TECHNICAL COMMENTARY

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SCHIZOPHRENIA LIBRARY

IQ

Introduction

Intelligence quotient (IQ) is derived from standardised tests used to measure general cognitive functioning. IQ is most commonly measured using the Wechsler Adult Intelligence Scale (WAIS). The WAIS is designed to measure all aspects of cognitive functioning and is divided into subtests measuring verbal IQ (verbal comprehension and working memory) and non-verbal IQ (perceptual organisation and processing speed).

Other tests used to assess IQ include the Mini-Mental State Examination (MMSE), which assesses cognitive impairment; the National Adult Reading Test (NART), which assesses premorbid intelligence; the Wide Range Achievement Test (WRAT), which assesses both verbal and mathematic ability; and the Raven's Progressive Matrices, which assesses general intelligence.

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 are prioritised 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[1]. Reviews with less than 50% of items 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 or 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)[2]. 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 36 systematic reviews that met our inclusion criteria[3-38].

- Compared to controls, moderate to high quality evidence finds a large effect of lower IQ in people with schizophrenia, including people with first episode, youth-onset or

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late-onset schizophrenia, with late-onset samples showing the greatest impairment.

- Moderate to high quality evidence shows a large effect of lower IQ in people with schizophrenia and violent behaviour compared to controls, and a small effect in people with antisocial personality disorder and violent behaviour.
- High quality evidence finds small effects of lower current and premorbid IQ in people at high-risk for psychosis compared to controls. Those at familial high risk were more impaired than those at clinical high risk. Moderate to high quality evidence shows a small effect of higher current IQ in people at clinical high-risk of psychosis than in people with first-episode psychosis.
- High quality evidence finds a small effect of lower current IQ, and a medium-sized effect of lower premorbid IQ, in people with psychosis and current cannabis use compared to people with psychosis and no cannabis use. However, there was a small effect of *better* global cognitive functioning in people with psychosis and any substance use disorder compared to people with psychosis with no substance use disorder.
- Moderate to high quality evidence shows a medium-sized association between higher IQ and better insight. There were small to medium-sized associations between higher IQ and less severe negative, disorganised and reality distortion symptoms.
- Moderate to high quality evidence suggests a small effect of lower general intelligence in people with schizophrenia and antisocial traits compared to people with schizophrenia without antisocial traits and compared to people with antisocial traits without schizophrenia.
- Moderate to high quality evidence shows greater improvements in global cognition in people taking second-generation antipsychotics compared to people taking first-generation antipsychotics. Specifically, there were improvements in global cognition post-treatment with quetiapine, olanzapine, clozapine and risperidone, and with low dose but not high dose haloperidol.
- Compared to people with affective psychoses, moderate to high quality evidence finds a small to medium-sized effect of lower current IQ, but not premorbid IQ, in people with schizophrenia. Premorbid IQ was lower in people with first-episode schizophrenia than in people with first-episode bipolar disorder.

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Aleman A, Agrawal N, Morgan KD, David AS

Insight in psychosis and neuropsychological function: Meta-analysis

British Journal of Psychiatry 2006; 189: 204-212

View review abstract online

Comparison	**Association between IQ and insight in people with schizophrenia.**
Summary of evidence	**Moderate to high quality evidence (small to medium-sized samples, direct, consistent, precise) suggests a medium-sized association between higher levels of overall cognition or IQ and higher levels of insight.**
IQ	
A medium effect size suggests higher overall cognition and WAIS IQ was associated with increased insight in people with schizophrenia; IQ: 4 studies, N = 174, r = 0.26, 95%CI 0.12 to 0.40, $p < 0.001$, $Q_w = 0.6$, $p = 0.89$ Overall cognition: 11 studies, N = 660, r = 0.23, 95%CI 0.15 to 0.30, $p < 0.0001$, $Q_w = 4.8$, $p = 0.91$	
Consistency in results‡	Consistent
Precision in results§	Precise
Directness of results‖	Direct

Bogaty SER, Lee RSC, Hickie IB, Hermens DF

Meta-analysis of neurocognition in young psychosis patients with current cannabis use

Journal of Psychiatric Research 2018; 99: 22-32

View review abstract online

Comparison	**Current and premorbid IQ in people with psychosis and current cannabis use vs. people with psychosis with no cannabis use.**
Summary of evidence	**High quality evidence (large samples, consistent, precise,**

	direct) shows a small effect of lower current IQ, and a medium-sized effect of lower premorbid IQ in people with psychosis and current cannabis use.
IQ	
Significant medium-sized effect of lower premorbid IQ and a small effect of lower current IQ in people with psychosis and current cannabis use; Premorbid IQ: 7 studies, N = 515, g = -0.40, 95%CI -0.59 to -0.20, $p < 0.001$, $I^2 = 0\%$ Current IQ: 6 studies, N = 747, g = -0.17, 95%CI -0.34 to -0.00, $p < 0.05$, $I^2 = 11\%$	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Bora E, Pantelis C

Meta-analysis of Cognitive Impairment in First-Episode Bipolar Disorder: Comparison With First-Episode Schizophrenia and Healthy Controls

Schizophrenia Bulletin 2015; 41(5): 1095-1104

View review abstract online

Comparison	**IQ in people with first-episode schizophrenia vs. people with first-episode bipolar disorder.**
Summary of evidence	**High quality evidence (large samples, consistent, precise, direct) shows a medium-sized effect of poorer premorbid IQ in people with first-episode schizophrenia compared to people with first-episode bipolar disorder. Moderate quality evidence (imprecise and inconsistent) also shows a medium-sized effect of poorer current IQ in people with first-episode schizophrenia.** **Moderate to high quality evidence (inconsistent) shows a small effect of poorer global cognition in people with first-episode schizophrenia compared to people with first-episode bipolar disorder.**
IQ	

A significant, medium-sized effect of lower premorbid and current IQ in people with first-episode schizophrenia compared with first-episode bipolar disorder; Premorbid IQ: 7 studies, N = 728, d = 0.50, 95%CI 0.30 to 0.69, $p < 0.001$, I^2 = 36.8%, p = 0.15 Current IQ: 6 studies, N = 533, d = 0.63, 95%CI 0.36 to 0.91, $p < 0.001$, I^2 = 67.9%, p = 0.05 Authors report no publication bias. No differences were found for males vs. females or younger vs. older patients.
Global cognition
A significant, small effect of poorer global cognition in people with first-episode schizophrenia compared with first-episode bipolar disorder; 14 studies, N = 1,427, d = 0.28, 95%CI 0.12 to 0.44, $p < 0.001$, I^2 = 48.8%, p = 0.02 Authors report no publication bias. No differences were found for males vs. females or younger vs. older patients.

Consistency in results	Consistent for premorbid IQ, inconsistent current IQ.
Precision in results	Precise for global cognition and premorbid IQ, imprecise for current IQ.
Directness of results	Direct

Bora E, Lin A, Wood SJ, Yung AR, McGorry PD, Pantelis C

Cognitive deficits in youth with familial and clinical high risk to psychosis: A systematic review and meta-analysis

Acta Psychiatrica Scandinavica 2014; 130(1): 1-15

View review abstract online

Comparison	**IQ in people at clinical high risk (UHR) and familial high risk (FHR) for psychosis.**
Summary of evidence	**High quality evidence (large samples, consistent, precise, direct) suggests people at familial high risk of psychosis are more impaired on premorbid and current IQ than those at clinical high risk.**
IQ	

Significant, small to medium size effect of poor premorbid IQ in UHR and FHR groups compared with controls, with the FHR group showing the greatest deficit; UHR: 9 studies, N = 1,370, *d* = 0.30, 95%CI 0.13 to 0.48, *p* < 0.001, I^2 = 0.04%, Q-test *p* = 0.02 FHR: 6 studies, N = 770, *d* = 0.63, 95%CI 0.47 to 0.79, *p* < 0.001, I^2 = 0%, Q-test *p* = 0.60 Q_B = 13.1, *p* < 0.001 *Significant, medium to large size effect of poor current IQ in UHR and FHR groups compared with controls, with the FHR group showing the greatest deficit;* UHR: 12 studies, N = 1,440, *d* = 0.40, 95%CI 0.25 to 0.54, *p* < 0.001, I^2 = 0.02%, Q-test *p* = 0.15 FHR: 8 studies, N = 900, *d* = 0.81, 95%CI 0.61 to 1.01, *p* < 0.001, I^2 = 0.04%, Q-test *p* = 0.07 Q_B = 20.0, *p* < 0.001 Meta-regression of the UHR studies showed that increased deterioration in functioning was associated with poor premorbid IQ. Lower transition to psychosis rate was significantly associated with higher IQ. Authors report no publication bias.

Consistency	Consistent
Precision	Precise
Directness	Direct

Bora E, Murray RM

Meta-analysis of cognitive deficits in ultra-high risk to psychosis and first-episode psychosis: Do the cognitive deficits progress over, or after, the onset of psychosis?

Schizophrenia Bulletin 2014; 40(43): 744-755

View review abstract online

Comparison	**Changes in global cognition over time in people at ultra-high risk of psychosis (UHR) vs. people with first-episode psychosis (FEP) or controls.**
Summary of evidence	**High quality evidence (large samples, precise, direct, consistent) suggests similar, small improvements in global cognition over time in people at ultra-high risk of psychosis, people with first-episode psychosis and controls.**

Global cognition	
Significant, small improvement in global cognition over time in UHR, FEP and controls, with no significant differences between groups; FEP: 17 studies, N = 905, *d* = 0.30, 95%CI 0.20 to 0.39, $p < 0.001$, $I^2 = 0\%$, Q-test $p = 0.54$ UHR: 14 studies, N = 560, *d* = 0.23, 95%CI 0.11 to 0.35, $p < 0.001$, $I^2 = 0\%$, Q-test $p = 0.95$ Controls: 11 studies, N = 405, *d* = 0.38, 95%CI 0.24 to 0.52, $p < 0.001$, $I^2 = 0\%$, Q-test $p = 0.94$ Q_B $p > 0.05$ Authors report no publication bias and no effects of medication status.	
Consistency	Consistent
Precision	Precise
Directness	Direct

Bora E, Yucel M, Pantelis C

Cognitive functioning in schizophrenia, schizoaffective disorder and affective psychoses: meta-analytic study

The British Journal of Psychiatry 2009; 195: 475-482

View review abstract online

Comparison	**IQ in people with schizophrenia vs. people with affective psychosis or schizoaffective disorder.** **Note: the schizophrenia group had more males, with a younger mean age and with fewer years of education, which may account for some observed effects.**
Summary of evidence	**Moderate quality evidence (unclear sample size, direct, precise, inconsistent) suggests a small effect of lower performance on the Wechsler Adult Intelligence Scale IQ test in people with schizophrenia.**
IQ	

A small significant effect of worse performance on the Wechsler Adult Intelligence Scale IQ test in schizophrenia compared with affective psychosis or schizoaffective disorder; 7 studies, d = 0.37, 95%CI 0.09 to 0.65, $p < 0.009$, Q_w $p < 0.03$

Consistency	Inconsistent
Precision	Precise
Directness	Direct

Bora E, Binnur Akdede B, Alptekin K

Neurocognitive impairment in deficit and non-deficit schizophrenia: a meta-analysis

Psychological Medicine 2017; 47: 2401-13

View review abstract online

Comparison	**Global cognition in people with deficit schizophrenia vs. people with non-deficit schizophrenia. Both groups were also compared to controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, mostly inconsistent, precise, direct) suggests people with deficit schizophrenia are more impaired than people with non-deficit schizophrenia on measures of global cognition.**

Global cognition

Significant, medium-sized effect of poorer global cognition in people with deficit schizophrenia compared to people with non-deficit schizophrenia;

21 studies, N = 2,287, d = 0.47, 0.37 to 0.58, $p < 0.001$, I^2 = 23%, p = 0.17

Significant, large effects of poorer global cognition in people with deficit schizophrenia compared to controls and in people with non-deficit schizophrenia compared to controls;

Deficit: 12 studies, N = 1,210, d = 1.35, 95%CI 1.14 to 1.56, $p < 0.001$, I^2 = 62%, p = 0.002

Non-deficit: 12 studies, N = 1,441, d = 0.91, 95%CI 0.75 to 1.06, $p < 0.001$, I^2 = 50%, p = 0.02

Consistency in results	Mostly inconsistent.
Precision in results	Precise

Directness of results	Direct

Christensen T

The influence of neurocognitive dysfunctions on work capacity in schizophrenia patients: a systematic review of the literature

International Journal of Psychiatry in Clinical Practice 2007; 11(2): 89-101

View review abstract online

Comparison	**Association between work capacity and cognitive performance in people with schizophrenia.** **Note: work capacity is the ability to obtain and maintain competitive work and work behaviours and skills.**
Summary of evidence	**Moderate to low quality evidence (small samples, direct, unable to assess consistency or precision) suggests lower work capacity is associated with poorer cognitive functioning and IQ.**
General cognition and IQ	
2 studies (N = 166) reported that poor *general neurocognitive functioning* was associated with worse work behaviour and employment status, whereas 2 studies (N = 140) found no association between neurocognitive functioning and employment or social functioning; 1 study (N = 53) reported that poor *WAIS non-verbal IQ* performance was associated with worse vocational functioning;	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

Cohen A, Saperstein A, Gold J, Kirkpatrick B, Carpenter W, Buchanan R

Neuropsychology of the deficit syndrome: New data and meta-analysis of findings to date

Schizophrenia Bulletin 2007; 33(5): 1201-1212

View review abstract online

Comparison	**IQ in people with deficit schizophrenia (predominantly negative symptoms) vs. people with non-deficit schizophrenia.**
Summary of evidence	**Moderate to low quality evidence (unclear sample size, direct, unable to assess consistency or precision) suggests people with deficit schizophrenia show greater impairments in IQ than people with non-deficit schizophrenia.**
IQ	
A medium effect size suggests greater IQ impairment in people with deficit schizophrenia compared with people with non-deficit schizophrenia; Tests included WAIS-full scale performance, WAIS-full scale IQ, sample sizes, effect sizes, Q and *p*-values are not reported, 6 studies, ES = 0.52, 95%CI 0.23 to 0.82.	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

Daban C, Martinez-Aran A, Torrent C, Tabarés-Seisdedos R, Balanzá-Martínez V, Salazar-Fraile J, Selva-Vera G, Vieta E

Specificity of cognitive deficits in bipolar disorder versus schizophrenia: A systematic review

Psychotherapy and Psychosomatics 2006; 75: 72-84

View review abstract online

Comparison	**IQ in people with schizophrenia vs. people with bipolar disorder.**

Summary of evidence	**Moderate quality evidence (large samples, direct, unable to assess consistency or precision) suggests people with schizophrenia may show impaired IQ (not premorbid) compared to people with bipolar disorder.**
IQ	
7 studies (N = 767) reported lower *IQ* scores (WAIS) in people with schizophrenia compared with people with bipolar disorder. 1 study (N = 137) reported no differences between groups. 6 studies reported lower *premorbid IQ* (NART 4 studies, N = 706; WAIS-R vocabulary 2 studies, N = 269) in people with schizophrenia compared with people with bipolar disorder. However, 8 studies (N = 818) reported no differences (NART, WRAT-R, WAIS-R vocabulary). Both groups performed worse than controls. 3 longitudinal studies reported no differences at baseline in adolescence later diagnosed with schizophrenia or bipolar disorder.	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

de Gracia Domingues M, Viechtbauer W, Simons C, van Os J

Are psychotic psychopathology and neurocognition orthogonal? A systematic review of their associations

Psychological Bulletin 2009; 135(1): 157-171

View review abstract online

Comparison	**Association between IQ and symptom dimensions in people with non-affective psychosis.**
Summary of evidence	**Moderate to high quality evidence (unclear sample size, direct, precise, consistent) suggests a medium association between increased negative and disorganised symptoms and lower IQ.**
IQ	
A significant medium association between increased negative symptoms and lower IQ; 13 studies, μ_p = -0.244, 95%CI -0.333 to -0.151, *p* = 0.00, I^2 = 52%	

A significant medium association between increased disorganised symptoms and lower IQ; 6 studies, μ_p = -0.205, 95%CI -0.327 to -0.076, *p* = 0.002, I^2 = 45% *No association with positive symptoms;* 10 studies, μ_p = 0.024, 95%CI -0.063 to 0.111, *p* = 0.591, I^2 = 26%	
Consistency	Consistent
Precision	Precise
Directness	Direct

Dibben CR, Rice C, Laws K, McKenna PJ

Is executive impairment associated with schizophrenic syndromes? A meta-analysis

Psychological Medicine 2009; 39(3): 381-392

View review abstract online

Comparison	**Association between IQ and negative symptoms in people with schizophrenia.**
Summary of evidence	**Moderate to high quality evidence (unclear sample size, consistent, precise, direct) shows a small effect of IQ impairment with negative symptoms.**
IQ	
Small effect size suggests an association of reduced intellectual function with negative symptoms; 30 studies, N not reported, *r* = -0.21, 95%CI -0.26 to -0.17, Q = not reported Excluding 6 outliers did not change results: *r* = -0.23, 95%CI -0.28 to -0.17, Q = not reported	
Consistency	Consistent
Precision	Precise
Directness	Direct
Comparison 2	**Association between IQ and disorganised symptoms in people with schizophrenia.**

Summary of evidence	**High quality evidence (consistent, precise, direct, large number of studies) shows a small association of IQ impairment with disorganised symptoms.**
IQ	
Small effect size suggests an association of reduced intellectual function with disorganised symptoms; N not reported, *r* = -0.21, 95%CI -0.28 to -0.14, Q = not reported Excluding 2 outliers, *r* = -0.28, 95%CI -0.35 to -0.19, Q = not reported	
Consistency	Consistent, no unexplained heterogeneity
Precision	Precise
Directness	Direct

Dickinson D, Ramsey ME, Gold JM

Overlooking the Obvious: A meta-analytic comparison of digit symbol coding tasks and other cognitive measures in schizophrenia

Archives of General Psychiatry 2007; 64: 532-542

View review abstract online

Comparison	**IQ in people with schizophrenia vs. healthy controls.**
Summary of evidence	**Moderate to high quality (large samples, direct, precise, unable to assess consistency) suggests a large effect of poorer performance on overall IQ, vocabulary, information, similarities and WRAT or NART reading (medium-sized effect) in people with schizophrenia.**
IQ	
Large effect size suggests people with schizophrenia showed poorer performance on intelligence tasks compared with controls on tasks including; IQ: 15 studies, N = 1,371, *g* = -1.19, SE = 0.15, 95%CI -1.48 to -0.90 Vocabulary: 10 studies, N = 1,194, *g* = -0.90, SE = 0.13, 95%CI -1.15 to -0.65 Information: 8 studies, N = 1,130, *g* = -0.82, SE = 0.10, 95%CI -1.01 to -0.64	

Similarities: 8 studies, N = 938, *g* = -1.01, SE = 0.08, 95%CI -1.16 to -0.86 *Medium effect size suggests people with schizophrenia showed poorer performance on the WRAT or NART reading test compared with controls;* 10 studies, N = 1,165, *g* = -0.59, SE = 0.11, 95%CI -0.81 to -0.37	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Precise
Directness	Direct

Donoghue K, Doody GA

Effect of Illegal Substance Use on Cognitive Function in Individuals With a Psychotic Disorder, A Review and Meta-Analysis

Neuropsychology 2012; 26(6): 785-801

View review abstract online

Comparison	**Cognitive functioning in people with a psychotic disorder and a substance use disorder vs. people with a psychotic disorder without a substance use disorder.**
Summary of evidence	**High quality evidence (large samples, consistent, precise, direct) suggests a small effect of better global cognitive functioning in people with a psychotic disorder and a substance use disorder than people with a psychotic disorder without a substance use disorder.**
Cognitive functioning in people with a polysubstance use disorder	
A significant small effect suggests people with a psychotic disorder and a polysubstance use disorder showed better global cognitive functioning than people with a psychotic disorder without a substance use disorder; Global cognitive functioning: 9 studies, N = 627, *g* = 0.175, 95%CI 0.008 to 0.343, *p* = 0.040, I^2 = 0%, *p* = 0.568	
Cognitive functioning in people with a cannabis use disorder	
A significant small effect suggests people with a psychotic disorder and a cannabis use disorder showed better global cognitive functioning than people with a psychotic disorder without a	

substance use disorder; Global cognitive functioning: 3 studies, N = 551, *g* = 0.237, 95%CI 0.083 to 0.390, *p* = 0.003, I^2 = 0%, *p* = 0.838	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Fioravant M, Bianchi V, Cinti ME

Cognitive deficits in schizophrenia: an updated meta-analysis of the scientific evidence

BMC Psychiatry 2012; 12: 64

View review abstract online

Comparison	**Global cognitive functioning in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) suggests people with schizophrenia showed lower IQ than controls.**
IQ	
A large effect of lower IQ, and a medium-sized effect of lower premorbid IQ in people with schizophrenia; *IQ:* 102 studies, N = 8,416, SMD = -0.96, 95%CI -1.07 to -0.85, *p* < 0.0001, I^2 = 80% Premorbid IQ: 48 studies, N = 3,568, SMD = -0.57, 95%CI -0.70 to -0.42, *p* < 0.0001, I^2 = 70% *Subgroup analyses showed a larger effect for inpatients vs. controls than outpatients vs. controls;* Inpatients: 27 studies, N = 1,800, SMD = -1.04, 95%CI -1.25 to -0.82, *p* < 0.00001, I^2 = 77% Outpatients: 27 studies, N = 2,274, SMD = -0.83, 95%CI -1.00 to -0.66, *p* < 0.00001, I^2 = 69%	
Consistency	Inconsistent
Precision	Precise
Directness	Direct

Forbes NF, Carrick LA, McIntosh AM, Lawrie SM

Working memory in schizophrenia: a meta-analysis

Psychological Medicine 2009; 39: 889-905

View review abstract online

Comparison	**Association between working memory and IQ in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate to low quality evidence (unclear sample size, direct, unable to assess consistency or precision) suggests higher IQ is associated with better performance on the memory task passage recall in people with schizophrenia.**
Association between memory and IQ	
Meta-regression analysis suggests a significant association between higher IQ and better performance on the memory test passage recall (b = -0.074, p = 0.001) in people with schizophrenia.	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

Guilera G, Pino O,Gomez-Benito J, Rojo JE

Antipsychotic effects on cognition in schizophrenia: A meta-analysis of randomised control trials

The European Journal of Psychiatry 2009; 23(2): 77-89

View review abstract online

Comparison	**Global cognition in people with schizophrenia on second generation antipsychotics vs. first generation antipsychotics.**
Summary of evidence	**Moderate to high quality evidence (large sample, direct, precise,**

	unable to assess consistency) suggests overall better global cognition in people with schizophrenia receiving second generation antipsychotics compared with those receiving first generation antipsychotics.
Global cognition	
A significant small effect size showed higher composite global cognition scores in people with schizophrenia receiving second-generation antipsychotics compared with those receiving first-generation antipsychotics; 18 RCTs, N = 1,808, *g* = 0.17, 95%CI 0.04 to 0.29, *p* < 0.01	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Precise
Directness	Direct

Hauser M, Zhang JP, Sheridan EM, Burdick KE, Mogil R, Kane JM, Auther A, Carrion RE, Cornblatt BA, Correll CU

Neuropsychological Test Performance to Enhance Identification of Subjects at Clinical High Risk for Psychosis and to Be Most Promising for Predictive Algorithms for Conversion to Psychosis: A Meta-Analysis

Journal of Clinical Psychiatry 2017; 78: e28-e40

View review abstract online

Comparison 1	**IQ in individuals at clinical high-risk of psychosis vs. controls.**
Summary of evidence	**High quality evidence (large samples, consistent, precise, direct) shows small effects of lower current and premorbid IQ in people at clinical high-risk for psychosis.**
IQ	
Significant, small effect of lower current IQ in people at clinical high-risk; 9 studies, N = 1,059, *g* = -0.21, 95%CI -0.35 to -0.07, *p* = 0.003, I^2 = 13% This effect was larger in longitudinal studies (follow-up 10.4 months, *g* = -0.70). The effect was significant in studies using Vocabulary and Block Design.	

Significant, small effect of lower premorbid IQ in people at clinical high-risk; 7 studies, N = 1,260, *g* = -0.25, 95%CI -0.39 to -0.11, *p* < 0.0001, I^2 = 17% This effect was significant in studies using the Mehrfachwortschatztest-B.	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct
Comparison 2	**IQ in individuals at clinical high-risk for psychosis vs. people with first-episode psychosis.**
Summary of evidence	**Moderate to high quality evidence (medium-sized sample, consistent, precise, direct) shows a small effect of higher current IQ in people at clinical high-risk of psychosis than people with first-episode psychosis.**
IQ	
Significant, small to medium-sized effect of higher current IQ in people at clinical high-risk; 3 studies, N = 418, *g* = 0.31, 95%CI 0.11 to 0.51, *p* = 0.003, I^2 = 0%	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct
Comparison 3	**IQ in individuals at clinical high-risk of psychosis that converted to psychosis vs. controls, and in people who did not convert to psychosis vs. controls.**
Summary of evidence	**Moderate to high quality evidence (small to medium-sized samples, consistent, precise, direct) found medium-sized effects of lower current IQ in both converters and non-converters compared to controls. There was a small effect of lower premorbid IQ in non-converters, and a large effect of lower premorbid IQ in converters vs. controls.**
IQ	
Significant, medium-sized effect of lower current IQ in non-converters vs. controls; 3 studies, N = 236, *g* = -0.61, 95%CI -0.88 to -0.34, *p* < 0.0001, I^2 = 3%	

Significant, medium to large effect of lower current IQ in converters vs. controls; 3 studies, N = 174, *g* = -0.72, 95%CI -1.04 to -0.39, *p* < 0.0001, I^2 = 0% *Significant, small effect of lower premorbid IQ in non-converters vs. controls;* 6 studies, N = 424, *g* = -0.30, 95%CI -0.49 to -0.11, *p* = 0.002, I^2 = 0% *Significant, medium to large effect of lower premorbid IQ in converters vs. controls;* 6 studies, N = 406, *g* = -0.75, 95%CI -1.01 to -0.49, *p* < 0.0001, I^2 = 8%

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

Hedman AM, van Haren NEM, van Baal CGM, Kahn RS, Pol HEH

IQ change over time in schizophrenia and healthy individuals: A meta-analysis

Schizophrenia Research 2013; 146(1-3): 201-8

View review abstract online

Comparison	**IQ changes over time in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate quality evidence (large sample, direct, inconsistent, unable to assess precision) suggests less improvement in global cognition tests over time in patients compared with controls.**

IQ

A significant, medium size effect of less test score improvement over time in patients vs. controls;
8 longitudinal studies, N = 586, *d* = −0.48, CI not reported, *p* = 0.01, I^2=73.93%, *p* < 0.001
The mean weighted IQ-change per year was +0.33 for patients and +2.08 for controls.
No significant differences were observed for change in verbal or performance IQ.
No publication bias.

Consistency	Inconsistent
Precision	Unable to assess; no measure of precision is reported.

Directness	Direct

Irani F, Kalkstein S, Moberg E, Moberg P

Neuropsychological performance in older patients with schizophrenia: A meta-analysis of cross-sectional and longitudinal studies

Schizophrenia Bulletin 2010; 37(6): 1318-1326

View review abstract online

Comparison	**IQ in older people with schizophrenia (mean age 64 years) vs. age-matched controls**
Summary of evidence	**Moderate quality evidence (unclear sample size, direct, inconsistent, precise or unable to assess) suggests older people with schizophrenia have poorer global cognition and IQ.**

IQ

A large effect suggests global cognition was significantly more impaired in older people with schizophrenia compared with the age-matched control group;

21 observational studies (cross-sectional), *d* = -1.19, 95%CI -1.29 to -1.11, *p* value not reported, Q_w = 325.96, *p* < 0.01

A large effect size suggesting poorer IQ in older people with schizophrenia compared with the age-matched control group (*d* = -0.84), Q and p-values are not reported.

Subgroup analysis suggests global cognition may be associated with age, sex, education, ethnicity, diagnosis, living status, age of onset/duration of illness and clinical symptoms.

Consistency	Inconsistent for overall global cognition, unable to assess for IQ.
Precision	Precise for overall global cognition, unable to assess for IQ.
Directness	Direct

Khandaker GM, Barnett JH, White IR, Jones PB

A quantitative meta-analysis of population-based studies of premorbid

intelligence and schizophrenia

Schizophrenia Research 2011; 132: 220-227

View review abstract online

Comparison	**Premorbid IQ in people with schizophrenia vs. population controls.**
Summary of evidence	**Moderate to high quality evidence (large sample, inconsistent, precise, direct) suggests a medium-sized effect of lower premorbid IQ in people with schizophrenia.**
IQ	
A significant medium effect of lower premorbid IQ in people with schizophrenia compared with population controls; 12 population studies, N = 750,116, *d* = -0.43, 95%CI -0.53 to -0.34, $p < 0.0001$, $I^2 = 77\%$, $p < 0.001$ Authors state this equates to a mean premorbid IQ of 93.6 in people who develop schizophrenia compared with a population mean of 100. They also report a dose-dependent relationship with a 3.7% increase in risk of schizophrenia with each one-point decrease in IQ (95% CI 3.4% to 3.9%, $p < 0.0001$).	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

Krabbendam L, Arts B, van Os J, Aleman A

Cognitive functioning in patients with schizophrenia and bipolar disorder: A quantitative review

Schizophrenia Research 2005; 80: 137-149

View review abstract online

Comparison	**Cognitive performance in people with schizophrenia vs. people with bipolar disorder.**
Summary of evidence	**Moderate quality evidence (medium-sized samples, inconsistent, precise, direct) suggests a small to medium-sized**

	effect of lower IQ in people with schizophrenia.
IQ	
A significant small to medium effect suggests people with schizophrenia showed impaired performance on various cognitive tests compared with people with bipolar disorder; 7 studies, N = 338, *d* = 0.36, 95%CI 0.01 to 0.71, *p* = 0.04, Q_w = 13.6, *p* = 0.03	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

Mesholam-Gately R, Giuliano A, Goff K, Faraone S, Seidman L

Neurocognition in first-episode schizophrenia: a meta analytic review.

Neuropsychology 2009; 23(3): 315-335

View review abstract online

Comparison	**General cognitive ability in people with first-episode schizophrenia vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large sample, direct, inconsistent, precise) suggests a large effect of poorer general cognitive ability in people with first-episode schizophrenia.**
General cognitive ability	
Large effect size shows people with first-episode schizophrenia have significantly poorer general cognitive ability than controls; 15 studies, N = 1,091, *d* = -0.91, 95%CI -1.21 to -0.61, *p* < 0.001, Q = 101.43, *p* < 0.001	
Consistency	Inconsistent
Precision	Precise
Directness	Direct

Nair A, Palmer EC, Aleman A, David AS

Relationship between cognition, clinical and cognitive insight in psychotic disorders: A review and meta-analysis

Schizophrenia Research 2014; 152: 191-200

View review abstract online

Comparison	**Associations between clinical and cognitive insight and cognitive functioning in people with schizophrenia.**
Summary of evidence	**Moderate to high quality evidence (medium to large samples, precise, consistent, direct) suggests small associations between increased clinical insight and increased IQ, and between reduced self-certainty and increased IQ.**
Associations between clinical insight (ability to identify symptoms as being a mental disorder) and IQ	
Significant, small association between increased clinical insight and increased IQ; 19 studies, N = 951, r = 0.20, 95%CI 0.13 to 0.26, p < 0.001, I^2 = 0%, p = 0.80 No publication bias.	
Relationship between cognitive insight (ability to evaluate symptoms as measured by the Beck Cognitive Insight Scale) and IQ	
Significant, small association between reduced self-certainty and increased IQ; Self-certainty: 3 studies, N = 251, r = −0.19, 95%CI −0.31 to −0.07, p < 0.001, I^2 = 0%, p = 0.88 *No associations between cognitive insight or self-reflectiveness and IQ;* Cognitive insight: 2 studies, N = 115, r = 0.15, 95%CI −0.14 to 0.42, p = 0.32, I^2 = 50.25%, p = 0.16 Self-reflectiveness: 3 studies, N = 251, r = −0.05, 95%CI −0.20 to 0.11, p = 0.55, I^2 = 30.64%, p = 0.24	
Consistency	Consistent
Precision	Precise
Directness	Direct

Nieto R, Castellanos F

A Meta-Analysis of Neuropsychological Functioning in Patients with Early Onset Schizophrenia and Paediatric Bipolar Disorder

Journal of Clinical Child & Adolescent Psychology 2012; 40(2): 266-280

View review abstract online

Comparison	**Cognitive performance in patients with early onset schizophrenia (EOS: mean age 15.8 years) and in paediatric bipolar disorder (PBD: mean age 13.6 years) vs. controls.**
Summary of evidence	**Moderate to high quality evidence (medium to large samples, inconsistent, precise, mostly direct) suggests a large effect of poor general cognitive ability in EOS vs. controls, and a medium effect of poor general cognitive ability in PBD vs. controls.**

General cognitive ability

Large effect in EOS and a medium effect in PBD of lower general cognitive ability vs. controls;

EOS: 9 studies, N = 667, g = -1.15, 95%CI -1.51 to -0.79, $p < 0.005$, Q = 17.19, $p = 0.03$

PBD: 6 studies, N = 358, g = -0.42, 95%CI -0.64 to -0.20, $p < 0.005$, Q = 22.75, $p < 0.001$

General cognitive ability was significantly lower in EOS vs. controls than PBD vs. controls ($p < 0.001$).

Moderator analyses revealed significantly smaller effect sizes in PBD studies with a lower rates of comorbid ADHD.

Authors report no publication bias.

Consistency	Inconsistent
Precision	Precise
Directness	Direct, apart from EOS vs. PBD

Quraishi S, Frangou S

Neuropsychology of bipolar disorder: a review

Journal of Affective Disorders 2002; 72: 209-225

View review abstract online

Comparison	**IQ in people with schizophrenia vs. bipolar disorder.**
Summary of evidence	**Moderate to low quality evidence (small to medium-sized samples, direct, unable to assess precision or consistency) suggests IQ may be more impaired in schizophrenia than in bipolar disorder.**
IQ	
6 studies reported lower IQ in people with schizophrenia compared with people with bipolar disorder, including general intelligence (2 studies, N = 216), reading (1 study, N = 308), full-scale IQ (1 study, N = 111) and verbal IQ (2 studies, N = 223). 1 study (N = 65) on general intelligence and another on performance IQ (N = 112) reported no differences between groups.	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

Rabin RA, Zakzanis KK, George TP

The effects of cannabis use on neurocognition in schizophrenia: a meta-analysis

Schizophrenia Research 2011; 128: 111-116

View review abstract online

Comparison	**IQ in people with schizophrenia and current cannabis use and vs. people with schizophrenia and no cannabis use.**
Summary of evidence	**Moderate to low quality evidence (unclear sample size, direct, unable to assess consistency or precision) suggests people with schizophrenia who use cannabis have a medium-sized increase in IQ.**
IQ	
A significant, medium-sized effect of higher general intelligence in patients using cannabis; 4 studies, $d = 0.48$, SD = 0.51, $p < 0.05$	

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

Rajji TK, Ismail Z, Mulsant BH

Age at onset and cognition in schizophrenia: meta-analysis

The British Journal of Psychiatry 2009; 195: 286-293

View review abstract online

Comparison	**Neurocognitive performance in people with schizophrenia with different age of onset (first-episode schizophrenia, youth-onset schizophrenia and late-onset schizophrenia) vs. controls.** **Note: maximum age for youth-onset was 19 years; minimum age for late-onset was 40 years; people with any other age at onset were classified as first-episode schizophrenia.**
Summary of evidence	**Moderate quality evidence (large samples, direct, unable to assess consistency or precision) suggests poorer performance on full scale IQ, verbal IQ and performance IQ in people with first-episode, youth-onset and late-onset schizophrenia compared with controls, with late-onset groups showing the greatest impairment.**

IQ performance

N = 5,010 (4,057 first-episode schizophrenia, 692 youth-onset schizophrenia, 261 late-onset schizophrenia)

Medium to large effect sizes suggest that people with first episode and late-onset schizophrenia showed a poorer measured of global cognition compared with controls, and with significant variation between patient groups;

First-episode schizophrenia: 7 studies, d = 0.67, SE 0.10

Late-onset schizophrenia: 7 studies, d = 1.67, SE 0.11

Q_B = 45.74, p < 0.001

Large effect sizes suggest that people with first episode, youth-onset and late-onset schizophrenia showed poorer full scale IQ compared with controls, and with significant variation between patient

groups; First-episode schizophrenia: 29 studies, *d* = 0.89, SE 0.04 Youth-onset schizophrenia: 15 studies, *d* = 1.77, SE 0.07 Late-onset schizophrenia: 4 studies, *d* = 1.61, SE 0.15 Q_B = 121.64, *p* < 0.001	
Large effect sizes suggest that people with first episode, youth-onset and late-onset schizophrenia showed poorer verbal IQ compared with controls; First-episode schizophrenia: 7 studies, *d* = 1.13, SE 0.08 Youth-onset schizophrenia: 4 studies, *d* = 1.19, SE 1.13 Late-onset schizophrenia: 3 studies, *d* = 1.34, SE 0.16	
Large effect sizes suggest that people with first episode, youth-onset and late-onset schizophrenia show poorer performance IQ compared with controls, and with significant variation between patient groups; First-episode schizophrenia: 5 studies, *d* = 1.73, SE 0.09 Youth-onset schizophrenia: 3 studies, *d* = 1.25, SE 0.15 Late-onset schizophrenia: 2 studies, *d* = 2.03, SE 0.23 Q_B = 11.75, *p* < 0.01	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

Schug R, Raine A

Comparative meta-analyses of neuropsychological functioning in antisocial schizophrenic persons

Clinical Psychological Review 2009; 29: 230-242

View review abstract online

Comparison	**IQ in people with schizophrenia and antisocial traits vs. people with schizophrenia without antisocial traits.** **Note: Antisocial behaviour was broadly defined as assaultive, criminal, psychopathic, or violent behaviours and included**

	individuals who had committed specific crimes (i.e. homicide, assault) or who had specific mental disorder diagnoses (i.e. antisocial personality disorder, psychopathy).
Summary of evidence	**Moderate to high quality evidence (unclear sample size, direct, consistent, precise) suggests a small effect size for reduced general intelligence in people with schizophrenia and antisocial traits.**
IQ	
Small effect size suggests people with schizophrenia and antisocial traits have significantly reduced general intelligence compared with people with schizophrenia without antisocial traits; General IQ: 19 studies, g = -0.275, 95%CI -0.384 to -0.166, $p < 0.001$, $Q_w = 27.605$, $p > 0.05$ *No significant difference on IQ subscales;* Verbal IQ: 10 studies, g = -0.131, 95%CI -0.285 to 0.024, $p > 0.05$, $Q_w = 20.268$, $p < 0.05$ Performance IQ: 10 studies, g = -0.097, 95%CI -0.276 to 0.082, $p > 0.05$, $Q_w = 25.866$, $p < 0.01$	
Consistency	Inconsistent for all measures except general intelligence
Precision	Precise
Directness	Direct
Comparison 2	**IQ in people with schizophrenia and antisocial traits vs. people without schizophrenia who have antisocial traits.**
Summary of evidence	**Moderate to high quality evidence (unclear sample size, direct, consistent, precise) suggests a small effect size for reduced general intelligence, verbal and performance IQ in people with schizophrenia and antisocial traits.**
IQ	
Small effect size suggests people with schizophrenia and antisocial traits show reduced; General IQ: 19 studies, g = -0.376, 95%CI -0.517 to -0.235, $p < 0.001$, $Q_w = 20.803$, $p > 0.05$ Verbal IQ: 11 studies, g = -0.321, 95%CI -0.530 to -0.111, $p < 0.01$, $Q_w = 9.660$, $p > 0.05$ Performance IQ: 12 studies, g = -0.365, 95%CI -0.572 to -0.158, $p < 0.01$, $Q_w = 5.950$, $p > 0.05$	
Consistency	Consistent
Precision	Precise
Directness	Direct

Sedgwick O, Young S, Baumeister D, Greer B, Das M, Kumari V

Neuropsychology and emotion processing in violent individuals with antisocial personality disorder or schizophrenia: The same or different? A systematic review and meta-analysis

Australian and New Zealand Journal of Psychiatry 2017; 51: 1178-97

View review abstract online

Comparison	**IQ in people with schizophrenia or antisocial personality disorder and violent behaviours vs. controls.**
Summary of evidence	**Moderate to high quality evidence (unclear sample size, consistent, precise, direct) shows a large effect of lower IQ in people with schizophrenia and a small effect in people with antisocial personality disorder.**
IQ	
A large effect of lower IQ in people with schizophrenia than controls; 6 studies, g = -0.78, 95%CI -1.05 to -0.52, $p < 0.001$, I^2 = 36%, p = 0.167 *A small effect of lower IQ in people with antisocial personality disorder than controls;* 8 studies, g = -0.30, 95%CI -0.50 to -0.10, p = 0.003, I^2 = 0%, p = 0.679	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Sprong M, Schothorst P, Vos E, Hox J, van Engeland H

Theory of mind in schizophrenia. Meta-analysis

British Journal of Psychiatry 2007; 191: 5-13

View review abstract online

Comparison	**Association between IQ and performance on Theory of Mind (ToM)**

	tasks in schizophrenia spectrum disorders vs. controls.
Summary of evidence	**Moderate quality evidence (large sample, unable to assess consistency or precision, direct) show no association between ToM performance and IQ in people with schizophrenia compared with controls.**
Combined ToM score	
29 observational studies, N = 831 Performance on ToM tasks in people with schizophrenia compared with controls showed no difference in results when IQ was added to the analysis. No publication bias.	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

Stefanopoulou E, Manoharan A, Landau S, Geddes J, Goodwin G, Frangou S

Cognitive functioning in patients with affective disorders and schizophrenia: A meta-analysis

International Review of Psychiatry 2009; 21(4):336-356

View review abstract online

Comparison	**General intelligence in people with schizophrenia vs. bipolar disorder.**
Summary of evidence	**Moderate to high quality evidence (unclear sample size, direct, some inconsistencies, precise) suggests a medium effect of lower IQ in people with schizophrenia.**
IQ	
A significant, medium effect suggests that people with schizophrenia had lower IQ scores than people with bipolar disorder; WAIS general IQ: SMD = 0.69, 95%CI 0.50 to 0.87, $p < 0.0001$, I^2 = not reported, $p = 0.27$ WAIS verbal IQ: SMD = 0.56, 95%CI 0.14 to 0.99, $p = 0.009$, $I^2 = 71\%$, $p = 0.004$	

WAIS performance IQ: SMD = 0.52, 95%CI 0.14 to 0.90, p = 0.007, I^2 = 63.4%, p = 0.01 *No difference in reading scores was reported between people with schizophrenia and people with bipolar disorder;* NART: SMD = 0.27, 95%CI -0.18 to 0.73, p = 0.24, I^2 = 60.5%, p = 0.05	
Consistency	Consistent except for verbal and performance IQ
Precision	Precise
Directness	Direct

Ventura J, Helleman GS, Thames AD, Koellner V, Nuechterlein KH

Symptoms as mediators of the relationship between neurocognition and functional outcome in schizophrenia: a meta-analysis

Schizophrenia Research 2009; 113(2-3): 189-99

View review abstract online

Comparison	**Association between positive (reality distortion) and negative symptoms and cognitive functioning.**
Summary of evidence	**Moderate quality evidence (large samples, direct, inconsistent, unable to assess precision) suggests that increased negative symptoms (but not positive symptoms) are significantly associated with reduced global cognitive functioning.**
Negative Symptoms	
Medium effect size suggests a significant association between increased negative symptom severity and reduced overall cognitive functioning; 53 studies, N = 4,929, r = -0.24, p < 0.01	
Positive Symptoms	
No association was reported between positive symptom severity and overall cognitive functioning; 25 studies, N = 1,297, r = -0.00, p = 0.97	
Consistency	Authors report all results are inconsistent
Precision	Unable to assess; no measure of precision is reported.

Directness	Direct

Ventura J, Thames AD, Wood RC, Guzik LH, Hellemann G

Disorganisation and reality distortion in schizophrenia: a meta-analysis of the relationship between positive symptoms and neurocognitive deficits

Schizophrenia Bulletin 2010; 121(1-3): 1-14

View review abstract online

Comparison	**Association between reality distortion and disorganised symptoms and overall cognitive functioning in people with schizophrenia.**
Summary of evidence	**Moderate to high quality evidence (large samples, direct, inconsistent, precise) suggests a small effect that overall reduced cognitive functioning may be associated with both increased disorganised and reality distortion symptoms.**
Disorganised symptoms and reality distortion	
Small, significant effect suggests an association between increased disorganised symptoms and reality distortion, and reduced cognitive functioning; 40 studies, N = 4,654, r = -0.05, p < 0.01, CI not reported	
Disorganised symptoms	
Medium sized, significant effect suggests an association between increased disorganised symptoms and reduced overall cognitive functioning; 69 studies, N = 4,002, r = -0.23, 95%CI -0.26 to -0.20, p < 0.01	
Reality distortion	
Small significant effect suggests an association between increased reality distortion and reduced overall cognitive functioning; 50 studies, N = 2,722, r = -0.04, 95%CI -0.08 to -0.01, p = 0.03	
Consistency	Authors report results are inconsistent.
Precision	Precise, unable to assess for combined symptoms.

Directness	Direct

Woodward ND, Purdon SE, Meltzer HY, Zald DH

A meta-analysis of neuropsychological change to clozapine, olanzapine, quetiapine, and risperidone in schizophrenia

International Journal of Neuropsychopharmacology 2005; 8: 457-472

View review abstract online

Comparison	**Global cognition in people with schizophrenia receiving second generation antipsychotics (clozapine, olanzapine, risperidone and quetiapine) vs. first generation antipsychotics (various) or pre- to post-treatment comparison with second generation antipsychotics.**
Summary of evidence	**High quality evidence (medium to large samples, consistent, precise, direct) shows greater improvements in global cognition in patients receiving second-generation antipsychotics compared with patients receiving first-generation antipsychotics.** **Moderate to high quality evidence (unable to assess precision) suggests improvement post-treatment with quetiapine, olanzapine, clozapine or risperidone.**

Global cognition

Greater improvements in global cognition were reported for patients receiving second generation antipsychotics compared with patients receiving first generation antipsychotics;

18 studies, N= 514, g = 0.24, 95%CI 0.114 to 0.37, $p < 0.001$, Q $p > 0.05$

Post-treatment, patients receiving the following second-generation antipsychotics showed improved global cognition;

Quetiapine: 7 studies, N = 118, g = 0.44, CI, not reported, $p < 0.05$, Q-test $p > 0.05$

Olanzapine: 13 studies, N = 690, g = 0.43, CI, not reported, $p < 0.05$, Q-test $p > 0.05$

Clozapine: 17 studies, N = 344, g = 0.29, CI, not reported, $p < 0.05$, Q-test $p > 0.05$

Risperidone: 13 studies, N = 361, g = 0.28, CI, not reported, $p < 0.05$, Q-test $p > 0.05$

Consistency	Consistent

Precision	Precise for first vs. second generation antipsychotics, unable to assess pre-post comparison.
Directness	Direct

Woodward ND, Purdon SE, Meltzer HY, Zald DH

A meta-analysis of cognitive changes with haloperidol in clinical trials of atypical antipsychotics: Dose effects and comparison to practice effects

Schizophrenia Research 2007; 89: 211-224

View review abstract online

Comparison	**Global cognition in people with schizophrenia receiving haloperidol to assess pre-post treatment effects.**
Summary of evidence	**Moderate to high quality evidence (small to medium-sized samples, consistent, precise, direct) suggests improved global cognitive performance post treatment with low dose, but not high dose haloperidol.**
Global cognition	
Significant, small effect of improved global cognitive performance post-treatment for low dose but not high dose haloperidol; Low dose: 6 studies, N = 392, *g* = 0.20, 95%CI 0.07 to 0.33, *p < 0.05* High dose: 6 studies, N = 173, *g* = 0.13, 95%CI -0.05 to 0.31, *p > 0.05*	
Consistency	Authors report all results are consistent (using fixed effects model)
Precision	Precise
Directness	Direct

Explanation of acronyms

CI = Confidence Interval, *d* = Cohen's *d* and *g* = Hedges' *g* = standardised mean differences (see below for interpretation of effect size), ES = effect size, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), IQ = Intelligence Quotient, ITAQ = Insight and Treatment Attitude Questionnaire, MMSE = Mini Mental State

Examination, N = number of participants, NART = National Adult Reading Test, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), PANSS = Positive and Negative Syndrome Scale, Q = Q statistic for the test of heterogeneity, Q_B = test for between group differences (heterogeneity between groups of studies for an outcome of interest), Q_w = test for within group differences (heterogeneity in study results within a group of studies – measure of study consistency), *r* = correlation coefficient, RAVENS = Raven's Progressive Matrices, RCT = randomised controlled trial, SAI = Schedule for the Assessment of Insight, SE = standard error, SMD = standard mean difference, SUMD = Scale to Assess Unawareness of Mental Disorders, ToM = Theory of Mind, vs = versus, WAIS-R = Wechsler Adult Intelligence Scale- Revised, WRAT-R = Wide Range Achievement Test- Revised, β = estimated regression coefficient, μ_p = estimated average correlation in the population, vs. = versus

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.[39]

† 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[39].

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[40]. lnOR stands for logarithmic OR where a lnOR 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 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.

‡ 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;[39]

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

§ 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 relaxed.[41]

‖ 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.

References

1. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMAGroup (2009): Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *British Medical Journal* 151: 264-9.
2. GRADEWorkingGroup (2004): Grading quality of evidence and strength of recommendations. *British Medical Journal* 328: 1490.
3. Aleman A, Agrawal N, Morgan KD, David AS (2006): Insight in psychosis and neuropsychological function: meta-analysis. *British Journal of Psychiatry* 189: 204-12.
4. Christensen TO (2007): The influence of neurocognitive dysfunctions on work capacity in schizophrenia patients: A systematic review of the literature. *International Journal of Psychiatry in Clinical Practice* 11: 89-101.
5. Cohen AS, Saperstein AM, Gold JM, Kirkpatrick B, Carpenter WT, Jr., Buchanan RW (2007): Neuropsychology of the deficit syndrome: new data and meta-analysis of findings to date. *Schizophrenia Bulletin* 33: 1201-12.
6. de Gracia Dominguez M, Viechtbauer W, Simons CJ, van Os J, Krabbendam L (2009): Are psychotic psychopathology and neurocognition orthogonal? A systematic review of their associations. *Psychological Bulletin* 135: 157-71.
7. Dickinson D, Ramsey ME, Gold JM (2007): Overlooking the obvious: a meta-analytic comparison of digit symbol coding tasks and other cognitive measures in schizophrenia. *Archives of General Psychiatry* 64: 532-42.
8. Forbes NF, Carrick LA, McIntosh AM, Lawrie SM (2009): Working memory in schizophrenia: a meta-analysis. *Psychological Medicine* 39: 889-905.
9. Guilera G, Pino O, Gómez-Benito J, Rojo JE (2009): Antipsychotic effects on cognition in schizophrenia: A meta-analysis of randomised controlled trials. *The European Journal of Psychiatry* 23: 77-89.
10. Irani F, Kalkstein S, Moberg EA, Moberg PJ (2011): Neuropsychological Performance in Older Patients With Schizophrenia: A Meta-Analysis of Cross-sectional and Longitudinal Studies. *Schizophrenia Bulletin* 37: 1318-26.
11. Mesholam-Gately RI, Giuliano AJ, Goff KP, Faraone SV, Seidman LJ (2009): Neurocognition in first-episode schizophrenia: a meta-analytic review. *Neuropsychology* 23: 315-36.
12. Quraishi S, Frangou S (2002): Neuropsychology of bipolar disorder: a review. *Journal of Affective Disorders* 72: 209-26.
13. Rajji TK, Ismail Z, Mulsant BH (2009): Age at onset and cognition in schizophrenia: meta-analysis. *British Journal of Psychiatry* 195: 286-93.
14. Schug RA, Raine A (2009): Comparative meta-analyses of neuropsychological functioning in antisocial schizophrenic persons. *Clinical Psychology Review* 29: 230-42.
15. Sprong M, Schothorst P, Vos E, Hox J, van Engeland H (2007): Theory of mind in schizophrenia: meta-analysis.[see comment]. *British Journal of Psychiatry* 191: 5-13.
16. Stefanopoulou E, Manoharan A, Landau S, Geddes JR, Goodwin G, Frangou S (2009): Cognitive functioning in patients with affective disorders and schizophrenia: a meta-analysis. *International Review of Psychiatry* 21: 336-56.
17. Ventura J, Hellemann GS, Thames AD, Koellner V, Nuechterlein KH (2009): Symptoms as mediators of the relationship between neurocognition and functional outcome in schizophrenia: a meta-analysis. *Schizophrenia Research* 113: 189-99.
18. Woodward ND, Purdon SE, Meltzer HY, Zald DH (2005): A meta-analysis of neuropsychological change to clozapine, olanzapine, quetiapine, and risperidone in schizophrenia. *International Journal of Neuropsychopharmacology* 8: 457-72.
19. Woodward ND, Purdon SE, Meltzer HY, Zald DH (2007): A meta-analysis of cognitive change with haloperidol in clinical trials of atypical antipsychotics: dose effects and comparison to practice effects. *Schizophrenia Research* 89: 211-24.

20. Dibben CR, Rice C, Laws K, McKenna PJ (2009): Is executive impairment associated with schizophrenic syndromes? A meta-analysis. *Psychological Medicine* 39: 381-92.
21. Bora E, Yucel M, Pantelis C (2009): Cognitive functioning in schizophrenia, schizoaffective disorder and affective psychoses: meta-analytic study. *British Journal of Psychiatry* 195: 475-82.
22. Daban C, Martinez-Aran A, Torrent C, Tabares-Seisdedos R, Balanza-Martinez V, Salazar-Fraile J, *et al.* (2006): Specificity of cognitive deficits in bipolar disorder versus schizophrenia. A systematic review. *Psychotherapy and Psychosomatics* 75: 72-84.
23. Krabbendam L, Arts B, van Os J, Aleman A (2005): Cognitive functioning in patients with schizophrenia and bipolar disorder: a quantitative review. *Schizophrenia Research* 80: 137-49.
24. Fioravanti M, Bianchi V, Cinti ME (2012): Cognitive deficits in schizophrenia: An updated metanalysis of the scientific evidence. *BMC Psychiatry* 12.
25. Khandaker GM, Barnett JH, White IR, Jones PB (2011): A quantitative meta-analysis of population-based studies of premorbid intelligence and schizophrenia. *Schizophrenia Research* 132: 220-7.
26. Nieto RG, Xavier Castellanos F (2012): A meta-analysis of neuropsychological functioning in patients with early onset schizophrenia and pediatric bipolar disorder. *Journal of Clinical Child and Adolescent Psychology* 40: 266-80.
27. Donoghue K, Doody GA (2012): Effect of illegal substance use on cognitive function in individuals with a psychotic disorder: a review and meta-analysis. *Neuropsychology* 26: 785-801.
28. Hedman AM, van Haren NEM, van Baal CGM, Kahn RS, Hulshoff Pol HE (2013): IQ change over time in schizophrenia and healthy individuals: A meta-analysis. *Schizophrenia Research* 146: 201-8.
29. Ventura J, Thames AD, Wood RC, Guzik LH, Hellman GS (2010): Disorganization and reality distortion in schizophrenia: A meta-analysis of the relationship between positive symptoms and neurocognitive deficits. *Schizophrenia Research* 121: 1-14.
30. Bora E, Lin A, Wood SJ, Yung AR, McGorry PD, Pantelis C (2014): Cognitive deficits in youth with familial and clinical high risk to psychosis: A systematic review and meta-analysis. *Acta Psychiatrica Scandinavica* 130: 1-15.
31. Bora E, Murray RM (2014): Meta-analysis of cognitive deficits in ultra-high risk to psychosis and first-episode psychosis: Do the cognitive deficits progress over, or after, the onset of psychosis? *Schizophrenia Bulletin* 40: 744-55.
32. Nair A, Palmer EC, Aleman A, David AS (2014): Relationship between cognition, clinical and cognitive insight in psychotic disorders: A review and meta-analysis. *Schizophrenia Research* 152: 191-200.
33. Bora E, Pantelis C (2015): Meta-analysis of cognitive impairment in first-episode bipolar disorder: Comparison with first-episode schizophrenia and healthy controls. *Schizophrenia Bulletin* 41: 1095-104.
34. Rabin RA, Zakzanis KK, George TP (2011): The effects of cannabis use on neurocognition in schizophrenia: a meta-analysis. *Schizophrenia Research* 128: 111-6.
35. Bogaty SER, Lee RSC, Hickie IB, Hermens DF (2018): Meta-analysis of neurocognition in young psychosis patients with current cannabis use. *Journal of Psychiatric Research* 99: 22-32.
36. Hauser M, Zhang JP, Sheridan EM, Burdick KE, Mogil R, Kane JM, *et al.* (2017): Neuropsychological Test Performance to Enhance Identification of Subjects at Clinical High Risk for Psychosis and to Be Most Promising for Predictive Algorithms for Conversion to Psychosis: A Meta-Analysis. *Journal of Clinical Psychiatry* 78: e28-e40.
37. Bora E, Binnur Akdede B, Alptekin K (2017): Neurocognitive impairment in deficit and non-deficit schizophrenia: a meta-analysis. *Psychological Medicine* 47: 2401-13.
38. Sedgwick O, Young S, Baumeister D, Greer B, Das M, Kumari V (2017): Neuropsychology and emotion processing in violent individuals with antisocial personality disorder or schizophrenia: The same or different? A systematic review and meta-analysis. *Australian and New Zealand Journal of Psychiatry* 51: 1178-97.
39. CochraneCollaboration (2008): Cochrane Handbook for Systematic Reviews of Interventions. Accessed 24/06/2011.

40. Rosenthal JA (1996): Qualitative Descriptors of Strength of Association and Effect Size. *Journal of Social Service Research* 21: 37-59.
41. GRADEpro (2008): [Computer program]. Jan Brozek, Andrew Oxman, Holger Schünemann. *Version 32 for Windows*