APPENDIX 17D: CLINICAL EVIDENCE PROFILES:

COGNITION, EMPLOYMENT AND EDUCATION

Abbreviations

CRT	cognitive remediation therapy
EPPIC	Early Psychosis Prevention and Intervention Centre, Australia
LOCF	last observation carried forward
OIS	optimal information size
RR	relative risk
SMD	standardised mean difference

Cognitive enhancement therapy (cognitive remediation therapy [CRT] and group-based social cognition therapy) versus psychoeducation at 104 weeks post-treatment

Outcome or subgroup	Study ID	Design	Risk of bias	Inconsistency	Indirectness	Impreci-sion	Other consider-ations	Number of studies / participants	Effect estimate (SMD or RR)	Quality of evidence (GRADE)[a]	Forest plot
Total symptoms (SMD)	EACK2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 58	-0.72 [-1.25, -0.19]*	Low[1, 2]	Appendix 14d (3.2)
Positive symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Negative symptoms (SMD)	EACK2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 58	-0.96 [-1.51, -0.41]*	Low[1, 2]	Appendix 14d (3.3)
General symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Global state (severity) (SMD)	-	-	-	-	-	-	-	-	-	-	-
Depression (SMD)	-	-	-	-	-	-	-	-	-	-	-
Mania (SMD)	-	-	-	-	-	-	-	-	-	-	-
Anxiety/depression (SMD)	EACK2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 58	-0.41 [-0.93, 0.11]	Low[1, 2]	Appendix 14d (3.1)
Psychosocial functioning (SMD)	EACK2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 58	-0.86 [-1.41, -0.32]*	Low[1, 2]	Appendix 14d (3.4)
Social functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Quality of life (SMD)	-	-	-	-	-	-	-	-	-	-	-
Social cognition (SMD)	EACK2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 58	-1.20 [-1.76, -0.64]*	Low[1, 2]	Appendix 14d (3.5)
Education	-	-	-	-	-	-	-	-	-	-	-
Sensitivity analysis: employment (assuming dropouts did not gain employment; RR)	EACK2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 58	2.83 [1.05, 7.65]*	Low[1, 2]	Appendix 14d (3.6)

Outcome or subgroup	Study ID	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of studies / participants	Effect estimate (SMD or RR)	Quality of evidence (GRADE)[a]	Forest plot
Leaving study early for any reason (RR)	EACK2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 58	1.22 [0.44, 3.40]	Low[1, 2]	Appendix 14d (3.15)

Note. [a]The GRADE approach was used to grade the quality of evidence for each outcome, see Section 3.5.5 in the full guideline for further detail.
*Favours CRT.
[1]Serious risk of bias (including unclear allocation concealment, unblind raters).
[2]Optimal information size (OIS) (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

CRT versus psychoeducation at 26 weeks post-treatment

Outcome or subgroup	Study ID	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of studies / participants	Effect estimate (SMD or RR)	Quality of evidence (GRADE)[a]	Forest plot
Total symptoms (SMD)	UELAND 2004	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	None	-0.19 [-0.98, 0.60]	Low[1, 2]	Appendix 14d (1.1)
Positive symptoms (SMD)	UELAND 2004	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 25	-0.33 [-1.13, 0.47]	Low[1, 2]	Appendix 14d (1.2)
Negative symptoms (SMD)	UELAND 2004	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 25	-0.17 [-0.96, 0.62]	Low[1, 2]	Appendix 14d (1.3)
General symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Global state (severity) (SMD)	-	-	-	-	-	-	-	-	-	-	-
Depression (SMD)	-	-	-	-	-	-	-	-	-	-	-
Mania (SMD)	-	-	-	-	-	-	-	-	-	-	-
Anxiety (SMD)	-	-	-	-	-	-	-	-	-	-	-
Psychosocial functioning (SMD)	UELAND 2004	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 26	-0.46 [-1.24, 0.32]	Low[1, 2]	Appendix 14d (1.4)
Social functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Quality of life (SMD)	-	-	-	-	-	-	-	-	-	-	-
Cognition	-	-	-	-	-	-	-	-	-	-	-
Education	-	-	-	-	-	-	-	-	-	-	-
Employment	-	-	-	-	-	-	-	-	-	-	-
Leaving study early for any reason (RR)	-	-	-	-	-	-	-	-	-	-	-

CRT versus psychoeducation at 52 weeks' follow-up

Outcome or subgroup	Study ID	Design	Risk of bias	Inconsistency	Indirectness	Imprec-ision	Other consid-erations	Number of studies / participants	Effect estimate (SMD or RR)	Quality of evidence (GRADE)[a]	Forest plot
Total symptoms (SMD)	UELAND 2004	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 24	-0.40 [-1.22, 0.42]	Low[1,2]	Appendix 14d (2.1)
Positive symptoms (SMD)	UELAND 2004	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 24	-0.35 [-1.17, 0.47]	Low[1,2]	Appendix 14d (2.2)
Negative symptoms (SMD)	UELAND 2004	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 24	-0.66 [-1.50, 0.17]	Low[1,2]	Appendix 14d (2.3)
General symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Global state (severity) (SMD)	-	-	-	-	-	-	-	-	-	-	-
Depression (SMD)	-	-	-	-	-	-	-	-	-	-	-
Mania (SMD)	-	-	-	-	-	-	-	-	-	-	-
Anxiety (SMD)	-	-	-	-	-	-	-	-	-	-	-
Psychosocial functioning (SMD)	UELAND 2004	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 25	-0.15 [-0.94, 0.64]	Low[1,2]	Appendix 14d (2.4)
Social functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Quality of life (SMD)	-	-	-	-	-	-	-	-	-	-	-
Cognition	-	-	-	-	-	-	-	-	-	-	-
Education	-	-	-	-	-	-	-	-	-	-	-
Employment	-	-	-	-	-	-	-	-	-	-	-
Leaving study early for any reason (RR)	-	-	-	-	-	-	-	-	-	-	-

Appendix 17d

CRT versus treatment as usual at 14 weeks post-treatment

Outcome or subgroup	Study ID	Design	Risk of bias	Inconsistency	Indirectness	Imprec-ision	Other consid-erations	Number of studies / participants	Effect estimate (SMD or RR)	Quality of evidence (GRADE)[a]	Forest plot
Total symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Positive symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Negative symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
General symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Global state (severity) (SMD)	-	-	-	-	-	-	-	-	-	-	-
Depression (SMD)	-	-	-	-	-	-	-	-	-	-	-
Mania (SMD)	-	-	-	-	-	-	-	-	-	-	-
Anxiety (SMD)	-	-	-	-	-	-	-	-	-	-	-
Psychosocial functioning	-	-	-	-	-	-	-	-	-	-	-
Social functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Quality of life (SMD)	-	-	-	-	-	-	-	-	-	-	-
Cognition	-	-	-	-	-	-	-	-	-	-	-
Education	-	-	-	-	-	-	-	-	-	-	-
Employment (RR)	-	-	-	-	-	-	-	-	-	-	-
Leaving study early for any reason (RR)	WYKES 2007	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 40	1.03 [0.75, 1.40]	Low[1,2]	Appendix 14d (4.1)

Note. [a]The GRADE approach was used to grade the quality of evidence for each outcome, see Section 3.5.5 in the full guideline for further detail.
[1]Serious risk of bias (including unclear sequence generation, unable to find trial registration, LOCF reported but high dropout).
[2] OIS (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

CRT versus treatment as usual at 26 weeks' follow-up

Outcome or subgroup	Study ID	Design	Risk of bias	Inconsistency	Indirectness	Imprec-ision	Other consid-erations	Number of studies / participants	Effect estimate (SMD or RR)	Quality of evidence (GRADE)[a]	Forest plot
Total symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Positive symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Negative symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
General symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Global state (severity) (SMD)	-	-	-	-	-	-	-	-	-	-	-
Depression (SMD)	-	-	-	-	-	-	-	-	-	-	-
Mania (SMD)	-	-	-	-	-	-	-	-	-	-	-
Anxiety (SMD)	-	-	-	-	-	-	-	-	-	-	-
Psychosocial functioning	-	-	-	-	-	-	-	-	-	-	-
Social functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Quality of life (SMD)	-	-	-	-	-	-	-	-	-	-	-
Cognition	-	-	-	-	-	-	-	-	-	-	-
Education	-	-	-	-	-	-	-	-	-	-	-
Employment (RR)	-	-	-	-	-	-	-	-	-	-	-
Leaving study early for any reason (RR)	WYKES 2007	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 40	0.97 [0.69, 1.35]	Low[1, 2]	Appendix 14d (5.1)

Note. [a]The GRADE approach was used to grade the quality of evidence for each outcome, see Section 3.5.5 in the full guideline for further detail.
[1]Serious risk of bias (including unclear sequence generation, unable to find trial registration, LOCF reported but high dropout)
[2]OIS (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

CRT versus computer games at 8 weeks post-treatment

Outcome or subgroup	Study ID	Design	Risk of bias	Inconsistency	Indirectness	Imprec-ision	Other consid-erations	Number of studies / participants	Effect estimate (SMD or RR)	Quality of evidence (GRADE)[a]	Forest plot
Total symptoms (SMD)	URBEN 2012	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 28	0.26 [-0.49, 1.00]	Very low[1,2,3]	Appendix 14d (6.1)
Positive symptoms (SMD)	URBEN 2012	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 28	0.35 [-0.39, 1.10]	Very low[1,2,3]	Appendix 14d (6.2)
Negative symptoms (SMD)	URBEN 2012	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 28	0.29 [-0.46, 1.04]	Very low[1,2,3]	Appendix 14d (6.3)
General symptoms (SMD)	URBEN 2012	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 28	0.23 [-0.52, 0.97]	Very low[1,2,3]	Appendix 14d (6.4)
Global state (severity) (SMD)	URBEN 2012	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 28	0.21 [-0.53, 0.96]	Very low[1,2,3]	Appendix 14d (6.5)
Depression (SMD)	-	-	-	-	-	-	-	-	-	-	-
Mania (SMD)	-	-	-	-	-	-	-	-	-	-	-
Anxiety (SMD)	-	-	-	-	-	-	-	-	-	-	-
Psychosocial functioning	-	-	-	-	-	-	-	-	-	-	-
Social functioning (SMD)	URBEN 2012	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 28	0.31 [-0.44, 1.06]	Very low[1,2,3]	Appendix 14d (6.6)
Quality of life (SMD)	-	-	-	-	-	-	-	-	-	-	-
Cognition	-	-	-	-	-	-	-	-	-	-	-
Education	-	-	-	-	-	-	-	-	-	-	-
Employment (RR)	-	-	-	-	-	-	-	-	-	-	-

Note. [a]The GRADE approach was used to grade the quality of evidence for each outcome, see Section 3.5.5 in the full guideline for further detail.

[1] Serious risk of bias (including unclear sequence generation and allocation concealment unblind raters, trial registration not found, available case analysis used).

[2] OIS (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

[3] Serious risk of indirectness (as sample contains participants at serious risk of psychosis).

CRT versus computer games at 26 weeks' follow-up

Outcome or subgroup	Study ID	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of studies / participants	Effect estimate (SMD or RR)	Quality of evidence (GRADE)[a]	Forest plot
Global state (severity) (SMD)	URBEN 2012	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 22	0.60 [-0.27, 1.46]	Very low[1, 2, 3]	Appendix 14d (7.1)
Leaving study early for any reason (RR)	URBEN 2012	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 32	1.17 [0.41, 3.35]	Very low[1, 2, 3]	Appendix 14d (7.2)

Note. [a]The GRADE approach was used to grade the quality of evidence for each outcome, see Section 3.5.5 in the full guideline for further detail.
[1] Serious risk of bias (including unclear sequence generation and allocation concealment unblind raters, trial registration not found, available case analysis used).
[2] OIS (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.
[3] Serious risk of indirectness (as sample contains participants at serious risk of psychosis).

Individual placement and support versus EPPIC treatment as usual at 26 weeks post-treatment

Outcome or subgroup	Study ID	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of studies / participants	Effect estimate (SMD or RR)	Quality of evidence (GRADE)[a]	Forest plot
Total symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Positive symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Negative symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
General symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Global state (severity) (SMD)	-	-	-	-	-	-	-	-	-	-	-
Depression (SMD)	-	-	-	-	-	-	-	-	-	-	-
Mania (SMD)	-	-	-	-	-	-	-	-	-	-	-
Anxiety (SMD)	-	-	-	-	-	-	-	-	-	-	-
Psychosocial functioning	-	-	-	-	-	-	-	-	-	-	-
Social functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Quality of life (SMD)	-	-	-	-	-	-	-	-	-	-	-

Cognition	-	-	-	-	-	-	-	-	-	-	-
Sensitivity analysis: Employed/ enrolled on a course (assuming dropouts did not gain employment; RR)	KILLACKEY 2008	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 41	6.83 [1.76, 26.51]*	Low[1, 2]	Appendix 14d (8.1)
Number of weeks worked (SMD)	KILLACKEY 2008	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 15	-0.49 [-1.99, 1.02]	Low[1, 2]	Appendix 14d (8.2)
Number of hours worked per week (SMD)	KILLACKEY 2008	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 15	-0.71 [-2.22, 0.81]	Low[1, 2]	Appendix 14d (8.3)
Leaving study early for any reason (RR)	KILLACKEY 2008	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 41	0.21 [0.03, 1.64]*	Low[1, 2]	Appendix 14d (8.4)

Note. [a]The GRADE approach was used to grade the quality of evidence for each outcome, see Section 3.5.5 in the full guideline for further detail.

*Favours individual placement and support.

[1] Serious risk of bias (including inadequate allocation concealment, unclear rater blinding, more people in the treatment as usual group were in marital or marital-like relationships tending to bias the study against finding success for the vocational intervention because people in marital relationships tend to function better socially and in employment).

[2] OIS (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.