APPENDIX 19: INTERVENTIONS FOR CHILDREN AND YOUNG PEOPLE – GRADE PROFILES

Pharmacological interventions....2
Selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs)....2
SSRIs and SNRIs compared with pill placebo....2
Fluoxetine compared with CBT....3
Pharmacotherapy for selective mutism: fluoxetine compared with pill placebo..4
Psychological interventions....5
Cognitive behavioural therapy (CBT)....5
CBT (individual and group) compared with waitlist....5
CBT (individual and group) compared with psychological placebo....6
CBT compared with pill placebo....7
CBT compared with CBT plus parent anxiety management....8
Other comparisons....9
CBT delivered via parents compared with waitlist....9
CBT delivered via parents compared with CBT via parents....11
Self-help compared with waitlist....12

Abbreviations

CBT	cognitive behavioural therapy
CI	confidence interval
OIS	optimal information size
RR	risk ratio/relative risk
SMD	standardised mean difference
SNRI	serotonin and noradrenaline reuptake inhibitor
SSRI	selective serotonin reuptake inhibitor

PHARMACOLOGICAL INTERVENTIONS

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS) AND SEROTONIN AND NORADRENALINE REUPTAKE INHIBITORS (SNRIS)

See Chapter 7, Section 7.4.1 of the guideline.

SSRIs and SNRIs compared with pill placebo

Quality assessment							No. of patients		Effect		Quality
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**SSRI/SNRI**	**Pill placebo**	**Relative (95% CI)**	**Absolute**	
3	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[1]	Reporting bias[2]	43/208 (20.7%)	12/194 (6.2%)	RR 0.85 (0.78 to 0.92)	9 fewer per 1000 (from 5 fewer to 14 fewer)	⊕⊕OO LOW
										8 fewer per 1000 (from 4 fewer to 12 fewer)	
3	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[1]	Reporting bias[2]	295	300	SMD 0.53 lower (0.69 to 0.36 lower)		⊕⊕OO LOW

[1] Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.
[2] Few trials were identified, trials in this area have not been registered, and previous reviews of medication for children and young people find evidence of important differences between published and unpublished studies.

Fluoxetine compared with CBT

Quality assessment							No. of patients		Effect		Quality
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**CBT**	**Fluoxetine**	**Relative (95% CI)**	**Absolute**	
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	30/59 (50.8%)	7/43 (16.3%)	RR 0.59 (0.44 to 0.79)	67 fewer per 1000 (from 34 fewer to 91 fewer)	⊕⊕OO LOW
										67 fewer per 1000 (from 34 fewer to 91 fewer)	
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[1]	Reporting bias[2]	57	33	SMD 0.15 higher (0.27 lower to 0.58 higher)		⊕⊕OO LOW

[1] Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.
[2] Few trials were identified, trials in this area have not been registered, and previous reviews of medication for children and young people find evidence of important differences between published and unpublished studies.

Pharmacotherapy for selective mutism: fluoxetine compared with pill placebo

Quality assessment							No. of patients		Effect	Quality
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fluoxetine	Pill placebo	Relative (95% CI)	
1	Randomised trials	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	Reporting bias[3]	6	9	SMD 0.74 lower (1.81 lower to 0.32 higher)	⊕OOO VERY LOW

[1] Methods poorly described.
[2] Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.
[3] Few trials were identified, trials in this area have not been registered, and previous reviews of medication for children and young people find evidence of important differences between published and unpublished studies.

PSYCHOLOGICAL INTERVENTIONS

See Chapter 7, Section 7.5 of the guideline.

COGNITIVE BEHAVIOURAL THERAPY (CBT)

See Section 7.5.1 of the guideline.

CBT (individual and group) compared with waitlist

Quality assessment							No. of patients		Effect		Quality
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	Waitlist	Relative (95% CI)	Absolute	
7	Randomised trials	No serious risk of bias	Serious[1]	No serious indirectness	Serious[2]	None	51/123 (41.5%)	3/94 (3.2%)	RR 0.65 (0.5 to 0.85)	11 fewer per 1000 (from 5 fewer to 16 fewer)	⊕⊕OO LOW
										-	
6	Randomised trials	No serious risk of bias	Serious[3]	No serious indirectness	Serious[2]	None	145	90	SMD 1.2 lower (1.97 to 0.43 lower)		⊕⊕OO LOW
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[2]	None	57	26	SMD 3.08 lower (3.75 to 2.41 lower)		⊕⊕OO LOW
2	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[2]	None	19	16	SMD 0.29 lower (0.96 lower to 0.38 higher)		⊕⊕OO LOW

[1] No explanation was provided.
[2] Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.
[3] Substantial and significant heterogeneity.

CBT (individual and group) compared with psychological placebo

Quality assessment							No. of patients		Effect		Quality
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	Psychological placebo	Relative (95% CI)	Absolute	
4	Randomised trials	No serious risk of bias	Serious[1]	No serious indirectness	Serious[2]	None	42/114 (36.8%)	8/89 (9%)	RR 0.72 (0.51 to 1.02)	25 fewer per 1000 (from 44 fewer to 2 more) 22 fewer per 1000 (from 38 fewer to 2 more)	⊕⊕OO LOW
3	Randomised trials	No serious risk of bias	Serious[1]	No serious indirectness	Very serious[2]	None	23/78 (29.5%)	6/58 (10.3%)	RR 0.79 (0.57 to 1.1)	22 fewer per 1000 (from 44 fewer to 10 more) 22 fewer per 1000 (from 45 fewer to 11 more)	⊕OOO VERY LOW
4	Randomised trials	No serious risk of bias	Serious[1]	No serious indirectness	Serious[2]	None	99	72	SMD 0.56 lower (1.16 lower to 0.04 higher)		⊕⊕OO LOW
3	Randomised trials	No serious risk of bias	Serious[1]	No serious indirectness	Serious[2]	None	68	50	SMD 0.54 lower (1.21 lower to 0.13 higher)		⊕⊕OO LOW
3	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[2]	None	69	53	SMD 0.19 higher (0.18 lower to 0.56 higher)		⊕⊕⊕O MODERATE
3	Randomised trials	No serious risk of bias	Serious[1]	No serious indirectness	Serious[2]	None	68	51	SMD 0.13 higher (0.82 lower to 1.09 higher)		⊕⊕OO LOW

[1] Substantial and significant heterogeneity.
[2] Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

CBT compared with pill placebo

Quality assessment							No. of patients		Effect		Quality
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	Pill placebo	Relative (95% CI)	Absolute	
1	Randomised trials	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	30/59 (50.8%)	1/37 (2.7%)	RR 0.51 (0.39 to 0.66)	13 fewer per 1000 (from 9 fewer to 16 fewer)	⊕⊕OO LOW
										13 fewer per 1000 (from 9 fewer to 16 fewer)	
1	Randomised trials	Serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	57	32	SMD 0.22 lower (0.66 lower to 0.21 higher)		⊕⊕OO LOW

[1] Risk of bias in several domains.
[2] Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

CBT compared with CBT plus parent anxiety management

Quality assessment							No. of patients		Effect		Quality
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	CBT with parent anxiety management	Relative (95% CI)	Absolute	
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	5/20 (25%)	4/21 (19%)	RR 1.31 (0.41 to 4.2)	59 more per 1000 (from 112 fewer to 610 more)	⊕⊕OO LOW
										59 more per 1000 (from 113 fewer to 611 more)	
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	7/20 (35%)	6/21 (28.6%)	RR 1.23 (0.5 to 3.02)	66 more per 1000 (from 143 fewer to 577 more)	⊕⊕OO LOW
										66 more per 1000 (from 143 fewer to 578 more)	
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	16	18	SMD 0.19 higher (0.48 lower to 0.87 higher)		⊕⊕OO LOW
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	16	14	SMD 0.58 higher (0.16 lower to 1.31 higher)		⊕⊕OO LOW
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	15	18	SMD 0.13 lower (0.81 lower to 0.56 higher)		⊕⊕OO LOW

1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	16	13	SMD 0.23 higher (0.51 lower to 0.96 higher)	⊕⊕OO LOW

[1] Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

OTHER COMPARISONS

See Section 7.5.2 and 7.5.3 of the guideline.

CBT delivered via parents compared with waitlist

Quality assessment							No. of patients		Effect		Quality
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**CBT via parents**	**Waitlist**	**Relative (95% CI)**		
4	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	20/62 (32.3%)	4/49 (8.2%)	RR 0.82 (0.64 to 1.06)	15 fewer per 1000 (from 29 fewer to 5 more)	⊕⊕OO LOW
										20 fewer per 1000 (from 40 fewer to 7 more)	
2	Randomised trials	No serious risk of bias	Serious[2]	No serious indirectness	Very serious[1]	None	5/27 (18.5%)	3/25 (12%)	RR 0.72 (0.19 to 2.67)	34 fewer per 1000 (from 97 fewer to 200 more)	⊕OOO VERY LOW
										40 fewer per 1000 (from 115 fewer to 237 more)	
2	Randomised	No	No serious	No serious	Very	None	19	17	SMD 0.15 lower (1.03 lower to		⊕⊕OO

	trials	serious risk of bias	inconsistency	indirectness	serious[1]				0.73 higher)	LOW
3	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	25	26	SMD 0.38 lower (0.96 lower to 0.19 higher)	⊕⊕OO LOW
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	6	9	SMD 0.72 lower (1.8 lower to 0.35 higher)	⊕⊕OO LOW

[1] Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.
[2] Substantial and significant heterogeneity.

CBT delivered via parents compared with CBT via parents

Quality assessment							No. of patients		Effect	Quality
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	CBT via parents	Relative (95% CI)	
2	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	19	21	SMD 0.01 lower (0.63 lower to 0.61 higher)	⊕⊕OO LOW
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	7	7	SMD 0.2 higher (0.85 lower to 1.25 higher)	⊕⊕OO LOW
2	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	19	20	SMD 0.21 higher (0.42 lower to 0.84 higher)	⊕⊕OO LOW
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	5	6	SMD 0.07 lower (1.25 lower to 1.12 higher)	⊕⊕OO LOW

[1] Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

Self-help compared with waitlist

Quality assessment							No. of patients		Effect		Quality
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Self-help	Waitlist	Relative (95% CI)	Absolute	
2	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	6/25 (24%)	2/21 (9.5%)	RR 0.85 (0.62 to 1.15)	14 fewer per 1000 (from 36 fewer to 14 more) 14 fewer per 1000 (from 35 fewer to 14 more)	⊕⊕OO LOW
3	Randomised trials	No serious risk of bias	Serious[2]	No serious indirectness	Serious[1]	None	32	30	SMD 0.47 lower (1.71 lower to 0.78 higher)		⊕⊕OO LOW
2	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	22	21	SMD 0.33 lower (0.94 lower to 0.27 higher)		⊕⊕OO LOW

[1] Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.
[2] Substantial and significant heterogeneity.