BEST in Mental Health
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Best Evidence Summaries of Topics in Mental Healthcare

BEST *in* MH *clinical question-answering service*

Question

"What is the most effective intervention for reducing/preventing psychotic symptoms and improving social functioning in people at risk of developing first episode psychosis"

Clarification of question using *PICO* structure

Patients:	*People with 'At Risk Mental States' for developing psychosis*
Intervention:	*Any Intervention*
Comparator:	*Any Intervention*
Outcome:	*Reduction/prevention in psychotic symptoms and improved social functioning*

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Clinical and research implications

There is some very limited evidence, from one generally well conducted systematic review, that cognitive behavioural therapy (CBT), integrated psychotherapy, pharmacotherapy (olanzapine), and dietary supplementation (omega 3 fatty acids) may be associated with reduced rates of transition to psychosis. However, as noted by the review authors, data were sparse and of limited quality; most comparisons were reported by a single study and analyses frequently included only those participants who completed the study.

Further research is needed to adequately assess the effectiveness of interventions for the treatment of people at high risk of psychosis.

What does the evidence say?

Number of included studies/reviews (number of participants)

We identified one systematic review that was relevant to this evidence summary. The review included only randomised controlled trials (RCTs) and assessed the effectiveness of any intervention (psychological, pharmacological, or nutritional) for preventing or delaying transition to psychotic disorders for people at high risk.

Main findings

The review included 11 studies reporting data to for eight comparisons. The summary estimate from five studies comparing CBT to supportive therapy indicated that CBT was associated with a reduction in transitions to psychosis at 6 to 12 months (relative risk (RR) 0.54 (95% CI: 0.34 to 0.86)). Data from one of these studies indicated that the addition of risperidone to CBT did not result in significant additional benefit. One small, placebo controlled trial of olanzapine reported a trend towards reduction in transition to psychosis at 6 to 12 months (RR 0.43 (95% CI: 0.17 to 1.08). Similarly, one small placebo controlled trial of omega 3 fatty acids reported a reduction in transition to psychosis at 6 to 12 months (RR 0.18 (95% CI: 0.04 to 0.75)). Two trials comparing integrated psychotherapy to supportive counselling and standard care both found that integrated psychotherapy was associated with a small reduction in transition to psychosis at 6 to 12 months: RRs 0.19 (95% CI: 0.04 to 0.81) and 0.24 (95% CI: 0.07 to 0.81), respectively.

Authors conclusions

The authors concluded that, although the evidence for benefits for any specific intervention is not conclusive, findings suggest that it may be possible to delay or prevent transition to psychosis in at risk individuals.

Reliability of conclusions/Strength of evidence

This evidence summary is based on the findings of one systematic review. The review was generally well conducted, however, as noted by the review authors, the available evidence was limited and included studies had a number of methodological weaknesses. The review authors' conclusions were appropriately cautious.

What do guidelines say?

The National Institute for Health and Care Excellence guidelines, 'Psychosis and schizophrenia in children and young people' (2013) provides the following comment on the most effective intervention for reducing psychotic symptoms and improving social functioning in people at risk of developing first episode psychosis:

"A number of interventions have been trialled in an attempt to avert the development of psychosis, including drugs, psychological interventions and other interventions. A relatively recent, moderate-sized randomised controlled trial of omega-3 fatty acids has shown the best evidence of any intervention, to date, reducing the rates of transition from 'high risk' states to a sustained psychosis. However, this is a single trial, which is underpowered, undertaken in one centre and lacks any health economic analysis. (p.40)

…After the first episode of psychosis, family intervention as an adjunct to antipsychotic medication substantially and significantly reduces relapse rates. A single small trial combining CBT family treatment with individual CBT without antipsychotic treatment suggested an important reduction in transition rates to the first psychosis." (p. 41)

Date question received: 29/04/2015
Date searches conducted: 19/05/2015
Date answer completed: 02/06/2015

References

Systematic reviews

Stafford, M. R., Jackson, H., Mayo-Wilson, E., Morrison, A. P., & Kendall, T. (2013). Early interventions to prevent psychosis: systematic review and meta-analysis. *The British Medical Journal*, *346*, f185. doi: 10.1136/bmj.f185

Guidelines

The National Institute for Health and Care Excellence (2013). *Psychosis and schizophrenia in children and young people.* Retrieved from http://www.nice.org.uk/guidance/cg155

Results

Systematic reviews

Author (year)	Search date	Inclusion criteria	Number of included studies	Summary of results	Risk of bias
Stafford et al (2013)	05/2015	*Participants*: -In eight studies, participants were selected if they scored over a threshold level on (i) the structured interview for prodromal symptoms, (ii) the positive and negative symptom scale (PANSS), (iii) the brief psychiatric rating scale (BPRS), or (iv) the comprehensive assessment of at risk mental states (CAARMS). -One study included adults meeting the international classification of diseases (ICD-10) for schizotypal disorder. -Two studies selected participants using the early recognition inventory (ERIraos); one study included those in the 'early initial prodromal state', and the other study failed to report the threshold employed. *Intervention and Comparator:* -Four studies compared cognitive behavioural therapy (CBT) to supportive counselling and monitoring. -Two studies compared CBT combined with Risperidone to supportive counselling (one of	11 (N: 1246*)	This systematic review aimed to assess the effectiveness of psychological, pharmacological, or nutritional interventions in preventing or delaying transition to psychotic disorders for people at high risk. Eleven studies reporting eight comparisons were included in the review; sample sizes ranged from 51 to 288. *CBT*: Five studies were included in a meta-analysis of CBT versus supportive counselling. CBT interventions provided manualised, problem focused, time limited treatments including normalisation, cognitive restructuring, and behavioural experiments. Supportive counselling and monitoring comparators were designed to match interventions for non-specific effects of treatment. There was some evidence to suggest that CBT may be	The research objective was clearly stated and appropriate inclusion criteria were defined. A range of bibliographic databases were searched and the search strategy was reported in full. Searches were supplemented by screening of the reference lists of included studies and reviews and by contact with study authors.

		these studies also compared risperidone and CBT to placebo and CBT). -One study each compared (i) olanzapine to placebo, (ii) integrated therapies to supportive counselling, (iii) integrated therapies to standard treatment, (iv) omega-3 fatty acids to placebo, and (v) amisulpride plus a needs based intervention to the needs- based intervention alone. *Outcome*: Transition to psychosis was the primary outcome, measured using: the ICD-10 diagnosis of psychotic disorder (1 study); diagnosis of schizophrenia spectrum disorders (1 study); Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) (1 study); a measure developed by the study authors (1 study); severity of symptoms according to PANNS (2 studies) and CAARMS (3 studies); and presence of positive psychotic symptoms (1 study). One study measured transition to sub-threshold psychosis. Outcome measures were grouped as: within six months of randomisation; between six and 12 months after randomisation; greater than 12 months after randomisation. *Study design*: Randomised controlled trials.		associated with a reduction in the rate of transition to psychosis at 6 to 12 months (relative risk (RR) 0.54 (95% CI: 0.34 to 0.86)) and at >12 months (RR 0.63 (95% CI: 0.40 to 0.99)). However, these analyses included only participants who completed the studies and it was unclear whether dropouts were evenly distributed between study arms. In sensitivity analyses, assuming that all dropouts had transitioned, only the effect at 12 months remained statistically significant. *CBT combined with pharmacotherapy*: There was some very limited evidence, from two RCTs, that CBT combined with risperidone may be associated with a reduction in the rate of transition to psychosis at six months compared to supportive counselling (RR 0.35 (95% CI: 0.13 to 0.95)). However, this analysis included only 130 participants and 17 events and the treatment effect did not remain statistically significant at 12 months and beyond. *Pharmacotherapy and food supplements*: Data from one study, comparing CBT plus risperidone to CBT plus placebo, indicated that the risperidone did not provide additional benefit. One small, placebo	The number of reviewers involved in study selection and data extraction was not reported and, therefore, the potential for error/bias in the review process cannot be assessed. The methodological quality of the included studies was independently assessed by two reviewers, using the Cochrane risk of bias tool for RCTs. Analysis methods were appropriate.

				controlled trial of olanzapine reported a trend towards reduction in transition to psychosis at 6 to 12 months (RR 0.43 (95% CI: 0.17 to 1.08). Similarly, one small placebo controlled trial of omega 3 fatty acids reported a reduction in transition to psychosis at 6 to 12 months (RR 0.18 (95% CI: 0.04 to 0.75)). *Integrated psychotherapy*: Two trials assessed the effectiveness of integrated psychotherapy compared to supportive counselling and to standard care. Integrated psychological therapies included CBT for individual patients, group skills training, cognitive remediation, and family treatments, with concomitant antipsychotic treatment in the second study. Both studies found that integrated psychotherapy was associated with a small reduction in transition to psychosis at 6 to 12 months: RRs 0.19 (95% CI: 0.04 to 0.81) and 0.24 (95% CI: 0.07 to 0.81), respectively. These effects were similar at >12 months. The main risk of bias in included studies was related to incomplete outcome data, reflecting high drop-out rates. Most studies were also rated as high risk of bias for	

				blinding of participants and study personnel, as blinding is not possible for psychological interventions.	

**N: Total no. of participants*

Risk of bias

Systematic reviews

Author (year)	RISK OF BIAS				
	Inclusion criteria	Searches	Review process	Quality assessment	Synthesis
Stafford 2013	☺	☺	?	☺	☺

☺ Low risk ☹ High risk ? Unclear risk

Search details

Source	Search Strategy	Number of hits	Relevant evidence identified
Guidelines			
NICE	at risk psychosis intervention	51	1
Systematic Reviews			
DARE	1 MeSH DESCRIPTOR Prodromal Symptoms EXPLODE ALL TREES 2 Delete 2 (At Risk Mental State) IN DARE 0 Delete 3 (At-Risk Mental State) IN DARE 0 Delete 4 (ARMS) IN DARE 1288 Delete 5 MeSH DESCRIPTOR Psychotic Disorders EXPLODE ALL TREES 158 Delete 6 #1 AND #5 0 Delete 7 #4 AND #5 3 Delete 8 (sub-threshold psychosis) IN DARE 0 Delete 9 (sub-threshold psychotic) IN DARE 0 Delete 10 (risk adj5 (psychosis OR psychotic)) IN DARE 12 Delete 11 (risk) IN DARE 14370 Delete 12 (first episode psychosis) IN DARE 14 Delete 13 #11 AND #12 6 Delete 14 #7 OR #10 OR #13 19 Delete	19	1
Primary Studies			
MEDLINE	14. Medline; BORDERLINE STATES/; 0 results. 15. Medline; AT RISK POPULATIONS/; 0 results. 16. Medline; "at risk mental state*".ti,ab; 248 results. 17. Medline; "at risk of psychosis".ti,ab; 52 results. 18. Medline; "first episode psychosis".ti,ab; 1591 results. 19. Medline; "psychotic symptoms".ti,ab; 5862 results.	99	0

	20. Medline; 14 OR 15 OR 16 OR 17 OR 18 OR 19; 7475 results. 21. Medline; "improved outcome".ti,ab; 3562 results. 22. Medline; EARLY INTERVENTION/; 0 results. 23. Medline; "social function*".ti,ab; 9536 results. 24. Medline; "reduc* symptoms".ti,ab; 2461 results. 25. Medline; 21 OR 22 OR 23 OR 24; 15540 results. 26. Medline; 20 AND 25; 227 results. 27. Medline; EARLY MEDICAL INTERVENTION/; 995 results. 28. Medline; 21 OR 23 OR 24 OR 27; 16521 results. 29. Medline; 20 AND 28; 279 results. 30. Medline; randomized.ab; 312928 results. 31. Medline; placebo.ab; 158896 results. 32. Medline; randomly.ab; 226647 results. 33. Medline; trial.ab; 315356 results. 34. Medline; groups.ab; 1422459 results. 35. Medline; "randomized controlled trial".pt; 386979 results. 36. Medline; "controlled clinical trial".pt; 88776 results. 37. Medline; 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36; 2064830 results. 38. Medline; 29 AND 37; 99 results.		
EMBASE	14. EMBASE; BORDERLINE STATES/; 0 results. 15. EMBASE; AT RISK POPULATIONS/; 0 results. 16. EMBASE; "at risk mental state*".ti,ab; 655 results. 17. EMBASE; "at risk of psychosis".ti,ab; 389 results. 18. EMBASE; "first episode psychosis".ti,ab; 3071 results. 19. EMBASE; "psychotic symptoms".ti,ab; 9246 results. 20. EMBASE; 14 OR 15 OR 16 OR 17 OR 18 OR 19; 12597 results. 21. EMBASE; "improved outcome".ti,ab; 5320 results. 22. EMBASE; EARLY INTERVENTION/; 12879 results. 23. EMBASE; "social function*".ti,ab; 14139 results. 24. EMBASE; "reduc* symptoms".ti,ab; 3373 results. 25. EMBASE; 21 OR 22 OR 23 OR 24; 35523 results.	194	0

	26. EMBASE; 20 AND 25; 1000 results. 27. EMBASE; BORDERLINE STATE/; 9525 results. 28. EMBASE; 16 OR 17 OR 18 OR 19 OR 27; 22019 results. 29. EMBASE; 25 AND 28; 1120 results. 30. EMBASE; random*.ti,ab; 966347 results. 31. EMBASE; factorial*.ti,ab; 24845 results. 32. EMBASE; (crossover* OR cross-over*).ti,ab; 73475 results. 33. EMBASE; placebo*.ti,ab; 213162 results. 34. EMBASE; (doubl* ADJ blind).ti,ab; 140522 results. 35. EMBASE; (singl* ADJ blind*).ti,ab; 15677 results. 36. EMBASE; assign*.ti,ab; 258218 results. 37. EMBASE; allocat*.ti,ab; 91894 results. 38. EMBASE; volunteer*.ti,ab; 186722 results. 39. EMBASE; CROSSOVER PROCEDURE/; 42723 results. 40. EMBASE; DOUBLE BLIND PROCEDURE/; 120104 results. 41. EMBASE; RANDOMIZED CONTROLLED TRIAL/; 369924 results. 42. EMBASE; SINGLE BLIND PROCEDURE/; 20148 results. 43. EMBASE; 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42; 1525783 results. 44. EMBASE; 29 AND 43; 194 results		
PsycINFO	1. PsycInfo; BORDERLINE STATES/; 4071 results. 2. PsycInfo; AT RISK POPULATIONS/; 31742 results. 3. PsycInfo; "at risk mental state*".ti,ab; 275 results. 4. PsycInfo; "at risk of psychosis".ti,ab; 61 results. 5. PsycInfo; "first episode psychosis".ti,ab; 1688 results. 6. PsycInfo; "psychotic symptoms".ti,ab; 6744 results. 7. PsycInfo; 1 OR 2 OR 3 OR 4 OR 5 OR 6; 43757 results. 8. PsycInfo; "improved outcome".ti,ab; 229 results. 9. PsycInfo; EARLY INTERVENTION/; 9149 results. 10. PsycInfo; "social function*".ti,ab; 8923 results. 11. PsycInfo; "reduc* symptoms".ti,ab; 1000 results. 12. PsycInfo; 8 OR 9 OR 10 OR 11; 19208 results.	388	0

	13. PsycInfo; 7 AND 12; 1648 results. 14. PsycInfo; random*.ti,ab; 141417 results. 15. PsycInfo; (doubl* ADJ blind*).ti,ab; 19294 results. 16. PsycInfo; (singl* ADJ blind*).ti,ab; 1686 results. 17. PsycInfo; groups.ti,ab; 386602 results. 18. PsycInfo; exp EXPERIMENTAL DESIGN/; 9762 results. 19. PsycInfo; controlled.ti,ab; 87531 results. 20. PsycInfo; (clinical adj3 study).ti,ab; 11777 results. 21. PsycInfo; trial.ti,ab; 74520 results. 22. PsycInfo; "randomized controlled trial".ti,ab; 9633 results. 23. PsycInfo; 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22; 597017 results. 24. PsycInfo; 13 AND 23; 388 results.		
CENTRAL	ID Search Hits #1 MeSH descriptor: [Prodromal Symptoms] explode all trees 7 #2 "prodrom*" 385 #3 "at risk mental state" 20 #4 "first episode psychosis" 284 #5 "bordeline state*" 0 #6 "psychotic symptoms" 884 #7 #1 or #2 or #3 or #4 or #5 or #6 1446 #8 MeSH descriptor: [Early Medical Intervention] explode all trees 95 #9 "early intervention*" 2024 #10 "improv* outcome" 1689 #11 "social function*" 2234 #12 "reduc* symptoms" 1180 #13 #8 or #9 or #10 or #11 or #12 6972 #14 #7 and #13 357 Central only 151	151	0

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