Appendix O: Clinical Evidence Profiles (GRADE)

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A.1 Risk markers associated with the development of behaviour that challenges

A.1.1 Auditory impairment

Table 1: Auditory impairment versus no auditory impairment as a risk factor for challenging behaviour

Quality asse	essment						Summary of	of Findings			
Participant s	Risk of bias	Inconsistency	Indirectnes s	Imprecisio n	Publicatio n bias	Overall quality of	Study event	rates (%)	Relative effect	Anticipated effects	absolute
(studies) Follow up						evidence	With no impairmen t	With auditory impairmen t	(95% CI)	Risk with no impairmen t	Risk difference with auditory impairmen t (95% CI)
All aggressi	on (phys	sical, verbal and	destructive)	(assessed with	ith: Validated	l questionnaire)				
1938 (2 studies)	no seriou s risk of bias	serious1	no serious indirectnes s	no serious imprecisio n	undetecte d	⊕⊖⊖⊖ VERY LOW1 due to inconsistency	380/1628 (23.3%)	35/310 (11.3%)	OR 0.97 (0.42 to 2.23)	233 per 1000	5 fewer per 1000 (from 120 fewer to 171 more)
Self-injury (assessed	d with: Validate	d questionnai	ire)							
2086 (3 studies)	no seriou s risk of bias	serious1	no serious indirectnes s	no serious imprecisio n	undetecte d	⊕⊖⊖⊖ VERY LOW1 due to inconsistency	419/1770 (23.7%)	37/316 (11.7%)	OR 1.05 (0.49 to 2.29)	237 per 1000	9 more per 1000 (from 105 fewer to 179 more)
Stereotypy	(assesse	d with: Validate	d questionna	ire)							
915 (1 study)	no seriou s risk of bias	no serious inconsistency	no serious indirectnes s	serious2	undetecte d	⊕⊖⊖⊖ VERY LOW2 due to imprecision	362/881 (41.1%)	16/34 (47.1%)	OR 1.27 (0.64 to 2.53)	411 per 1000	59 more per 1000 (from 102 fewer to 227 more)
1 I2 > 40%											

Quality assessment

Summary of Findings

2 Optimal information size not met; single study

A.2 Autism diagnosis

 Table 2: Autism diagnosis versus no autism diagnosis as a risk factor for challenging behaviour

Quality ass	essment						Summary	of Findings	5		
Participant s	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study ever	nt rates (%)	Relative effect	Anticipated effects	labsolute
(studies) Follow up							With no autism diagnosis	With autism diagnosis	(95% CI)	Risk with no autism diagnosis	Risk difference with autism diagnosis (95% CI)
All aggress	ion (phys	ical, verbal and	destructive) (a	assessed with	n: Validated o	questionnaires, i	nterviews a	nd medical	records)		
1938 (2 studies)	no seriou s risk of bias	serious1	no serious indirectness	no serious imprecision	undetecte d	⊕⊖⊖⊖ VERY LOW1 due to inconsistency	337/1718 (19.6%)	78/220 (35.5%)	OR 1.76 (1.17 to 2.65)	196 per 1000	104 more per 1000 (from 26 more to 197 more)
Destruction	of prope	rty (assessed w	ith: Questionr	naire and inter	rviews with b	oth service use	r and carer)				
2376 (2 studies)	no seriou s risk of bias	very serious2	no serious indirectness	no serious imprecision	undetecte d	 ⊕⊖⊖⊖ VERY LOW2,3 due to inconsistency, large effect 	121/1285 (9.4%)	279/1091 (25.6%)	OR 5.6 (1.39 to 22.56)	94 per 1000	274 more per 1000 (from 32 more to 607 more)
Physical ag	gression	(assessed with	Validated que	estionnaires,	interviews ar	nd medical recor	ds)				
5637 (4 studies)	no seriou s risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	undetecte d	⊕⊕⊕⊝ MODERATE3 due to large effect	712/4468 (15.9%)	357/1169 (30.5%)	RR 2.80 (1.98 to 3.98)	159 per 1000	287 more per 1000 (from 156 more to

Quality ass	essment			Summary of Findings									
											475 more)		
Self-injury (assessed with: Validated questionnaires and interviews with both service user and carer)													
4338 (5 studies)	no seriou s risk of bias	very serious2	no serious indirectness	no serious imprecision	undetecte d	 ⊕⊖⊖ VERY LOW2,3 due to inconsistency, large effect 	416/3015 (13.8%)	390/1323 (29.5%)	OR 3.11 (1.81 to 5.35)	138 per 1000	194 more per 1000 (from 87 more to 323 more)		
1 I2 > 40% 2 I2 > 75% 3 RR >2													

A.2.1 Degree of learning disability

Table 3: Mild/moderate learning disability versus severe/profound learning disability as a risk factor for challenging behaviour

Quality ass	essmen	t					Summary of Findings					
Participant s	Risk of	Inconsistenc y	Indirectne ss	Imprecisio n	Publicatio n bias	Overall quality of	Study event	Study event rates (%)		Anticipated absolute effects		
(studies) Follow up	bias					evidence	With Mild/ moderate LD	With Severe/profoun d LD	(95% C I)	Risk with Mild/ moderat e LD	Risk difference with Severe/profoun d LD (95% CI)	
All aggress	ion (phy	/sical, verbal a	and destructi	ve) (assesse	d with: Vali	dated questior	nnaires)					
1918 (2 studies)	no serio us risk of bias	very serious1	no serious indirectnes s	no serious imprecisio n	undetecte d	⊕⊖⊖⊖ VERY LOW1 due to inconsistenc y	300/1398 (21.5%)	111/520 (21.3%)	OR 1.70 (0.81 to 3.57)	215 per 1000	103 more per 1000 (from 33 fewer to 279 more)	
Challenging	g behavi	iour (global) (a	ssessed wit	h: Survey)								
822	no	no serious	no serious	serious2	undetecte	$\oplus \oplus \ominus \ominus$	40/604	51/218	OR	66 per	168 more per	

Quality ass	sessmen	it					Summary of	of Findings			
(1 study)	serio us risk of bias	inconsistenc y	indirectnes s		d	LOW2,3 due to imprecision, large effect	(6.6%)	(23.4%)	4.31 (2.75 to 6.74)	1000	1000 (from 97 more to 257 more)
Destruction	n of prop	perty (assesse	d with: Valid	ated questic	onnaire)						
3160 (1 study) 12 months	no serio us risk of bias	no serious inconsistenc y	no serious indirectnes s	serious2	undetecte d	 ⊕⊖⊖ VERY LOW2 due to imprecision 	496/2165 (22.9%)	259/995 (26%)	OR 1.18 (1 to 1.41)	229 per 1000	31 more per 1000 (from 0 more to 66 more)
Inappropria	ate sexu	al behaviour (assessed wit	h: Validated	questionna	lire)					
3160 (1 study) 12 months	no serio us risk of bias	no serious inconsistenc y	no serious indirectnes s	serious2	undetecte d	 ⊕⊖⊖ VERY LOW2 due to imprecision 	211/2165 (9.7%)	99/995 (9.9%)	OR 1.02 (0.8 to 1.32)	97 per 1000	2 more per 1000 (from 18 fewer to 27 more)
Physical ag	ggressio	on - inpatient s	etting (asses	sed with: Su	urvey)						
11139 (1 study)	no serio us risk of bias	no serious inconsistenc y	serious4	serious2	undetecte d	 ⊕⊖⊖ VERY LOW2,4 due to indirectness, imprecision 	731/2485 (29.4%)	1885/8654 (21.8%)	OR 0.67 (0.6 to 0.74)	294 per 1000	76 fewer per 1000 (from 58 fewer to 94 fewer)
Physical ag	ggressio	on - mixed sett	ing (assesse	d with: Valid	lated questi	onnaires, inter	views, obser	vations and med	dical recor	ds)	
43864 (6 studies)	no serio us risk of bias	very serious1	no serious indirectnes s	no serious imprecisio n	undetecte d	⊕⊖⊖⊖ VERY LOW1 due to inconsistenc y	2831/2079 4 (13.6%)	4189/23070 (18.2%)	OR 1.76 (1.4 to 2.2)	136 per 1000	81 more per 1000 (from 45 more to 121 more)
Self-injury	(assess	ed with: Valida	ated questior	nnaires, surv	veys and me	dical records)					
85888 (12 studies)	no serio us	very serious1	no serious indirectnes s	no serious imprecisio	undetecte d	⊕⊖⊝⊖ VERY LOW1,3	2144/4081 1 (5.3%)	7584/45077 (16.8%)	OR 3.75 (2.62 to	53 per 1000	120 more per 1000 (from 74 more

Quality ass	essmen	ıt					Summary of Findings					
0 to 36 months	risk of bias			n		due to inconsistenc y, large effect			5.38)		to 177 more)	
Stereotypy	(assess	ed with: Valid	ated questio	nnaires and	surveys)							
23946 (4 studies)	no serio us risk of bias	very serious1	no serious indirectnes s	no serious imprecisio n	undetecte d	⊕⊖⊖⊖ VERY LOW1,3 due to inconsistenc y, large effect	1153/1784 7 (6.5%)	2740/6099 (44.9%)	OR 6.38 (1.42 to 28.65)	65 per 1000	241 more per 1000 (from 25 more to 600 more)	
Verbal agg	ression	(assessed wit	h: Validated	questionnair	.е)							
3160 (1 study)	no serio us risk of bias	no serious inconsistenc y	no serious indirectnes s	serious2	undetecte d	 ⊕⊖⊖ VERY LOW2 due to imprecision 	896/2165 (41.4%)	293/995 (29.4%)	OR 0.59 (0.5 to 0.69)	414 per 1000	120 fewer per 1000 (from 86 fewer to 153 fewer)	
3 RR > 2		n size not met; / to review popu		isk inpatient								

A.2.2 Expressive communication difficulties

 Table 4: Expressive communication difficulties versus no expressive communication difficulties as a risk factor for challenging behaviour

Quality as	sessmen	t			Summary of Findings						
Participan	Risk of	Inconsisten	Indirectne	Imprecisi	Publicati	Overall	Study event ra	tes (%)	Relativ	Anticipated ab	solute effects
ts (studies) Follow up	bias	су	SS	on	on bias	quality of evidence	With no expressive communicati	With expressive communicati	e effect (95%	Risk with no expressive communicati	Risk difference with

Quality as	sessmen	t					Summary of I	Findings			
							on difficulties	on difficulties	CI)	on difficulties	expressive communicati on difficulties (95% CI)
All aggres	sion (phy	/sical, verbal a	and destruct	ive) (asses	sed with: Va	alidated quest	ionnaire)				
1936 (2 studies)	no seriou s risk of bias	no serious inconsisten cy	no serious indirectne ss	no serious imprecisi on	undetect ed	⊕⊕⊝⊝ LOW	300/1310 (22.9%)	115/626 (18.4%)	OR 1.41 (1.08 to 1.86)	229 per 1000	66 more per 1000 (from 14 more to 127 more)
Physical a	aggressio	n- adult popu	lation (asses	ssed with: C	Questionnai	re)					
3662 (1 study)	seriou s1	no serious inconsisten cy	no serious indirectne ss	serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	784/2994 (26.2%)	250/668 (37.4%)	OR 1.69 (1.41 to 2.01)	262 per 1000	113 more per 1000 (from 72 more to 154 more)
Physical a	aggressio	n- mixed pop	ulation (asse	essed with:	Non-validat	ted questionna	aire)				
211 (1 study)	seriou s3	no serious inconsisten cy	no serious indirectne ss	serious2	undetect ed	⊕⊕⊖⊖ LOW2,3,4 due to risk of bias, imprecision, large effect	52/166 (31.3%)	2/45 (4.4%)	OR 0.10 (0.02 to 0.44)	313 per 1000	270 fewer per 1000 (from 146 fewer to 304 fewer)
Self injury	(assesse	ed with: Ques	tionnaires, ii	nterviews a	nd formal a	ssessments)					
7502 (9 studies) 0 to 3 years	no seriou s risk of bias	very serious5	no serious indirectne ss	no serious imprecisi on	undetect ed	⊕⊖⊖⊖ VERY LOW5,6 due to inconsisten cy, large effect	821/5630 (14.6%)	566/1872 (30.2%)	OR 2.93 (1.8 to 4.78)	146 per 1000	188 more per 1000 (from 89 more to 304 more)

Quality as:	sessmen	t					Summary of Findings					
Stereotypy (assessed with: Validated questionnaire)												
915 (1 study)	no seriou s risk of bias	no serious inconsisten cy	no serious indirectne ss	serious2	undetect ed	 ⊕⊖⊖ VERY LOW2 due to imprecision 	290/769 (37.7%)	88/146 (60.3%)	OR 2.51 (1.74 to 3.6)	377 per 1000	226 more per 1000 (from 136 more to 308 more)	
2 Optimal in	nformation naire for r	cklist for risk ar n size not met; isk and outcon	single study		alidated							

A.2.4 Receptive communication difficulties

 Table 5: Receptive communication difficulties versus no receptive communication difficulties as a risk factor for challenging behaviour

Quality as	sessme	nt					Summary of Findings						
Participan ts (studies) Follow up	Risk of bias	Inconsisten cy	Indirectne ss	Imprecisi on	Publicati on bias	Overall quality of evidence	Study event ra With no receptive communicati	With receptive communicati	Relativ e effect (95% CI)	Anticipated abs Risk with no receptive communicati	Risk difference with		
							on difficulties	on difficulties		on difficulties	receptive communicati on difficulties (95% CI)		
Self-injury	(assess	sed with: Que	stionnaire a	nd interview	')								
1321 (3 studies)	no serio us	no serious inconsisten cy	no serious indirectne ss	no serious imprecisi	undetect ed	⊕⊕⊕⊝ MODERAT E1	148/1098 (13.5%)	82/223 (36.8%)	OR 3.46 (2.5 to	135 per 1000	215 more per 1000 (from 146		

Quality as	ssessment			Summary of F	indings		
0 to 3 years	risk of bias	on	due to large effect		4.79)	more to 293 more)
1 RR > 2							

A.2.5 Gender

Table 6: Male gender versus female gender as a risk factor for challenging behaviour

Quality asse	essment						Summary	of Findings			
Participant s	Risk of bias	Inconsistency	Indirectness	Imprecisio n	Publicatio n bias	Overall quality of	Study even	t rates (%)	Relative effect	Anticipated effects	absolute
(studies) Follow up						evidence	With female gender	With male gender	(95% CI)	Risk with female gender	Risk difference with male gender (95% CI)
All aggressi	on (phys	ical, verbal and	destructive) (assessed wit	h: Validated	questionnaire a	and observa	tion)			
2046 (3 studies)	no seriou s risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	undetecte d	⊕⊕⊝⊝ LOW	237/898 (26.4%)	238/1148 (20.7%)	OR 0.63 (0.51 to 0.79)	264 per 1000	80 fewer per 1000 (from 43 fewer to 109 fewer)
Challenging	behavio	ur (global) (ass	essed with: Va	alidated surve	ey)						
816 (1 study)	no seriou s risk of bias	no serious inconsistency	no serious indirectness	serious1	undetecte d	⊕⊖⊖⊖ VERY LOW1 due to imprecision	34/370 (9.2%)	56/446 (12.6%)	OR 1.42 (0.9 to 2.23)	92 per 1000	34 more per 1000 (from 8 fewer to 92 more)
Destruction	of prope	rty (assessed v	vith: Validated	questionnair	.е)						
3461 (2 studies)	no seriou	no serious inconsistency	no serious indirectness	no serious imprecision	undetecte d	⊕⊕⊝⊝ LOW	0/3461 (0%)2	-2	Not estimabl	See comment	-

0 to 12 s ris months of bi						Carmany	of Findings			
								е	2	
Inappropriate sex	kual behaviour	assessed with: C	Questionnaire							
3160no(1 study)serie12 monthss risof bi	k	no serious cy indirectness	serious1	undetecte d	⊕⊖⊖⊖ VERY LOW1 due to imprecision	116/1527 (7.6%)	194/1633 (11.9%)	OR 1.64 (1.29 to 2.09)	76 per 1000	43 more per 1000 (from 20 more to 71 more)
Physical aggress	sion (assessed v	vith: Validated qu	uestionnaires,	, interviews,	observations ar	nd medical r	ecords)			
6925no(5 studies)serio0 to 12s rismonthsof bi	k	no serious indirectness	no serious imprecision	undetecte d	⊕⊖⊖⊖ VERY LOW3 due to inconsistency	0/6925 (0%)2	-2	Not estimabl e	See comment 2	-
Self-injury - mixe	d settings (ass	ssed with: Ques	tionnaire and	survey)						
6174no(6 studies)serie0 to 12s rismonthsof bit	k	no serious cy indirectness	no serious imprecision	undetecte d	⊕⊕⊝⊝ LOW	827/2820 (29.3%)	879/3354 (26.2%)	OR 0.81 (0.69 to 0.96)	293 per 1000	42 fewer per 1000 (from 8 fewer to 71 fewer)
Self-injury- inpati	ient setting (ass	essed with: Non	validated que	estionnaire, s	survey and inter	view)				
18227no(5 studies)serio0 to 3s risyearsof bit	sk	s4 no serious indirectness	no serious imprecision	undetecte d	⊕⊖⊖⊖ VERY LOW4 due to inconsistency	1008/824 6 (12.2%)	1220/998 1 (12.2%)	OR 0.97 (0.76 to 1.23)	122 per 1000	3 fewer per 1000 (from 27 fewer to 24 more)
Stereotypy (asse	ssed with: Valio	ated questionna	ire)							
915 no (1 study) seric s ris of bi	k	no serious cy indirectness	serious1	undetecte d	⊕⊖⊖⊖ VERY LOW1 due to imprecision	169/411 (41.1%)	209/504 (41.5%)	RR 1.01 (0.86 to 1.18)	411 per 1000	4 more per 1000 (from 58 fewer to 74 more)
Verbal aggressio	n (assessed wi	h: Validated que	stionnaire)							
3461 no	no serious	no serious	no serious	undetecte	See	0/3461	-2	Not	See	-

Quality asse	essment			Summary of Findings							
(2 studies) 0 to 12 months	seriou s risk of bias	inconsistency	indirectness	imprecision	d	comment	(0%)2		estimabl e	comment 2	
1 Optimal inf 2 N/A; Gener 3 I2 > 40% 4 I2 > 75%		size not met; sin e variance	gle study								

A.2.6 Mental health needs

Table 7: Mental health needs versus no mental health needs as a risk factor for challenging behaviour

Quality asso	essment						Summary of	f Findings			
Participant s	Risk of bias	Inconsistency	Indirectnes s	Imprecisio n	Publicatio n bias	Overall quality of	Study event	rates (%)	Relative effect	Anticipated effects	absolute
(studies) Follow up						evidence	With no mental health needs	With mental health needs	(95% CI)	Risk with no mental health needs	Risk difference with mental health needs (95% CI)
All aggress	ion (phys	sical, verbal and	destructive)	(assessed wi	th: Validated	questionnaire)					
1938 (2 studies)	no seriou s risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	undetecte d	⊕⊕⊝⊝ LOW	377/1837 (20.5%)	38/101 (37.6%)	OR 2.03 (1.3 to 3.15)	205 per 1000	139 more per 1000 (from 46 more to 243 more)
Destruction	of prope	erty (assessed v	with: Validated	l questionnai	re and surve	у)					
30874 (2 studies)	no seriou s risk	very serious1	no serious indirectness	no serious imprecision	undetecte d	⊕⊝⊝⊖ VERY LOW1 due to	0/30874 (0%)2	-2	Not estimabl e	See comment 2	-

Quality asse	essment						Summary of	Findings			
	of bias					inconsistency					
Physical ag	gression	(assessed with	: Validated qu	estionnaire a	and survey)						
30874 (2 studies)	no seriou s risk of bias	very serious1	no serious indirectness	no serious imprecision	undetecte d	⊕⊖⊖⊖ VERY LOW1 due to inconsistency	0/30874 (0%)2	-2	Not estimabl e	See comment 2	-
Self-injury (assessed	d with: Validated	d questionnai	res and surve	ey)						
32516 (3 studies)	no seriou s risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	undetecte d	⊕⊕⊝⊝ LOW	2690/28860 (9.3%)	450/365 6 (12.3%)	OR 1.4 (1.26 to 1.56)	93 per 1000	33 more per 1000 (from 21 more to 45 more)
Stereotypy	(assesse	d with: Validate	d questionnai	re and surve	y)						
31493 (2 studies)	no seriou s risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	undetecte d	⊕⊕⊝⊝ LOW	1970/27876 (7.1%)	293/361 7 (8.1%)	OR 1.26 (1.1 to 1.43)	71 per 1000	17 more per 1000 (from 7 more to 27 more)
Verbal aggr	ession (a	ssessed with:	/alidated ques	stionnaire and	d survey)						
30874 (2 studies)	no seriou s risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	undetecte d	⊕⊕⊕⊝ MODERATE3 due to large effect	0/30874 (0%)2	-2	Not estimabl e	See comment 2	-
1 I2 > 75% 2 N/A; Gene 3 RR > 2	ric inverse	e variance									

A.2.7 Mobility impairment

Table 8: Mobility impairment versus no mobility impairment as a risk factor for challenging behaviour

Quality assessment	Summary of Findings
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Quality ass	sessment						Summary of	of Findings			
Participant s	Risk of bias	Inconsistency	Indirectness	Imprecisio n	Publicatio n bias	Overall quality of	Study event	rates (%)	Relative effect	Anticipated effects	absolute
(studies) Follow up						evidence	With no impairmen t	With mobility impairment	(95% CI)	Risk with no impairmen t	Risk difference with mobility impairment (95% CI)
All aggress	sion (phys	ical, verbal and	l destructive) ((assessed w	ith: Validated	questionnair	e)				
1023 (1 study)	no seriou s risk of bias	no serious inconsistency	no serious indirectness	serious1	undetecte d	⊕⊖⊖⊖ VERY LOW1 due to imprecision	78/775 (10.1%)	22/248 (8.9%)	OR 0.87 (0.53 to 1.43)	101 per 1000	12 fewer per 1000 (from 45 fewer to 37 more)
Self-injury-	adult pop	oulation (assess	sed with: Valio	lated questic	onnaire)						
1023 (1 study)	no seriou s risk of bias	no serious inconsistency	no serious indirectness	serious1	undetecte d	⊕⊖⊖⊖ VERY LOW1 due to imprecision	78/775 (10.1%)	22/248 (8.9%)	OR 0.87 (0.53 to 1.43)	101 per 1000	12 fewer per 1000 (from 45 fewer to 37 more)
Self-injury-	children	and young peo	ple population	(assessed v	with: Validate	d questionna	ire)				
147 (1 study)	no seriou s risk of bias	no serious inconsistency	no serious indirectness	serious1	undetecte d	⊕⊖⊖⊖ VERY LOW1 due to imprecision	64/134 (47.8%)	9/13 (69.2%)	OR 2.46 (0.72 to 8.38)	478 per 1000	215 more per 1000 (from 81 fewer to 407 more)

A.2.8 Visual impairment

 Table 9: Visual impairment versus no visual impairment as a risk factor for challenging behaviour

Quality assessment

Quality asse	essment						Summary o	of Findings			
Participant s	Risk of bias	Inconsistency	Indirectness	Imprecisio n	Publicatio n bias	Overall quality of	Study event	rates (%)	Relative effect	Anticipated effects	absolute
(studies) Follow up						evidence	With No impairmen t	With Visual impairmen t	(95% CI)	Risk with No impairmen t	Risk difference with Visual impairment (95% CI)
All aggressi	on (phys	ical, verbal and	destructive)	assessed wit	th: Validated	questionnair	e)				
1938 (2 studies)	no seriou s risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	undetecte d	⊕⊕⊝⊝ LOW	349/1422 (24.5%)	66/516 (12.8%)	OR 1.22 (0.78 to 1.92)	245 per 1000	39 more per 1000 (from 43 fewer to 139 more)
Self-injury (a	assessed	d with: Validated	d questionnaiı	re)							
2086 (3 studies)	no seriou s risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	undetecte d	⊕⊕⊝⊝ LOW	384/1564 (24.6%)	73/522 (14%)	OR 1.45 (1.02 to 2.06)	246 per 1000	75 more per 1000 (from 4 more to 156 more)
Stereotypy (assesse	d with: Validate	d questionnai	re)							
915 (1 study)	no seriou s risk of bias	no serious inconsistency	no serious indirectness	serious1	undetecte d	 ⊕⊖⊖ VERY LOW1 due to imprecision 	356/880 (40.5%)	22/35 (62.9%)	OR 2.49 (1.24 to 5.01)	405 per 1000	224 more per 1000 (from 53 more to 368 more)
1 Optimal inf	ormation	size; single stud	у								

A.3 Interventions aimed at the prevention of behaviour that challenges

A.3.1 Educational intervention versus attention control

 Table 10: Learning Experiences and Alternative Program for Pre-schoolers and Their Parents (LEAP) - full replication condition versus manual-only attention control

Quality ass	essment						Summa	ry of Findings	5		
Participant s	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Publicatio n bias	Overall quality of	Study ev	rent rates (%)	Relative effect	Anticipat effects	ed absolute
(studies) Follow up						evidence	With attentio n control	With educationa I interventio n	(95% CI)	Risk with attentio n control	Risk difference with educational intervention (95% CI)
Behaviour	that challe	enges (severity)	- post-treatm	ent (measure	ed with: Cha	nge score1; Be	etter indic	ated by lowe	r values)		
294 (1 study)	serious 2	no serious inconsistenc y	serious3	serious4	undetecte d	⊕⊖⊖⊖ VERY LOW2,3,4 due to risk of bias, indirectness , imprecision	117	177	-		The mean behaviour that challenges (severity) - post- treatment in the intervention groups was 0.19 standard deviations lower (0.42 lower to 0.04 higher)
Adaptive fu	Inctioning	(social) - post-	treatment (Be	tter indicated	d by lower va	alues)					
294 (1 study)	serious 2	no serious inconsistenc y	serious3	serious4	undetecte d	⊕⊖⊖⊖ VERY LOW2,3,4 due to risk of bias, indirectness ,	117	177	-		The mean adaptive functioning (social) - post- treatment in the intervention groups was

Quality ass	essment						Summar	y of Findings	5	
						imprecision				0.76 standard deviations higher (0.52 to 1 higher)
Adaptive fu	nctioning	(communicatio	on) - post-trea	tment (Better	indicated by	y lower values)			
294 (1 study)	serious 2	no serious inconsistenc y	serious3	serious4	undetecte d	⊕⊖⊖ VERY LOW2,3,4 due to risk of bias, indirectness , imprecision	117	177	-	The mean adaptive functioning (communication) - post-treatment in the intervention groups was 0.94 standard deviations higher (0.7 to 1.19 higher)

1 Due to significant baseline differences, standard deviation of change and estimates of mean change were derived using initial and final mean values and utilising r = 0.5. Sensitivity analyses were used to explore the impact of altering assumptions about the calculation of the effect size, but this resulted in no change to conclusions.

2 Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect

A.3.2 Home-based EBI versus centre-based EBI

Table 11: Home-based Building Blocks programme versus centre-based Building Blocks programme

Quality ass	essment						Summary	of Findings			
Participant	Risk of	Inconsistenc	Indirectnes	Imprecisio	Publicatio	Overall	Study even	t rates (%)	Relativ	Anticipated	absolute effects
s (studies) Follow up	bias	У	S	n	n bias	quality of evidence	With centre- based early	With home- based early	e effect (95% C I)	Risk with centre- based early	Risk difference with home- based early behavioural

Quality ass	sessment						Summary of	of Findings			
							behaviour al interventio n	behaviour al interventio n		behaviour al interventio n	intervention (95% CI)
Behaviour	that challe	enges (severity	/) - post-treat	ment (Better	indicated by	/ lower value	es)				
44 (1 study)	serious 1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetecte d	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecisio n	22	22	-		The mean behaviour that challenges (severity) - post-treatment in the intervention groups was 0.11 standard deviations lower (0.7 lower to 0.48 higher)
	unctioning	g (social) - post	t-treatment (E	Setter indicat							
56 (1 study)	serious 1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetecte d	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecisio n	29	27	-		The mean adaptive functioning (social) - post- treatment in the intervention groups was 0.63 standard deviations lower (1.17 to 0.09 lower)
Adaptive fu	unctioning	g (communicat	ion) - post-tre	atment (Bett	er indicated	by lower va	lues)				
55 (1 study)	serious 1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetecte d	 ⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, 	29	26	-		The mean adaptive functioning (communication) - post-

Quality assessment			Summary of Findings		
		imprecisio n			treatment in the intervention groups was 0.46 standard deviations lower (1 lower to 0.07 higher)
1 Crucial limitation for one criterion or 2 Optimal information size not met; sm	some limitations for multiple criteria suffi nall, single study	icient to lowe	r ones confidence in the e	stimate of effect	

A.3.3 EIBI versus parent training

Table 12: EIBI (UCLA model) versus parent training

Quality asse	essment						Summa	ry of F	indings		
Participant s	Risk of bias	Inconsistency	Indirectnes s	Imprecisio n	Publication bias	Overall quality of	Study ev rates (%)		Relative effect	Anticipate	ed absolute effects
(studies) Follow up						evidence	With parent training	Wit h EIB I	(95% CI)	Risk with parent training	Risk difference with EIBI (95% CI)
Behaviour t	hat challe	nges (severity)	- post-treatme	ent (measure	d with: Paren	t-rated; Better i	indicated	by lov	ver values)		
28 (1 study)	no serious risk of bias	no serious inconsistency	serious1	very serious2	undetected	⊕⊖⊖⊖ VERY LOW1,2 due to indirectness, imprecision	13	15	-		The mean behaviour that challenges (severity) - post- treatment in the intervention groups was 0.36 standard deviations lower (1.1 lower to 0.39 higher)

Quality asse	essment						Summa	ry of F	indings	
28 (1 study)	no serious risk of bias	no serious inconsistency	serious1	very serious2	undetected	⊕⊖⊖ VERY LOW1,2 due to indirectness, imprecision	13	15	-	The mean behaviour that challenges (severity) - post- treatment in the intervention groups was 0.47 standard deviations higher (0.28 lower to 1.23 higher)
Adaptive fu	nctioning	(communicatio	n) - post-treat	ment (Better	indicated by	lower values)				
28 (1 study)	no serious risk of bias	no serious inconsistency	serious1	very serious2	undetected	⊕⊖⊖ VERY LOW1,2 due to indirectness, imprecision	13	15	-	The mean adaptive functioning (communication) - post-treatment in the intervention groups was 0.63 standard deviations higher (0.13 lower to 1.39 higher)
Adaptive fu	nctioning	(global) - post-t	treatment (Bet	ter indicated	by lower val	ues)				
28 (1 study)	no serious risk of bias	no serious inconsistency	serious1	very serious2	undetected	⊕⊖⊖⊖ VERY LOW1,2 due to indirectness, imprecision	13	15	-	The mean adaptive functioning (global) - post-treatment in the intervention groups was 0.11 standard deviations higher (0.64 lower to 0.85 higher)

2 Optimal information size not met; small, single study

High supervision EIBI versus low supervision EIBI A.3.4

Table 13: High supervision EIBI (clinic-directed UCLA model) versus low supervision EIBI (parent-directed UCLA model)

Quality ass	essment						Summary of	of Findings			
Participant	Risk of	Inconsistenc	Indirectnes	Imprecisio	Publicatio	Overall	Study event	t rates (%)	Relativ	Anticipated	absolute effects
s (studies) Follow up	bias	У	S	n	n bias	quality of evidence	With low supervisio n EIBI (parent- directed)	With high supervisio n EIBI (clinic- directed)	e effect (95% C I)	Risk with low supervisio n EIBI (parent- directed)	Risk difference with high supervision EIBI (clinic- directed) (95% CI)
Adaptive fu	Inctioning	(communicati	ion) -post-tre	atment (Bett	er indicated	by lower valu	es)				
23 (1 study)	serious 1	no serious inconsistenc y	serious2	very serious3	undetecte d	⊕⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectnes s, imprecision	10	13	-		The mean adaptive functioning (communication) -post- treatment in the intervention groups was 0.25 standard deviations lower (1.08 lower to 0.57 higher)

2 Applicability concerns: autism population; no information reported concerning learning disability 3 Optimal information size not met; small, single study

A.3.5 Parent training versus any control

Table 14: Parent training (plus centre based EBI) versus treatment as usual (centre-based EBI)

Quality asse	essment						Summa	ary of Fin	dings		
Participant s	Risk of bias	Inconsistency	Indirectness	Imprecisio n	Publication bias	Overall quality of	Study e rates (%		Relative effect	Anticipa	ted absolute effects
(studies) Follow up						evidence	With contro I	With parent trainin g	(95% CI)	Risk with contro I	Risk difference with parent training (95% CI)
Behaviour t	hat challen	ges (severity) -	post-treatmen	t (Better indi	cated by low	er values)					
57 (1 study)	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊝ LOW1 due to imprecision	28	29	-		The mean behaviour that challenges (severity) - post- treatment in the intervention groups was 0.4 standard deviations lower (0.93 lower to 0.12 higher)
Behaviour t	hat challen	ges (severity) -	follow up (Bet	ter indicated	by lower value	ues)					
117 (2 studies) 26 to 52 weeks	serious2	no serious inconsistency	no serious indirectness	serious3	undetecte d	⊕⊕⊖⊖ LOW2,3 due to risk of bias, imprecision	58	59	-		The mean behaviour that challenges (severity) - follow up in the intervention groups was 0.37 standard deviations lower (0.79 lower to 0.05 higher)
Adaptive fu	nctioning (global) - post-tr	eatment (Bette	er indicated b	y lower value	es)					
58 (1 study)	no serious	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊝⊝ LOW1	28	30	-		The mean adaptive functioning (global) -

Quality asse	essment						Summa	ary of Fin	dings	
	risk of bias					due to imprecision				post-treatment in the intervention groups was 0.25 standard deviations higher (0.27 lower to 0.77 higher)
Adaptive fu	nctioning (global) - follow-	up (Better indi	icated by low	er values)					
119 (2 studies) 26 to 52 weeks	serious2	no serious inconsistency	no serious indirectness	serious3	undetecte d	⊕⊕⊖⊖ LOW2,3 due to risk of bias, imprecision	56	63	-	The mean adaptive functioning (global) - follow-up in the intervention groups was 0.52 standard deviations higher (0.15 to 0.88 higher)
Adaptive fu	nctioning (communication) - follow-up (E	Better indicat	ed by lower v	/alues)				
68 (1 study) 26 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊝⊖ LOW1 due to imprecision	33	35	-	The mean adaptive functioning (communication) - follow-up in the intervention groups was 0.75 standard deviations higher (0.26 to 1.25 higher)

2 Most information is from studies at moderate risk of bias

3 Optimal information size not met

- A.4 Interventions aimed at reducing health risks and increasing understanding of physical illness in relation to the prevention or management of behaviour that challenges
- A.4.1 Hand-held health record versus treatment as usual

Table 15: Advocacy Skills Kit Diary or Personal Health Profile versus treatment as usual

Quality ass	essment						Summary	of Finding	js		
Participant s	Risk of bias	Inconsistency	Indirectness	Imprecisio n	Publication bias	Overall quality of	Study ever (%)	nt rates	Relative effect	Anticipated effects	absolute
(studies) Follow up						evidence	With treatment as usual	With hand- held health record	(95% CI)	Risk with treatment as usual	Risk difference with hand- held health record (95% CI)
Health pron	notion (blo	od pressure che	ecked)								
119 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊖⊖ LOW1 due to imprecision	32/68 (47.1%)	28/51 (54.9%)	RR 1.17 (0.82 to 1.66)	471 per 1000	80 more per 1000 (from 85 fewer to 311 more)
Health pron	notion (cor	nstipation invest	tigation)								
119 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊝⊝ LOW1 due to imprecision	1/68 (1.5%)	5/51 (9.8%)	RR 6.67 (0.8 to 55.33)	15 per 1000	83 more per 1000 (from 3 fewer to 799 more)
Health pron	notion (hea	aring test)									
119 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊖⊖ LOW1 due to imprecision	2/68 (2.9%)	3/51 (5.9%)	RR 2 (0.35 to 11.53)	29 per 1000	29 more per 1000 (from 19 fewer to 310 more)

Quality ass	sessment						Summary	of Finding	js		
Health pro	motion (visi	ion test)									
119 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊝⊖ LOW1 due to imprecision	4/68 (5.9%)	7/51 (13.7%)	RR 2.33 (0.72 to 7.55)	59 per 1000	78 more per 1000 (from 16 fewer to 385 more)
Health pro	motion (wei	ght measured)									
119 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊝⊖ LOW1 due to imprecision	17/68 (25%)	18/51 (35.3%)	RR 1.41 (0.81 to 2.46)	250 per 1000	102 more per 1000 (from 47 fewer to 365 more)
Health pro	motion (wei	ght manageme	nt plan)								
119 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊝⊖ LOW1 due to imprecision	12/68 (17.6%)	5/51 (9.8%)	RR 0.56 (0.21 to 1.48)	176 per 1000	78 fewer per 1000 (from 139 fewer to 85 more)
Health pro	motion (epi	lepsy review)									
119 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊝⊖ LOW1 due to imprecision	8/68 (11.8%)	11/51 (21.6%)	RR 1.83 (0.8 to 4.23)	118 per 1000	98 more per 1000 (from 24 fewer to 380 more)
Service use by higher va		e of health proble	ems (measured	with: Knowled	dge of Health	Problems and	Terminology	/ Checklist	(unvalidate	d measure);	Better indicated
66 (1 study)	serious2	no serious inconsistency	no serious indirectness	very serious1	undetecte d	 ⊕⊖⊖ VERY LOW1,2 due to risk of bias, imprecision 	32	34	-		The mean service user knowledge of health problems in the intervention groups was

Quality ass	essment						Summary	of Finding	js	
										0.32 standard deviations lower (0.81 lower to 0.16 higher)
Carer know indicated b			measured wit	h: Knowledge	e of Health P	roblems and 1	Ferminology	/ Checklis	t (unvalidated measu	ıre); Better
144 (1 study)	serious2	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	74	70	-	The mean carer knowledge of health problems in the intervention groups was 0 standard deviations higher (0.33 lower to 0.33 higher)
Carer satis	faction (Bet	tter indicated by	/ lower values)						
101 (1 study)	serious2	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	52	49	-	The mean carer satisfaction in the intervention groups was 0 standard deviations higher (0.39 lower to 0.39 higher)
Service use	er satisfacti	on (Better indic	ated by lower	values)						
36 (1 study)	serious2	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊝⊝⊖ VERY	20	16	-	The mean service user

Quality ass	essment						Summary	of Finding	IS		
						LOW1,2 due to risk of bias, imprecision					satisfaction in the intervention groups was 0.6 standard deviations higher (0.08 lower to 1.27 higher)
Premature of	death										
169 (1 study)	serious2	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	2/88 (2.3%)	5/81 (6.2%)	RR 2.72 (0.54 to 13.61)	23 per 1000	39 more per 1000 (from 10 fewer to 287 more)

2 Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect

A.4.2 Annual health check versus treatment as usual

Table 16: Comprehensive Health Assessment Program versus treatment as usual

Quality asse	essment				Summary of Findings						
s bi	Risk of bias	Inconsistency	Indirectness	Imprecisio n	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect	Anticipated absolute effects	
(studies) Follow up							With treatment as usual	With annual health check	(95% CI)	Risk with treatment as usual	Risk difference with annual health check (95% CI)

Health promotion (blood pressure checked)

Quality ass	essment						Summary	of Finding	S		
574 (2 studies) 52 weeks	no serious risk of bias	very serious1	no serious indirectness	serious2	undetecte d	⊕⊖⊖⊖ VERY LOW1,2 due to inconsistency, imprecision	131/287 (45.6%)	143/287 (49.8%)	RR 1.09 (0.92 to 1.30)	456 per 1000	41 more per 1000 (from 37 fewer to 137 more)
Health pron	notion (co	onstipation investion	stigation)								
121 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊕⊖ LOW3 due to imprecision	1/68 (1.5%)	4/53 (7.5%)	RR 5.13 (0.59 to 44.58)	15 per 1000	61 more per 1000 (from 6 fewer to 641 more)
Health pron	notion (he	earing test)									
574 (2 studies) 52 weeks	no serious risk of bias	serious4	no serious indirectness	serious2	undetecte d	⊕⊕⊖⊖ LOW2,4 due to inconsistency, imprecision	3/287 (1%)	42/287 (14.6%)	RR 12.22 (2.43 to 61.49)	10 per 1000	117 more per 1000 (from 15 more to 632 more)
Health pron	notion (vis	sion test)									
574 (2 studies) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	serious2	undetecte d	⊕⊕⊕⊖ MODERATE2 due to imprecision	16/287 (5.6%)	60/287 (20.9%)	RR 3.75 (2.21 to 6.36)	56 per 1000	153 more per 1000 (from 67 more to 299 more)
Health pron	notion (ac	uity corrected b	oy glasses)								
453 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊕⊖⊖ LOW3 due to imprecision	0/219 (0%)	3/234 (1.3%)	RR 6.55 (0.34 to 126.14)	0 per 1000	-
Health pron	notion (ot	oscopic examin	ation)								
453 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊕⊖⊖ LOW3 due to imprecision	50/219 (22.8%)	92/234 (39.3%)	RR 1.72 (1.29 to 2.3)	228 per 1000	164 more per 1000 (from 66 more to

Quality asse	essment						Summary	of Finding	IS		
											297 more)
Health prom	notion (we	eight measurem	ent)								
574 (2 studies) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	serious2	undetecte d	⊕⊕⊕⊖ MODERATE2 due to imprecision	53/287 (18.5%)	129/287 (44.9%)	RR 2.46 (1.87 to 3.23)	185 per 1000	270 more per 1000 (from 161 more to 412 more)
Health prom	notion (we	eight manageme	ent plan)								
574 (2 studies) 52 weeks	no serious risk of bias	serious4	no serious indirectness	serious2	undetecte d	⊕⊕⊖⊖ LOW2,4 due to inconsistency, imprecision	13/287 (4.5%)	22/287 (7.7%)	RR 2.32 (0.66 to 8.14)	45 per 1000	60 more per 1000 (from 15 fewer to 323 more)
Health prom	notion (ep	oilepsy review)									
121 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊕⊖⊖ LOW3 due to imprecision	8/68 (11.8%)	9/53 (17%)	RR 1.44 (0.6 to 3.49)	118 per 1000	52 more per 1000 (from 47 fewer to 293 more)
Identificatio	n of phys	sical health prob	olem (hearing l	oss)							
453 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊕⊝⊝ LOW3 due to imprecision	0/219 (0%)	15/234 (6.4%)	RR 29.02 (1.75 to 482.11)	0 per 1000	-
Identificatio	n of phys	sical health prob	olem (visual im	pairment)							
453 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊕⊝⊝ LOW3 due to imprecision	1/219 (0.46%)	7/234 (3%)	RR 6.55 (0.81 to 52.82)	5 per 1000	25 more per 1000 (from 1 fewer to 237 more)
Identificatio	n of phys	sical health prob	olem (obesity)								
453 (1 study)	no serious	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊕⊝⊖ LOW3	4/219 (1.8%)	17/234 (7.3%)	RR 3.98 (1.36 to	18 per 1000	54 more per 1000

Quality ass	essment						Summary	of Finding	S		
52 weeks	risk of bias					due to imprecision			11.64)		(from 7 more to 194 more)
Premature	death										
453 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊕⊝⊖ LOW3 due to imprecision	1/219 (0.46%)	1/234 (0.43%)	RR 0.94 (0.06 to 14.87)	5 per 1000	0 fewer per 1000 (from 4 fewer to 63 more)
1 I2 > 75% 2 Optimal in 3 Optimal in 4 I2 > 40%		size not met size not met; sm	all, single study								

A.4.3 Annual health check versus hand-held health record

Table 17: Comprehensive Health Assessment Program versus Advocacy Skills Kit Diary

Quality ass	essment						Summary of Findings				
Participant s	Risk of bias	Inconsistency	Indirectness	Imprecisio n	Publication bias	Overall quality of	Study event rates (%)		Relative effect	Anticipated absolute effects	
(studies) Follow up				evidence	With hand- held health record	With annual health check	(95% CI)	Risk with hand- held health record	Risk difference with annual health check (95% CI)		
Health pron	notion (blo	ood pressure ch	ecked)								
104 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetected	⊕⊕⊝⊖ LOW1 due to imprecision	28/51 (54.9%)	26/53 (49.1%)	RR 0.89 (0.62 to 1.29)	549 per 1000	60 fewer per 1000 (from 209 fewer to 159 more)

Quality ass	essment						Summary of Findings					
Health pror	notion (co	nstipation inves	tigation)									
104 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetected	⊕⊕⊝⊖ LOW1 due to imprecision	5/51 (9.8%)	4/53 (7.5%)	RR 0.77 (0.22 to 2.71)	98 per 1000	23 fewer per 1000 (from 76 fewer to 168 more)	
Health pror	notion (he	aring test)										
104 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetected	⊕⊕⊝⊖ LOW1 due to imprecision	3/51 (5.9%)	10/53 (18.9%)	RR 3.21 (0.94 to 10.99)	59 per 1000	130 more per 1000 (from 4 fewer to 588 more)	
Health pror	notion (vis	sion test)										
104 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetected	⊕⊕⊝⊝ LOW1 due to imprecision	7/51 (13.7%)	11/53 (20.8%)	RR 1.51 (0.64 to 3.60)	137 per 1000	70 more per 1000 (from 49 fewer to 357 more)	
Health pror	notion (we	ight measured)										
104 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetected	⊕⊕⊝⊖ LOW1 due to imprecision	18/51 (35.3%)	29/53 (54.7%)	RR 1.55 (0.99 to 2.42)	353 per 1000	194 more per 1000 (from 4 fewer to 501 more)	
Health pror	notion (we	ight manageme	nt plan)									
104 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetected	⊕⊕⊝⊝ LOW1 due to imprecision	5/51 (9.8%)	15/53 (28.3%)	RR 2.89 (1.13 to 7.36)	98 per 1000	185 more per 1000 (from 13 more to 624 more)	
Health pror	notion (ep	ilepsy review)										
104 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetected	⊕⊕⊝⊖ LOW1 due to imprecision	11/51 (21.6%)	9/53 (17%)	RR 0.79 (0.36 to 1.74)	216 per 1000	45 fewer per 1000 (from 138 fewer to 160	

Quality assessment				Summary	of Finding	IS	
							more)
1 Optimal information	size not met; sma	ll, single study					

A.4.4 Annual health check and hand-held health record versus treatment as usual

 Table 18: Comprehensive Health Assessment Program and Advocacy Skills Kit Diary versus treatment as usual

Quality asse	essment						Summary	of Findings			
Participant s	Risk of bias	Inconsistency	Indirectness	Imprecisio n	Publication bias	Overall quality of	Study ever	it rates (%)	Relative effect	Anticipated effects	absolute
(studies) Follow up						evidence	With treatment as usual	With annual health check + hand- held health record	(95% CI)	Risk with treatment as usual	Risk difference with annual health check + hand-held health record (95% CI)
Health prom	notion (blo	ood pressure ch	necked)								
138 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊝⊝ LOW1 due to imprecision	32/68 (47.1%)	46/70 (65.7%)	RR 1.4 (1.03 to 1.89)	471 per 1000	188 more per 1000 (from 14 more to 419 more)
Health prom	notion (co	nstipation inve	stigation)								
138 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊝⊖ LOW1 due to imprecision	1/68 (1.5%)	4/70 (5.7%)	RR 3.89 (0.45 to 33.89)	15 per 1000	42 more per 1000 (from 8 fewer to 484 more)
Health prom	notion (he	aring test)									
138 (1 study)	no serious	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊝⊝ LOW1	2/68 (2.9%)	10/70 (14.3%)	RR 4.86 (1.1 to	29 per 1000	114 more per 1000

Quality ass	essment						Summary	of Finding	S		
52 weeks	risk of bias					due to imprecision			21.36)		(from 3 more to 599 more)
Health pron	notion (vis	sion test)									
138 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊝⊖ LOW1 due to imprecision	4/68 (5.9%)	20/70 (28.6%)	RR 4.86 (1.75 to 13.47)	59 per 1000	227 more per 1000 (from 44 more to 734 more)
Health pron	notion (we	eight measured))								
138 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊝⊝ LOW1 due to imprecision	17/68 (25%)	41/70 (58.6%)	RR 2.34 (1.48 to 3.7)	250 per 1000	335 more per 1000 (from 120 more to 675 more)
Health pron	notion (we	eight manageme	ent plan)								
138 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊝⊝ LOW1 due to imprecision	12/68 (17.6%)	7/70 (10%)	RR 0.57 (0.24 to 1.35)	176 per 1000	76 fewer per 1000 (from 134 fewer to 62 more)
Health pron	notion (ep	ilepsy review)									
138 (1 study) 52 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious1	undetecte d	⊕⊕⊝⊝ LOW1 due to imprecision	8/68 (11.8%)	7/70 (10%)	RR 0.85 (0.33 to 2.22)	118 per 1000	18 fewer per 1000 (from 79 fewer to 144 more)

A.5 Environmental change interventions aimed at reducing and managing behaviour that challenges

A.5.1 Sensory intervention versus any control

Table 19: Multisensory room or vibroacoustic chair versus any control

Quality ass	essment						Summa	ary of Finding	S		
Participant s	Risk of bias	Inconsistency	Indirectness	Imprecisio n	Publication bias	Overall quality of	Study e (%)	event rates	Relative effect	Anticipa effects	ted absolute
(studies) Follow up		evidend aviour that challenges (global) - post-treatment (measured with: Change		evidence	With any contro I	With sensory intervention	(95% CI)	Risk with any contro I	Risk difference with sensory intervention (95% CI)		
Targeted be	haviour th	nat challenges (global) - post-	treatment (m	easured with	: Change sco	re1; Bett	er indicated b	oy lower va	lues)	
89 (1 study)	serious 2	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊖⊖ VERY LOW2,3 due to risk of bias, imprecision	41	48	-		The mean targeted behaviour that challenges (global) - post- treatment in the intervention groups was 1.69 standard deviations higher (1.2 to 2.18 higher)
Targeted be	haviour th	nat challenges (global) - follov	v-up (measur	ed with: Cha	nge score1; E	Better inc	licated by low	ver values)		
89 (1 study) 12 weeks	serious 2	no serious inconsistency	no serious indirectness	very serious3	undetecte d	 ⊕⊖⊖ VERY LOW2,3 due to risk of bias, 	41	48	-		The mean targeted behaviour that challenges (global) - follow-

Quality ass	essment						Summa	ary of Finding	s		
						imprecision					up in the intervention groups was 0.00 standard deviations higher (0.42 lower to 0.42 higher)
Targeted be	haviour th	nat challenges (self-injurious	behaviour, se	everity) - pos	t-treatment (B	Better inc	licated by low	er values)		
20 (1 study)	serious 2	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊖⊖ VERY LOW2,3 due to risk of bias, imprecision	10	10	-		The mean targeted behaviour that challenges (self- injurious behaviour, severity) - post- treatment in the intervention groups was 0.2 standard deviations lower (1.08 lower to 0.68 higher)
Targeted be	haviour th	nat challenges (self-injurious	behaviour, fr	equency) - po	ost-treatment	(Better i	ndicated by lo	ower values	5)	
20 (1 study)	serious 2	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊖⊖ VERY LOW2,3 due to risk of bias, imprecision	10	10	-		The mean targeted behaviour that challenges (self- injurious behaviour, frequency) - post- treatment in the intervention groups was 0.25 standard deviations lower (1.14 lower to

Quality ass	essment						Summ	ary of Finding	S		
											0.63 higher)
Targeted be	ehaviour th	nat challenges (stereotypical I	behaviour, se	everity) - post	t-treatment (B	etter ind	licated by low	er values)		
20 (1 study)	serious 2	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊖⊖ VERY LOW2,3 due to risk of bias, imprecision	10 (Detter i	10	-		The mean targeted behaviour that challenges (stereotypical behaviour, severity) - post- treatment in the intervention groups was 0.33 standard deviations higher (0.55 lower to 1.21 higher)
-		nat challenges (-	ower values		
20 (1 study)	serious 2	no serious inconsistency	no serious indirectness	very serious3	undetecte d	 ⊕⊖⊖ VERY LOW2,3 due to risk of bias, imprecision 	10	10	-		The mean targeted behaviour that challenges (stereotypical behaviour, frequency) - post- treatment in the intervention groups was 0.22 standard deviations lower (1.1 lower to 0.66 higher)
Targeted be	ehaviour th	nat challenges (aggressive/ de	estructive bel	haviour, seve	erity) - post-tr	eatment	(Better indica	ted by lowe	er values)	
20 (1 study)	serious 2	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊝⊝⊖ VERY LOW2,3	10	10	-		The mean targeted behaviour that

Quality ass	essment						Summa	ary of Finding	S		
		nat challenges (aggrossivo/ de		haviour from	due to risk of bias, imprecision				worvalu	challenges (aggressive/ destructive behaviour, severity) - post- treatment in the intervention groups was 0.15 standard deviations lower (1.03 lower to 0.72 higher)
										wer valu	
20 (1 study)	serious 2	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊖⊖⊖ VERY LOW2,3 due to risk of bias, imprecision	10	10	-		The mean targeted behaviour that challenges (aggressive/ destructive behaviour, frequency) - post- treatment in the intervention groups was 0.22 standard deviations lower (1.1 lower to 0.66 higher)
Adaptive fu	nctioning	- post-treatmen	t (measured w	ith: Change	score1; Bette	er indicated by	higher	values)			
89 (1 study)	serious 2	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊖⊖⊖ VERY LOW2,3 due to risk of bias, imprecision	41	48	-		The mean adaptive functioning - post- treatment in the intervention groups was 1.12 standard

Quality ass	essment						Summa	ary of Finding	S	
										deviations lower (1.57 to 0.67 lower)
Adaptive fu	nctioning	- follow-up (mea	asured with: C	hange score	1; Better indi	icated by high	er value	s)		
89 (1 study) 12 weeks	serious 2	no serious inconsistency	no serious indirectness	very serious3	undetecte d	⊕⊖⊖⊖ VERY LOW2,3 due to risk of bias, imprecision	41	48	-	The mean adaptive functioning - follow-up in the intervention groups was 0.48 standard deviations lower (0.9 to 0.05 lower)

1 Due to significant baseline differences, standard deviation of change and estimates of mean change were derived using initial and final mean values and utilising r = 0.5. Sensitivity analyses were used to explore the impact of altering assumptions about the calculation of the effect size, but this resulted in no change to conclusions.

2 Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect 3 Optimal information size not met; small, single study

A.5.2 Structured activity versus unstructured activity

Table 20: Special Olympics Sports Skill Instructional Program versus free play

Quality asso	essment						Summary of	Findings			
Participant s	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Publicatio n bias	Overall quality of	Study event i	ates (%)	Relative effect	Anticipated a effects	bsolute
(studies) Follow up						evidence	With unstructure d activity	With structure d activity	(95% CI)	Risk with unstructure d activity	Risk difference with structured activity (95% CI)

Targeted behaviour that challenges (severity) - post-treatment (measured with: Change score1; Better indicated by lower values)

Quality ass	essment						Summary of	Findings		
26 (1 study)	serious 2	no serious inconsistency	no serious indirectnes s	very serious3	undetecte d	⊕⊖⊖ VERY LOW2,3 due to risk of bias, imprecisio n	13	13	-	The mean targeted behaviour that challenges (severity) - post- treatment in the interventio n groups was 0.87 standard deviations lower (1.68 to 0.06 lower)
Targeted be	ehaviour t	hat challenges	(severity) - fo	llow-up (mea	sured with: (Change score	e1; Better indi	cated by low	ver values	
26 (1 study) 6 weeks	serious 2	no serious inconsistency	no serious indirectnes s	very serious3	undetecte d	⊕⊖⊖⊖ VERY LOW2,3 due to risk of bias, imprecisio n	13	13	-	The mean targeted behaviour that challenges (severity) - follow-up in the interventio n groups was 0.95 standard deviations lower (1.77 to 0.13 lower)

Quality assessment

Summary of Findings

1 Due to significant baseline differences, standard deviation of change and estimates of mean change were derived using initial and final mean values and utilising r = 0.5. Sensitivity analyses were used to explore the impact of altering assumptions about the calculation of the effect size, but this resulted in no change to conclusions.

2 Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect 3 Optimal information size not met; small, single study

A.6 Parent training interventions aimed at reducing and managing behaviour that challenges

A.6.1 Parent training versus any control

Table 21: Parent training versus any control

Quality as	ssessme	ent					Summa	ary of Fi	ndings		
Participa nts	Risk of	Inconsisten cy	Indirectne ss	Imprecisio n	Publication bias	Overall quality of evidence	Study e rates (%		Relati ve	Anticip	ated absolute effects
(studies) Follow up	bias						With any contr ol	With parent trainin g	effect (95% CI)	Risk with any contr ol	Risk difference with parent training (95% CI)
Targeted	behavio	our that challe	nges (severit	ty) - post-tre	atment (Bette	r indicated by lowe	r values)				
841 (14 studies)	serio us1	no serious inconsisten cy	no serious indirectnes s	no serious imprecisio n	undetected	⊕⊕⊕⊖ MODERATE1 due to risk of bias	390	451	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.41 standard deviations lower (0.58 to 0.24 lower)
Targeted	behavio	our that challe	nges (severit	y) - follow-u	p (Better indi	cated by lower valu	es)				
342 (3 studies)	serio us1	no serious inconsisten cy	serious2	serious3	reporting bias strongly	⊕⊖⊝⊖ VERY LOW1,2,3,4	156	186	-		The mean targeted behaviour that challenges (severity) - follow-up in the

Quality a	ssessm	ent					Summ	ary of Fi	ndings		
26- 52 weeks					suspected4	due to risk of bias, indirectness, imprecision, publication bias					intervention groups was 0.13 standard deviations lower (0.34 lower to 0.08 higher)
Targeted	behavio	our that challe	nges (severit	ty, non-impro	ovement) - po	st-treatment					
428 (8 studies)	serio us1	no serious inconsisten cy	no serious indirectnes s	no serious imprecisio n	undetected	⊕⊕⊕⊖ MODERATE1 due to risk of bias	174/1 97 (88.3 %)	131/2 31 (56.7 %)	RR 0.67 (0.59 to 0.77)	883 per 1000	291 fewer per 1000 (from 203 fewer to 362 fewer)
Targeted	behavio	our that challe	nges (freque	ncy) - post-t	reatment (Bet	ter indicated by lov	ver value	es)			
633 (9 studies)	serio us1	serious5	no serious indirectnes s	no serious imprecisio n	undetected	⊕⊕⊖⊖ LOW1,5 due to risk of bias, inconsistency	294	339	-		The mean targeted behaviour that challenges (frequency) - post- treatment in the intervention groups was 0.54 standard deviations lower (0.8 to 0.28 lower)
Targeted	behavio	our that challe	nges (freque	ncy) - follow	-up (Better in	dicated by lower va	lues)				
258 (12 studies) 26 weeks	serio us6	no serious inconsisten cy	no serious indirectnes s	serious7	reporting bias strongly suspected4	 ⊕⊖⊖ VERY LOW4,6,7 due to risk of bias, imprecision, publication bias 	123	135	-		The mean targeted behaviour that challenges (frequency) - follow-up in the intervention groups was 0.23 standard deviations lower (0.47 lower to 0.02 higher)
Targeted	behavio	our that challe	nges (freque	ncy, non-im	provement) - j	post-treatment					
343 (6 studies)	serio us1	no serious inconsisten cy	serious2	no serious imprecisio n	undetected	$\oplus \oplus \ominus \ominus$ LOW1,2 due to risk of bias, indirectness	147/1 55 (94.8 %)	105/1 88 (55.9 %)	RR 0.63 (0.55 to 0.73)	948 per 1000	351 fewer per 1000 (from 256 fewer to 427 fewer)

Quality a	ssessm	ent					Sumn	nary of F	indings	
Adaptive	functio	ning (commur	nication) - po	ost-treatmen	t (Better indica	ated by higher value	es)			
124 (1 study)	serio us6	no serious inconsisten cy	serious2	very serious7	undetected	⊕⊖⊖⊖ VERY LOW2,6,7 due to risk of bias, indirectness, imprecision	49	75	-	The mean adaptive functioning (communication) - post- treatment in the intervention groups was 0.47 standard deviations higher (0.11 to 0.84 higher)
Adaptive	functio	ning (total) - p	ost-treatme	nt (Better inc	dicated by high	ner values)				
135 (2 studies)	serio us1	no serious inconsisten cy	serious2	serious3	undetected	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	53	82	-	The mean adaptive functioning (total) - post- treatment in the intervention groups was 0.51 standard deviations higher (0.15 to 0.86 higher)
2 Concerr 3 Optimal 4 Publicat 5 I2 > 40% 6 Crucial	ns with a informa ion bias % limitatior	n is from studie pplicability - dif tion size not me strongly suspe n for one criterie tion size not me	iferent popula et ected on or some li	ations mitations for I	multiple criteria	sufficient to lower or	nes conf	idence ir	n the estimat	(0.15 to 0.86 higher)

A.6.2 Individual parent training versus group parent training

 Table 22: Individual parent training versus group parent training

Quality as	ssessme	ent					Summa	ry of Finding	gs		
Participa nts	Risk of	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of	Study ev (%)	vent rates	Relativ e	Anticipate	ed absolute effects
(studies) Follow	bias					evidence	With group	With individual	effect (95%	Risk with	Risk difference with individual parent training

Quality as	ssessm	ent					Summa	ry of Findir	ngs		
up							parent training	parent training	CI)	group parent training	(95% CI)
Targeted	behavio	our that challer	nges (severity	/) - post-tre	eatment (Be	etter indicated	l by lower	values)			
38 (1 study)	serio us1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	 ⊕ ⊖ ⊖ ∨ERY LOW1,2 due to risk of bias, imprecision 	15	23	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.38 standard deviations lower (1.04 lower to 0.28 higher)
Targeted	behavio	our that challer	nges (severity	/) - follow-ı	up (Better i	ndicated by lo	wer value	es)			
38 (1 study) 26 weeks	serio us1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	 ⊕⊖⊖ VERY LOW1,2 due to risk of bias, imprecision 	15	23	-		The mean targeted behaviour that challenges (severity) - follow-up in the intervention groups was 0.05 standard deviations lower (0.7 lower to 0.61 higher)
Targeted	behavio	our that challer	nges (frequen	cy) - post-	treatment (Better indicate	ed by low	er values)			
31 (1 study)	serio us1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	13	18	-		The mean targeted behaviour that challenges (frequency) - post-treatment in the intervention groups was 0.34 standard deviations lower (1.06 lower to 0.38 higher)
Targeted	behavio	our that challer	nges (frequen	cy) - follov	v-up (Bette	r indicated by	lower val	ues)			
31 (1 study) 26 weeks	serio us1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias,	13	18	-		The mean targeted behaviour that challenges (frequency) - follow-up in the intervention groups was 0.12 standard deviations

Quality assessment							Summary of Findings					
				imprecision			higher (0.59 lower to 0.84 higher)					
1 Crucial limitation for 2 Optimal information				e criteria sufficient to	lower ones c	confidence in the es	stimate of effect					

A.6.3 Parent training plus optimism training versus parent training alone

Table 23: Parent training plus optimism training versus parent training alone

Quality as	ssessme	ent					Summar	y of Findings			
Participa	Risk	Inconsistenc	Indirectnes	Imprecis	Publicati	Overall	Study ev	ent rates (%)	Relativ	Anticipate	ed absolute effects
nts (studies) Follow up	of bias	У	S	ion	on bias	quality of evidence	With parent training alone	With parent training plus optimism training	e effect (95% CI)	Risk with parent training alone	Risk difference with parent training plus optimism training (95% CI)
Targeted	behavio	our that challer	nges (severity	/) - post-tre	eatment (Be	etter indicated	l by lower	values)			
35 (1 study)	very serio us1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	17	18	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.8 standard deviations lower (1.49 to 0.11 lower)
Targeted	behavio	our that challer	nges (severity	, non-imp	rovement) -	post-treatme	ent				
35 (1 study)	very serio us1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	 ⊕⊖⊖ VERY LOW1,2 due to risk of bias, imprecision 	11/17 (64.7%)	5/18 (27.8%)	RR 0.43 (0.19 to 0.98)	647 per 1000	369 fewer per 1000 (from 13 fewer to 524 fewer)
Carer sati	isfactior	n - post-treatm	ent (Better in	dicated by	higher value	ues)					

Quality as	ssessme	ent					Summar	y of Findings				
35 (1 study)	very serio us1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	17	18	-	The mean carer satisfaction - post- treatment in the intervention groups was 0.22 standard deviations higher (0.44 lower to 0.89 higher)		
	1 Crucial limitation for one or more criteria sufficient to substantially lower ones confidence in the estimate of effect 2 Optimal information size not met; small, single study											

A.6.4 Enhanced parent training versus standard parent training

Table 24: Enhanced parent training versus standard parent training

Quality as	ssessmer	nt					Summary	/ of Finding	js		
Participa nts	Risk of bias	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of	Study eve (%)	ent rates	Relativ e	Anticipated	absolute effects
(studies) Follow up						evidence	With standar d parent training	With enhance d parent training	effect (95% CI)	Risk with standard parent training	Risk difference with enhanced parent training (95% CI)
Targeted	behaviou	r that challeng	ges (severity)	- post-trea	atment (Bet	ter indicated	by lower v	values)			
50 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious1	undetect ed	⊕⊕⊝⊖ LOW1 due to imprecisio n	26	24	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.06 standard deviations lower (0.62 lower to 0.49 higher)
Targeted	behaviou	r that challeng	ges (severity)	- follow-u	p (Better in	dicated by lo	wer values	5)			
42 (1 study)	no serious	no serious inconsistenc	no serious indirectnes	very serious1	undetect ed	⊕⊕⊝⊝ LOW1	19	23	-		The mean targeted behaviour that challenges

Quality a	ssessmer	nt					Summary	of Finding	js		
52 weeks	risk of bias	У	S			due to imprecisio n					(severity) - follow-up in the intervention groups was 0.56 standard deviations lower (1.18 lower to 0.06 higher)
Targeted	behaviou	r that challeng	ges (severity,	non-impro	ovement) - I	post-treatme	nt				
50 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious1	undetect ed	⊕⊕⊝⊖ LOW1 due to imprecisio n	10/26 (38.5%)	13/24 (54.2%)	RR 1.41 (0.77 to 2.59)	385 per 1000	158 more per 1000 (from 88 fewer to 612 more)
Targeted	behaviou	r that challeng	ges (severity,	non-impro	ovement) - f	follow-up					
42 (1 study) 52 weeks	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious1	undetect ed	⊕⊕⊖⊖ LOW1 due to imprecisio n	11/19 (57.9%)	12/23 (52.2%)	RR 0.9 (0.52 to 1.56)	579 per 1000	58 fewer per 1000 (from 278 fewer to 324 more)
Targeted	behaviou	r that challeng	ges (frequenc	y) - post-ti	reatment (B	Setter indicate	ed by lowe	r values)			
50 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious1	undetect ed	⊕⊕⊝⊖ LOW1 due to imprecisio n	26	24	-		The mean targeted behaviour that challenges (frequency) - post- treatment in the intervention groups was 0.04 standard deviations higher (0.52 lower to 0.59 higher)
Targeted	behaviou	r that challeng	ges (frequend	y) - follow	-up (Better	indicated by	lower valu	es)			
42 (1 study) 52 weeks	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious1	undetect ed	⊕⊕⊖⊖ LOW1 due to imprecisio n	19	23	-		The mean targeted behaviour that challenges (frequency) - follow-up in the intervention groups was 0.04 standard deviations higher (0.56 lower to 0.65 higher)

Quality as	ssessmer	nt					Summary	/ of Finding	js		
Targeted	behaviou	r that challeng	ges (frequend	y, non-imp	provement)	- post-treatn	nent				
50 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious1	undetect ed	⊕⊕⊝⊝ LOW1 due to imprecisio n	11/26 (42.3%)	8/24 (33.3%)	RR 0.79 (0.38 to 1.62)	423 per 1000	89 fewer per 1000 (from 262 fewer to 262 more)
Targeted	behaviou	r that challeng	ges (frequenc	y, non-imp	provement)	- follow-up					
42 (1 study) 52 weeks	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious1	undetect ed	⊕⊕⊝⊝ LOW1 due to imprecisio n	4/19 (21.1%)	8/23 (34.8%)	RR 1.65 (0.59 to 4.65)	211 per 1000	137 more per 1000 (from 86 fewer to 768 more)
Carer sat	isfaction-	post-treatmer	nt (Better indi	cated by h	igher value	es)					
50 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious1	undetect ed	⊕⊕⊝⊝ LOW1 due to imprecisio n	26	24	-		The mean carer satisfaction- post-treatment in the intervention groups was 0.18 standard deviations higher (0.38 lower to 0.74 higher)

1 Optimal information size not met; small, single study

A.7 Psychosocial interventions aimed at reducing and managing behaviour that challenges

A.7.1 Cognitive behavioural interventions versus any control

Table 25: Cognitive behaviour interventions versus any control

Quality as	ssessmen	t					Summary of Findings					
Participa nts	Risk of bias	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of	Study (%)	event rates	Relativ e	Anticipa	ated absolute effects	
(studies)						evidence	With	With	effect	Risk	Risk difference with	

Quality as	ssessmen	t					Summ	nary of Finding	s		
Follow up							any contr ol	cognitive behavioural interventions	(95% CI)	with any contr ol	cognitive behavioural interventions (95% CI)
Targeted	behaviou	r that challeng	es (severity)	- post-trea	tment (mea	sured with: Far	nily car	er rated; Bette	r indicate	d by low	ver values)
103 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious1	undetect ed	⊕⊕⊝⊝ LOW1 due to imprecision	58	45	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.24 standard deviations lower (0.63 lower to 0.15 higher)
Targeted	behaviou	r that challeng	es (severity)	- follow-up	(measured	d with: Family c	arer rate	ed; Better indi	cated by	lower va	lues)
83 (1 study) 31 weeks	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious1	undetect ed	⊕⊕⊖⊖ LOW1 due to imprecision	41	42	-		The mean targeted behaviour that challenges (severity) - follow-up in the intervention groups was 0.03 standard deviations lower (0.46 lower to 0.4 higher)
Targeted	behaviou	r that challeng	es (severity,	non-impro	vement) - p	ost-treatment (a	assesse	ed with: Paid c	arer rated	d)	
38 (1 study)	serious 2	no serious inconsistenc y	no serious indirectnes s	very serious1	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision 	15/2 0 (75%)	9/18 (50%)	RR 0.67 (0.39 to 1.13)	750 per 1000	247 fewer per 1000 (from 458 fewer to 97 more)
Targeted	behaviou	r that challeng	es (severity)	- post-trea	tment (mea	sured with: Pai	d carer	rated; Better in	ndicated	by lower	r values)
194 (2 studies)	no serious risk of bias	serious3	no serious indirectnes s	serious4	undetect ed	⊕⊕⊖⊖ LOW3,4 due to inconsistency , imprecision	102	92	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was

Quality as	ssessmen	t					Summ	nary of Finding	S	
										0.03 standard deviations lower (0.48 lower to 0.42 higher)
Targeted	behaviou	r that challeng	es (severity)	- follow-up	(measured	d with: Paid car	er rated	; Better indica	ted by lower valu	es)
176 (2 studies) 17- 31 weeks	no serious risk of bias	serious3	no serious indirectnes s	serious4	undetect ed	⊕⊕⊖⊖ LOW3,4 due to inconsistency , imprecision	86	90	-	The mean targeted behaviour that challenges (severity) - follow-up in the intervention groups was 0.13 standard deviations lower (0.58 lower to 0.33 higher)
Adaptive	functionir	ng - post-treatr	ment (measu	red with: P	aid carer ra	ated; Better indi	cated b	y higher value	s)	
28 (1 study)	serious 2	no serious inconsistenc y	no serious indirectnes s	very serious1	undetect ed	 ⊕⊖⊖ VERY LOW1,2 due to risk of bias, imprecision 	10	18	-	The mean adaptive functioning - post- treatment in the intervention groups was 1.32 standard deviations higher (0.46 to 2.18 higher)
Quality of	f life - pos	t-treatment (m	easured with	: Self rated	l; Better ind	dicated by high	er value	s)		
129 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious1	undetect ed	⊕⊕⊖⊖ LOW1 due to imprecision	67	62	-	The mean quality of life - post-treatment in the intervention groups was 0.16 standard deviations lower (0.5 lower to 0.19 higher)
Quality of	f life - follo	ow-up (measur	ed with: Self	rated; Bet	ter indicate	d by lower valu	es)			
140 (1 study) 31 weeks	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious1	undetect ed	⊕⊕⊖⊖ LOW1 due to imprecision	70	70	-	The mean quality of life - follow-up in the intervention groups was 0.02 standard deviations lower (0.35 lower to 0.32 higher)

Quality assessmentSummary of Findings2 Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect3 I2 > 40%

4 Optimal information size not met

A.7.2 Behavioural therapy versus any control

Table 26: Behavioural therapy versus any control

Quality as	ssessme	ent					Summ	ary of Findi	ngs		
Participa nts	Risk of	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of	Study (%)	event rates	Relativ e	Anticipa	ted absolute effects
(studies) Follow up	bias					evidence	With Any contr ol	With Behaviou ral therapy	effect (95% CI)	Risk with Any control	Risk difference with Behavioural therapy (95% CI)
Targeted	behavio	ur that challen	ges (severity) - post-trea	atment (Bet	tter indicated	by lower	values)			
61 (1 study)	seriou s1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	30	31	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.47 standard deviations lower (0.98 lower to 0.04 higher)
Targeted	behavio	ur that challen	ges (severity) - follow-u	p (Better in	dicated by lov	ver valu	es)			
63 (1 study) 78 weeks	seriou s1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	30	33	-		The mean targeted behaviour that challenges (severity) - follow-up in the intervention groups was 0.33 standard deviations lower (0.85 lower to 0.19 higher)

1 Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect

2 Optimal information size not met; small, single study

A.8 Sleep interventions aimed at reducing and managing behaviour that challenges

A.8.1 Sleep interventions versus any control

 Table 27: Sleep interventions versus any control

Quality as	ssessme	ent					Summa	ary of Findi	ngs		
Participa nts	Risk of	Inconsisten cy	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of evidence	Study e (%)	event rates	Relativ e	Anticip	ated absolute effects
(studies) Follow up	bias						With any contr ol	With sleep interventi ons	effect (95% CI)	Risk with any contr ol	Risk difference with sleep interventions (95% CI)
Targeted	behavio	our that challer	nges (global	problem sl	eep behavi	our, non-improve	ement) -	post-treatm	ent		
69 (1 study)	serio us1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	21/34 (61.8 %)	5/35 (14.3%)	RR 0.23 (0.1 to 0.54)	618 per 1000	476 fewer per 1000 (from 284 fewer to 556 fewer)
Targeted	behavio	our that challer	nges (global	problem sl	eep behavi	our) - post-treatm	nent (Bet	ter indicate	d by low	er value	s)
154 (4 studies)	serio us4	no serious inconsistenc y	no serious indirectnes s	serious5	undetect ed	 ⊕⊕⊖⊖ LOW4,5 due to risk of bias, imprecision 	77	77	-		The mean targeted behaviour that challenges (global problem sleep behaviour) - post-treatment in the intervention groups was 1.05 standard deviations lower (1.48 to 0.63 lower)
Targeted	behavio	our that challer	nges (global	problem sl	eep behavi	our) - follow-up (l	Better in	dicated by	lower val	ues)	
130 (3	serio us4	serious6	no serious indirectnes	serious5	undetect ed		55	75	-		The mean targeted behaviour that challenges (global

Quality as	ssessme	ent					Summa	ary of Findi	ngs	
studies) 6 to 26 weeks			S			LOW4,5,6 due to risk of bias, inconsistency, imprecision				problem sleep behaviour) - follow-up in the intervention groups was 0.92 standard deviations lower (1.6 to 0.24 lower)
Targeted	behavio	our that challer	nges (total sl	eep time) -	post-treatr	ment (measured v	vith: Act	igraph; Bett	er indicate	ed by higher values)
96 (2 studies)	serio us4	no serious inconsistenc y	no serious indirectnes s	serious5	undetect ed	 ⊕⊕⊖ LOW4,5 due to risk of bias, imprecision 	48	48	-	The mean targeted behaviour that challenges (total sleep time) - post-treatment in the intervention groups was 0.62 standard deviations higher (0.2 to 1.03 higher)
Targeted	behavio	our that challer	nges (sleep e	fficiency)	post-treat	ment (measured v	with: Act	tigraph; Bet	ter indicate	ed by higher values)
96 (2 studies)	serio us4	no serious inconsistenc y	no serious indirectnes s	serious5	undetect ed	 ⊕⊕⊖⊖ LOW4,5 due to risk of bias, imprecision 	48	48	-	The mean targeted behaviour that challenges (sleep efficiency) - post-treatment in the intervention groups was 0.24 standard deviations higher (0.26 lower to 0.74 higher)
Targeted	behavio	our that challer	nges (total sl	eep time) -	follow-up	(measured with: A	Actigrap	h; Better ind	licated by	higher values)
46 (1 study) 26 weeks	serio us1	no serious inconsistenc y	no serious indirectnes s	very serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	23	23	-	The mean targeted behaviour that challenges (total sleep time) - follow-up in the intervention groups was 0.14 standard deviations higher (0.44 lower to 0.71 higher)
Targeted	behavio	our that challer	nges (sleep e	fficiency)	follow-up	(measured with:	Actigrap	h; Better in	dicated by	lower values)
46 (1 study) 26	serio us1	no serious inconsistenc y	no serious indirectnes s	very serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,3 due to risk of	23	23	-	The mean targeted behaviour that challenges (sleep efficiency) - follow-up in the

Quality as	ssessme	ent					Summa	ary of Findi	ngs	
weeks						bias, imprecision				intervention groups was 0.11 standard deviations lower (0.69 lower to 0.46 higher)
Targeted	behavio	our that challer	nges (sleep o	nset laten	cy) - post-tı	reatment (measur	ed with:	Actigraph;	Better in	dicated by lower values)
69 (1 study)	serio us1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖ ∨ERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	34	35	-	The mean targeted behaviour that challenges (sleep onset latency) - post-treatment in the intervention groups was 0.59 standard deviations lower (1.07 to 0.11 lower)
Targeted	behavio	our that challer	nges (wake a	fter sleep o	onset) - pos	st-treatment (mea	sured wi	ith: Actigrap	oh; Bette	r indicated by lower values)
96 (2 studies)	serio us4	serious6	no serious indirectnes s	serious5	undetect ed	 ⊕⊖⊖ ∨ERY LOW4,5,6 due to risk of bias, inconsistency, imprecision 	48	48	-	The mean targeted behaviour that challenges (wake after sleep onset) - post-treatment in the intervention groups was 0.31 standard deviations lower (1.13 lower to 0.51 higher)
Targeted	behavio	our that challer	nges (wake a	fter sleep o	onset) - foll	ow-up (measured	with: A	ctigraph; Be	etter indi	cated by lower values)
46 (1 study) 26 weeks	serio us1	no serious inconsistenc y	no serious indirectnes s	very serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	23	23	-	The mean targeted behaviour that challenges (wake after sleep onset) - follow-up in the intervention groups was 0.29 standard deviations higher (0.29 lower to 0.88 higher)
Targeted	behavio	our that challer	nges (total sl	eep time) p	ost-treatm	ent (measured wi	th: Sleep	o diary; Bet	ter indica	ated by higher values)
30 (1 study)	serio us1	no serious inconsistenc y	no serious indirectnes s	very serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	15	15	-	The mean targeted behaviour that challenges (total sleep time) post-treatment in the intervention groups was 0.3 standard deviations lower

Targeted behavio30serio(1 study)us1	no serious				ent (measured wit	h: Sleep	diary; Bette	er indica	ted by lo	(1.02 lower to 0.42 higher)
30 serio	no serious				ent (measured wit	h: Sleep	diary; Bette	er indica	ted by lo	ower values)
		no serious								· · · · · · · · · · · · · · · · · · ·
	inconsistenc y		very serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	15	15	-		The mean targeted behaviour that challenges (activity score) - post-treatment in the intervention groups was 0.28 standard deviations higher (0.44 lower to 1 higher)
Carer Satisfaction	n (non-satisfie	d) - post-treati	ment							
30 serio (1 study) us1	no serious inconsistenc y		very serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	2/17 (11.8 %)	1/13 (7.7%)	RR 0.65 (0.07 to 6.45)	118 per 1000	41 fewer per 1000 (from 109 fewer to 641 more)

A.8.2 Face-to-face sleep intervention versus booklet only

 Table 28: Face-to-face sleep intervention versus booklet only

Quality as	ssessm	ent					Summ	ary of Findin	gs		
Participa nts	Risk of	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of	Study (%)	Study event rates (%)		Anticipa	ted absolute effects
(studies) Follow up	bias					evidence	With bookl et only	With face- to-face sleep interventio	effect (95% CI)	Risk with bookle t only	Risk difference with face-to- face sleep intervention (95% CI)

Quality as	ssessm	ent					Summ	ary of Findin	gs				
								n					
Targeted	Targeted behaviour that challenges (global problem sleep behaviour) - follow-up (Better indicated by lower values)												
42 (1 study) 26 weeks	serio us1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	22	20	-		The mean targeted behaviour that challenges (global problem sleep behaviour) - follow-up in the intervention groups was 0.07 standard deviations lower (0.68 lower to 0.53 higher)		
	1 Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect 2 Optimal information size not met; small, single study												

A.9 Pharmacological interventions aimed at reducing and managing behaviour that challenges

A.9.1 Risperidone versus placebo in children and young people

 Table 29: Risperidone versus placebo in children and young people

Quality as	ssessme	ent					Summ	ary of Fin	dings		
Participa nts	Risk of	Inconsistenc y	Indirectnes s	Imprecisio n	Publicati on bias	Overall quality of evidence	-	Study event rates (%)		Anticipa	ated absolute effects
(studies) Follow up	bias						With With place risperid bo one		effect (95% CI)	Risk with place bo	Risk difference with risperidone (95% CI)
Targeted	behavio	our that challen	nges (severity	/) - post-treat	ment (mea	sured with: End-po	oint sco	int score; Better indicated by lower values)			er values)
257 (4 studies)	serio us1	no serious inconsistenc y	no serious indirectnes s	serious2	undetect ed	$\oplus \oplus \bigcirc \bigcirc$ LOW1,2 due to risk of bias, imprecision	141	116	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 1.09 standard deviations lower (1.39 to 0.79 lower)

Quality as	ssessm	ent					Summ	ary of Fir	dings		
Targeted	behavio	ur that challenge	es (severity) -	post-treatme	nt (measured	d with: Change score	e; Better	· indicated	by lower	values)	
66 (1 study)	serio us3	no serious inconsistenc y	serious4	very serious5	undetect ed	⊕⊖⊖⊖ VERY LOW3,4,5 due to risk of bias, indirectness, imprecision	35	31	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.98 standard deviations lower (1.49 to 0.47 lower)
Targeted	behavio	our that challer	nges (severity	y, non-impro	vement) - p	ost-treatment					
153 (2 studies)	serio us1	no serious inconsistenc y	no serious indirectnes s	serious2	undetect ed	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision	68/80 (85%)	25/73 (34.2%)	RR 0.42 (0.28 to 0.64)	850 per 1000	493 fewer per 1000 (from 306 fewer to 612 fewer)
Adaptive higher va		ning (social) -	post-treatmei	nt (measured	d with: Niso	nger Child Behavio	our Rati	ng Form -	Social C	omplian	ce6; Better indicated by
155 (3 studies)	serio us1	no serious inconsistenc y	no serious indirectnes s	serious2	undetect ed	⊕⊕⊝⊝ LOW1,2 due to risk of bias, imprecision	88	67	-		The mean adaptive functioning (social) - post- treatment in the intervention groups was 0.86 standard deviations higher (0.42 to 1.3 higher)
Adverse	events (elevated prola	ctin, non-occ	urence) - po	st-treatmen	t					
228 (2 studies)	serio us1	no serious inconsistenc y	no serious indirectnes s	serious2	undetect ed	⊕⊕⊝⊝ LOW1,2 due to risk of bias, imprecision	119/1 20 (99.2 %)	97/108 (89.8%)	RR 0.91 (0.85 to 0.97)	992 per 1000	89 fewer per 1000 (from 30 fewer to 149 fewer)
Adverse	events (prolactin-relat	ed adverse ev	vent; oligom	enorrhea, n	on-occurence) - po	ost-treat	ment			
66 (1 study)	serio us3	no serious inconsistenc y	serious4	very serious5	undetect ed	⊕⊖⊝⊖ VERY LOW3,4,5 due to risk of bias,	35/35 (100 %)	30/31 (96.8%)	RR 0.97 (0.89 to	1000 per 1000	30 fewer per 1000 (from 110 fewer to 50 more)

Quality as	ssessm	ent					Summ	ary of Fin	dings		
						indirectness, imprecision			1.05)		
Adverse	events (prolactin level	; ng/ml) - pos	st-treatment (Better indic	ated by lower valu	es)				
241 (3 studies)	serio us3	no serious inconsistenc y	serious4	serious2	undetect ed	⊕⊖⊖⊖ VERY LOW2,3,4 due to risk of bias, indirectness, imprecision	125	116	-		The mean adverse events (prolactin level; ng/ml) - post-treatment in the intervention groups was 3.22 standard deviations higher (1.68 to 4.75 higher)
Adverse	events (weight; kg) - p	ost-treatmen	t (measured	with: Chang	ge score; Better ind	dicated	by lower v	values)		
282 (3 studies)	serio us1	no serious inconsistenc y	no serious indirectnes s	serious2	undetect ed	$\oplus \oplus \bigcirc \bigcirc$ LOW1,2 due to risk of bias, imprecision	150	132	-		The mean adverse events (weight; kg) - post-treatment in the intervention groups was 0.82 standard deviations higher (0.57 to 1.06 higher)
Adverse	events (weight; kg) - p	ost-treatmen	t (measured	with: Endpo	oint score; Better in	ndicated	by lowe	r values)		
53 (1 study)	serio us3	no serious inconsistenc y	serious4	very serious5	undetect ed	⊕⊖⊖⊖ VERY LOW3,4,5 due to risk of bias, indirectness, imprecision	28	25	-		The mean adverse events (weight; kg) - post-treatment in the intervention groups was 0.39 standard deviations higher (0.16 lower to 0.93 higher)
Adverse	events (weight gain, n	on-occurrenc	e) - post-trea	atment						
277 (3 studies)	serio us1	no serious inconsistenc y	serious4	serious2	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2,4 due to risk of bias, indirectness, imprecision 	147/1 48 (99.3 %)	115/12 9 (89.1%)	RR 0.91 (0.85 to 0.96)	993 per 1000	89 fewer per 1000 (from 40 fewer to 149 fewer)

Quality as	ssessm	ent					Summ	ary of Fin	dings				
550 (6 studies)	serio us1	serious7	serious4	no serious imprecisio n	undetect ed	⊕⊖⊖⊖ VERY LOW1,4,7 due to risk of bias, inconsistency, indirectness	249/2 83 (88%)	138/26 7 (51.7%)	RR 0.58 (0.44 to 0.77)	880 per 1000	370 fewer per 1000 (from 202 fewer to 493 fewer)		
Adverse	events (seizure, non-o	ccurrence) -	post-treatme	nt								
101 (1 study)	serio us3	no serious inconsistenc y	no serious indirectnes s	very serious5	undetect ed	 ⊕⊖⊖⊖ VERY LOW3,5 due to risk of bias, imprecision 	51/52 (98.1 %)	49/49 (100%)	RR 1.02 (0.97 to 1.08)	981 per 1000	20 more per 1000 (from 29 fewer to 78 more)		
Adverse	Adverse events (discontinuation due to adverse events, non-occurrence) - post-treatment												
340 (4 studies)	serio us1	no serious inconsistenc y	serious4	no serious imprecisio n2	undetect ed	⊕⊕⊖⊖ LOW1,2,4 due to risk of bias, indirectness	175/1 78 (98.3 %)	158/16 2 (97.5%)	RR 0.99 (0.96 to 1.03)	983 per 1000	10 fewer per 1000 (from 39 fewer to 29 more)		
Adverse	events (discontinuatio	n due other r	easons, non	-occurrence	e) - post-treatment							
450 (5 studies)	serio us1	serious7	serious4	no serious imprecisio n	undetect ed	⊕⊖⊖⊖ VERY LOW1,4,7 due to risk of bias, inconsistency, indirectness	170/2 35 (72.3 %)	190/21 5 (88.4%)	RR 1.19 (1.06 to 1.34)	723 per 1000	137 more per 1000 (from 43 more to 246 more)		

2 Optimal information size not met

3 Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect
4 Applicability - different populations
5 Optimal information size not met; small, single study
6 Combined adaptive social and compliant/calm subscales

7 l2 > 40%

A.9.2 Withdrawal of risperidone versus continuation of risperidone in children and young people

 Table 30: Withdrawal of risperidone versus continuation of risperidone in children and young people

Quality as	ssessme	ent					Summary of	f Findings				
Participa	Risk	Inconsistenc	Indirectn	Imprecis	Publicati	Overall quality	Study event	rates (%)	Relativ	Anticipated at	osolute effects	
nts (studies) Follow up	of bias	У	ess	ion	on bias	of evidence	With continuatio n of risperidone	With withdrawal of risperidon e	e effect (95% CI)	Risk with continuation of risperidone	Risk difference with withdrawal of risperidone (95% CI)	
Targeted	Targeted behaviour that challenges (relapse) - post-treatment											
32 (1 study)	seriou s1	no serious inconsistenc y	serious2	very serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	2/16 (12.5%)	10/16 (62.5%)	RR 5 (1.3 to 19.3)	125 per 1000	500 more per 1000 (from 37 more to 1000 more)	

3 Optimal information size not met; small, single study

A.9.3 Aripiprazole versus placebo in children and young people

 Table 31: Aripiprazole versus placebo in children and young people

Quality as	ssessme	ent			Summ	ary of Fin	dings		
Participa nts	Risk of	Inconsistenc y	Indirectn essImprecis ionPublicati on biasOverall quality of evidenceStudy even rates (%)	e (%)		Anticipated absolute effects			
(studies) Follow up	bias				With place bo	With aripipra zole	effect (95% CI)	Risk with place bo	Risk difference with aripiprazole (95% CI)

Quality a	ssessm	ent					Summ	ary of Fin	dings			
Targeted	behavio	our that challer	nges (sever	ity) - post-	treatment (Better indicated by lo	wer valu	ies)				
308 (2 studies)	serio us1	no serious inconsistenc y	serious2	serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	98	210	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.64 standard deviations lower (0.91 to 0.36 lower)	
Targeted	behavio	our that challer	nges (sever	ity, non-im	provement) - post-treatment						
308 (2 studies)	serio us1	no serious inconsistenc y	serious2	serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	74/98 (75.5 %)	100/21 0 (47.6%)	RR 0.65 (0.5 to 0.84)	755 per 1000	264 fewer per 1000 (from 121 fewer to 378 fewer)	
Quality of life - post-treatment (Better indicated by higher values)												
243 (2 studies)	serio us1	very serious4	serious2	serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,2,3,4 due to risk of bias, inconsistency, indirectness, imprecision	76	167	-		The mean quality of life - post-treatment in the intervention groups was 0.6 standard deviations higher (0.17 lower to 1.37 higher)	
Adverse	events (elevated prola	ctin, non-o	ccurrence)	- post-trea	tment						
313 (2 studies)	serio us1	no serious inconsistenc y	serious2	serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	96/10 1 (95%)	211/21 2 (99.5%)	RR 1.05 (0.99 to 1.1)	950 per 1000	48 more per 1000 (from 10 fewer to 95 more)	
Adverse	events (weight gain; kg	g) - post- tr	eatment (B	etter indica	ated by lower values)						
216 (1 study)	serio us5	no serious inconsistenc y	serious2	very serious6	undetect ed	⊕⊖⊖⊖ VERY LOW2,5,6 due to risk of bias, indirectness, imprecision	51	165	-		The mean adverse events (weight gain; kg) - post- treatment in the intervention groups was 0.48 standard deviations higher	

Quality a	ssessm	ent					Summ	ary of Fin	dings		
											(0.17 to 0.8 higher)
Adverse	events (weight gain; cl	linically sig	., non-occi	urrence)						
313 (2 studies)	serio us1	no serious inconsistenc y	serious2	serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	94/10 1 (93.1 %)	156/21 2 (73.6%)	RR 0.79 (0.71 to 0.88)	931 per 1000	195 fewer per 1000 (from 112 fewer to 270 fewer)
Adverse	events (sedation, non-	occurrence	e) - post-tre	eatment						
313 (2 studies)	serio us1	no serious inconsistenc y	serious2	serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	96/10 1 (95%)	165/21 2 (77.8%)	RR 0.83 (0.76 to 0.91)	950 per 1000	162 fewer per 1000 (from 86 fewer to 228 fewer
Adverse	events (seizure, non-o	ccurrence)	- post-trea	tment						
216 (1 study)	serio us5	no serious inconsistenc y	serious2	very serious6	undetect ed	⊕⊖⊖⊖ VERY LOW2,5,6 due to risk of bias, indirectness, imprecision	50/51 (98%)	165/16 5 (100%)	RR 1.03 (0.98 to 1.08)	980 per 1000	29 more per 1000 (from 20 fewer to 78 more)
Adverse	events (discontinuatio	n due to ad	lverse evei	nts, non-oc	currence) - post-trea	tment				
316 (2 studies)	serio us1	no serious inconsistenc y	serious2	serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	96/10 3 (93.2 %)	191/21 3 (89.7%)	RR 0.96 (0.89 to 1.04)	932 per 1000	37 fewer per 1000 (from 103 fewer to 37 more
Adverse	events (discontinuatio	n due to ot	her reason	s, non-occ	urrence) - post-treatr	nent				
316 (2 studies)	serio us1	no serious inconsistenc y	serious2	serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	81/10 3 (78.6 %)	201/21 3 (94.4%)	RR 1.19 (1.07 to 1.33)	786 per 1000	149 more per 1000 (from 55 more to 260 more)

2 Applicability - different populations

Quality assessment

Summary of Findings

3 Optimal information size not met
4 I2 > 75%
5 Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect.
6 Optimal information size not met; small, single study

A.9.4 Aripiprazole versus risperidone in children and young people

Table 32: Aripiprazole versus risperidone in children and young people

Quality as	ssessme	ent					Summar	y of Findi	ngs		
Participa nts	Risk of	Inconsistenc y	Indirectn ess	Imprecis ion	Publicati on bias	Overall quality of evidence	Study eve (%)	ent rates	Relativ e	Anticipate	d absolute effects
(studies) Follow up	bias						With Risperi done	With Aripipra zole	effect (95% CI)	Risk with Risperid one	Risk difference with Aripiprazole (95% CI)
Targeted	behavio	our that challer	nges (sever	ity) - post-	treatment (Better indicated b	by lower va	alues)			
59 (1 study)	serio us1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	30	29	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.38 standard deviations higher (0.14 lower to 0.9 higher)
Adverse	events (drowsiness, no	on-occurre	nce) - post	-treatment						
59 (1 study)	serio us1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	25/30 (83.3%)	23/29 (79.3%)	RR 0.95 (0.74 to 1.22)	833 per 1000	42 fewer per 1000 (from 217 fewer to 183 more)
Adverse	events (seizure, non-o	ccurrence)	- post-trea	itment						
59	serio	no serious	serious2	very	undetect	$\Theta \Theta \Theta \Theta$	29/30	29/29	RR	967 per	29 more per 1000

Quality as	ssessm	ent					Summar	y of Findi	ngs		
(1 study)	us1	inconsistenc y		serious3	ed	VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	(96.7%)	(100%)	1.03 (0.94 to 1.13)	1000	(from 58 fewer to 126 more)
Adverse	events (discontinuatio	n due to ac	lverse eve	nts, non-oc	currence) - post-	treatment				
59 (1 study)	serio us1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	29/30 (96.7%)	29/29 (100%)	RR 1.03 (0.94 to 1.13)	967 per 1000	29 more per 1000 (from 58 fewer to 126 more)
Adverse	events (discontinuatio	n due to ot	her reason	ns, non-occ	urrence) - post-ti	reatment				
59 (1 study)	serio us1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	28/30 (93.3%)	27/29 (93.1%)	RR 1 (0.87 to 1.14)	933 per 1000	0 fewer per 1000 (from 121 fewer to 131 more)
2 Applicat	oility - dif	n for one criterio ferent populatio tion size not me	ns		or multiple ci	riteria sufficient to	lower ones	confidenc	e in the e	stimate of e	ffect

A.9.5 Withdrawal of aripiprazole versus continuation of aripiprazole in children and young people

Table 33: Withdrawal of aripiprazole versus continuation of aripiprazole in children and young people

Quality as	ssessme	ent					Summary of	Findings			
Participa	Risk	Inconsistenc	Indirectn	Imprecis	Publicati	Overall quality	Study event	rates (%)	Relativ	Anticipated ab	solute effects
nts (studies)	of bias	У	ess	ion	on bias	of evidence	With	With	e effect	Risk with	Risk difference

Quality as	ssessme	ent					Summary of	Findings			
Follow up							continuatio n of aripiprazole	withdrawal of aripiprazol e	(95% CI)	continuation of aripiprazole	with withdrawal of aripiprazole (95% CI)
Targeted	behavio	our that challen	iges (relaps	se) - post-ti	reatment						
85 (1 study)	seriou s1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	14/41 (34.1%)	23/44 (52.3%)	RR 1.53 (0.92 to 2.55)	341 per 1000	181 more per 1000 (from 27 fewer to 529 more)
Adverse	events (v	weight gain; cl	inically sig	., non-occı	irrence)						
85 (1 study)	seriou s1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	39/41 (95.1%)	43/44 (97.7%)	RR 1.03 (0.95 to 1.12)	951 per 1000	29 more per 1000 (from 48 fewer to 114 more)
Adverse	events (discontinuatio	n due to ad	verse ever	nts, non-oco	currence) - post-tr	eatment				
85 (1 study)	seriou s1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	41/41 (100%)	43/44 (97.7%)	RR 0.98 (0.92 to 1.04)	1000 per 1000	20 fewer per 1000 (from 80 fewer to 40 more)
Adverse e	events (discontinuatio	n due to otl	ner reason	s, non-occı	irrence) - post-tre	atment				
85 (1 study)	seriou s1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖ VERY LOW1,2,3 due to risk of bias, 	22/41 (53.7%)	20/44 (45.5%)	RR 0.85 (0.55 to 1.3)	537 per 1000	80 fewer per 1000 (from 241 fewer to 161 more)

Quality assessment		Summary of Findings						
		indirectness, imprecision						
1 Crucial limitation for one crite 2 Applicability - different popul 3 Optimal information size not	ations	multiple criteria sufficient to lo	wer ones confi	dence in the e	estimate c	f effect		

A.9.6 Olanzapine versus haloperidol in children and young people

 Table 34: Olanzapine versus haloperidol in children and young people

Quality as	ssessme	ent					Summar	y of Find	ings			
Participa nts	Risk of	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of	Study ev (%)	ent rates	Relativ e effect	Anticipated absolute effects		
(studies) Follow up	bias					evidence	With haloper idol	With olanza pine	(95% CI)	Risk with haloperi dol	Risk difference with olanzapine (95% CI)	
Targeted	behavio	ur that challen	ges (severity)	- post-trea	tment (Bett	er indicated b	y lower va	lues)				
12 (1 study)	very seriou s1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	6	6	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 1.4 standard deviations lower (2.73 to 0.08 lower)	
Adverse e	events (o	drowsiness, no	n-occurrence) - post-tre	atment							
12 (1 study)	very seriou s1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	 ⊕⊖⊖ VERY LOW1,2 due to risk of bias, imprecision 	4/6 (66.7%)	1/6 (16.7%)	RR 0.25 (0.04 to 1.63)	667 per 1000	500 fewer per 1000 (from 640 fewer to 420 more)	
Adverse e	events -	(weight gain; k	g) - post-treat	tment (Bett	er indicated	d by lower val	ues)					
12	very	no serious	no serious	very	undetect	$\Theta \Theta \Theta$	6	6	-		The mean adverse events -	

(1 study)	seriou s1	inconsistenc y	indirectnes s	serious2	ed	VERY LOW1,2 due to risk of bias, imprecision					(weight gain; kg) - post- treatment in the intervention groups was 1.26 standard deviations higher (0.03 lower to 2.54 higher)
Adverse	events (v	weight gain) - p	ost-treatmen	t							
12 (1 study)	very seriou s1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	6/6 (100%)	5/6 (83.3%)	RR 0.85 (0.55 to 1.31)	1000 per 1000	150 fewer per 1000 (from 450 fewer to 310 more)
		for one or more ion size not met			antially lowe	er ones confider	nce in the e	estimate o	f effect.		

A.9.7 Topiramate (plus risperidone) versus placebo (plus risperidone) in children and young people

Table 35: Topiramate (plus risperidone) versus placebo (plus risperidone) in children and young people

Quality as	Quality assessment							of Findings			
Participa	Risk of	Inconsisten	Indirectn	Imprecis	Publicati	Overall	Study ever	nt rates (%)	Relativ	Anticipated	absolute effects
nts (studies) Follow up	bias	су	ess	ion	on bias	quality of evidence	With placebo plus risperido ne	With topiramat e plus risperidon e	e effect (95% CI)	Risk with Placebo plus risperidon e	Risk difference with topiramate plus risperidone (95% CI)
Targeted	behaviou	ir that challeng	ges (severi	ty) - post-ti	reatment (E	Better indicate	d by lower v	values)			
40 (1 study)	no seriou s risk of bias	no serious inconsistenc y	serious1	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to indirectness , imprecision	20	20	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 1.88 standard deviations lower

Quality a	ssessmei	nt					Summary	of Findings			
											(2.63 to 1.12 lower)
Adverse	events (s	edation, non-c	occurrence) - post-trea	atment						
40 (1 study)	no seriou s risk of bias	no serious inconsistenc y	serious1	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to indirectness , imprecision	16/20 (80%)	19/20 (95%)	RR 1.19 (0.93 to 1.51)	800 per 1000	152 more per 1000 (from 56 fewer to 408 more)
Adverse	events (w	eight at endpo	oint; <mark>kg) -</mark> p	ost-treatm	ent (Better	indicated by l	ower values	5)			
40 (1 study)	no seriou s risk of bias	no serious inconsistenc y	serious1	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to indirectness , imprecision	20	20	-		The mean adverse events (weight at endpoint; kg) - post- treatment in the intervention groups was 0.24 standard deviations lower (0.87 lower to 0.38 higher)

2 Optimal information size not met; small, single study

A.9.8 Valproate versus placebo in children and young people

Table 36: Topiramate (plus risperidone) versus placebo (plus risperidone) in children and young people

Quality as	ssessme	ent					Summ	ary of Fi	ndings		
Participa nts	Risk of	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of evidence	Study rates (Relativ e effect	Anticipa	ated absolute effects
(studies) Follow up	bias						With place bo	With valpro ate	(95% CI)	Risk with place bo	Risk difference with valproate (95% CI)

Targeted	behavio	ur that challen	ges (severity)	- post-trea	itment (Bett	er indicated by low	er value				
57 (2 studies)	seriou s1	serious2	no serious indirectnes s	serious3	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, inconsistency, imprecision 	25	32	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.06 standard deviations lower (0.75 lower to 0.63 higher)
Targeted	behavio	ur that challen	ges (severity,	non-impro	vement) - p	ost-treatment					
27 (1 study)	seriou s4	no serious inconsistenc y	no serious indirectnes s	very serious5	undetect ed	⊕⊖⊖⊖ VERY LOW4,5 due to risk of bias, imprecision	10/11 (90.9 %)	6/16 (37.5 %)	RR 0.41 (0.21 to 0.8)	909 per 1000	536 fewer per 1000 (from 182 fewer to 718 fewer)
Adverse e	events (v	veight gain; kg) - post-treatr	nent (meas	ured with:	Change score; Bett	er indica	ated by I	ower valu	ies)	
57 (2 studies)	seriou s1	no serious inconsistenc y	no serious indirectnes s	serious3	undetect ed	$\oplus \oplus \ominus \ominus$ LOW1,3 due to risk of bias, imprecision	25	32	-		The mean adverse events (weight gain; kg) - post- treatment in the intervention groups was 0.29 standard deviations higher (0.24 lower to 0.82 higher)
Adverse e	events (v	weight gain, no	n-occurrence	e) - post-tre	atment						
30 (1 study)	seriou s4	no serious inconsistenc y	no serious indirectnes s	very serious5	undetect ed	 ⊕⊖⊖⊖ VERY LOW4,5 due to risk of bias, imprecision 	10/14 (71.4 %)	9/16 (56.3 %)	RR 0.79 (0.46 to 1.36)	714 per 1000	150 fewer per 1000 (from 386 fewer to 257 more)
Adverse e	events (s	somnolence/se	dation, non-o	ccurrence)	- post-trea	tment					
57 (2 studies)	seriou s1	no serious inconsistenc y	no serious indirectnes s	serious3	undetect ed	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision	19/25 (76%)	29/32 (90.6 %)	RR 1.19 (0.9 to 1.56)	760 per 1000	144 more per 1000 (from 76 fewer to 426 more)
Adverse e	events (o	discontinuation	n due to adver	rse events,	non-occuri	rence) - post-treatm	ent				
57 (2	seriou s1	no serious inconsistenc	no serious indirectnes	serious3	undetect ed	⊕⊕⊝⊝ LOW1,3	25/25 (100	30/32 (93.8	RR 0.95 (0.83	1000 per	50 fewer per 1000 (from 170 fewer to 80 more)

studies)		у	S			due to risk of bias, imprecision	%)	%)	to 1.08)	1000	
Adverse	events (d	discontinuation	due to other	reasons, r	on-occurre	ence) - post-treatme	nt				
27 (1 study)	seriou s4	no serious inconsistenc y	no serious indirectnes s	very serious5	undetect ed	⊕⊖⊖⊖ VERY LOW4,5 due to risk of bias, imprecision	10/11 (90.9 %)	15/16 (93.8 %)	RR 1.03 (0.82 to 1.29)	909 per 1000	27 more per 1000 (from 164 fewer to 264 more)
2 I2 > 40% 3 Optimal 4 Crucial I	6 informati imitation	is from studies ion size not met for one criterion ion size not met	or some limita	ations for m	ultiple criteri	a sufficient to lower o	ones con	fidence i	n the estir	nate of e	ffect

A.9.9 N-acetylcysteine versus placebo in children and young people

Table 37: N-acetylcysteine versus placebo in children and young people

nts of y ess ion on bias of evidence (%) e (studies) bias bias Follow (%) effect (95%) (95%)	Anticipated absolute effects Risk Risk difference with N-
Follow place acetylcyste (95%	Risk Risk difference with N-
	with acetylcysteine (NAC) place (95% CI) bo
Targeted behaviour that challenges (severity) - post-treatment (Better indicated by lower values)	
29 (1 study)serio us1no serious inconsistenc yserious2very serious3undetect ed⊕⊙⊙ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision1514-	The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.70 standard deviations lower (1.46 lower to 0.05 higher)

Quality assessment						Summary of Findings					
33 (1 study)	serio us1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	18/18 (100 %)	14/15 (93.3%)	RR 0.93 (0.78 to 1.11)	1000 per 1000	70 fewer per 1000 (from 220 fewer to 110 more)
Adverse events (discontinuation due to other reasons, non-occurrence) - post-treatment											
33 (1 study)	serio us1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	12/18 (66.7 %)	14/15 (93.3%)	RR 1.4 (0.98 to 1.99)	667 per 1000	267 more per 1000 (from 13 fewer to 660 more)
 Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect Applicability - different populations Optimal information size not met; small, single study 											

A.9.10 Ginkgo biloba (plus risperidone) versus placebo (plus risperidone) in children and young people

Table 38: Ginkgo biloba (plus risperidone) versus placebo (plus risperidone) in children and young people

Quality assessment							Summary of Findings					
Participa Ri	Risk of	Inconsisten	Indirectn	Imprecis	Publicati	Overall	Study event rates (%)		Relativ	Anticipated absolute effects		
nts bia (studies) Follow up	vias	су	ess	ion	on bias	quality of evidence	With placebo plus risperido ne	With ginkgo biloba plus risperidon e	e effect (95% CI)	Risk with placebo plus risperidon e	Risk difference with ginkgo biloba plus risperidone (95% CI)	

Targeted behaviour that challenges (severity) - post-treatment (Better indicated by lower values)

Quality as	ssessmer	nt					Summary	of Findings			
47 (1 study)	no seriou s risk of bias	no serious inconsistenc y	serious1	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to indirectness , imprecision	24	23	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.1 standard deviations higher (0.47 lower to 0.67 higher)
Adverse	events (d	rowsiness, no	n-occurren	ce) - post-	treatment						
47 (1 study)	no seriou s risk of bias	no serious inconsistenc y	serious1	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to indirectness , imprecision	17/24 (70.8%)	17/23 (73.9%)	RR 1.04 (0.73 to 1.49)	708 per 1000	28 more per 1000 (from 191 fewer to 347 more)
	-	erent population		le study							

A.9.11 Omega-3 versus placebo in children and young people

 Table 39: Omega-3 versus placebo in children and young people

Quality as	ssessme	ent					Summ	ary of F	indings		
Participa nts	Risk of	Inconsistenc y	Indirectn ess	Imprecis ion	Publicati on bias	Overall quality of evidence	Study e rates (9		Relativ e effect	Anticipa	ated absolute effects
(studies) Follow up	bias						With place bo	With omeg a-3	(95% CI)	Risk with place bo	Risk difference with omega-3 (95% CI)
Targeted	behavio	ur that challen	ges (severi	ty) - post-t	reatment (B	Better indicated by	lower va	alues)			
12	seriou	no serious	serious2	very	undetect	$\oplus \ominus \ominus \ominus$	5	7	-		The mean targeted behaviour

Quality as	ssessme	ent					Summ	ary of F	indings		
(1 study)	s1	inconsistenc y		serious3	ed	VERY LOW1,2,3 due to risk of bias, indirectness, imprecision					that challenges (severity) - post- treatment in the intervention groups was 0.37 standard deviations higher (0.79 lower to 1.53 higher)
Adverse	events (discontinuatior	n due to ad	verse even	ts, non-occ	urence) - post-trea	tment				
13 (1 study)	seriou s1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	5/6 (83.3 %)	7/7 (100 %)	RR 1.19 (0.78 to 1.83)	833 per 1000	158 more per 1000 (from 183 fewer to 692 more)
2 Applicat	oility - dif	for one criterior ferent population ion size not met	าร		r multiple crit	eria sufficient to low	er ones	confide	nce in the	estimate	of effect

A.9.12 Piracetam (plus risperidone) versus placebo (plus risperidone) in children and young people

Table 40: Piracetam (plus risperidone) versus placebo (plus risperidone) in children and young people

Quality as	ssessme	ent					Summary of	f Findings			
Participa	Risk	Inconsistenc	Indirectn	Imprecis	Publicati	Overall quality	Study event	rates (%)	Relativ	Anticipated al	osolute effects
nts (studies) Follow up	of bias	У	ess	ion	on bias	of evidence	With placebo (plus risperidone)	With piracetam (plus risperidone)	e effect (95% CI)	Risk with placebo (plus risperidone)	Risk difference with piracetam (plus risperidone) (95% CI)
Adverse	events (e	drowsiness, no	n-occurren	ce) - post-l	treatment						
40 (1 study)	seriou s1	no serious inconsistenc y	serious2	very serious3	undetect ed	⊕⊖⊝⊖ VERY LOW1,2,3 due to risk of	11/20 (55%)	13/20 (65%)	RR 1.18 (0.71 to	550 per 1000	99 more per 1000 (from 160 fewer to 534 more)

	bias, indirectness, imprecision	1.97)	
 Crucial limitation for one criterion or some limitations for mu Applicability - different populations Optimal information size not met; small, single study 	Itiple criteria sufficient to lower ones co	nfidence in the estimate of effect	

A.9.13 Risperidone versus placebo in adults

Table 41: Risperidone versus placebo in adults

Quality a	ssessmen	t					Summ	ary of Fin	dings		
Participa nts	Risk of bias	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of evidence	Study rates (Relativ e	Anticipa	ated absolute effects
(studies) Follow up							With place bo	With risperid one	effect (95% CI)	Risk with place bo	Risk difference with risperidone (95% CI)
Targeted	behaviou	r that challenge	es (severity) -	post-treat	ment (meas	ured with: End-	point so	ore; 12 w	eek; Bett	er indica	ated by lower values)
88 (2 studies)	no serious risk of bias	serious1	no serious indirectnes s	serious2	undetect ed	⊕⊕⊝⊝ LOW1,2 due to inconsistency, imprecision	45	43	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.25 standard deviations lower (0.94 lower to 0.44 higher)
Targeted	behaviou	r that challenge	es (severity) -	post-treat	ment (meas	sured with: Char	nge-sco	re; 12 wee	k; Better	indicate	ed by lower values)
74 (1 study)	serious 3	no serious inconsistenc y	no serious indirectnes s	very serious4	undetect ed	 ⊕⊖⊖ VERY LOW3,4 due to risk of bias, imprecision 	37	37	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.44 standard deviations lower (0.9 lower to 0.02 higher)

Quality as	ssessmen	t					Summ	ary of Fin	dings		
Targeted	behaviou	r that challenge	es (severity) -	post-treat	ment (meas	sured with: End	ooint-sc	ore; 26 w	eks5; Be	tter indi	cated by lower values)
37 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious4	undetect ed	⊕⊕⊝⊝ LOW4 due to imprecision	20	17	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.16 standard deviations higher (0.48 lower to 0.81 higher)
Quality of	f life - pos	t-treatment (me	easured with:	12 weeks;	Better indi	cated by higher	values)				
58 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious4	undetect ed	⊕⊕⊝⊝ LOW4 due to imprecision	29	29	-		The mean quality of life - post-treatment in the intervention groups was 0.27 standard deviations higher (0.25 lower to 0.79 higher)
Quality of	f life - pos	t-treatment (me	easured with:	26 weeks5	5; Better ind	licated by highe	er values	5)			
40 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious4	undetect ed	⊕⊕⊖⊖ LOW4 due to imprecision	21	19	-		The mean quality of life - post-treatment in the intervention groups was 0.2 standard deviations higher (0.42 lower to 0.82 higher)
Adaptive	functionir	ng (social) - po	st-treatment (Better indi	cated by lo	wer values)					
30 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious4	undetect ed	⊕⊕⊝⊝ LOW4 due to imprecision	16	14	-		The mean adaptive functioning (social) - post- treatment in the intervention groups was 1.36 standard deviations lower (2.17 to 0.56 lower)
Adverse e	events (we	eight gain, non	-occurrence)	- post-trea	tment						
31 (1 study)	no serious risk of bias	no serious inconsistenc y	serious6	very serious4	undetect ed	⊕⊖⊝⊖ VERY LOW4,6 due to	16/16 (100 %)	13/15 (86.7%)	RR 0.87 (0.69 to	1000 per 1000	130 fewer per 1000 (from 310 fewer to 90 more)

ssessmen	t					Summ	ary of Fin	dings		
					indirectness, imprecision			1.09)		
events (so	mnolence/sed	ation, non-oc	currence) ·	- post-treat	ment					
no serious risk of bias	very serious7	no serious indirectnes s	serious2	undetect ed	 ⊕⊖⊖ VERY LOW2,7 due to inconsistency, imprecision 	48/54 (88.9 %)	36/54 (66.7%)	RR 0.65 (0.28 to 1.47)	889 per 1000	311 fewer per 1000 (from 640 fewer to 418 more)
events (dis	scontinuation	due to advers	e events, r	non-occurre	ence) - post-trea	tment				
no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	serious4	undetect ed	⊕⊕⊕⊝ MODERATE4 due to imprecision	45/45 (100 %)	41/44 (93.2%)	RR 0.95 (0.87 to 1.04)	1000 per 1000	50 fewer per 1000 (from 130 fewer to 40 more)
events (dis	scontinuation	due to other r	easons, no	on-occurrer	nce) - post-treatr	nent				
no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	serious4	undetect ed	⊕⊕⊕⊝ MODERATE4 due to imprecision	67/83 (80.7 %)	70/83 (84.3%)	RR 1.04 (0.92 to 1.18)	807 per 1000	32 more per 1000 (from 65 fewer to 145 more)
•	events (so no serious risk of bias events (dis risk of bias events (dis no serious risk of	no very serious serious7 risk of bias events (discontinuation no no serious risk of y bias events (discontinuation y bias events (discontinuation risk of y bias	events (somnolence/sedation, non-ocnoveryno seriousseriousserious7indirectnesrisk ofserious7sbiasno serioussevents (discontinuation due to adversnono seriousno seriousinconsistencno seriousindirectnesrisk ofysbiasss	events (somnolence/sedation, non-occurrence)noveryno seriousserious2seriousserious7indirectnesserious2risk ofssssbiasno serioussssevents (discontinuation due to adverse events, rno seriousserious4nono seriousno seriousserious4risk ofysssbiasysssevents (discontinuation due to other reasons, noserious4nono seriousno seriousserious4nono seriousno seriousserious4events (discontinuation due to other reasons, noserious4nono seriousno seriousseriousinconsistencindirectnes5seriousinconsistencsseriousinconsistencsseriousinconsistencsserioussseriouss	events (somnolence/sedation, non-occurrence) - post-treationnoveryno seriousserious2undetectseriousserious7indirectnesserious2undetectrisk ofseriousssssevents (discontinuation due to adverse events, non-occurrentno seriousno seriousserious4undetectnono seriousno seriousno seriousserious4undetectednono seriousno seriousserious4undetectedseriousyssserious4undetectedevents (discontinuation due to other reasons, non-occurrentno seriousserious4undetectednono seriousno seriousserious4undetectedevents (discontinuation due to other reasons, non-occurrentno seriousserious4undetectnono seriousno seriousserious4undetectnoseriousssserious4undetectrisk ofyssserious4undetect	events (somnolence/sedation, non-occurrence) - post-treatmentnoveryno seriousserious2undetect⊕ ⊖ ⊖ ⊖seriousserious7indirectnesserious2undetect⊕ ⊖ ⊖ ⊖risk ofserious7seriousserious2undetect⊕ ⊖ ⊖ ⊖biasveryserious7serious2undetectedVERYLOW2,7due toinconsistency,imprecisionevents (discontinuation due to adverse events, non-occurrence) - post-treatno seriousindirectnesnono seriousno seriousserious4undetect⊕ ⊕ ⊕noseriousindirectnesserious4undetectedMODERATE4biasvseriousno seriousno seriousserious4undetectedMODERATE4nono seriousno seriousserious4undetectedMODERATE4noserious4inconsistencserious4undetectedMODERATE4noserious4inconsistenc5serious4undetectedMODERATE4noserious4inconsistenc5serious4undetectedMODERATE4noserious4serious4undetectedMODERATE4ue to	events (somolence/sedation, non-occurrence) - post-treatmentno serious risk of biasvery serious7no serious indirectnes sserious2 serious2undetect ed⊕ ⊖ ⊖ ⊖ VERY UOW2,7 due to inconsistency, imprecision48/54 (88.9) %)events (discontinuation due to adverse events, non-occurrence) - post-treatmentno serious risk of biasno serious indirectnes sserious4 undetect⊕ ⊕ ⊕ ⊖ MODERATE4 due to imprecision45/45 (100 %)events (discontinuation due to other reasons, non-occurrence) - post-treatmentno serious risk of biasno serious sserious4 sundetect ed⊕ ⊕ ⊕ ⊖ MODERATE4 due to imprecision45/45 (100 %)events (discontinuation due to other reasons, non-occurrence) - post-treatmentno serious risk of biasno serious indirectnes sserious4 serious4undetect ed⊕ ⊕ ⊕ ⊖ MODERATE4 (100 %)	events (somolence/sedation, non-occurrence) - post-treatmentindirectness, imprecisionindirectness, imprecisionno serious risk of biasvery serious7no serious indirectnes sserious2 serious2undetect ed $\bigcirc \bigcirc (88.9)(VERYLOW2,7due toinconsistency,imprecision48/54(88.9)(66.7%(66.7%)(66.7%)(66.7%)(66.7%)(66.7%)(66.7%)(66.7%)(66.7%)(66.7%)36/54(66.7%)(66.7%)(66.7%)(66.7%)(66.7%)(60.7%)events (discontinuation due to adverse events, non-occurrence) - post-treatmentinconsistency,inconsistencyyno seriousseriousserioussno seriousseriousseriousno seriousserioussserious4edundetected\oplus \oplus \oplus \bigcirc \\ \% \otimes 0(100)(100)(100)(100)(100)(100)(9).2%)41/44(93.2%)(9).2%)noseriousrisk ofbiasno seriousinconsistencyno seriousserioussserious4serious4undetected\oplus \oplus \oplus \odot \otimes (57/83)(80.7(80.7)(80.7)70/83(84.3%)(84.3%)$	events (sorrolence/sedation, non-occurrence) - post-treatmentindirectness, imprecisionindirectness, imprecision1.09)serious risk of biasvery serious7no serious indirectnes sserious2 serious2undetect ed $\oplus \bigcirc \bigcirc \bigcirc$ VERY LOW2,7 due to inconsistency, imprecision48/54 (88.9 (66.7%)36/54 (0.65 (0.28) 	IndicationIndicationIndicationIndicationIndicationindirectness, imprecisionindirectness, seriousIndirectness, indirectnessIndirectness, indirectnessIndirectness, indirectnesIndicationIndirectnesIndication

2 Optimal information size not met

3 Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect

4 Optimal information size not met; small, single study

5 Participants agreed to take the study drug for 12 weeks, with the option of continuing until 26 weeks, unless at 12 weeks other options were preferred. Posttreatment data is therefore provided at both 12 and 26 week end of treatment.

6 Applicability - different populations

7 |2 > 75%

A.9.14 Haloperidol versus placebo in adults

Table 42: Haloperidol versus placebo in adults

Quality asse	essment						Summa	ry of Findings			
Participants	Risk of	Inconsiste	Indirectne	Imprecisio	Publicatio	Overall	Study ev	vent rates (%)	Relativ	Anticipa	ted absolute effects
(studies) Follow up	bias	ncy	SS	n	n bias	quality of evidence	With placeb o	With haloperidol	e effect (95% CI)	Risk with placeb o	Risk difference with haloperidol (95% CI)
Targeted beh	naviour that c	hallenges (se	everity) - post-	treatment (me	easured with:	12 weeks1; B	etter indic	ated by lower	/alues)		
57 (1 study)	no serious risk of bias	no serious inconsiste ncy	no serious indirectnes s	very serious2	undetecte d	⊕⊕⊖⊖ LOW2 due to imprecisio n	29	28	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.48 standard deviations lower (1 lower to 0.05 higher)
Targeted beh	naviour that c	hallenges (se	everity) - post-	treatment (me	easured with:	26 weeks1; B	etter indic	ated by lower	/alues)		
40 (1 study)	no serious risk of bias	no serious inconsiste ncy	no serious indirectnes s	very serious2	undetecte d	⊕⊕⊖⊖ LOW2 due to imprecisio n	20	20	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.25 standard deviations lower (0.87 lower to 0.37 higher)
Quality of life	- post-treatr	ment (measure	ed with: 12 we	eeks1; Better	indicated by h	nigher values)					
57	no	no serious	no serious	very	undetecte	$\oplus \oplus \ominus \ominus$	29	28	-		The mean quality of

Quality asse	essment						Summa	ry of Findings	;		
(1 study)	serious risk of bias	inconsiste ncy	indirectnes s	serious2	d	LOW2 due to imprecisio n					life - post-treatment in the intervention groups was 0.17 standard deviations lower (0.69 lower to 0.35 higher)
Quality of life	- post-treatr	ment (measure	ed with: 26 we	eeks1; Better	indicated by h	nigher values)					
41 (1 study)	no serious risk of bias	no serious inconsiste ncy	no serious indirectnes s	very serious2	undetecte d	⊕⊕⊖⊖ LOW2 due to imprecisio n	21	20	-		The mean quality of life - post-treatment in the intervention groups was 0.18 standard deviations lower (0.79 lower to 0.43 higher)
Adverse ever	nts (seizure,	non-occurren	ce) - post-trea	atment							
57 (1 study)	no serious risk of bias	no serious inconsiste ncy	no serious indirectnes s	very serious2	undetecte d	⊕⊕⊖⊖ LOW2 due to imprecisio n	29/29 (100%)	27/28 (96.4%)	RR 0.96 (0.88 to 1.06)	1000 per 1000	40 fewer per 1000 (from 120 fewer to 60 more)
Adverse ever	nts (discontir	nuation due to	adverse ever	nts, non-occu	rrence) - post	-treatment					
57 (1 study)	no serious risk of bias	no serious inconsiste ncy	no serious indirectnes s	very serious2	undetecte d	⊕⊕⊖⊖ LOW2 due to imprecisio n	29/29 (100%)	26/28 (92.9%)	RR 0.93 (0.82 to 1.05)	1000 per 1000	70 fewer per 1000 (from 180 fewer to 50 more)
Adverse ever	nts (discontir	nuation due to	other reasons	s, non-occurr	ence) - post-t	reatment					
57 (1 study)	no serious risk of bias	no serious inconsiste ncy	no serious indirectnes s	very serious2	undetecte d	⊕⊕⊝⊝ LOW2 due to imprecisio	21/29 (72.4%)	23/28 (82.1%)	RR 1.13 (0.85 to	724 per 1000	94 more per 1000 (from 109 fewer to 369 more)

Quality ass	essment					Summa	ry of Findings		
					n			1.51)	
	greed to take ata is therefor				uing until 26 w	eeks, unle	ess at 12 weeks	s other options we	re preferred. Post-
2 Optimal in	formation size	e not met; sm	all, single trial						

A.9.15 Risperidone versus haloperidol in adults

Table 43: Risperidone versus haloperidol in adults

Quality as	ssessmen	t					Summar	y of Find	ings		
Participa nts	Risk of bias	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of	Study ev (%)	ent rates	Relativ e	Anticipate	d absolute effects
(studies) Follow up						evidence	With haloper idol	With risperid one	effect (95% CI)	Risk with haloperi dol	Risk difference with risperidone (95% CI)
Targeted	behaviou	r that challeng	es (severity)	- post-treat	tment (mea	sured with: 12	2 weeks1;	Better in	dicated b	y lower va	lues)
57 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊕⊝⊝ LOW2 due to imprecision	28	29	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.49 standard deviations higher (0.03 lower to 1.02 higher)
Targeted	behaviou	r that challeng	es (severity)	- post-treat	tment (mea	sured with: 20	6 weeks1;	Better in	dicated b	y lower va	lues)
36 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊕⊝⊝ LOW2 due to imprecision	19	17	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.39 standard deviations higher (0.28 lower to 1.05 higher)

Quality of life - post-treatment (measured with: 12 weeks1; Better indicated by higher values)

Quality as	ssessmen	t					Summa	ry of Find	ings		
57 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊕⊝⊝ LOW2 due to imprecision	28	29	-		The mean quality of life - post-treatment in the intervention groups was 0.43 standard deviations higher (0.09 lower to 0.96 higher)
Quality of	f life - pos	t-treatment (m	easured with	: 26 weeks	1; Better in	ndicated by hi	gher valu	es)			
39 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊕⊖⊖ LOW2 due to imprecision	20	19	-		The mean quality of life - post-treatment in the intervention groups was 0.41 standard deviations higher (0.23 lower to 1.04 higher)
Adverse e	events (se	eizure, non-occ	urrence) - po	st-treatme	nt						
57 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊕⊖⊖ LOW2 due to imprecision	27/28 (96.4%)	29/29 (100%)	RR 1.04 (0.94 to 1.14)	964 per 1000	39 more per 1000 (from 58 fewer to 135 more)
Adverse e	events (di	scontinuation	due to advers	se events)	- post-treat	ment					
57 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊕⊖⊖ LOW2 due to imprecision	26/28 (92.9%)	28/29 (96.6%)	RR 1.04 (0.92 to 1.18)	929 per 1000	37 more per 1000 (from 74 fewer to 167 more)
Adverse e	events (di	scontinuation	due to other	reasons) -	post-treatm	nent					
57 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊕⊝⊝ LOW2 due to imprecision	24/28 (85.7%)	23/29 (79.3%)	RR 0.93 (0.73 to 1.18)	857 per 1000	60 fewer per 1000 (from 231 fewer to 154 more)

1 Patients agreed to take the study drug for 12 weeks, with the option of continuing until 26 weeks, unless at 12 weeks other options were preferred. Post-treatment data is therefore provided at both 12 and 26 week end of treatment. 2 Optimal information size not met; small, single study

A.9.16 Olanzapine versus risperidone in adults

Table 44: Olanzapine versus risperidone in adults

Quality as	ssessme	ent					Summa	ry of Find	ings		
Participa nts	Risk of	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of	Study ev (%)	ent rates	Relativ e	Anticipate	d absolute effects
(studies) Follow up	bias					evidence	With risperid one	With olanza pine	effect (95% CI)	Risk with risperido ne	Risk difference with olanzapine (95% CI)
Targeted	behavio	ur that challen	ges (frequend	cy) - post-tr	eatment (B	etter indicated	l by lower	values)			
62 (1 study)	seriou s1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	 ⊕⊖⊖ VERY LOW1,2 due to risk of bias, imprecision 	31	31	-		The mean targeted behaviour that challenges (frequency) - post-treatment in the intervention groups was 0.2 standard deviations higher (0.3 lower to 0.7 higher)
Adverse e	events (e	elevated prolac	tin) - post-tre	atment							
62 (1 study)	seriou s1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	30/31 (96.8%)	22/31 (71%)	RR 0.73 (0.58 to 0.93)	968 per 1000	261 fewer per 1000 (from 68 fewer to 406 fewer)
Adverse e	events (v	weight gain, no	n-occurrence	e) - post-tre	atment						
62 (1 study)	seriou s1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	28/31 (90.3%)	24/31 (77.4%)	RR 0.86 (0.69 to 1.07)	903 per 1000	126 fewer per 1000 (from 280 fewer to 63 more)
Adverse e	events (s	sedation, non-o	occurrence) -	post-treatn	nent						
62	seriou	no serious	no serious	very	undetect	$\Theta \Theta \Theta \Theta$	26/31	24/31	RR	839 per	67 fewer per 1000

(1 study)	s2	inconsistenc y	indirectnes s	serious2	ed	VERY LOW2 due to risk of bias, imprecision	(83.9%)	(77.4%)	0.92 (0.72 to 1.18)	1000	(from 235 fewer to 151 more)
		for one criterior ion size not met			ultiple criteri	a sufficient to lo	ower ones	confidenc	e in the e	stimate of el	fect

A.9.17 Lithium versus placebo in adults

Table 45: Lithium versus placebo in adults

Quality as	ssessmer	nt					Summa	ary of Fi	ndings			
Participa nts	Risk of bias	Inconsistency	Indirectness	Imprecis ion	Publicatio n bias	Overall quality of evidence	Study e rates (%		Relative effect	Anticipate	ed absolute effects	
(studies) Follow up							With place bo	With lithiu m	(95% CI)	Risk with placebo	Risk difference with lithium (95% CI)	
Targeted	Fargeted behaviour that challenges (frequency, non-improvement)											
42 (1 study)	serious no serious no serious very undetecte $\oplus \ominus \ominus \ominus$ 14/20 6/22 RR 0.39 700 per 427 fewer per											
	1 Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect 2 Optimal information size not met; small, single study											

A.9.18 Withdrawal of zuclopenthixol versus continuation of zuclopenthixol in adults

Table 46: Withdrawal of zuclopenthixol versus continuation of zuclopenthixol in adults

Quality as	ssessm	ent					Summary o	f Findings				
Participa	Risk	Inconsisten	Indirectne	Imprecis	Publicati	Overall quality	Study event	rates (%)	Relati	Anticipated absolute effects		
nts	of	су	SS	ion	on bias	of evidence	With	With	ve	Risk with	Risk difference with	

(studies) Follow up	bias						continuatio n of zuclopenthi xol	withdrawal of zuclopenthi xol	effect (95% CI)	continuation of zuclopenthi xol	withdrawal of zuclopenthixol (95% CI)
Targeted	behavio	our that challe	nges (relaps	e) - post-tr	eatment						
39 (1 study)	serio us1	no serious inconsisten cy	no serious indirectne ss	very serious2	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision 	12/19 (63.2%)	19/20 (95%)	RR 1.5 (1.05 to 2.15)	632 per 1000	316 more per 1000 (from 32 more to 726 more)
Targeted	behavio	our that challe	nges (severi	ty) - post-t	reatment (n	neasured with: E	End-point sco	ore; Better ind	licated b	y lower values	s)
39 (1 study)	serio us1	no serious inconsisten cy	no serious indirectne ss	very serious2	undetect ed	 ⊕⊖⊖ ∨ERY LOW1,2 due to risk of bias, imprecision 	19	20	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.56 standard deviations higher (0.08 lower to 1.2 higher)
Targeted	behavio	our that challe	nges (severi	ty) - post-t	reatment (n	neasured with: (Change score	; Better indic	ated by I	ower values)	
85 (1 study)	serio us1	no serious inconsisten cy	no serious indirectne ss	very serious2	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision 	45	40	-		The mean targeted behaviour that challenges (severity) - post-treatment in the intervention groups was 0.68 standard deviations higher (0.24 to 1.11 higher)
Targeted	behavio	our that challe	nges (proble	ems in man	agement) -	post-treatment					
43 (1 study)	serio us3	no serious inconsisten cy	no serious indirectne ss	very serious2	undetect ed	⊕⊝⊝ VERY LOW2,3	5/24 (20.8%)	7/19 (36.8%)	RR 1.77 (0.67	208 per 1000	160 more per 1000 (from 69 fewer to 771 more)

						due to risk of bias, imprecision			to 4.7)		
Adaptive	function	ning (social) -	post-treatme	ent (Better	indicated b	y higher values)				
85 (1 study)	serio us1	no serious inconsisten cy	no serious indirectne ss	very serious2	undetect ed	 ⊕⊖⊖ VERY LOW1,2 due to risk of bias, imprecision 	45	40	-		The mean adaptive functioning (social) - post-treatment in the intervention groups was 0.47 standard deviations lower (0.9 to 0.04 lower)
Adverse e	events (weight gain; k	(g) - post- tre	eatment (Be	etter indica	ted by lower val	ues)				
39 (1 study)	serio us1	no serious inconsisten cy	no serious indirectne ss	very serious2	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision 	19	20	-		The mean adverse events (weight gain; kg) - post- treatment in the intervention groups was 0.55 standard deviations lower (1.19 lower to 0.09 higher)
Adverse e	events (drowsiness, r	non-occurren	ice) - post-	treatment						
42 (1 study)	serio us1	no serious inconsisten cy	no serious indirectne ss	very serious2	undetect ed	 ⊕⊖⊖ VERY LOW1,2 due to risk of bias, imprecision 	19/20 (95%)	21/22 (95.5%)	RR 1 (0.88 to 1.15)	950 per 1000	0 fewer per 1000 (from 114 fewer to 142 more)
Adverse e	events (discontinuatio	on due to adv	verse even	ts, non-occ	urrence) - post-	treatment				
204 (3 studies)	serio us4	serious5	no serious indirectne ss	serious6	undetect ed	⊕⊖⊖⊖ VERY LOW4,5,6 due to risk of bias, inconsistency,	98/103 (95.1%)	80/101 (79.2%)	RR 0.86 (0.71 to 1.04)	951 per 1000	133 fewer per 1000 (from 276 fewer to 38 more)

						imprecision							
Adverse	dverse events (discontinuation due to other reasons, non-occurrence) - post-treatment												
91 (2 studies)	serio us4	very serious7	no serious indirectne ss	serious6	undetect ed	 ⊕⊖⊖ VERY LOW4,6,7 due to risk of bias, inconsistency, imprecision 	38/46 (82.6%)	29/45 (64.4%)	RR 0.73 (0.33 to 1.64)	826 per 1000	223 fewer per 1000 (from 553 fewer to 529 more)		

A.9.19 Melatonin versus placebo in children and young people

 Table 47: Melatonin versus placebo in children and young people

Quality as	ssessmen	t					Summary of Findings					
Participa							Study rates (Relativ	Anticipa	ated absolute effects	
nts (studies) Follow up	Risk of bias	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of evidence	With place bo	With melat onin	e effect (95% CI)	Risk with place bo	Risk difference with melatonin (95% CI)	

Targeted behaviour that challenges (global problem sleep behaviour) - post-treatment (measured with: Children's Sleep Habits Questionnaire; Better indicated by lower values)

66 (1 study) Targeted	serious 1 behaviou	no serious inconsistenc y r that challeng	serious2 es (global pr	very serious3 oblem slee	undetect ed p behaviou	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	32 nt (meas	34 sured wi	- th: Comp	posite SI	The mean targeted behaviour that challenges (global problem sleep behaviour) - post- treatment in the intervention groups was 1.81 standard deviations lower (2.39 to 1.23 lower) eep Disturbance Index; Better
indicated	by lower	values)			-				-		•
125 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious3	undetect ed	⊕⊕⊖⊖ LOW3 due to imprecision	65	60	-		The mean targeted behaviour that challenges (global problem sleep behaviour) - post- treatment in the intervention groups was 0.26 standard deviations lower (0.62 lower to 0.09 higher)
Targeted	behaviou	r that challeng	jes (non-impi	ovement o	f global pr	oblem sleep beha	viour) -	post-tre	atment		
66 (1 study)	serious 1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	32/32 (100 %)	21/34 (61.8 %)	RR 0.62 (0.48 to 0.81)	1000 per 1000	380 fewer per 1000 (from 190 fewer to 520 fewer)
Targeted	behaviou	r that challeng	jes (sleep effi	iciency) - p	ost-treatm	ent (measured wi	th: Actig	graph; B	etter indi	cated by	v higher values)
124 (2 studies)	no serious risk of bias	very serious4	no serious indirectnes s	serious5	undetect ed	⊕⊖⊖⊖ VERY LOW4,5 due to inconsistency, imprecision	60	64	-		The mean targeted behaviour that challenges (sleep efficiency) - post-treatment in the intervention groups was 1.46 standard deviations higher (0.51 lower to 3.42 higher)
Targeted	behaviou	r that challeng	es (total slee	p time) - p	ost-treatme	ent (measured wit	th: Actig	raph; B	etter indi	cated by	higher values)
125 (2 studies)	no serious risk of	very serious4	no serious indirectnes s	serious5	undetect ed	⊕⊖⊖⊖ VERY LOW4,5 due to	61	64	-		The mean targeted behaviour that challenges (total sleep time) - post-treatment in the intervention groups was

Quality as	ssessmen	t					Summ	ary of Fi	indings		
Participa							Study rates (Relativ	Anticip	ated absolute effects
nts (studies) Follow up	Risk of bias	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of evidence	With place bo	With melat onin	e effect (95% CI)	Risk with place bo	Risk difference with melatonin (95% CI)
		r that challeng lower values)		oblem slee	ep behaviou	ur) - post-treatme	nt (meas	sured wi	th: Childr	en's Sle	eep Habits Questionnaire;
66 (1 study)	serious 1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	32	34	-		The mean targeted behaviour that challenges (global problem sleep behaviour) - post- treatment in the intervention groups was 1.81 standard deviations lower (2.39 to 1.23 lower)
	bias					inconsistency, imprecision					1.01 standard deviations highe (0.26 lower to 2.28 higher)
Targeted	behaviou	r that challeng	es (wake afte	er sleep on	set) - post-	treatment (measu	red with	h: Actigr	aph; Bett	er indic	ated by lower values)
115 (2 studies)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	serious5	undetect ed	⊕⊕⊕⊖ MODERATE5 due to imprecision	57	58	-		The mean targeted behaviour that challenges (wake after sleep onset) - post-treatment in the intervention groups was 0.76 standard deviations lower (1.14 to 0.38 lower)
Targeted	behaviou	r that challeng	es (sleep on	set latency) - post-trea	atment (measured	d with: A	Actigraph	n; Better i	ndicate	d by lower values)
66 (1 study)	serious 1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	32	34	-		The mean targeted behaviour that challenges (sleep onset latency) - post-treatment in the intervention groups was 1.23 standard deviations lower (1.75 to 0.7 lower)
Targeted	behaviou	r that challeng	es (total slee	p time) - p	ost-treatme	ent (measured wit	h: Sleep	o diary; E	Better ind	icated b	y higher values)
169	no	serious6	no serious	serious5	undetect	$\oplus \oplus \ominus \ominus$	85	84	-		The mean targeted behaviour

Quality a	ssessmen	it					Summ	ary of Fi	ndings		
Participa							Study of rates (Relativ	Anticip	ated absolute effects
nts (studies) Follow up	Risk of bias	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of evidence	With place bo	With melat onin	e effect (95% CI)	Risk with place bo	Risk difference with melatonir (95% CI)
		r that challeng lower values)		oblem slee	p behaviou	ur) - post-treatme	nt (meas	sured wit	th: Childr	en's Sle	ep Habits Questionnaire;
66 (1 study)	serious 1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	32	34	_		The mean targeted behaviour that challenges (global proble sleep behaviour) - post- treatment in the intervention groups was 1.81 standard deviations lowe (2.39 to 1.23 lower)
(3 studies)	serious risk of bias		indirectnes s		ed	LOW5,6 due to inconsistency, imprecision					that challenges (total sleep time) - post-treatment in the intervention groups was 0.34 standard deviations high (0.37 lower to 1.05 higher)
Targeted	behaviou	r that challeng	es (number d	of wakes p	er night) - p	oost-treatment (m	easured	with: SI	eep diary	; Better	indicated by lower values)
164 (3 studies)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	serious5	undetect ed	⊕⊕⊕⊖ MODERATE5 due to imprecision	81	83	-		The mean targeted behaviour that challenges (number of wakes per night) - post- treatment in the intervention groups was 0.06 standard deviations lowe (0.49 lower to 0.37 higher)
Targeted	behaviou	r that challeng	es (wake afte	er sleep on	set) - post-	treatment (measu	ured with	n: Sleep	diary; Be	tter indi	cated by lower values)
172 (3 studies)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	serious5	undetect ed	⊕⊕⊕⊖ MODERATE5 due to imprecision	85	87	-		The mean targeted behaviour that challenges (wake after sleep onset) - post-treatment the intervention groups was 0.64 standard deviations lowe

Quality as	ssessmen	t					Summ	ary of Fi	ndings		
Participa							Study rates (Relativ	Anticip	ated absolute effects
nts (studies) Follow up	Risk of bias	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of evidence	With place bo	With melat onin	e effect (95% CI)	Risk with place bo	Risk difference with melatonin (95% CI)
		r that challeng lower values)		oblem slee	p behaviou	ur) - post-treatme	nt (meas	sured wit	h: Childr	en's Sle	ep Habits Questionnaire;
66 (1 study)	serious 1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	32	34	_		The mean targeted behaviour that challenges (global problem sleep behaviour) - post- treatment in the intervention groups was 1.81 standard deviations lower (2.39 to 1.23 lower)
											(1.03 to 0.25 lower)
Targeted	behaviou	r that challeng	es (duration	of wakes)	 post-treat 	ment (measured)	with: Sle	eep diary	; Better i	ndicate	d by lower values)
163 (3 studies)	no serious risk of bias	serious6	no serious indirectnes s	serious5	undetect ed	⊕⊕⊖⊖ LOW5,6 due to inconsistency, imprecision	81	82	-		The mean targeted behaviour that challenges (duration of wakes) - post-treatment in the intervention groups was 0.23 standard deviations higher (0.36 lower to 0.82 higher)
Adverse	events (so	olomnence/sed	lation, non-o	ccurrence)	- post-trea	tment					
146 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious3	undetect ed	⊕⊕⊝⊖ LOW3 due to imprecision	66/76 (86.8 %)	61/70 (87.1 %)	RR 1 (0.89 to 1.14)	868 per 1000	0 fewer per 1000 (from 96 fewer to 122 more)
Adverse	events (di	scontinuation	due to adver	se events,	non-occur	rence) - post-trea	tment				
146 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious3	undetect ed	⊕⊕⊖⊖ LOW3 due to imprecision	74/76 (97.4 %)	69/70 (98.6 %)	RR 1.01 (0.97 to 1.06)	974 per 1000	10 more per 1000 (from 29 fewer to 58 more)

Quality as	ssessmen	t					Summ	ary of Fi	indings		
Participa							Study rates (Relativ	Anticip	ated absolute effects
nts (studies) Follow up	Risk of bias	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of evidence	With place bo	With melat onin	e effect (95% CI)	Risk with place bo	Risk difference with melatonin (95% CI)
		r that challeng lower values)		oblem slee	ep behaviou	ur) - post-treatme	ent (meas	sured wi	th: Childr	en's Sle	ep Habits Questionnaire;
66 (1 study)	serious 1	no serious inconsistenc y	serious2	very serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	32	34	-		The mean targeted behaviour that challenges (global problem sleep behaviour) - post- treatment in the intervention groups was 1.81 standard deviations lower (2.39 to 1.23 lower)
Adverse	events (di	scontinuation	due to other	reasons, r	on-occurre	ence) - post-treat	ment				
284 (3 studies)	no serious risk of bias	serious6	no serious indirectnes s	serious5	undetect ed	⊕⊕⊖⊖ LOW5,6 due to inconsistency, imprecision	127/1 44 (88.2 %)	130/1 40 (92.9 %)	RR 1.06 (0.94 to 1.2)	882 per 1000	53 more per 1000 (from 53 fewer to 176 more)
Adverse	events (se	izure, non-oco	currence) - po	ost-treatme	ent						
146 (1 study)	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	very serious3	undetect ed	⊕⊕⊝⊝ LOW3 due to imprecision	75/76 (98.7 %)	70/70 (100 %)	RR 1.01 (0.98 to 1.05)	987 per 1000	10 more per 1000 (from 20 fewer to 49 more)

2 Applicability- different populations 3 Optimal information size not met; small, single study 4 I2 > 75%

5 Optimal information size not met 6 I2 > 40%

A.9.20 Melatonin versus cognitive behavioural therapy in children and young people

 Table 48: Melatonin versus cognitive behavioural therapy in children and young people

Quality as	ssessme	ent					Sumn	nary of F	indings		
Participa nts	Risk of	Inconsistenc y	Indirectn ess	Imprecis ion	Publicati on bias	Overall quality of evidence	Study rates	event (%)	Relativ e effect	Antici	pated absolute effects
(studies) Follow up	bias						With CBT	With melato nin	(95% CI)	Risk with CBT	Risk difference with melatonin (95% CI)
Targeted indicated			ges (global	problem s	leep behavi	iour) - post-treatm	ent (me	easured v	vith: Chilo	lren's \$	Sleep Habits Questionnaire; Better
67 (1 study)	seriou s1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕ ⊖ ⊖ ∨ERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	33	34	-		The mean targeted behaviour that challenges (global problem sleep behaviour) - post-treatment in the intervention groups was 0.94 standard deviations lower (1.45 to 0.44 lower)
Targeted	behavio	ur that challen	ges (non-in	nprovemen	t of global s	sleep problem beh	aviour)) - post-tr	eatment		
67 (1 study)	seriou s1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕ ⊖ ⊖ ∨ERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	30/3 3 (90. 9%)	21/34 (61.8 %)	RR 0.68 (0.51 to 0.9)	909 per 100 0	291 fewer per 1000 (from 91 fewer to 445 fewer)
Targeted	behavio	ur that challen	ges (sleep o	onset laten	cy) - post-t	reatment (measure	ed with	: Actigra	oh; Better	indica	ted by lower values)
67 (1 study)	seriou s1	no serious inconsistenc y	serious2	very serious3	undetect ed	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	33	34	-		The mean targeted behaviour that challenges (sleep onset latency) - post-treatment in the intervention groups was 0.54 standard deviations lower (1.03 to 0.05 lower)

Targeted	behavio	ur that challen	ges (wake a	after sleep	onset) - pos	st-treatment (mea	sured w	ith: Actig	graph; Be	tter ind	licated by lower values)
67 (1 study)	seriou s1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	33	34	-		The mean targeted behaviour that challenges (wake after sleep onset) - post-treatment in the intervention groups was 0.73 standard deviations lower (1.22 to 0.23 lower)
Targeted	behavio	ur that challen	ges (total s	leep time)	- post-treat	ment (measured	with: Act	igraph; I	Better ind	icated	by higher values)
67 (1 study)	seriou s1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	33	34	-		The mean targeted behaviour that challenges (total sleep time) - post- treatment in the intervention groups was 0.76 standard deviations higher (0.26 to 1.26 higher)
Targeted	behavio	ur that challen	ges (sleep	efficiency)	- post-treat	ment (measured	with: Ac	tigraph;	Better inc	licated	by higher values)
67 (1 study)	seriou s1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	33	34	-		The mean targeted behaviour that challenges (sleep efficiency) - post- treatment in the intervention groups was 0.89 standard deviations higher (0.39 to 1.4 higher)
Adverse e	events (o	discontinuatior	n due to oth	er reasons	s, non-occu	rrence) - post-tre	atment				
80 (1 study)	seriou s1	no serious inconsistenc y	serious2	very serious3	undetect ed	 ⊕⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision 	36/4 0 (90 %)	36/40 (90%)	RR 1 (0.86 to 1.16)	900 per 100 0	0 fewer per 1000 (from 126 fewer to 144 more)

Crucial limitation for one criterion or some limitations for
 Applicability- different populations
 Optimal information size not met; small, single study

A.10 Interventions aimed at improving the health and well-being of carers of people with learning disabilities

A.10.1 Cognitive behavioural interventions for family carers versus any control

 Table 49: Cognitive behavioural interventions for family carers versus any control

Quality as	sessme	ent					Summa	ary of Finding	S		
Participa nts	Risk of	Inconsisten cy	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of evidence	Study e (%)	event rates	Relativ e	Anticip	ated absolute effects
(studies) Follow up	bias						With Any contro I	With cognitive behavioural intervention	effect (95% CI)	Risk with any contr ol	Risk difference with cognitive behavioural intervention (95% CI)
Carer hea	Ith and	well-being (de	pression) - po	ost-treatme	ent (Better i	indicated by lowe	r values)				
428 (5 studies)	serio us1	no serious inconsistenc y	no serious indirectnes s	serious2	undetect ed	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision	177	251	-		The mean carer health and well-being (depression) - post-treatment in the intervention groups was 0.35 standard deviations lower (0.54 to 0.15 lower)
Carer hea	Ith and	well-being (de	pression) - fo	llow-up (B	etter indica	ated by lower valu	es)				
130 (2 studies) 46 to 104 weeks	serio us1	no serious inconsistenc y	no serious indirectnes s	serious2	undetect ed	 ⊕⊕⊖ LOW1,2 due to risk of bias, imprecision 	66	64	-		The mean carer health and well-being (depression) - follow-up in the intervention groups was 0.41 standard deviations lower (0.79 to 0.04 lower)
Carer hea	Ith and	well-being (clir	nically depres	ssed) - pos	st-treatmen	t					
111	serio	no serious	no serious	very	undetect	$\oplus \ominus \ominus \ominus$	13/58	3/53	RR	224	168 fewer per 1000

Quality as	sessme	ent					Summa	ary of Findi	ngs		
(1 study)	us1	inconsistenc y	indirectnes s	serious3	ed	VERY LOW1,3 due to risk of bias, imprecision	(22.4 %)	(5.7%)	0.25 (0.08 to 0.84)	per 1000	(from 36 fewer to 206 fewer)
Carer hea	Ith and	well-being (an	kiety, trait) - j	oost-treatm	nent (Better	indicated by low	er values	s)			
68 (2 studies)	serio us1	no serious inconsistenc y	no serious indirectnes s	serious2	undetect ed	 ⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision 	31	37	-		The mean carer health and well-being (anxiety, trait) - post-treatment in the intervention groups was 0.5 standard deviations lower (1.03 lower to 0.03 higher)
Carer hea	Ith and	well-being (an	kiety, state) -	post-treat	ment (Bette	er indicated by low	ver value	es)			
36 (1 study)	serio us4	no serious inconsistenc y	no serious indirectnes s	very serious3	undetect ed	⊕⊖⊖⊖ VERY LOW3,4 due to risk of bias, imprecision	18	18	-		The mean carer health and well-being (anxiety, state) - post-treatment in the intervention groups was 0.46 standard deviations lower (1.12 lower to 0.2 higher)
Carer hea	Ith and	well-being (me	ntal ill health	n) - post-tre	eatment (Be	tter indicated by	lower va	lues)			
58 (1 study)	serio us4	no serious inconsistenc y	no serious indirectnes s	very serious3	undetect ed	 ⊕⊖⊖ VERY LOW3,4 due to risk of bias, imprecision 	29	29	-		The mean carer health and well-being (mental ill health) - post-treatment in the intervention groups was 2.19 standard deviations lower (2.85 to 1.53 lower)
Carer hea	Ith and	well-being (qua	ality of life) -	post-treatr	nent (Bette	r indicated by low	ver value	es)			
58 (1 study)	serio us4	no serious inconsistenc y	no serious indirectnes s	very serious3	undetect ed	⊕⊖⊖⊖ VERY LOW3,4 due to risk of bias,	29	29	-		The mean carer health and well-being (quality of life) - post-treatment in the intervention groups was

Quality as	ssessme	ent					Summ	ary of Findi	ngs		
						imprecision					0.87 standard deviations higher (0.33 to 1.41 higher)
Carer hea	Ith and	well-being (str	ess) - post-tr	eatment (B	Better indica	ated by lower val	ues)				
384 (3 studies)	serio us1	serious5	no serious indirectnes s	serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2,5 due to risk of bias, inconsistency, imprecision	159	225	-		The mean carer health and well-being (stress) - post- treatment in the intervention groups was 0.45 standard deviations lower (0.78 to 0.12 lower)
Carer hea	Ith and	well-being (str	ess) - follow-	up (Better	indicated b	y lower values)					
76 (1 study) 104 weeks	serio us4	no serious inconsistenc y	no serious indirectnes s	very serious3	undetect ed	⊕⊖⊖⊖ VERY LOW3,4 due to risk of bias, imprecision	27	49	-		The mean carer health and well-being (stress) - follow- up in the intervention groups was 0.43 standard deviations lower (0.9 lower to 0.05 higher)
Carer hea	Ith and	well-being (cli	nically stress	ed) - post-	treatment						
111 (1 study)	serio us4	no serious inconsistenc y	no serious indirectnes s	very serious3	undetect ed	⊕⊖⊖⊖ VERY LOW3,4 due to risk of bias, imprecision	17/58 (29.3 %)	2/53 (3.8%)	RR 0.13 (0.03 to 0.53)	293 per 1000	255 fewer per 1000 (from 138 fewer to 284 fewer)

2 Optimal information size not met

3 Optimal information size not met; small, single study
4 Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect 5 l2 > 40%

A.10.2 Psychoeducational interventions for family carers versus any control

 Table 50: Psychoeducational interventions for family carers versus any control

Quality as	ssessme	ent					Summ	nary of Findin	gs		
Participa nts	Risk of	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of	Study (%)	event rates	Relativ e	Anticipa	ted absolute effects
(studies) Follow up	bias					evidence	With any contr ol	With psychoedu cation	effect (95% CI)	Risk with any contro I	Risk difference with psychoeducation (95% CI)
Carer hea	alth and	well-being (de	pression) - fo	llow-up (Be	etter indica	ted by lower v	alues)				
75 (1 study) 4 weeks	seriou s1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	 ⊕⊖⊖ VERY LOW1,2 due to risk of bias, imprecision 	35	40	-		The mean carer health and well-being (depression) - follow-up in the intervention groups was 0.84 standard deviations lower (1.31 to 0.36 lower)
Carer hea	alth and	well-being (bu	rnout) - follov	v-up (Bette	r indicated	by lower valu	es)				
90 (1 study) 8 weeks	seriou s1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	 ⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision 	45	45	-		The mean carer health and well-being (burnout) - follow- up in the intervention groups was 0.35 standard deviations lower (0.77 lower to 0.06 higher)

1 Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect 2 Optimal information size not met; small, single study

A.10.3 Support interventions for family carers versus any control

Table 51: Parent advisor scheme versus treatment as usual

Quality as	ssessme	ent				Summ	ary of Findin	gs			
Participa nts	Risk of	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of	Study (%)	event rates	Relativ e	Anticipa	ted absolute effects
(studies) Follow up	bias					evidence	With any contr ol	With support interventio ns	effect (95% CI)	Risk with any control	Risk difference with support interventions (95% CI)
Carer hea	alth and	well-being (stre	ess) - post-tre	eatment (Be	etter indicat	ted by lower v	alues)				
28 (1 study)	seriou s1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	12	16	-		The mean carer health and well-being (stress) - post- treatment in the intervention groups was 1.21 standard deviations lower (2.04 to 0.39 lower)

2 Optimal information size not met; small, single study

A.10.4 Mindfulness interventions for paid carers versus any control

Table 52: Mindfulness interventions for paid carers versus any control

Quality as	ssessme	ent				Summary of Findings					
Participa nts	Risk of	Inconsistenc y	Indirectnes s	Imprecis ion	Publicati on bias	Overall quality of evidence	Study (%)	event rates	Relativ e	Anticipa	ated absolute effects
(studies) Follow up	bias						With any contr	With mindfulnes s	effect (95% CI)	Risk with any	Risk difference with mindfulness interventions (95% CI)

Quality a	ssessm	ent					Sumn	nary of Findir	ngs		
							ol	interventio ns		contro I	
Carer hea	alth and	well-being (me	ental well-bei	ng) - post-	treatment (Better indicated b	y highe	r values)			
120 (1 study)	serio us1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	54	66	-		The mean carer health and well-being (mental well- being) - post-treatment in the intervention groups was 0.17 standard deviations higher (0.19 lower to 0.53 higher)
Carer hea	alth and	well-being (me	ental well-bei	ng) - follov	v-up (Bette	r indicated by higl	ner valu	ies)			
120 (1 study) 6 weeks	serio us1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	54	66	-		The mean carer health and well-being (mental well- being) - follow-up in the intervention groups was 0.28 standard deviations higher (0.08 lower to 0.64 higher)
Carer hea	alth and	well-being (me	ental ill healtl	h) - post-tre	eatment (Be	etter indicated by	lower v	alues)			
154 (2 studies)	serio us3	serious4	no serious indirectnes s	serious2	undetect ed	 ⊕⊖⊖ ∨ERY LOW2,3,4 due to risk of bias, inconsistency, imprecision 	70	84	-		The mean carer health and well-being (mental ill health - post-treatment in the intervention groups was 0.54 standard deviations lower (1.06 to 0.02 lower)
Carer hea	alth and	well-being (me	ental ill health	h) - follow-	up (Better i	ndicated by lower	values)			
154 (2 studies) 6-13 weeks	serio us3	serious4	no serious indirectnes s	serious2	undetect ed	 ⊕⊖⊖ VERY LOW2,3,4 due to risk of bias, inconsistency, imprecision 	70	84	-		The mean carer health and well-being (mental ill health - follow-up in the intervention groups was 0.24 standard deviations lower (0.72 lower to 0.24 higher)

Quality as	ssessm	ent					Sumn	nary of Fir	ndings	
Carer hea	alth and	well-being (str	ress) - post-ti	reatment (E	Better indic	ated by lower valu	les)			
120 (1 study)	serio us1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	54	66	-	The mean carer health and well-being (stress) - post- treatment in the intervention groups was 0.17 standard deviations higher (0.19 lower to 0.53 higher)
Carer hea	alth and	well-being (sti	ress) - follow	-up (Better	indicated b	oy lower values)				
120 (1 study) 6 weeks	serio us1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	54	66	-	The mean carer health and well-being (stress) - follow- up in the intervention groups was 0.05 standard deviations lower (0.41 lower to 0.31 higher)
			1 1 1		-	icated by lower va				
34 (1 study)	serio us1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	 ⊕⊖⊖ VERY LOW1,2 due to risk of bias, imprecision 	16	18	-	The mean carer health and well-being (burnout) - post- treatment in the intervention groups was 0.18 standard deviations lower (0.86 lower to 0.49 higher)
Carer hea	alth and	well-being (bu	irnout) - follo	w-up (Bette	er indicated	d by lower values)				
34 (1 study) 13 weeks	serio us1	no serious inconsistenc y	no serious indirectnes s	very serious2	undetect ed	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	16	18	-	The mean carer health and well-being (burnout) - follow-up in the intervention groups was 0.08 standard deviations lower (0.76 lower to 0.59 higher)

2 Optimal information size not met; small, single study

Quality assessment

3 Most information is from studies at moderate risk of bias 4 I2 > 40%

Summary of Findings