TECHNICAL COMMENTARY

Treatments for first-episode psychosis

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Introduction

People with a first episode of psychosis may experience distressing symptoms such as unusual beliefs or abnormal behaviour (positive symptoms) and/or withdrawal or loss of interest in work or school (negative symptoms). A first episode of psychosis may be distinct from a first episode of schizophrenia, which has significantly more stringent requirements for diagnosis.

Early intervention paradigms for schizophrenia and psychosis are often combined into multi-element programs comprising both pharmaceutical and psychosocial therapies or enriched therapies that are tailored to individuals' needs[1-8]. Consequently, this table presents the evidence for interventions utilising either, or both antipsychotic medications and/or cognitive or behavioural therapies for treating early psychosis and preventing relapse.

The conclusions presented here are based on group data, and as such individual treatment programs need to be tailored by trained clinicians. Individual response to treatment can vary in terms of both symptoms and adverse effects.

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 which describes a preferred way to present a meta-analysis[9]. Reviews reporting less than 50% of items 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)[10]. 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).

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Results

We found 11 reviews that met our inclusion criteria[2, 3, 6-8, 11-16].

- High quality evidence suggests multi-element first-episode psychosis programs involving both antipsychotic medication and psychosocial treatments provide a small reduction in the risk of relapse and symptom severity after a first episode of psychosis compared to treatment as usual. Moderate quality evidence suggests these programs may also improve social function, quality of life, treatment adherence, and treatment satisfaction. The addition of Cognitive Behavioural Therapy or Relapse Prevention Therapy does not further reduce the rate of relapse or suicide, but may further improve negative symptoms, social function and quality of life.
- Moderate to high quality evidence suggests early intervention programs using assertive case management can reduce the number of hospital bed days compared to treatment as usual. Moderate quality evidence finds they may also reduce the number of hospitalisations.
- Moderate to high quality evidence suggests no differences in long-term outcomes when medication is delayed for a short period of time and psychosocial treatments are provided in a research setting when compared to immediate commencement of medication without psychosocial treatment.
- Moderate to low quality evidence suggests no significant benefit of group therapy over individual therapy for negative symptoms, functioning and quality of life, but some benefit for improving psychotic symptoms, treatment adherence and treatment satisfaction.

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Alvarez-Jimenez M, Parker AG, Hetrick SE, McGorry PD, Gleeson JF

Preventing the Second Episode: A Systematic Review and Meta-analysis of Psychosocial and Pharmacological Trials in First-Episode Psychosis

Schizophrenia Bulletin 2011; 37(3): 619-30

View review abstract online

Comparison 1	**Specialist first-episode psychosis programs comprising multidisciplinary teams administering unspecified low-dose atypical antipsychotics, manualised cognitive-behavioural strategies, individualised management plans and counselling, and psychoeducation vs. treatment as usual.**
Summary of evidence	**High quality evidence (large samples, consistent, precise, direct) suggests a small effect of specialist first-episode psychosis programs reducing the risk of relapse compared to treatment as usual. Moderate to high quality evidence (unable to assess precision) suggests they may also reduce the length of hospital stay following relapse.**
Relapse rate	
Small effect size significantly favours first-episode psychosis programs for preventing relapse; 3 RCTs, N = 679, † OR = 1.80, 95%CI 1.31 to 2.48, $p < 0.001$, $I^2 = 0\%$, $p = 0.82$ The number needed to treat to prevent one relapse was approximately 8	
Days in hospital	
The number of days in hospital following relapse was significantly lower in the specialist treatment group compared to treatment as usual; 3 RCTs, N = 402, WMD = -26.20, 95%CI -7.35 to -45.06, $p < 0.01$, $I^2 = 0\%$, $p = 0.71$	
Consistency in results	Consistent
Precision in results	Precise for relapse, unable to assess days in hospital (measure not standardised).
Directness of results	Direct
Comparison 2	**Cognitive based therapies vs. various comparison treatments.**

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Summary of evidence	**Moderate to low quality evidence (small to medium-sized samples, consistent, imprecise, indirect) suggests the addition of either cognitive behavioural therapy or relapse prevention therapy to specialist first-episode psychosis programs does not significantly improve the rate of relapse.**
Individual cognitive behavioural therapy for relapse prevention	
2 RCTs administered specialist first-episode psychosis programs alone, compared with a specialist first-episode psychosis program in addition to individual cognitive behavioural therapy (10-20 sessions over 3 months). *No significant benefit of additional cognitive behavioural therapy over first-episode psychosis programs for reducing relapse rates;* N = 90, OR = 1.95, 95%CI 0.76 to 5.00, p = 0.17, I^2 = 0%, p = 0.48	
1 RCT, N = 193, administered individual cognitive behavioural therapy (15-20 sessions over 5 weeks) compared with other therapies (supportive counselling or treatment as usual). *No significant benefit of cognitive behavioural therapy was reported for reducing relapse rates compared to;* Supportive counselling: OR = 1.11, 95% CI 0.63 to 1.95, p = 0.72 Treatment as usual: OR = 1.15, 95% CI 0.65 to 2.04, p = 0.62	
Cognitive-based relapse prevention therapy for relapse prevention	
1 RCT administered specialist first-episode psychosis programs alone, compared with a specialist first-episode psychosis program in addition to individual and family cognitive-based relapse prevention therapy (follow up at 7 months). *Non-significant (trend) benefit of relapse prevention therapy for reducing relapse rates;* N = 81, OR = 0.21, 95%CI 0.04 to 1.03, p = 0.06	
Consistency in results	Consistent where applicable
Precision in results	Imprecise
Directness of results	Indirect (control conditions combined)
Comparison 3	**Family therapy (psychoeducation) vs. treatment as usual.**
Summary of evidence	**Moderate to low quality evidence (small to medium-sized sample, inconsistent, imprecise, direct) suggests family therapy did not reduce relapse rates compared to treatment as usual.**

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Relapse prevention	
2 RCTs compared family therapy (6 - 18 sessions of psychoeducation or counselling for families over 9 - 18 months) with standard outpatient care. *No significant benefit of family therapy was reported over standard care for reducing relapse rates;* N = 184, OR = 2.82, 95%CI 0.54 to 14.75, $p = 0.22$, $I^2 = 76\%$, $p < 0.05$	
Consistency in results	Inconsistent
Precision in results	Imprecise
Directness of results	Direct

Bird V, Premkuma P, Kenall T, Whittington C, Mitchell J, Kuipers E

Early intervention services, cognitive-behavioural therapy and family intervention in early psychosis: systematic review

The British Journal of Psychiatry 2010; 197(5): 350-356

View review abstract online

Comparison	**Any early intervention service (incorporating intensive case management, medication management, and various psychosocial interventions 'as-required' such as cognitive behavioural therapy, social skills training, family interventions and vocational rehabilitation) vs. standard care. Treatment duration 9 months to 2 years.**
Summary of evidence	**High quality evidence (large samples, consistent, precise, direct) shows that early intervention services may improve positive and negative symptoms compared to standard care.** **Moderate to high quality evidence (medium to large samples, direct, consistent, some imprecision) suggests early intervention may reduce relapse rates, hospital admission, dropout rates and improve rate of contact with the index mental health team compared to standard care.** **Moderate to low quality evidence (direct, imprecise, inconsistent) suggests early intervention services may increase the likelihood of receiving psychological interventions compared to standard care.**

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Symptoms **Measured by PANSS or SAPS**
The early intervention group showed significant small effect of reduced positive symptoms at end of treatment; 2 RCTs, N = 468, SMD = -0.21, 95%CI -0.42 to -0.01, $p < 0.05$, $I^2 = 9\%$, $p = 0.29$ *The early intervention group showed significant medium effect of reduced negative symptoms at end of treatment;* 2 RCTs, N = 468, SMD = -0.39, 95%CI -0.57 to -0.20, $p < 0.05$, $I^2 = 0\%$, $p = 0.38$
Relapse and Hospital admission rates
A medium effect showed that the early intervention group were significantly less likely to relapse at end of treatment; 2 RCTs, N = 172, RR = 0.66, 95%CI 0.47 to 0.94, $p < 0.05$, NNTB = 6, 95%CI 3 to 25, $I^2 = 0\%$, $p = 0.67$ *A medium effect showed that the early intervention group were significantly less likely to be admitted to hospital at end of treatment;* 3 RCTs, N = 622, RR = 0.67, 95%CI 0.54 to 0.83, $p < 0.05$, NNTB = 7, 95%CI 5 to 7, $I^2 = 0\%$, $p = 1.00$
Dropout rate and adherence
Significant medium effect of lower discontinuation rate for the early intervention group; 4 RCTs, N = 800, RR = 0.71, 95%CI 0.53 to 0.94, $p < 0.05$, NNTB = 8, 95%CI 5 to 14, $I^2 = 40\%$, $p = 0.17$ *Medium effect shows that the early intervention group were significantly more likely to remain in contact with the index mental health team;* 2 RCTs, N = 580, RR = 0.60, 95%CI 0.39 to 0.92, $p < 0.05$, NNTB = 13, 95%CI 4 to NR, $I^2 = 0\%$, $p = 0.079$ *Medium effect showed that the early intervention group were significantly more likely to receive psychological intervention;* 3 RCTs, N = 630, RR = 0.67, 95%CI 0.46 to 0.97, $p < 0.05$, NNTB = 5, 4 to 6, $I^2 = 74\%$, $p = 0.02$

Consistency in results	Inconsistent for likelihood to receive psychological intervention, consistent for all other outcomes
Precision in results	Imprecise for likelihood to relapse, remain in contact with the index mental health team and receive psychological intervention, precise for all other measures

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Directness of results	Direct

Bola JR

Medication-free research in early episode schizophrenia: evidence of long-term harm?

Schizophrenia Bulletin 2006; 32(2): 288-96

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Comparison	**Delaying antipsychotic medication (mostly first generation) vs. placebo or psychosocial treatments for an average of 2 months to assess the effects of delaying medication administration.**
Summary of evidence	**Moderate to high quality evidence (large sample, consistent, precise, indirect) suggests no significant difference in long-term outcomes when medication is delayed for a short period (in clinical trials) and psychosocial treatments are provided, compared to immediate commencement of medication without psychosocial treatment.**

Long term effects at 1-7 year post-treatment on relapse, hospitalisation, global function, clinical improvement and employment

Seven studies (4 RCT, 3 quasi-experimental)

No significant differences reported from pooled effect sizes in long-term outcomes for medication compared to placebo or psychosocial treatments;

N = 623, r = 0.09, 95%CI -0.27 to 0.09, $p > 0.05$

No significant differences between study results;

$\chi^2 = 2.32$, $p > 0.05$

Subgroup analysis

Both RCT and quasi-experimental studies showed no difference in long-term outcomes, no significant difference between groups;

RCT, r = 0.01, 95%CI, p not reported

Quasi, r = -0.15, 95%CI, p not reported

$t = 1.58$, $p > 0.05$

Subgroup analysis

A medium effect advantage of active psychosocial comparison vs. placebo comparison for long

term outcomes; Active, *r* = -0.16, 95%CI, *p* not reported Placebo, *r* = 0.11, 95%CI, *p* not reported *t* = 6.63, *p* = 0.00	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Indirect comparison (mixed control conditions combined)

Correll CU, Galling B, Pawar A, Krivko A, Bonetto C, Ruggeri M, Craig TJ, Nordentoft M, Srihari VH, Guloksuz S, Hui CLM, Chen EYH, Valencia M, Juarez F, Robinson DG, Schooler NR, Brunette MF, Mueser KT, Rosenheck RA, Marcy P, Addington J, Estroff SE, Robinson J, Penn D, Severe JB, Kane JM

Comparison of early intervention services vs treatment as usual for early-phase psychosis: A systematic review, meta-analysis, and meta-regression

JAMA Psychiatry 2018; 75: 555-65

View review abstract online

Comparison	**Integrated early intervention services specifically designed for people with early-phase psychosis (pharmaceutical and psychosocial such as case management, psychotherapy, supported employment and education, and family support) vs. treatment as usual. Mean trial duration = 16.2 months (range 9-24 months).**
Summary of evidence	**Moderate to high quality evidence (large samples, mostly consistent, precise, indirect) finds small effects of fewer relapses and hospitalisations, more remission and recovery, greater improvements in symptoms, functioning and quality of life, and less all-cause treatment discontinuation with early intervention services. These effects were similar across most time points (6, 9-12, and 18-24 months). There were few moderating variables. Studies including fidelity monitoring had fewer hospitalisations than those without fidelity monitoring. Larger study sample size was associated with lower**

	hospitalisation risk. Younger age, male sex, higher baseline symptom severity and more patients with schizophrenia were each associated with greater improvements in total symptoms.
Hospitalisation and relapse	
A small, significant effects of fewer hospitalisations and relapses with early intervention services; At least one hospitalisation: 10 RCTs, N = 2,105, RR = 0.74, 95%CI 0.61 to 0.90, $p = 0.003$, $I^2 = 47\%$, $p = 0.047$ Number of hospitalisations: 8 RCTs, N = 1,412, SMD = -0.17, 95%CI -0.31 to -0.03, $p = 0.018$, $I^2 = 35\%$, $p = 0.157$ Duration of hospitalisation: 6 RCTs, N = 1,107, SMD = -0.17, 95%CI -0.28 to -0.05, $p = 0.006$, $I^2 = 0\%$, $p = 0.470$ Relapse: 7 RCTs, N = 1,275, RR = 0.71, 95%CI 0.53 to 0.93, $p = 0.014$, $I^2 = 37\%$, $p = 0.143$ In subgroup analyses, the only significant between-subgroup difference was that studies including fidelity monitoring had fewer hospitalisations vs. tau than those without fidelity monitoring (RR = 0.88 vs. 0.50, $p = 0.001$). Meta-regression showed larger study sample size was associated with lower hospitalisation risk (coefficient = 0.001, $p = 0.002$). There were no moderating effects of region, blinding, type of psychosocial component (family therapy, crisis response, social skills, vocational), number of sites, duration of treatment, number of treatment components, ratio of number of visits in intervention vs. control groups, study risk of bias, diagnosis, baseline symptoms and functioning, age, gender, duration of treated or untreated psychosis, prior antipsychotic treatment, attrition rates.	
Symptoms	
Small, significant effects of greater improvements in symptoms with early intervention services; Total symptoms: 8 RCTs, N = 1,179, SMD = -0.32, 95%CI -0.47 to -0.17, $p < 0.001$, $I^2 = 32\%$, $p = 0.175$ General symptoms: 8 RCTs, N = 1,118, SMD = -0.30, 95%CI -0.47 to -0.13, $p < 0.001$, $I^2 = 40\%$, $p = 0.111$ Positive symptoms: 10 RCTs, N = 1,532, SMD = -0.22, 95%CI -0.32 to -0.11, $p < 0.001$, $I^2 = 0.5\%$, $p = 0.433$ Negative symptoms: 10 RCTs, N = 1,532, SMD = -0.28, 95%CI -0.42 to -0.14, $p < 0.001$, $I^2 = 38\%$, $p = 0.102$ Depressive symptoms: 5 RCTs, N = 874, SMD = -0.19, 95%CI -0.35 to -0.03, $p = 0.017$, $I^2 = 18\%$, $p = 0.301$ Meta-regressions showed moderating effects of younger age, male sex, higher baseline symptom severity and the percentage of patients with schizophrenia vs. other psychoses were each associated with greater improvements in total symptoms with early intervention services.	

There were no moderating effects on total symptoms in other subgroup or meta-regression analyses (see the hospitalisation section for a full list of variables assessed).	
Remission and recovery	
Small, significant effects of more remission and recovery with early intervention services; Remission: 7 RCTs, N = 1,229, RR = 1.29, 95%CI 1.07 to 1.55, $p = 0.007$, $I^2 = 69\%$, $p = 0.004$ Recovery: 3 RCTs, N = 640, RR = 1.24, 95%CI 1.03 to 1.50, $p = 0.022$, $I^2 = 0\%$, $p = 0.689$	
Functioning and quality of life	
Small, significant effects of greater improvements in functioning and quality of life with early intervention services; Overall functioning: 7 RCTs, N = 1,005, SMD = 0.21, 95%CI 0.08 to 0.34, $p < 0.001$, $I^2 = 0\%$, $p = 0.590$ Involvement in school or work: 6 RCTs, N = 1,743, RR = 1.13, 95%CI 1.03 to 1.24, $p = 0.01$, $I^2 = 0\%$, $p = 0.659$ Quality of life: 4 RCTs, N = 505, SMD = 0.23, 95%CI 0.004 to 0.46, $p = 0.046$, $I^2 = 34\%$, $p = 0.208$ There were no moderating variables.	
Risks	*There was less all-cause treatment discontinuation with early intervention services;* 10 RCTs, N = 2,173, RR = 0.70, 95%CI 0.61 to 0.80, $p < 0.001$, $I^2 = 0.4\%$, $p = 0.434$
Consistency in results	Consistent, apart from remission and at least one hospitalisation.
Precision in results	Precise
Directness of results	Indirect (mixed interventions combined).

Harvey PO, Lepage M, Malla A

Benefits of enriched intervention compared with standard care for patients with recent-onset psychosis: a metaanalytic approach

Canadian Journal of Psychiatry 2007; 52(7): 464-72

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Comparison	**Enriched intervention programs (EI, comprising high carer to patient ratio and antipsychotic therapy plus psychosocial treatments relevant to this phase of illness) plus standard care compared to standard care alone (SC, comprising antipsychotic therapy and case management).**
Summary of evidence	**Moderate to low quality evidence (large sample, inconsistent, precise, indirect) suggests enriched interventions may be more effective than standard care for improving symptom severity but not global function.**
Symptom severity (PANSS or BPRS)	
EI programs administered for a minimum of 6 months, or well-identified psychosocial therapy (such as family interventions, social skills training, cognitively oriented therapy, supportive therapy) targeted to the early phase of illness administered for minimum 3 months) and administered for a minimum of 3 months. Only results from the randomised studies are reported here. Five EI trials were compared with three SC trials, total N = 875. Follow up duration up to 2 years. *Significant benefit of EI over SC for reducing symptom severity;* Total symptoms Effect of EI: *d* = -1.79 (95%CI -1.95 to -1.63) Effect of SC: *d* = -1.26 (95%CI, -1.49 to -1.03) Between group comparison: Q_B = 13.5, *p* < 0.001 Positive symptoms Effect of EI: *d* = -1.81 (95%CI, -1.93 to -1.69) Effect of SC: *d* = -1.07 (95%CI, -1.19 to -1.00) Between group comparison: Q_B = 74.4, *p* < 0.001 Negative symptoms Effect of EI: *d* = -0.67 (95%CI, -0.80 to -0.55) Effect of SC: *d* = -0.18 (95%CI, -0.32 to -0.05) Between group comparison: Q_B = 26.2, *p* < 0.001 An extended sample including non-randomised studies (eleven EI and six SC, total N = 1553) reported similar magnitude and direction of effect and significance.	
Global function (GAF)	

Levels of functioning, N = 875 No significant difference between EI and SC Effect of EI: *d* = 0.78 (95%CI, 0.61 to 0.95) Effect of SC: *d* = 0.58 (95%CI, 0.43 to 0.73) Between group comparison: Q_B = 3.02, *p* = NS An extended sample including non-randomised studies (eleven EI and six SC, total N = 1553) reported a significant benefit of EI over SC for improving global function (*p* < 0.001).	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Indirect

Marshall M, Rathbone J

Early Intervention for psychosis

Cochrane Database of Systematic Reviews, 2011 Issue 6. Art. No.: CD004718. DOI: 10.1002/14651858.CD004718.pub3

View review abstract online

Comparison	**LifeSPAN - 8 to 10 sessions of cognitive behavioural therapy + specialised team vs. specialised team alone.** **Participants were acutely suicidal (score of 4-7 on BPRS suicide subscale).**
Summary of evidence	**Moderate to low quality evidence (small sample, imprecise, direct) is uncertain as to the benefit of cognitive behavioural therapy + specialised team over specialised team alone for treatment retention and preventing suicide.**
Leaving the study early	
No treatment effect for CBT over the specialised team alone at 6 months; 1 RCT, N = 56, RR 2.02 95%CI 0.72 to 5.66, *p* = 0.18	
Suicide rate	

No significant treatment effect for CBT over the specialised team alone at 6 months; 1 RCT, N = 56, RR 0.81 95%CI 0.05 to 12.26, *p* = 0.88	
Consistency in results	Not applicable, 1 RCT only
Precision in results	Imprecise
Directness of results	Direct
Comparison 2	**12 months of behavioural family therapy (18 sessions) + individual-orientated therapy (supportive therapy including maintenance medication and stress management assistance) vs. supportive therapy alone.**
Summary of evidence	**Moderate to low quality evidence (small sample, imprecise, direct) is uncertain as to the benefit of behavioural family therapy + individual-orientated therapy over individual-orientated therapy alone for improving relapse rates.**
Relapse by end of treatment	
No significant treatment effect for family therapy over supportive therapy alone at 1 year; 1 RCT, N = 76, RR 1.05 95%CI 0.37 to 2.98, *p* = 0.92	
Consistency in results	Not applicable, 1 RCT only
Precision in results	Imprecise
Directness of results	Direct
Comparison 3	**Family psychoeducation – individual and group + standard care (including outpatient care, and maintenance medication) vs. standard care alone.**
Summary of evidence	**Moderate to low quality evidence (small sample, imprecise, direct) is uncertain as to the benefit of family therapy over standard care.**
Leaving the study early	
No significant treatment effect for family therapy + standard care over standard care alone at 18 months; 1 RCT N = 83, RR 1.46, 95%CI 0.26 to 8.31, *p* = 0.67	

Hospital admissions	
Small effect size favouring intervention group for decreased hospital admissions at 18 months; 1 RCT N = 83, RR 0.28 95%CI 0.13-0.62, *p* = 0.0017, NNT = 3, 95%CI 2 to 6	
Treatment adherence	
Trend effect favouring family therapy + standard care over standard care at 18 months; 1 RCT N = 83, RR 0.57, 95%CI 0.31 to 1.04, *p*=0.065	
Consistency in results	Not applicable, 1 RCT only
Precision in results	Imprecise
Directness of results	Direct
Comparison 4	**Integrated, assertive community treatment – specialised team including family involvement, social skills training and maintenance medication vs. standard care (community health care and maintenance medication).**
Summary of evidence	**Moderate to high quality evidence (large sample, precise, direct, 1 RCT) suggests a small benefit of specialised integrated assertive community treatment over standard care for improved treatment adherence, ability to work or sustain education and a medium benefit for improved global function in the short term, and improved service satisfaction for up to 2 years. No benefit was reported for suicide rate or ability to live independently.**
Leaving the study early	
Small effect size favouring specialised team therapy over standard care at 1 year; 1 RCT, N = 547, RR 0.59, 95%CI 0.43 to 0.81, *p* = 0.0012, NNT= 9, 95%CI 6 to 18 *Small effect size favouring specialised team therapy over standard care at 2 years;* 1 RCT, N = 547, RR 0.64 95%CI 0.50 to 0.82, *p* = 0.00048, NNT=7, 95%CI 6 to 14	
Global state **Measured by GAF-symptom, average endpoint score**	

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Medium effect size favouring specialised team therapy over standard care at 1 year; 1 RCT, N = 419, *d* = -0.24 95%CI -0.43 to -0.05, *p* = 0.01 *No treatment effect for specialised team therapy over standard care at 2 years;* 1 RCT, N = 369, *d* = -0.16 95%CI -0.37 to 0.04. *p* = 0.12
Global state **Measured by GAF-function, average endpoint score**
No treatment effect for specialised team therapy over standard care at 1 year; 1 RCT, N = 419, *d* = -0.15 95%CI -0.35 to 0.04, *p* = 0.12 *Medium effect size favouring specialised team therapy over standard care at 2 years;* 1 RCT, N = 369, *d* = -0.26 95%CI -0.47 to -0.05, *p* = 0.01
User satisfaction **Measured by CSQ-8 average endpoint score**
Medium effect size favouring specialised team therapy over standard care at 1 year; 1 RCT, N = 419, *d* = -0.32 95%CI -0.52 to -0.13, *p* = 0.001 *Medium effect size favouring specialised team therapy over standard care at 2 years;* 1 RCT, N = 369, *d* = -0.72 95%CI -0.93 to -0.51, *p* < 0.00001
Treatment adherence
Small effect size favouring specialised team therapy over standard care at 1 year; 1 RCT, N = 507, RR 0.20 95%CI 0.10 to 0.42, *p* = 0.000023, NNT=9, 95%CI 8 to 12
Hospitalisation
No treatment effect for specialised team therapy over standard care at 2 years; 1 RCT, N = 436, RR -0.67 95%CI -1.88 to 0.54, *p* = 0.28
Suicide
No treatment effect for specialised team therapy over standard care at 1 year; 1 RCT, N = 506, RR 0.93 95%CI 0.06 to 14.81, *p* = 0.96
Social outcomes

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Living independently at 2 years *No treatment effect for specialised team therapy over standard care;* 1 RCT, N = 436, RR 0.74 95%CI 0.36 to 1.53, *p* = 0.41 Working or in education at 2 years *Small effect size favouring specialised team therapy over standard care;* 1 RCT, N = 436, RR 0.72 95%CI 0.54 to 0.97, *p* = 0.029, NNT 11, 95%CI 7 to 99	
Consistency in results	Not applicable, 1 RCT only
Precision in results	Precise for all outcomes except living independently, suicide, and hospitalisation
Directness of results	Direct
Comparison 5	**Cognitive behavioural therapy + antipsychotics vs. befriending vs. antipsychotics.** **Maximum of 20 sessions of CBT over 14 weeks for approximately 45 minutes.**
Summary of evidence	**Moderate to low quality evidence (small sample, unable to assess precision or consistency, direct) is uncertain as to the benefit of Needs Focused Intervention plus amisulpride over Needs Focused Intervention for improving mental state, depression, global state or study retention.**
Leaving the study early	
No treatment effect for CBT over befriending; 1 RCT, N = 62, RR 0.57 95%CI 0.19 to 1.76, *p* = 0.33	
Hospitalised by 12 months	
No treatment effect for CBT over befriending; 1 RCT, N = 62, RR 1.08 95%CI 0.59 to 1.99, *p* = 0.80	
Suicide by 12 months	
No treatment effect for CBT over befriending; 1 RCT, N = 62, RR 5.00 95%CI 0.25 to 100.08, *p* = 0.29	
Social functioning **Measured by the SOFRAS**	

No treatment effect for CBT over befriending; Total score: 1 RCT, N = 62, MD -1/30 95%CI -8.86 to 6.26, *p* = 0.74 Total score: 1 RCT, N = 62, MD 0.35 95%CI -1.86 to 2.56, *p* = 0.76 Total score: 1 RCT, N = 62, MD 4.89 95%CI -1.58 to 11.36, *p* = 0.14	
Consistency in results	Not applicable, 1 RCT only
Precision in results	Imprecise
Directness of results	Direct
Comparison 6	**3 months of Ethyl-Eicosapentaenoic Acid oil (E-EPA dose 500 mg/twice a day) plus second generation antipsychotics vs. placebo plus second generation antipsychotics.**
Summary of evidence	**Moderate to low quality evidence (small sample, imprecise, direct) is uncertain as to the benefit of E-EPA.**
Leaving the study early	
No differences between groups at 12 weeks; 1 RCT, N = 80, RR = 0.83, 95%CI 0.28 to 2.51, *p* = 0.75	
Global state **Not responded to treatment by 12 weeks**	
No differences between groups at 12 weeks; 1 RCT, N = 80, RR = 0.90, 95%CI 0.57 to 1.43, *p* = 0.65	
Consistency in results	Not applicable, 1 RCT only
Precision in results	Imprecise
Directness of results	Direct
Comparison 7	**Brief intervention plus treatment as usual vs. treatment as usual.** **Brief intervention consists of seven, one-hourly sessions, including information gathering from a relative; an educational component on psychotic illness, symptoms and early warning signs, treatment, and help seeking; coping strategies, problem solving and communication with the patient.**

Summary of evidence	**Moderate to low quality evidence (small to medium-sized sample, imprecise, direct) is uncertain as to the benefit of brief intervention.**
Leaving the study early	
No differences between groups at 12 weeks; 1 RCT, N = 106, RR = 0.72, 95%CI 0.34 to 1.51, *p* = 0.38	
Hospitalised	
No differences between groups; *< 4 months:* 1 RCT, N = 106, RR = 1.19, 95%CI 0.89 to 1.58, *p* = 0.25 *At 4 months:* 1 RCT, N = 106, RR = 0.75, 95%CI 0.41 to 1.38, *p* = 0.36 *4-9 months:* 1 RCT, N = 106, RR = 0.86, 95%CI 0.43 to 1.74, *p* = 0.67	
Consistency in results	Not applicable, 1 RCT only
Precision in results	Imprecise
Directness of results	Direct
Comparison 8	**Phase specific intervention plus treatment as usual vs. supportive therapy plus treatment as usual.** **Phase specific intervention consists of 14 sessions lasting between 30-45 minutes over six months. It is a manual-based psychotherapy consisting of 4 phases: (1) establishing therapeutic alliance; (2) promoting treatment adherence; (3) developing a plan for maintenance treatment and (4) rehabilitation.** **Supportive therapy had two phases (1) establishment of the therapeutic relationship and (2) emotional support and discussion of non-illness issues or topics.**
Summary of evidence	**Moderate to low quality evidence (small sample, imprecise direct) is uncertain as to the benefit of phase specific intervention.**
Leaving the study early	
No differences between groups at 6 months; 1 RCT, N = 24, RR = 1.27, 95%CI 0.26 to 6.28, *p* = 0.77	

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Mental state **PANSS**	
No differences between groups; *PANSS total:* 1 RCT, N = 17, MD = -4.80, 95%CI -18.42 to 8.82, *p* = 0.49 *PANSS positive:* 1 RCT, N = 17, MD = -1.58, 95%CI -4.88 to 1.72, *p* = 0.33 *PANSS negative:* 1 RCT, N = 17, MD = -1.64, 95%CI -8.05 to 4.77, *p* = 0.62 *PANSS general:* 1 RCT, N = 17, MD = -1.57, 95%CI -7.65 to 4.51, *p* = 0.61	
Depression **Calgary Depression Rating Scale**	
No differences between groups; 1 RCT, N = 17, MD = -1.46, 95%CI -4.17 to 1.25, *p* = 0.29	
Quality of life	
No differences between groups; 1 RCT, N = 17, MD = -2.93, 95%CI -25.59 to 19.73, *p* = 0.80	
Consistency in results	Not applicable, 1 RCT only
Precision in results	Imprecise
Directness of results	Direct
Comparison 9	**Phase specific vocational intervention plus treatment as usual vs. treatment as usual.** **A time-unlimited intervention, continuing after employment is obtained, and adapted to the needs of the individual.**
Summary of evidence	**Moderate to low quality evidence (small sample, imprecise direct) is uncertain as to the benefit of vocational intervention**
Leaving the study early	
No differences between groups; 1 RCT, N = 41, RR = 0.21, 95%CI 0.03 to 1.64, *p* = 0.14	
Employment	
Less unemployment in the intervention group;	

1 RCT, N = 41, RR = 0.39, 95%CI 0.21 to 0.71, *p* = 0.0024	
Consistency in results	Not applicable, 1 RCT only
Precision in results	Imprecise
Directness of results	Direct
Comparison 10	**Cannabis and Psychosis Therapy vs. psychoeducation.** **A cognitive behavioural orientated programme delivered in weekly sessions by trained clinicians over 3 months (mean 8 sessions).**
Summary of evidence	**Moderate to low quality evidence (small sample, imprecise, direct) is uncertain as to the benefit of cannabis and psychosis therapy.**
Cannabis use in the last 4 weeks	
No differences between groups; By 3 months: 1 RCT, N = 47, RR = 1.04, 95%CI 0.62 to 1.74, *p* = 0.87 By 9 months (6 month follow up): 1 RCT, N = 47, RR = 1.30, 95%CI 0.79 to 2.15, *p* = 0.30	
Global state **KAPQ**	
No differences between groups; By 3 months: 1 RCT, N = 47, MD = 0.80, 95%CI -1.78 to 3.38, *p* = 0.54 By 9 months (6 month follow up): 1 RCT, N = 47, MD = 0.90, 95%CI -1.42 to 3.22, *p* = 0.45	
Mental state **BPRS**	
No differences between groups; By 3 months: 1 RCT, N = 47, MD = -3.60, 95%CI -12.81 to 5.61, *p* = 0.44 By 9 months (6 month follow up): 1 RCT, N = 47, MD = 0.80, 95%CI -7.47 to 9.07, *p* = 0.85	
Social functioning **SOFAS**	
No differences between groups; By 3 months: 1 RCT, N = 47, MD = -0.80, 95%CI -9.95 to 8.35, *p* = 0.86	

By 9 months (6 month follow up): 1 RCT, N = 47, MD = -4.70, 95%CI -14.52 to 5.12, *p* = 0.35	
Consistency in results	Not applicable, 1 RCT only
Precision in results	Imprecise
Directness of results	Direct
Comparison 11	**Crisis intervention vs. usual care.** **GP education in early detection with access to Lambeth Early Onset Crisis Assessment Team**
Summary of evidence	**Moderate to low quality evidence (small to medium-sized sample, imprecise, direct) suggests no differences between groups.**
Hospitalisation or referred to emergency services or mental health services	
No differences between groups; 1 RCT, N = 98, RR = 0.85, 95%CI 0.57 to 1.27, *p* = 0.44	
Consistency in results	Not applicable, 1 RCT only
Precision in results	Imprecise
Directness of results	Direct

Oliver D, Davies C, Crossland G, Lim S, Gifford G, McGuire P, Fusar-Poli P

Can We Reduce the Duration of Untreated Psychosis? A Systematic Review and Meta-Analysis of Controlled Interventional Studies

Schizophrenia bulletin 2018; 44: 1362-72

View review abstract online

Comparison	**First episode psychosis services, clinical high risk services, community interventions, healthcare professional training, or multifocus interventions vs. control conditions.**
Summary of evidence	**Moderate to high quality evidence (large samples, mostly consistent, precise, indirect) finds no differences in the duration of untreated psychosis between various early intervention**

	services and controls conditions.
Duration of untreated psychosis	
There were no differences between groups; 16 studies, N = 1,964, *g* = -0.12, 95%CI -0.25 to 0.01, *p* > 0.05, I^2 = 66%, *p* < 0.001 Subgroup analysis of intervention type showed only clinical high-risk services significantly reduced the duration of untreated psychosis compared to treatment as usual, but this was based on only one trial. Meta-regression showed that defining the duration of untreated psychosis *onset* as the onset of frank psychotic positive symptoms or by using the PANSS was associated with a significantly greater decrease in duration of untreated psychosis compared to other onset definitions. There were no moderating effects of age, marital status, length of interventions, quality of studies, publication year, continent, healthcare system type, study design, definition of duration of untreated psychosis, or length of duration of untreated psychosis in the control groups.	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Indirect (mixed interventions combined).

Penn DL, Waldheter EJ, Perkins DO, Mueser KT, Lieberman JA

Psychosocial Treatment for First-Episode Psychosis: A Research Update

American Journal of Psychiatry 2005; 162(12): 2220-32

View review abstract online

Comparison 1	**Multi-element psychosocial intervention programs – including antipsychotics, CBT, individual and group programs, family therapy, assertive community therapy and case management. No control group, pre-post analysis.**
Summary of evidence	**Moderate quality evidence (medium to large samples, unable to assess consistency or precision, direct) suggest some benefit of multi-element early intervention programs for improved symptoms, social functioning, quality of life and remission.**
Prevention and Early Intervention Program for Psychosis (PEPP)	
Single group design – no control group. 3 observational studies, total N = 192	

At 1 year, 3 studies showed significant improvement from baseline for both positive and negative symptoms (BPRS, SAPS, PANSS, SANS). 2 studies (N = 107) showed significant improvement from baseline in social functioning and quality of life (QOL, WQOLI, GAF). 1 study (N = 85) showed significant reduction in rate of relapse – 70% in remission.
Calgary Early Intervention Program
Single group design – no control group. 5 studies, total N = 868 At 1 year 1 study, N = 180, showed significant improvement from baseline for positive symptoms but not negative symptoms (BPRS, SAPS, PANSS, SANS). 1 study, N = 177, showed significant improvement in social functioning and quality of life (QOL, WQOLI, GAF).
Early Psychosis Prevention and Intervention Centre (EPPIC)
3 studies, total N = 583 Symptoms (BPRS, SAPS, PANSS, SANS) 1 single-group study, N = 231 reported significant improvement in positive symptoms at 3 months. 1 quasi-experimental, N = 102, reported significant improvement in negative symptoms at 1 year.
Relapse 1 single-group study N = 231 reported significant reduction in relapse at 3 months – 63% in remission. 1 quasi-experimental N = 102 reported significant reduction in relapse at 1 year.
Social functioning and quality of life (QOL, WQOLI, GAF) 2 quasi-experimental studies, N = 352, reported improved function at 1 year.
Integrated treatment, combining low-dose atypical antipsychotics with family psychoeducation and therapy, assertive community treatment and social skills training vs. standard treatment
1 RCT, N = 341, not blind, raters independent Significant treatment effect favouring OPUS program for both positive and negative symptoms (BPRS, SANS, SAPS, PANSS), social functioning and quality of life (QOL, WQOLI, GAF) at 1 year.
Integrated treatment with low-dose atypical antipsychotics with individual and family therapy, case management and continuity of care (parachute program)

1 quasi-experimental study, N = 297, at 1 year follow up reported significantly reduced relapse and improved social function and quality of life (QOL, WQOLI, GAF), but no difference in symptom severity (BPRS, SAPS, PANSS, SANS).	
Consistency in results	No measures of heterogeneity reported
Precision in results	No confidence intervals reported
Directness of results	Direct
Comparison 2	**Individual cognitive behavioural therapy or supportive counselling + routine care vs. routine care alone.**
Summary of evidence	**Moderate quality evidence (large samples, unable to assess consistency or precision, direct) suggests some benefit of individual therapy over routine care for positive symptoms.**
Positive Symptoms	
Symptom severity (BPRS, PSRS, PANSS, SANS) 5 RCTs, N = 827, up to 24 months follow up 2 of 5 studies reported CBT improved positive symptom severity more than supportive counselling or routine care.	
Relapse rates	
Relapse (Medical records, hospital admissions, and Life Chart Schedule score); 5 RCTs, N = 827, up to 24 months follow up, reported no overall difference in relapse rates.	
Consistency in results	No measures of heterogeneity reported
Precision in results	No confidence intervals reported
Directness of results	Direct
Comparison 3	**Individual cognitive behavioural therapy + EPPIC multi-element care vs. EPPIC services + routine care.**
Summary of evidence	**Moderate to low quality evidence (small to medium-sized sample, unable to assess consistency or precision, direct) suggests there may be a benefit of cognitive behavioural therapy + EPPIC multi-element care over routine care for negative symptoms, social functioning and quality of life.**

Symptom severity	
Symptom severity (BPRS, PSRS, PANSS, SANS) 2 quasi-experimental studies, N = 131, up to 12 months follow up No overall difference reported in positive symptom severity. 1 of 2 studies reported cognitive behavioural therapy improved negative symptoms.	
Relapse rates	
Medical records or hospital readmission 2 quasi-experimental studies, N = 131, up to 12 months follow up No overall difference reported in relapse or hospital readmission rates.	
Social functioning/quality of life	
Measures include Quality of Life Scale, Global Assessment of Functioning Scale score, and Life Chart Schedule; 2 quasi-experimental studies, N = 131, up to 12 months follow up 1 of 2 studies reported CBT improved social function and quality of life.	
Consistency in results	No measure of heterogeneity is reported.
Precision in results	No measures of precision is reported.
Directness of results	Direct
Comparison 4	**LifeSPAN therapy (cognitive behavioural therapy targeted for suicide) + EPPIC care vs. EPPIC care alone.**
Summary of evidence	**Moderate to low quality evidence (small sample, unable to assess consistency or precision, direct) is uncertain of the benefit of LifeSPAN CBT.**
Hopelessness and suicide	
1 RCT, N = 56, 6 months follow up Targeted CBT was better than control for hopelessness, social function and quality of life; both groups improved on suicidal ideation and suicide attempts.	
Consistency in results	No measures of heterogeneity is reported.

Precision in results	No confidence intervals is reported.
Directness of results	Direct
Comparison 5	**Group therapies (weekly during treatment period, including EPPIC multi-element programs and cognitively based therapies) vs. individual therapy (EPPIC or cognitive).**
Summary of evidence	**Moderate to low quality evidence (small to medium-sized sample, unable to assess consistency or precision direct) suggests no benefit of group therapy over individual therapy for negative symptoms, functioning and quality of life, but may improve psychotic symptoms, treatment adherence and treatment satisfaction.**
Symptom severity	
Symptom severity (BPRS, PSRS, PANSS, SANS) 2 quasi-experimental studies, 1 single-group study, N = 177 No overall difference reported in negative symptom severity, though group participants reportedly had more negative symptoms at baseline. Single group study (N = 5) reported some improvement in psychotic symptoms.	
Social functioning/Quality of life	
Quality of life scale, Global Assessment of Functioning Scale, and Life Chart Schedule 2 quasi-experimental studies, 1 single group study, N = 177 No overall difference reported in social function or quality of life scores, though group participants reportedly had better treatment adherence and higher treatment satisfaction.	
Consistency in results	No measure of heterogeneity reported
Precision in results	No confidence intervals reported
Directness of results	Direct
Comparison 6	**Behavioural family therapy (communication and problem-solving skill training, reducing expressed emotion) + individual therapy vs. individual therapy alone.**
Summary of evidence	**Moderate to low quality evidence (small to medium-sized samples, unable to assess consistency or precision, direct) suggests no benefit of behavioural family therapy + individual therapy vs. individual therapy alone for relapse, social function and quality of**

	life.
Relapse rates	
Medical records or hospital readmission 3 RCTs, N = 222, up to 5 year follow up No overall difference reported in relapse or hospital readmission rates.	
Social functioning/Quality of life	
Measures include Quality of Life Scale, Global Assessment of Functioning Scale score, and Life Chart Schedule 1 RCT, N = 73, 5 year follow up No overall difference reported in quality of life or social function scores.	
Consistency in results	No measure of heterogeneity reported
Precision in results	No confidence intervals reported
Directness of results	Direct
Comparison 7	**Family therapy (psychoeducation, stress management, communication training) and routine care vs. individual care.**
Summary of evidence	**Moderate to low quality evidence (small to medium-sized samples, unable to assess consistency or precision, direct) suggests some benefit of family therapy over individual care for improving hospital readmission rate, positive symptom severity and social functioning.**
Relapse rates	
Medical records or hospital readmission 1 RCT, 1 quasi-experimental study, N = 164, up to 5 year follow up Significantly reduced relapse or hospital readmission rates in family therapy group, up to 3.5 fold reduction.	
Positive Symptoms	
Symptom severity (BPRS, PSRS, PANSS, SANS) 1 RCT, 1 quasi-experimental study, N = 164, up to 5 year follow up Significant improvement in positive symptom severity favouring family therapy.	

Social functioning/Quality of life	
Measures include Quality of Life Scale, Global Assessment of Functioning Scale score, and Life Chart Schedule 1 RCT, N = 83, 18 month follow up Significant improvement in social function and quality of life, favouring family therapy.	
Consistency in results	No measure of heterogeneity reported
Precision in results	No confidence intervals reported
Directness of results	Direct

Randall JR, Vokey S, Loewen H, Martens PJ, Brownell M, Katz A, Nickel NC, Burland E, Chateau D

A Systematic Review of the Effect of Early Interventions for Psychosis on the Usage of Inpatient Services

Schizophrenia Bulletin 2015; 41(6): 1379-1386

View review abstract online

Comparison	**Early intervention programs using assertive case management vs. treatment as usual.**
Summary of evidence	**Moderate to high quality evidence (large samples, precise, inconsistent, direct) suggests early intervention programs using assertive case management may reduce the number of hospital bed days compared to treatment as usual.** **Moderate quality evidence (large samples, inconsistent, imprecise, direct) suggests early intervention programs using assertive case management may reduce the number of hospitalisations compared to treatment as usual.**
Bed days and hospitalisations	
A significant, medium-sized effect of fewer bed days in the early intervention group; 11 studies (RCTs and observational), N = 3,292, SMD = -0.38, 95%CI -0.53 to -0.24, $p < 0.00001$, $I^2 = 67\%$, $p = 0.0007$	

A significant, small effect of fewer bed days in the early intervention group from RCTs; 3 RCTs, N = 741, SMD = -0.18, 95%CI -0.33 to -0.03, $p < 0.05$, I^2 not reported *A significant, medium-sized effect of fewer hospitalisations in the early intervention group;* 13 studies (RCT and observational), N = 3,793, OR = 0.33, 95%CI 0.18 to 0.63, $p = 0.0007$, $I^2 = 91\%$, $p < 0.00001$ *A near significant, small effect of fewer hospitalisations in the early intervention group from RCTs;* 3 RCTs, N = 741, OR = 0.73, 95%CI 0.53 to 1.00, $p = 0.05$, I^2 not reported Authors report possible publication bias for the hospitalisation outcome but not the bed-days outcome. Most of the studies were rates as low risk of bias, the remainder were rated as unclear risk of bias, and observational studies frequently found differences in demographic variables, but it was unclear how much these factors bias the outcome.	
Consistency in results	Inconsistent
Precision in results	Precise for bed days, imprecise for hospitalisations.
Directness of results	Direct

Rathbone J, Variend H, Mehta H

Cannabis and schizophrenia

Cochrane Database of Systematic Reviews 2008, Issue 3. Art. No.: CD004837. DOI: 10.1002/14651858.CD004837.pub2

View review abstract online

Comparison	**Cannabis and Psychosis Therapy (CAP), consisting of 3 months of individually delivered CBT orientated programme vs. psychoeducaton (PE).**
Summary of evidence	**Moderate to low quality evidence (small sample, imprecise, direct) is uncertain as to the benefit of CAP for patients in their first episode of psychosis who are using cannabis.**
Substance use **Cannabis and Substance Use Assessment Schedule (CASUS)**	
No significant differences between groups; At 3 months (immediately post treatment): 1 RCT, N = 47, RR = 1.04, 95%CI = 0.62 to 1.74, $p = 0.87$	

By 9 months (6 months after treatment): 1 RCT, N = 47, RR = 1.30, 95%CI = 0.79 to 2.15, *p* = 0.30
Knowledge About Psychosis Questionnaire (KAPQ)
No significant differences between groups; At 3 months: 1 RCT, N = 47, WMD = 0.80, 95%CI = -1.78 to 3.38, *p* = 0.54 By 9 months: 1 RCT, N = 47, WMD = 0.90, 95%CI = -1.42 to 3.22, *p* = 0.45
Brief Psychiatric Rating Scale-E (BPRS-E)
No significant differences between groups; At 3 months: 1 RCT, N = 47, WMD = -3.60, 95%CI = -12.81 to 5.61, *p* = 0.44 By 9 months: 1 RCT, N = 47, WMD = 0.80, 95%CI = -7.47 to 9.07, *p* = 0.85
Social and Occupational Functioning Assessment Scale (SOFAS)
No significant differences between groups; At 3 months: 1 RCT, N = 47, WMD = -0.80, 95%CI = -9.95 to 8.35, *p* = 0.86 By 9 months: 1 RCT, N =47, WMD = -4.70, 95%CI = -14.52 to 5.12, *p* = 0.35

Risks	Not reported
Consistency in results	Not applicable (1 RCT)
Precision in results	Imprecise
Directness of results	Direct

Welch M, Welch T

Early psychosis in rural areas

Australian and New Zealand Journal of Psychiatry 2007; 41(6): 485-494

View review abstract online

Comparison	**Psychosocial intervention programs (including community and group or family therapies, education, case management and routine treatment) for people in rural areas with early psychosis.**

	No control group.
Summary of evidence	**Moderate to low quality evidence (unclear sample size, unable to assess consistency or precision, direct) is uncertain as to the effectiveness of integrated intervention programs for identifying and treating early psychosis in rural areas. Authors report that a lack of primary studies in rural areas.**
Southern Area First Episode (SAFE) Program	
The SAFE program is based in rural NSW and provides primary care, community and education services to people with early psychosis. One report describes the service provision and one study evaluates the program (total N not reported). From 225 potential cases available to mental health services, 43 were deemed appropriate for inclusion in SAFE and around 11 were assessed to be early intervention clients. SAFE was reported to be inconsistently implemented between service sectors, with high fidelity to protocol in the medical aspects of care, but low fidelity in terms of psychoeducation, family therapies and cognitive behavioural interventions. It was reported that outcomes (such as clinical profile, drop-out rate) were better when SAFE was implemented according to protocol. Registration in SAFE was the strongest predictor for best-practice intervention for early psychosis.	
South Fraser Area Health Program	
The South Fraser program is based in British Colombia, Canada and provides primary care from a team of clinicians, and community case management services to people with early psychosis, in a mix of rural and urban settings. One study reported the program received 93 referrals from a total population of 590 000 within the first year of operation.	
Consistency in results	No measure of heterogeneity reported
Precision in results	No confidence intervals reported
Directness of results	Direct

Explanation of acronyms

BPRS = Brief Psychiatric Rating Scale, CBT = cognitive behavioural therapy, CI = Confidence Interval, CSQ-8 = Client Satisfaction Questionnaire, *d* = Cohen's *d* and *g* = Hedges' *g* =

standardised mean differences (see below for interpretation of effect size), EI = enriched intervention, EPPIC = Early Psychosis Prevention and Intervention Centre, FEP = first episode psychosis, GAF = Global Assessment of Function test, KAPQ = Knowledge About Psychosis Questionnaire; MD = mean difference, N = number of participants, NNTB = Number Needed to Treat for Benefit, NS = non-significant, OR = odds ratio, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), PANSS = Positive and Negative Syndrome Scale, PEPP = Prevention and Early Interventions Program for Psychosis, PSRS = Psychotic Symptom Rating Scale, 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), QOL = Quality of Life, *r* = coefficient, RPT = Relapse Prevention Therapy, RR = relative risk, vs. = versus, SAFE = Southern Area First Episode Program, SANS = Scale for the Assessment of Negative Symptoms, SAPS = Scale for the Assessment of Positive Symptoms, SC = standard care, SOFRAS = Social and Occupational Functioning Assessment Scale, vs = versus, WMD = weighted mean difference, WQOLI = Wisconsin Quality of Life Index, χ^2 = Chi-square test for heterogeneity between groups.

Explanation of technical terms

† Different effect measures are reported by different reviews.

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. 0.2 represents a small effect, 0.5 a moderate effect, and 0.8 and over represents a large effect[17].

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

Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They are an 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.

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‡ 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[17];

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

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§ 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

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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[19].

‖ 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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