TECHNICAL COMMENTARY

Telemental health

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Introduction

There is a growing need to deliver low-cost treatments tailored to individual needs and delivered in a continuous way (e.g. all year long) from any location. Telemental health (or "ehealth") has the potential to meet this need.

Telemental health refers to any mental health treatment that is provided electronically, either by telephone or internet (such as online health programs, or video conferencing). This type of intervention involves structured counselling and generally aims to increase medication adherence and prevent relapse. Importantly, it also removes geographic barriers to care.

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2000 that report results separately for people with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder or first episode schizophrenia. Reviews were identified by searching the databases MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO and the Cochrane library. Hand searching reference lists of identified reviews was also conducted. When multiple copies of reviews were found, only the most recent version was included. Reviews with pooled data are prioritised for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis[1]. Reviews with less than 50% of items checked have been excluded from the Library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)[2]. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

Results

We found six systematic reviews that met inclusion criteria[3-8].

- Moderate to high quality evidence suggests small effects of increased quality of life and decreased symptoms with social media interventions. However social support and self-management were decreased with social media interventions. Low quality evidence from one small RCT is unable to

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determine the effects of social media interventions on self-rated stress levels.

- Moderate quality evidence suggests a large effect of increased medication adherence with telemental medication management compared to standard care, pill counting, or early warning signs of relapse checklist. There was greater satisfaction with telemental communication than with standard care, non-web-based communications, or provision of information.
- Moderate quality evidence finds better medication adherence with regular telephone calls prior to a psychiatric visit. Moderate to low quality evidence suggests no reduction in cardiovascular risk factors with adjunctive telephone-delivered interventions compared to face-to-face interventions aimed at reducing these risk factors.
- Moderate quality evidence suggests internet peer-support delivered via Listserv may provide adequate social support. Review authors conclude that when peer-to-peer interactions were moderated by facilitators, retention, engagement, acceptability, and efficacy were higher than for interventions with no facilitators. Studies involving service users in intervention design showed higher rates of acceptability.
- Moderate to low quality evidence suggests PharmCAT (an app of environmental supports maintained on weekly home visits by a case worker) and MedeMonitor (smart-pill container capable of cueing the taking of medication and alerting staff of missed medication) is better at improving adherence than treatment as usual.
- Moderate to low quality evidence suggests the Information Technology–Aided Relapse Prevention Program in Schizophrenia (ITAREPS) can improve treatment adherence and reduce rehospitalisations.

Baker AL, Turner A, Beck A, Berry K, Haddock G, Kelly PJ, Bucci, S.

Telephone-delivered psychosocial interventions targeting key health priorities in adults with a psychotic disorder: systematic review

Psychological Medicine 2018; 48: 2637-57

View review abstract online

Comparison 1	**Telephone-delivered interventions vs. standard care.**
Summary of evidence	**Moderate quality evidence (large sample, unable to assess consistency or precision, direct) suggests greater medication adherence with regular telephone calls prior to psychiatric visit. Lower quality evidence (mostly small samples) is unable to determine any benefit for relapse prevention.**

Relapse prevention

1 pilot RCT (N = 13) assessed two phone calls to check on welfare after hospital discharge and to remind about clinic appointments, plus the provision of a nurse available by telephone 24 hours/day during first 2 weeks after discharge and as needed during following 4-6 weeks. There were no significant differences in the number of hospital readmission days, or for compliance with outpatient appointments.

1 partially randomised trial (N = 89) assessed telephone supported therapy plus manual guided and telephone delivered recovery-oriented CBT incorporating a self-help manual. Some patients also received group sessions that focused on shared ideas and experiences and explored recovery. There were no benefits for symptoms, recovery, distress, or functioning over standard care.

Medication adherence

1 RCT (N = 928) assessed three monthly telephone calls for 3 months prior to psychiatric visit and found significant increases in medication adherence over psychiatric visit alone. There was also greater clinical improvement.

1 RCT (N = 140) assessed 3 months of planned behaviour guided intervention delivered by nurses who expressed and reinforced the value of adherence, educated the participant about adherence benefits, and problem solved adherence barriers. There were no significant benefits for medication adherence or symptoms.

1 RCT (N = 32) assessed 1 year of verbal reinforcement for adherence, encouraging discussion, validating treatment experience, and problem-solving improvements in self-care. There were no significant benefits for medication adherence or symptoms.

1 pilot RCT (N = 13) assessed two phone calls to check on welfare after hospital discharge and to remind about clinic appointments, plus the provision of a nurse available by telephone 24 hours/day

during first 2 weeks after discharge and as needed during following 4-6 weeks. There were no benefits for compliance with medications.	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct
Comparison 2	**Telephone-delivered interventions vs. active control.**
Summary of evidence	**Moderate to low quality evidence (medium-sized sample, unable to assess consistency or precision, direct) suggests no reduction in cardiovascular risk factors with adjunctive telephone-delivered interventions over face-to-face interventions aimed at reducing these risk factors. Lower quality evidence (small samples) is unable to determine any benefit for relapse prevention.**
Behaviour	
1 RCT (N = 235) assessed 24 weeks of telephone plus face-to-face vs. face-to-face sessions only to reduce smoking and other cardiovascular disease risk factors (medication side effects, nicotine withdrawal, distress, smoking behaviour, diet, weight and physical activity). There were no significant differences in these risk factors, functioning, quality of life, or symptom severity.	
Relapse prevention	
1 RCT (N = 45) assessed 1 year of weekly phone calls administering the 10-item Early Warning Sign Questionnaire. If the score exceeded a given threshold, patients were instructed to increase their antipsychotic by 20% of within the next 24 hours. Nurses also visited patients' homes to verify increases in oral medication. The comparison group was assessed weekly (no details were provided). There was less risk of rehospitalisation in the treatment group (HR = 0.21, 95%CI 0.04 to 0.99, p = 0.049), and fewer days in hospital if hospitalised (37 vs. 710, p = 0.023). There were no significant differences in the number of non-hospitalised relapses, however total BPRS scores at relapse were lower in the treatment group (change score 11.3 vs. 7.2, p = 0.019). 1 pilot RCT (N = 47) assessed 3 months of weekly 10-min phone calls vs. 2 assessments. All patients received routine community care. There were no significant differences in the number of days until first psychiatric rehospitalisation or in the length or frequency of rehospitalisation.	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

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Batra S, Baker RA, Wang T, Forma F, DiBiasi F, Peters-Strickland T

Digital health technology for use in patients with serious mental illness: A systematic review of the literature

Medical Devices: Evidence and Research 2017; 10: 237-51

View review abstract online

Comparison	**Digital interventions for people with schizophrenia.**
Summary of evidence	**Moderate to low quality evidence (medium-sized sample, unable to assess consistency or precision, direct) suggests PharmCAT (an app of environmental supports maintained on weekly home visits by a case worker) and MedeMonitor (smart-pill container capable of cueing the taking of medication and alerting staff of missed medication) is better at improving adherence than treatment as usual. Low quality evidence (small samples) is unable to determine benefits of other digital interventions.**

Various outcomes

Electronic pill container

1 RCT (N = 132) assessed 9 months of PharmCAT (an app of environmental supports maintained on weekly home visits by a case worker), MedeMonitor (smart-pill container capable of cueing the taking of medication and alerting staff of missed medication), and treatment as usual. The study found PharmCAT and MedeMonitor were significantly better at improving adherence than treatment as usual, but they were not significantly different from each other. There were no significant differences in symptoms, functioning, or health care utilisation.

Mobile apps

1 uncontrolled study (N = 24) assessed 1 week of Experience Sampling Program 4.0; an ecological momentary assessment (EMA) program involving taking real-time measures of current location, company, activity, positive affect, negative affect, psychotic symptoms, and self-stigma. The study found participants spent 63% of their time at home, were often alone (60%) or with family (20%), spent much time inactive (39%) and eating (21%), or engaged in other activities (20%). There was a significant improvement in self-stigma when doing unspecified “other” activities compared to eating. There were no other significant differences. One non-randomised study (N = 50) assessed 1 week of mobile EMA compared to retrospective ratings and found mean retrospective ratings were lower than mean EMA ratings in both groups.

1 uncontrolled study (N = 12) assessed usability of FOCUS involving three smartphone apps and

found that all participants were confident in using the system and were satisfied with the ease of use. Another non-controlled study (N = 32) assessed 3 x daily for 1 month FOCUS use for medication adherence, social, mood, auditory hallucinations, or sleep difficulties, and found 93.7% of patients were satisfied with ease of use of the app and thought components of FOCUS worked well together. There was a significant reduction in symptoms by the end of the trial. Beliefs about medication did not change.

1 non-randomised study (N = 34) assessed a visit mobile app version of a scale for functioning capacity assessment (UPSA-Mobile) vs. the full UPSA. Patients with schizophrenia found the device somewhat difficult to operate, with controls achieving significantly higher scores on UPSA-M than patients with schizophrenia. UPSA-M scores correlated with clinical assessment scales and UPSA-M was able to accurately differentiate adults with schizophrenia from controls 80% of the time.

1 uncontrolled study (N = 44) assessed ClinTouch, a mobile app for retrospective momentary assessment of mood and symptoms. Assessment questions were related to items on clinical scales. Correlations with standard clinical scales were generally good, although there was variability; positive symptoms showed moderate to strong correlation with corresponding items on CDS and PANSS scales. Mobile assessments showed some instability across time.

Digital medicine with sensors

1 non-randomised study (N = 28) assessed 4 weeks of DHFS, which electronically confirms ingestion of oral medication embedded with an ingestion sensor and acquires physiological metrics. The study found physiological metrics did not differ between schizophrenia and bipolar groups. 70% found DHFS was easy to understand and 89% thought it could be useful.

1 uncontrolled study (N = 49) assessed 8 weeks of a digital medicine system comprising medication embedded with an ingestible sensor, a wearable sensor, and software apps and found 82.1% of patients independently or with minimal assistance were able to complete tasks associated with the app of wearable sensor and pairing with smartphone app. 78% were somewhat to extremely satisfied with the system. Five device-related adverse events led to study discontinuation (details of the events were not described).

Adhesive patch/wearable sensor

1 non-randomised study (N = 35) assessed 4 weeks of an adhesive patch to monitor locomotor activity and heart rate paired to a mobile device and found a combination of heart rate and locomotor activity provided 95.3% classification accuracy vs. heart rate (78.5%) or locomotor activity (85.5%) alone.

Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Bell IH, Lim MH, Rossell SL, Thomas N

Ecological momentary assessment and intervention in the treatment of psychotic disorders: A systematic review

Psychiatric Services 2017; 68: 1172-81

View review abstract online

Comparison	**Ecological momentary assessments (EMA) for people with schizophrenia.**
Summary of evidence	**Moderate to low quality evidence (small to medium-sized sample, unable to assess consistency or precision, direct) suggests the Information Technology–Aided Relapse Prevention Program in Schizophrenia (ITAREPS) can improve treatment adherence and reduce hospitalisations. Low quality evidence (small samples) is unable to determine benefits of other EMA interventions.**

Various outcomes

1 RCT (N = 158) assessed 52 weeks of Information Technology–Aided Relapse Prevention Program in Schizophrenia (ITAREPS) and found more adherence in the treatment group. There were reduced hospitalisations only in participants whose treatment team followed the protocol (HR = 0.11), and fewer inpatient days (2.1 vs. 19.7).

1 RCT (N = 55) assessed 52 weeks of ITAREPS involving telephone assessments plus nurse visits to deliver medication protocol in response to alerts. There were fewer hospitalisations in the treatment group (0 vs. 8, HR = 0.21) and fewer rehospitalisation days. The ratio of relapses to hospitalisations was lower in the treatment group.

1 non-randomised study (N = 73) assessed 104 weeks of ITAREPS with remote monitoring of signs of relapse completed weekly by patients and family members by SMS with alert sent to treatment team if relapse is indicated, requiring medication increase and heightened monitoring. There were significant reductions in the number of hospitalisations and hospitalisation days during the intervention compared with same period before the trial.

1 uncontrolled study (N = 55) assessed 12 weeks of Mobile Assessment and Treatment for Schizophrenia (MATS) where users were prompted 12 times daily to complete assessment items with response-driven, empirically derived feedback designed to promote medication adherence, socialisation, and coping with auditory hallucinations. Helpfulness of the program was between moderate to very helpful, and reports of helpfulness increased over time, although some people reported technical issues related to usability. There was increased adherence to and positive beliefs about medication over time. There was an increased amount and positive perception of socialisation over time, and decreased reports of severity and of level of perceived uncontrollability

of hallucinations. There were no significant pre-post changes in other symptoms.

1 quasi-randomised study (N = 62) assessed 7 weeks of a SMS based intervention where users were prompted to complete personalised goals for daily living and record their achievement. The study found 20% of goals were achieved during the intervention. 70% provided positive feedback, 20% neutral feedback and 10% negative feedback. 41% reported the intervention was effective, 33% were neutral and 26% said it was ineffective. 47% were willing to continue, 22% were unsure, and 31% were unwilling. Percentage of overall goals achieved rose from 47% during baseline to 62% during the intervention and fell to 40% at follow-up. Appointment attendance improved but not medication adherence, inhibition of undesirable behaviour, or attendance of training program.

1 uncontrolled study (N = 14) assessed 6 weeks of Mobus where patients reported personalised goals to caregivers and are then prompted to complete these at appropriate times. Patients logged 43% of the activities initially listed and symptoms were recorded once per week on average. There were increased living skills (on a food subscale only), and a reduction in thinking time, but no improvement in symptoms.

1 uncontrolled study (N = 33) assessed 3 x daily for 1 month FOCUS use for medication adherence, social, mood, auditory hallucinations, or sleep difficulties, and found over 90% of patients were satisfied with the app, however 12% to 18% requested more training or support or felt the intervention was complicated. There was a significant reduction in symptoms by the end of the trial.

1 pilot study (N = 9) assessed 24 weeks of Skills Training and Empowerment Program (STEP) involving 12 fortnightly face-to-face living skills training plus weekly 20-minute phone calls to reinforce uptake of skills. 57% reported enjoying the intervention, 14% reported that the intervention helped them very much and 57% reported that it helped them moderately. There were improved functioning scores in the intervention group compared to a matched sample. 86% reported some or a lot of skill utilisation.

Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Biagianti B, Quraishi SH, Schlosser DA

Potential benefits of incorporating peer-to-Peer interactions into digital interventions for psychotic disorders: A systematic review

Psychiatric Services 2018; 69: 377-88

View review abstract online

Comparison	**Digital peer-to-peer interactions for people with schizophrenia.**

Summary of evidence	**Moderate quality evidence (large sample, unable to assess consistency or precision, direct) suggests internet peer-support via Listserv may provide adequate social support. Low quality evidence (small samples) is unable to determine benefits of other digital peer-to-peer formats. Review authors conclude that when peer-to-peer interactions were moderated by facilitators, retention, engagement, acceptability, and efficacy were higher than for interventions with no facilitators. Studies involving service users in intervention design showed higher rates of acceptability.**

Various outcomes

1 RCT (N = 300) assessed 1 year of internet peer-support Listserv and a peer support bulletin board vs. waiting list. 30% reported having read the messages at least weekly and sent at least five messages. Perceived relevance, support, and satisfaction were rated as moderate. There were no differences in quality of life, empowerment or symptoms.

1 RCT (N = 16) assessed 1 year of Schizophrenia Online Access to Resources (SOAR), involving in-person psychoeducation followed by online psychoeducation, therapy groups, moderated peer discussion forums, and questions via e-mail vs. usual care. 100% of participants engaged with treatment. 68.8% to 81.4% found SOAR moderately to extremely easy to use. 93.8% would have liked to be involved in SOAR after study conclusion. There were reductions in positive symptoms, improvements in perceived social support and stress, and increase in schizophrenia knowledge. Compared to other web sites SOAR showed good ease of use.

1 uncontrolled pilot study (N = 20) assessed 4 weeks of HORYZONS, an online interactive psychosocial intervention and moderated social networking program. 100% of participants engaged with treatment, 60% used the program for the full four weeks, 70% for at least three weeks. 75% had a positive experience and 90% would recommend it to others. 70% felt it would be a useful long-term treatment option. 100% agreed or strongly agreed that HORYZONS was safe and confidential, and 90% felt that moderation had contributed to safety. There were moderate to large reductions in depression, 60% reported increased perceived social connectedness, 55% felt empowerment in their recovery process and 70% found the system to be useful after discharge from hospital.

1 uncontrolled pilot study (N = unclear) assessed 12 weeks of Personalised Real-Time Intervention for Motivation Enhancement (PRIME) involving SMS-based motivational coaching from trained therapists, individualised goal setting in various psychosocial domains and social networking via direct peer-to-peer messaging, with a community “moments feed” to capture and reinforce rewarding experiences and goal achievements. Average number of logins per week was 4.1, challenge completion was 84.9%, average number of user-initiated peer interactions was 74.2, average number of user-initiated coach interactions was 56.6, average number of challenges completed was 19.4, and average times active per week was 7.52. Overall satisfaction rating 8/10.

1 uncontrolled pilot study (N = 21) assessed 6 weeks of Creating Live Interactions to Mitigate Barriers (CLIMB) program involving computerised social cognition training, remote weekly group

therapy sessions, and moderated group texting. 78% attended 84% of the group therapy sessions, completed a median of 9.5 hours of training, and posted a median of 5.2 messages per week on the group text chat. Ratings out of 5 for enjoyment/satisfaction was 2.99, for program clarity and ease of use 4.18, for ease of fitting into daily schedule 2.91, and for perceived benefits 3.25. There were significant improvements in social emotion, identification abilities, and trend-level improvements in aspects of quality of life, with no improvements in symptoms.	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Valimaki M, Athanasopoulou C, Lahti M, Adams CE

Effectiveness of Social Media Interventions for People With Schizophrenia: A Systematic Review and Meta-Analysis

Journal of Medical Internet Research 2016; 18(4): e92

View review abstract online

Comparison	**Social media interventions (12 months duration; online psychoeducation or peer support) vs. standard care.**
Summary of evidence	**Moderate to high quality evidence (large sample, some inconsistency, precise, direct) suggests small effects of increased quality of life and decreased symptoms with social media interventions. However social support and self-management were decreased with social media interventions. Low quality evidence from one small RCT (imprecise) is unable to determine the effects of social media interventions on stress.**
Symptoms, quality of life, social support, self-management and perceived stress	
A significant, small increase in quality of life in the social media group at 12 months; 2 RCTs, N = 600, median difference 0.15, 95%CI 0.14 to 0.17, $p < 0.001$, I^2 83%, $p = 0.02$ *A significant, small decrease in symptoms in the social media group at 6 months;* 1 study, N = 300, median difference -0.14, 95%CI -0.15 to -0.13, $p < 0.001$ *A significant, small decrease in level of social support in the social media group at 6 months;* 2 RCTs, N = 330, median difference 0.22, 95%CI 0.02 to 0.42, $p = 0.03$, I^2 40%, $p = 0.20$	

A significant, small decrease in self-management in the social media group at 12 months; 2 RCTs, N = 600, median difference 0.07, 95%CI 0.07 to 0.08, $p < 0.001$, I^2 80%, $p = 0.03$ *A significant, small decrease in self-rated stress in the social media group at 6 months;* 1 study, N = 30, median difference -0.51, 95%CI -0.90 to -0.12, $p = 0.01$	
Consistency in results	Consistent for social support, inconsistent for self-management and quality of life, not applicable for symptoms and stress (1 study).
Precision in results	CIs appear precise, apart from self-rated stress.
Directness of results	Direct

van der Krieke L, Wunderink L, Emerencia AC, de Jonge P, Sytema S

E–Mental Health Self-Management for Psychotic Disorders: State of the Art and Future Perspectives

Psychiatric services 2014; 65(1): 33-49

View review abstract online

Comparison 1	**Telemental medication management vs. standard care, pill counting, or early warning signs checklist.**
Summary of evidence	**Moderate quality evidence (medium to large sample, unable to assess consistency, precise, indirect) suggests a large effect of increased medication adherence with telemental medication management.**
Medication adherence	
A large, significant effect of increased medication adherence with telemental medication management; 3 RCTs, N = 422, $g = 0.920$, 95%CI 0.509 to 1.331, $p < 0.001$	
Consistency in results	No measure of consistency is reported.
Precision in results	Precise
Directness of results	Indirect comparison (mixed control conditions).
Comparison 2	**Telemental communication/shared decision making vs. standard care, non-web-based communications, or provision of**

	information.
Summary of evidence	**Moderate quality evidence (large sample, unable to assess consistency, precise, indirect) suggests a small effect of greater satisfaction with telemental communication.**
Satisfaction	
A small, significant effect of greater satisfaction with telemental communication; 3 RCTs, N = 834, *g* = 0.205, 95%CI 0.030 to 0.380, *p* = 0.022	
Consistency in results	Heterogeneity measure not reported
Precision in results	Precise
Directness of results	Indirect comparison (mixed control conditions).
Comparison 3	**Telemental psychoeducation vs. conventional psychoeducation or medication instruction.**
Summary of evidence	**Moderate quality evidence (large sample, unable to assess consistency, precise, indirect) suggests no differences between telemental psychoeducation and conventional psychoeducation for improving knowledge.**
Knowledge	
No significant differences between groups; 3 RCTs, N = 342, *g* = 0.369, 95%CI -0.065 to 0.803, *p* = 0.096	
Consistency in results	No measure of consistency is reported.
Precision in results	Precise
Directness of results	Indirect (mixed control conditions).

Explanation of acronyms

CBT = Cognitive Behavioural Therapy, CI = Confidence Interval, *g* = Hedges' *g,* standardised mean differences (see below for interpretation of effect size), N = number of participants, *p* = statistical probability of obtaining that result (*p* < 0.05 generally regarded as significant), 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[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).

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 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

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

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

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

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