TECHNICAL COMMENTARY

Visuospatial ability

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Introduction

Visuospatial ability refers to a person's capacity to identify visual and spatial relationships among objects. Visuospatial ability is measured in terms of the ability to imagine objects, to make global shapes by locating small components, or to understand the differences and similarities between objects.

Several tests have been designed to assess visuospatial ability. The Weschler Adult Intelligence Scale (WAIS) block-design subtest requires subjects to use small blocks to recreate a larger block pattern. The WAIS picture arrangement subtest assesses perceptual skills and involves study participants placing pictures in a logical order[1]. The WAIS Object Assembly subtest assesses speed and accuracy of jigsaw puzzle completion. The WAIS Picture Completion task requires participants to visually scan an image and identify what is missing. The WAIS Matrix Reasoning subtest requires participants to select the missing design in a patterned sequence. The Benton Judgement of Line Orientation Test requires participants to identify the orientation of a line in comparison to a target line; and both the Rey-Osterrieth Complex Figure Test (ROCFT) and the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) visuospatial/constructional subtest, involve replicating a complex figure from memory[2].

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. Due to the high volume of systematic reviews we have now limited inclusion to systematic meta-analyses. Where no systematic meta-analysis exists for a topic, systematic reviews without meta-analysis are included for that topic. 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.

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[3]. 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,

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

precise and direct with low associated risks (see end of table for an explanation of these terms)[4]. 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 12 systematic reviews that met our inclusion criteria[1, 5-15].

- High quality evidence shows a medium to large effect of poorer visuospatial memory in people with schizophrenia compared to controls. Moderate to high quality evidence suggests a large effect of poorer global visuospatial ability in people with first-episode schizophrenia.
- Moderate quality evidence suggests a medium to large effect of poorer perceptual problem solving, including block design and line orientation compared to controls.
- High quality evidence suggests no differences in visuospatial processing between patients taking first generation or second generation antipsychotics. Moderate to high quality evidence suggests patients taking olanzapine show improvement after treatment, and patients receiving clozapine or risperidone show no improvement.
- Moderate to low quality evidence suggests a medium to large association between impaired understanding, appreciation, reasoning and lower levels of occupational activity and poorer visuospatial ability.
- High quality evidence suggests people at clinical high risk of psychosis are more impaired on visuospatial working memory than those at familial high risk of psychosis.
- Moderate to low quality evidence suggests patients using cannabis have a small to medium-sized effect of better visuospatial ability compared to patients who do not use cannabis.

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

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	**Cognitive functioning in people at clinical high risk (UHR) and familial high risk (FHR) for psychosis.**
Summary of evidence	**High quality evidence (consistent, precise, direct, large samples) suggests people at clinical high risk of psychosis were more impaired on visuospatial working memory than people at familial risk of psychosis.**
Visuospatial working memory	
Significant, small to medium size effect of poor visuospatial working memory in UHR and FHR groups compared with controls, with the UHR group showing the greatest deficit; UHR: 9 studies, N = 802, $d^{\dagger}$ = 0.71, 95%CI 0.39 to 1.04, $p < 0.001$, $I^2 = 0.18\%$, Q-test $p < 0.001$ FHR: 4 studies, N = 426, d = 0.35, 95%CI 0.01 to 0.71, $p = 0.04$, $I^2 = 0.09\%$, Q-test $p = 0.02$ $Q_B = 4.6$, $p = 0.03$ Authors report no publication bias.	
Consistency[‡]	Consistent (low I^2 statistics)
Precision[§]	Precise
Directness[‖]	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 (direct, unable to assess consistency or precision) suggests that lower levels of occupational activity and functioning are associated with poor visuospatial ability.**
Visuospatial ability	
2 studies (N = 128) reported that poor *visuospatial processing/ ability, visual recall and visual scanning* was associated with worse occupational activity and functioning.	
Consistency in results	Unable to assess
Precision in result	Unable to assess
Directness of results	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	**Perceptual problem solving in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate quality (direct, unable to assess consistency, precise) suggests a medium to large effect size of poorer performance on perceptual problem solving tasks, including block design, and line orientation.**
Perceptual problem solving	

Large effect size suggests people with schizophrenia showed poorer performance on the block design task compared with controls; 10 studies, N = 1300, *g* = -0.84, 95%CI -1.06 to -0.61, *p* < 0.05 *Medium effect size suggests people with schizophrenia showed poorer performance on a line orientation task compared with controls;* 5 studies, N = 624, *g* = -0.62, 95%CI -0.94 to -0.30, *p* < 0.05	
Consistency	Unable to assess
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	**Working memory performance in people with schizophrenia vs. controls.**
Summary of evidence	**High quality evidence (direct, mostly consistent and precise) suggests a medium to large effect showing poorer performance in people with schizophrenia compared with controls on visuospatial memory.**

Visuospatial memory

Significant medium effect size of poorer performance on the following visuospatial memory tests in people with schizophrenia compared to controls;

Visual paired associate learning test: 6 studies, *d* = -0.91, 95%CI -1.24 to -0.57, *p* < 0.001, I^2 = 51.5, *p* = 0.067

Benton visual retention test: 9 studies, *d* = -1.29, 95%CI -1.73 to -0.85, *p* < 0.001, I^2 = 83, *p* < 0.001

Complex figure reproduction (errors): 3 studies, *d* = 0.95, 95%CI 0.49 to 1.41, *p* < 0.001, I^2 = 18.1, *p* = 0.295

Tests of immediate facial recognition: 15 studies, *d* = -0.82, 95%CI -1.02 to -0.61, *p* < 0.001, I^2 = 44.1, *p* = 0.034

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

Tests of pattern recognition: 9 studies, *d* = -0.84, 95%CI -1.04 to -0.64, *p* < 0.001, I² = 42.5, *p* = 0.85 Spatial delayed response task (error distance): 3 studies, *d* = 0.85, 95%CI 0.5 to 1.19, *p* < 0.001, I² = 0, *p* = 0.955 Test of spatial recognition: 5 studies, *d* = -0.76, 95%CI -0.96 to -0.56, *p* < 0.001, I² = 0, *p* = 0.41 Spatial span backwards: 6 studies, *d* = -0.99, 95%CI -1.27 to -0.72, *p* < 0.001, I² = 27.6, *p* <= 0.227 Spatial span forward: 19 studies, *d* = -0.94, 95%CI -1.08 to -0.79, *p* < 0.001, I² = 39.1, *p* = 0.042 Immediate visual recall tests: 33 studies, *d* = -0.87, 95%CI -1.01 to -0.72, *p* < 0.001, I² = 63.2, *p* < 0.001 *Visuospatial span - forwards and backwards:* 3 studies, *d* = -0.51, 95%CI -0.88 to -0.16, *p* < 0.001, I² = 53.4, *p* = 0.117 Meta-regression analysis suggests a significant association between longer duration of illness and poorer performance on visual paired associate learning test (*b* = -0.15, *p* = 0.017) and immediate visual recall test (*b* = -0.062*p* = 0.005).	
Consistency	Inconsistent for all except visual paired associate learning test
Precision	Precise
Directness	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	**Visuospatial ability in people with first-episode schizophrenia vs. controls.** **Note: participants defined as 'first-episode' had either a first presentation of psychosis, initial psychiatric hospitalisation, or a minimal duration of illness/treatment.**
Summary of evidence	**Moderate to high quality evidence (direct, large sample, inconsistent, precise) suggests a large effect of poorer global visuospatial ability in people with first-episode schizophrenia compared with controls, including impaired task-specific performance on the WAIS block design and ROCFT Copy task.**

	High quality evidence (consistent) supported this effect in WAIS picture arrangement, object assembly, picture completion and Benton test.
Visuospatial abilities	
Large effect sizes suggest people with first-episode schizophrenia showed significantly poorer visuospatial ability compared with controls, including in global measures as well as in specific subtests; Global Assessment: 12 studies, N = 1685 d = -0.88, 95%CI -1.01 to -0.75, $p < 0.001$, $Q_w = 64.79$, $p < 0.001$ Small effect size associated with a higher proportion of males, $p = 0.05$ WAIS-R Picture Arrangement: 2 studies, N = 529, d = -1.36, 95%CI -1.57 to -1.14, $p < 0.001$, $Q_w = 0.05$, $p = 0.83$ WAIS Block Design: 7 studies, N = 1009, d = -0.90, 95%CI -1.14 to -0.66, $p < 0.001$, $Q_w = 14.12$, $p = 0.03$ WAIS-R Object Assembly: 3 studies, N = 697, d = -0.90, 95%CI -1.17 to -0.63, $p < 0.001$, $Q_w = 3.19$, $p = 0.14$ WAIS-R Picture Completion: 2 studies, N = 709, d = -0.86, 95%CI -1.04 to -0.69, $p < 0.001$, $Q_w = 1.62$, $p = 0.45$ Benton Judgement of Line Orientation: 3 studies, N = 292, d = -0.83, 95%CI -1.08 to -0.59, $p < 0.001$, $Q_w = 0.39$, $p = 0.82$ ROCFT Copy: 5 studies, N = 902, d = -0.61, 95%CI -0.91 to -0.31, $p < 0.001$, $Q_w = 12.44$, $p = 0.01$	
Consistency	Consistent for all measures except global visuospatial ability, WAIS Block Design and ROCFT Copy.
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

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Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

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 quality evidence (inconsistent) suggests a large effect of poor visuospatial ability in EOS vs. controls.** **High quality evidence suggests a large effect of poor visuospatial ability in PBD vs. controls.** **Low quality evidence (indirect) is unable to determine the differences in cognition in EOS vs. PBD.**
Visuospatial ability	
Large effect in EOS and a medium effect in PBD of poorer visuospatial ability vs. controls; EOS: 7 studies, N = 540, *g* = -0.96, 95%CI -1.28 to -0.64, *p* < 0.005, Q = 14.69, *p* = 0.02 PBD: 3 studies, N = 234, *g* = -0.44, 95%CI -0.79 to -0.09, *p* = 0.02, Q = 1.56 *p* = 0.46 Visuospatial ability was significantly lower in EOS vs. controls than PBD vs. controls (*p* < 0.001). Moderator analyses revealed significantly smaller effect sizes in studies with a higher percentage of males in both diagnostic groups. No publication bias.	
Consistency	Consistent for PBD, inconsistent for EOS
Precision	Precise
Directness	Direct, apart from EOS vs. PBD

Palmer BW, Savla GN

The association of specific neuropsychological deficits with capacity to consent to research or treatment

Journal of the International Neuropsychological Society 2007; 13: 1047-1059

View review abstract online

Comparison	**Association between visuospatial ability and capacity to consent to treatment and research in people with schizophrenia spectrum disorders, in terms of their *understanding* of the information; *appreciation* of the context; and *reasoning* of the**

	consequences of their decision.
Summary of evidence	**Moderate to low quality evidence (direct, unable to assess precision or consistency, mostly small samples) suggests that impaired understanding, appreciation and reasoning were associated with poorer visuospatial ability (medium to large effect) in people with schizophrenia.**
Capacity to consent (understanding, appreciation and reasoning) and visuospatial ability	
1 study (N = 25) reported medium associations between understanding and RBANS and Matrix reasoning (r = 0.44 to 0.71, $p < 0.05$). 1 study (N = 108) reported a medium association between understanding and perceptual organisation (r = 0.31, $p < 0.05$). 1 study (N = 25) reported a medium association between appreciation and Matrix reasoning (r = 0.64, $p < 0.05$). 2 studies (N = 55) reported a medium association between appreciation and RBANS visuospatial/constructional (r = 0.24-0.54, $p < 0.05$). 1 study (N = 25) reported a medium association between reasoning and Matrix reasoning (r = 0.45, $p < 0.05$). 1 study (N = 108) reported a medium association between reasoning and perceptual organisation (r = 0.47 $p < 0.01$).	
Consistency	Unable to assess – authors report inconsistency
Precision	Unable to assess
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

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Comparison	**Relationship between current cannabis use and cognitive ability in people with schizophrenia.**

Summary of evidence	**Moderate to low quality evidence (unable to assess consistency or precision, direct) suggests patients using cannabis have a small to medium-sized effect of better visuospatial ability compared to patients who do not use cannabis.**
Visuospatial ability	
A significant, small to medium-sized effect of better visuospatial ability in patients with cannabis use; 3 studies, d = 0.33, SD = 0.27, $p < 0.05$	
Consistency in results	Unable to assess
Precision in results	Unable to assess
Directness of results	Direct

Rajji TK, Mulsant BH

Nature and course of cognitive function in late-life schizophrenia: a systematic review

Schizophrenia Research 2008; 102: 122-140

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Comparison	**Visuospatial ability in people with schizophrenia aged over 50 years (late-life schizophrenia, LLS).**
Summary of evidence	**Low to moderate quality evidence (large samples, direct, unable to assess consistency or precision) suggests people with late-life schizophrenia may have impaired visuospatial ability.**
Visuospatial ability	
Visuospatial ability was consistently found to be impaired in ten studies in LLS. One study (N = 181) reported LLS were impaired in composite measures of visuospatial ability; three studies (N = 445) reported LLS impairments in visuospatial tasks combined with information processing tasks, and six further studies (N = 951) reported impairments in individual tests of visuospatial ability. These deficits were consistent across hospitalised patients, ambulatory subjects and mixed subject groups, but may be more prevalent in late onset schizophrenia. One study (N = 75) additionally	

reported no difference in visuospatial ability in hospitalised patients compared with ambulatory patients, after controlling for illness severity and medication.	
Consistency	Unable to assess
Precision	Unable to assess
Directness	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

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Comparison	**Visuospatial 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, and people with any other age at onset were classified as first-episode schizophrenia.**
Summary of evidence	**Low to moderate quality evidence (direct, unable to assess consistency or precision, large sample) suggests poorer performance in visuospatial construction in people with first-episode, youth-onset and late-onset schizophrenia compared with controls.**
Visuospatial construction	
N = 4057 first-episode schizophrenia, 692 youth-onset schizophrenia, 261 late-onset schizophrenia. *All three groups showed considerable visuospatial impairment, with significant between group variability;* First-episode schizophrenia: 34 studies, d = 0.83, SE 0.03, $p < 0.05$ Youth-onset schizophrenia: 10 studies, d = 0.98, SE 0.08, $p < 0.05$ Late-onset schizophrenia: 3 studies, d = 1.41, SE 0.18, $p < 0.05$ $Q_B = 12.97$, $p < 0.01$	
Consistency	Unable to assess

Precision	Unable to assess (appears imprecise)
Directness	Direct

Szöke A, Tranfafir A, Dunpont ME, Méary A, Schürhoff F

Longitudinal studies of cognition in schizophrenia: meta-analysis

The British Journal of Psychiatry 2008; 192: 248-257

View review abstract online

Comparison	**Visuospatial ability in people with schizophrenia tested on two separate occasions more than 1 month apart.**
Summary of evidence	**Moderate to high quality evidence (precise, direct, unable to assess consistency, large samples) suggests that people with schizophrenia may show improved performance on the WAIS block design task, but not on the ROCFT.**
Visuospatial	
Significant small effect of improved performance on the WAIS block design test but not the ROCFT at retest compared with baseline; WAIS block design: 9 studies, N = 368, g = 0.22, 95%CI 0.08 to 0.37, $p < 0.05$ ROCFT: 5 studies, N = 157, g = 0.09, 95%CI -0.14 to 0.31, $p > 0.05$	
Consistency	Unable to assess
Precision	Precise
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	**Visuospatial processing in people with schizophrenia receiving second generation antipsychotics (clozapine, olanzapine, risperidone and quetiapine).**
Summary of evidence	**High quality evidence (consistent, precise, direct) shows no differences in visuospatial processing between patients receiving first or second generation antipsychotics.** **Moderate to high quality evidence (unable to assess precision) suggests that patients receiving olanzapine show improvement pre- to post-treatment, however patients receiving clozapine or risperidone show no improvement. Low quality evidence (very small N) is unable to determine the effect of quetiapine on visuospatial processing.**
Visuospatial processing	
No difference in attention was reported between patients receiving second generation antipsychotics compared with patients receiving first generation antipsychotics; 10 studies, N= 253, *g* = 0.00, 95%CI - 0.18 to 0.02, *p* = 0.988, Q-test *p* > 0.05 *Post-treatment, patients receiving olanzapine showed improved performance;* Olanzapine: 5 studies, N = 144, *g* = 0.50, (CI not reported), *p* > 0.006, Q-test *p* > 0.05 *Patients receiving clozapine or risperidone or quetiapine showed no significant improvement post medication;* Clozapine: 9 studies, N = 179, *g* = 0.20, (CI not reported), *p* > 0.05, Q-test *p* > 0.05 Risperidone: 3 studies, N = 65, *g* = 0.39, (CI not reported), *p* > 0.05, Q-test *p* > 0.05 Quetiapine: 1 studies, N = 11, *g* = 0.56, (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

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

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), LLS = Late Life Schizophrenia, N = number of participants, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), Q = Q statistic for the test of heterogeneity, Q_B = test for between group differences (heterogeneity between groups of studies for an outcome of interest), RBANS = Repeatable Battery for the Assessment of Neuropsychological Status, RCT = randomised controlled trail, ROCFT = Rey-Osterrieth Complex Figure Test, SE = standard error, SMD = Standardised Mean Difference, vs = versus, WAIS-R = Wechsler Adult Intelligence Scale (Revised)

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

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[16].

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† Different effect measures are reported by different reviews.

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

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

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect[16].

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[17]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

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

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

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‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula[16];

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

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§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, these criteria should be relaxed.[18]

‖ 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.

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

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