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DATA SUPPLEMENT

TABLE DS1 **Randomised controlled trials of interventions in patients at ultra-high risk (UHR) of psychosis**

Study	Clinical inclusion criteria	Treatment	Control	Summary of main outcomes and issues
McGorry *et al*, 2002; Phillips *et al*, 2007 Single-blind randomised	PACE UHR criteria Age 14–30 years	Risperidone (1–2 mg/day) + modified CBT + needs-based interventions (case management, support with vocational and family problems) Duration: 6 months 31 participants	Needs-based interventions (case management, support with vocational and family problems) 28 participants	Rate of transition to psychosis in the treatment group was significantly less at the end of the treatment phase (P=0.03, NNT=4), but at 1 year post baseline this effect was lost (P=0.24). Extrapyramidal side-effects and sedation reported. Adherence to risperidone variable. Within 3–4 years 41 out of the 59 original participants were followed up. There was no significant difference between the two groups in terms of transition rate, level of symptomatology or functioning.
Morrison *et al*, 2004, 2007 Single-blind randomised	PACE UHR criteria Age 16–36 years	CBT (26 sessions over 6 months) Duration: 6 months 37 participants	Monitoring only 23 participants	At 1 year, there was significantly lower transition rate in the treatment group than the control group (P=0.028). Positive psychotic symptoms also were significantly improved in the treatment group at 12 months. Median number of CBT sessions was 11. Within 3 years, transition rates were not significantly different: treatment group, 20.0%; control group, 30.4%. Reasonably high drop-out at longer-term follow-up.
McGlashan *et al*, 2006 Double-blind randomised	UHR equivalent criteria for prodromal states (COPS) using Structured Interview for Prodromal Symptoms (SIPS) Age 12–45 years	Olanzapine (5–15 mg/day) Duration: 12 months 31 participants	Placebo 21 participants	Non-significantly lower rate of transition to psychosis at the end the treatment period (P=0.08; NNT=4.5). Weight gain (8.8 kg) in the olanzapine group). Relatively high number dropped out. Partly funded by an investigator-initiated pharmaceutical company grant. 1 year following the treatment phase only 12 of the 60 were followed up – the transition rates were similar in the two groups (33% olanzapine, 25% placebo).
Amminger *et al*, 2010, 2015 Double-blind randomised	PACE UHR criteria Age 13–25 years	1.2 g/day of omega-3 polyunsaturated fatty acids (PUFAs), comprising 700 mg EPA/480 mg DHA Duration: 12 weeks 41 participants	Placebo 40 participants	At 12 months post study entry those in the treatment arm had a significantly lower rate of transition to psychosis (P=0.007). Positive, negative and general symptoms were also all significantly more improved in the omega-3 group. Drop out was low and there were no differences in adverse events between the 2 groups. At median of 6.7 years' follow-up the differences in transition rates, psychotic symptoms and functioning between the omega-3 and placebo group were maintained; 87.7% were followed up. Younger age range and female predominance compared with other trials.
Yung *et al*, 2010; McGorry *et al*, 2013 Double-blind randomised	PACE UHR criteria Age 14–30 years	Treatment group 1: CBT + risperidone (0.5–2 mg/day) (43 participants) Treatment group 2: CBT + placebo (44 participants) Duration: 6 months	Supportive therapy + placebo 28 participants	At 6 months there was no significant difference in transition rates between the 3 groups: 4.7% in the CBT + risperidone group; 9.1% in the CBT + placebo group; 7.1% in the supportive therapy + placebo group. There were similar findings at 12-month follow-up. All 3 randomised groups showed significant improvement in BPRS total, BPRS psychotic subscale and HDRS scores (depression). All groups significantly increased in functioning. There were no significant differences in side-effects between the 3 groups. Therapists partially 'blind'.
Addington *et al*, 2011 Single-blind randomised	UHR-equivalent COPS, using SIPS Age 14–30 years	CBT Duration: 6 months 27 participants	Active supportive therapy 24 participants	No significant difference in transition rates between the groups but there were small numbers and very few transitions (only 3 individuals in the monitoring group and none in the CBT group transitioned to psychosis over the course of the study). Both groups improved on symptoms but there was no significant difference between the treatment and control groups Relatively low rates of treatment exposure (mean 12/20 sessions).

(continued)

TABLE DS1 ***Continued***

Study	Clinical inclusion criteria	Treatment	Control	Summary of main outcomes and issues
Morrison *et al*, 2012 Single-blind randomised	PACE-equivalent UHR criteria Age 14–35 years	CBT + treatment as usual Duration: up to 26 weeks 144 participants	Monitoring, including supportive listening, signposting, crisis management + treatment as usual 144 participants	No significant difference between the groups on rates of transition: at 12 months 6.9% in treatment group and 9.0% in the control group (P=0.45). Overall transition rate lower than anticipated. CBT did reduce the frequency and intensity of psychotic symptoms but did not significantly affect either distress related to psychotic symptoms or levels of depression, social anxiety and satisfaction with life. Low rates of treatment exposure (mean 9/26 sessions). A number of breaks of 'blinding' (22%).
Van der Gaag *et al*, 2012 Single-blind randomised	PACE UHR criteria Age 14–35 years	CBT + treatment as usual Duration: up to 26 weeks 95 participants	Treatment as usual 101 participants	Significantly more transitions in the control (treatment as usual) group than the treatment (CBT) group over the 18-month follow-up (P=0.03) and significantly more remissions from the UHR state. At 18-month follow-up, NNT for preventing transition to psychosis was 9 (95% CI 4.7–89.9). No differences between the CBT and control groups in outcome measures assessing the severity of depression and anxiety. In both groups, depression and anxiety severity scores were reduced at the follow-up assessments. Low rates of treatment exposure (mean 10/26 sessions).

Table adapted from Bucur & Whale (2012), with permission.

BPRS, Brief Psychiatric Rating Scale; CBT, cognitive–behavioural therapy; COPS, Criteria for Prodromal States; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; HDRS, Hamilton Depression Rating Scale; NNT, number needed to treat; PACE, Personal Assistance and Clinical Evaluation Clinic; POPS, Presence of Psychosis Scale; SIPS, Structured Interview for Prodromal Symptoms.

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