2016;67(2):227–233.

32. Harrison G, Amin S, Singh SP, Croudace T, Jones P. Outcome of psychosis in people of African-Caribbean family origin. Population-based first-episode study. *Br J Psychiatry.* 1999;175:43–49.

33. Johannesson JO, Joa I, Auestad B, et al. First-episode psychosis patients recruited into treatment via early detection teams versus ordinary pathways: course and health service use during 5 years. *Early Interv Psychiatry.* 2011;5(1):70–75.

34. Malla AK, Norman RM, Manchanda R, et al. Status of patients with first-episode psychosis after one year of phase-specific community-oriented treatment. *Psychiatr Serv.* 2002;53(3):458–463.

35. Pina-Camacho L, Garcia-Prieto J, Parellada M, et al. Predictors of schizophrenia spectrum disorders in early-onset first episodes of psychosis: a support vector machine model. *Ear Child Adolesc Psychiatry.* 2015;24(4):427–440.

36. Enderami A, Monesi FS, Zarghami M. One-year follow-up of patients with a diagnosis of first episode psychosis. *Mater Sociomed.* 2017;29(1):21–25.

37. Pina-Camacho L, Garcia-Prieto J, Parellada M, et al. Predictors of schizophrenia spectrum disorders in early-onset first episodes of psychosis: a support vector machine model. *Ear Child Adolesc Psychiatry.* 2015;24(4):427–440.

38. Rufino AC, Uchida RR, Vilela JA, Marques JM, Zuardi AW, Del-Ben CM. Stability of the diagnosis of first-episode psychosis made in an emergency setting. *Gen Hosp Psychiatry.* 2005;27(3):189–193.

39. Shah D, Chand P, Bandawar M, Benegal V, Murthy P. Cannabis induced psychosis and subsequent psychiatric disorders. *Asian J Psychiatry.* 2017;30:180–184.

40. Zandian A, Wingård L, Nilsson H, et al. Untargeted screening for novel autoantibodies with prognostic value in first-episode psychosis. *Transl Psychiatry.* 2017;7(7):e1177.

41. Rahm C, Cullberg J. Diagnostic stability over 3 years in a total group of first-episode psychosis patients. *Nord J Psychiatry.* 2007;61(3):189–193.

42. Salvatore P, Baldessarini RJ, Tohen M, et al. McLean-Harvard international first-episode project: two-year stability of DSM-IV diagnoses in 500 first-episode psychotic disorder patients. *J Clin Psychiatry.* 2009;70(4):458–466.

43. Sauras R, Keymer A, Alonso-Solis A, et al. Volumetric and morphological characteristics of the hippocampus are associated with progression to schizophrenia in patients with first-episode psychosis. *Ear Psychiatry.* 2017;45:1–5.

44. Schanzer BM, First MB, Dominguez B, Hasin DS, Caton CL. Diagnosing psychotic disorders in the emergency department in the context of substance use. *Psychiatr Serv.* 2006;57(10):1468–1473.

45. Thompson A, Marwaha S, Winsper C, et al. Short-term outcome of substance-induced psychotic disorder in a large UK first episode psychosis cohort. *Acta Psychiatr Scand.* 2016;134(4):321–328.

46. Leucht S, Rothe P, Davis JM, Engel RR. Equipercentile linking of the BPRS and the PANSS. *Eur Neuropsychopharmacol.* 2013;23(8):956–959.

47. Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Non-Randomized Studies in Meta-Analysis. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed February 17, 2019.

48. Borenstein M, Hedges L, Higgins J, Rothstein H. *Comprehensive Meta Analysis (CMA) Version 3.* Englewood, NJ: Biostat; 2013.

49. Aadamsoo K, Saluveer E, Külünarpuu H, Vasar V, Maron E. Diagnostic stability over 2 years in patients with acute and transient psychotic disorders. *Nord J Psychiatry.* 2011;65(6):381–388.

50. Alderson HL, Semple DM, Blayney C, Queirazza F, Chekuri V, Lawrie SM. Risk of transition to schizophrenia following first admission with substance-induced psychotic disorder: a population-based longitudinal cohort study. *Psychol Med.* 2017;47:2548–2555.

51. Amin S, Singh SP, Brewin J, Jones PB, Medley I, Harrison G. Diagnostic stability of first-episode psychosis. Comparison of ICD-10 and DSM-III-R systems. *Br J Psychiatry.* 1999;175:537–543.

52. Amini H, Alaghband-rad J, Omid A, et al. Diagnostic stability in patients with first-episode psychosis. *Australas Psychiatry.* 2005;13(4):388–392.

53. Arendt M, Mortensen PB, Rosenberg R, Pedersen CB, Waltoft BL. Familial predisposition for psychiatric disorder: comparison of subjects treated for cannabis-induced psychosis and schizophrenia. *Arch Gen Psychiatry.* 2008;65(11):1269–1274.

54. Bachmann S, Bottmer C, Schroder J. One-year outcome and its prediction in first-episode schizophrenia—a naturalistic study. *Psychopathology.* 2008;41(2):115–123.

55. Baldwin P, Browne D, Scully PJ, et al. Epidemiology of first-episode psychosis: illustrating the challenges across diagnostic boundaries through the Cavan-Monaghan study at 8 years. *Schizophr Bull.* 2005;31(3):624–638.

56. Björkenstam E, Björkenstam C, Hjern A, Reutjors J, Boden R. A five year diagnostic follow-up of 1,840 patients after a first episode non-schizophrenia and non-affective psychosis. *Schizophr Res.* 2013;150(1):205–210.

57. Bromet EJ, Kotov R, Fochtman L, et al. Diagnostic shifts during the decade following first admission for psychosis. *Am J Psychiatry.* 2011;168(11):1186–1194.

58. Castagnini A, Bertelsen A, Berrios GE. Incidence and diagnostic stability of ICD-10 acute and transient psychotic disorders. *Compr Psychiatry.* 2008;49(3):255–261.

59. Castro-Fornieles J, Baeza I, de la Serna E, et al. Two-year diagnostic stability in early-onset first-episode psychosis. *J Child Psychol Psychiatry.* 2011;52(10):1089–1098.

60. Chang WC, Pang SL, Chung DW, Chan SS. Five-year stability of ICD-10 diagnoses among Chinese patients presented with first-episode psychosis in Hong Kong. *Schizophr Res.* 2009;115(2-3):351–357.

61. Chen WL, Hsieh CH, Chang HT, Hung CC, Chan CH. The epidemiology and progression time from transient to permanent psychiatric disorders of substance-induced psychosis in Taiwan. *Addict Behav.* 2015;47:1–4.

62. Crebbin K, Mitford E, Paxton R, Turkington D. First-episode drug-induced psychosis: a medium term follow up study reveals a high-risk group. *Soc Psychiatry Psychiatr Epidemiol.* 2009;44(9):710–715.

63. Frugas D, de Castro MJ, Medina O, et al. Does diagnostic classification of early-onset psychosis change over follow-up? *Child Psychiatry Hum Dev.* 2008;39(2):137–145.

64. Haahr U, Friis S, Larsen TK, et al. First-episode psychosis: diagnostic stability over one and two years. *Psychopathology.* 2008;41(5):322–329.

65. Heslin M, Lomas B, Lappin JM, et al. Diagnostic change 10 years after a first episode of psychosis. *Psychol Med.* 2015;45(13):2757–2769.

66. Jarbin H, von Knorring AL. Diagnostic stability in adolescent onset psychotic disorders. *Ear Child Adolesc Psychiatry.* 2003;12(1):15–22.
67. Kim JS, Baek JH, Choi JS, Lee D, Kwon JS, Hong KS. Diagnostic stability of first-episode psychosis and predictors of diagnostic shift from non-affective psychosis to bipolar disorder: a retrospective evaluation after recurrence. *Psychiatry Res*. 2011;188(1):29–33.

68. Kingston T, Scully PJ, Browne DJ, et al. Diagnostic trajectory, interplay and convergence/divergence across all 12 DSM-IV psychotic diagnoses: 6-year follow-up of the Cavan-Monaghan First Episode Psychosis Study (CAMFEPS). *Psychol Med*. 2013;43(12):2523–2533.

69. Komuravelli A, Poole R, Higgo R. Stability of the diagnosis of first-episode drug-induced psychosis. *The Psychiatrist* 2011;35(6):224–227.

70. Marneros A, Pillmann F, Haring A, Balzuweit S, Blöink R. What is schizophrenic in acute and transient psychotic disorder? *Schizophr Bull*. 2003;29(2):311–323.

71. Mauri MC, Di Pace C, Reggiari A, Paletta S, Colasanti A. Primary psychosis with comorbid drug abuse and drug-induced psychosis: diagnostic and clinical evolution at follow up. *Asian J Psychiatr*. 2017;29:117–122.

72. Medhus S, Rognli EB, Gossop M, Holm B, Morland J, Bramness JG. Amphetamine-induced psychosis: transition to schizophrenia and mortality in a small prospective sample. *Am J Addict*. 2015;24(7):586–589.

73. Narayanawamy JC, Shamugam VH, Ravendranathan D, Viswanath B, Muralidharan K. Short-term diagnostic stability of acute psychosis: data from a tertiary care psychiatric center in South India. *Indian J Psychiatr Med*. 2012;34(2):176–178.

74. Pillmann F, Haring A, Balzuweit S, Blöink R, Marneros A. The concordance of ICD-10 acute and transient psychosis and DSM-IV brief psychotic disorder. *Psychol Med*. 2002;32(3):525–533.

75. Poon JY, Leung CM. Outcome of first-episode acute and transient psychotic disorder in Hong Kong Chinese: a 20-year retrospective follow-up study. *Nord J Psychiatry*. 2017;71(2):139–144.

76. Pope MA, Joober R, Malla AK. Diagnostic stability of first-episode psychotic disorders and persistence of comorbid psychiatric disorders over 1 year. *Can J Psychiatry*. 2013;58(10):588–594.

77. Rusaka M, Rancâns E. First-episode acute and transient psychotic disorder in Latvia: a 6-year follow-up study. *Nord J Psychiatry*. 2014;68(1):24–29.

78. Rusaka M, Rancans E. A prospective follow-up study of first-episode acute transient psychotic disorder in Latvia. *Ann Gen Psychiatry* 2014;13:4.

79. Schimmelmann BG, Conus P, Edwards J, McGorry PD, Lambert M. Diagnostic stability 18 months after treatment initiation for first-episode psychosis. *J Clin Psychiatry*. 2005;66(10):1239–1246.

80. Schwartz JE, Fennig S, Tanenberg-Karant M, et al. Congruence of diagnoses 2 years after a first-admission diagnosis of psychosis. *Arch Gen Psychiatry*. 2000;57(6):593–600.

81. Shinn AK, Bolton KW, Karmacharya R, et al. McLean OnTrack: a translational program for early intervention in first-episode psychosis. *Early Interv Psychiatry*. 2017;11(1):83–90.

82. Singal A, Bhat PS, Srivastava K, Prakash J. The study of primary psychotic disorders with concurrent substance abuse in terms of their diagnostic stability. *Indian J Psychiatry*. 2015;57(3):224–228.

83. Singh SP, Burns T, Amin S, Jones PB, Harrison G. Acute and transient psychotic disorders: precursors, epidemiology, course and outcome. *Br J Psychiatry*. 2004;185:452–459.

84. Subramaniam M, Pek E, Verma S, Chan YH, Chong SA. Diagnostic stability 2 years after treatment initiation in the early psychosis intervention programme in Singapore. *Aust N Z J Psychiatry*. 2007;41(6):495–500.

85. Suda K, Hayashi N, Hiraga M. Predicting features of later development of schizophrenia among patients with acute and transient psychotic disorder. *Psychiatry Clin Neurosci*. 2005;59(2):146–150.

86. Veen ND, Selten JP, Schols D, et al. Diagnostic stability in a Dutch psychosis incidence cohort. *Br J Psychiatry*. 2004;185:460–464.

87. Whitty P, Clarke M, McTigue O, et al. Diagnostic shift from non-affective psychosis to bipolar disorder? *Br J Psychiatry*. 2015;207(5):383–387.

88. Wright HH, Cole EA, Batey SR, Hanna K. Phencyclidine-induced psychosis: eight-year follow-up of ten cases. *South Med J*. 1988;81(5):565–567.

89. Zhang-Wong J, Beiser M, Bean G, Iacono WG. Five-year course of schizophreniform disorder. *Psychiatry Res*. 1995;59(1-2):109–117.

90. Naz B, Bromet EJ, Mojtabai R. Distinguishing between first-admission schizophreniform disorder and schizophrenia. *Schizophr Res*. 2003;62(1-2):51–58.

91. Sara G, Burgess P, Malhi GS, Whiteford H, Hall W. Differences in associations between cannabis and stimulant disorders in first admission psychosis. *Schizophr Res*. 2013;147(2-3):216–222.

92. Lambert M, Conus P, Lubman DI, et al. The impact of substance use disorders on clinical outcome in 643 patients with first-episode psychosis. *Acta Psychiatr Scand*. 2005;112(2):141–148.

93. Gage SH, Hickman M, Zammit S. Association between cannabis and psychotic disorders: epidemiologic evidence. *Biol Psychiatry*. 2016;79(7):549–556.

94. Lappin JM, Sara GE, Farrell M. Methamphetamine-related psychosis: an opportunity for assertive intervention and prevention. *Addiction*. 2017;112(6):927–928.

95. Wade D, Harrigan S, McGorry PD, Burgess PM, Whelan G. Impact of severity of substance use disorder on symptomatic and functional outcome in young individuals with first-episode psychosis. *J Clin Psychiatry*. 2007;68(5):767–774.

96. Sara GE, Burgess PM, Malhi GS, Whiteford HA, Hall WC. Cannabis and stimulant disorders and readmission 2 years after first-episode psychosis. *Br J Psychiatry*. 2014;204(6):448–453.

97. Drake RE, McHugo GJ, Xie H, Fox M, Packard J, Helmstetter B. Ten-year recovery outcomes for clients with co-occurring schizophrenia and substance use disorders. *Schizophr Bull*. 2006;32(3):464–473.

98. Drake RE, Luciano AE, Mueser KT, et al. Longitudinal course of clients with co-occurring schizophrenia-spectrum and substance use disorders in urban mental health centers: a 7-year prospective study. *Schizophr Bull*. 2016;42(1):202–211.

99. Kendler KS, Ohlsson H, Sundquist J, Sundquist K. Prediction of onset of substance-induced psychotic disorder and its progression to schizophrenia in a Swedish national sample. *Am J Psychiatry*. 2019;176(9):711–719.

100. Hall W, Degenhardt L. Cannabis and the increased incidence of psychotic disorders: systematic review-based meta-analyses: a systematic review of empirical studies. *Int J Technol Assess Health Care*. 2012;28(2):138–144.