TECHNICAL COMMENTARY

Drug and alcohol use

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Introduction

Drug and alcohol misuse, abuse or dependence are concerns for people with schizophrenia due to the association with poorer clinical and social outcomes including high rates of suicide, HIV, homelessness, aggression and incarceration. Moreover, substance use places additional burden on patients, families, psychiatric services, and government resources due to high rates of treatment non-adherence and relapse[1]. This topic covers rates of comorbid substance use in people with schizophrenia. For treatments for comorbid substance use, please see the topic; 'all treatments for dual diagnosis'. For the effects of substance use on the course and outcome of the disorder, please see the topic; 'Illness Course and Outcome – drug and alcohol use'.

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2000 that report results separately for people with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder or first episode schizophrenia. Reviews were identified by searching the databases MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO and the Cochrane library. Hand searching reference lists of identified reviews was also conducted. When multiple copies of reviews were found, only the most recent version was included. Reviews with pooled data were given priority for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis[2]. Reviews rated as having less than 50% of items checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate, low or very low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)[3]. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

Results

We found eight systematic reviews that met our inclusion criteria[4-11].

- Moderate quality evidence suggests the lifetime prevalence rates of any illicit drug misuse, abuse or dependence range from

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17% in rehabilitation and long-term settings to 70% in community health settings**.** Any lifetime substance use, particularly cannabis, is associated with an earlier age of onset of psychosis.

- Moderate quality evidence suggests the lifetime prevalence rates of alcohol misuse, abuse or dependence in people with schizophrenia range from 29% in rehabilitation and long-term settings to 75% in community health settings. Prevalence is higher in studies using DSM-III-R diagnostic criteria compared to studies using DSM-IV, ICD-9 or ICD-10. Prevalence is higher in samples aged 30 to 40 years compared to other age groups, and in studies published between 1990 and 1995 compared to earlier publications.
- Moderate quality evidence suggests prevalence of any cannabis use in first episode psychosis patients is around 33-38%, and low to moderate quality evidence suggests lifetime prevalence of cannabis use disorders in people with schizophrenia is around 27%, with current prevalence around 16%. Prevalence is higher in males compared to females, in people under 30 years of age compared to people over 30 years of age, and in patients with first episode schizophrenia compared to patients with chronic schizophrenia. The initiation of cannabis use is around 6-7 years prior to the onset of psychosis, and continuation of cannabis use declines after treatment.
- Moderate quality evidence suggests the rate of stimulant use disorders in people with psychosis is around 9%. Studies including patients with affective psychosis, inpatients, cannabis users, and those from USA and Australia reported the highest rates of stimulant use.

Carra G, Johnson S

Variation in rates of comorbid substance use in psychosis between mental health settings and geographical areas in the UK. A systematic review

Social Psychiatry and Psychiatric Epidemiology 2009; 44: 429-447

View review abstract online

Comparison	**Prevalence of drug and alcohol misuse in people with schizophrenia in the UK.**
Summary of evidence	**Moderate quality evidence (mostly large samples, direct, unable to assess consistency or precision) suggests the lifetime prevalence rates of alcohol misuse, abuse or dependence range from 29% in rehabilitation and long-term settings to 75% in community health settings. Lifetime prevalence rates of drug misuse, abuse or dependence range from 17% in rehabilitation and long-term settings to 70% in community health settings.**

Alcohol use – misuse, abuse or dependence

Community mental health teams;

Lifetime prevalence: 1 study, N = 82, 75%

Current prevalence: 1 study, N = 851, 7%

1 year prevalence: 2 studies, N = 453, 25 - 32%

6 month prevalence: 2 studies, N = 382, 12 - 20%

Forensic settings;

Lifetime prevalence: 1 study, N = 63, 62%

Current prevalence: 2 studies, N = 964, 6 - 42%

1 year prevalence: 2 studies, N = 1,159, 2.3 - 37%

Crisis resolution teams and inpatient wards;

Current prevalence: 1 study, N = 200, 49%

1 year prevalence: 1 study, N = 57, 9%

6 month prevalence: 1 study, N = 342, 21%

Assertive outreach teams;

Current prevalence: 2 studies, N = 341, 24 - 48%

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1 year prevalence: 1 study, N = 1,369, 26 - 45% 6 month prevalence: 2 studies, N = 420, 16 - 29% *Early intervention services;* Lifetime prevalence: 2 studies, N = 275, 27 - 43% *Catchment areas and GPs;* Lifetime prevalence: 2 studies, N = 668, 15 - 39% 1 year prevalence: 2 studies, N = 1,685, 7- 24% *Rehabilitation and long-term settings;* Lifetime prevalence: 1 study, N = 185, 29% 1 year prevalence: 1 study, N = 588, 3% 6 month prevalence: 1 study, N = 185, 11 - 18% *Addiction services;* Current prevalence: 1 study, N = 368, 6% 1 year prevalence: 1 study, N = 282, 9% 6 month prevalence: 1 study, N = 342, 12%
Drug use – misuse, abuse or dependence
Community mental health teams; Lifetime prevalence: 2 studies, N = 124, 35 - 70% Current prevalence: 1 study, N = 851, 9% 1 year prevalence: 2 studies, N = 453, 16 - 30% 6 month prevalence: 2 studies, N = 382, 12 - 13% *Early intervention services;* Lifetime prevalence: 2 studies, N = 275, 68% for all drugs, 51% cannabis Current prevalence: 3 studies, N = 579, 19 - 35% 1 year prevalence: 1 study, N = 51, 24% *Forensic settings;* Lifetime prevalence: 1 study, N = 63, 62% Current prevalence: 2 studies, N = 964, 6-75% for all drugs, 30% stimulants, 18% opiates 1 year prevalence: 2 studies, N = 1,159, 3.3-15% for all drugs, 35% stimulants, 42% heroin, 19% cannabis, 17 amphetamines, 29% cocaine *Crisis resolution teams and inpatient wards;* Lifetime prevalence: 2 studies, N = 315, 58% for all drugs, 71% cannabis

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Current prevalence: 7 studies, N = 1,217, 21-49% for all drugs, 39-60% cannabis 6 month prevalence: 1 study, N = 342, 33% *Assertive outreach teams;* Current prevalence: 2 studies, N = 341, 29 - 48% 1 year prevalence: 1 study, N = 1,369, 26 - 45% 6 month prevalence: 2 studies, N = 420, 20 - 29% *Catchment areas and GPs;* Lifetime prevalence: 2 studies, N = 668, 15 - 19% 1 year prevalence: 3 studies, N = 1,001,685, 6 - 24% *Rehabilitation and long-term settings;* Lifetime prevalence: 1 study, N = 185, 17% 1 year prevalence: 1 study, N = 588, 7% for all drugs, 5% cannabis, 1% ecstasy, 1% stimulant and 2% sedatives 6 month prevalence: 1 study, N = 185, 4 - 10%
Any substance use – misuse, abuse or dependence
Crisis resolution teams and inpatient wards; Current prevalence: 5 studies, N = 1,071, 21 - 49% *Early intervention services;* Current prevalence: 1 study, N = 304, 19% 1 year prevalence: 1 study, N = 51, 24% *Community mental health teams;* Current prevalence: 1 study, N = 1,271, 18%

Consistency in results	Unable to assess
Precision in results	Unable to assess
Directness of results	Direct

Curran C, Byrappa N, McBride A

Stimulant psychosis: Systematic review

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British Journal of Psychiatry 2004; 185: 196-204 View review abstract online	
Comparison	**Characteristics of people with schizophrenia who use cocaine vs. people with schizophrenia who do not use cocaine.**
Summary of evidence	**Low quality evidence (small sample, direct, unable to assess precision or consistency) is unclear of the effects of cocaine use in schizophrenia.**
Age at onset, hospitalization and symptoms	
2 case-control studies (N = 79) found a younger age of onset/first admission in people with schizophrenia who use cocaine compared to people with schizophrenia who do not use cocaine. 1 study (N = 43) found fewer negative symptoms, and 1 study (N = 62) found increased hallucinations in people with schizophrenia who use cocaine. 1 study (N = 70) found lower education and increased prior hospitalisation rates in people with schizophrenia using cocaine compared to people with schizophrenia who use cocaine.	
Consistency in results	Unable to assess
Precision in results	Unable to assess
Directness of results	Direct

Koskinen J, Löhönen J, Koponen H, Isohanni M, Miettunen J

Prevalence of alcohol use disorder in schizophrenia – a systematic review and meta-analysis

Acta Psychiatrica Scandinavica 2009; 120: 85-96

View review abstract online

Comparison	**Prevalence of Alcohol Use Disorder (AUD) in people with schizophrenia.**

Summary of evidence	**Moderate to low quality evidence (large overall sample, direct, inconsistent, unable to assess precision) suggests overall AUD prevalence in people with schizophrenia is around 18%. Prevalence is higher in studies using DSM-III-R diagnostic criteria compared to DSM-IV, ICD-9 or ICD-10, in samples aged 30 to 40 compared to other age groups, and in studies published between 1990 and 1995 compared to earlier publications.**

Alcohol Use Disorder (AUD) prevalence

Overall AUD prevalence: 60 studies, N = 60,317, median = 17.8%, range 1.1% to 57.0%

Authors report significant heterogeneity ($p < 0.001$)

Lifetime total: 47 studies, median = 20.6%, range 1.3% to 57.0%

Lifetime abuse: 19 studies, median = 13.5%, range 1.5% to 47.1%

Lifetime dependence: 10 studies, median = 18.7%, range 3.8% to 46.9%

Current total: 18 studies, median = 9.4%, range 1.1% to 38.8%

Current abuse: 9 studies, median = 4.6%, range 1.1% to 38.8%

Current dependence: 4 studies, median = 11.4%, range 5.9% to 23.4%

Significantly higher total AUD prevalence in studies using DSM-III-R diagnostic criteria compared to studies using DSM-IV, ICD-9 or ICD-10 ($p < 0.001$);

DSM-III-R: 21 studies, median = 32.3%, range 1.1% to 57.0%

DSM-IV: 23 studies, median = 16.1%, range 1.9% to 47.1%

ICD-9: 5 studies, median = 10.3%, range 2.6% to 23.7%

ICD-10: 5 studies, median = 5.9%, range 3.4% to 9.1%

Significantly higher lifetime AUD prevalence in people with schizophrenia aged 30-39 years compared to the younger or older age groups ($p = 0.01$);

Lifetime AUD < 30 years: 7 studies, median = 11.0%, range 1.9% to 32.3%

Lifetime AUD 30-40 years: 26 studies, median = 24.0%, range 1.3% to 57.0%

Lifetime AUD > 40 years: 8 studies, median = 16.8%, range 2.5% to 47.1%

No significant differences in current AUD prevalence ($p = 0.23$);

Current AUD below 30 years: 3 studies, median = 8.0%, range 1.1% to 22.0%

Current AUD 30-40 years: 7 studies, median = 10.1%, range 1.4% to 24.5%

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Current AUD over 40 years: 5 studies, median = 10.9%, range 5.9% to 38.8% *Significantly higher total AUD prevalence in studies published from 1990 to 1995 compared to studies published from 1960 to 1989 (p = 0.01);* 1960-1989: 6 studies, median = 19%, range 12% to 30% 1990-1995: 10 studies, median = 36%, range 21% to 54%	
Consistency in results	Inconsistent for total prevalence, unable to assess subgroup analyses
Precision in results	Unable to assess
Directness of results	Direct

Koskinen J, Löhönen J, Koponen H, Isohanni M, Miettunen J

Rate of cannabis use disorders in clinical samples of patients with schizophrenia: A meta-analysis

Schizophrenia Bulletin 2010; 36(6): 1115-1130

View review abstract online

Comparison	**Prevalence of Cannabis Use Disorder (CUD) in people with schizophrenia.**
Summary of evidence	**Moderate to low quality evidence (large sample, direct, inconsistent, unable to assess precision) suggests the median lifetime CUD prevalence in people with schizophrenia is around 27%, with current prevalence rates being around 16%. Prevalence is higher in males compared to females, in people under 30 years compared to people over 30 years of age, and in people with first episode schizophrenia compared to people with chronic schizophrenia.**
Cannabis Use Disorder (CUD) prevalence	
Total prevalence: 35 studies, (N = 5,572), median = 27.0%, range 0.0% to 65.5% Authors report significant heterogeneity (p < 0.001) Lifetime prevalence: 28 studies, median = 27.1%, IQR 12.% to 38.5% Current prevalence: 10 studies, median = 16.0%, IQR 8.6% to 28.6%	

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Significantly higher current (p = 0.02) and lifetime (p = 0.02) prevalence of CUD in younger people with schizophrenia (< 30 years) compared to older people with schizophrenia (≥ 30 years);

< 30 years lifetime CUD: 6 studies, median = 45.0%, range 13.7% to 65.6%

< 30 years current CUD: 2 studies, median = 38.5%, range 28.6% to 48.3%

≥ 30 years lifetime CUD: 18 studies, median = 17.9%, range 0.0% to 44.4%

≥ 30 years current CUD: 6 studies, median = 16.0%, range 8.2% to 53.5%

Significantly higher prevalence of CUD in samples with a higher proportion of males (p = 0.002);

> 67% males: 18 studies, median = 33.8%, range 4.9% to 65.6%

< 67% males: 12 studies, median = 13.2%, range 0.0% to 41.0%

Significantly higher lifetime (p = 0.001), but not current (p = 0.09) CUD prevalence in first-episode schizophrenia compared to chronic schizophrenia;

First-episode lifetime CUD: 9 studies, median = 44.4%, range 13.7% to 65.6%

First-episode current CUD: 3 studies, median = 38.6%, range 8.2% to 48.3%

Long-term lifetime CUD: 12 studies, median = 12.2%, range 0.0% to 36.0%

Long-term current CUD: 4 studies, median = 22.0%, range 12.9% to 53.5%

No differences in prevalence rates in studies using difference diagnostic measures, using different samples, or from different locations (all p > 0.05);

ICD-10: 3 studies, median = 30.0%, range 12.0% to 45.6%

DSM-III-R: 12 studies, median = 27%.1, range 0.0% to 65.6%

DMS-IV: 19 studies, median = 18.5%, range 2.0% to 53.5%

Inpatients: 15 studies, median = 31.3%, range 8.6% to 53.5%

Outpatients: 6 studies, median = 25.2%, range 4.9% to 52.8%

Europe: 15 studies, median = 18.5%, range 0.0% to 52.8%

North America: 11 studies, median = 27.2%, range 6.3% to 48.0%

Consistency in results	Inconsistent for total prevalence, unable to assess subgroup analyses
Precision in results	Unable to assess
Directness of results	Direct

Large M, Sharma S, Compton MT, Slade T, Nielssen O

Cannabis use and earlier onset of psychosis

Archives of General Psychiatry 2011; 68(6): 555-561

View review abstract online

Comparison	**Age at onset in people with schizophrenia who have comorbid substance use, compared to people with schizophrenia and no substance use.**
Summary of evidence	**Moderate quality evidence (inconsistent, mostly precise, direct) suggests lifetime substance use, particularly cannabis, is associated with an earlier age of onset of psychosis.**

Age at onset

Overall (any substance)

Patients who had used any substance had a significantly younger age of onset than those who had not used any substances;

131 studies, N = 22,519, d = -0.264, 95% CI -0.453 to -0.075, p = 0.006, I^2 = 78.1%, p < 0.001

No significant differences when males and females were analysed separately;

Females: 13 studies, d = -0.365, 95%CI -0.622 to -0.108

Males 24 studies, d = -0.325, 95%CI -0.513 to -0.138

No significant difference between heavy and light substance use (p = 0.42);

Light/discontinued use: 10 studies, d = -0.301, 95%CI -0.522 to -0.08

Heavy/continuous use: 10 studies, d = -0.428, 95%CI -0.644 to -0.211

Lifetime cannabis use

Patients who had used cannabis had a significantly younger age of onset than those who had not used cannabis'

41 studies, d = -0.414, 95% CI -0.526 to -0.301, p < 0.001

Alcohol use

There was no significant differences in age of onset between patients with and without alcohol use;

22 studies, d = -0.038, 95% CI -0.196 to 0.120, p = 0.64

Consistency in results	Inconsistent
Precision in results	Mostly precise
Directness of results	Direct

Myles H, Myles N, Large M

Cannabis use in first episode psychosis: Meta-analysis of prevalence, and the time course of initiation and continued use

Australian & New Zealand Journal of Psychiatry 2015; 50(3): 208-219

View review abstract online

Comparison	**Prevalence, initiation and continuation of cannabis use in people with first-episode psychosis.**
Summary of evidence	**Moderate quality evidence (inconsistent, precise, direct) suggests prevalence of cannabis use in first episode psychosis patients is around 33-38%. Initiation of cannabis use is around 6-7 years prior to onset of psychosis, and continuation of cannabis use declines after treatment.**

Cannabis use

Prevalence

About one third of people with first episode psychosis were using cannabis at the time;

35 studies, prevalence rate 33.7%, 95%CI 29% to 38%, I^2 = 92.1%, $p < 0.001$

Sub-group analyses found a significant difference in prevalence rates according to geographical region, with the highest rate of cannabis use recorded in studies from Australia, followed by Europe, the United Kingdom and North America. Comparatively low rates of cannabis use were recorded in studies conducted in the years prior to 1995, peak rates were in 1995–2000, followed by a steady decline in 2000–2005, 2005–2010 and after 2010. There were no differences in results according to sex or age. Sensitivity analysis removing 5 samples that may have biased the results increased the prevalence estimate to 38.0% (95%CI 33.0% to 43.3%).

Initiation

A large effect shows regular cannabis use begins around 6.3 years before age at onset of psychosis;

Earlier vs. later initiation: 10 studies, SMD = 1.56, 95%CI 1.40 to 1.72, I^2 = 49.6%, p = 0.04 Sensitivity analysis removing 3 samples that may have biased the results increased the SMD to 1.65 (95%CI 1.48 to 1.82), equating to an increased initiation interval of 9 months. Continuation *A medium to large effect shows continued cannabis use reduces from baseline between 2 months and 10 years of follow-up after the first episode of psychosis;* 19 studies, OR 0.56, 95%CI 0.40 to 0.79, I^2 = 84.2%, p < 0.001 Meta-regression found that studies with a higher proportion of users at baseline tended to have a greater reduction of use at follow up. Sub-group analyses found no differences in results according to length of follow-up. Sensitivity analysis removing 1 sample that may have biased the result resulted in an OR of 0.65 (95%CI 0.45 to 0.91).

Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

Sara GE, Large MM, Matheson SL, Burgess PM, Malhi GS, Whiteford HA, Hall WD

Stimulant use disorders in people with psychosis: A meta-analysis of rate and factors affecting variation

Australian & New Zealand Journal of Psychiatry 2015; 49(2): 106-117

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Comparison	**Rates of stimulant use by people with psychosis.**
Summary of evidence	**Moderate quality evidence (inconsistent, unable to assess precision, direct, large sample) suggests the rate of stimulant use disorders in people with psychosis is around 9%. Between-study variance could be explained by studies that included affective psychosis, inpatients, cannabis users and studies from USA and Australia as these factors were related to higher stimulant use.**
Stimulant use disorders	
Sixty-four studies provided estimates of lifetime or recent stimulant use disorders in 22,500 people with psychosis.	

The pooled rate of stimulant use disorders was 8.9%, 95%CI 7.4% to 10.5%, I^2 91.0%. Adjustment for possible publication bias resulted in a pooled estimate of 10.5%, 95%CI 8.9% to 12.4%. Higher rates of stimulant use disorders were reported in studies of affective psychosis, studies from inpatient settings, studies from the USA and Australia, studies with higher rates of cannabis disorder. A multiple meta-regression analysis suggested these factors explained 68% of between-study variance. Rates of stimulant use disorder were stable over time, and unrelated to age, sex, stage of psychosis, type of stimulant or study methodology.	
Consistency in results	Inconsistent, however the multiple-regression analysis model explained 68% of between study variance
Precision in results	Unable to assess formally (not standardised CI), but appears precise
Directness of results	Direct

Thornton LK, Baker AL, Johnson MP, Lewin TJ

Attitudes and perceptions towards substances among people with mental disorders: a systematic review

Acta Psychiatrica Scandinavica 2012; 126: 87-105

View review abstract online

Comparison	**Attitudes towards substances in people with schizophrenia.**
Summary of evidence	**Low quality evidence (unable to assess consistency or precision, direct) is unclear as to the key reasons for substance use in people with schizophrenia.**
Attitudes to substances	
Drugs (predominantly cannabis) and alcohol 7 studies (N = 673) reported that people with schizophrenia who used substances cited reasons for use including: relaxation, pleasure, intoxication, depression/dysphoria relief, social interaction, and to relieve hallucinations/suspiciousness. Smoking 5 studies (N = 959) reported that people with schizophrenia who smoked cited reasons for use including: relaxation/stress reduction, dysphoria relief, sociability, craving/addiction. 1 study (N = 298) reported reasons for quitting included: self-control, health concerns, social	

influence.	
Consistency in results	Unable to assess
Precision in results	Unable to assess
Directness of results	Direct

Explanation of acronyms

AUD = Alcohol Use Disorder, CI = Confidence Interval, CUD = Cannabis Use Disorder, *d* = Cohen's *d* and *g* = Hedges' *g* = standardised mean differences (see below for interpretation of effect sizes), DSM = Diagnostic and Statistical Manual of Mental Disorders by the American Psychiatry Association, GP = general practitioner, ICD = International Classification of Disease by World Health Organisation, IQR = inter-quartile range, N = number of participants, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), Q = Q statistic for the test of heterogeneity, UK = United Kingdom, vs = versus, z = z-transformation of the effect size, χ^2 = chi-squared test of heterogeneity

Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small[12].

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† Different effect measures are reported by different reviews.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect[12].

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2[13]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios

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measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They can provide an indirect indication of prediction, but do not confirm causality due to possible and often unforseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (*b*) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

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‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula[12];

$$I^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

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§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, these criteria should be relaxed[14].

‖ Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and/or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available and is therefore inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

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References

1. Cleary M, Hunt G, Matheson S, Siegfried N, Walter G. Psychosocial interventions for people with both severe mental illness and substance misuse. *Cochrane Database of Systematic Reviews*. 2008; (1): CD001088.
2. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMAGroup. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *British Medical Journal*. 2009; **151**(4): 264-9.
3. GRADEWorkingGroup. Grading quality of evidence and strength of recommendations. *British Medical Journal*. 2004; **328**: 1490.
4. Myles H, Myles N, Large M. Cannabis use in first episode psychosis: Meta-analysis of prevalence, and the time course of initiation and continued use. *Australian and New Zealand Journal of Psychiatry*. 2015; **50**(3): 208-19.
5. Carra G, Johnson S. Variations in rates of comorbid substance use in psychosis between mental health settings and geographical areas in the UK. A systematic review. *Social Psychiatry & Psychiatric Epidemiology*. 2009; **44**(6): 429-47.
6. Curran C, Byrappa N, McBride A. Stimulant psychosis: systematic review. *British Journal of Psychiatry*. 2004; **185**: 196-204.
7. Koskinen J, Lohonen J, Koponen H, Isohanni M, Miettunen J. Prevalence of alcohol use disorders in schizophrenia - A systematic review and meta-analysis. *Acta Psychiatrica Scandinavica*. 2009; **120**(2): 85-96.
8. Koskinen J, Löhönen J, Koponen H, Isohanni M, Miettunen J. Rate of Cannabis Use Disorders in Clinical Samples of Patients With Schizophrenia: A Meta-analysis. *Schizophrenia Bulletin*. 2010; **36**(6): 1115-30.
9. Large M, Sharma S, Compton MT, Slade T, Nielssen O. Cannabis use and earlier onset of psychosis: a systematic meta-analysis. *Archives of General Psychiatry*. 2011; **68**(6): 555-61.
10. Thornton LK, Baker AL, Johnson MP, Lewin TJ. Attitudes and perceptions towards substances among people with mental disorders: A systematic review. *Acta Psychiatrica Scandinavica*. 2012; **126**(2): 87-105.
11. Sara GE, Large MM, Matheson SL, Burgess PM, Malhi GS, Whiteford HA, Hall WD. Stimulant use disorders in people with psychosis: A meta-analysis of rate and factors affecting variation. *Australian and New Zealand Journal of Psychiatry*. 2015; **49**(2): 106-17.
12. CochraneCollaboration. Cochrane Handbook for Systematic Reviews of Interventions. 2008: Accessed 24/06/2011.
13. Rosenthal JA. Qualitative Descriptors of Strength of Association and Effect Size. *Journal of Social Service Research*. 1996; **21**(4): 37-59.
14. GRADEpro. [Computer program]. Jan Brozek, Andrew Oxman, Holger Schünemann. *Version 32 for Windows*. 2008.