

## Reasoning

### Introduction

Reasoning refers to the ability to logically gather information to solve problems and form conclusions. Reasoning bias may affect problem solving skills and is measured in three ways: 'jumping to conclusions' (JTC); 'belief inflexibility'; and an 'externalising attribution style'. JTC can be measured with the Bead task that presents participants with two jars containing different ratios of coloured beads (eg. 80 red: 20 blue). Beads are drawn from one of the jars, and based on the string of coloured beads drawn, participants must guess which jar they were drawn from. Within the JTC task, "draws to decision" refers to the number of beads required to decide which jar they were drawn from. Extreme JTC responding refers to when a decision is made after little information is gathered. The "draws to certainty" condition is when participants are asked about their certainty regarding which jar beads are being drawn from. "Response to disconfirmatory evidence" refers to the change in certainty after a single bead contradicts their response. "Response to reversal" is when a participant makes a decision based on the initial evidence, then reverses their decision based on later evidence. Belief inflexibility is an inability to change a belief when presented with contradictory evidence and can be measured by the Bias Against Disconfirmatory or Confirmatory Evidence (BADE/BACE) tasks. Liberal acceptance (LA) can also be measured, which involves overrating the plausibility of absurd interpretations. Attribution bias refers to when available evidence is incorrectly used to attribute an event to internal or external causes and is measured by the Pragmatic Inference Task or Attribution questionnaire where participants are asked to explain events. Reasoning and problem solving may also be measured using Mazes or the Matrix Reasoning where participants select the missing design in a patterned sequence.

### 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<sup>1</sup>. 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

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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)<sup>2</sup>. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

### Results

We found 17 systematic reviews that met our inclusion criteria<sup>3-19</sup>.

- High quality evidence finds a medium-sized association between more severe delusions and more belief inflexibility.
- Moderate to high quality evidence finds medium to large effects of more JTC, BADE, BACE, and LA in people with schizophrenia with current delusions than controls. In people with schizophrenia without delusions there were small to medium-sized effects of more BADE and LA, with no differences in JTC or BACE.
- When directly comparing people with schizophrenia with or without delusions, high quality evidence finds small to medium-sized effects of more JTC, BADE, BACE, and LA in those with delusions.
- There were no differences in JTC, BADE, BACE, and LA between people with schizophrenia with delusions or people with other psychiatric disorders with delusions, however when compared to people with

other psychiatric disorders without delusions, there were medium to large effects of more JTC, BADE, BACE and LA in people with schizophrenia with delusions.

- Moderate to high quality evidence finds medium-sized effects that people with psychosis require less information to form conclusions and show more extreme responding than controls.
- Moderate to high quality evidence finds a medium-sized effect that people with psychosis require less information to form conclusions and a large effect of more extreme responding than people with nonpsychotic mental disorders.
- Moderate to high quality evidence finds small effects that people with psychosis and delusions require less information to form conclusions and display more extreme responding than people with psychosis and not delusions.
- Moderate to high quality evidence shows a small association between poorer reasoning ability and more severe negative symptoms. Moderate quality evidence also suggests an association with more severe disorganised symptoms and, to a lesser extent, more severe reality distortion symptoms.
- Moderate to high quality evidence shows a medium-sized effect of better social problem solving and social skills being associated with increased reasoning ability. Greater community functioning and better social behaviour show a weaker association with increased reasoning ability.
- Moderate to high quality evidence suggests medium to strong associations between poorer reasoning ability and problem solving and poorer verbal learning, processing speed, working memory, attention and vigilance, and verbal fluency. There are weaker associations between poorer reasoning ability and problem solving and poorer emotion perception, social



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perception, facial recognition and emotion processing.

- Moderate to high quality evidence suggests no difference in reasoning and problem-solving ability in people with schizophrenia taking second generation antipsychotics compared to those taking first generation antipsychotics.
- Moderate quality evidence suggests better problem solving and reasoning ability is found in people with schizophrenia with a cannabis use disorder compared to people with schizophrenia without any substance use disorder.
- Moderate to high quality evidence shows a small effect of poorer reasoning in people at clinical high-risk of psychosis compared to controls. High quality evidence finds a medium-sized effect of poorer reasoning in people at high-risk for psychosis who converted to psychosis compared to controls, and a small effect in those who did not convert to psychosis.



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*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](#)

<b>Comparison</b>	<b>Cognitive functioning in people with first-episode schizophrenia vs. people with first-episode bipolar disorder.</b>
<b>Summary of evidence</b>	<b>Moderate quality evidence (small to medium-sized samples, direct, precise, inconsistent) shows no differences in reasoning ability.</b>
<b>Reasoning</b>	
<p><i>No significant differences in reasoning;</i>                  2 studies, N = 218, <math>d = 0.23</math>, 95%CI -0.09 to 0.56, <math>p = 0.16</math>, <math>I^2 = 26.3%</math>, <math>p = 0.24</math>                  Authors report no publication bias.                  No differences were found for males vs. females or younger vs. older patients.</p>	
<b>Consistency in results<sup>†</sup></b>	Consistent
<b>Precision in results<sup>§</sup></b>	Imprecise
<b>Directness of results<sup>  </sup></b>	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](#)

<b>Comparison</b>	<b>Association between reasoning ability and symptom dimensions in people with non-affective psychosis.</b>
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<b>Summary of evidence</b>	<b>Moderate to high quality evidence (unclear sample size, direct, consistent, precise) shows a small association between lower reasoning ability and more severe negative symptoms. Moderate quality evidence (inconsistent) also suggests an association with more severe disorganised symptoms.</b>
<b>Reasoning ability</b>	
<p><i>A significant weak association between increased negative symptoms and lower reasoning and problem solving;</i>            33 studies, <math>\mu_p = -0.140</math>, 95%CI -0.197 to -0.081, <math>p = 0.00</math>, <math>I^2 = 58\%</math></p> <p><i>A significant small to medium association between increased disorganised symptoms and lower reasoning and problem solving;</i>            15 studies, <math>\mu_p = -0.197</math>, 95%CI -0.336 to -0.048, <math>p = 0.009</math>, <math>I^2 = 81\%</math></p> <p><i>No association with positive symptoms;</i>            27 studies, <math>\mu_p = -0.013</math>, 95%CI -0.066 to 0.041, <math>p = 0.639</math>, <math>I^2 = 37\%</math></p>	
<b>Consistency</b>	Consistent apart from disorganised symptoms
<b>Precision</b>	Precise
<b>Directness</b>	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](#)

<b>Comparison</b>	<b>Baseline cognitive functioning 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.</b>
<b>Summary of evidence</b>	<b>Moderate to low quality evidence (unclear sample size, inconsistent, imprecise, direct) suggests no differences in reasoning ability.</b>
<b>Reasoning ability</b>	



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No significant differences between groups in reasoning ability;  
8 studies,  $g = 0.39$ , 95%CI -0.32 to 1.10,  $p = 0.279$ , Q-test  $p = 0.000$

<b>Consistency</b>	Inconsistent
<b>Precision</b>	Imprecise
<b>Directness</b>	Direct

*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](#)

<b>Comparison</b>	Association between individual and composite measures of reasoning and problem-solving ability and other neuropsychological tests on people with schizophrenia.
<b>Summary of evidence</b>	Moderate to high quality evidence (large samples, direct, unable to assess consistency, precise) suggests a medium to strong association between increased scores of reasoning ability and problem solving (WISC mazes and WCST variables) and increased scores on other Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) domains including verbal learning, processing speed, working memory, vigilance, category and letter fluency, digit symbol, Hopkins verbal learning test (HVLTL), visuospatial working memory variables, letter-number sequencing and identical pairs Continuous Performance Test (CPT) variable in people with schizophrenia.

#### Reasoning and problem solving

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 reasoning tasks was associated



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with increased performance on other cognitive tests,  $r = 0.45$ , 95%CI 0.35 to 0.54,  $p < 0.001$ .

1 study (N > 1,123), reported a significant strong association between increased reasoning ability and problem solving (WCST variables and WISC mazes) and increased verbal learning, processing speed, working memory and vigilance;  $r = 0.50$ , 95%CI 0.47 to 0.53.

1 study (N = 120), reported a strong association between increased scores on individual measures of reasoning ability (matrix reasoning) and increased scores on WAIS-III measures, block design, arithmetic, digit span, letter-number sequencing, digit symbol and symbol search;  $r = 0.49$ , 95%CI 0.46 to 0.53.

1 study (N > 1,123), reported a medium association between increased scores on individual measures of reasoning ability (WISC mazes) and increased scores on the WCST variables, category and letter fluency, digit symbol, HVLT, visuospatial working memory variables, letter-number sequencing, identical pairs CPT variable;  $r = 0.33$ , 95%CI 0.24 to 0.41.

<b>Consistency</b>	Unable to assess; no measure of consistency is reported.
<b>Precision</b>	Precise
<b>Directness</b>	Direct

*Dudley R, Taylor P, Wickham S, Hutton P*

### **Psychosis, Delusions and the "Jumping to Conclusions" Reasoning Bias: A Systematic Review and Meta-analysis**

**Schizophrenia Bulletin 2016; 42: 652-65**

[View review abstract online](#)

<b>Comparison 1</b>	<b>Reasoning bias in people with psychosis vs. controls.</b>
<b>Summary of evidence</b>	<b>Moderate to high quality evidence (large samples, inconsistent, some imprecision, direct) finds medium-sized effects that people with psychosis require less information to form conclusions and show more extreme responding.</b>
<b>Draws to decision</b>	
<i>A significant, medium-sized effect of less information required to form conclusions in people with psychosis;</i>	
33 studies, N = 1,935, $g = -0.53$ , 95%CI -0.69 to -0.36, $p < 0.05$ , $I^2 = 66%$ , $p < 0.001$	
<b>Extreme responding</b>	



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<p><i>A significant, medium-sized effect of more extreme responding in people with psychosis; 22 studies, N = 2,001, OR = 3.82, 95%CI 2.69 to 5.43, p &lt; 0.05, I<sup>2</sup> = 44%, p = 0.01</i></p>	
<b>Consistency</b>	Inconsistent
<b>Precision</b>	Precise for draws to decision, imprecise for extreme responding.
<b>Directness</b>	Direct
<b>Comparison 2</b>	<b>Reasoning bias in people with psychosis vs. people with nonpsychotic mental health disorders.</b>
<b>Summary of evidence</b>	<b>Moderate to high quality evidence (medium to large samples, consistent, some imprecision, direct) finds a medium-sized effect that people with psychosis require less information to form conclusions and a large effect of more extreme responding (JTC).</b>
<b>Draws to decision</b>	
<p><i>A significant, medium-sized effect of less information required to form conclusions in people with psychosis; 13 studies, N = 667, g = -0.58, 95%CI -0.80 to -0.35, p &lt; 0.05, I<sup>2</sup> = 46%, p = 0.03</i></p>	
<b>Extreme responding</b>	
<p><i>A significant, large effect of more extreme responding in people with psychosis; 4 studies, N = 291, OR = 5.55, 95%CI 2.32 to 13.28, p &lt; 0.05, I<sup>2</sup> = 20%, p = 0.29</i></p>	
<b>Consistency</b>	Consistent
<b>Precision</b>	Precise for draws to decision, imprecise for extreme responding.
<b>Directness</b>	Direct
<b>Comparison 3</b>	<b>Reasoning bias in people with psychosis and delusions vs. people with psychosis without delusions.</b>
<b>Summary of evidence</b>	<b>Moderate to high quality evidence (medium to large samples, consistent, some imprecision, direct) finds small effects that people with psychosis and delusions require less information to form conclusions and display more extreme responding (JTC).</b>
<p><i>A significant, small effect of less information required to form conclusions in people with psychosis</i></p>	



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*and delusions;*

8 studies, N = 456,  $g = -0.29$ , 95%CI -0.48 to -0.09,  $p < 0.05$ ,  $I^2 = 0\%$ ,  $p = 0.72$

*There was also a small correlation between increased delusion severity and less information required;*

18 studies, N = 794,  $g = -0.09$ , 95%CI -0.21 to 0.03,  $p < 0.10$ ,  $I^2 = 54\%$ ,  $p = 0.03$

### Extreme responding

*A significant, small effect of more extreme responding in people with psychosis and delusions;*

14 studies, N = 770, OR = 1.52, 95%CI 1.12 to 2.05  $p < 0.05$ ,  $I^2 = 13\%$ ,  $p = 0.31$

<b>Consistency</b>	Consistent, apart from the correlation analysis.
<b>Precision</b>	Precise for draws to decision, imprecise for extreme responding.
<b>Directness</b>	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](#)

<b>Comparison</b>	<b>Association between reasoning bias and functional outcomes (community function, social behaviour, social problem solving, social skills) in patients with schizophrenia.</b>
<b>Summary of evidence</b>	<b>Moderate to high quality evidence (mixed samples, direct, consistent, precise) reports that better social problem-solving and social skills show a medium association with increased reasoning ability. Greater community functioning and better social behaviour show a weak association with increased reasoning ability.</b>
<b>Community functioning (work performance, social interaction)</b>	
<i>Significant small association between increased performance on reasoning and problem-solving tasks and increased community functioning;</i>	
16 studies, N = 901, $r = 0.19$ , 95%CI 0.12 to 0.26, $p < 0.001$ , $I^2 = 9.95\%$ , $p > 0.05$	



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<b>Social behaviour</b>	
<i>Significant small association between increased performance on reasoning and problem-solving tasks and increased social behavior;</i>	
5 studies, N = 257, r = 0.23, 95%CI 0.11 to 0.35, p < 0.001, I <sup>2</sup> = 0%, p > 0.05	
<b>Social problem solving</b>	
<i>Significant small to medium association between increased performance on reasoning and problem-solving tasks and increased social problem solving;</i>	
3 studies, N = 90, r = 0.29, 95%CI 0.08 to 0.47, p = 0.008, I <sup>2</sup> = 0%, p > 0.05	
<b>Social skills</b>	
<i>Significant small to medium association between increased performance on reasoning and problem-solving tasks and increased social skills;</i>	
3 studies, N = 119, r = 0.34, 95%CI 0.17 to 0.50, p < 0.001, I <sup>2</sup> = 0%, p > 0.05	
<b>Consistency</b>	Consistent
<b>Precision</b>	Precise
<b>Directness</b>	Direct

*Fine C, Gardner M, Graigie J, Gold I*

**Hopping, skipping or jumping to conclusions? Clarifying the role of the JTC bias in delusions**

**Cognitive Neuropsychiatry 2007; 12(1): 46-77**

[View review abstract online](#)

<b>Comparison</b>	<b>Association between delusions and reasoning bias (jumping to conclusions – JTC) in people with schizophrenia with delusions vs. people with schizophrenia without delusions vs. psychiatric patients vs. healthy controls.</b>
<b>Summary of evidence</b>	<b>Low quality evidence (unclear sample size, direct, unable to assess consistency or precision) is unable to determine differences in reasoning bias between patients with schizophrenia with delusions compared to patients with schizophrenia without delusions or compared to other</b>



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	<b>psychiatric disorders or controls.</b>
<b>Schizophrenia vs. other psychiatric disorders and healthy controls</b>	
<p>Authors report that people with schizophrenia or delusional disorder had more “draws to decisions” (<math>p &lt; 0.001</math>) and “draws to certainty” (<math>p &lt; 0.001</math>) compared to other psychiatric patients.</p> <p>Authors report that people with schizophrenia or delusional disorder had more “response to disconfirmatory evidence” compared to healthy controls (<math>p &lt; 0.001</math>). No differences were reported with other psychiatric patients (<math>p = 0.56</math>).</p> <p>Authors report no differences in “response to reversal” between people with schizophrenia or delusional disorder and other psychiatric patients (<math>p = 0.38</math>) or healthy controls (<math>p = 0.105</math>).</p>	
<b>Schizophrenia with delusions vs. schizophrenia without delusions</b>	
<p>1 study reported an association between JTC “extreme responding” and the presence of delusions, however, 3 studies reported no differences on “draws to decision” variable.</p>	
<b>Consistency</b>	Unable to assess; no measure of consistency is reported.
<b>Precision</b>	Unable to assess; no measure of precision is reported.
<b>Directness</b>	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](#)

<b>Comparison</b>	<b>Reasoning and problem-solving ability in people with schizophrenia receiving second generation antipsychotics vs. first generation antipsychotics.</b>
<b>Summary of evidence</b>	<b>Moderate to high quality evidence (large sample, direct, precise, unable to assess consistency) suggests no difference in reasoning and problem-solving ability in people with schizophrenia taking second generation antipsychotics compared to those taking first generation antipsychotics.</b>



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Reasoning and problem solving	
<p><i>No significant difference in reasoning and problem-solving ability in people with schizophrenia receiving second generation antipsychotics compared to first generation antipsychotics;</i></p> <p>12 RCTs, N = 1,569, <math>g = 0.07</math>, 95%CI -0.07 to 0.21, <math>p = 0.33</math></p>	
<b>Consistency</b>	Unable to assess; no measure of consistency is reported.
<b>Precision</b>	Precise
<b>Directness</b>	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](#)

<b>Comparison 1</b>	Reasoning in individuals at clinical high-risk of psychosis vs. controls.
<b>Summary of evidence</b>	Moderate to high quality evidence (large sample, inconsistent, precise, direct) shows a small effect of poorer reasoning in people at clinical high-risk of psychosis.
Reasoning	
<p><i>Significant, small effect of poorer reasoning in people at clinical high-risk of psychosis;</i></p> <p>8 studies, N = 969, <math>g = -0.24</math>, 95%CI -0.49 to 0.004, <math>p = 0.05</math>, <math>I^2 = 70\%</math></p> <p>This effect was significant on the Wisconsin Card Sorting Test preservation errors, but not preservation response.</p>	
<b>Consistency in results</b>	Inconsistent
<b>Precision in results</b>	Precise
<b>Directness of results</b>	Direct



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<b>Comparison 2</b>	<b>Reasoning in individuals at clinical high-risk for psychosis vs. people with first-episode psychosis.</b>
<b>Summary of evidence</b>	<b>Moderate quality evidence (medium to large sample, inconsistent, imprecise, direct) finds no differences in reasoning.</b>
<b>Reasoning</b>	
<p><i>No significant differences in reasoning;</i>                      3 studies, N = 441, <math>g = -0.08</math>, 95%CI -0.26 to 0.42, <math>p = 0.642</math>, <math>I^2 = 66\%</math></p>	
<b>Consistency in results</b>	Inconsistent
<b>Precision in results</b>	Imprecise
<b>Directness of results</b>	Direct
<b>Comparison 3</b>	<b>Cognitive functioning in individuals at clinical high-risk of psychosis that converted or did not convert to psychosis vs. controls.</b>
<b>Summary of evidence</b>	<b>High quality evidence (medium to large samples, consistent, precise, direct) finds a medium-sized effect of poorer reasoning in converters and a small effect in non-converters.</b>
<b>Reasoning</b>	
<p><i>Significant, small effect of poorer reasoning in non-converters vs. controls;</i>                      5 studies, N = 420, <math>g = -0.34</math>, 95%CI -0.59 to -0.09, <math>p = 0.008</math>, <math>I^2 = 38\%</math>                      This effect was not significant on the Wisconsin Card Sorting Test preservation errors test.</p> <p><i>Significant, medium-sized effect of poorer reasoning in converters vs. controls;</i>                      5 studies, N = 328, <math>g = -0.50</math>, 95%CI -0.73 to -0.27, <math>p &lt; 0.0001</math>, <math>I^2 = 0\%</math>                      This effect was not significant on the Wisconsin Card Sorting Test preservation errors test.</p>	
<b>Consistency in results</b>	Consistent
<b>Precision in results</b>	Precise
<b>Directness of results</b>	Direct

*McLean BF, Mattiske JK, Balzan RP*

**Association of the Jumping to Conclusions and Evidence Integration Biases With Delusions in Psychosis: A Detailed Meta-analysis**

Schizophrenia Bulletin 2017; 43: 344-54

[View review abstract online](#)

<b>Comparison 1</b>	<b>Reasoning bias in people with schizophrenia with current delusions vs. controls.</b>
<b>Summary of evidence</b>	<b>Moderate to high quality evidence (medium to large sample size, some inconsistency, precise, direct) finds medium to large effects that people with schizophrenia display more JTC, BADE, BACE and LA than controls.</b>
<b>Jumping to conclusions (JTC)</b>	
<i>A medium to large effect of more JTC in people with schizophrenia;</i> 21 studies, N = 1,131, $g = 0.71$ , 95%CI 0.51 to 0.90, $p < 0.05$ , $I^2 = 58%$ , $p < 0.0001$	
<b>Bias against disconfirmatory evidence (BADE)</b>	
<i>A medium to large effect of more BADE in people with schizophrenia;</i> 7 studies, N = 369, $g = 0.56$ , 95%CI 0.28 to 0.83, $p < 0.05$ , $I^2 = 38%$ , $p = 0.14$	
<b>Bias against confirmatory evidence (BACE)</b>	
<i>A medium to large effect of more BACE in people with schizophrenia;</i> 7 studies, N = 369, $g = 0.53$ , 95%CI 0.32 to 0.78, $p < 0.05$ , $I^2 = 0%$ , $p = 0.49$	
<b>Liberal acceptance (LA)</b>	
<i>A medium to large effect of more LA in people with schizophrenia;</i> 6 studies, N = 338, $g = 0.79$ , 95%CI 0.45 to 1.11, $p < 0.05$ , $I^2 = 51%$ , $p = 0.07$	
<b>Consistency</b>	Inconsistent for JTC, consistent for BADE, BACE, and LA.
<b>Precision</b>	Precise
<b>Directness</b>	Direct



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<b>Comparison 2</b>	<b>Reasoning bias in people with schizophrenia without current delusions vs. controls.</b>
<b>Summary of evidence</b>	<b>High quality evidence (medium to large samples, consistent, precise, direct) finds small to medium-sized effects that people with schizophrenia without delusions display more BADE and LA than controls, with no differences in JTC and BACE.</b>
<b>Jumping to conclusions (JTC)</b>	
<i>No significant differences between groups;</i> 7 studies, N = 385, $g = 0.12$ , 95%CI -0.17 to 0.41, $p > 0.05$ , $I^2 = 47%$ , $p = 0.08$	
<b>Bias against disconfirmatory evidence (BADE)</b>	
<i>A small to medium-sized effect of more BADE in people with schizophrenia without delusions;</i> 7 studies, N = 455, $g = 0.35$ , 95%CI 0.15 to 0.55, $p < 0.05$ , $I^2 = 0%$ , $p = 0.69$	
<b>Bias against confirmatory evidence (BACE)</b>	
<i>No significant differences between groups;</i> 7 studies, N = 455, $g = 0.22$ , 95%CI -0.01 to 0.44, $p > 0.05$ , $I^2 = 9%$ , $p = 0.28$	
<b>Liberal acceptance (LA)</b>	
<i>A medium-sized effect of more LA in people with schizophrenia without delusions;</i> 6 studies, N = 409, $g = 0.48$ , 95%CI 0.17 to 0.78, $p < 0.05$ , $I^2 = 49%$ , $p = 0.08$	
<b>Consistency</b>	Consistent
<b>Precision</b>	Precise
<b>Directness</b>	Direct
<b>Comparison 3</b>	<b>Reasoning bias in people with schizophrenia with current delusions vs. people with schizophrenia without current delusions.</b>
<b>Summary of evidence</b>	<b>High quality evidence (medium to large samples, consistent, precise, direct) finds small to medium-sized effects that people with schizophrenia with delusions display more JTC, BADE, BACE and LA than people with schizophrenia without delusions.</b>
<b>Jumping to conclusions (JTC)</b>	



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<p><i>A small to medium-sized effect of more JTC in people with schizophrenia with delusions; 20 studies, N = 834, g = 0.33, 95%CI 0.19 to 0.46, p &lt; 0.05, I<sup>2</sup> = 0%, p = 0.53</i></p>	
<p><b>Bias against disconfirmatory evidence (BADE)</b></p>	
<p><i>A small to medium-sized effect of more BADE in people with schizophrenia with delusions; 8 studies, N = 466, g = 0.31, 95%CI 0.02 to 0.60, p &lt; 0.05, I<sup>2</sup> = 50%, p = 0.05</i></p>	
<p><b>Bias against confirmatory evidence (BACE)</b></p>	
<p><i>A small to medium-sized effect of more BACE in people with schizophrenia with delusions; 7 studies, N = 426, g = 0.39, 95%CI 0.12 to 0.54, p &lt; 0.05, I<sup>2</sup> = 0%, p = 0.55</i></p>	
<p><b>Liberal acceptance (LA)</b></p>	
<p><i>A small to medium-sized effect of more LA in people with schizophrenia with delusions; 6 studies, N = 383, g = 0.38, 95%CI 0.15 to 0.62, p &lt; 0.05, I<sup>2</sup> = 9%, p = 0.36</i></p>	
<b>Consistency</b>	Consistent
<b>Precision</b>	Precise
<b>Directness</b>	Direct
<b>Comparison 4</b>	<b>Reasoning bias in people with schizophrenia with current delusions vs. people with other psychiatric disorders with current delusions.</b>
<b>Summary of evidence</b>	<b>Moderate quality evidence (small sample, consistent, precise, direct) finds no significant differences in JTC.</b>
<p><b>Jumping to conclusions (JTC)</b></p>	
<p><i>No significant differences between groups; 2 studies, N = 86, g = 0.20, 95%CI -0.23 to 0.63, p &gt; 0.05, I<sup>2</sup> = 0%, p = 0.95</i></p>	
<b>Consistency</b>	Consistent
<b>Precision</b>	Precise
<b>Directness</b>	Direct
<b>Comparison 5</b>	<b>Reasoning bias in people with schizophrenia with current delusions vs. people with other psychiatric disorders without current delusions.</b>

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<b>Summary of evidence</b>	<b>Moderate to high quality evidence (small to medium-sized samples, consistent, precise, direct) finds a large effect of more JTC, and medium-sized effects of more BADE, BACE and LA in people with schizophrenia with delusions.</b>
<b>Jumping to conclusions (JTC)</b>	
<i>A large effect of more JTC in people with schizophrenia with delusions; 10 studies, N = 409, g = 0.84, 95%CI 0.64 to 1.04, p &lt; 0.05, I<sup>2</sup> = 0%, p = 0.67</i>	
<b>Bias against disconfirmatory evidence (BADE)</b>	
<i>A medium-sized effect of more BADE in people with schizophrenia with delusions; 4 studies, N = 221, g = 0.68, 95%CI 0.34 to 1.01, p &lt; 0.05, I<sup>2</sup> = 20%, p = 0.29</i>	
<b>Bias against confirmatory evidence (BACE)</b>	
<i>A medium-sized effect of more BACE in people with schizophrenia with delusions; 4 studies, N = 221, g = 0.48, 95%CI 0.19 to 0.78, p &lt; 0.05, I<sup>2</sup> = 0%, p = 0.47</i>	
<b>Liberal acceptance (LA)</b>	
<i>A medium-sized effect of more LA in people with schizophrenia with delusions; 4 studies, N = 221, g = 0.50, 95%CI 0.20 to 0.79, p &lt; 0.05, I<sup>2</sup> = 0%, p = 0.51</i>	
<b>Consistency</b>	Consistent
<b>Precision</b>	Precise
<b>Directness</b>	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](#)

<b>Comparison</b>	<b>Cognitive functioning in people with schizophrenia with a substance use disorder (SUD) vs. people with schizophrenia</b>
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	without a SUD.
<b>Summary of evidence</b>	<b>Moderate quality evidence (small sample, direct, precise, unable to assess consistency) suggests better problem-solving and reasoning ability is found in people with schizophrenia with a cannabis SUD compared to people with schizophrenia without any SUD.</b>
<b>Reasoning and problem-solving</b>	
<p>Problem solving and reasoning composite (based on MATRICS groupings)</p> <p><i>A significant large effect suggests better problem solving and reasoning in people with schizophrenia with cannabis SUD compared to people with schizophrenia without any SUD;</i></p> <p>Cannabis SUD: 2 studies, N = 99, <math>g = 0.789</math>, 95%CI 0.366 to 1.212, <math>p = 0.0001</math></p>	
<b>Consistency</b>	Unable to assess; no measure of consistency is reported.
<b>Precision</b>	Precise
<b>Directness</b>	Direct

So S, Garety P, Peters E, Kapur S

### **Do antipsychotics improve reasoning biases? A review**

**Psychosomatic Medicine 2010; 72: 681-693**

[View review abstract online](#)

<b>Comparison</b>	Reasoning bias in people with a schizophrenia spectrum disorder.
<b>Summary of evidence</b>	<b>Moderate to low quality evidence (small samples, direct, unable to access precision, some inconsistencies) suggests an associated between more severe positive symptoms (usually delusions) and greater belief inflexibility, internalising, externalising and personalising attribution bias. It is unable to determine any clear relationships between JTC or evidence evaluation and schizophrenia, nor the effects of antipsychotics on JTC or attribution style.</b>
<b>Symptoms</b>	



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### *Jumping to conclusions (JTC)*

1 longitudinal study (N = 19 with current hallucinations or delusions) reported that greater delusion symptom scores were associated with poorer performance on the fish task with earlier termination of information gathering.

1 observational study (N = 81: 23 with delusions, 22 psychiatric controls, 36 healthy controls) reported that greater positive and delusional symptoms were associated with fewer beads drawn, and anxiety disorder was associated with a greater number of beads drawn on the Beads task.

1 observational study (N = 100 with current delusions) reported a trend effect of greater positive and delusional symptoms (measured by PANSS) being associated with poorer performance on the Beads task.

No association was reported between severity of delusional symptoms and change in number of 'draws to decision' (1 observational study, N = 19), or JTC performance (1 observational study, N = 128 with schizophrenia, and 1 longitudinal study N = 55: 17 with delusions, 18 psychiatric controls, 20 controls).

### *Attribution style*

1 observational study (N = 81: 23 with delusions, 22 psychiatric controls, 36 healthy controls) reported that deluded patients made significantly more internalizing attributions than healthy controls. Patients with "bad me" delusions showed the greatest self-serving bias and patients with "poor me" delusions showed a depressive attributional style. No association was reported between attribution style and clinical measures at baseline.

1 observational study (N = 136: 40 with acute delusions, 25 with remitted delusions, 35 depressed, 36 healthy controls) reported that people with acute delusions showed significantly greater personalizing bias than patients with remitted delusional symptoms. All patients with delusions (acute or remitted) showed externalizing bias for negative events. Greater attribution bias was significantly associated with increased symptom severity.

1 observational study (N = 71 with schizophrenia) reported that people with increased persecutory and grandiose beliefs showed greater externalizing attribution for negative events.

1 longitudinal study (N = 55: 17 with delusions, 18 psychiatric controls, 20 healthy controls) reported an increase in self-serving bias at follow-up across all groups.

1 observational study (N = 86 with schizophrenia) reported that greater overall psychopathology was associated with less externalizing bias, however no association was reported between externalizing or internalizing bias and delusions specifically.

### *Belief flexibility*

1 observational study (N = 100 with current delusions) reported that poorer belief flexibility was associated with greater delusional symptoms. No association was reported between belief flexibility and severity of psychosis.

1 observational study (N = 100 with current delusions) reported that poorer belief flexibility was associated with greater delusional symptoms and hallucinations (measured by PANSS). No association was reported between belief flexibility and negative or general symptoms.



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1 observational study (N = 76: 36 with active delusions, 16 with remitted delusions, 24 healthy controls) reported that patients with active delusions were less responsive to disconfirmatory evidence than remitted patients.

1 observational study (N = 69: 17 with delusions, 17 without delusions, 35 healthy controls) reported that the deluded and non-deluded groups showed poorer belief flexibility compared to controls, with only the comparison between non-deluded and controls reaching significance. No association was reported between groups on personally meaningful beliefs.

### *Evidence evaluation*

1 longitudinal study (N = 95: 29 schizophrenia, 31 anxious, 35 healthy controls) reported no association between individual psychiatric symptom severity and performance on a probability judgment task, however the effect of confirmatory and disconfirmatory evidence on probability judgment was stronger in remitted patients than non-remitted patients.

### **Effects of antipsychotic medication on task performance**

#### *Jumping to conclusions (JTC)*

1 longitudinal study (N = 19 with schizophrenia: 12 initially drug free) reported that emotionally salient task Beads task 'draws to decision' improved in response to treatment, but not on the neutral version of the task.

1 observational study (N = 128: 39 currently paranoid, 29 remitted paranoid, 27 non-psychotic depressed, 33 healthy controls) reported no association between medication dosage and JTC performance.

#### *Attribution style*

1 longitudinal study (N = 17 with schizophrenia, all initially drug free) reported that antipsychotics had little effect, with only modest improvement on externalising bias. Internalising style was associated with a poorer response to antipsychotic medication.

<b>Consistency</b>	Unable to assess; no measure of consistency is reported.
<b>Precision</b>	Unable to assess; no measure of precision is reported.
<b>Directness</b>	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](#)



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<b>Comparison</b>	<b>Association between reasoning and problem-solving ability and positive and negative symptoms in people with schizophrenia.</b>
<b>Summary of evidence</b>	<b>Moderate quality evidence (large sample, direct, inconsistent, unable to assess precision) suggests a small effect of increased negative symptoms (but not positive symptoms) being significantly associated with poorer reasoning and problem-solving ability. Symptom severity may act as a mediator between reasoning and problem solving and functional impairment.</b>
<b>Positive Symptoms</b>	
<i>No significant association was reported between positive symptom severity and reasoning and problem solving;</i> 16 studies, N = 797, $r = 0.00$ , $p = 0.94$	
<b>Negative Symptoms</b>	
<i>Small effect size suggests a significant association between increased negative symptom severity and poorer reasoning and problem solving;</i> 27 studies, N = 3,039, $r = -0.13$ , $p < 0.01$	
<i>Subgroup analysis examined the potential for negative symptom severity to mediate the effect of neurocognitive performance on functional outcomes;</i> The relationship between reasoning and problem solving with community function appears to be at least partially mediated by negative symptom severity, $p < 0.01$ . The relationship between reasoning and problem solving with skills assessment also appears to be mediated by negative symptom severity, $p < 0.01$ .	
<b>Consistency</b>	Authors report all results are inconsistent.
<b>Precision</b>	Unable to assess; no measure of precision is reported.
<b>Directness</b>	Direct for symptom relationships, indirect subgroup analysis.

*Ventura J, Thames AD, Wood RC, Guzik LH, Helleman 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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[View review abstract online](#)

<b>Comparison</b>	<b>Association between reasoning and problem solving and reality distortion and disorganised symptoms in people with schizophrenia.</b>
<b>Summary of evidence</b>	<b>Moderate to high quality evidence (large samples, direct, inconsistent, precise) suggests a small effect of poorer reasoning and problem solving being associated with increased disorganised symptoms and to a lesser degree, reality distortion.</b>
<b>Disorganised symptoms</b>	
<i>Small effect size suggests a significant association between increased disorganised symptoms and poorer reasoning and problem solving;</i> 38 studies, N = 2,300, $r = -0.24$ , 95%CI -0.28 to -0.19, $p < 0.01$	
<b>Reality distortion</b>	
<i>Very small effect size suggests a significant association between increased reality distortion and poorer reasoning and problem solving;</i> 27 studies, N = 1,427, $r = -0.06$ , 95%CI -0.11 to -0.05, $p = 0.03$	
<b>Consistency</b>	Authors report results are inconsistent.
<b>Precision</b>	Precise
<b>Directness</b>	Direct

*Ventura J, Wood RC, Helleman 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](#)

<b>Comparison</b>	<b>Association between social cognition, symptom domains and cognitive functioning in people with schizophrenia.</b>
<b>Summary of evidence</b>	<b>Moderate to high quality evidence (large samples, consistent, direct, unable to assess precision) suggests small associations between poor performance on emotion perception, social</b>

	<b>perception and Theory of Mind tasks and decreased reasoning and problem-solving ability.</b>
<b>Associations between social cognition and reasoning</b>	
<p><i>Small association between poor emotion perception and poor reasoning/ problem solving;</i> 15 studies, N = 870, <math>r = 0.30</math>, <math>Q_w = 17.38</math>, <math>p = 0.30</math></p> <p><i>Small association between poor social perception and poor reasoning/ problem solving;</i> 8 studies, N = 540, <math>r = 0.33</math>, <math>Q_w = 4.98</math>, <math>p = 0.76</math></p> <p><i>Small association between poor Theory of Mind and poor reasoning/ problem solving;</i> 17 studies, N = 747, <math>r = 0.34</math>, <math>Q_w = 15.58</math>, <math>p = 0.48</math></p>	
<b>Consistency in results</b>	Consistent
<b>Precision in results</b>	Unable to assess; no measure of precision is reported.
<b>Directness of results</b>	Direct

<p><i>Ventura J, Wood RC, Jimenez AM, Helleman GS</i></p> <p><b>Neurocognition and symptoms identify links between facial recognition and emotion processing in schizophrenia: Meta-analytic findings</b></p> <p><b>Schizophrenia Research 2013; 151: 78-84</b></p> <p><a href="#">View review abstract online</a></p>	
<b>Comparison</b>	<b>Association between social cognition, symptom domains and cognitive functioning in people with schizophrenia.</b>
<b>Summary of evidence</b>	<b>Moderate quality evidence (mixed samples, consistent, unable to assess precision, direct) suggests small to medium size associations between poor facial recognition and emotion processing and decreased reasoning and problem-solving ability.</b>
<b>Associations between social cognition and reasoning</b>	
<p><i>Medium size association between poor facial recognition and poor reasoning/ problem solving;</i> 2 studies, N = 68, <math>r = 0.45</math>, <math>Q_w = 3.81</math>, <math>p = 0.15</math></p> <p><i>Small association between poor emotion processing (facial stimuli) and poor reasoning/ problem solving;</i> 15 studies, N = 972, <math>r = 0.28</math>, <math>Q_w = 17.71</math>, <math>p = 0.28</math></p>	



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*Small association between poor emotion processing (voice prosody) and poor reasoning/ problem solving;*

2 studies, N = 68,  $r = 0.30$ ,  $Q_w = 2.10$ ,  $p = 0.35$

<b>Consistency in results</b>	Consistent
<b>Precision in results</b>	Unable to assess; no measure of precision is reported.
<b>Directness of results</b>	Direct

*Zhu C, Sun X, So SH*

### **Associations between belief inflexibility and dimensions of delusions: A meta-analytic review of two approaches to assessing belief flexibility**

**British Journal of Clinical Psychology 2018; 57: 59-81**

[View review abstract online](#)

<b>Comparison</b>	<b>Association between delusions and belief inflexibility in people with schizophrenia spectrum disorders vs. controls.</b>
<b>Summary of evidence</b>	<b>High quality evidence (large sample, consistent, precise, direct) finds a medium-sized association between more severe delusions and more belief inflexibility.</b>

#### **Belief inflexibility and delusions**

*A significant, medium-sized association between more severe delusions and more belief inflexibility;*

4 studies, N = 849,  $g = 0.452$ , 95%CI 0.303 to 0.600,  $p < 0.001$ ,  $I^2 = 0\%$ ,  $p = 0.940$

The effect was similar in the analysis of patients with active delusions.

In the analysis of delusion dimensions, the effect was largest for conviction ( $g = 0.678$ ), then preoccupation ( $g = 0.274$ ), then distress ( $g = 0.20$ ).

<b>Consistency</b>	Consistent
<b>Precision</b>	Precise
<b>Directness</b>	Direct



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### Explanation of acronyms

BADE task – Bias Against Disconfirmatory Evidence, CI = Confidence Interval, CPT = Continuous Performance Test,  $d$  = Cohen's  $d$  and  $g$  = Hedges'  $g$  = standardized mean differences (see below for interpretation of effect size), HVLT = Hopkins verbal learning test,  $I^2$  = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), JTC = Jumping to Conclusions, MATRICS = Measurement and Treatment Research to Improve Cognition in Schizophrenia, OR = odds ratio, N = number of participants, N/A = not applicable,  $p$  = 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),  $r$  = correlation coefficient RCT = Randomised Control Trial, WAIS-III = Wechsler Adult Intelligence Scale, Third Edition, WCST = Wisconsin card sorting task, WISC = Wechsler Intelligence Scale for Children, vs. = versus, Z = z-transformation of the effect size,  $\mu_p$  = 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<sup>20</sup>.

† 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<sup>20</sup>.

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  $< 0.2$ <sup>21</sup>. InOR stands for logarithmic OR where a InOR 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 unforeseen confounding variables. An  $r$  of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised ( $b$ ) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate.  $I^2$  is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity.  $I^2$  can be calculated from  $Q$  (chi-square) for the test of heterogeneity with the following formula;<sup>20</sup>

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

§ 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<sup>22</sup>.

|| 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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