TECHNICAL COMMENTARY

Personality and temperament

Introduction

Personality and temperament are inter-related and are thought to be relatively stable over time. Temperament is a basic inherited style and refers to aspects like emotions, sensitivity, introversion, and extraversion, while personality refers to characteristics like behaviours, feelings, and thoughts.

One of the main personality/temperament models is the Five-Factor Model which includes five traits of; 1) neuroticism: vulnerability to emotional instability and self-consciousness, 2) extraversion: predisposition towards sociability, assertiveness, and social interaction, 3) openness: cognitive disposition to new experiences, creativity, and aesthetics, 4) agreeableness: tendency towards being sympathetic, trusting, and altruistic, and 5) conscientiousness: tendency towards dutifulness and competence.

Impulsivity was originally thought to be part of the extraversion construct but is now viewed as a separate personality construct. It involves a predisposition towards unplanned reactions to internal or external stimuli, without regard to the consequences. Impulsivity is a major feature in a variety of psychiatric disorders.

Method

We have included only systematic reviews with detailed literature search, methodology, and inclusion/exclusion criteria that were published in full text, in English, from the year 2010. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. Reviews with pooled data are prioritized for inclusion. Reviews reporting fewer than 50% of items on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA[1]) checklist have been excluded from the library. The evidence was graded guided by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach[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 six systematic reviews that met our inclusion criteria[3-8].

Compared to controls

- Moderate to high quality evidence suggests large effects of more harm avoidance, highs and lows, depression, irritability, and anxiousness, and less self-directedness and excessive positive mood in people with bipolar disorder. There were medium-sized effects of more self-transcendence and less cooperativeness and excessive positive mood, and small effects of more novelty seeking and less reward dependence in people with bipolar disorder.
- Moderate to high quality evidence found medium-sized effects of more impulsivity on tasks assessing response inhibition, delayed gratification, attention, decision making, and risk-taking in people with bipolar disorder compared to controls. Moderate to low quality evidence found increased impulsivity in non-planning, motor, and general cognitive domains in people with bipolar disorder during remission of the disorder.
- In first-degree relatives of people with bipolar disorder, there were large effects of more highs and lows, irritability, and anxiousness, and medium-sized effects of more harm avoidance and less self-directedness than in controls.

Compared to first-degree relatives

- Moderate to high quality evidence suggests large effects of more harm avoidance, highs and lows, irritability, and anxiousness, and less self-directedness in people with bipolar disorder than in first-degree relatives. There were also medium-sized effects of less cooperativeness, and more novelty seeking and self-transcendence in people with bipolar disorder.

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

Compared to bipolar disorder II

- Moderate to high quality evidence suggests a small effect of more depression in people with bipolar disorder I.

Compared to other psychiatric disorders

- Moderate to high quality evidence suggests medium-sized effects of more novelty seeking, highs and lows, irritability, and excessive positive mood in people with bipolar disorder than in people with major depression. There are also small effects of more self-transcendence and less harm avoidance in people with bipolar disorder.
- Moderate to high quality evidence found no significant differences in levels of overall rumination between people with bipolar disorder and people with major depression. Rumination on positive mood states but not depressive mood states showed increased levels in people with bipolar disorder (both I and II).
- Compared to people with borderline personality disorder, moderate quality evidence suggests large effects of less depression, irritability, and anxiousness, and a medium-sized effect of more excessive positive mood in people with bipolar disorder.
- There were no significant differences in the comparisons with ADHD.

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

Amlung M, Marsden E, Holshausen K, Morris V, Patel H, Vedelago L, Naish KR, Reed DD, McCabe RE

Delay Discounting as a Transdiagnostic Process in Psychiatric Disorders: A Meta-analysis

JAMA Psychiatry 2019; 76: 1176-86

View review abstract online

Comparison	**Monetary delay discounting in people with bipolar disorder vs. controls.** **Monetary delay discounting involves preferring immediate but smaller monetary rewards over delayed but larger monetary rewards.**
Summary of evidence	**Moderate to high quality evidence (medium to large sample, consistent, precise, direct) suggests increased monetary delay discounting in people with bipolar disorder.**
Monetary delay discounting	
A medium-sized effect showed more impulsive delay discounting in people with bipolar disorder; 4 studies, N = 349, g = 0.68, 95%CI 0.37 to 0.98, $p < 0.001$, I^2 = 39%	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Kovacs LN, Takacs ZK, Toth Z, Simon E, Schmelowszky A, Kokonyei G

Rumination in major depressive and bipolar disorder - a meta-analysis

Journal of Affective Disorders 2020; 276: 1131-41

View review abstract online

Comparison	**Rumination in people with bipolar disorder vs. people with major depressive disorder.**

	Depressive rumination is a response style where a person reacts to their own negative mood states by dwelling on them passively and repeatedly. Ruminating on positive mood states involves constantly recalling rewarding past events and positive mood, which amplifies and sustains the positive feeling. Reflection is a more adaptive form of rumination where analysing feelings and thoughts may help problem solving.
Summary of evidence	**Moderate to high quality evidence (large sample, inconsistent, precise, direct) found no significant differences in levels of overall rumination between people with bipolar disorder and people with major depressive disorder. Only rumination on positive mood states showed increased levels in people with bipolar disorder (both I and II) compared to people with major depression.**
Rumination	
There were no significant differences in levels of overall rumination; 12 studies, N = 2,071, g = 0.16, 95%CI -0.06 to 0.38, p = 0.16, I^2 = 79% Subgroup analysis of bipolar disorder type (I or II) showed a non-significant trend effect for greater overall rumination in people with bipolar I disorder compared to people with major depression, with no significant or trend differences between bipolar II disorder and major depression. Subgroup analysis of rumination type showed no significant differences in depressive rumination or reflection, however rumination on positive mood was greater in people with bipolar disorder (g = 0.46), and in the sub-analysis of bipolar types (bipolar I g = 0.51, bipolar II g = 0.44). There were no moderating effects of publication year, sex, age, or study quality score.	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

Ramirez-Martin A, Ramos-Martin J, Mayoral-Cleries F, Moreno-Kustner B, Guzman-Parra J

Impulsivity, decision-making and risk-taking behaviour in bipolar disorder: a systematic review and meta-analysis

Psychological medicine 2020; 50: 2141-53

View review abstract online

Comparison	**Impulsivity and decision making in people with bipolar disorder vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large sample, some inconsistency, precise, direct) found medium-sized effects of poorer performance in people with bipolar disorder on tasks assessing response inhibition, delayed gratification, attention, decision making, and risk-taking.**
Impulsivity **Various tasks**	
Medium-sized effects showed poorer performance on the following measures of impulsivity in people with bipolar disorder; Response inhibition: 13 studies, N = 1,164, g = 0.49, 95%CI 0.36 to 0.62, $p < 0.0001$, I^2 = 26% Delayed gratification: 5 studies, N = 1,913, g = 0.57, 95%CI 0.37 to 0.77, $p < 0.0001$, I^2 = 37% Inattention: 4 studies, N = 645, g = 0.49, 95%CI 0.33 to 0.65, $p < 0.0001$, I^2 = 0% Decision making: 13 studies, N = 1,696, g = -0.61, 95%CI -0.93 to -0.23, p = 0.0002, I^2 = 89% Risk-taking: 6 studies, N = 607, g = 0.41, 95%CI -0.02 to 0.84, p = 0.0598, I^2 = 81% For response inhibition, the effect size was small and not significant in the bipolar I disorder in a euthymic state subgroup. For risk-taking, the effect size was large and significant in the bipolar I disorder in a euthymic state subgroup. For decision making, the effect size was large but not significant in the depressed subgroup, large and significant in the manic subgroup, and small and significant in the euthymic subgroup. It was large and significant in the bipolar I disorder in a euthymic state subgroup.	
Consistency in results	Consistent for response inhibition, delayed gratification, and inattention.
Precision in results	Precise
Directness of results	Direct

Saddichha S, Schuetz C

Is impulsivity in remitted bipolar disorder a stable trait? A meta-analytic review

Comprehensive Psychiatry 2014; 55: 1479-84

View review abstract online	
Comparison	**Impulsivity during remission/euthymia in people with bipolar disorder vs. controls.**
Summary of evidence	**Moderate to low quality evidence (large sample, direct, inconsistent, imprecise) suggests increased impulsivity in non-planning, motor, and cognitive domains in people with bipolar disorder during remission of illness compared to controls.**
Impulsivity **Measured with the Barratt Impulsivity Scale**	
Total scores: 17 studies, N = 1,469, WMD = 12.80, 95%CI 8.03 to 17.56, $p < 0.00001$, $I^2 = 97\%$ Non-planning: 14 studies, N = 1,254, WMD = 4.94, 95%CI 3.66 to 6.22, $p < 0.00001$, $I^2 = 79\%$ Motor: 14 studies, N = 1,254, WMD = 4.32, 95%CI 2.65 to 5.98, $p < 0.00001$, $I^2 = 90\%$ Cognitive: 14 studies, N = 1,254, WMD = 4.10, 95%CI 2.85 to 5.35, $p < 0.00001$, $I^2 = 87\%$	
Consistency in results	Inconsistent
Precision in results	Appears imprecise
Directness of results	Direct

Solmi M, Zaninotto L, Toffanin T, Veronese N, Lin K, Stubbs B, Fornaro M, Correll CU

A comparative meta-analysis of TEMPS scores across mood disorder patients, their first-degree relatives, healthy controls, and other psychiatric disorders

Journal of Affective Disorders 2016; 196: 32-46

View review abstract online

Comparison 1	**Assessment of temperament in people with bipolar disorder vs. controls on the Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego (TEMPS) scale.**
Summary of evidence	**Moderate quality evidence (large samples, inconsistent, imprecise, direct) suggests large effects of increased**

	cyclothymic, depressive, irritable, and anxious temperament scores, with decreased hyperthymic temperament scores, in people with bipolar disorder.
TEMPS	
Large, significant effects of increased TEMPS scores in people with bipolar disorder on the following scales; Cyclothymic (highs and lows): 14 studies, N = 2452, SMD = 2.22, 95%CI 1.61 to 2.84, $p < 0.00001$, $I^2 = 97\%$, $p < 0.00001$ Depressive: 14 studies, N = 2452, SMD = 1.19, 95%CI 0.55 to 1.82, $p = 0.0002$, $I^2 = 97\%$, $p < 0.00001$ Irritable: 14 studies, N = 2452, SMD = 1.29, 95%CI 0.86 to 1.72, $p < 0.00001$, $I^2 = 95\%$, $p < 0.00001$ Anxious: 12 studies, N = 1928, SMD = 1.38, 95%CI 0.66 to 2.09, $p = 0.0002$, $I^2 = 97\%$, $p < 0.00001$ *Medium-sized, significant effect of decreased hyperthymic scores in people with bipolar disorder;* Hyperthymic (excessive positive mood): 14 studies, N = 2452, SMD = -0.44, 95%CI -0.74 to -0.15, $p = 0.004$, $I^2 = 90\%$, $p < 0.00001$	
Consistency in results	Inconsistent
Precision in results	Imprecise, apart from hyperthymic.
Directness of results	Direct
Comparison 2	**Assessment of temperament in first-degree relatives of people with bipolar disorder vs. controls.**
Summary of evidence	**Moderate quality evidence (large samples, inconsistent, imprecise, direct) suggests large effects of increased cyclothymic, irritable, and anxious temperament scores in relatives of people with bipolar disorder.**
TEMPS	
Large, significant effects of increased TEMPS scores in relatives of people with bipolar disorder on the following scales; Cyclothymic: 4 studies, N = 1018, SMD = 1.54, 95%CI 0.43 to 2.65, $p = 0.007$, $I^2 = 98\%$, $p < 0.00001$ Irritable: 4 studies, N = 1018, SMD = 0.98, 95%CI 0.48 to 1.47, $p = 0.0001$, $I^2 = 97\%$, $p < 0.00001$ Anxious: 4 studies, N = 1018, SMD = 2.11, 95%CI 0.50 to 3.72, $p = 0.01$, $I^2 = 99\%$, $p < 0.00001$ There were no significant differences on hyperthymic and depressive scales.	
Consistency in results	Inconsistent

Precision in results	Imprecise
Directness of results	Direct
Comparison 3	**Assessment of temperament in people with bipolar disorder vs. first-degree relatives.**
Summary of evidence	**Moderate quality evidence (large samples, inconsistent, imprecise, direct) suggests large effects of increased cyclothymic, irritable, and anxious temperament scores in people with bipolar disorder compared to relatives of people with bipolar disorder.**
TEMPS	
Large, significant effects of increased TEMPS scores in relatives of people with bipolar disorder on the following scales; Cyclothymic: 4 studies, N = 795, SMD = 2.89, 95%CI 1.48 to 4.29, $p < 0.0001$, $I^2 = 98\%$, $p < 0.00001$ Irritable: 4 studies, N = 795, SMD = 1.90, 95%CI 0.77 to 3.04, $p = 0.001$, $I^2 = 98\%$, $p < 0.00001$ Anxious: 4 studies, N = 795, SMD = 2.71, 95%CI 0.23 to 5.18, $p = 0.03$, $I^2 = 99\%$, $p < 0.00001$ There were no significant differences on hyperthymic and depressive scales.	
Consistency in results	Inconsistent
Precision in results	Imprecise
Directness of results	Direct
Comparison 4	**Assessment of temperament in people with bipolar disorder I vs. bipolar disorder II.**
Summary of evidence	**Moderate to high quality evidence (medium to large sample, consistent, precise, direct) suggests a small effect of decreased depressive temperament scores in people with bipolar disorder I compared to people with bipolar disorder II.**
TEMPS	
Small, significant effect of less depressive scores in people with bipolar disorder I; Depressive: 3 studies, N = 671, SMD = -0.25, 95%CI -0.41 to -0.09, $p = 0.002$, $I^2 = 0\%$, $p = 0.61$ There were no significant differences on cyclothymic, irritable, anxious, and hyperthymic scales.	
Consistency in results	Consistent

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

Precision in results	Precise
Directness of results	Direct
Comparison 5	**Assessment of temperament in people with bipolar disorder vs. other psychiatric disorders.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) suggests medium-sized effects of increased cyclothymic, irritable, and hyperthymic temperament scores in people with bipolar disorder compared to people with major depression.** **Moderate quality evidence (small samples, consistent, precise, direct) suggests a medium-sized effect of increased hyperthymic temperament scores, and large effects of decreased depressive, irritable, and anxious scores in people with bipolar disorder compared to people with borderline personality disorder.**
TEMPS	
Compared to major depression *Medium-sized, significant effects of increased TEMPS scores in people with bipolar disorder on the following scales;* Cyclothymic: 12 studies, N = 2204, SMD = 0.54, 95%CI 0.38 to 0.71, $p < 0.00001$, $I^2 = 65\%$, $p = 0.0009$ Hyperthymic: 12 studies, N = 2204, SMD = 0.39, 95%CI 0.18 to 0.60, $p = 0.0002$, $I^2 = 78\%$, $p < 0.00001$ Irritable: 12 studies, N = 2204, SMD = 0.41, 95%CI 0.22 to 0.60, $p < 0.00001$, $I^2 = 73\%$, $p < 0.0001$ There were no significant differences on depressive and anxious subscales. Compared to borderline personality disorder *Large, significant effects of decreased TEMPS scores in people with bipolar disorder on the following scales;* Depressive: 2 studies, N = 80, SMD = -1.24, 95%CI -1.73 to -0.76, $p < 0.00001$, $I^2 = 0\%$, $p = 0.67$ Irritable: 2 studies, N = 80, SMD = -0.91, 95%CI -1.38 to -0.45, $p < 0.0001$, $I^2 = 0\%$, $p = 0.46$ Anxious: 2 studies, N = 80, SMD = -1.42, 95%CI -1.91 to -0.92, $p < 0.00001$, $I^2 = 0\%$, $p = 0.43$ *Medium-sized, significant effect of increased TEMPS hyperthymic scores in people with bipolar disorder;* Hyperthymic (excessive positive mood): 2 studies, N = 80, SMD = 0.69, 95%CI 0.23 to 1.14, $p = 0.003$, $I^2 = 0\%$, $p = 0.81$	

There were no significant differences on the cyclothymic scale. <u>Compared to ADHD</u> There were no significant differences on depressive, cyclothymic, irritable, anxious, and hyperthymic scales.	
Consistency in results	Inconsistent for major depression comparison. Consistent for borderline personality disorder comparison.
Precision in results	Precise
Directness of results	Direct

Zaninotto L, Solmi M, Toffanin T, Veronese N, Cloninger CR, Correll CU

A meta-analysis of temperament and character dimensions in patients with mood disorders: Comparison to healthy controls and unaffected siblings

Journal of Affective Disorders 2016; 194: 84-97

View review abstract online

Comparison 1	**Assessment of temperament in people with bipolar disorder vs. controls on the Tridimensional Personality Questionnaire (TPQ) and the Temperament and Character Inventory (TCI) scales.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) suggests large effects of increased harm avoidance and decreased self-directedness; medium-sized effects of increased self-transcendence and decreased cooperativeness; small effects of increased novelty seeking and decreased reward dependence in people with bipolar disorder.**
TPQ/TCI	
Large, significant effect of increased harm avoidance in people with bipolar disorder; 18 studies, N = 4504, SMD = 0.86, 95%CI 0.67 to 1.06, $p < 0.0005$, $I^2 = 88\%$ The harm avoidance subscales of anticipatory worry, fear of uncertainty, shyness with strangers, and fatigability all showed medium to large increases in people with bipolar disorder. *Large, significant effect of decreased self-directedness in people with bipolar disorder;* 14 studies, N = 3527, SMD = -0.85, 95%CI -1.12 to -0.58, $p < 0.0005$, $I^2 = 92\%$ The self-directedness subscales of responsibility, purposefulness, resourcefulness, self-acceptance, and enlightened second nature all showed medium to large decreases in people with	

bipolar disorder. *Medium-sized, significant effect of increased self-transcendence in people with bipolar disorder;* 14 studies, N = 3527, SMD = 0.45, 95%CI 0.23 to 0.66, $p < 0.0005$, $I^2 = 88\%$ The self-transcendence subscales of self-forgetfulness and spiritual acceptance showed small to medium-sized increases in people with bipolar disorder, with no significant differences in transpersonal identification. *Medium-sized, significant effect of decreased cooperativeness in people with bipolar disorder;* 14 studies, N = 3527, SMD = -0.46, 95%CI -0.61 to -0.31, $p < 0.0005$, $I^2 = 73\%$ The cooperation subscales of social acceptance, empathy, helpfulness, and pure-hearted conscience all showed small to medium-sized decreases in people with bipolar disorder, with no significant differences in compassion. *Small, significant effect of increased novelty seeking in people with bipolar disorder;* 18 studies, N = 4504, SMD = 0.22, 95%CI 0.03 to 0.41, $p < 0.05$, $I^2 = 88\%$ The novelty seeking subscales of impulsiveness, extravagance, and disorderliness all showed small to medium-sized increases, while exploratory excitability showed small decreases in people with bipolar disorder. *Small, significant effect of decreased reward dependence in people with bipolar disorder;* 16 studies, N = 3801, SMD = -0.11, 95%CI -0.01 to -0.21, $p < 0.05$, $I^2 = 46\%$ The reward dependence subscales of attachment and dependence showed small decreases in people with bipolar disorder, while there were no differences in sentimentality or openness to warm communication. There were no significant differences on the persistence scales.	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct
Comparison 2	**Assessment of temperament in first-degree relatives of people with bipolar disorder vs. controls.**
Summary of evidence	**Moderate to high quality evidence (medium-sized samples, consistent, precise, direct) suggests medium-sized effects of increased harm avoidance and decreased self-directedness in relatives of people with bipolar disorder.**
TPQ/TCI	
Medium-sized, significant effect of increased harm avoidance in relatives of people with bipolar disorder;	

3 studies, N = 499, SMD = 0.64, 95%CI 0.44 to 0.83, $p < 0.0005$, $I^2 = 11\%$ *Medium-sized, significant effect of decreased self-directedness in people with bipolar disorder;* 3 studies, N = 499, SMD = -0.64, 95%CI -0.89 to -0.38, $p < 0.0005$, $I^2 = 46\%$ There were no significant differences in self-transcendence, cooperativeness, novelty seeking, reward dependence, or persistence.	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct
Comparison 3	**Assessment of temperament in people with bipolar disorder vs. first-degree relatives.**
Summary of evidence	**Moderate to high quality evidence (medium-sized samples, consistent, precise, direct) suggests large effects of increased harm avoidance and decreased self-directedness, and medium-sized effects of decreased cooperativeness, and increased novelty seeking and self-transcendence in people with bipolar disorder.**
TPQ/TCI	
Large, significant effect of decreased self-directedness in people with bipolar disorder; 3 studies, N = 412, SMD = -0.95, 95%CI -1.16 to -0.74, $p < 0.0005$, $I^2 = 3\%$ *Large, significant effect of increased harm avoidance in people with bipolar disorder;* 3 studies, N = 412, SMD = 0.76, 95%CI 0.55 to 0.96, $p < 0.0005$, $I^2 = 0\%$ *Medium-sized, significant effect of decreased cooperativeness in people with bipolar disorder;* 3 studies, N = 412, SMD = -0.53, 95%CI -0.87 to -0.19, $p < 0.005$, $I^2 = 64\%$ *Medium-sized, significant effect of increased self-transcendence in people with bipolar disorder;* 3 studies, N = 412, SMD = 0.50, 95%CI 0.24 to 0.77, $p < 0.0005$, $I^2 = 41\%$ *Medium-sized, significant effect of increased novelty seeking in people with bipolar disorder;* 3 studies, N = 412, SMD = 0.48, 95%CI 0.28 to 0.68, $p < 0.0005$, $I^2 = 0\%$ There were no significant differences on the reward dependence or persistence scales.	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Personality and temperament

Comparison 4	**Assessment of temperament in people with bipolar disorder vs. major depression.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) suggests a medium-sized effect of increased novelty seeking, and small effects of increase self-transcendence and decreased harm avoidance in people with bipolar disorder.**
TPQ/TCI	
Medium-sized, significant effect of increased novelty seeking in people with bipolar disorder; 14 studies, N = 2728, SMD = 0.54, 95%CI 0.25 to 0.83, $p < 0.0005$, $I^2 = 91\%$ *Small, significant effect of increased self-transcendence in people with bipolar disorder;* 11 studies, N = 2430, SMD = 0.33, 95%CI 0.15 to 0.51, $p < 0.005$, $I^2 = 73\%$ *Small, significant effect of decreased harm avoidance in people with bipolar disorder;* 14 studies, N = 2728, SMD = -0.34, 95%CI -0.65 to -0.03, $p < 0.05$, $I^2 = 92\%$	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

Explanation of acronyms

CI = confidence interval, *g* = Hedges' standardised mean difference, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), N = number of participants, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), SMD = standardised mean difference, TCI = Temperament and Character Inventory, TEMPS = Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego scale, TPQ = Tridimensional Personality Questionnaire vs. = versus

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

Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small.[9]

† 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).

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[9].

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[10]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

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

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula;[9]

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

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data 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[11].

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

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

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