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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 2000. 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 10 systematic reviews that met our inclusion criteria[3-12].

- Moderate to high quality evidence finds a large increase in neuroticism and a large decrease in extraversion in people with schizophrenia compared to controls. There were also medium-sized decreases in openness, agreeableness, and conscientiousness in people with schizophrenia.
- Moderate to high quality evidence finds a large increase in trait anhedonia (inability to feel pleasure) in people with schizophrenia compared to controls.
- High quality evidence shows a large increase in harm avoidance, and small decreases in novelty seeking, reward dependence, and persistence in people with schizophrenia compared to controls.
- Moderate to high quality evidence found medium-sized increases in maladaptive strategies (using suppression, rumination, and self-blaming) in people with schizophrenia compared to controls. There were also decreased adaptive strategies (cognitive reappraisal and distraction) in patients. There was a medium-sized association between increased maladaptive strategies and increased positive symptoms.
- Moderate to high quality evidence finds medium to large increases in negative emotion and less positive emotion in people with schizophrenia compared to controls.
- Moderate to high quality evidence finds a medium to large effect of poor emotion regulation, and more dissociation and alexithymia (inability to identify and describe

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one's own emotions) in people with schizophrenia compared to controls.

- High quality evidence finds a medium-sized increase in aversion and arousal to neutral stimuli, increased aversion to positive stimuli, and increased hedonic (pleasure) response to negative stimuli in people with schizophrenia compared to controls.
- Moderate to high quality evidence suggests increased monetary delay discounting (preference for immediate smaller monetary rewards) indicating more impulsivity in people with schizophrenia than in controls.
- Moderate to high quality evidence finds people with a psychotic disorder and a substance use disorder showed medium-sized effects of higher scores on negative urgency, low premeditation, sensation seeking, and unconscientious disinhibition than people with a psychotic disorder and no substance use disorder.

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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 schizophrenia vs. controls.** **Monetary delay discounting involves preferring immediate but smaller monetary rewards over delayed but larger monetary rewards. It is a proposed measure of impulsivity.**
Summary of evidence	**Moderate to high quality evidence large sample, inconsistent, precise, direct) suggests increased monetary delay discounting in people with schizophrenia.**
Impulsivity	
A medium-sized effect showed more monetary delay discounting in people with schizophrenia; 12 studies, N = 766, g = 0.46, 95%CI 0.14 to 0.77, $p < 0.001$, I^2 = 79%	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

Cho H, Gonzalez R, Lavaysse LM, Pence S, Fulford D, Gard DE

Do people with schizophrenia experience more negative emotion and less positive emotion in their daily lives? A meta-analysis of experience sampling studies

Schizophrenia Research 2017; 183: 49-55

View review abstract online	
Comparison	**Negative and positive emotion in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, some inconsistency, precise, direct) finds medium to large effects of more negative emotion and less positive emotion in people with schizophrenia.**
Emotion	
Medium to large effects of more negative emotion and less positive emotion in people with schizophrenia; Negative emotion: 12 studies, N = 1,349, SMD = 0.84, 95%CI, 0.73 to 0.95, $p < 0.0001$, $I^2 = 23\%$ Positive emotion: 12 studies, N = 1,349, SMD = -0.75, 95%CI, -1.03 to -0.46, $p < 0.0001$, $I^2 = 71\%$	
Consistency in results	Consistent for negative emotion, inconsistent for positive emotion.
Precision in results	Precise
Directness of results	Direct

Cohen AS, Minor KS

Emotional experience in patients with schizophrenia revisited: Meta-analysis of laboratory studies

Schizophrenia Bulletin 2010; 36(1): 143-150

View review abstract online

Comparison	**Emotional response following positive, negative, or neutral stimuli in people with schizophrenia vs. controls.** **Note: "Positive" refers to stimuli generating pleasure. "Negative" refers to stimuli evoking avoidant, threat, sadness, or other negative emotional states. "Neutral" refers to stimuli that are neither positive nor negative. Hedonic and aversive emotions refer to positive or negative emotions following stimuli presentation. "Bipolar ratings" refers to a subjective rating scale set up with hedonic and aversive emotions on opposing ends of a spectrum.**
Summary of evidence	**High quality evidence (large samples, consistent, precise,**

	direct) suggests a medium-sized effect of greater aversion to positive and neutral stimuli, and greater hedonic response to negative stimuli in people with schizophrenia. There were similar hedonic responses to positive and neutral stimuli, and similar aversive responses to negative stimuli between patients and controls.
Positive stimuli	
A medium to large-sized effect suggests people with schizophrenia experienced greater aversion to positive stimuli, compared with controls; 11 studies, N = 605, *d* = 0.72, 95%CI 0.53 to 0.91, no *p*-value reported, Q = 5.36 *A small to medium-sized effect suggests people with schizophrenia experienced greater aversion (lower 'bipolar ratings') to positive stimuli, compared with controls;* 12 studies, N = 627, *d* = -0.33, 95%CI -0.57 to -0.10, no *p*-value reported, Q = 10.68 *No difference was reported in hedonic response to positive stimuli between people with schizophrenia and controls;* 14 studies, N = 770, *d* = -0.16, 95%CI -0.40 to 0.07, no *p*-value reported, Q = 13.72	
Negative stimuli	
A small effect suggests people with schizophrenia experienced greater hedonic response to negative stimuli, compared with controls; 10 studies, N = 544, *d* = 0.28, 95%CI 0.03 to 0.59, no *p*-value reported, Q = 10.86 *No difference was reported in aversive response to negative stimuli between people with schizophrenia and controls;* 9 studies, N = 697, *d* = 0.24, 95%CI -0.03 to 0.45, no *p*-value reported, Q = 8.56 *No difference was reported in 'bipolar ratings' to negative stimuli between people with schizophrenia and controls;* 12 studies, N = 594, *d* = 0.12, 95%CI -0.12 to 0.36, no *p*-value reported, Q = 11.80	
Neutral stimuli	
A medium effect suggests that people with schizophrenia experienced greater aversion to neutral stimuli, compared with controls; 7 studies, N = 321, *d* = 0.64, 95%CI 0.34 to 0.93, no *p*-value reported, Q = 4.76 *No difference was reported in hedonic response to neutral stimuli between people with schizophrenia and controls;* 7 studies, N = 321, *d* = 0.25, 95%CI -0.25 to 0.73, no *p*-value reported, Q = 6.24 *No difference was reported in 'bipolar ratings' to neutral stimuli between people with schizophrenia*	

and controls; 9 studies, N = 452, *d* = 0.07, 95%CI -0.15 to 0.29, no *p*-value reported, Q = 8.01 Subgroup analysis suggests stimulus type, gender and medication did not significantly affect emotion induction.	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Llerena K, Strauss GP, Cohen AS

Looking at the other side of the coin: A meta-analysis of self-reported emotional arousal in people with schizophrenia

Schizophrenia Research 2012; 142(1-3): 65-70

View review abstract online

Comparison	**Emotional arousal in people with schizophrenia vs. controls.**
Summary of evidence	**High quality evidence (large samples, consistent, precise, direct) shows a medium-sized effect of increased arousal to neutral emotive stimuli compared to controls, but no differences with positive or negative emotive stimuli.**
Emotional arousal using subjective arousal ratings	
A medium effect of increased arousal to neutral emotive stimuli in patients compared to controls; 22 studies, N = 1,588, *g* = 0.43, 95%CI 0.23 to 0.63, *p* < 0.001, Q = 22.29, *p* > 0.05 *No differences between in arousal for positive or negative emotive stimuli;* Positive: 24 studies, N = 1,530, *g* = -0.05, 95%CI -0.19 to 0.09, *p* > 0.05, Q = 22.19, *p* > 0.05 Negative: 26 24 studies, N = 1,827, *g* = -0.14, 95%CI -0.32 to 0.04, *p* > 0.05, Q = 26.93, *p* > 0.05 Authors report no evidence of publication bias.	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Ludwig L, Werner D, Lincoln TM

The relevance of cognitive emotion regulation to psychotic symptoms - a systematic review and meta-analysis

Clinical Psychology Review 2019; 72: 101746

View review abstract online

Comparison	**Emotion regulation in people with a schizophrenia spectrum disorder vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, some inconsistency, mostly precise, direct) found medium-sized effects of people with schizophrenia using maladaptive strategies more often than controls (suppression, rumination, and self-blaming), and adaptive strategies less often (cognitive reappraisal and distraction). There was a medium-sized association between increased maladaptive strategies and increased positive symptoms, and no association between adaptive strategies and positive symptoms.**

Emotion regulation

42 studies, N = 5,879

Medium-sized effects showed people with schizophrenia used the following maladaptive strategies more often than controls;

Suppression: 16 studies, g = -0.36, 95%CI -0.56 to -0.16, $p < 0.05$, $I^2 = 72\%$

Rumination: 6 studies, g = -0.67, 95%CI -0.85 to -0.48, $p < 0.05$, $I^2 = 0\%$

Self-blaming: 4 studies, g = -0.56, -0.76 to -0.37, $p < 0.05$, $I^2 = 4\%$

Medium-sized effects showed people with schizophrenia used the following adaptive strategies less often than controls;

Cognitive reappraisal: 22 studies, g = 0.41, 95%CI 0.28 to 0.55, $p < 0.05$, $I^2 = 59\%$

Distraction: 2 studies, g = 0.55, 95%CI 0.11 to 0.98, $p < 0.05$, $I^2 = 0\%$

There were no significant differences in;

Acceptance: 3 studies, g = 0.30, 95%CI -0.54 to 1.14, $p < 0.05$, $I^2 = 91\%$

Managing emotions: 12 studies, g = 0.93, 95%CI 0.75 to 1.11, $p < 0.05$, $I^2 = 56\%$

There was a medium-sized association between maladaptive strategies and positive symptoms;

6 studies, r = 0.34, 95%CI 0.22 to 0.44, $p < 0.05$, $I^2 = 0\%$

There was no relationship with adaptive strategies;

6 studies, r = -0.16, 95%CI -0.37 to 0.06, $p < 0.05$, $I^2 = 63\%$	
Consistency in results	Some inconsistency (when $I^2 > 50\%$).
Precision in results	Mostly precise
Directness of results	Direct

Miettunena J, Raevuoric A

A meta-analysis of temperament in axis I psychiatric disorders

Comprehensive Psychiatry 2012; 53: 152-166

View review abstract online

Comparison	**Temperament in people with schizophrenia vs. controls.**
Summary of evidence	**High quality evidence (large samples, consistent, precise, direct) suggests a large effect of more harm avoidance, and small effects of less novelty seeking, reward dependence, and persistence in people with schizophrenia compared to controls.**
Harm avoidance	
A large effect of more harm avoidance in people with schizophrenia than controls; 13 studies, N = 6,481, d = 1.15, $p < 0.05$	
Novelty seeking or risk taking	
A small effect of less novelty seeking in people with schizophrenia; 13 studies, N = 6,481, d = -0.16, $p < 0.05$	
Reward dependence	
A small to medium-sized effect of less reward dependence in people with schizophrenia; 10 studies, N = not reported, d = -0.36, $p < 0.05$	
Persistence	
A small effect of less persistence in people with schizophrenia; 10 studies, N = not reported, d = -0.23, $p < 0.05$	

Consistency in results	Authors report results are consistent.
Precision in results	Graphs indicate data are precise.
Directness of results	Direct

O'Driscoll C, Laing J, Mason O

Cognitive emotion regulation strategies, alexithymia and dissociation in schizophrenia, a review and meta-analysis

Clinical Psychology Review 2014; 34: 482-495

View review abstract online

Comparison	**Cognitive emotion regulation, alexithymia (inability to identify and describe own emotions), and dissociation (detachment from reality) in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, mostly inconsistent or imprecise, direct) suggests a medium to large effect of poor emotion regulation, more dissociation, and more alexithymia in people with schizophrenia than controls.**

Cognitive emotion regulation

A medium to large-sized effect of poor emotion regulation in people with schizophrenia, with less emotion management and cognitive reappraisal, and more attentional deployment, worry, rumination, and experiential avoidance;

Emotion management: 13 studies, N = 1,204, g = 0.96, 95%CI 0.77 to 1.14, $p < 0.00001$, I^2 = 45%, p = 0.06

Cognitive reappraisal: 11 studies, N = 1,395, g = 0.49, 95%CI 0.32 to 0.66, $p < 0.00001$, I^2 = 51%, p = 0.03

Attentional deployment: 17 studies, N = 2,001, g = -0.96, 95%CI -1.18 to -0.75, $p < 0.00001$, I^2 = 76%, $p < 0.00001$

Worry: 12 studies, N = 1,559, g = -1.06, 95%CI -1.33 to -0.79, $p < 0.00001$, I^2 = 80%, $p < 0.00001$

Rumination: 5 studies, N = 442, g = -0.67, 95%CI -0.86 to -0.47, $p < 0.00001$, I^2 = 0%, p = 0.41

Experiential avoidance: 9 studies, N = 713, g = -0.44, 95%CI -0.59 to -0.29, $p < 0.00001$, I^2 = 1%, p = 0.42

Dissociation

A large effect of more dissociation in people with schizophrenia; Overall: 7 studies, N = 767, *g* = -0.86, 95%CI -1.13 to -0.60, *p* < 0.00001, I^2 = 50%, *p* = 0.06 Amnesia: 4 studies, N = 545, *g* = -0.73, 95%CI -1.03 to -0.44, *p* < 0.05, I^2 = 36%, *p*-value not reported Absorption: 5 studies, N = 587, *g* = -0.70, 95%CI -1.03 to -0.37, *p* < 0.05, I^2 = 54%, *p*-value not reported Depersonalisation / derealisation: 4 studies, N = 545, *g* = -0.95, 95%CI -1.19 to -0.72, *p* < 0.05, I^2 = 0%, *p*-value not reported
Alexithymia
A large effect of more alexithymia in people with schizophrenia; 8 studies, N = 710, *g* = -1.05, 95%CI -1.45 to -0.65, *p* < 0.00001, I^2 = 83%, *p* < 0.00001

Consistency in results	Consistent for rumination, experiential avoidance, depersonalisation, and dissociation.
Precision in results	Imprecise for amnesia, absorption, and alexithymia.
Directness of results	Direct

Oh H, Jang SK, Lee HS, Lee EB, Choi KH

Personality Traits in Individuals with the Dual Diagnosis of Psychosis and Substance Use Disorders: A Comprehensive Review and Meta-Analysis

Journal of Dual Diagnosis 2021; 17(1): 34-51

View review abstract online

Comparison	**Impulsivity personality traits in people with a psychotic disorder (mostly schizophrenia) plus a substance use disorder (dual diagnosis) vs. people with a psychotic disorder only (mostly schizophrenia).**
Summary of evidence	**Moderate to high quality evidence (medium-sized samples, mostly consistent, precise, direct) finds people with a psychotic disorder and a substance use disorder showed medium-sized effects of higher scores on negative urgency, low premeditation, sensation seeking, and unconscientious disinhibition than people with a psychotic disorder and no substance use disorder.**

Impulsivity personality traits	
People with a dual diagnosis showed medium-sized effects of higher scores on the following impulsivity measures; Negative urgency: 4 studies, N = 262, SMD = 0.59, 95%CI 0.34 to 0.84, $p < 0.05$, $I^2 = 0\%$ Low premeditation: 5 studies, N = 349, SMD = 0.60, 95%CI 0.39 to 0.80, $p < 0.05$, $I^2 = 0\%$ Sensation seeking: 7 studies, N = 550, SMD = 0.63, 95%CI 0.17 to 1.09, $p < 0.05$, $I^2 = 86\%$ Unconscientious disinhibition: 5 studies, N = 291, SMD = 0.36, 95%CI 0.13 to 0.59, $p < 0.05$, $I^2 = 0\%$ There were no significant differences in low perseverance, disagreeable disinhibition, positive or negative affect, and trait anhedonia.	
Consistency in results	Inconsistent for sensation seeking only.
Precision in results	Precise
Directness of results	Direct

Ohi K, Shimada T, Nitta Y, Kihara H, Okubo H, Uehara T, Kawasaki Y

The Five-Factor Model personality traits in schizophrenia: A meta-analysis

Psychiatry Research 2016; 240: 34-41

View review abstract online

Comparison	**Assessment of the five-factor model of personality (neuroticism, extraversion, openness, agreeableness, and conscientiousness) in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) suggests large effects of increased neuroticism and decreased extraversion, and medium-sized effects of decreased openness, agreeableness, and conscientiousness in people with schizophrenia compared to controls.**
Five-factor model of personality **Assessed using the NEO Five-Factor Inventory**	
Large effects of higher scores on neuroticism and lower scores on extraversion in people with schizophrenia compared to controls; 9 studies, N = 946	

Neuroticism: *g* = 1.10, 95%CI 0.77 to 1.43, *p* < 0.05 Extraversion: *g* = -0.79, 95%CI -1.00 to -0.59, *p* < 0.05 *Medium-sized effects of lower scores on openness, agreeableness and conscientiousness in people with schizophrenia compared to controls;* 8 studies, N = 870 Openness: *g* = -0.38, 95%CI -0.62 to -0.14, *p* < 0.05 Agreeableness: *g* = -0.51, 95%CI -0.86 to -0.15, *p* < 0.05 Conscientiousness: *g* = -0.59, 95%CI -0.87 to -0.31, *p* < 0.05 Moderator analysis showed that having more males in the study was associated with lower levels of agreeableness compared to controls. There were no moderating effects of age. Authors report no evidence of publication bias.

Consistency in results	Authors state all results are inconsistent, although removing one study from each of the extraversion, openness and agreeableness analyses reduced heterogeneity.
Precision in results	Precise
Directness of results	Direct

Yan C, Cao Y, Zhang Y, Song L, Cheung EFC, Chan RCK

Trait and State Positive Emotional Experience in Schizophrenia: A Meta-Analysis

PLoS ONE 2012; 7(7): e40672

View review abstract online

Comparison	**Positive emotional experience in people with schizophrenia vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) suggests a large effect of more trait anhedonia in people with schizophrenia compared with controls.**
Positive emotional experience	
A large effect of more trait anhedonia symptoms (inability to experience pleasure) in people with schizophrenia compared with controls; 47 studies, N = 3,722, *d* = 0.81, 95%CI 0.73 to 0.90, *p* < 0.05, Q = 113.30, *p* < 0.001	

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A small effect of less hedonia, and no differences in exciting experience; Hedonic: 40 studies, N = 2,264, *d* = -0.24, 95%CI -0.37 to -0.11, *p* < 0.05, Q = 106.61.30, *p* < 0.001 Exciting: 21 studies, N = 1,258, *d* = 0.01, 95%CI -0.14 to 0.16, *p* > 0.05, Q = 38.14, *p* = 0.009 Authors report no evidence of publication bias.	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

Explanation of acronyms

CI = confidence interval, *d* = Cohen's *d* and *g* = Hedges' *g* = standardised mean differences, 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), Q = Q statistic for the test of heterogeneity, *r* = correlation coefficient, SMD = standardised mean difference, vs. = versus

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Personality and temperament

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.[13]

† 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[13].

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[14]. 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.

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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;[13]

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

§ 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[15].

‖ 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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