

Schizophrenia diagnosis

Introduction

Diagnostic scales are widely used within clinical practice and research settings to ensure consistency of illness ratings. These scales have been extensively validated and provide a set of criteria that is used to define and diagnose an illness. Two key examples include the American Psychiatric Association's *Diagnostic and Statistical Manual* (DSM) and the World Health Organisation's *International Classification of Diseases* (ICD), which both provide a comprehensive definition of schizophrenia. Both the DSM and ICD criteria are regularly updated, and the most recent versions are the DSM-5 and the ICD-11.

For a DSM-5 diagnosis of schizophrenia, at least two symptoms need to have been present for at least six months, and for a significant portion of time over a one-month period. Symptoms include delusions, hallucinations, disorganized speech and behaviour, catatonic behaviour, and negative symptoms such as diminished emotional expression, poverty of speech, and lack of purposeful action. At least one symptom of delusions, hallucinations, or disorganized speech needs to be present, and there also needs to be significant social or occupational dysfunction.

For an ICD-11 diagnosis of schizophrenia, at least two symptoms must be present, including positive, negative, depressive, manic, psychomotor, and cognitive deficits. One core symptom needs to be present, including delusions, thought insertion/thought withdrawal, hallucinations, and thought disorder. Symptoms should have been present for most of the time during a period of at least one month.

Method

We have included only systematic reviews with detailed literature search, methodology, and inclusion/exclusion criteria that were published in full text, in English, from the year 2000. Reviews were identified by searching the databases MEDLINE, EMBASE, and

PsycINFO. Reviews with pooled data are prioritized for inclusion. Reviews reporting fewer than 50% of items on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA¹) checklist have been excluded from the library. The evidence was graded guided by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach². 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 17 systematic reviews that met our inclusion criteria³⁻¹⁹.

- Moderate to high quality evidence suggests the DSM-III, DSM-III-R or DSM-IV diagnostic criteria assigns significantly more males with psychosis to a schizophrenia diagnosis, rather than any other psychosis diagnosis, compared to the ICD-9, which shows no differences in gender distribution across diagnoses.
- Moderate quality evidence suggests moderate predictive value and good kappa agreement for schizophrenia and schizophrenia spectrum diagnoses, good predictive value, and kappa agreement for psychotic disorder, but poor predictive value and kappa agreement for schizoaffective disorder.
- Moderate to high quality evidence suggests better test-retest reliability for a diagnosis of schizophrenia than for a diagnosis of schizoaffective disorder, but lower test-retest reliability than for a diagnosis of bipolar disorder or unipolar depression.
- Moderate to high quality evidence suggests poorer interrater reliability for a diagnosis of schizoaffective disorder than for a diagnosis of schizophrenia, bipolar disorder, or unipolar depression.

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- Moderate quality evidence suggests excellent specificity (91%) and good sensitivity (71%) of latent semantic analysis in recognising a diagnosis of schizophrenia. Latent semantic analysis quantifies the degree of incoherence in language use.
- Moderate quality evidence suggests support vector machines combined with other machine learning techniques applied to neuroimaging data may assist with clinical diagnosis of schizophrenia. There were no differences in sensitivity ratings between deep and shallow (support vector) machine learning techniques.
- Moderate to high quality evidence suggests a significant association of increased deficit schizophrenia (predominately negative symptoms) vs. non-deficit schizophrenia in males, a finding that was not moderated by sampling method, diagnosis criteria, or duration of illness.
- Moderate quality evidence suggests Black people in the United States are more likely to be diagnosed with schizophrenia than White people in the United States. The effect size was largest in studies with more males, more White patients, more young patients, studies in hospital or military settings, and studies conducted in the Midwest, Southeast, National, or multistate USA. There were no differences in risk according to diagnostic method (structured vs. unstructured), DSM version (DSM-III or DSM-IV), or study year.
- Moderate to high quality evidence suggests the proportion of first-episode psychosis patients retaining a diagnosis of schizophrenia over time is around 90% and 72% for schizoaffective disorder. Diagnostic stability for schizophreniform disorder is 29% over time.
- Moderate quality evidence suggests the rate of a schizophrenia diagnosis following a diagnosis of schizophreniform disorder is around 65% (over 4 years). Following brief, atypical, or not otherwise specified psychoses, the rate of a schizophrenia

diagnosis is around 36%. Following a substance-induced psychosis, the rate of a schizophrenia diagnosis is around 25%. The rates were highest for cannabis, hallucinogens, and amphetamines, and lowest for opioids, alcohol, and sedatives.

Beauchamp G, Gagnon A

Influence of diagnostic classification on gender ratio in schizophrenia

Social Psychiatry and Psychiatric Epidemiology 2004; 39: 1017–1022

[View review abstract online](#)

Comparison	Assessment of the gender distribution in schizophrenia vs. other psychoses, depending on the diagnostic tool used.
Summary of evidence	Moderate to high quality evidence (consistent, imprecise, direct, large sample) suggests the DSM-III, DSM-III-R or DSM-IV diagnostic criteria assigns significantly more males with psychosis to a schizophrenia diagnosis, rather than any other psychosis diagnosis, compared to the ICD-9, which shows no differences in gender distribution across diagnoses.
Gender distribution	
<p>A male with psychosis is significantly more likely to obtain a diagnosis of schizophrenia than a female with psychosis.</p> <p>12 studies, N = 827, OR = 1.70, 95%CI 1.27 to 2.30, $p = 0.0003$, $Q_w = 11.1$, $p = 0.43$</p> <p>However, this finding depends on the diagnostic tool used as when the ICD-9 and DSM were analysed separately, only the DSM criteria assigned significantly greater proportions of males to a schizophrenia diagnosis.</p> <p>ICD-9: OR = 1.13, 95%CI 0.69 to 1.85 DSM: OR = 2.41, 95%CI 1.60 to 3.61 $Q_B = 5.7$, $p = 0.017$</p>	
Consistency in results[†]	Consistent
Precision in results[§]	Imprecise
Directness of results	Direct

Bracher-Smith M, Crawford K, Escott-Price V

Machine learning for genetic prediction of psychiatric disorders: a systematic review

Molecular Psychiatry 2021; 26(1): 70-9

[View review abstract online](#)

Comparison	Assessment of machine learning techniques from genetic studies of schizophrenia.
Summary of evidence	Moderate to low quality evidence (unclear sample size, inconsistent, unable to assess precision, direct) is unclear of the diagnostic usefulness of machine learning techniques of genetic data.
Accuracy	
7 genetic studies (N = unclear), accuracy ranged from AUC = 0.54 to 0.95 Authors reported that there was widespread high risk of bias.	
Consistency in results	Inconsistent
Precision in results	Unable to assess; no measure of precision is reported
Directness of results	Direct

Chang WC, Chan SSM, Chung DWS

Diagnostic Stability of Functional Psychosis: a Systematic Review

Hong Kong Journal of Psychiatry 2009; 19: 30-41

[View review abstract online](#)

Comparison	Assessment of the stability over time of schizophrenia diagnosis (the degree to which the diagnosis remains the same over subsequent clinical evaluations). Note: this review also reports on other psychoses, the results here are only reported for schizophrenia.
Summary of evidence	Moderate quality evidence (unable to assess consistency or precision, direct, large sample) suggests a schizophrenia

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	diagnosis is associated with reasonably high stability over subsequent evaluations (>70% consistency).
Diagnostic stability	
<p>12/14 studies reported over 70% consistency of a first-episode schizophrenia diagnosis, with 9/12 reporting over 90% consistency.</p> <p>11/14 studies reported over 70% consistency of a schizophrenia diagnosis. The remaining 3 studies reported considerable shift between schizophrenia, bipolar and schizoaffective disorder diagnoses.</p>	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Davis KAS, Sudlow CLM, Hotopf M

**Can mental health diagnoses in administrative data be used for research?
A systematic review of the accuracy of routinely collected diagnoses**

BMC Psychiatry 2016; 16: 263

[View review abstract online](#)

Comparison	Diagnostic integrity in administrative databases using ICD-10 vs. reference comparison (e.g., clinical chart or research diagnosis).
Summary of evidence	Moderate quality evidence (unable to assess consistency, appears imprecise, direct, large samples) suggests moderate predictive value and kappa agreement for schizophrenia and schizophrenia spectrum diagnoses, good predictive value, and kappa agreement for psychotic disorder, but poor predictive value and kappa agreement for schizoaffective disorder.
Diagnostic integrity	
<p><i>Moderate predictive value and kappa agreement for schizophrenia and schizophrenia spectrum diagnoses, good predictive value and kappa agreement for psychotic disorder, but poor predictive value and kappa agreement for schizoaffective disorder;</i></p> <p>Schizophrenia: 18 studies, N = 5,016, median PPV ~75% (range 40-100%), Kappa ~0.45 (range 0-72%).</p> <p>Schizophrenia spectrum (any non-affective psychosis, including schizophrenia): 13 studies, N = 2,662, median PPV ~85% (range 55-95%), Kappa ~0.45 (range 20-65%).</p>	

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<p>Psychotic disorder: 4 studies, N = 1,561, median PPV ~90% (range 85-100%), Kappa ~0.80 (range 35-90%).</p> <p>Schizoaffective disorder: 5 studies, N = 823, median PPV ~50% (range 10-58%), Kappa ~0.38 (range 10-45%).</p>	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Appears imprecise
Directness of results	Direct

de Boer JN, Voppel AE, Begemann MJH, Schnack HG, Wijnen F, Sommer IEC

Clinical use of semantic space models in psychiatry and neurology: A systematic review and meta-analysis

Neuroscience and Biobehavioral Reviews 2018; 93: 85-92

[View review abstract online](#)

Comparison	<p>Specificity and sensitivity of semantic space calculations for recognising people with a diagnosis of schizophrenia vs. people without a clinical diagnosis.</p> <p>Semantic space calculations quantify the degree of incoherence in spoken language using latent semantic analysis.</p> <p>Most of the sample included people with schizophrenia, and some studies included people with first-episode psychosis.</p>
Summary of evidence	<p>Moderate quality evidence (medium-sized sample, unable to assess consistency, appears precise, direct) suggests excellent specificity (91%) and good sensitivity (71%).</p>
Specificity and sensitivity	
<p><i>Excellent specificity and good sensitivity;</i></p> <p>4 studies, N = 298, specificity = 91%, 95%CI 0.87% to 0.93%</p> <p>4 studies, N = 298, sensitivity = 71%, 95%CI 0.63% to 0.78%</p>	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Appears precise
Directness of results	Direct

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De Filippis R, Carbone EA, Gaetano R, Bruni A, Pugliese V, Segura-Garcia C, De Fazio P

Machine learning techniques in a structural and functional MRI diagnostic approach in schizophrenia: A systematic review

Neuropsychiatric Disease and Treatment 2019; 15: 1605-27

[View review abstract online](#)

Comparison	<p>Assessment of machine learning techniques on functional and structural neuroimaging data as a diagnostic tool for schizophrenia.</p> <p>Machine learning techniques are most useful when analysing highly complex datasets. They include support vector machines which is a high-dimensional, pattern recognition, supervised learning algorithm. Other techniques include multivariate pattern analysis and random forest analysis.</p>
Summary of evidence	<p>Moderate quality evidence (large samples, unable to assess consistency, appears imprecise, direct) suggests support vector machines combined with other machine learning techniques applied to neuroimaging data may assist the clinical evaluation of schizophrenia.</p>
Accuracy	
<p>27 functional neuroimaging studies (N = 4,137), accuracy ranged from 41% to 99%</p> <p>9 structural neuroimaging studies (N = 1,767), accuracy ranged from 70% to 88%</p> <p>Authors reported that accuracy was greatest in studies using support vector machine plus other machine learning techniques, and that the prefrontal and temporal cortices appeared to be the most useful brain regions for diagnosis.</p>	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Appears imprecise for the functional studies.
Directness of results	Direct

Fusar-Poli P, Cappucciati M, Rutigliano G, Heslin M, Stahl D, Brittenden Z, Caverzasi E, McGuire P, Carpenter WT

Diagnostic Stability of ICD/DSM First Episode Psychosis Diagnoses: Meta-

analysis	
Schizophrenia Bulletin 2016; 42(6): 1395-406 View review abstract online	
Comparison	Diagnostic stability in people with first-episode psychosis using ICD or DSM over 4-5 years.
Summary of evidence	Moderate to high quality evidence (unable to assess consistency, precise, direct, large sample) suggests the proportion of first-episode psychosis patients retaining the diagnosis of schizophrenia over time is around 90% and 72% for schizoaffective disorder. Diagnostic stability for schizophreniform disorder is 29% over time.
Diagnostic stability	
<p>42 studies N = 14 484, follow-up average 4.5 years</p> <p><i>The proportion of first-episode psychosis patients retaining the diagnosis of schizophrenia over time is around 90% and 72% for schizoaffective disorder, but only 29% for schizophreniform disorder;</i></p> <p>Schizophrenia: 0.90, 95%CI 0.85 to 0.95 Schizoaffective disorder: 0.72, 95%CI 0.61 to 0.73 Schizophreniform disorder: 0.29, 95%CI 0.22 to 0.38</p> <p><i>Other diagnoses;</i></p> <p>All affective spectrum psychoses: 0.84, 95%CI 0.79 to 0.89 Substance-induced psychotic disorder: 0.66, 95%CI 0.51 to 0.81 Delusional disorder: 0.59, 95%CI 0.47 to 0.71 Acute and transient psychotic disorder/brief psychotic disorder: 0.56, 95%CI 0.62 to 0.60 Psychosis not otherwise specified: 0.36, 95%CI 0.27 to 0.45</p> <p>About 10% of patients with diagnosis of affective spectrum psychoses changed to schizophrenia spectrum psychoses over time.</p> <p>Moderator analyses revealed more recent studies and studies of inpatient (vs. mixed) settings had higher diagnostic instability over time. There was no effect on diagnostic stability according to patients' age, gender, substance abuse, baseline ICD-10 or DSM-IV diagnostic criteria, baseline functioning level and duration of follow-up.</p>	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Precise
Directness of results	Direct

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Linscott RJ, Allardyce J, van Os J

Seeking verisimilitude in a class: a systematic review of evidence that the critical clinical symptoms of schizophrenia are taxonic.

Schizophrenia Bulletin 2010; 26(4): 811-829

[View review abstract online](#)

Comparison	Assessment of the latent structure of the schizophrenia diagnosis: if the symptoms of schizophrenia can be organised into discrete (latent) classes vs. a dimensional (continuum) scale.
Summary of evidence	Low quality evidence (unclear sample size, appears inconsistent, unable to assess precision, direct) is unclear as to any latent structure underlying the schizophrenia diagnosis.
Latent classes	
<p>There was no consistent evidence from 24 studies to support a two-, three-, four-, five-, or six-class interpretation of a latent class structure of schizophrenia symptoms (e.g., positive, negative, disorganisation, affective).</p> <p>Fourteen analyses identified a two-class structure of schizophrenia; five analyses identified a three-class structure; six analyses identified a four-class structure; three analyses identified five classes; and two studies identified six latent classes.</p>	
Consistency in results	Appears imprecise.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Menezes N, Milovan E

First-episode psychosis: a comparative review of diagnostic evolution and predictive variables in adolescents versus adults

Canadian Journal of Psychiatry 2000; 45: 710-716

[View review abstract online](#)

Comparison	Assessment of the diagnostic stability over time of first-episode psychosis in adolescents and adults (the degree to which the
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	diagnosis remains the same over subsequent clinical evaluations).
Summary of evidence	Low quality evidence (unclear sample size, unable to assess consistency or precision, direct) is unable to ascertain any differences in stability of diagnosis of psychosis in adults compared to adolescents.
Diagnostic stability	
Four studies reported higher rates of misdiagnosis in adolescents compared to adults, and an overall high rate of diagnostic shift for psychosis. Two studies report a comparative stability of the schizophrenia diagnosis.	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Murrie B, Lappin J, Large M, Sara G

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

Schizophrenia Bulletin 2019; 46(5): 505-516

[View review abstract online](#)

Comparison	Diagnosis of schizophrenia following a diagnosis of schizophreniform, brief, atypical, not otherwise specified (NOS), or substance-induced psychoses.
Summary of evidence	Moderate quality evidence (large samples, inconsistent, mostly precise, direct) suggests the rate of a schizophrenia diagnosis following a diagnosis of schizophreniform disorder is around 65%. Following brief, atypical, or NOS psychoses, the rate of a schizophrenia diagnosis is around 36%. Following a substance-induced psychosis, the rate of a schizophrenia diagnosis is around 25%. The rates were highest for cannabis (34%), hallucinogens (26%), and amphetamines (22%), and lowest for opioids (12%), alcohol (10%), and sedatives (9%).
Diagnosis of schizophrenia	
<i>Diagnosis of schizophrenia at follow-up;</i>	

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<p>Schizophreniform: 20 estimates, N = 590, rate = 65%, 95%CI 57% to 72%, I² = 54%</p> <p>Brief, atypical and NOS: 34 estimates, N = 5,969, rate = 36%, 95%CI 30% to 43%, I² = 92%</p> <p>Substance induced: 25 estimates, N = 34,244, rate = 25%, 95%CI 18% to 35%, I² = 99%</p> <p>The rates were highest for cannabis (34%), hallucinogens (26%), and amphetamines (22%), and lowest for opioids (12%), alcohol (10%), and sedatives (9%).</p> <p>Mean follow-up period was 4 years.</p>	
Consistency in results	Inconsistent
Precision in results	Appears mostly precise.
Directness of results	Direct

<p><i>Olbert CM, Nagendra A, Buck B</i></p> <p>Meta-analysis of black vs. white racial disparity in schizophrenia diagnosis in the United States: Do structured assessments attenuate racial disparities?</p> <p>Journal of Abnormal Psychology 2018; 127: 104-15</p> <p>View review abstract online</p>	
Comparison	<p>Racial disparity (Black vs. White) in the diagnosis of schizophrenia.</p> <p>Studies primarily used the DSM-III or DSM-IV for diagnosis of schizophrenia.</p>
Summary of evidence	<p>Moderate quality evidence (large sample, inconsistent, imprecise, direct) suggests Black people in the United States are more likely to be diagnosed with schizophrenia than White people in the United States. The effect size was largest in studies with more males, more White patients, more young patients, studies in hospital or military settings, and studies conducted in the Midwest, Southeast, National, or multistate USA. There were no differences in risk according to diagnostic method (structured vs. unstructured), DSM version (DSM-III or DSM-IV), or study year.</p>
Racial disparity	
<p><i>A medium-sized, significant effect of greater rates of diagnosis of schizophrenia in Black individuals;</i></p> <p>52 studies, N = 2,099,506, OR = 2.42, 95%CI 1.59 to 3.66, p = 0.00003, I² = 98%, p < 0.001</p> <p>The effect size was largest in studies with more males, more White patients, more young patients,</p>	

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studies in hospital or military settings, and studies conducted in the Midwest, Southeast, National, or multistate USA.

There were no significant moderating effects of diagnostic method (structured vs. unstructured), DSM version, or study year.

Authors report there was little evidence of publication bias.

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

Quaak M, van de Mortel L, Thomas RM, van Wingen G

Deep learning applications for the classification of psychiatric disorders using neuroimaging data: Systematic review and meta-analysis

NeuroImage: Clinical 2021; 30

[View review abstract online](#)

Comparison	Assessment of deep vs. shallow machine learning (e.g., support vector) from functional and structural neuroimaging studies of schizophrenia.
Summary of evidence	Moderate to low quality evidence (unclear sample size, inconsistent, imprecise, direct) finds no difference in sensitivity between deep and shallow machine learning techniques.
Accuracy	
<p><i>No significant differences in sensitivity between deep and shallow machine learning;</i> 9 studies, difference in sensitivity = 0.086, 95%CI -0.558 to 0.729, $p = 0.794$ A model is a deep model when it included two or more stacked layers and therefore learns features through a hierarchical learning process.</p>	
Consistency in results	Authors report data are inconsistent
Precision in results	Appears imprecise
Directness of results	Direct

Roy MA, Maziade M, Labbe A, Merette C

Male gender is associated with deficit schizophrenia: a meta-analysis

Schizophrenia Research 2001; 47(2-3): 141-147

[View review abstract online](#)

<p>Comparison</p>	<p>Association of male sex in deficit schizophrenia compared to non-deficit schizophrenia.</p> <p>Note: deficit schizophrenia is a descriptive rather than diagnostic term and reflects severe negative symptoms.</p>
<p>Summary of evidence</p>	<p>Moderate to high quality evidence (consistent, imprecise, direct, large sample) suggests significant association of increased deficit schizophrenia in males. This effect was not moderated by sampling method, diagnosis criteria, or duration of illness.</p>
<p>Association with sex</p>	
<p>23 studies, N = 1765 consider the association of sex with deficit schizophrenia.</p> <p>The sample contained 28.7% of people with deficit schizophrenia.</p> <p>A large effect size suggests a significant association of increased number of males with deficit schizophrenia vs. non-deficit schizophrenia.</p> <p>OR = 1.75, 95%CI 1.39 to 2.21, $p = 0.000002$, $Q = 15.87$, $p = 0.82$</p>	
<p><i>Subgroup analyses</i></p> <p>No effect of sampling method was reported: no significant difference in effect size between convenience and systematic sampling, $Q = 0.04$, $p = 0.86$</p> <p>No effect of deficit assessment method was reported: no significant difference in effect size between three assessment methods:</p> <p>Schedule for the Deficit Syndrome (SDS) vs Proxy Deficit Syndrome (PDS), $Q = 0.32$, $p = 0.57$</p> <p>SDS vs detailed review (DR), $Q = 0.85$, $p = 0.36$</p> <p>PDS vs. DR, $Q = 0.85$, $p = 0.18$</p> <p>Unlike SDS and DR, the pooled OR for PDS alone did not yield a significant association with male gender, 3 studies, OR = 1.33, 95%CI 0.86 to 2.05</p> <p>No effect of diagnosis inclusion criteria: no significant difference between schizophrenia or schizoaffective disorder, $Q = 0.49$, $p = 0.49$</p> <p>Pooled OR for schizophrenia alone was significantly different to pooled OR including schizoaffective: OR = 1.68, 95%CI 1.29 to 2.19</p> <p>No effect of duration of illness: no significant difference between duration less than or greater than</p>	

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10 years, $Q = 1.17$, $p = 0.28$

Consistency in results	Consistent
Precision in results	Imprecise
Directness of results	Direct

Roy MA, Merette C, Maziade M

Subtyping Schizophrenia According to Outcome or Severity: A Search for Homogeneous Subgroups

Schizophrenia Bulletin 2001; 27(1): 115-138

[View review abstract online](#)

Comparison	Validity of three potential schizophrenia diagnostic subdivisions: deficit vs. nondeficit; Kraepelinian vs. non-Kraepelinian and congenital vs. adult-onset.
Summary of evidence	Low quality evidence (unclear sample size, unable to assess consistency or precision, direct) is unclear as to the reliability of defining schizophrenia in terms of deficit vs. non-deficit, Kraepelinian vs. non-Kraepelinian, or congenital vs. adult-onset.

Schizophrenia subgroups

Deficit vs. non-deficit schizophrenia

Deficit schizophrenia is defined by the presence of at least two negative symptoms for at least 12 months. 31 studies have compared deficit and non-deficit schizophrenia.

People with deficit schizophrenia were reported to have more severe negative symptoms but less severe depressive symptoms. There was no difference between deficit and non-deficit in positive symptom severity (hallucinations or delusions).

Deficit schizophrenia has been associated with poorer premorbid adjustment and social functioning, is more common in males, and has a high degree of stability over time.

Kraepelinian vs. non-Kraepelinian

Kraepelinian schizophrenia is defined by either continuous hospitalisation or complete dependence on care; lack of useful employment; and absence of complete remission. Six studies have compared Kraepelinian and non-Kraepelinian schizophrenia.

Kraepelinian schizophrenia has been associated with more severe negative symptoms and more severe disorganisation, and poorer social functioning, but no difference in positive symptoms (hallucination and delusions). Kraepelinian schizophrenia has also been associated with poorer

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<p>treatment response.</p> <p><i>Congenital vs. adult-onset</i></p> <p>Congenital schizophrenia occurs before age 25, with poor premorbid adjustment, and a chronic course. Adult-onset schizophrenia is defined by abrupt onset at any age, without significant premorbid impairment, with acute psychotic episodes. 1 study assessed congenital vs. adult-onset schizophrenia.</p> <p>There was preliminary evidence that congenital psychosis was associated with familial psychosis, and adult-onset schizophrenia associated with familial depression.</p>	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Santelmann H, Franklin J, Busshoff J, Baethge C

Interrater reliability of schizoaffective disorder compared with schizophrenia, bipolar disorder, and unipolar depression - A systematic review and meta-analysis

Schizophrenia Research 2016; 176: 357-63

[View review abstract online](#)

Comparison	Interrater reliability of diagnosis of schizoaffective disorder compared to schizophrenia, bipolar disorder and unipolar depression.
Summary of evidence	Moderate to high quality evidence (inconsistent, appears precise, direct, large sample) suggests lower interrater reliability for a diagnosis of schizoaffective disorder than for a diagnosis of schizophrenia, bipolar disorder or unipolar depression.
Interrater reliability	
<p>25 studies, N = 7,912</p> <p><i>Interrater reliability for schizoaffective disorder is lower than for schizophrenia, bipolar disorder and unipolar depression;</i></p> <p>Schizoaffective disorder = Cohen's kappa = 0.57, 95%CI 0.41 to 0.73, I² = 98%</p> <p>Schizophrenia = Cohen's kappa = 0.80, 95%CI 0.76 to 0.84, I² = 70%</p> <p>Bipolar disorder = Cohen's kappa = 0.82, 95%CI 0.77 to 0.86, I² = 38%</p> <p>Unipolar depression = Cohen's kappa = 0.75, 95%CI 0.70 to 0.81, I² = 82%</p>	

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These results did not change according to diagnostic or kappa method used, sample size, number of differential diagnoses, or year of publication. There was no evidence of publication bias.	
Consistency in results	Inconsistent
Precision in results	Appears precise
Directness of results	Direct

<p><i>Santelmann H, Franklin J, Bushoff J, Baethge C</i></p> <p>Test-retest reliability of schizoaffective disorder compared with schizophrenia, bipolar disorder, and unipolar depression-a systematic review and meta-analysis</p> <p>Bipolar Disorders 2015; 17: 753-68</p> <p>View review abstract online</p>	
Comparison	Test-retest reliability of a schizophrenia diagnosis compared to a bipolar disorder, schizoaffective disorder or unipolar depression.
Summary of evidence	Moderate to high quality evidence (inconsistent, appears precise, direct, large sample) suggests better test-retest reliability for a diagnosis of schizophrenia than for a diagnosis of schizoaffective disorder, but lower than for a diagnosis of bipolar disorder or unipolar depression.
Test-retest reliability	
49 studies, N = 14,314	
<i>Test-retest reliability is higher for a diagnosis of schizophrenia than for a diagnosis of schizoaffective disorder, with similar test- retest reliability when comparing schizophrenia to bipolar disorder or unipolar depression;</i>	
Schizophrenia = 42 studies, Cohen's kappa = 0.69, 95%CI 0.64 to 0.74, I ² = 90%	
Schizoaffective disorder = 48 studies, Cohen's kappa = 0.50, 95%CI 0.40 to 0.59, I ² = 96%	
Bipolar disorder = 33 studies, Cohen's kappa = 0.77, 95%CI 0.73 to 0.82, I ² = 92%	
Unipolar depression = 35 studies, Cohen's kappa = 0.73, 95%CI 0.66 to 0.79, I ² = 91%	
In studies of schizophrenia, kappa was significantly higher in; blinded vs. non-blinded studies; studies using consistent vs. inconsistent use of diagnostic interview; studies with a short vs. long follow-up period (< 2 months vs. > 12 months).	
There were no differences in kappa according to; diagnostic tool (ICD-10 vs. DSM 111, DSM 1V or	

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DSM 5); risk of bias in studies; similar vs. different rater identity; first-episode vs. chronic illness; or inpatient vs. outpatient status.	
Consistency in results	Inconsistent
Precision in results	Appears precise
Directness of results	Direct

Soares-Weiser K, Maayan N, Bergman H, Davenport C, Kirkham AJ, Grabowski S, Adams CE

First rank symptoms for schizophrenia

Cochrane Database of Systematic Reviews 2015; 1: CD010653-CD

[View review abstract online](#)

Comparison	Assessment of first rank symptoms in identifying people with schizophrenia vs. other mental disorders. First rank symptoms include hallucinations, hearing voices, and thinking that other people can hear one's thoughts.
Summary of evidence	Moderate to high quality evidence (large sample, inconsistent, appears precise, direct) finds moderate sensitivity and good specificity of first rank symptoms for identifying people with schizophrenia compared to other psychotic and non-psychotic mental disorders.
Accuracy	
21 studies, N = 6,253	
First rank symptoms differentiated schizophrenia from all other diagnoses with moderate sensitivity of 57% (50.4% to 63.3%), and good specificity of 81.4% (74% to 87.1%).	
First rank symptoms differentiated schizophrenia from non-psychotic mental health disorders with moderate sensitivity of 61.8% (51.7% to 71%) and good specificity of 94.1% (88% to 97.2%).	
First rank symptoms differentiated schizophrenia from other types of psychosis with moderate sensitivity of 58% (50.3% to 65.3%) and good specificity of 74.7% (65.2% to 82.3%).	
Consistency in results	Authors report some inconsistency
Precision in results	Appears precise
Directness of results	Direct

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Explanation of acronyms

AUC = area under the curve, CI = confidence interval, DSM = American Psychiatric Association's Diagnostic and Statistical Manual, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), ICD = World Health Organisation's International Classification of Diseases, N = number of participants, OR = odds ratio, p = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), PDS = Proxy Deficit Syndrome (measurement tool to assess Deficit schizophrenia), PPV = Positive Predictive Value; the percentage of patients with a positive test who actually have the disease, Q = Q statistic for the test of heterogeneity, Q_w = test for within group differences (heterogeneity in study results within a group of studies – measure of study consistency), Q_B = test for between group differences (heterogeneity between groups of studies for an outcome of interest), SDS = Schedule for the Deficit Syndrome (measurement tool to assess deficit schizophrenia), vs. = versus

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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 small²⁰.

† 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. 0.2 represents a small effect, 0.5 a moderate effect, and 0.8 and over represents a large effect²⁰.

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 ²¹. InOR stands for logarithmic OR where a InOR of 0 shows no difference between groups. Hazard ratios 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

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indirect indication of prediction, but do not confirm causality due to possible and often unforeseen 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.

‡ 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 formula²⁰;

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

§ 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 relaxed²².

|| 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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