TECHNICAL COMMENTARY

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Information processing

Introduction

Information processing involves several cognitive functions including perception, attention, memory and decision making, as well as the speed at which these cognitive functions are executed. Any impairment in information processing can also reflect impairments in these other cognitive domains.

Information processing can be assessed using various tests. The Wechsler Adult Intelligence Scale (WAIS) digit symbol coding test presents participants with paired numbers and symbols and when shown several numbers, participants must write down the missing corresponding symbols as quickly as possible. The Wisconsin Card Sorting Task (WCST) requires an ability to shift cognitive sets; participants are told to match stimulus cards containing varying coloured shapes, based first on colour, then quantity, then design. The participant is then given additional cards and asked to match each one without being told any matching rules, so participants usually match according to the previous rule. Feedback is provided as to whether their match was correct or incorrect, based on a new and undisclosed matching rule, that changes during the task. The Trail Making Test (TMT) requires participants to connect, in order, letters and/or numbers as quickly as possible. The Stroop Colour Word Test (SCWT), presents colour names printed in an ink congruent to the colour name (e.g. blue), or incongruent to the colour name (e.g. blue). Participants are asked to either read the word or name the ink colour. Category fluency (e.g. animal naming) is an oral test that requires participants to name as many of a category (e.g. types of animals) in one minute. The Stockings of Cambridge (SOC) planning task requires participants to mentally plan a sequence of moves needed to complete a task in the fewest number of moves before beginning the task.

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 checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons,

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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 28 systematic reviews that met our inclusion criteria[3-30].

- Compared to controls, high quality evidence shows a large effect of poorer information processing in people with schizophrenia. This result was found regardless of medication status, and on a variety of tasks including digit symbol coding, TMT-A, and SCWT, and covered both first episode and chronic schizophrenia. Moderate quality evidence also suggests poorer performance in people with youth-onset or late-onset schizophrenia.
- Compared with affective psychoses moderate to high quality evidence shows a small effect of poorer information processing on TMT-A, TMT-B, and WCST categories, but not on WCST perseverative errors or on the SCWT in patients with schizophrenia.
- Moderate to high quality evidence shows a weak association between increased positive, negative or disorganised symptoms and poorer information processing. Moderate quality evidence suggests greater impairment in deficit schizophrenia (predominately negative symptoms) compared with non-deficit schizophrenia in both speeded and non-speeded tasks.
- High quality evidence shows greater improvements in processing speed in patients receiving second-generation antipsychotics compared with patients receiving first-generation antipsychotics. Moderate to high quality evidence suggests that patients receiving olanzapine, clozapine or risperidone showed improvements from pre- to post-treatment, while patients receiving quetiapine showed no improvement. High quality evidence suggests no improvement in processing speed post-treatment with haloperidol.
- High quality evidence shows better information processing may have a medium association with increased community functioning. Symptom severity may act as a mediator between speed of processing and functional impairment.
- Moderate to high quality evidence finds medium-sized effects of fewer number of perfect solutions on the SOC task, and more subsequent thinking time in people with schizophrenia, with no differences in initial thinking time.
- Moderate to high quality evidence suggests medium to strong associations between increased speed of processing and increased scores on memory, executive functioning, verbal learning, visual learning, attention/ vigilance, reasoning, abstraction and flexibility tasks.
- Moderate to high quality evidence suggests better speed of processing in people with schizophrenia with any substance use disorder compared with people with schizophrenia without any substance use disorder.
- High quality evidence suggests people at clinical high risk or familial high risk of

psychosis are similarly impaired on processing speed.

- Moderate to high quality evidence shows a medium-sized effect of slower processing speed in people at clinical high-risk for psychosis than controls. There was a large effect of poorer processing speed in people at high risk who converted to psychosis compared to controls, and a small effect in non-converters compared to controls. Moderate quality evidence shows a medium-sized effect of better processing speed in people at clinical high-risk of psychosis than people with first-episode psychosis.
- High quality evidence shows similar, small improvements in processing speed over time (1 to 5 years) in people at high risk of psychosis, in people with first-episode psychosis, and in controls.
- Moderate to high quality evidence suggests small associations between slower processing speed and poorer emotion perception, social perception, Theory of Mind, facial recognition, and emotion processing.

Information processing

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	**Processing speed 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 clinical high risk of psychosis and familial high risk of psychosis are similarly impaired on processing speed.**
Processing speed	
Significant, small to medium size effect of poor processing speed in UHR and FHR groups compared to controls, with no significant differences between groups; UHR: 8 studies, N = 974, d = 0.47, 95%CI 0.27 to 0.66, $p < 0.001$, I^2 = 0.04%, Q-test p = 0.04 FHR: 13 studies, N = 1,494, d = 0.35, 95%CI 0.22 to 0.49, $p < 0.001$, I^2 = 0.02%, Q-test p = 0.13 Q_B $p > 0.05$ In FHR studies, symptomatic subjects were significantly more impaired than asymptomatic subjects. 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

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View review abstract online	
Comparison	**Changes in processing speed over time in people at ultra-high risk of psychosis (UHR) compared with people with first-episode psychosis (FEP) or controls.**
Summary of evidence	**High quality evidence (medium to large samples precise, direct, consistent) suggests similar, small improvements in processing speed over time in people at ultra-high risk of psychosis, people with first-episode psychosis and controls.**
Cognitive functioning over time (1 to 5 years)	
Significant, small improvement in processing speed over time in UHR, FEP and controls, with no significant differences between groups; FEP: 12 studies, N = 627, d = 0.19, 95%CI 0.08 to 0.30, $p < 0.001$, I^2 = 0%, Q-test p = 0.84 UHR 9 studies, N = 242, d = 0.18, 95%CI 0.0 to 0.36, p = 0.05, I^2 = 0%, Q-test p = 0.64 Controls: 8 studies, N = 299, d = 0.38, 95%CI 0.21 to 0.54, $p < 0.001$, I^2 = 0%, Q-test p = 0.85 Q_B $p > 0.05$ Authors report no publication bias and no effects of medication status.	
Consistency	Consistent
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	**Processing speed 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, mostly precise, direct) suggests people with deficit**

	schizophrenia are more impaired than people with non-deficit schizophrenia on measures of processing speed.
Processing speed	
Significant, medium-sized effects of poorer processing speed in people with deficit schizophrenia compared to people with non-deficit schizophrenia; Processing speed: 14 studies, N = 1,855, d = 0.43, 95%CI 0.26 to 0.60, $p < 0.001$, I^2 = 59%, p = 0.003 TMT A: 8 studies, N = 793, d = 0.44, 95%CI 0.15 to 0.74, p = 0.003, I^2 = 71%, $p < 0.001$ Symbol coding: 5 studies, N = 1,171, d = 0.52, 95%CI 0.33 to 0.71, $p < 0.001$, I^2 = 46%, p = 0.12 *Significant, large effects of poorer processing speed in people with deficit schizophrenia compared to controls and in people with non-deficit schizophrenia compared to controls;* Deficit: 6 studies, N = 822, d = 1.26, 95%CI 0.68 to 1.83, $p < 0.001$, I^2 = 92%, $p < 0.001$ Non-deficit: 6 studies, N = 907, d = 0.80, 95%CI 0.44 to 1.16, $p < 0.001$, I^2 = 83%, $p < 0.001$	
Consistency in results	Mostly inconsistent.
Precision in results	Mostly precise.
Directness of results	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	**Performance speed in people with deficit schizophrenia (predominantly negative symptoms) vs. people with non-deficit schizophrenia.**
Summary of evidence	**Moderate quality evidence (large samples, unable to assess consistency or precision, direct) suggests greater impairment in deficit schizophrenia compared to non-deficit schizophrenia in both speeded and non-speeded tasks.**
Performance speed	

Information processing

Greater impairment in people with deficit schizophrenia compared to non-deficit schizophrenia for both speeded and non-speeded tasks (letter cancellation, trails A, WAIS-R digit symbol); $Q_B = 0.17$, $p > 0.05$ *Small effect for speeded tasks;* 8 studies, N = 467, 19 measures, mean weighted ES (unspecified) = 0.46, 95%CI 0.26 to 0.67, $Q_w = 4.95$ *Small effect for non-speeded tasks;* 13 studies, N = 719, 90 measures, ES = 0.42, 95%CI 0.26 to 0.57, $Q_w = 13.03$	
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 speed of processing and symptoms dimensions in people with on-affective psychosis.**
Summary of evidence	**Moderate to high quality evidence (unclear sample size, direct, precise, consistent) finds a weak association between increased symptoms and slower processing speed.**
Information processing	
*A significant weak association between increased **negative symptoms** and lower speed of processing;* 23 studies, $\mu_p = -0.167$, 95%CI -0.241 to -0.09, $p = 0.00$, $I^2 = 53\%$ *A significant weak association between increased **disorganised symptoms** and lower speed of processing;* 13 studies, $\mu_p = -0.171$, 95%CI -0.275 to -0.062, $p = 0.002$, $I^2 = 56\%$ *A significant very weak association between increased **positive symptoms** and lower speed of*	

processing; 20 studies, μ_p = -0.089, 95%CI -0.164 to -0.012, *p* = 0.023, I^2 = 46%	
Consistency	Consistent
Precision	Precise
Directness	Direct

De Herdt A, Wampers M, Vancampfort D, De Hert M, Vanhees L, Demunter H, Van Bouwel L, Brunner E, Probst M

Neurocognition in clinical high risk young adults who did or did not convert to a first schizophrenic psychosis: a meta-analysis

Schizophrenia Research 2013; 149(1-2): 48-55

View review abstract online

Comparison	**Baseline processing speed in people at clinical high risk for psychosis who transitioned to psychosis at follow-up compared with those who did not transition to psychosis at follow-up.**
Summary of evidence	**Moderate to low quality evidence (unclear sample size, inconsistent, imprecise, direct) suggests no differences in processing speed.**
Processing speed	
No significant differences between groups; 7 studies, *g* = -0.52, 95%CI -1.21 to 0.17, *p* = 0.138, Q-test *p* < 0.0001	
Consistency	Inconsistent
Precision	Imprecise
Directness	Direct

Dickinson D, Ramsey ME, Gold JM

Information processing

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	**Processing speed in people with schizophrenia vs. healthy controls.**
Summary of evidence	**High quality evidence (large samples, direct, consistent, precise) suggests a large effect of poorer performance in schizophrenia patients on digit symbol coding compared to controls.** **Moderate to high quality evidence (unable to assess consistency) also suggests a large effect of poorer performance on TMT-A and Stroop word-reading conditions.**

Processing speed

Large effect size suggests people with schizophrenia showed poorer processing speed performance compared to controls on tasks including;

Digit symbol coding: 37 studies, N = 3,405, *g* = -1.57, SE = 0.05, 95%CI -1.66 to -1.48, Q = 40.7, *p* = 0.21

TMT-A: 19 studies, N = 1,770, *g* = -0.88, SE = 0.07, 95%CI -1.01 to -0.75

Stroop word-reading condition: 3 studies, N = 212, *g* = -0.97, SE = 0.15, 95%CI -1.26 to -0.67

Subgroup analysis suggests better performance on digit symbol coding in younger people with shorter duration of illness (*g* = 1.44, 95%CI -1.63 to -1.25, Q_w = 14.18) compared to older people with chronic illness (*g* = -1.62, 95%CI -1.77 to -1.47, Q_w = 21.43).

People with early onset schizophrenia performed more poorly on digit symbol coding (*g* = -1.72, 95%CI -2.09 to -1.34, Q_w = 4.39).

No association was reported with medication, symptom severity or education.

Consistency	Consistent, unable to assess for trial making A or Stroop word-reading condition
Precision	Precise
Directness	Direct

Information processing

Dickinson D, Gold JM

Less unique variance than meets the eye: Overlap among traditional neuropsychological dimensions in schizophrenia

Schizophrenia Bulletin 2008; 34(3): 423-434

View review abstract online

Comparison	**Association between individual and composite measures of speed of processing and other neuropsychological tests on people with schizophrenia.**
Summary of evidence	**Moderate to high quality evidence (large sample, direct, unable to assess consistency, precise) suggests a medium to strong association between increased scores on speed of processing and increased scores on other Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) domains including memory, executive functioning, verbal learning, visual learning, attention/ vigilance, reasoning, abstraction and flexibility.**

Speed of processing

9 studies (N = 1,860)

Meta-analysis combined multiple correlations within each study into a single study-level effect size, and then calculated an overall weighted effect size between studies.

Weighted effect size of these 9 studies indicated a significant correlation across composite MATRICS cognitive scores; such that increased performance on speed of processing tasks was associated with increased performance on other cognitive tests, $r = 0.45$, 95%CI 0.35 to 0.54, $p < 0.001$.

1 study (148 outpatients), reported a strong association between increased processing speed (symbol cancellation, trail making test A and category fluency) and increased verbal learning, visual learning and executive functioning; $r = 0.61$, 95%CI 0.56 to 0.66.

1 study (N > 1,123 outpatients), reported a strong association between increased processing speed (letter fluency, category fluency, digit symbol, grooved pegboard) and increased verbal learning, reasoning, working memory, vigilance; $r = 0.50$, 95%CI 0.47 to 0.53.

1 study (N = 40 first episode), reported a medium association between increased processing speed (trails making test A, digit symbol coding and Stroop variables) and increased verbal learning, visual learning and working memory; $r = 0.35$, 95%CI 0.21 to 0.47.

1 study (N = 120 outpatients), reported a strong association between increased scores on individual measures of processing speed (digit symbol coding) and increased scores on block design, matrix

reasoning, arithmetic, digit span, letter-number sequencing and symbol search; *r* = 0.49, 95%CI 0.46 to 0.53. 1 study (N = 53 inpatients), reported a strong association between increased scores on individual measures of processing speed (letter fluency) and increased scores on verbal series CPT, trail making B, symbol digit, HVLT (immediate), digit span, WCST, Stroop; *r* = 0.43, 95%CI 0.38 to 0.47. 1 study (N > 1,123 outpatients), reported a strong association between increased scores on individual measures of processing speed (category and letter fluency, digit symbol coding) and increased scores on WCST, WISC mazes, HVLT, visuospatial working memory, letter-number sequencing and identical pairs CPT; *r* = 0.40, 95%CI 0.37 to 0.44. 1 study (N = 32 outpatients), reported a strong association between increased scores on individual measures of processing speed (letter fluency, digit symbol and trail making A) and increased scores on WCST (perseverative errors), Penn conditional exclusion test, trail making B and HVLT (immediate); *r* = 0.40, 95%CI 0.28 to 0.50. 1 study (N = 36 inpatients), reported a medium association between increased scores on individual measures of processing speed (letter fluency) and scores on letter-number span, WCST (perseverative errors), trail making B, digit span and Gordon's CPT; *r* = 0.44, 95%CI 0.33 to 0.54. 1 study (N = ~140 inpatients and outpatients), reported a medium association between increased scores on individual measures of processing speed (category and letter fluency, symbol digit coding) and increased scores on verbal list learning, digit sequencing and tower of London; *r* = 0.33, 95%CI 0.24 to 0.41. 1 study (N = 169 inpatients), reported a medium association between increased scores on individual measures of processing speed (digit symbol coding) and increased scores on digit span, arithmetic and block design; *r* = 0.32, 95%CI 0.25 to 0.39. 1 study (N = 219 first-episode), reported a medium association between increased scores on individual measures of processing speed (trails making A) and increased scores on CVLT (immediate), WCST (perseverative errors), letter fluency, trails making B and identical pairs CPT; *r* = 0.31, 95%CI 0.27 to 0.34. 1 study (N = 118 first or second episode), reported a medium association between increased scores on individual measures of processing speed (category fluency) and increased scores on CVLT (immediate), Rey complex figure memory, Stroop and Gordon's CPT; *r* = 0.30, 95%CI 0.24 to 0.36. 1 study (N = 30 inpatients), reported a medium association between increased scores on individual measures of processing speed (trail making A and digit symbol coding) and increased scores on trail making B, Rey AVLT, WCST, identical pairs CPT and letter-number sequencing; *r* = 0.30, 95%CI 0.18 to 0.41. 1 study (N = 30 inpatients), reported a medium association between increased scores on individual measures of processing speed (digit symbol coding) and increased scores on visuospatial working memory, digit span (backwards) and WCST (perseverative errors); *r* = 0.24, 95%CI 0.01 to 0.46.	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Precise

Directness	Direct

Fatouros-Bergman H, Cervenka S, Flyckt L, Edman G, Farde L

Meta-analysis of cognitive performance in drug-naïve patients with schizophrenia

Schizophrenia Research 2014; 158: 156-162

View review abstract online

Comparison	**Cognitive performance in people with schizophrenia who have never been medicated vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large sample, direct, inconsistent, precise) shows poorer performance on speed of processing tasks in never-medicated people with schizophrenia compared with controls.**
Speed of processing	
Significant, medium to large effect of poorer executive functioning in never-medicated patients; 7 studies, N = 672, SMD -1.03, 95%CI -1.23 to -0.82, $p < 0.001$, $I^2 = 66\%$, $p < 0.0001$ Tests used were; Verbal fluency letter "S" (amount of words), Verbal fluency animal naming (amount of words), TMT A (time), WAIS-R Digit Symbol (number of digits).	
Consistency	Inconsistent
Precision	Precise
Directness	Direct

Fett AK, Viechtbauer W, Dominguez M, Penn D, van Os J, Krabbendam L

The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: A meta-analysis

Neuroscience and Biobehavioural Reviews 2011; 35: 573-588

View review abstract online

Information processing

Comparison	**Association between functional outcomes (community function, social behaviour, social problem solving, social skills) and information processing performance in schizophrenia.**
Summary of evidence	**High quality evidence (medium to large sample, direct, consistent, precise) shows that better information processing may have a medium association with increased community functioning.**
Community functioning (work performance, social interaction)	
Significant medium positive association between increased performance on a processing speed task and better community functioning; 8 studies, N = 465, r = 0.25, 95%CI 0.13 to 0.37, p <0.001, Q = 12.36, I^2 = 43%, p > 0.05	
Consistency	Consistent
Precision	Precise
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	**Information processing 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 quicker processing speed in people with schizophrenia receiving second-generation antipsychotics compared to those receiving first-generation antipsychotics.** **Moderate to low quality evidence (small sample, imprecise) suggests no difference in perceptual processing.**
Information processing	

Information processing

A significant small effect size showed quicker speed of processing in people with schizophrenia receiving second-generation antipsychotics compared to those receiving first-generation antipsychotics; 11 RCT, N = 909, *g* = 0.26, 95%CI 0.13 to 0.39, *p* < 0.01 *No significant difference in perceptual processing in people with schizophrenia receiving second-generation antipsychotics compared to first-generation antipsychotics;* 2 RCT, N = 136, *g* = 0.04, 95%CI -0.50 to 0.58, *p* = 0.89	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Imprecise for perceptual processing
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	**Information processing in individuals at clinical high-risk of psychosis vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large sample, inconsistent, precise, direct) shows a medium-sized effect of slower processing speed in people at clinical high-risk for psychosis than controls.**
Information processing	
Significant, medium-sized effect of poorer processing speed in people at clinical high-risk; 12 studies, N = 1,664, *g* = -0.43, 95%CI -0.61 to -0.24, *p* < 0.0002, I^2 = 68% This effect was similar in longitudinal studies (follow-up 10.4 months, *g* = -0.45). The effect was significant in studies using the Controlled Oral Word Association Test, Trail-Making A and B, and digit symbol, but not the Finger Tapping Test.	

Information processing

Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct
Comparison 2	**Information processing in individuals at clinical high-risk for psychosis vs. people with first-episode psychosis.**
Summary of evidence	**Moderate quality evidence (medium to large samples, inconsistent, precise, direct) shows a medium-sized effect of better processing speed in people at clinical high-risk of psychosis than people with first-episode psychosis.**
Information processing	
Significant, small effect of better speed of processing in people at clinical high-risk; 5 studies, N = 527, *g* = 0.29, 95%CI 0.03 to 0.56, *p* = 0.03, I^2 = 55% This effect was significant in studies using the Controlled Oral Word Association Test and Verbal Fluency Semantic Categories, but not Trail-Making B.	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct
Comparison 3	**Information processing in individuals at clinical high-risk of psychosis that converted or did not convert to psychosis vs. controls.**
Summary of evidence	**Moderate to high quality evidence (medium to large samples, consistent, precise, direct) found a large effect of poorer speed of processing in converters and a small effect in non-converters.**
Information processing	
Significant, small effect of poorer speed of processing in non-converters vs. controls; 7 studies, N = 528, *g* = -0.34, 95%CI -0.53 to -0.16, *p* < 0.0001, I^2 = 0% This effect was significant on the Trail-Making Test A and Digit Symbol, but not Trail-Making Test B or the Verbal Fluency Test. *Significant, large effect of poorer speed of processing in converters vs. controls;* 7 studies, N = 429, ***g*** = -0.80, 95%CI -1.02 to -0.58, *p* < 0.0001, I^2 = 0%	

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This effect was significant on the Trail-Making Test A and B, Digit Symbol and the Verbal Fluency Test.	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Knowles E, David A, Reichenberg A

Processing speed deficits in schizophrenia: Reexamining the evidence

American Journal of Psychiatry 2010; 167: 828-835

View review abstract online

Comparison	**Information processing (measured by digit symbol coding performance) in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large sample, direct, inconsistent, precise) suggests a large effect of impaired information processing in people with schizophrenia compared to controls.**
Information processing	
A large effect size suggests impaired performance on digit symbol coding in people with schizophrenia compared to controls; 47 studies, N = 6,427, g = -1.50, 95%CI -1.63 to -1.35, I^2 = 78%, p < 0.001	
Consistency	Inconsistent
Precision	Precise
Directness	Direct

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

Neurocognition in first-episode schizophrenia: a meta analytic review

Information processing

Neuropsychology 2009; 23(3): 315-335 View review abstract online	
Comparison	**Information processing 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 processing speed in people with first-episode schizophrenia compared to controls.**
Processing speed	
Large effect size suggests people with first-episode schizophrenia showed significantly poorer processing speed compared to controls; 25 studies, N = 3,017, d = -0.96, 95%CI -1.05 to -0.86, $p < 0.001$, Q = 313.72, $p < 0.001$ Smaller effects were reported in studies with a higher proportion of right-handed patients, male patients, and in more recent publications.	
Consistency	Inconsistent
Precision	Precise
Directness	Direct

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 processing speed 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 quality evidence (large samples, direct, unable to assess precision or consistency) suggests a small effect of**

	impaired understanding, appreciation and reasoning may be associated with poorer processing speed in people with schizophrenia.
Processing speed	
3 studies (N = 1,625) reported a significant association between impaired processing speed and poorer understanding (r = 0.19 to 0.30, p < 0.05). 1 study (N = 1,447) reported a significant association between impaired processing speed and poorer appreciation (r = 0.19, p < 0.05). 2 studies (N = 1,555) reported a significant association between impaired processing speed and poorer reasoning ability (r = 0.21 to 0.43, p < 0.05).	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

Potvin S, Joyal CC, Pelletier J, Stip E

Contradictory cognitive capacities among substance-abusing patients with schizophrenia: a meta-analysis

Schizophrenia Research 2008; 100: 242-251

View review abstract online

Comparison	**Cognitive functioning in people with schizophrenia with a comorbid substance use disorder (SUD) vs. people with schizophrenia without an SUD.**
Summary of evidence	**Moderate to high quality evidence (large sample, direct, precise, unable to assess consistency) suggests better speed of processing in people with schizophrenia with any SUD compared to people with schizophrenia without any SUD.**
Speed of processing	
Speed of processing composite (based on MATRICS groupings): *A significant small effect suggests better speed of processing in people with schizophrenia with any SUD compared to people with schizophrenia without any SUD;*	

Any SUD: 16 studies, N = 1,245, *g* = 0.211, 95%CI 0.013 to 0.409, *p* = 0.037	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Precise
Directness	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	**Information processing in people with schizophrenia aged over 50 years (late-life schizophrenia, LLS) vs. controls.**
Summary of evidence	**Moderate quality evidence (medium to large samples, direct, unable to assess consistency or precision) suggests people with late-life schizophrenia are impaired on information processing speed combined with motor speed and visuospatial performance.**
Information processing	
Three studies (N = 487) reported impaired motor speed and speed of information processing in ambulatory patients with late-life schizophrenia compared to controls. Three studies (N = 445) reported LLS impairments in visuospatial tasks combined with information processing tasks.	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

Information processing

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	**Information processing 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 sample, direct, unable to assess consistency or precision) suggests poorer performance in psychomotor speed of processing and digit symbol coding in people with first-episode, youth-onset and late-onset schizophrenia compared to controls.**
Information processing	
N = 5,010 *All three groups showed considerable digit symbol coding impairment, with significant between group variability;* First-episode schizophrenia: 15 studies, *d* = 1.46, SE 0.05 Youth-onset schizophrenia: 10 studies, *d* = 1.46, SE 0.09 Late-onset schizophrenia: 1 study, *d* = 0.29, SE 0.22 $Q_B = 27.18$, $p < 0.001$ *All three groups showed considerable psychomotor speed of processing impairment, with significant between group variability;* First-episode schizophrenia: 62 studies, *d* = 0.65, SE 0.02 Youth-onset schizophrenia: 17 studies, *d* = 0.92, SE 0.06 Late-onset schizophrenia: 2 studies, *d* = 1.01, SE 0.21 $Q_B = 19.68$, $p < 0.01$	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.

Directness	Direct

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

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Comparison	**Information processing in people with schizophrenia vs. bipolar disorder.**
Summary of evidence	**Moderate to high quality evidence (unclear sample size, direct, consistent, precise) shows a small effect of lower performance on TMT-A, TMT-B, and WCST categories, but not on WCST perseverative errors or the STROOP test in patients with schizophrenia compared to patients with bipolar disorder.**

Information processing

A significant, small effect suggests people with schizophrenia were more impaired on the following tests than people with bipolar disorder;

TMT-A: (number of studies not reported) SMD = -0.23, 95%CI -0.44 to 0.03, $p = 0.02$, I^2 = not reported, $p = 0.06$

TMT-B: SMD = -0.42, 95%CI -0.63 to 0.21, $p < 0.0001$, I^2 = not reported, $p = 0.08$

WCST Categories achieved: SMD = 0.37, 95%CI 0.22 to 0.51, $p < 0.0001$, I^2 = not reported, $p = 0.30$

No differences were reported for the following tests;

WCST perseverative errors: SMD = -0.14, 95%CI -0.33 to 0.03, $p = 0.10$, I^2 = not reported, $p = 0.14$

Stroop Colour Word Test: SMD = 0.18, 95%CI -0.16 to 0.58, $p = 0.34$, I^2 = not reported, $p = 0.21$

Consistency	Consistent
Precision	Precise
Directness	Direct

Information processing

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

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Comparison	**Information processing in people with schizophrenia tested on two separate occasions more than 1 month apart.**
Summary of evidence	**Moderate quality evidence (small samples, precise, direct, unable to assess consistency) suggests that people with schizophrenia show improved performance when retested on the digit symbol substitution test, with no improvement in controls.**
Psychomotor processing	
Significant small effect size suggesting that people with schizophrenia showed improved performance on the digit symbol substitution at retest compared to baseline; 7 studies, N = 215, g = 0.28, 95%CI 0.10 to 0.48, $p < 0.05$ *No difference between controls and people with schizophrenia on improvement levels;* 5 studies, N = 136, g = 0.38, 95%CI 0.13 to 0.63, $p > 0.05$	
Consistency	Unable to assess; no measure of consistency is reported.
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	**Relationship between information processing, positive symptoms and negative symptoms in people with**

	schizophrenia.
Summary of evidence	**Moderate quality evidence (large samples, direct, inconsistent, unable to assess precision) suggests that negative symptoms (but not positive symptoms) are significantly associated with poorer speed of processing. Symptom severity may act as a mediator between speed of processing and functional impairment.**
Positive Symptoms	
No significant relationship between positive symptom severity and speed of processing; 18 studies, N = 1,040, r = 0.04, p = 0.21	
Negative Symptoms	
Small effect size suggests a significant relationship between negative symptom severity and poorer speed of processing; 33 studies, N = 3,899, r = -0.26, p < 0.01 *Subgroup analysis examined the potential for negative symptoms to mediate the effect of neurocognitive performance on functional outcomes;* The relationship between speed of processing and community function appears to be at least partially mediated by negative symptom severity. The relationship between speed of processing and skills assessment also appears to be mediated by negative symptom severity.	
Consistency	Authors report all results are inconsistent.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct for symptom relationships, indirect subgroup analysis.

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

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Information processing

Comparison	**Relationship between information processing and disorganised symptoms and reality distortion in people with schizophrenia.**
Summary of evidence	**Moderate to high quality evidence (large samples, direct, inconsistent, precise) suggests a small effect that impaired speed of processing may be associated with disorganised symptoms in people with schizophrenia. No relationship between speed of processing and reality distortion is observed.**
Disorganised symptoms	
Small significant relationship between disorganised symptoms and speed of processing; 42 studies, N = 2,473, r = -0.26, 95%CI -0.30 to -0.22, $p < 0.01$	
Reality distortion	
No significant relationship between reality distortion and speed of processing; 33 studies, N = 1,870, r = -0.03, 95%CI -0.07 to 0.02, $p > 0.05$.	
Consistency	Authors report results are inconsistent.
Precision	Precise
Directness	Direct

Ventura J, Wood RC, Hellemann GS

Symptom Domains and Neurocognitive Functioning Can Help Differentiate Social Cognitive Processes in Schizophrenia: A Meta-Analysis

Schizophrenia Bulletin 2013; 39(1): 102-111

View review abstract online

Comparison	**Association between social cognition, symptom domains and cognitive functioning in people with schizophrenia.**
Summary of evidence	**Moderate to high quality evidence (large samples, consistent, direct, unable to assess precision) suggests small associations between poor performance on emotion perception, social perception and Theory of Mind tasks and decreased speed of processing.**

Information processing

Associations between social cognition and speed of processing	
Small association between poor emotion perception and poor speed of processing; 16 studies, N = 943, r = 0.29, Q_w = 18.28, p = 0.31 *Small association between poor social perception and poor speed of processing;* 7 studies, N = 478, r = 0.24, Q_w = 3.83, p = 0.80 *Small association between poor Theory of Mind and poor speed of processing;* 11 studies, N = 683, r = 0.18, Q_w = 8.18, p = 0.70	
Consistency in results	Consistent
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Ventura J, Wood RC, Jimenez AM, Hellemann GS

Neurocognition and symptoms identify links between facial recognition and emotion processing in schizophrenia: Meta-analytic findings

Schizophrenia Research 2013; 151: 78-84

View review abstract online

Comparison	**Association between social cognition, symptom domains and cognitive functioning in people with schizophrenia.**
Summary of evidence	**Moderate quality evidence (mixed samples, consistent, unable to assess precision, direct) suggests small associations between poor facial recognition and emotion processing and decreased speed of processing.**
Associations between social cognition and speed of processing	
Small association between poor emotion processing (facial stimuli) and poor speed of processing; 17 studies, N = 1,037, r = 0.29, Q_w = 15.97, p = 0.53 *Small association between poor emotion processing (voice prosody) and poor speed of processing;* 1 study, N = 35, r = 0.34, Q_w = N/A *Small association between poor facial recognition and poor speed of processing;*	

1 study, N = 35, r = 0.24, Q_w = N/A	
Consistency in results	Consistent
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Watson AJ, Joyce EM, Fugard AJB, Leeson VC, Barnes TRE, Huddy V

More haste less speed: A meta-analysis of thinking latencies during planning in people with psychosis

Psychiatry Research 2017; 258: 576-82

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Comparison	**Speed of information processing in people with psychotic disorders (mostly schizophrenia) vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) finds medium-sized effects of fewer number of perfect solutions and more subsequent thinking time in people with schizophrenia, with no differences in initial thinking time.**

Speed of information processing

Measured using the SOC planning task

Overall 11 studies, N = 1,159

Significant, medium-sized effect of fewer number of perfect solutions in people with schizophrenia;

8 studies, N = unclear, SMD = -0.66, 95%CI -0.85 to -0.46, $p < 0.001$, $I^2 = 48\%$, $p = 0.059$

This effect was larger in the subgroup analysis of more difficult tasks than easier tasks (SMD = -1.61 vs. -0.58).

There were no significant differences in initial thinking time;

8 studies, N = unclear, SMD = -0.10, 95%CI -0.52 to 0.33, $p = 0.655$, $I^2 = 90\%$, $p < 0.001$

This effect was larger and significant in the subgroup analysis of more difficult tasks but not for easier tasks (SMD = -0.40 vs. 0.22).

Significant, medium-sized effect of more subsequent thinking time in people with schizophrenia;

8 studies, N = unclear, SMD = 0.50, 95%CI 0.32 to 0.68, $p < 0.001$, $I^2 = 43\%$, $p = 0.095$

This effect was similar in the subgroup analysis of task difficulty (SMD = 0.39 vs. 0.47).

Information processing

Consistency in results	Inconsistent for initial thinking time, trend inconsistent for number of perfect solutions and subsequent thinking time.
Precision in results	Precise
Directness of results	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

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Comparison	**Processing speed 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 processing speed patients receiving second generation antipsychotics.** **Moderate to high quality evidence (unable to assess precision) suggests that patients receiving olanzapine, clozapine or risperidone showed improvements from pre to post treatment, while patients receiving quetiapine showed no improvement.**

Processing speed

Greater improvements in processing speed were reported for patients receiving second generation antipsychotics compared to patients receiving first generation antipsychotics;

15 studies, N= 451, g = 0.21, 95%CI 0.07 to 0.35, p = 0.003, Q-test $p > 0.05$

Post-treatment, patients receiving clozapine, olanzapine or risperidone showed improved processing speed;

Clozapine: 16 studies, N = 326, g = 0.35, CI, not reported, $p < 0.006$, Q-test $p > 0.05$

Olanzapine: 12 studies, N = 648, g = 0.43, CI, not reported, $p < 0.006$, Q-test $p > 0.05$

Risperidone: 9 studies, N = 299, g = 0.30, CI, not reported, $p < 0.006$, Q-test $p > 0.05$

No improvements were reported for patients on quetiapine; *Quetiapine:* 6 studies, N = 107, *g* = 0.35, 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 comparisons.
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

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Comparison	**Processing speed in people with schizophrenia receiving haloperidol to assess before and after treatment effects.**
Summary of evidence	**Moderate to high quality evidence (small to medium-sized samples, consistent, precise, direct) suggests no improvement in processing speed post-treatment with haloperidol.**
Processing speed	
No improvement on digit symbol/ modalities test post treatment; Low dose: 5 studies, N = 344, SMD = 0.13, 95%CI -0.02 to 0.28, *p* > 0.05 High dose: 4 studies, N = 131, SMD = 0.13, 95%CI -0.09 to 0.35, *p* > 0.05 *Or on TMT-B;* All studies: 11 studies, N = 384, SMD = 0.09, 95%CI -0.04 to 0.23, *p* > 0.05 Low dose: 4 studies, N = 179, SMD = 0.02, 95%CI -0.18 to 0.22, *p* > 0.05 High dose: 6 studies, N = 178, SMD = 0.12, 95%CI -0.08 to 0.32, *p* > 0.05	
Consistency	Consistent
Precision	Precise
Directness	Direct

Information processing

Yücel M, Bora E, Lubman DI, Solowij N, Brewer WJ, Cotton SM, Conus P, Takagi MJ, Fornito A, Wood SJ, McGorry PD, Pantelis C

The impact of cannabis use on cognitive functioning in patients with schizophrenia: a meta-analysis of existing findings and new data in first-episode sample

Schizophrenia Bulletin 2012; 38(2):316-330

View review abstract online

Comparison	**Cognition in people with schizophrenia and comorbid cannabis use vs. people with schizophrenia without cannabis use.**
Summary of evidence	**Moderate to high quality evidence (small to medium-sized sample, direct, consistent, precise) suggests a medium-sized effect of people with schizophrenia with lifetime comorbid cannabis faster speed of processing than people with schizophrenia without a history of cannabis use.**
Speed of processing	
People with schizophrenia with lifetime cannabis use showed better processing speed than people with schizophrenia without a history of cannabis use; Processing speed: 5 studies, N = 227, *d* = 0.65, 95%CI 0.38 to 0.92, *p* = 0.001, Q = 1.72, *p* > 0.05	
Consistency	Consistent
Precision	Precise
Directness	Direct

Information processing

Explanation of acronyms

AVLT = auditory verbal learning test, β = estimated regression coefficient, CI = Confidence Interval, CPT = Continuous Performance Task, CVLT = California Verbal Learning Test, *d* = Cohen's *d* and *g* = Hedges' *g* = standardized mean differences (see below for interpretation of effect size), ES = effect size, HVLT = Hpokins Verbal Learning Test, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance),LLS = late life schizophrenia, MATRICS = Measurement and Treatment Research to Improve Cognition in 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_w = test for within group differences (heterogeneity in study results within a group of studies – measure of study consistency), Q_B = test for between group differences (heterogeneity between groups of studies for an outcome of interest), *r* = correlation coefficient, SE = standard error, SMD = standard mean difference, vs. = versus, WAIS-R = Wechsler Adult Intelligence Scale- Revised, WCST = Wisconsin Card Sorting Task, WISC = Wechsler Intelligence Scale for Children, μ_p = = estimated average correlation in the population

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Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small[31].

† 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[31].

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

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

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

‡ 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[31];

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

§ 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[33].

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

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