

Social skills therapies

Introduction

Social and interpersonal skills are a key aspect preventing some people with schizophrenia from integrating within the community and living a satisfying life. Programs targeting the development of social skills are designed to allow people with severe mental disorders such as schizophrenia to achieve greater social and community functioning.

Such programs may involve training in social interactions, social perception and cognition, self- and illness-management skills, community participation, and workplace skills. These programs can be organised through a day-centre unit, attended by residents of either hospitals or the community, on an individual basis or in a group setting.

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 MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO and the Cochrane Library databases. 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-analysis¹. Reviews rated as less than 50% of items checked have now 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 (RCT) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms). 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 seven systematic reviews that met our inclusion criteria²⁻⁸.



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- Moderate to high quality evidence shows a large benefit of social skills training for improving social interactions, community functioning, symptom severity (particularly negative symptoms), and reducing relapse rates. Moderate to low quality evidence also finds improved quality of life.
- Moderate quality evidence shows a medium to large benefit of social cognitive skills programs for improving emotion perception and Theory of Mind, particularly for patients with longer illness durations.
- Moderate to low quality evidence shows a large effect of focussed facial affect recognition training for improving facial affect recognition and social functioning, with no benefits for symptoms.



Almerie MQ, Okba AI, Marhi M, Jawoosh M, Alsabbagh M, Matar HE, Maayan N, Bergman H

Social skills programmes for schizophrenia

Cochrane Database of Systematic Reviews 2015; Issue 6. Art. No.: CD009006. DOI: 10.1002/14651858.CD009006.pub2.

[View review abstract online](#)

Comparison	Social skills training vs. standard care.
Summary of evidence	Moderate quality evidence (small to medium-sized samples, consistent, imprecise, direct) shows a medium-sized benefit of social skills training for reducing relapse and rehospitalisation and improving negative symptoms. Moderate to low quality evidence (small samples) also finds improved mental state and quality of life.
Mental state	
<p><i>A significant, medium-sized effect of fewer relapses and rehospitalisations with social skills training;</i> Relapse: 2 RCTs, N = 263, RR = 0.52, 95% CI 0.34 to 0.79, $p < 0.05$, $I^2 = 40%$, $p = 0.20$ Rehospitalisation: 1 RCT, N = 143, RR = 0.53, 95% CI 0.30 to 0.93, $p < 0.05$ <i>A significant, small effect of better mental state with social skills training;</i> Global state: 1 RCT, N = 67, RR = 0.29, 95% CI 0.12 to 0.68, $p < 0.05$ Overall mental state: 1 RCT, N = 91, MD = -4.01, 95% CI -7.52 to -0.50, $p < 0.05$ Positive symptoms: 1 RCT, N = 120, MD = -1.90, 95% CI -3.37 to -0.43, $p < 0.05$ Negative symptoms: 2 RCTs, N = 187, MD = -8.92, 95% CI -10.46 to -7.38, $p < 0.05$, $I^2 44%$, $p = 0.18$</p> <p>Authors report possible risk of bias in primary studies.</p> <p>No significant differences were reported when comparing social skills training to a discussion group activity.</p>	
Quality of life	
General well-being schedule	
<p><i>A significant effect of better quality of life with social skill training;</i> 1 RCT, N = 112, MD = -7.60, 95% CI -12.18 to -3.02, $p < 0.05$ Authors report possible risk of bias in primary studies.</p> <p>No significant differences were reported when comparing social skills training to a discussion group</p>	



activity.	
Consistency in results	Consistent for comparisons with > 1 RCT.
Precision in results	Imprecise, unable to assess MDs.
Directness of results	Direct

Bordon N, O'Rourke S, Hutton P

The feasibility and clinical benefits of improving facial affect recognition impairments in schizophrenia: Systematic review and meta-analysis

Schizophrenia Research 2017; 188: 3-12

[View review abstract online](#)

Comparison	Facial affect recognition training vs. various control conditions.
Summary of evidence	Moderate to low quality evidence (small to medium-sized samples, consistent, some imprecision, indirect) shows a large effect of focussed facial affect recognition training for improving facial affect recognition and social functioning, with no effects on symptoms.

Facial affect recognition

Large, significant effects of improved facial affect recognition with focussed treatment;

8 studies, N = 300, $g = 1.26$, 95%CI 0.92 to 1.60, $p < 0.05$, $I^2 = 41\%$

Authors report the studies were generally at high risk of various forms of bias

Social functioning

Large, significant effects of improved social functioning with focussed treatment;

3 studies, N = 109, $g = 0.98$, 95%CI 0.37 to 1.36, $p < 0.05$, $I^2 = 38\%$

Authors report the studies were generally at high risk of various forms of bias

Symptoms

No significant differences between groups;

Negative symptoms: 4 studies, N = 173, $g = -0.11$, 95%CI -0.41 to 0.20, $p > 0.05$, $I^2 = 0\%$

Positive symptoms: 3 studies, N = 135, $g = 0.10$, 95%CI -0.25 to 0.45, $p > 0.05$, $I^2 = 0\%$

General psychopathology: 3 studies, N = 135, $g = 0.12$, 95%CI -0.44 to 0.69, $p > 0.05$, $I^2 = 56\%$



Authors report the studies were generally at high risk of various forms of bias.

Consistency in results	Consistent
Precision in results	Precise for facial affect recognition, negative symptoms, and positive symptoms
Directness of results	Indirect comparison (mixed control conditions combined).

Kurtz MM, Mueser KT

A meta-analysis of controlled research on social skills training for schizophrenia

Journal of Consulting & Clinical Psychology 2008; 76(3): 491-504

[View review abstract online](#)

Comparison	Individual or group social skills training vs. standard care or an active control intervention. Treatment duration 4-72 weeks, frequency 1-5 sessions per week.
Summary of evidence	Moderate to high quality evidence (medium to large samples, mostly consistent, precise, indirect) shows a large benefit of social skills training for improving social interactions (particularly for inpatients), as well as a medium benefit for community functioning and negative symptom severity, and a small benefit for relapse rates.

Functioning

Results are reported from the highest quality 'unbiased' studies only

A significant, large effect of improved 'content mastery' in the trained skills with social skills training;
6 RCTs, N = 254, $d = 1.16$, 95%CI 0.89 to 1.43, p not reported, $Q = 1.77$, $p > 0.05$, I^2 not reported;
fail-safe N = 29

A significant, medium-sized effect of improved social ability with social skills training;
5 RCTs, N = 377, $d = 0.48$, 95%CI 0.27 to 0.69, p not reported, $Q = 31.48$, $p < 0.01$, I^2 not reported;
fail-safe N = 7

This effect was larger in inpatients ($d = 0.82$) than in outpatients ($d = 0.42$), $Q_B = 3.5$, $p = 0.06$, and larger in the treatment as usual comparison ($d = 0.87$) than in the active control comparison ($d = 0.09$), $Q_B = 16.4$, $p < 0.0005$.

A significant, medium-sized effect of improved community or institutional functioning with social



<i>skills training;</i>	
4 RCTs, N = 230, $d = 0.41$, 95%CI 0.15 to 0.68, p not reported, $Q = 11.63$, $p > 0.05$, I^2 not reported; fail-safe N = 4	
Mental state	
<i>A significant, small effect of reduced rates of relapse with social skills training;</i>	
9 RCTs, N = 485, $d = 0.23$, 95%CI 0.04 to 0.41, p not reported, $Q = 4.32$, $p > 0.05$, I^2 not reported	
<i>A significant, medium-sized effect of improved negative symptom severity with social skills training;</i>	
5 RCTs, N = 287, $d = 0.47$, 95%CI 0.24 to 0.71, p not reported, $Q = 17.26$, $p < 0.05$, I^2 not reported, fail-safe N = 7	
<i>No significant differences between groups in overall symptom severity;</i>	
7 RCTs, N = 411, $d = 0.20$, 95%CI 0.00 to 0.39, p not reported, $Q = 9.84$, $p > 0.05$, I^2 not reported	
Consistency in results	Consistent, except for negative symptoms and performance-based social skills assessment.
Precision in results	Precise
Directness of results	Indirect comparison (mixed control conditions combined).

<i>Kurtz MM, Richardson CL</i>	
Social Cognitive Training for Schizophrenia: A Meta-Analytic Investigation of Controlled Research	
Schizophrenia Bulletin 2012; 38(5): 1092-1104	
View review abstract online	
Comparison	Individual or group social cognitive skills training, (involving emotion perception, social perception, facial affect recognition or Theory of Mind) vs. standard care or an active control involving problem solving, supportive therapy, or illness management groups. Treatment duration 1-62 weeks.
Summary of evidence	Moderate quality evidence (medium to large samples, inconsistent, precise, indirect) shows a medium to large benefit of social cognitive skills programs for improving emotion perception, Theory of Mind, and overall symptoms and functioning.
Emotion and social perception	



<p><i>A medium to large effect of improved facial affect identification and discrimination with social cognitive skills training;</i></p> <p>Identification: 15 studies, N = 488, $d = 0.71$, 95%CI 0.52 to 0.90, $p < 0.01$, $Q_w = 34.9$, $p < 0.01$</p> <p>Discrimination: 3 studies, N = 89, $d = 1.01$, 95%CI 0.56 to 1.47, $p < 0.01$, $Q_w = 5.61$, $p < 0.01$</p> <p><i>No significant differences between groups in social perception with social cognitive skills training;</i></p> <p>8 studies, N = 261, $d = 0.13$, 95%CI -0.12 to 0.38, $p > 0.01$, $Q_w = 24.74$, $p > 0.01$</p>	
Theory of Mind	
<p><i>A significant, medium-sized effect of improved Theory of Mind with social cognitive skills training;</i></p> <p>7 studies, N = 186, $d = 0.46$, 95%CI 0.15 to 0.78, $p < 0.01$, $Q_w = 40.31$, $p < 0.01$</p> <p>Increased illness duration was related to increased treatment effects ($p < 0.001$); increased education was related to decreased treatment effects ($p < 0.01$); static measures of Theory of Mind showed larger effects than dynamic measures ($p < 0.001$).</p>	
Attributional style	
<p><i>No significant differences between groups in attribution style;</i></p> <p>Aggression bias: 4 studies, N = 119, $d = 0.25$, 95%CI -0.12 to 0.62, $p > 0.01$, $Q_w = 4.42$, $p > 0.01$</p> <p>Hostility bias: 4 studies, N = 119, $d = 0.15$, 95%CI -0.24 to 0.53, $p > 0.01$, $Q_w = 23.95$, $p > 0.01$</p> <p>Blame bias: 4 studies, N = 119, $d = 0.07$, 95%CI -0.30 to 0.45, $p > 0.01$, $Q_w = 11.08$, $p > 0.01$</p>	
Mental state	
<p><i>A significant, medium to large effect of improved overall symptoms with social cognitive skills training;</i></p> <p>7 studies, N = 166, $d = 0.68$, 95%CI 0.33 to 1.02, $p < 0.01$, $Q_w = 58.36$, $p < 0.01$</p> <p><i>No significant differences between groups on individual symptom domains;</i></p> <p>Negative symptoms: 10 studies, N = 306, $d = 0.15$, 95%CI -0.08 to 0.38, $p > 0.05$, $Q_w = 16.37$, $p > 0.01$</p> <p>Positive symptoms: 8 studies, N = 258, $d = 0.26$, 95%CI -0.01 to 0.52, $p > 0.05$, $Q_w = 60.31$, $p > 0.01$</p>	
Functioning	
<p><i>A significant, medium to large effect size of improved community and institutional functioning with social cognitive skills training;</i></p> <p>4 studies, N = 187, $d = 0.78$, 95%CI 0.45 to 1.11, $p < 0.01$, $Q_w = 73.65$, $p < 0.01$</p>	
Consistency in results	Inconsistent for all significant findings, consistent for all non-significant findings.



Precision in results	Precise
Directness of results	Indirect comparison (mixed control conditions combined).

Pfammatter M, Junghan UM, Brenner HD

Efficacy of psychological therapy in schizophrenia: conclusions from meta-analyses

Schizophrenia Bulletin 2006; 32(Suppl 1): S64-80

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Comparison	Social skills training vs. undefined control plus standard care. Treatment duration, frequency of treatment not reported.
Summary of evidence	Moderate to high quality evidence (large samples, consistent, precise, indirect) suggests social skills training provides a medium to large benefit over control conditions for social skills and social function, assertiveness and general psychopathology. Improvements in social function were maintained at follow up (duration unspecified).
Mental state	
<p><i>A significant, small effect of improved general psychopathology with social skills training;</i> Post-treatment: 8 RCTs, N = 349, $g = 0.23$, 95%CI 0.01 to 0.44, p not reported, $Q = 13.25$, $p = 0.07$</p> <p><i>A significant, small effect of reduced hospitalisation rates with social skills training;</i> At follow-up: 2 RCTs, N = 110, $g = 0.48$, 95%CI 0.11 to 0.86, p not reported, $Q = 0.02$, $p = 0.89$</p>	
Functioning	
Post-treatment	
<p><i>A significant, medium to large effect of improved social skills with social skills training;</i> 14 RCTs, N = 688, $g = 0.77$, 95%CI 0.62 to 0.93, p not reported, $Q = 16.54$, $p = 0.22$</p> <p><i>A significant, medium-sized effect of increased assertiveness with social skills training;</i> 5 RCTs, N = 160, $g = 0.43$, 95%CI 0.11 to 0.76, p not reported, $Q = 2.63$, $p = 0.62$</p> <p><i>A significant, medium-sized effect of improved social functioning with social skills training;</i> 6 RCTs, N = 342, $g = 0.39$, 95%CI 0.19 to 0.59, p not reported, $Q = 1.22$, $p = 0.94$</p> <p style="text-align: center;">At follow up (unspecified duration)</p>	



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*A significant, medium-sized effect of improved social skills with social skills training;
6 RCTs, N = 295, g = 0.52, 95%CI 0.28 to 0.77, p not reported, Q = 5.57, p = 0.35*
*A significant, small effect of improved social functioning with social skills training;
3 RCTs, N = 210, g = 0.32, 95%CI 0.08 to 0.56, p not reported, Q = 0.90, p = 0.64*

Consistency in results	Consistent
Precision in results	Precise
Directness of results	Indirect comparison (mixed control conditions combined).

Pilling S, Pebbington P, Kuipers P, Garety P, Geddes J, Martindale B, Orbach G, Morgan C

Psychological treatments in schizophrenia: II. Meta-analyses of randomized controlled trials of social skills training and cognitive remediation

Psychological Medicine 2002; 32(5): 783-91

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Comparison	Social skills training interventions vs. undefined control conditions. Treatment duration 4-72 weeks, 1-12 hours per week.
Summary of evidence	Moderate quality evidence (medium-sized samples, consistent, imprecise, indirect) suggests no significant benefit of social skills training over control conditions for relapse or global function. There was no difference between groups for treatment drop-out rates.

Mental state

No significant differences between groups for preventing relapse;
 < 1 year during treatment: 4 RCTs, N = 125, OR = 0.74, 95%CI 0.40 to 1.39, p not reported, Q = 3.71, p = 0.29
 1-2 years during treatment: 2 RCTs, N = 264, OR = 3.88, 95%CI 0.22 to 69.67, p not reported, Q = 5.06, p = 0.02
 1 year post treatment: 3 RCTs, N = 155, OR = 0.62, 95%CI 0.29 to 1.35, p not reported, Q = 1.25, p = 0.54

Functioning



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No significant differences between groups for global functioning (measured by the Global Adjustment Scale or the Nurses Global Impression Scale);

2 RCTs, N = 92, ES = -0.153, 95%CI -0.56 to 0.26, *p* not reported, Q = 0.35, *p* = 0.56

No significant differences between groups for treatment non-compliance;

6 RCTs, N = 235, OR = 1.31, 95%CI 0.78 to 2.20, *p* not reported, Q = 3.36, *p* = 0.64

Consistency in results	Consistent
Precision in results	Imprecise
Directness of results	Direct

Turner DT, McGlanaghy E, Cuijpers P, Van Der Gaag M, Karyotaki E, MacBeth A
A Meta-Analysis of Social Skills Training and Related Interventions for Psychosis

Schizophrenia Bulletin 2018; 44: 475-91

[View review abstract online](#)

Comparison	Social skills training vs. treatment as usual (TAU) or other active interventions.
Summary of evidence	<p>Moderate to high quality evidence (unclear sample sizes, consistent, precise, indirect) suggests a small effect of improved overall and negative symptoms with social skills training when compared to treatment as usual. There was no benefit for positive symptoms.</p> <p>Moderate to low quality evidence (unclear sample size, mostly inconsistent, precise, indirect) finds no significant differences when compared to other active treatments.</p>
Mental state	
<p><i>A significant, small effect of improved overall symptoms with social skills training when compared to treatment as usual but not an active comparator;</i></p> <p>vs. TAU: 6 RCTs, N = not reported, <i>g</i> = 0.28, 95%CI 0.05 to 0.51, <i>p</i> = 0.018, <i>I</i>² = 0%, <i>p</i> > 0.05</p> <p>vs. active: 18 RCTs, N = not reported, <i>g</i> = 0.07, 95%CI -0.15 to 0.29, <i>p</i> = 0.55, <i>I</i>² = 63%, <i>p</i> < 0.05</p> <p><i>A significant, small effect of improved negative symptoms with social skills training when compared to treatment as usual but not an active comparator;</i></p> <p>vs. TAU: 6 RCTs, N = not reported, <i>g</i> = 0.31, 95%CI 0.08 to 0.54, <i>p</i> = 0.009, <i>I</i>² = 0%, <i>p</i> > 0.05</p>	



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vs. active: 11 RCTs, N = not reported, $g = 0.14$, 95%CI -0.07 to 0.34, $p = 0.196$, $I^2 = 38\%$, $p > 0.05$
 After excluding studies with a high risk of bias, the comparison with active treatments became significant (6 RCTS, $g = 0.28$)

No significant differences between groups for positive symptoms;

vs. TAU: 5 RCTs, N = not reported, $g = 0.15$, 95%CI -0.10 to 0.40, $p = 0.235$, $I^2 = 0\%$, $p > 0.05$

vs. active: 8 RCTs, N = not reported, $g = 0.08$, 95%CI -0.22 to 0.38, $p = 0.62$, $I^2 = 65\%$, $p < 0.05$

Social competency

No significant differences between groups;

vs. TAU: 5 RCTs, N = not reported, $g = 0.20$, 95%CI -0.14 to 0.54, $p = 0.248$, $I^2 = 25\%$, $p > 0.05$

vs. active: 12 RCTs, N = not reported, $g = 0.13$, 95%CI 0.23 to 0.50, $p = 0.482$, $I^2 = 82\%$, $p < 0.05$

Consistency in results	Consistent for TAU comparisons and active comparison for negative symptoms only.
Precision in results	Precise
Directness of results	Direct for TAU comparison, indirect for active comparison (mixed control conditions combined).

Explanation of acronyms

CI = Confidence Interval, d = Cohen's d and g = Hedges' g = standardised mean differences (see below for interpretation of effect size), ES = effect size, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), N = number of participants, OR = Odds ratio, p = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), Q = Q statistic for the test of heterogeneity, Q_w = test for within group differences (heterogeneity in study results within a group of studies – measure of study consistency), Q_B = test for between group differences (heterogeneity between groups of studies for an outcome of interest), RCT = randomised controlled trial, SANS = Scale for the Assessment of Negative Symptoms, SAPS = Scale for the Assessment of Negative Symptoms, TAU = treatment as usual, vs. = versus



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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.

† 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) which 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 effect⁹.

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 ⁹. InOR stands for logarithmic OR where a InOR 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



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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;

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

§ 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.

|| 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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