APPENDIX 13A: CLINICAL EVIDENCE STUDY CHARACTERISTICS TABLES:

AT RISK MENTAL STATES FOR PSYCHOSIS AND SCHIZOPHRENIA IN CHILDREN AND YOUNG PEOPLE: RECOGNITION AND MANAGEMENT

Abbreviations

BPRS	Brief Psychiatric Rating Scale
CAARMS	Comprehensive Assessment of At Risk Mental States
CBT	cognitive behavioural therapy
COPS	Criteria of Prodromal Syndromes
DSM-IV	*Diagnostic and Statistical Manual of Mental Disorders* – 4th edition
EDIE	Early Detection and Intervention Evaluation trial
EPPIC	Early Psychosis Prevention and Intervention Centre, Australia
GAF	Global Assessment of Functioning
GP	general practitioner
HAM-D	Hamilton Depression Rating Scale
ITT	intention to treat
MADRS	Montgomery-Åsberg Depression Rating Scale
MANSA	Manchester Short Assessment of Quality of Life
N	number of participants
N/A	
PACE	Personal Assessment and Crisis Evaluation Clinic, Australia
PANSS	Positive and Negative Syndrome Scale
PRIME	Prevention through Risk Identification Management and Education
QLS	Quality of Life Scale
RCT	randomised controlled trial
SANS	Scale for the Assessment of Negative Symptoms
SAS	Simpson-Angus Extrapyramidal Side Effects Scale
SIAS	Social Interaction Anxiety Scale
SOPS	Scale of Prodromal Symptoms
YMRS	Young Mania Rating Scale

Included studies

Study ID	ADDINGTON2011
Bibliographic reference	Addington, J., Epstein, I., Liu, L., *et al.* (2011) A randomized controlled trial of cognitive behavioural therapy for individuals at clinical high risk of psychosis. *Schizophrenia Research*, *125*, 54-61.
General information	Funding source: Ontario Mental Health Research Foundation. Published or unpublished data: Published.
Method	Type of study: Individual randomised trial. Type of analysis: Not reported. Blindness: Only raters blind. Duration: Number of weeks of treatment – 26 weeks; length of follow-up – 78 weeks. Raters: Independent of treatment. Design: Single-site (Toronto, Canada) randomised controlled trial (RCT). Number of people screened, excluded and reasons: 562 individuals referred, 302 assessed suitable after phone screen, 112 met Criteria of Prodromal Syndromes (COPS) criteria, 37 refused any study, 19 refused but consented to a non-treatment study, 56 consented, 51 participants were then randomised. Notes about study methods: Recruitment of participants was sought from a variety of sources including family physicians, student counsellors, and community mental health teams and practitioners. Recruitment and ascertainment methods included advertisement on radio, public transport and local newspaper.
Participants	Diagnosis: At risk mental state. Diagnostic tool: COPS. Inclusion criteria: • aged 14 and 30 • meet the COPS. Exclusion criteria: • met criteria for any current or lifetime axis I psychotic disorder • prior history of treatment with an antipsychotic • IQ <70 • past or current history of a clinically significant central nervous system disorder that may confound or contribute to prodromal symptoms. Total sample size: Number randomised = 51 Gender: 71% male

	Age: Mean 20.9 years (range not reported). Ethnicity: 57% white Setting: Specialist centre - Prevention through Risk Identification Management and Education (PRIME) Clinic.
Interventions	Intervention: group 1: cognitive behavioural therapy (CBT) - up to 20 sessions within 26 weeks, N = 27; group 2: supportive counselling - up to 20 sessions within 26 weeks, N = 24.
Extractable outcomes	Transition to psychosis (*Diagnostic and Statistical Manual of Mental Disorders* – 4th edition [DSM-IV]): Number of participants. Mental state: Scale of Prodromal Symptoms (SOPS), Calgary Depression Scale for Schizophrenia. Functioning: Global Assessment of Functioning (GAF), Simpson-Angus Extrapyramidal Side Effects Scale (SAS), Social Interaction Anxiety Scale (SIAS). Leaving the study early: Leaving due to any reason.
Quality	Sequence generation: Low risk. Allocation concealment: Unclear risk. Participants blinded: High risk. Providers blinded: High risk. Outcome assessors blinded: Low risk. Missing outcome data: High risk. Selective outcome reporting: Unclear risk. Other bias: High risk.
Related publications	None.

Study ID	**AMMINGER2010**
Bibliographic reference	Amminger, G. P., Schäfer, M. R., Papageorgiou, K., *et al.* (2010) Long-chain omega-3 fatty acids for indicated prevention of psychotic disorders: a randomized, placebo-controlled trial. *Archives of General Psychiatry*, *67*, 146–154.
General information	Funding source: Stanley Medical Research Institute. Published or unpublished data: Published.
Method	Type of study: Individual randomised trial. Type of analysis: Intention to treat (ITT). Blindness: Participants, providers and outcome assessors were blind. Duration: Number of weeks of treatment – 12 weeks; length of follow-up – 52 weeks. Raters: Independent of treatment. Design: Single-site (Vienna, Austria) RCT. Number of people screened, excluded and reasons: 256 individuals assessed for eligibility, 175 excluded (150 did not meet

	inclusion criteria or met exclusion criteria and 25 refused to participate), 81 participants were randomised. Notes about study methods: No additional information provided by AMMINGER2010,
Participants	Diagnosis: At risk mental state. Diagnostic tool: Positive and Negative Syndrome Scale (PANSS). Inclusion criteria: • aged 13 to 25 years • meeting criteria for one or more of three operationally defined and well-validated groups of risk factors for psychosis. Exclusion criteria: • a history of a previous psychotic disorder or manic episode (both treated or untreated) • substance-induced psychotic disorder • acute suicidal or aggressive behaviour • a current DSM-IV diagnosis of substance dependence (except cannabis dependence) • neurological disorders (for example, epilepsy) • IQ <70 • structural brain changes apparent on magnetic resonance imaging, except for enlargement of the ventricles or sulci or other minor abnormalities without pathological relevance (for example, white matter lucencies or temporal horn asymmetry) • previous treatment with an antipsychotic or mood-stabilising agent (>1week) • having taken omega-3 supplements within 8 weeks of being included in the trial • laboratory values more than 10% outside the normal range for transaminases, thyroid hormones, C-reactive protein, or bleeding parameters. • another severe intercurrent illness that may have put the person at risk or influenced the results of the trial or affected their ability to take part in the trial. Total sample size: Number randomised = 81. Gender: 33% male. Age: Mean 16 years (range not reported). Ethnicity: Not reported. Setting: Specialist clinic – Psychosis Detection Unit of the Department of Child and Adolescent Psychiatry, Medical University of Vienna.
Interventions	Intervention: group 1: long-chain omega-3 fatty acids (fish oil), 1,200 mg per day for 12 weeks, N = 41; group 2: placebo (coconut oil), N = 40. Notes about the interventions: Placebo capsules were carefully matched in appearance and flavour with the active treatment; they

	also contained the same amount of vitamin E as the omega-3 capsules and 1% fish oil to mimic taste.
Extractable outcomes	Transition to psychosis (DSM-IV): Number of participants. Mental state: PANSS, Scale for the Assessment of Negative Symptoms (SANS), SAPS, Montgomery-Åsberg Depression Rating Scale (MADRS). Psychosocial functioning: GAF. Leaving the study early: Leaving due to any reason.
Quality	Sequence generation: Low risk. Allocation concealment: Low risk. Participants blinded: Low risk. Providers blinded: Low risk. Outcome assessors blinded: Low risk. Missing outcome data: High risk. Selective outcome reporting: High risk. Other bias: High risk.
Related publications	Marshall, M. & Rathbone, J. (2011) Early intervention for psychosis. *Cochrane Database of Systematic Reviews, Issue 6,* Art. No.: CD004718.

Study ID	**BECHDOLF2012**
Bibliographic reference	Bechdolf, A., Wagner, M., Ruhrmann, S., *et al.* (2012) Preventing progression to first-episode psychosis in early initial prodromal states. *British Journal of Psychiatry*, *200*, 22–29.
General information	Funding source: German Federal Ministry for Education and Research (Bundesministerium für Bildung und Forschung). Published or unpublished data: Published.
Method	Type of study: Individual randomised trial. Type of analysis: ITT. Blindness: Participants, providers and raters were not blind – 'Although ratings were mainly carried out by people, who were not involved in treatment, raters could have been aware of the treatment allocation, which raises the possibility that rating bias could have influenced the results.' Duration: Number of weeks of treatment – 52 weeks; length of follow-up – 104 weeks. Raters: Independent of treatment. Design: Multisite (at four early detection and intervention centres located at the Departments of Psychiatry and Psychotherapy at the Universities of Cologne, Bonn, Düsseldorf and Munich, Germany) RCT. Number of people screened, excluded and reasons: 1,597 individuals assessed, 232 met early initial prodromal state inclusion

	criteria, and 168 were eligible for randomisation. 128 participants were randomised (22 refused research participation, 15 refused treatment, two were lost during assessment and one developed psychosis). Notes about study methods: No additional information provided byBECHDOLF2012.
Participants	Diagnosis: At risk mental state. Diagnostic tool: Early Recognition Inventory Inclusion criteria: • self-experienced cognitive thought and perception deficits • one or more of the following basic symptoms in the last 3 months several times a week: - thought interferences - thought perseveration - thought pressure - thought blockages - disturbances of receptive language, either heard or read - decreased ability to discriminate between ideas and perception, fantasy and true memories - unstable ideas of reference (subject-centrism) - derealisation - visual perception disturbances (blurred vision, transitory blindness, partial sight, hypersensitivity to light, and so on) - acoustic perception disturbances (hypersensitivity to sounds or noise, acoasms, and so on) - and/or • reduction in the GAF score (DSM-IV) of at least 30 points (within the past year) and at least one of the following risk factors: - first-degree relative with a lifetime-diagnosis of schizophrenia or a schizophrenia spectrum disorder - pre- or perinatal complications. Exclusion criteria: • attenuated or brief limited intermittent psychotic symptoms • present or past diagnosis of a schizophrenic, schizophreniform, schizoaffective, delusional or bipolar disorder according to DSM-IV • present or past diagnosis of a brief psychotic disorder according to DSM-IV with a duration of more than 1 week or within the last 4 weeks regardless of its duration • diagnosis of delirium, dementia, amnestic or other cognitive disorder, mental retardation, psychiatric disorders due to a somatic factor or related to the consumption of psychotropic substances according to DSM-IV • alcohol or drug dependence within the last 3 months prior to inclusion according to DSM-IV

	• organic brain disease (inflammatory, traumatic, epilepsy, and so on) • previous treatment with antipsychotics • acute suicidality • aged below 17 years and above 35 years. Total sample size: Number randomised = 128. Gender: 66% male. Age: Mean 25.8 years (range not reported). Ethnicity: Not reported. Setting: Specialist early detection and intervention centres (specialised outpatient departments designed to provide a low-threshold, non-stigmatising environment).
Interventions	Intervention: group 1: integrated psychological therapies, delivered weekly or bi-weekly for 52 weeks, N = 63; group 2: supportive counselling, a maximum of 30 session over 52 weeks, N = 65. Notes about the interventions: Integrated psychological therapies: 25 individual CBT sessions; 15 group therapy sessions; 12 cognitive remediation therapy sessions; three sessions of information and counselling of relatives. Supportive counselling: Designed to provide a minimal level of support for individuals who were seeking help and were clearly in need of support as a result of psychiatric symptoms or concerns relating to functional domains. Basic assessment, basic psychoeducation about the at risk mental state and counselling in a supportive, warm, genuine, empathic and unstructured style were delivered.
Extractable outcomes	Transition to psychosis (PANSS, DSM-IV): Number of participants. Leaving the study early: Leaving due to any reason.
Quality	Sequence generation: Low risk. Allocation concealment: Low risk. Participants blinded: High risk. Providers blinded: High risk. Outcome assessors blinded: Low risk. Missing outcome data: High risk. Selective outcome reporting: High risk. Other bias: High risk.
Related publications	Bechdolf, A., Wagner, M., Veith, V., *et al.* (2007) Randomized controlled multicentre trial of cognitive behaviour therapy in the early initial prodromal state: effects on social adjustment post treatment. *Early Intervention in Psychiatry*, *1*, 71–78.

Study ID	MCGLASHAN2003
Bibliographic reference	McGlashan, T. H., Zipursky, R. B., Perkins, D., *et al.* (2003) The PRIME North America randomized double-blind clinical trial of olanzapine versus placebo in patients at risk of being prodromally symptomatic for psychosis: I. Study rationale and design. *Schizophrenia Research, 61*, 7-18.
General information	Funding source: Eli Lilly. Published or unpublished data: Published.
Method	Type of study: Individual randomised trial. Type of analysis: Last observation carried forward. Blindness: Participants, providers and outcome assessors blind. Duration: Number of weeks of treatment – 52 weeks; length of follow-up – 104 weeks. Raters: Independent of treatment. Design: Multisite (Yale University, New Haven, US; University of Toronto, Canada; University of North Carolina, Chapel Hill, US; and University of Calgary, Canada) RCT. Number of people screened, excluded and reasons: 71 consented, 11 were excluded (six did not meet inclusion criteria, one was not prodromal, four met psychosis criteria, and one had an IQ <80, four withdrew consent, one did not return) and 60 were randomised. Notes about study methods: No additional information provided by MCGLASHAN2003.
Participants	Diagnosis: At risk mental state. Diagnostic tool: COPS. Inclusion criteria: • treatment-seeking outpatients • 12 to 45 years old • meeting a definition of prodromal syndrome. Exclusion criteria: • meeting criteria for past or current DSM-IV psychotic disorder • judged clinically to have a treatable psychiatric disorder (for example, mania, depression, attention deficit hyperactivity disorder) that could account for the inclusion symptoms • judged clinically to be too suicidal or homicidal to risk randomisation to placebo • presenting with inclusion symptoms occurring primarily as sequelae to drug or alcohol use • IQ <80 • took non-protocol psychotropic medication within 1 week of randomisation. Total sample size: Number randomised = 60.

	Gender: 65% male. Age: Mean: 17.8 years (range 12 to 36). Ethnicity: 67% white. Setting: A specialist outpatient clinic for prodromal patients called the PRIME Clinic.
Interventions	Intervention: Group 1: olanzapine 8 mg/day for 52 weeks, N = 31; group 2: placebo for 52 weeks, N = 29. Notes about the interventions: individual and family psychosocial interventions with supportive and psycho educational components were available to each participant.
Extractable outcomes	Transition to psychosis (presence of psychosis scale): Number of people. Mental state: SOPS, PANSS, Young Mania Rating Scale (YMRS), MADRS. Global state: Clinical Global Impression – Severity. Psychosocial functioning: GAF. Side effects: Blood pressure, pulse, weight, SAS, Abnormal Involuntary Movement Scale, Barnes Akathisia Rating Scale Leaving the study early: Leaving due to any reason.
Quality	Sequence generation: Unclear risk. Allocation concealment: Unclear risk. Participants blinded: Low risk. Providers blinded: Low risk. Outcome assessors blinded: Low risk. Missing outcome data: High risk. Selective outcome reporting: Unclear risk. Other bias: Low risk.
Related publications	McGlashan, T. H., Zipursky, R. B., Perkins, D., *et al.* (2006) Randomized, double-blind trial of olanzapine versus placebo in patients prodromally symptomatic for psychosis. *The American Journal of Psychiatry*, *163*, 790-799. Woods, S. W., Breier, A., Zipursky, R. B., *et al.* (2003) Randomized trial of olanzapine versus placebo in the symptomatic acute treatment of the schizophrenic prodrome. *Biological Psychiatry*, *54*, 453-464.

Study ID	MCGORRY2002
Bibliographic reference	McGorry, P. D., Yung, A. R., Phillips, L. J. *et al.* (2002) Randomized controlled trial of interventions designed to reduce the risk of progression to first-episode psychosis in a clinical sample with subthreshold symptoms. *Archives of General Psychiatry*, *59*, 921–928.
General information	Funding source: The Commonwealth Government of Australia Research and Development Grants Advisory Committee and Janssen- Cilag Pharmaceuticals. Funding for the follow-up component was provided by an Australian Rotary Health Research Fund. Published or unpublished data: Published
Method	Type of study: Individual randomised trial. Type of analysis: ITT. Blindness: 'Designed as a single-blind RCT with research interviewers intended to be blind to the interventions received. However, this was difficult to achieve because the two intervention groups were treated by different clinicians, a feature that was difficult to conceal from raters.' Duration: Number of weeks of treatment – 26 weeks; length of follow-up – 156 to 208 weeks. Raters: Independent of treatment. Design: Single-site (Melbourne, Australia) RCT. Number of people screened, excluded and reasons: 522 individuals were referred to the Personal Assessment and Crisis Evaluation (PACE) clinic, 135 met study criteria, 43 refused research participation, 92 agreed to participation, 59 participants were randomised. Notes about study methods: No additional information provided by MCGORRY2002.
Participants	Diagnosis: At risk mental state. Diagnostic tool: Not reported. Inclusion criteria: • aged 14 to 30 years • lived in the Melbourne metropolitan area • met criteria for one or more of three operationally defined ultra-high risk groups. Exclusion criteria: • a previous psychotic or manic episode • previous treatment with an antipsychotic or mood stabilising agent • a substance-induced psychotic disorder • IQ <70 • an inadequate command of the English language.

	Total sample size: Number randomised = 59. Gender: 58% male. Age: Mean 20 (range 14 to 28) years. Ethnicity: Not reported. Setting: Specialist clinic – PACE Clinic, an extension of the Early Psychosis Prevention and Intervention Centre (EPPIC).
Interventions	Intervention: group 1: specific preventative intervention – risperidone 1.3 mg/day + cognitive behavioural therapy (CBT) for 26 weeks, N = 31; group 2: needs based intervention for 26 weeks, N = 28. Notes about the interventions: N/A Specific preventative intervention: Involved all elements of NBI and two additional treatment components – risperidone and CBT. CBT was conducted according to a manual. The overall aims were to develop an understanding of the symptoms experienced, to learn strategies to enhance control of these symptoms and to reduce associated distress. Modules on the following were offered flexibly: stress management, depression/negative symptoms, positive symptoms and other comorbidities (including substance misuse, obsessive-compulsive features and social anxiety). Needs based intervention: Focused on the presenting symptoms and problems already manifest. Participants assigned to this group received needs-based supportive psychotherapy primarily focusing on pertinent issues such as social relationships and vocational and family issues. Therapists also performed a case management role, providing assistance with accommodation, education or employment, and family education and support. Although people in this group did not receive antipsychotic medication, they could receive antidepressants (sertraline hydrochloride) if moderate to severe depression was present or benzodiazepines for insomnia (usually temazepam).
Extractable outcomes	Transition to psychosis: Number of people. Mental state: Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Rating Scale (HAM-S), Brief Psychiatric Rating Scale (BPRS), SANS, YMRS. Psychosocial functioning: GAF. Quality of life: Quality of Life Scale (QLS). Leaving the study early: Leaving due to any reason.
Quality	Sequence generation: Unclear risk. Allocation concealment: Unclear risk. Participants blinded: High risk. Providers blinded: High risk. Outcome assessors blinded: High risk. Missing outcome data: High risk. Selective outcome reporting: Unclear risk. Other bias: High risk.

Related publications	Phillips, L. J., McGorry, P. D., Yuen, H. P., *et al.* (2007) Medium term follow-up of a randomized controlled trial of interventions for young people at ultra high risk of psychosis. *Schizophrenia Research*, 96, 25–33.

Study ID	**MORRISON2004**
Bibliographic reference	Morrison, A. P., French, P., Walford, L., *et al.* (2004) Cognitive therapy for the prevention of psychosis in people at ultra-high risk: randomised controlled trial. *The British Journal of Psychiatry*, *185*, 291–297.
General information	Funding source: North West NHS Research and Development Executive and the Stanley Foundation. Published or unpublished data: Published.
Method	Type of study: Individual randomised trial. Type of analysis: ITT. Blindness: The Early Detection and Intervention Evaluation (EDIE) trial was designed as a pragmatic, single-masked (rater) RCT. Assessors were intended to be masked to the condition to which the patient was allocated; however, this proved difficult in practice because the participants often divulged information about their therapist or used language that suggested they were receiving cognitive therapy. Duration: Number of weeks of treatment – 26 weeks; length of follow-up – 156 weeks. Raters: Independent of treatment. Design: Single-site (Manchester, UK) RCT. Number of people screened, excluded and reasons: 134 individuals referred for assessment, 14 did not attend and 14 refused participation, therefore 106 were assessed for eligibility. 46 individuals were excluded (27 did not meet inclusion criteria, three refused participation, 12 had an untreated first episode of psychosis and four were receiving antipsychotic medication) and 60 participants were randomised. Notes about study methods: No additional information provided by MORRISON2004.
Participants	Diagnosis: At risk mental state. Diagnostic tool: PANSS, GAF. Inclusion criteria: • brief limited intermittent psychotic symptoms or attenuated (subclinical) psychotic symptoms Or • trait plus state risk factors - operationally defined by the presence of an at risk mental state – defined for the purposes of this study as scoring for caseness on the General Health Questionnaire and/or a recent deterioration in function of 30 points or more on the GAF – plus either a family history, indicated by a first-degree relative with a history of any psychotic disorder, or a diagnosis of schizotypal personality disorder in the participant. • aged 16 to 36 years old.

	Exclusion criteria: • current or past receipt of antipsychotic medication. Total sample size: Number randomised = 60. Gender: 67% male. Age: Mean 22 (range 16 to 36) years. Ethnicity: Not reported. Setting: Recruitment of participants was sought from a variety of sources, including primary care teams (general practitioners [GPs], practice nurses, and psychological therapists), student counselling services, accident and emergency departments, specialist services (for example, community drug and alcohol teams, child and adolescent psychiatry and adult psychiatry services) and voluntary sector agencies (such as carers' organisations).
Interventions	Intervention: group 1: cognitive therapy + monitoring, a maximum of 26 sessions over 26 weeks, N = 37; group 2: monitoring, N = 23. Notes about the interventions: Cognitive therapy + monitoring: Followed the principles developed by A. Beck (*Cognitive Therapy and the Emotional Disorders*. International Universities Press: New York, 1976). It was problem-oriented, time-limited and educational; it encouraged collaborative empiricism, used guided discovery and homework tasks, and was based on a written manual. It was based on the cognitive model most appropriate to the disorder that was prioritised on a problem list agreed between the therapist and the participant. Monitoring: Both monitoring and therapy conditions incorporated elements of case management in order to resolve crises regarding social issues and mental health risks.
Extractable outcomes	Transition to psychosis (PANSS, DSM-IV): Number of participants. Leaving the study early: Leaving due to any reason.
Quality	Sequence generation: Low risk. Allocation concealment: Low risk. Participants blinded: High risk. Providers blinded: High risk. Outcome assessors blinded: Low risk. Missing outcome data: High risk. Selective outcome reporting: Low risk. Other bias: High risk.
Related publications	Morrison, A. P., Bentall, R. P., French, P., *et al.* (2002) Randomised controlled trial of early detection and cognitive therapy for preventing transition to psychosis in high-risk individuals. Study design and interim analysis of transition rate and psychological risk factors. *The British Journal of Psychiatry*, 181, s78-s84.

	Morrison, A. P., French, P., Parker, S., *et al.* (2007) Three-year follow-up of a randomized controlled trial of cognitive therapy for the prevention of psychosis in people at ultrahigh risk. *Schizophrenia Bulletin*, 33, 682-687.

Study ID	**MORRISON2011**
Bibliographic reference	Morrison, A. P., Stewart, S. L., French, P., *et al.* (2011) Early detection and intervention evaluation for people at high-risk of psychosis-2 (EDIE-2): trial rationale, design and baseline characteristics. *Early Intervention in Psychiatry*, *5*, 24-32.
General information	Funding source: Medical Research Council and the Department of Health. Published or unpublished data: Published.
Method	Type of study: Individual randomised trial. Type of analysis: ITT. Blindness: Only raters blind. Duration: Number of weeks of treatment – 26 weeks; length of follow-up – 104 weeks. Raters: Independent of treatment. Design: Multisite (Manchester, Birmingham/ Worcestershire, Glasgow, Cambridgeshire and Norfolk, UK) RCT. Number of people screened, excluded and reasons: 634 individuals assessed for eligibility and 346 excluded (321 due to not meeting entry criteria, 36 due to antipsychotic medication, 91 due to current psychosis at initial baseline, 29 due to current psychosis at second baseline, 110 due to being subthreshold for an at risk mental state, 45 due to not being help-seeking, 10 due to other reasons, 16 lost contact before assessment was complete and nine declined involvement before assessment was complete). 288 participants were randomised. Notes about study methods: No additional information provided by MORRISON2011.
Participants	Diagnosis: At risk mental state. Diagnostic tool: Comprehensive Assessment of At Risk Mental States (CAARMS) Inclusion criteria: • brief limited intermittent psychotic symptoms, attenuated symptoms or state-plus-trait factors • aged between 14 and 35 years, and seeking help for symptoms. Exclusion criteria: • current or previous receipt of antipsychotic medication • moderate to severe learning disability • organic impairment • insufficient fluency in English. Total sample size: Number randomised = 288. Gender: 63% male.

	Age: Mean 20.7 (range 14 to 34) years. Ethnicity: 88% white. Setting: Variable as conducted over multiple sites.
Interventions	Intervention – group 1: cognitive therapy + monitoring, sessions were offered on a weekly basis for up to a maximum of 26 weeks, plus up to four booster sessions in the subsequent 6 months, N = 144; group 2: monitoring, for 26 weeks, N = 144. Notes about the interventions: Both conditions were in addition to treatment as usual, which will have been highly variable and dependent on local service configurations and specific source of referral to the trial; therefore, randomisation was stratified by site in an attempt to control for this variation. Cognitive therapy + monitoring: Cognitive therapy requires an individualised, problem-orientated approach and incorporates a process of assessment and formulation, which is manualised. The specific interventions depend on individual goals and formulations, but the range of permissible interventions is described in the manual. Key ingredients of the approach are the development of a problem and goal list, early formulation (both longitudinal and maintenance), a focus upon normalising psychotic-like experiences, and an active therapy stance utilising behavioural experiments and evaluation of appraisals. Monitoring: Incorporating a CAARMS assessment from a research assistant, which represents an enhancement over routine care since it aimed to provide warm, empathic and non-judgmental face-to-face contact, supportive listening, signposting to appropriate local services for unmet needs and crisis management when required (usually by referral to a local crisis team, early intervention in psychosis service or psychiatric liaison within emergency departments). Monitoring ensured that all participants had a GP with whom they were encouraged to stay in regular contact and a personalised 'crisis card', which provided contact details for local sources of help in a psychiatric emergency.
Extractable outcomes	Transition to psychosis (CAARMS): Number of participants. Mental state: CAARMS-Severity, Beck Depression Inventory for Primary Care, SIAS. Quality of life: Manchester Short Assessment of Quality of Life (MANSA). Leaving the study early: Leaving due to any reason.
Quality	Sequence generation: Low risk. Allocation concealment: Low risk. Participants blinded: High risk. Providers blinded: High risk. Outcome assessors blinded: Low risk. Missing outcome data: High risk. Selective outcome reporting: Low risk. Other bias: Low risk.
Related publications	Morrison, A. P., French, P., Stewart, S. L., *et al.* (2012) Early detection and intervention evaluation for people at risk of psychosis: Multisite randomised controlled trial. *BMJ*, *344*, 2233.

Study ID	PHILLIPS2009
Bibliographic reference	Phillips, L. J., Nelson, B., Yuen, H. P., *et al.* (2009) Randomized controlled trial of interventions for young people at ultra-high risk of psychosis: study design and baseline characteristics. *Australian and New Zealand Journal of Psychiatry*, *43*, 818–829.
General information	Funding source: Janssen-Cilag Pharmaceuticals. Published or unpublished data: Published.
Method	Type of study: Individual randomised trial. Type of analysis: ITT – multiple imputation was used to impute missing values. Blindness: Research interviewers and psychiatrists involved with the study were blind to treatment group. Psychologists were blind to treatment group as far as the design would allow (to the pharmacological but not to the psychological intervention). Duration: Number of weeks of treatment – 52 weeks; length of follow-up – 104 weeks. Raters: Independent of treatment. Design: Single-site (Melbourne, Australia) RCT. Number of people screened, excluded and reasons: 1,428 referred to PACE Clinic, 464 met study criteria, 225 agreed to research participation, 30 entered a lithium trial, two were subsequently found not to meet criteria for randomisation. 115 participants were randomised, 78 refused randomisation but agreed to research assessment and follow-up. Notes about study methods: The 78 people who formed the monitoring group were excluded from this systematic review owing to the absence of randomisation.
Participants	Diagnosis: At risk mental state. Diagnostic tool: CAARMS. Inclusion criteria: • aged between 14 and 30 years • living in the Melbourne metropolitan area • meeting criteria for one or more of three ultra-high risk groups. Exclusion criteria: • history of a previous psychotic or manic episode (treated or untreated) • history of a medical condition that may account for symptoms leading to initial referral (for example, epilepsy) • clinically relevant neurological, biochemical or haematological abnormalities • serious coexisting illnesses • previous use of neuroleptic medication (greater than the equivalent of 5 mg of haloperidol for 3 weeks or longer) • any previous or current use of mood stabilising medication • history of severe drug allergy • intellectual disability (IQ <70)

	• pregnant or lactating • insufficient English language skills to participate in research interviews or psychological treatment without assistance from an interpreter. Total sample size: No. randomised – 115. Gender: 39% male. Age: Mean 18 (range not reported) years. Ethnicity: Not reported. Setting: Specialist clinic – PACE Clinic, an extension of EPPIC..
Interventions	Intervention – group 1: CBT (35 sessions was aimed at) + risperidone 2 mg/day), for 52 weeks, N = 43; group 2: CBT (35 sessions was aimed at) + placebo, for 52 weeks, N = 44; group 3: supportive counselling (35 sessions was aimed at) + placebo, N = 28. Notes about the interventions: CBT: Provided by trained clinical psychologists using a manualised programme consisting of four modules: stress management, depression/ negative symptoms, positive symptoms and other comorbidities. Supportive counselling: Was provided by the same clinical psychologists and aimed to provide the participant with emotional and social support, as well as basic problem solving, stress management and psychoeducation about psychosis.
Extractable outcomes	Transition to psychosis (CAARMS): Number of participants. Mental state: BPRS, SOPS, HAM-D. Psychosocial functioning: GAF. Quality of life: QLS. Side effects: Udvalg for Kliniske Undersøgelser (UKU) Side Effect Rating Scale. Leaving the study early: Leaving due to any reason.
Quality	Sequence generation: Low risk. Allocation concealment: Low risk. Participants blinded: Low risk. Providers blinded: Low risk. Outcome assessors blinded: Low risk. Missing outcome data: High risk. Selective outcome reporting: Unclear risk. Other bias: High risk.
Related publications	McGorry, P. D., Nelson, B., Phillips, L. J., *et al*. (unpublished) Randomized controlled trial of interventions for young people at ultra-high risk of psychosis: 12-month outcome. Yung, A. R., Phillips, L. J., Nelson, B. *et al*. (2011) Randomized controlled trial of interventions for young people at ultra high risk for psychosis: 6-month analysis. *Journal of Clinical Psychiatry*, 72, 430–440.

Study ID	VANDERGAAG2012
Bibliographic reference	Van der Gaag, M., Nieman, D., Rietdijk, J., *et al.* (in press) Cognitive behavioural therapy for subjects at ultra-high risk for developing psychosis: a randomised controlled trial. *Schizophrenia Bulletin*, published online: 1 September 2012. DOI: 10.1093/schbul/sbs105.
General information	Funding source: Netherlands Health Research Council. Published or unpublished data: Published.
Method	Type of study: Multi-site RCT. Type of analysis: ITT analyses on primary outcomes, analyses on secondary outcomes were based on 164 patients that did not make a transition to psychosis in the study period. Blindness: Only outcome assessors blind Duration: Each patient was treated for 6 months; length of follow-up 18 months. Raters: Only outcome assessors blind. Design: Multisite RCT. Participants were recruited at four sites in the Netherlands (Mental Health Centre PsyQ Haaglanden, the Hague, Academic Medical Centre and Mental Health Centre PsyQ, Amsterdam, Mental Health Centre Rivierduinen, Leiden and surroundings and Mental Health Institute Friesland in the province of Friesland). Number of people screened, excluded and reasons: Discrepancy in reporting of number of individuals screened (5,800 in flow diagram and 5,705 in text). 5,497 excluded (4,841 did not meet initial Prodromal Questionnaire criteria, 373 did not meet criteria for ultra high risk, 104 had psychosis, eight had a history of psychosis, 16 used antipsychotic medication, 50 had scores that were too high on the Social and Occupational Functioning Assessment Scale [SOFAS], three were not in the age range, one died, 57 refused to participate, 22 lost contact, 22 'other 'reasons, up to 102 participants not accounted for due to discrepancy in reporting number screened). 201 participants were randomised. Notes about study methods: No additional information provided by VANDERGAAG2012.
Participants	Diagnosis: At risk mental state. Diagnostic tool: CAARMS. Inclusion criteria: • age 14 to 35 years • a genetic risk or CAARMS scores in the range of the at risk mental state • an impairment in social functioning (a score on the SOFAS of 50 or less, and/or a reduction by 30% on the SOFAS for at least 1 month in the past year). Exclusion criteria: • current or previous use of antipsychotic medication

	• severe learning impairment • problems due to an organic condition • insufficient competence in the Dutch language • history of psychosis. Total sample size: Number randomised = 201. Gender: 49% male. Age: Mean 22.74 years (range not reported). Ethnicity: Not reported. Setting: Mental health centres (multi-site).
Interventions	Intervention group: CBT + psychoeducation on dopamine and cognitive biases + treatment as usual were offered on a weekly basis for up to a maximum of 26 weeks. The mean number of sessions was 10. N = 98. Control group: treatment as usual, N = 103. Notes about the interventions: Both conditions were in addition to treatment as usual, which will have been highly variable and dependent on local service configurations and specific source of referral to the trial; therefore, randomisation was stratified by site in an attempt to control for this variation. CBT + psychoeducation on dopamine and cognitive biases + treatment as usual: The CBT component of the intervention involved using the French and Morrison protocol, a CBT protocol designed for use with people at high risk of developing psychosis. The protocol was enriched with education on dopamine supersensitivity, explaining how this affects perception and thinking. Exercises were also added to experience cognitive biases; becoming aware of cognitive biases may lead to corrected secondary appraisals. Treatment as usual: Both the experimental and the control group were treated with evidence-based active treatment for the axis 1 or 2 disorder that they were experiencing.
Extractable outcomes	Transition to psychosis (CAARMS): Number of participants. Severity of psychosis, if transition had taken place: PANSS. Mental state: Beck Depression Inventory-II, Calgary Depression Scale, SIAS. Quality of life: MANSA. Social functioning: SOFAS. Personal beliefs about illness: Personal Beliefs about Illness Questionnaire-Revised. Leaving the study early: Leaving due to any reason.
Quality	Sequence generation: Low risk. Allocation concealment: Low risk. Participants blinded: High risk. Providers blinded: High risk.

	Outcome assessors blinded: Low risk. Missing outcome data: High risk. Selective outcome reporting: Low risk. Other bias: Low risk.
Related publications	Rietdijk., J., Dragt, S., Klaassen, R., *et al*. (2010) A single blind randomized controlled trial of cognitive behavioural therapy in a help-seeking population with an at risk mental state for psychosis: the Dutch Early Detection and Intervention Evaluation (EDIE-NL) trial. *Trials*, *11*, 30.

Excluded studies

A generic search was conducted in order to address review questions across each section of the guideline. Studies relevant to an at risk population were identified from a list of included RCTs of pharmacological, psychological, psychosocial or dietary interventions (see Appendices 13b and 13c) and therefore no list of excluded studies was generated for Appendix 13a.