APPENDIX 17B: CLINICAL EVIDENCE PROFILES: PSYCHOLOGICAL AND PSYCHOSOCIAL INTERVENTIONS

Abbreviations

CBT	cognitive behavioural therapy
ECT	electroconvulsive therapy
EPPIC	Early Psychosis Prevention and Intervention Centre, Australia
OIS	optimal information size
RR	relative risk
SMD	standardised mean difference

PSYCHOLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 25 YEARS AND YOUNGER

Cognitive behavioural therapy (CBT) versus treatment as usual: 26 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)	JACKSON2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 46	-0.29 [-0.87, 0.30]	Low[1,2]	Appendix 14b (1.1)
Mania (SMD)	-	-	-	-	-	-	-	-	-	-	-
Anxiety (SMD)	-	-	-	-	-	-	-	-	-	-	-
Psychosocial functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Social functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Quality of life (SMD)	-	-	-	-	-	-	-	-	-	-	-
Relapse	-	-	-	-	-	-	-	-	-	-	-
Remission (RR)	-	-	-	-	-	-	-	-	-	-	-

Mortality (including suicide) (RR)	-	-	-	-	-	-	-	-	-	-	-
Leaving the study early for any reason (RR)	JACKSON2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 66	1.94 [0.85, 4.43]	Low[1,2]	Appendix 14b (1.2)

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 allocation concealment, trial registration not found and missing data).
[2] Optimal information size (OIS) (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

CBT versus treatment as usual: 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)	-	-	-	-	-	-	-	-	-	-	-
Positive symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Negative symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
General symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Global state (severity) (SMD)	-	-	-	-	-	-	-	-	-	-	-
Depression (SMD)	JACKSON 2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 46	-0.05 [-0.65, 0.54]	Low[1,2]	Appendix 14b (2.1)
Mania (SMD)	-	-	-	-	-	-	-	-	-	-	-
Anxiety (SMD)	-	-	-	-	-	-	-	-	-	-	-
Psychosocial functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Social functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Quality of life (SMD)	-	-	-	-	-	-	-	-	-	-	-
Relapse	-	-	-	-	-	-	-	-	-	-	-
Remission (RR)	-	-	-	-	-	-	-	-	-	-	-
Mortality (including suicide) (RR)	-	-	-	-	-	-	-	-	-	-	-
Leaving the study early for any reason (RR)	JACKSON 2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 66	1.77 [0.89, 3.52]	Low[1,2]	Appendix 14b (2.2)

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 allocation concealment, trial registration not found and missing data).
[2] OIS (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

CBT versus EPPIC treatment as usual: 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)	JACKSON 2008	-	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 62	-0.05 [-0.55, 0.45]	Very low[1,2,3]	Appendix 14b (3.1)
Negative symptoms (SMD)	JACKSON 2008	-	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 62	-0.46 [-0.96, 0.05]	Very low[1,2,3]	Appendix 14b (3.2)
General symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Global state (severity) (SMD)	-	-	-	-	-	-	-	-	-	-	-
Depression (SMD)	-	-	-	-	-	-	-	-	-	-	-
Mania (SMD)	-	-	-	-	-	-	-	-	-	-	-
Anxiety (SMD)	-	-	-	-	-	-	-	-	-	-	-
Psychosocial functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Social functioning (SMD)	JACKSON 2008	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 62	-0.40 [-0.90, 0.11]	Very low[1,2,3]	Appendix 14b (3.3)
Quality of life (SMD)	-	-	-	-	-	-	-	-	-	-	-
Relapse	-	-	-	-	-	-	-	-	-	-	-
Remission (RR)	-	-	-	-	-	-	-	-	-	-	-
Mortality (including suicide) (RR)	-	-	-	-	-	-	-	-	-	-	-
Leaving the study early for any reason (RR)	JACKSON 2008	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 62	0.57 [0.19, 1.76]	Very low[1,2,3]	Appendix 14b (3.4)

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.
[1] Serious risk of bias (including unclear allocation concealment, trial registration not found).
[2] OIS (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.
[3]Serious risk of indirectness as 21% of participants had bipolar disorder and 8.1% of participants were receiving electroconvulsive therapy (ECT).

CBT versus EPPIC treatment as usual: 52 weeks' follow-up

Outcome or subgroup	Study ID	Design	Risk of bias	Inconsistency	Indirect-ness	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)	JACKSON 2008	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 62	-0.08 [-0.58, 0.42]	Very low[1,2,3]	Appendix 14b (4.1)
Negative symptoms (SMD)	JACKSON 2008	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 62	-0.37 [-0.87, 0.13]	Very low[1,2,3]	Appendix 14b (4.2)
General symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Global state (severity) (SMD)	-	-	-	-	-	-	-	-	-	-	-
Depression (SMD)	-	-	-	-	-	-	-	-	-	-	-
Mania (SMD)	-	-	-	-	-	-	-	-	-	-	-
Anxiety (SMD)	-	-	-	-	-	-	-	-	-	-	-
Psychosocial functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Social functioning (SMD)	JACKSON 2008	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 62	-0.08 [-0.58, 0.41]	Very low[1,2,3]	Appendix 14b (4.3)
Quality of life (SMD)	-	-	-	-	-	-	-	-	-	-	-
Relapse (number of participants requiring hospitalisation) (RR)	JACKSON 2008	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 57	1.35 [0.65, 2.80]	Very low[1,2,3]	Appendix 14b (4.4)
Remission (RR)	-	-	-	-	-	-	-	-	-	-	-
Suicide (number of participants; assuming dropouts did not die by suicide) (RR)	JACKSON 2008	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 62	5.00 [0.25, 100.08]	Very low[1,2,3]	Appendix 14b (4.5)
Leaving the study early for any reason (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 allocation concealment, trial registration not found).
[2] OIS (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.
[3]Serious risk of indirectness as 21% of participants had bipolar disorder and 8.1% of participants were receiving ECT.

CBT versus EPPIC treatment as usual in acutely suicidal participants: 10 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 (SMD)	-	-	-	-	-	-	-	-	-	-	-
Social functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Quality of life (SMD)	POWER 2003	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 42	-0.04 [-0.54, 0.47]	Very low[1,2,3]	Appendix 14b (5.1)
Relapse	-	-	-	-	-	-	-	-	-	-	-
Remission (RR)	-	-	-	-	-	-	-	-	-	-	-
Mortality (number of deaths by suicide) (RR)	POWER 2003	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 56	Not estimable (no events)	Very low[1,2,3]	Appendix 14b (5.3)
Leaving the study early for any reason (RR)	POWER 2003	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 56	2.02 [0.72, 5.66]	Very low[1,2,3]	Appendix 14b (5.2)

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, trial registration not found and missing data analysis not reported).
[2] OIS (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met
[3]Serious risk of indirectness as participants were acutely suicidal

CBT versus EPPIC treatment as usual in acutely suicidal participants: 36 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 (SMD)	-	-	-	-	-	-	-	-	-	-	-
Social functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Quality of life (SMD)	POWER 2003	RCT	Serious [1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 33	0.03 [-0.66, 0.71]	Very low[1,2,3]	Appendix 14b (6.1)
Relapse	-	-	-	-	-	-	-	-	-	-	-
Remission (RR)	-	-	-	-	-	-	-	-	-	-	-
Suicide (number of participants; assuming dropouts did not die by suicide) (RR)	POWER 2003	RCT	Serious [1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 56	0.81 [0.05, 12.26]	Very low[1,2,3]	Appendix 14b (6.2)
Leaving the study early for any reason (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, trial registration not found and missing data analysis not reported).
[2] OIS (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.
[3]Serious risk of indirectness as participants were acutely suicidal.

CBT + clozapine versus clozapine in participants whose symptoms have not adequately responded to treatment: 12 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)	EDWARDS 2012	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 25	0.19 [-0.60, 0.98]	Low[1, 2]	Appendix 14b (7.1)
Negative symptoms (SMD)	EDWARDS 2012	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 25	-0.30 [-1.09, 0.50]	Low[1, 2]	Appendix 14b (7.2)
General symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Global state (severity) (SMD)	EDWARDS 2012	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 25	0.00 [-0.79, 0.79]	Low[1, 2]	Appendix 14b (7.3)
Depression (SMD)	EDWARDS 2012	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 1, N = 25	0.56 [-0.25, 1.37]	Low[1, 2]	Appendix 14b (7.4)
Mania (SMD)	-	-	-	-	-	-	-	-	-	-	-
Anxiety (SMD)	-	-	-	-	-	-	-	-	-	-	-
Psychosocial functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Social functioning (SMD)	EDWARDS 2012	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 25	0.18 [-0.61, 0.97]	Low[1, 2]	Appendix 14b (7.5)
Quality of life (SMD)	EDWARDS 2012	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 25	-0.04 [-0.83, 0.75]	Low[1, 2]	Appendix 14b (7.6)
Relapse	-	-	-	-	-	-	-	-	-	-	-
Remission (RR)	-	-	-	-	-	-	-	-	-	-	-
Mortality (including suicide) (RR)	-	-	-	-	-	-	-	-	-	-	-

Leaving the study early for any reason (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 & allocation concealment, single blind trial but unclear if it is providers, participants or raters who were blind, trial registration not found and missing data not reported, average daily dose of clozapine was 44.8 mg/day higher in the clozapine only group than the clozapine+CBT group).
[2] OIS (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met

CBT + clozapine versus clozapine in participants whose symptoms have not adequately responded to treatment: 24 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)	EDWARDS 2012	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 25	-0.24 [-1.03, 0.55]	Low[1, 2]	Appendix 14b (8.1)
Negative symptoms (SMD)	EDWARDS 2012	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 25	-0.28 [-1.07, 0.51]	Low[1, 2]	Appendix 14b (8.2)
General symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Global state (severity) (SMD)	EDWARDS 2012	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 25	0.12 [-0.67, 0.91]	Low[1, 2]	Appendix 14b (8.3)
Depression (SMD)	EDWARDS 2012	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 25	0.62 [-0.19, 1.43]	Low[1, 2]	Appendix 14b (8.4)
Mania (SMD)	-	-	-	-	-	-	-	-	-	-	-
Anxiety (SMD)	-	-	-	-	-	-	-	-	-	-	-
Psychosocial functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Social functioning (SMD)	EDWARDS 2012	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 14b (8.5)

Quality of life (SMD)	EDWARDS 2012	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 25	-0.56 [-1.36, 0.25]	Low[1, 2]	Appendix 14b (8.6)
Relapse	-	-	-	-	-	-	-	-	-	-	-
Sensitivity analysis: remission (number of participants: assuming dropouts did not achieve remission) (RR)	EDWARDS 2012	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 25	1.09 [0.51, 2.31]	Low[1, 2]	Appendix 14b (8.7)
Mortality (including suicide) (RR)	-	-	-	-	-	-	-	-	-	-	-
Leaving the study early for any reason (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 & allocation concealment, single blind trial but unclear if it is providers, participants or raters who were blind, trial registration not found and missing data not reported, average daily dose of clozapine was 44.8 mg/day higher in the clozapine only group than the clozapine+CBT group).
[2] OIS (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

Individual CBT versus family CBT: 52 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 (SMD)	-	-	-	-	-	-	-	-	-	-	-
Social functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Quality of life (SMD)	-	-	-	-	-	-	-	-	-	-	-

Sensitivity analysis: relapse (number of participants: assuming dropouts relapsed) (RR)	LINSZEN 1996	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 76	0.95 [0.34, 2.68]	low[1,2]	Appendix 14b (9.1)
Remission (RR)	-	-	-	-	-	-	-	-	-	-	-
Mortality (including suicide) (RR)	-	-	-	-	-	-	-	-	-	-	-
Leaving the study early for any reason (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, only raters were blind, trial registration not found, and missing data analysis was not reported)
[2] OIS (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

Individual and family CBT versus EPPIC treatment as usual: 30.33 weeks post-treatment

Outcome or subgroup	Study ID	Design	Risk of bias	Inconsistency	Indirectness	Imprec-ision	Other conside rations	Number of studies / participants	Effect estimate (SMD or RR)	Quality of evidence (GRADE)[a]	Forest plot
Total symptoms (SMD)	GLEESON 2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 81	-0.08 [-0.51, 0.36]	Low[1,2]	Appendix 14b (10.1)
Positive symptoms (SMD)	GLEESON 2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 81	-0.28 [-0.72, 0.15]	Low[1,2]	Appendix 14b (10.2)
Negative symptoms (SMD)	GLEESON 2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 81	-0.03 [-0.46, 0.41]	Low[1,2]	Appendix 14b (10.3)
General symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Global state (severity) (SMD)	-	-	-	-	-	-	-	-	-	-	-
Depression (SMD)	GLEESON 2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 81	-0.24 [-0.68, 0.20]	Low[1,2]	Appendix 14b (10.4)
Mania (SMD)	-	-	-	-	-	-	-	-	-	-	-
Anxiety (SMD)	-	-	-	-	-	-	-	-	-	-	-
Psychosocial functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-

Social functioning (SMD)	GLEESON 2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 81	0.06 [-0.37, 0.50]	Low[1,2]	Appendix 14b (10.6)
Quality of life (SMD)	GLEESON 2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 81	0.00 [-0.44, 0.44]	Low[1,2]	Appendix 14b (10.5)
Relapse (time in days)	GLEESON 2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 81	-3.26 [-3.94, -2.59]*	Low[1,2]	Appendix 14b (10.7)
Relapse (number of participants: assuming dropouts relapsed) (RR)	GLEESON 2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 81	0.24 [0.06, 1.08]	Low[1,2]	Appendix 14b (10.8)
Remission (RR)	-	-	-	-	-	-	-	-	-	-	-
Mortality (including suicide) (RR)	-	-	-	-	-	-	-	-	-	-	-
Leaving the study early for any reason (RR)	GLEESON 2009	RCT	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	K = 1, N = 82	1.40 [0.48, 4.05]	Low[1,2]	Appendix 14b (10.9)

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 CBT (individual and family).
[1] Serious risk of bias (unclear allocation concealment and missing data).
[2] OIS (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

Any psychological intervention in addition to EPPIC treatment as usual versus EPPIC treatment as usual: 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)	EDWARDS2012 GLEESON2009 JACKSON2008	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 3, N = 150	-0.11 [-0.43, 0.21]	Very low[1,2,3]	Appendix 14b (11.1)
Negative symptoms (SMD)	EDWARDS2012 GLEESON2009 JACKSON2008	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 3, N = 150	-0.25 [-0.57, 0.08]	Very low[1,2,3]	Appendix 14b (11.2)

General symptoms (SMD)	-	-	-	-	-	-	-	-	-	-	-
Global state (severity) (SMD)	-	-	-	-	-	-	-	-	-	-	-
Depression (SMD)	EDWARDS2012 GLEESON2009	RCT	Serious[1]	Serious[4]	No serious indirectness	Serious[2]	None	K = 2, N = 63	0.10 [-0.68, 0.87]	Very low[1,2,4]	Appendix 14b (11.3)
Mania (SMD)	-	-	-	-	-	-	-	-	-	-	-
Anxiety (SMD)	-	-	-	-	-	-	-	-	-	-	-
Psychosocial functioning (SMD)	-	-	-	-	-	-	-	-	-	-	-
Social functioning (SMD)	EDWARDS2011 GLEESON2009 JACKSON2008	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 3, N = 150	-0.10 [-0.45, 0.24]	Very low[1,2,3]	Appendix 14b (11.5)
Quality of life (SMD)	EDWARDS2011 GLEESON2009 POWER2003	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 3, N = 148	-0.02 [-0.34, 0.30]	Very low[1,2,3]	Appendix 14b (11.4)
Relapse	-	-	-	-	-	-	-	-	-	-	-
Remission (RR)	-	-	-	-	-	-	-	-	-	-	-
Suicide (number of participants; assuming dropouts did not die by suicide) (RR)	JACKSON2008 POWER2003	RCT	Serious[1]	No serious inconsistency	Serious[3]	Serious[2]	None	K = 2, N = 104	2.06 [0.28, 15.34]	Very low[1,2,3]	Appendix 14b (11.6)
Leaving the study early for any reason (RR)	GLEESON2009 JACKSON2008	RCT	Serious[1]	Serious[4]	Serious[3]	Serious[2]	None	K = 2, N = 144	0.91 [0.38, 2.19]	Very low[1,2,3,4]	Appendix 14b (11.7)

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 psychological intervention .
[1] Serious risk of bias (including unclear sequence generation and allocation concealment, unblinded, trial registration not found, missing data, 64.3% of clozapine only group were male compared with 90.9% of clozapine+CBT group and the average daily dose of clozapine was 44.8 mg/day, more serious in the clozapine only group than the clozapine+CBT group).
[2] OIS (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.
[3]Serious risk of indirectness (including acutely suicidal participants, participants with bipolar disorder and participants receiving ECT).
[4] $I^2 \geq 50\%$, $p<.05$.