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1.1 INTERVENTIONS TO IMPROVE THE CARER'S EXPERIENCE OF SERVICES - CRITICAL OUTCOMES

1.1.1 Enhanced psychoeducation versus standard psychoeducation for carers of adults with severe mental illness - clinical evidence profile

			Quality as	ssessment			No of p	oatients	Ef	fect		Importan
No of studie	Design	Risk of bias	Inconsisten cy	Indirectne ss	Imprecisi on	Other consideratio ns	Enhanced Psychoeducati on	Standard	Relativ e (95% CI)	Absolut e	Quality	ce
Experi	ence of car	e givin	g, End of in	tervention	Better indi	cated by high	ner values)					
	randomise d trials		inconsistenc	no serious indirectnes s		none	24	19	-	SMD 0.64 higher (0.03 to 1.25 higher)	MODERAT E	CRITICA L
Carer 1	nental hea	lth - E1	nd of interve	ntion (Bette	er indicated	by lower val	ues)	<u>, </u>				
	randomise d trials		inconsistenc	no serious indirectnes s		none	24	19	-	SMD 0.32 higher (0.29 lower to 0.92 higher)	MODERAT E	CRITICA L
Self-ca	re - End of	interv	ention (Bette	er indicated	by lower v	values)						
	randomise d trials		inconsistenc	no serious indirectnes s		none	24	19	-	SMD 0.68 lower	MODERAT E	CRITICA L

of			(1.31 to	
bias			0.06	
			lower)	

¹ Confidence interval crosses clinical decision threshold

Appendix 17

1.1.2 Standard psychoeducation (practitioner versus post delivery) for carers of adults with severe mental illness - clinical evidence profile

			Quality as	sessment			No of patients Effect				Qualit	Importanc
No of studie s	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Standard Psychoeducation (PRACTITIONE R	POST delivery)	Relativ e (95% CI)	Absolut e	v	e
Family	burden, En	d of int	ervention (Be	tter indicate	d by lower v	alues)						
1	randomise d trials		no serious inconsistency			none	20	20	-	SMD 0.41 lower (1.04 lower to 0.21 higher)	LOW	CRITICAL
Family	burden - uj	p to 6 m	onth follow-u	p (Better inc	dicated by lo	wer values)						
1	randomise d trials		no serious inconsistency			none	20	20	-	SMD 0.41 lower (1.03 lower to 0.22 higher)	LOW	CRITICAL
Psycho	logical dist	ress - Er	d of interven	tion (Better i	indicated by	lower values)						!
1	randomise d trials		no serious inconsistency			none	20	20	-	SMD 0.38 lower (1 lower to	LOW	CRITICAL

										* 1P P	CHUIN 17	
										0.25		
										higher)		
Psycho	logical dist	ress - up	to 6 month f	ollow-up (Be	etter indicate	ed by lower va	lues)					
1	randomise	serious	no serious	no serious	serious ²	none	20	20	-	SMD 0		CRITICAL
	d trials	1	inconsistency	indirectness						higher	LOW	
										(0.62		
										lower to		
										0.61		
										higher)		

Concerns regarding risk of bias
 Confidence interval crosses clinical decision threshold

1.1.3 Psychoeducation versus any control for carers of adults with severe mental illness - clinical evidence profile

			Quality as	sessment			No of patients Effect				— Qualit	Importanc
No of studie	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Psychoeducatio n	Any contro 1	Relativ e (95% CI)	Absolut e	y	e
Experie	ence of care	giving,	End of interv	ention (Bette	r indicated l	y higher value	es)	•				
8	randomise d trials	serious 1	very serious ²	no serious indirectness		none	229	199	-	SMD 1.03 higher (0.36 to 1.69 higher)	VERY LOW	CRITICAL
Experie	ence of care	giving -	up to 6 month	n follow-up (Better indica	ated by higher	values)					
4	randomise d trials	serious 1	very serious ²	no serious indirectness		none	128	87	-	SMD 0.92 higher (0.32 to 1.51 higher)	VERY LOW	CRITICAL
Experie	ence of care	giving -	> 6 month fol	low-up (Bett	er indicated	by higher valu	ies)					
3	randomise d trials	serious 1	very serious ²	no serious indirectness		None	88	63	-	SMD 1.29 higher (0.18 to 2.4 higher)	VERY LOW	CRITICAL

Oualita	Quality of Life - End of intervention (Better indicated by higher values)											
Quality	1	1	· ·			,	00	10		C) (D)		CDITICAT
1	randomise				serious ³	none	23	18	-	SMD		CRITICAL
	d trials	1	inconsistency	indirectness						0.31	LOW	
										higher (-		
										0.31		
										lower to		
										0.93		
										higher)		
Satisfa	ction with s	ervices -	End of interv	ention (Bette	er indicated	by higher valu	es)					
1	randomise	serious	no serious	no serious	serious ³	none	19	20	-	SMD		CRITICAL
	d trials	1	inconsistency	indirectness						0.42	LOW	
										higher		
										(0.22		
										lower to		
										1.06		
										higher)		
Satisfa	ction with s	ervices -	up to 6 mont	h follow-up (Better indi	cated by higher	values)			, ,		
1	randomise	1			serious ³	none	19	20	_	SMD		CRITICAL
	d trials		inconsistency							0.41	LOW	
										higher (-		
										0.23		
										lower to		
										1.04		
										higher)		
Psvcho	logical distr	ress - En	d of intervent	ion (Better in	ndicated by	lower values)				0 - /		
2	_		serious ²		serious ³	none	44	42	_	SMD 0.3		CRITICAL
	d trials	1		indirectness	2011000		11			lower	VERY	
	a triais									(0.84	LOW	
										lower to	LOW	
										0.24		
										higher)		
										mgner)		

Psycho	Psychological distress- up to 6 month follow-up (Better indicated by lower values)													
2	randomise	serious	no serious	no serious	serious³	none	44	42	-	SMD		CRITICAL		
	d trials	1	inconsistency	indirectness						0.34	LOW			
										lower				
										(0.76				
										lower to				
										0.08				
										higher)				
Psycho	logical distr	ess - > 6	month follow	v-up (Better i	ndicated by	lower values)								
1	randomise	no	no serious	no serious	no serious	none	13	5	-	SMD		CRITICAL		
	d trials	serious	inconsistency	indirectness	imprecision					1.79	HIGH			
		risk of								lower				
		bias								(3.01 to				
										0.56				
										lower)				

1.1.4 Support groups versus any control for carers of adults with severe mental illness - clinical evidence profile

			Quality ass	sessment		No of patients Effect				0 114	_	
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Support groups	Any	Relative (95% CI)	Absolute	Quality	Importance
Experie	nce of care g	iving , E	nd of intervent	tion (Better in	ndicated by h	igher values)						
	randomised trials	serious ¹	serious²		no serious imprecision	none	97	97	-	SMD 1.16 higher	VERY	CRITICAL

Concerns regarding risk of bias
 Concerns regarding heterogeneity
 CI crosses clinical decision threshold

										<i>11p</i>	penuix 1.	
										(0.36 to 1.96 higher)	LOW	
Experie	nce of care g	iving - u	p to 6 month f	ollow-up (Be	tter indicated	by higher valu	es)	<u>.</u>				
3	randomised trials		no serious inconsistency	serious ³	no serious imprecision	none	91	75	-	SMD 0.67 higher (0.35 to 0.99 higher)	LOW	CRITICAL
Experie	nce of care g	iving - >	6 month follo	w-up (Better	indicated by	higher values)						
2	randomised trials	serious ¹	very serious ²	serious ³	serious ⁴	none	70	53	-	SMD 1.95 lower (4.22 lower to 0.31 higher)		CRITICAL
Psychol	logical distre	ss - End	of intervention	n (Better indi	cated by low	er values)						
	randomised trials		inconsistency	serious ³	no serious imprecision	none	35	35	-	SMD 0.99 lower (1.48 to 0.49 lower)		CRITICAL
Psychol	logical distre	ss- up to	6 month follo	w-up (Better	indicated by	lower values)						
1	randomised trials		no serious inconsistency	serious ³	no serious imprecision	none	35	35	-	SMD 0.99 lower (1.48 to 0.49 lower)		CRITICAL

¹ Concerns regarding risk of bias

 ² Concerns regarding heterogeneity
 ³ Studies all based in East Asia - may not be applicable to UK setting

⁴ Confidence interval crosses clinical decision threshold

Appendix 17
1.1.5 Psychoeducation plus support group versus any control for carers of adults with severe mental illness - clinical evidence profile

			Quality as	sessment			No of patients Effect			fect	Orralit	Tananautana
No of studie	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Psychoeducatio n + support group	Any contro	Relativ e (95% CI)	Absolut e	v	Importanc e
Experie	ence of care	giving -	> 6 month fol	low-up (Bett	er indicated	by higher valu	ies)					
1	randomise d trials	1	inconsistency			none	26	23	-	SMD 0.05 higher (0.51 lower to 0.61 higher)	LOW	CRITICAL

¹ Concerns regarding risk of bias

1.1.6 Problem-solving bibliotherapy versus any control for carers of adults with severe mental illness - clinical evidence profile

		Quality as		No of patients		Ef	fect		Townselsons			
No of studie s	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	solving bibliotherap y		Relativ e (95% CI)	Absolut e	Quality	Importanc e
Experie	ence of care	giving,	End of interv	ention (Bette	er indicated	by higher valu	ies)					
	randomise d trials		no serious inconsistency		serious²	none	56	58	-	SMD 0.17 higher	LOW	CRITICAL

² Confidence interval crosses decision making threshold

								•			пррении 1.	<u>'</u>
										(2.11		
										lower to		
										2.45		
										higher)		
Experie	ence of care	giving -	up to 6 mont	h follow-up	(Better indic	ated by higher	values)					
1	randomise	serious	no serious	no serious	serious ²	none	56	58	-	SMD		CRITICAL
	d trials	1	inconsistency	indirectness						1.09	LOW	
			_							higher		
										(0.34		
										lower to		
										2.52		
										higher)		
Quality	y of Life - Er	nd of int	ervention (Be	etter indicate	d by higher	values)						
1	randomise	serious	no serious	no serious	serious ²	none	56	58	-	SMD		CRITICAL
	d trials	1	inconsistency	indirectness						0.14	LOW	
			_							higher		
										(0.23)		
										lower to		
										0.5		
										higher)		
Quality	y of life - up	to 6 mo	nth follow-uj	(Better ind	icated by hig	gher values)						
	randomise					none	56	58	-	SMD 0.5		CRITICAL
	d trials	1	inconsistency	indirectness						higher	LOW	
										(0.12 to		
										0.87		
										higher)		
Psycho	logical distr	ess - En	d of interven	tion (Better i	ndicated by	lower values)						
1	randomise		no serious			none	56	58	-	SMD		CRITICAL
	d trials	1	inconsistency	indirectness	imprecision					1.57	MODERAT	
										lower	Е	

											11ppcnuix 11	
										(1.79 to		
										1.35		
										lower)		
Psyc	hological dist	ress- up	to 6 month fo	llow-up (Bet	ter indicated	d by lower valu	ıes)					
1	randomise	serious	no serious	no serious	no serious	none	53	58	-	SMD		CRITICAL
	d trials	1	inconsistency	indirectness	imprecision					1.54	MODERAT	
										lower	E	
										(1.95 to		
										1.13		
										lower)		

¹ Concerns regarding risk of bias

1.1.7 Self-management versus any control for carers of adults with severe mental illness - clinical evidence profile

	Quality assessment Other							ents	Ef	fect		Tooloogia
No of studie	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Self- managemen t	any	Relativ e (95% CI)	Absolut e	Quality	Importanc e
Experie	ence of care	giving	End of interv	ention (Bette	er indicated	by higher valu	es)	<u> </u>				
1	randomise	no	no serious	no serious	serious ¹	none	41	45	-	SMD		CRITICAL
	d trials	seriou	inconsistency	indirectness						0.19	MODERAT	
		s risk								higher	E	
		of bias								(0.20		
										lower to		
										0.58		
										higher)		
Psycho	logical distr	ess - Er	nd of interven	tion (Better i	ndicated by	lower values)						

² Confidence intervals cross clinical decision making threshold

			_	_								
1	randomise	no	no serious	no serious	serious ¹	none	41	45	-	SMD		CRITICAL
	d trials	seriou	inconsistency	indirectness						0.32	MODERAT	
		s risk								lower	Е	
		of bias								(0.73)		
										lower to		
										0.09		
										higher)		

¹ Confidence interval crosses clinical decision threshold

1.2 INTERVENTIONS TO PREVENT PSYCHOSIS

1.2.1 Interventions to prevent psychosis versus any alternative management strategy- health economic profile

Interventi	ions to prever	nt psychosis v	ersus any alternative man	agement strat	egy		
Study & country	Limitation s	Applicabili ty	Other comments	Incrementa 1 cost (£) ¹	Incrementa 1 effect	ICER (£/effect)	Uncertainty
McCron e et al, 2013 UK	Potentially ² serious limitations	Partially ³ applicable	Cost analysis Time horizon: 6 months	-£5,120	NA	NA	EIS more expensive if: probability of admission following psychosis for EIS increased from 0.58 to 0.86; probability of SC service users with psychosis being admitted reduced from 0.58 to 0.29-0.4; length of stay for EIS service users in excess of 97% that of SC; in excess of 67% of service users referred to EIS have psychosis; less than 36% of those referred to SC have psychosis
Valmag gia et al, 2009 UK	Potentially serious limitations	Partially applicable ⁵	Measure of outcome: probability of transition to psychosis Time horizon: 24 months	£1,305	-0.15	£8,701	None reported for the findings from health sector perspective

Phillips et al, 2009 Australi a	Potentially serious limitations	Partially applicable7	Cost minimisation analysis Measure of outcome: probability of transition to psychosis Time horizon: 36 months	0-6 months: £986 6-12 months: £620 12-36 months - £9,934	No difference	Dominant	None reported
---	---------------------------------	--------------------------	---	---	------------------	----------	---------------

- 1.In non-UK studies costs converted to UK pounds using purchasing power parities (PPP) exchange rates (http://www.oecd.org/std/ppp); all costs uplifted to 2011/2012 UK pounds using the UK HCHS inflation index
- 2.Effectiveness data from various published sources and supplemented by authors' assumptions; resource use based on variety of published sources, data provided by mental health trust, and authors' assumptions; time horizon only 6 months and may not be sufficiently long enough to reflect all important differences in costs
- 3. Cost analysis, hasn't considered health effects, mental health services perspective
- 4. Effectiveness data from observational studies; second year costs are not discounted
- 5. Cost implication study, no treatment outcomes measured
- 6. The time duration of the model is short to capture lifelong characteristics of psychosis and some of the data used are not from RCTs
- 7.Cost implication study, no treatment outcomes measured, £3% discount rate used and Australian healthcare system not exactly similar to the UK

1.3 INTERVENTIONS TO PROMOTE PHYSICAL HEALTH - CRITICAL OUTCOMES

1.3.1 Physical activity versus any alternative management strategy- clinical evidence profile

	Quality assessment							f patients	Ef	fect		
No of studie s	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n		Physica 1 Activity	Any alternative managemen t strategy	Relativ e (95% CI)	Absolut e	Quality	Importanc e
Physic	al health, w	eight/BI	MI - End of in	tervention -	Body weigh	t (Better indica	ited by lo	ower values)				
		serious risk of bias	no serious inconsistency		serious ²	reporting bias ³	64	41	-	SMD 0.20 higher (0.2 lower to 0.59 higher)	VERY LOW	CRITICAL
Quality	y of Life - E	nd of in	tervention (Be	etter indicate	d by higher	values)						
	randomise d trials	serious 4	serious ⁵	serious ¹	serious ²	none	52	31	-	SMD 0.62 higher (0.41 lower to 1.66	VERY LOW	CRITICAL

				,							тррении 1	
										higher)		
Iinut	tes walked - 1	End of i	ntervention (l	Better indica	ted by high	er values)						
	randomise	serious	no serious	no serious	serious ²	none	48	49	-	SMD		CRITICAL
	d trials	6	inconsistency	indirectness						0.24	LOW	
										higher		
										(0.16		
										lower to		
										0.64		
										higher)		
intern	ational Phys	ical Act	ivity Question	nnaire: Short	Form-Tele	phone Format (Better in	dicated by h	igher val	lues)		
1	randomise	serious	no serious	no serious	no serious	none	37	16	-	SMD		CRITICAL
	d trials	6	inconsistency	indirectness	imprecision					0.32	MODERAT	
										higher	E	
										higher (0.27	E	
										_	Е	
										(0.27	Е	
										(0.27 lower to	Е	
Minut	tes walked -	up to 6 1	month follow-	-up (Better ir	ndicated by	higher values)				(0.27 lower to 0.91	E	
Minut	randomise			_ `	ndicated by serious ²	higher values)	48	49	-	(0.27 lower to 0.91	E	CRITICAL
Minut		serious		no serious	serious ²	,	48	49	-	(0.27 lower to 0.91 higher)		CRITICAL
Minut	randomise	serious	no serious	no serious	serious ²	,	48	49	-	(0.27 lower to 0.91 higher)		CRITICAL
Minut	randomise	serious	no serious	no serious	serious ²	,	48	49	-	(0.27 lower to 0.91 higher) SMD 0.34		CRITICAL

						Tipperionse ir	
					0.74		
					higher)		

¹ Concern as to the applicability of intervention and population.

² Confidence interval (CI) crosses the clinical decision threshold

³ Suspicion of publication bias

⁴ Most information is from studies at moderate risk of bias

⁵ Evidence of very serious heterogeneity of study effect size

⁶ Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect

1.3.2 Physical activity and healthy eating versus any alternative management strategy-clinical evidence profile

			Quality as	sessment			No o	f patients	Ef	fect		
No of studie	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration	Physica 1 Activity & Healthy Eating	Any alternative managemen	Relativ e (95% CI)	Absolut e	Quality	Importanc e
Body n	nass, weight	t - End o	f interventior	- Weight (B	etter indica	ted by lower va	alues)					
14	randomise d trials	serious 1		no serious indirectness		none	564	547	-	MD 2.8 lower (3.6 to 1.99 lower)	LOW	CRITICAL
Body n	nass, weight	t -up to	6 month follo	w-up- Weigh	nt (Better inc	dicated by low	er values)				
5	randomise d trials		no serious inconsistency		serious ³	none	221	228	-	MD 2.33 lower (3.31 to 1.34 lower)	LOW	CRITICAL
Body n	nass- weigh	t - > 12 1	nonth follow-	up (Better ir	dicated by	lower values)						

	1 .	ı	I		1		1	1			71ppenaix 17	
1	randomise	serious	no serious	no serious	no serious	none	119	128	-	MD 3.20		CRITICAL
	d trials	1	inconsistency	indirectness	imprecision					lower	MODERAT	
										(5.17 to	E	
										1.23		
										lower)		
										,		
Qualit	y of Life - Eı	nd of in	tervention (Be	etter indicate	ed by higher	values)						
6	randomise	serious	no serious	no serious	serious ³	none	177	176	-	SMD		CRITICAL
	d trials	1	inconsistency	indirectness						0.24	LOW	
										higher		
										(0.01 to		
										0.47		
										higher)		
Satisfa	ction - End	of interv	vention (Bette	r indicated b	y higher va	lues)						
1	randomise	serious	no serious	no serious	no serious	none	34	37	-	SMD		CRITICAL
	d trials	4	inconsistency	indirectness	imprecision					0.75	MODERAT	
										higher	E	
										(0.26 to		
										1.23		
										higher)		
Physic	al health - E	xercise -	- End of interv	ention - Cli	nical Global	Impression (C	GI): Acti	ivity Level (B	Setter inc	licated by	y higher valu	ies)
1	randomise	serious	no serious	no serious	serious ³	none	23	11	-	SMD		CRITICAL
	d trials	4	inconsistency	indirectness						1.04	LOW	
										higher		
			1			ı						

	(0.28 to
	1.81
	higher)
Physical health - Exercise - End of intervention - Accelerometry- total minutes of activity (Better	indicated by higher values)
randomise serious no serious no serious serious³ none 28 29	- SMD CRITICAL
d trials 4 inconsistency indirectness	0.56 LOW
	higher
	(0.03 to
	1.09
	higher)
	1 ('7040 1 () /0 () '1 ()
Physical health - Exercise - End of intervention - International Physical Activity Questionnaire-s	short version (IPAQ-short) (Better indicated
by higher values)	
1 randomise no no serious no serious no serious none 60 66	- SMD CRITICAL
d trials serious inconsistency indirectness imprecision	0.01 HIGH
risk of	higher
	(0.34
bias	(0.34
bias	lower to
bias	
bias	lower to
	lower to 0.36 higher)
Physical health - Exercise - up to 6 month follow-up - Accelerometry- total minutes of activity (B	lower to 0.36 higher) setter indicated by higher values)
	lower to 0.36 higher)
Physical health - Exercise - up to 6 month follow-up - Accelerometry- total minutes of activity (B	lower to 0.36 higher) setter indicated by higher values)

						1 ippertette 17	
					(0.33)		
					lower to		
					0.76		
					higher)		

¹ Most studies included are at moderate risk of bias

1.3.3 Physical activity and healthy eating versus any alternative management strategy- health economic profile

Physical activity a	and healthy ea	ting intervention	ons versus any alternative	management	strategy		
Study & country	Limitations	Applicability	Other comments	Incremental cost (£)1	Incremental QALY	ICER (£/QALY)	Uncertainty
Winterbourne et al, in publication UK	Minor limitations ²	Partially applicable ³	Cost utility Time horizon: lifetime	£18	0.07	£251	Probability intervention cost effective at WTP £20,000-30,000 per QALY is 0.93-0.94; using lower estimate of intervention effect cost per QALY £150,609; using 10-year time frame cost per QALY £54,446; for female cohort intervention dominant

1. All costs uplifted to 2011/2012 UK pounds using the UK HCHS inflation index

 $^{^2}$ Evidence of serious heterogeneity of study effect size

³ CI crosses clinical decision threshold

⁴ Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect

- 2. Effectiveness and resource use based on RCT review, authors' assumptions, and other published sources; costs of treating schizophrenia and pharmacotherapy side effects excluded
- 3. UK NHS perspective; costs relevant from PSS perspective excluded however these were expected to account only for a small proportion of costs

1.3.4 Physical activity (yoga) versus physical activity (aerobic) - clinical evidence profile

			Quality as	sessment			No of j	patients	Ef	ffect	0131	T
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	l ()ther	Activity	Physical Activity (Aerobic)	(95%	Absolute	Quality	Importance
Quality	of Life - up	to 6 mo	nth follow-up	(Better indica	ated by lower	r values)						
1	randomised	no	no serious	no serious	no serious	none	21	20	-	SMD 0.34		CRITICAL
	trials	serious	inconsistency	indirectness	imprecision					higher	HIGH	
		risk of								(0.06		
		bias								lower to		
										0.74		
										higher)		

1.3.5 Bupropion versus placebo for smoking cessation and reduction-clinical meta- analysis

			Quality as	sessment			No of pa	tients	Ef	fect		Turned
No of studie	Design	bias	Inconsistenc y	S	n	s	Bupropio n versus placebo	Contro 1	Relativ e (95% CI)	Absolut e	Quality	Importanc e
			1 1	,		versus Placebo		T	ı	T	T	
	randomise d trials		no serious inconsistency			none	5/51 (9.8%)	2/53 (3.8%) 3.6%	RR 2.19 (0.5 to 9.63)	45 more per 1000 (from 19 fewer to 326 more) 43 more per 1000 (from 18 fewer to 311 more)	LOW	CRITICAL
Abstin	ence at 6-mo	nth foll	ow-up (prima	ry outcome)	- Bupropion	+ TNP versus	Placebo + T	NP				
	d trials		no serious inconsistency		serious ²	none	9/55 (16.4%)	2/55 (3.6%)		88 more per 1000 (from 5 fewer to 447 more)	MODERAT E	CRITICAL

											търсник т.	
										94 more		
										per 1000		
								3.9%		(from 5		
								3.9%		fewer to		
										480		
										more)		
Absti	nence at end	of interv	vention (secon	dary outcom	e) - Bupropi	on + TNP versu	ıs. Placebo	+ TNP				
2	randomise	no	serious ³	no serious	serious ²	none	17/55	6/55	RR 2.92	209 more		CRITICAL
	d trials	serious		indirectness			(30.9%)	(10.9%)	(0.75 to	per 1000	LOW	
		risk of							11.33)	(from 27		
		bias								fewer to		
										1000		
										more)		
										217 more		
										per 1000		
								11.3%		(from 28		
								11.570		fewer to		
										1000		
										more)		
Absti	nence at end	of interv	vention (secon	dary outcom	e) - Bupropi	on versus. Place	ebo					
5	randomise					none	27/115			139 more		CRITICAL
	d trials	4	inconsistency	indirectness	imprecision		(23.5%)	(5.2%)			MODERAT	
									8.14)	(from 34	E	
										more to		
										373		
										more)		
								6.3%		168 more		
										per 1000		

											трреник т	
										(from 42		
										more to		
										450		
										more)		
	ion - Expire ed by lower		vel at the end	of interventi	on (seconda	ry outcome) - ab	stinence st	tudies -	Studies	using fina	ıl measureme	ents (Better
3		no	no serious		serious ⁵	none	74	76	-	MD 6.01		CRITICAL
	d trials		inconsistency	indirectness						lower	MODERAT	
		risk of								(10.2 to	E	
		bias								1.83		
										lower)		
	ion - Expire indicated b			of interventi	on (seconda	ry outcome) - ab	stinence st	tudies -	Studies	using cha	nge from bas	eline
1		no	no serious	no serious	very	none	10	9		MD 14.8		CRITICAL
			inconsistency		5	none	10	9	-	lower	LOW	CKITICAL
	u triais	risk of	liconsistency	manechiess	serious					(28.15 to	LOW	
		bias								1.45		
										lower)		
Depres	sive sympto	ms at th	e end of inter	vention (fina	ıl measurem	ients)				/		
3	randomise					none	-	-	-	_		
	d trials							0%		-		
	ion - Expire ed by lower			follow-up (s	secondary o	utcome) - abstin	ence studio	es - Stud	lies usin	g final me	easurements	(Better
2	1	1	very serious ⁶	no serious	serious ²	none	50	54	-	MD 2.08		CRITICAL
	d trials	serious	, ,	indirectness						lower	VERY LOW	
		risk of								(17.76		
		bias								lower to		
										13.59		
										higher)		

	ion - Expire ed by lower		vel at 6-month	follow-up (s	secondary o	utcome) - abstin	ence studio	es - Stud	lies usin	g change	from baselin	e (Better
1	randomise d trials	no serious risk of bias	no serious inconsistency		very serious ⁵	none	10	9	1	MD 14.3 lower (27.2 to 1.4 lower)	LOW	CRITICAL
	ion - Chang er values)	e in nun	nber of CPD f	rom baseline	e at the end	of intervention	(secondary	outcom	e) - absti	nence stu	dies (Better i	ndicated
	d trials	1	serious ³	indirectness	serious ⁵	none	90	94	-	MD 10.77 lower (16.52 to 5.01 lower)	VERY LOW	CRITICAL
Reduct lower v	U	e in nun	nber of CPD f	rom baseline	e at 6-month	follow-up (seco	ondary outo	come) <i>- a</i>	bstinen	ce studies	(Better indic	cated by
	randomise d trials		no serious inconsistency	no serious indirectness	very serious ^{2,5}	none	50	54	-	MD 0.4 higher (5.72 lower to 6.53 higher)	LOW	CRITICAL
Reduct lower v		e in nun	nber of CPD f	rom baseline	at the end	of intervention	(secondary	outcom	e) - redu	ction stuc	lies (Better ir	ndicated by
	randomise d trials		no serious inconsistency		serious ²	none	61	32	-	MD 2.61 lower (7.99 lower to 2.77 higher)	LOW	CRITICAL

- ¹ Most information is from studies at moderate risk of bias
- ² Confidence interval (CI) cross the clinical decision threshold
- ³ Evidence of serious heterogeneity of study effect size
- ⁴ Most information is from studies at moderate risk of bias
- ⁵ Optimal information size not met
- ⁶ Evidence of very serious heterogeneity of study effect size

1.3.6 Bupropion in combination with CBT and NRT versus standard care- health economic profile

Study & country	Limitations	Applicability	Other comments	Incremental cost (£)1	Incremental QALY	ICER (£/QALY)	Uncertainty
Winterbourne et al, in publication UK	Minor limitations ²	Partially applicable ³	Cost utility Time horizon: lifetime	£620	0.6	£1,033	Probability intervention cost effective at WTP £20,000-30,000 per QALY is 0.95; with alternative 12-month follow-up data on efficacy intervention dominated; changing gender, smoking status, baseline BMI, diagnosis cost per QALY ranges between £705-1,034

- 1. All costs uplifted to 2011/2012 UK pounds using the UK HCHS inflation index
- 2. Effectiveness and resource use based on RCT review, authors' assumptions, published sources, QDiabetes and QRISK2-2012 calculators; resource use based on authors' assumptions and RCT review
- 3. UK NHS perspective; costs relevant from PSS perspective excluded however these were expected to account only for a small proportion of costs

1.3.7 Varenicline versus placebo for smoking cessation and reduction-clinical meta- analysis

			Quality as	sessment			No of pat	tients	Ef	fect	015	T
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Varenicline versus placebo	Control	Relative (95% CI)	Absolute	Quality	Importance
Abstine	ence at 6-mo	nth follo	w-up (primary	y outcome)				•				
	randomised trials			no serious indirectness	serious ²	none	10/85 (11.8%)	1/43 (2.3%)	RR 5.06 (0.67 to 38.24)	per 1000 (from 8 fewer to 866 more) 93 more	LOW	CRITICAL
								2.3%		per 1000 (from 8 fewer to 857 more)		
			ention (second			T	I					
	randomised trials			no serious indirectness	serious ⁴	none	19/89 (21.3%)	2/48 (4.2%)	RR 4.74 (1.34 to 16.71)	156 more per 1000 (from 14 more to 655 more)	LOW	CRITICAL
								2.3%		86 more per 1000 (from 8 more to		

					1 1/1	cittitic 11	
					361 more)		

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

² Confidence interval (CI) cross the clinical decision threshold

³ Most information is from studies at moderate risk of bias

⁴ Optimal information size not met

1.4 PEER PROVIDED INTERVENTIONS - CRITICAL OUTCOMES

1.4.1 Mutual support versus any alternative management strategy- clinical evidence profile

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Mutual Support	(ontrol	Relative (95% CI)	Absolute		
Recovery- Post-intervention (Better indicated by higher values)												
	randomised trials			no serious indirectness	serious ²	reporting bias ³	200	100	-	SMD 0.11 higher (0.13 lower to 0.35 higher)	VERY	CRITICAL
Empow	Empowerment- Post-intervention (Better indicated by higher values)											
	randomised trials	serious ⁴	,	no serious indirectness	serious ²	reporting bias ³	1206	1060	-	SMD 1.44 higher (0.09 to 2.79 higher)	VERY LOW	CRITICAL
Quality of Life- Post-intervention (Better indicated by higher values)												
	randomised trials			no serious indirectness	serious ⁶	reporting bias ³	200	100	-	SMD 1.42 higher	VERY	CRITICAL

			1								pennin 1	
										(1.16 to	LOW	
										1.69		
										higher)		
Service use, contact- Post-intervention												
1	randomised	serious ¹	no serious	no serious	serious ²	reporting bias ³	21/40	10/40	RR 0.63	93 fewer		CRITICAL
	trials		inconsistency	indirectness			(52.5%)	(25%)	(0.44 to	per 1000	VERY	
			-						0.92)	(from 20	LOW	
										fewer to		
										140 fewer)		
										ŕ		
										93 fewer		
										per 1000		
								25%		(from 20		
										fewer to		
										140 fewer)		
Service use, hospitalisation- Post-intervention												
1	randomised	serious ¹	no serious	no serious	serious ²	reporting bias ³	7/40	14/40	RR 0.5	175 fewer		CRITICAL
	trials		inconsistency	indirectness			(17.5%)	(35%)	(0.23 to	per 1000	VERY	
			, and the second				,	, ,	1.11)	(from 269	LOW	
									,	fewer to 39		
										more)		
										,		
										175 fewer		
								35%		per 1000		
								20 70		(from 269		
										fewer to 39		

			<i>1</i> 1 <i>f</i>	periorise 11	'
			more)		

- ¹ Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect
- ² Confidence interval (CI) cross the clinical decision threshold
- ³ Suspicion of publication bias
- ⁴ Most information is from studies at moderate risk of bias
- ⁵ Evidence of very serious heterogeneity of study effect size
- ⁶ Optimal information size not met

1.4.2 Peer mental health service providers versus any alternative management strategy- clinical evidence profile

			Quality ass	sessment			No of pa	tients	Ef	fect		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Peer Mental Health Service Providers	Control	Relative (95% CI)	Absolute	Quality	Importance
Service	use, hospita	lisation-	Post-interven	tion								
	randomised trials			no serious indirectness	serious ²	reporting bias ³	21/57 (36.8%)	31/57 (54.4%) 54.4%		174 fewer per 1000 (from 299 fewer to 16 more) 174 fewer per 1000 (from 299 fewer to 16 more)	VERY	CRITICAL
Satisfac	tion, questi	onnaire-	Post-intervent	ion (Better ir	ndicated by l	ower values)						
1	randomised trials			no serious indirectness	serious ⁴	reporting bias ³	43	44	-	SMD 0.48 higher (0.05 to	VERY	CRITICAL

					- 1 P	perior 1	*
					0.91	LOW	
					higher)		

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

 $^{^{\}rm 2}$ Confidence interval (CI) cross the clinical decision threshold

³ Suspicion of publication bias

⁴ Optimal information size not met

1.4.3 Peer support providers versus any alternative management strategy-clinical evidence profile

			Quality as	sessment			No of p	atients	Ef	fect	Ouality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Peer Support	('ontrol	Relative (95% CI)	Absolute		•
Recover	ry- post-inte	rvention	(Better indicat	ed by higher	values)							
Recover 2	ry, Up to 6 m randomised trials	serious risk of bias onths fo	serious ¹ Ilow-up (Bette no serious inconsistency	no serious indirectness r indicated by no serious indirectness		reporting bias ³ es) reporting bias ³	217	222	-	SMD 0.24 higher (0.09 to 0.39 higher) SMD 0.23 higher (0.09 to 0.37 higher)	VERY LOW	CRITICAL
Empow	erment- pos	t-interve	ntion (Better in	dicated by hi	igher values)							
	randomised trials	serious ⁴	very serious ⁵	no serious indirectness	serious²	reporting bias ³	152	134	-	SMD 2.34 lower (7.68 lower to 3.00		CRITICAL

				,	,					210	rpenaix 1	/
										higher)		
Empov	verment- up t	to 6 mon	th follow-up (H	Better indicate	ed by higher	values)						
2	randomised trials		inconsistency	no serious indirectness	serious ²	reporting bias ³	278	260	-	SMD 0.25 higher (0.07 to 0.43 higher)	VERY LOW	CRITICAL
Function	oning/Disab	oility- pos	st-intervention	(Better indic	ated by lowe	r values)						
1	randomised trials	serious ⁶	no serious inconsistency	no serious indirectness	serious ²	reporting bias ³	95	70	-	SMD 0.37 higher (0.06 to 0.68 higher)	VERY LOW	CRITICAL
Quality	y of life - pos	t-interve	ntion (Better i	ndicated by h	igher values							
5	randomised trials	serious ⁴	serious ¹	no serious indirectness	serious ²	reporting bias ³	494	545	-	SMD 0.04 lower (0.24 lower to 0.16 higher)		CRITICAL
Quality	y of life- up to	o 6 mont	h follow-up (B	etter indicate	d by higher	values)					<u> </u>	
2	randomised	serious ⁴	no serious	no serious	serious ²	reporting bias ³	323	316	-	SMD 0.24 higher	VERY	CRITICAL

	1	1	1		1	ı	ı	1			<i>рениі</i> х 1.	,
	trials		inconsistency	indirectness						(0.08 to	LOW	
										0.40 lower)		
Service	use, contact-	- post-int	ervention (Bet	ter indicated	by lower val	ues)						
2	randomised		1				122	100		SMD 0.22		CRITICAL
3		serious	serious	no serious	serious ²	reporting bias ³	132	123	-			CRITICAL
	trials			indirectness						lower (0.72		
										lower to	LOW	
										0.28		
										higher)		
Contrico	l la bossita	lication	post-intervent	ion								
Service	use, nospita	115at1011-	post-intervent	1011								
1	randomised	serious ⁶	no serious	no serious	serious ²	reporting bias ³	11/24	9/21	RR 1.07	30 more		CRITICAL
	trials			indirectness			1	(42.9%)	(0.55 to	per 1000	VERY	
							(/	(,,	2.07)	(from 193	LOW	
									,	fewer to		
										459 more)		
										los more)		
										30 more		
										per 1000		
								42.9%		(from 193		
										fewer to		
										459 more)		
Satisfa	tion anestic	nnaire.	 post-interventi	on (Better in	licated by hi	gher values)						
Saciola	ciion, questic	Jiiidiic	Post interventi	on (Detter Int	indica by in	Siler varaes)						
3	randomised	serious ⁴	no serious	no serious	serious ²	reporting bias ³	180	152	-	SMD 0.02		CRITICAL
	trials		inconsistency	indirectness						lower (0.23	VERY	
										lower to		
		l										

					- 1 P	periona 1	•
					0.20	LOW	
					higher)		

¹ Evidence of serious heterogeneity of study effect size

² Confidence interval (CI) cross the clinical decision threshold

³ Suspicion of publication bias

⁴ Most information is from studies at moderate risk of bias

⁵ Evidence of very serious heterogeneity of study effect size

⁶ Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect

1.5 SELF-MANAGEMENT INTERVENTIONS - CRITICAL OUTCOMES

1.5.1 Self-management versus any alternative management strategy-clinical evidence profile

			Quality as	sessment			No of pat	ients	Ef	fect		
No of studie		Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Self- managemen t	Contro 1	Relativ e (95% CI)	Absolut e	Quality	Importanc e
Psycho	sis (total sy	mptoms) - End of inte	rvention (Be	tter indicate	d by lower val	ues)					
	d trials	1	very serious ²	indirectness		none	142	141	-	SMD 0.40 lower (1.02 lower to 0.22 higher)	VERY LOW	CRITICAL
Psycho	sis (positive	sympto	oms) - End of	intervention	(Better indi	cated by lower	values)					
10	randomise d trials	serious 1		no serious indirectness	serious ³	none	526	524	-	SMD 0.31 lower (0.56 lower to 0.07	VERY LOW	CRITICAL

											Appenaix 17	·
										lower)		
Psycho	sis (negativ	e sympt	oms) - End of	intervention	(Better ind	icated by lower	r values)					
8	randomise	serious	serious ⁴	no serious	serious³	none	265	262	-	SMD		CRITICAL
	d trials	1		indirectness						0.38	VERY LOW	
										lower		
										(0.67 to		
										0.08		
										lower)		
Psycho	sis (total sy	mptoms) - up to 6 mo	nth follow-u	p (Better inc	licated by lowe	er values)					
1	randomise	serious	no serious	no serious	serious³	none	39	45	-	SMD		CRITICAL
	d trials	5	inconsistency	indirectness						0.23	LOW	
										lower		
										(0.66		
										lower to		
										0.2		
										higher)		
Psycho	sis (positive	sympto	oms) - up to 6	month follow	w-up (Better	indicated by 1	ower values)					
4	randomise	serious	very serious ²	no serious	serious ³	none	156	159	-	SMD		CRITICAL
	d trials	1		indirectness						0.24	VERY LOW	
										lower		
										(0.69		
										lower to		
										0.21		

											Аррепиіх 1.	
										higher)		
Psycho	sis (negativ	e sympt	oms) - up to 6	month follo	w-up (Better	indicated by I	lower values)					
4	randomise	serious	very serious ²	no serious	serious³	none	156	159	-	SMD		CRITICAL
	d trials	1		indirectness						0.33	VERY LOW	
										lower		
										(0.88		
										lower to		
										0.22		
										higher)		
Psycho	sis (total sy	mptoms) - 7-12 month	follow-up (Better indica	ted by lower v	alues)					
1	randomise	no	no serious	no serious	no serious	none	44	44	-	SMD		CRITICAL
	d trials	serious	inconsistency	indirectness	imprecision					1.49	HIGH	
		risk of								lower		
		bias								(1.96 to		
										1.01		
										lower)		
Psycho	sis (positive	sympto	oms) - 7-12 mo	nth follow-u	ıp (Better in	dicated by low	er values)					
3	randomise	no	very serious ²	no serious	serious³	none	317	322	-	SMD		CRITICAL
	d trials	serious		indirectness						0.49	VERY LOW	
		risk of								lower		
		bias								(1.28		
										lower to		
										0.3		

											Appenaix 17	<u>'</u>
										higher)		
Psycho	osis (negativ	e sympt	oms) - 7-12 m	onth follow-	up (Better in	dicated by low	ver values)					
2	randomise d trials	no serious risk of bias	very serious ²	no serious indirectness	serious ³	none	97	94	-	SMD 0.77 lower (2.17 lower to 0.63 higher)	VERY LOW	CRITICAL
Psycho	osis (total sy	mptoms) - >12 month	follow-up (H	Better indica	ted by lower v	alues)					
1	randomise d trials		no serious inconsistency		no serious imprecision	none	19	19	-	SMD 1.36 lower (2.07 to 0.65 lower)	MODERAT E	CRITICAL
Psycho	sis (positive	e sympto	oms) - >12 mo	nth follow-u	p (Better inc	dicated by lowe	er values)					
2	randomise d trials		no serious inconsistency		no serious imprecision	none	72	69	-	SMD 0.72 lower (1.06 to 0.37 lower)	MODERAT E	CRITICAL

											Прреник 17	
Psycho	sis (negativ	e sympt	oms) - >12 mo	onth follow-u	ıp (Better in	dicated by low	er values)					
2	randomise	serious	very serious ²	no serious	serious ³	none	72	69	-	SMD		CRITICAL
	d trials	1		indirectness						0.92	VERY LOW	
										lower		
										(1.93		
										lower to		
										0.09		
										higher)		
										11181101)		
Global	state - Func	tioning,	, disability - E	nd of interve	ention (Bette	er indicated by	lower values)				
_	1 , .	T .	I						T	6) (F)		CDITTI C A I
7	randomise	serious	serious ⁴			none	271	255	-	SMD		CRITICAL
	d trials	1		indirectness	imprecision					0.07	LOW	
										lower		
										(0.33		
										lower to		
										0.2		
										higher)		
C1.1.1			1. 1.1.		C 11	(D (1 1 1 1	11 1	1 \				
Global	state - Func	tioning,	, aisability - u	p to 6 month	follow-up (Better indicate	a by lower va	aiues)				
4	randomise	serious	serious ⁴	no serious	serious ³	none	156	159	_	SMD		CRITICAL
	d trials	1		indirectness						0.37	VERY LOW	
										lower		
										(1.05		
										lower to		
										0.32		
				<u> </u>								

											Аррепаіх 1.	/
										higher)		
Global	state - Fund	ctioning	, disability - 7	-12 month fo	llow-up (Be	etter indicated b	oy lower valu	es)				
1	randomise d trials		no serious inconsistency		serious ³	none	53	50	-	SMD 044 lower (0.83 to 0.05 lower)	LOW	CRITICAL
Global	state - Fund	tioning	disability - >	12 month fol	llow-up (Be	tter indicated b	y lower value	es)				
	d trials	1	very serious ²	indirectness		none	93	90	-	SMD 0.56 lower (1.99 lower to 0.87 higher)	VERY LOW	CRITICAL
Quality	y of Life - Eı	nd of in	tervention (Be	etter indicate	d by higher	values)						
9	randomise d trials	no serious risk of bias	serious ⁴	no serious indirectness	serious ³	none	678	659	-	SMD 0.24 higher (0.14 to 0.35 higher)	LOW	CRITICAL

Qualit	y of Life - u _l	p to 6 m	onth follow-u	p (Better ind	icated by hi	gher values)					11ррениіх 1	,
2	randomise d trials		no serious inconsistency		serious ³	none	127	113	-	SMD 0.24 higher (0.01 lower to 0.50 higher)	LOW	CRITICAL
Qualit	y of Life - 7-	12 mont	h follow-up (Better indica	ted by high	er values)						
3	randomise d trials	no serious risk of bias	serious ⁴	no serious indirectness	serious ³	none	300	300	-	SMD 0.34 higher (0.09 to 0.60 higher)	LOW	CRITICAL
Qualit	y of Life - >1	12 mont	h follow-up (l	Better indicat	ted by highe	er values)						
2	randomise d trials		no serious inconsistency		serious	none	59	59	-	SMD 0.23 higher (0.13 lower to 0.60 higher)	LOW	CRITICAL

Empov	verment - Er	nd of int	tervention (Be	etter indicated	d by higher	values)					Аррениіх 17	
3	randomise d trials	serious 1	very serious ²	no serious indirectness	very serious	none	187	159	-	SMD 1.44 higher (0.08 lower to 2.97 higher)	VERY LOW	CRITICAL
Empov	verment - up	to 6 m	onth follow-u	p (Better ind	icated by hi	gher values)					1	
2	d trials	risk of bias	no serious inconsistency	indirectness	serious	none	278	260	-	SMD 0.25 higher (0.07 to 0.43) higher)	MODERAT E	CRITICAL
Service	e use, contac	t - End o	of intervention	n								
1	randomise d trials	serious ⁵	no serious inconsistency		no serious imprecision	none	4/27 (14.8%)	17/27 (63%)	,		MODERAT E	CRITICAL

											пррении 17	
										fewer)		
								0%		-		
ervice	Use - Hosp	italisati	on - End of in	tervention -	Days hospit	alised (Better i	ndicated by		lues)			
	randomise	serious	no serious	no serious	no serious	none	49	73		SMD		CRITICAL
	d trials	5	inconsistency	indirectness	imprecision					0.03	MODERAT	
			-		-					lower	E	
										(0.39		
										lower to		
										0.34		
										higher)		
				tervention								
	randomise d trials		no serious inconsistency	no serious	serious	none	15/49 (30.6%)			17 more per 1000 (from 112 fewer to	LOW	CRITICAL
				no serious		none	•	(28.8%)	(0.61 to	per 1000 (from 112		CRITICAL
	d trials		inconsistency	no serious indirectness		none	•		(0.61 to	per 1000 (from 112 fewer to 245		CRITICAL
ervice	d trials			no serious indirectness		none	•	(28.8%)	(0.61 to	per 1000 (from 112 fewer to 245 more)		CRITICAL
ervico	d trials	italisati	inconsistency on - up to 6 m	no serious indirectness		none	(30.6%)	(28.8%) 0%	(0.61 to 1.85)	per 1000 (from 112 fewer to 245 more) -	LOW	CRITICAL

									0.7)	fewer to	E	
										108		
										fewer)		
										,		
								0%		-		
Servic	Use - Hosp	italisati	on - 7-12 mon	th follow-up)					<u> </u>		
	•			1								
,	randomise	serious	no serious	no serious	serious	none	16/122	21/116	RR 0.77	42 fewer		CRITICA
	d trials	1	inconsistency	indirectness			(13.1%)	(18.1%)	(0.43 to	per 1000	LOW	
									1.39)	(from		
										103		
										fewer to		
										71 more)		
								0%		-		
Servic	use - Hosp	oitalisati	on - >12 mont	th follow-up				0%				
Servic				_		hone	25 /156		PP 0 44	-		CDITICAL
Servic	randomise			no serious	serious	none	25/156	35/182		- 65 fewer		CRITICA
Servic				_	serious	none	25/156 (16%)	35/182	(0.23 to	65 fewer per 1000	UIII VERY LOW	CRITICA
Servic	randomise			no serious	serious	none	Ī	35/182		65 fewer per 1000 (from		CRITICA
Servic	randomise			no serious	serious	none	Ī	35/182	(0.23 to	65 fewer per 1000 (from 148		CRITICAI
Servico !	randomise			no serious	serious	none	Ī	35/182	(0.23 to	65 fewer per 1000 (from 148 fewer to		CRITICAI
Service	randomise			no serious	serious	none	Ī	35/182	(0.23 to	65 fewer per 1000 (from 148 fewer to 177		CRITICAI
Servic	randomise			no serious	serious	none	Ī	35/182	(0.23 to	65 fewer per 1000 (from 148 fewer to		CRITICA
Servic	randomise			no serious	serious	none	Ī	35/182	(0.23 to	65 fewer per 1000 (from 148 fewer to 177		CRITICAI

1	randomise	serious	no serious	no serious	no serious	none	49	73	-	SMD		CRITICAL
	d trials	5	inconsistency	indirectness	imprecision					0.15	MODERAT	
										higher	Е	
										(0.21		
										lower to		
										0.51		
										higher)		

¹ Most information is from studies at moderate risk of bias

² Evidence of very serious heterogeneity of study effect size

³ Confidence interval (CI) cross the clinical decision threshold

⁴ Evidence of serious heterogeneity of study effect size

⁵ Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect

1.6 PSYCHOLOGICAL MANAGEMENT OF TRAUMA IN PSYCHOSIS AND SCHIZOPHRENIA - CRITICAL OUTCOMES

1.6.1 Cognitive therapy plus treatment as usual versus treatment as usual for trauma-clinical meta- analysis

			Quality as:	sessment			No of pat	ients	Ef	ffect	019	T
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Cognitive therapy + TAU	ITAII	Relative (95% CI)	Absolute	Quality	Importance
Anxiety	symptoms,	End of i	ntervention (B	etter indicated	d by lower v	alues)						
	randomised trials			no serious indirectness	serious ²	none	22	24	1	SMD 0.34 lower (0.93 lower to 0.24 higher)		CRITICAL
Anxiety	symptoms,	up to 6 1	nonth follow-u	p (Better ind	icated by lov	ver values)						
	randomised trials			no serious indirectness	serious ²	none	22	24	-	SMD 0.47 lower (1.06 lower to 0.11 higher)		CRITICAL
Depress	sion sympto	ms, End	of interventior	(Better indic	ated by low	er values)			1		l	
1	randomised	serious ¹	no serious	no serious	serious ²	none	22	24	-	SMD 0.29		CRITICAL

										219		
	trials		inconsistency	indirectness						lower (0.87	LOW	
										lower to		
										0.3 higher)		
										0 /		
Depre	ession sympto	ms, up to	o 6 month follo	ow-up (Better	indicated by	y lower values)						
	randomised	serious ¹	no serious	no serious	serious ²	none	22	24	-	SMD 0.05		CRITICAL
	trials		inconsistency	indirectness						lower (0.63	LOW	
										lower to		
										0.52		
										higher)		
										ingrei)		
Aissi :	ng data, any re	eason - E	nd of interven	tion				•				
	randomised	serious ¹	no serious	no serious	serious ²	none	14/36	6/30	RR 1.94	188 more		CRITICAL
•	trials			indirectness	Serio dis		(38.9%)	(20%)		per 1000	LOW	011110112
	triais		niconsistency	maneethess			(50.570)	(2070)	4.43)	(from 30	LOW	
									4.43)	(110111 50		
										forezon to		
										fewer to		
										fewer to 686 more)		
										686 more)		
										686 more) 188 more		
								20%		686 more) 188 more per 1000		
								20%		686 more) 188 more per 1000 (from 30		
								20%		188 more per 1000 (from 30 fewer to		
								20%		686 more) 188 more per 1000 (from 30		
Missii	ng data, any re	eason - U	Jp to 6 month f	ollow-up				20%		188 more per 1000 (from 30 fewer to		
Missii	ng data, any re		<u>-</u>	follow-up no serious	serious ²	none	14/36	20%	RR 1.94	188 more per 1000 (from 30 fewer to		CRITICAL

trials	inconsistency	indirectness	(38.9%)	(20%)	4.43)	(from 30	LOW	
						fewer to		
						686 more)		
						188 more		
						per 1000		
				20%		(from 30		
						fewer to		
						686 more)		
	I I			1		1		

¹ Studies included at moderate risk of bias

² CI crosses clinical decision threshold

1.7 TEAM AND SERVICE-LEVEL INTERVENTIONS - CRITICAL OUTCOMES

1.7.1 Early intervention services versus any alternative management strategy-clinical evidence profile

			Quality as	sessment			No of pat	ients	Efi	fect		
No of studie s	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Early Interventio n Services	Contro 1	Relativ e (95% CI)	Absolut e	Quality	Importance
Advers	se events - S	uicide	(actual and att	tempted), en	d of interve	ntion						
			no serious inconsistency		serious ¹	none	1/346 (0.29%)		(0.05 to	11 fewer per 1000 (from 14 fewer to 9 more)	MODERAT	CRITICAL
Advers	se events - S	uicide	(actual and at	tempted), >1	2months fo	llow-up						
			no serious inconsistency		serious ¹	none	3/275 (1.1%)	•	(0.17 to 3.28)	4 fewer per 1000 (from 12 fewer to 34 more)	MODERAT E	CRITICAL
Service	use - hospi	talisati	on, End of int	tervention		l						

											Аррениіх	17
3	randomise	no	no serious	no serious	serious ¹	none	219/374	242/35	RR 0.88	81 fewer		CRITICAL
	d trials	seriou	inconsistency	indirectness			(58.6%)	9	(0.79 to	per 1000	MODERAT	
		s risk						(67.4%)	0.98)	(from 13	E	
		of bias								fewer to		
										142		
										fewer)		
Sorvic	e usa - hosn	italicati	ion (number o	f had days)	and of inter	vention (Better	r indicated h	w lower	values)			
Servic	e use - nosp.	itali5ati	ion (number o	i bed days),	end of filter	vention (better	i iliaicatea t	y lower	varuesj			
2	randomise	no	no serious	no serious	serious ¹	none	344	339	-	SMD		CRITICAL
	d trials	seriou	inconsistency	indirectness						0.18	MODERAT	
		s risk								lower	E	
		of bias								(0.33 to		
										0.03		
										lower)		
Servic	e use - hosp	italisati	ion (no. of adı	 nissions), en	d of interve	ntion (Better in	ndicated by	lower va	lues)			
1	randomise	no	no serious	no serious	serious ¹	none	69	67	_	SMD		CRITICAL
1	d trials		inconsistency			rioric	07	07	_	0.46	MODERAT	CRITICILE
	u trais	s risk	liteorisistericy	manechiess						lower	E	
		of bias								(0.8 to	L	
		OI DIGS								0.12		
										lower)		
										10 (()		
Servic	e use - hosp	italisati	ion, >12 mont	h follow-up								
2	randomise	no	no serious	no serious	serious ¹	none	136/330	141/31	RR 0.93	31 fewer		CRITICAL
	d trials	seriou	inconsistency	indirectness			(41.2%)	6			MODERAT	

											Аррениіх	17
		s risk						(44.6%)	1.11)	(from 98	E	
		of bias								fewer to		
										49 more)		
										Í		
Service	e use - hospi	talisati	on (no. bed d	ays), >12 mo	nths follow	-up (Better ind	icated by lov	ver valu	es)			
2	randomise	no	no serious	no serious	serious ¹	none	320	326	-	SMD		CRITICAL
	d trials	seriou	inconsistency	indirectness						0.08	MODERAT	
		s risk								lower	E	
		of bias								(0.24		
										lower to		
										0.07		
										higher)		
Service	use - hospi	talisati	on (no. of adr	nissions), >1	.2 month fol	llow-up (Better	indicated by	y lower v	values)			
1	randomise	no	no serious	no serious	serious ¹	none	45	54	-	SMD 0.2		CRITICAL
	d trials	seriou	inconsistency	indirectness						lower	MODERAT	
		s risk								(0.6	E	
		of bias								lower to		
										0.2		
										higher)		
										,		
Service	e use - conta	ct, (not	in contact wi	th services- i	ndex team),	end of interve	ntion					
2	randomise	no	no serious	no serious	serious ¹	none	27/314	42/266	RR 0.61	62 fewer		CRITICAL
	d trials	seriou	inconsistency	indirectness			(8.6%)	(15.8%)	(0.4 to	per 1000	MODERAT	
		s risk							0.93)	(from 11	E	
		of bias								fewer to		

											Аррениіх	17		
										95				
										fewer)				
Service use - contact, (not in contact with services- mental health service), end of intervention														
1	randomise no no serious no serious serious¹ none 11/71 27/73 RR 0.42 215 ☐☐☐ CRITICAL													
						none	-	•				CRITICAL		
			inconsistency	indirectness			(15.5%)	(37%)	(0.23 to	fewer	MODERAT			
		s risk							0.78)	per 1000	E			
		of bias								(from 81				
										fewer to				
										285				
										fewer)				
Clobal	state Dolar	nco (fui	ll or partial), e	and of interv	ontion									
Global	State - Kela	pse (ru	ii oi partiai), t	end of interv	ention									
2 1	randomise	no	no serious	no serious	serious ¹	none	32/91	42/81	RR 0.65	181		CRITICAL		
	d trials	seriou	inconsistency	indirectness			(35.2%)	(51.9%)	(0.46 to	fewer	MODERAT			
		s risk					, ,	, ,	0.93)	per 1000	E			
		of bias							,	(from 36				
										fewer to				
										280				
										fewer)				
										,				
Global	state - Rem	ission ((full or partial	l), end of int	ervention									
2 1	randomise	no	serious ²	no serious	serious ¹	none	19/96	27/85	RR 0.66	108		IMPORTAN		
	d trials	seriou		indirectness			(19.8%)	(31.8%)	(0.32 to	fewer	LOW	T		
		s risk					` '	, ,	1.39)	per 1000				
1									<i>'</i>	1				
		of bias								(from				

											Аррепиіх	17
										216		
										fewer to		
										124		
										more)		
										·		
Global	state - Fund	tioning	g/Disability	(GAF), end o	of interventi	on (Better indi	cated by low	er value	es)			
2	randomise	no	serious ²	no serious	serious ¹	reporting	259	208	-	SMD		CRITICAL
	d trials	seriou		indirectness		bias ³				0.32	VERY LOW	
		s risk								lower		
		of bias								(0.51 to		
										0.14		
										lower)		
Global	state - Func	tioning	g/Disability	(GAF), >12 n	nonth follov	v-up (Better in	dicated by lo	wer valı	ues)			
1	randomise	no	no serious	no serious	serious ¹	none	151	150	-	SMD		CRITICAL
	d trials	seriou	inconsistency	indirectness						0.07	MODERAT	
		s risk								lower	E	
		of bias								(0.29		
										lower to		
										0.16		
										higher)		
Total S	ymptoms (I	'ANSS), end of inter	vention (Bet	ter indicate	d by lower valu	ies)					
1	randomise	no	no serious	no serious	serious ¹	reporting	55	44	-	SMD		CRITICAL
	d trials	seriou	inconsistency	indirectness		bias ³				0.52	LOW	
		s risk								lower		
	i	·				1					i	

		of bias								(0.92 to 0.11 lower)	Пррении	
Positiv	ve Symptom	s (PAN	SS or SAPS),	end of interv	vention (Bet	ter indicated b	y lower valu	es)				
2			no serious inconsistency		serious ¹	reporting bias ³	260	208	-	SMD 0.21 lower (0.39 to 0.03 lower)	LOW	CRITICAL
Negati	ive Sympton	ns (PAI	NSS or SANS)	, end of inte	rvention (B	etter indicated	by lower val	ues)				
2			no serious inconsistency		serious ¹	reporting bias ³	260	208	-	SMD 0.39 lower (0.57 to 0.2 lower)	LOW	CRITICAL
Positiv	ve Symptom	s (PAN	(SS), >12 mon	th follow-up	(Better ind	icated by lower	r values)					
1			no serious inconsistency		serious ¹	none	151	150	-	SMD 0.06 higher (0.16 lower to	MODERAT E	CRITICAL

		1						•		1	Пррениіх	17
										0.29		
										higher)		
Negati	ve Sympton	ns (PAN	NSS), >12 mor	nth follow-u	p (Better inc	licated by lowe	r values)					
Ü	, ,	,	•	•	•		ŕ					
1	randomise	no	no serious	no serious	serious ¹	none	151	150	-	SMD		CRITICAL
	d trials	seriou	inconsistency	indirectness						0.07	MODERAT	
		s risk	_							lower	E	
		of bias								(0.29		
										lower to		
										0.16		
										higher)		
										ingrici		
Emplo	vment and l	Educati	on, end of int	ervention		<u> </u>						
	<i>y</i>		,									
1	randomise	no	no serious	no serious	serious ¹	none	61/243	67/193	RR 0.72	97 fewer		CRITICAL
	d trials	seriou	inconsistency	indirectness			(25.1%)	(34.7%)	(0.54 to	per 1000	MODERAT	
		s risk					,	, ,		(from 10		
		of bias							,	fewer to		
										160		
										fewer)		
										icweij		
Emplo	yment and l	Educati	on, >12 montl	n follow-up		1						
				1								
1	randomise	no	no serious	no serious	serious ¹	none	159/275	148/27	RR 1.06	33 more		CRITICAL
	d trials	seriou	inconsistency	indirectness			(57.8%)	2	(0.92 to	per 1000	MODERAT	
		s risk					,	(54.4%)	`	(from 44		
		of bias						<u> </u>	,	fewer to		
										125		
L										120		

						1 ipperionic	<u> </u>	_
					more)			

¹ Confidence interval (CI) cross the clinical decision threshold

1.7.2 Early intervention services versus any alternative management strategy- health economic profile

EIS versus any alternative management strategy

Study & country	Limitations	Applicability	Other comments	Incremental cost (£)1	Incremental effect	ICER (£/effect)	Uncertainty
Cocchi et al, 2011 Italy	Potentially serious limitations ²	Partially applicable ³	Measure of outcome: change in Health of the Nation Outcome Scale (HoNOS) score Time horizon 5 years	-£2,865	18.20%	EI dominant	EI favourable irrespective of discount rate
Hastrup et al, 2013 Denmark	Minor limitations ⁴	Partially applicable ⁵	Measure of outcome: change in Global Assessment of Functioning (GAF) scale score Time horizon 5 years	-£23,973	1.19	EI dominant	Probability EI cost effective at WTP: €0 for point increase on GAF scale 0.95; €2,000 for point increase on GAF scale 0.97
McCrone et al, 2010 UK	Minor limitations ⁶	Directly applicable ⁷	Measure of outcome: change in Manchester Short Assessment (MANSA) of quality of life score; vocational recovery Time horizon 18 months	-£2,989	6 MANSA 11.8% vocational recovery	EI dominant	Probability EI cost effective at WTP: £0 for point improvement in MANSA score is 0.92; £0 for someone making vocational recovery is 0.76

² Evidence of serious heterogeneity of study effect size

³ Suspicion of publication bias

Appendix 17

McCrone et al, 2009 UK	Minor limitations ⁸	Directly applicable ⁹	Cost analysis Time horizon 1 and 3 years	-£5,687 year 1 -£16,296 year 3	NA	NA	Increasing readmission probabilities in EI by 50% never results in EI exceeding base-case SC cost; reducing readmission probabilities in SC by 50% cost break even
Mihalopoulos et al, 2009 Australia	Potentially serious limitations ¹⁰	Partially applicable ¹¹	Outcome measure: change in Brief Psychiatric Rating Scale score Time horizon up to 7.2 years	-£4,165	2.8	EI dominant	EI less costly and more favourable in 100% of cases; results robust to unit cost estimates
Serretti et al, 2009 Italy	Potentially serious limitations ¹²	Partially applicable ¹³	Cost analysis Time horizon 1 year	-£486	NA	NA	EI less costly in 75% of cases

- 1. In non-UK studies costs converted to UK pounds using purchasing power parities (PPP) exchange rates (http://www.oecd.org/std/ppp); all costs uplifted to 2011/2012 UK pounds using the UK HCHS inflation index
- 2. Effectiveness data derived from small prospective cohort study (n=46); limited sensitivity analysis; health effects not discounted
- 3. Italian NHS perspective; local unit costs used; discount rates of 3% and 5% for costs
- 4. Resource use estimates were derived from one RCT (n=547) and national registers
- 5. Danish public sector payer perspective; discount rate of 3% for costs
- 6. Resource use from one RCT (n=144), hospital administrative system, annual reports and accounts, other published sources; time horizon may not be sufficiently long to reflect all important differences in costs and outcomes
- 7. Analysis from NHS and PSS and criminal justice sector perspective, however NHS and PSS costs were reported separately
- 8. Resource use data based on review of RCTs, audit data, DoH, expert opinion, and other published sources
- 9. Analysis from NHS and PSS perspective

- 10. Modelling study based on small prospective cohort study with historical controls (n=65); resource use derived from a variety of sources; unclear what resource use included; limited sensitivity analysis; discount rate of 3% on costs
- 11. Australian public mental health service perspective
- 12. Modelling study based on retrospective prevalence-based multi-centre study, published sources and authors' assumptions; unclear source of unit costs; unclear if all costs relevant to NHS and PSS perspective included; limited sensitivity analysis; time horizon may not be sufficiently long to reflect all important differences in costs
- 13. Italian NHS perspective

1.7.3 ICM versus any alternative management strategy- clinical evidence profile

	Quality assessment							of patients	Eff	fect		
No of studie	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	ICM	Any alternative management s strategy		Absolut e	Quality	Importanc e
Service	e use: Avera	ge numl	oer of days in	hospital per	month - by	about 24 mont	hs (Bet	ter indicated b	y lower	values)		
	d trials	1	serious ² vith psychiatr	indirectness	-		1846	1749	-	MD 0.86 lower (1.37 to 0.34 lower)	LOW	CRITICAL
	randomise d trials	,	no serious inconsistency		serious ⁴	none	10/48 (20.8%)			176 fewer per 1000 (from 276 fewer to 19 more)	VERY LOW	CRITICAL

											търрсник т	
Not rer	naining in c	ontact v	vith psychiatr	ic services- r	nedium tern	n follow-up						
3	randomise	serious	no serious	no serious	no serious	none	65/527	132/536	RR 0.51	121		CRITICAL
	d trials	1	inconsistency	indirectness	imprecision		(12.3%	(24.6%)	(0.36 to	fewer	MODERAT	
					-)	,	0.71)	per 1000	E	
										(from 71		
										fewer to		
										158		
										fewer)		
									-			
								0%		-		
Not rer	naining in o	ontact v	vith psychiatr	ric services- l	ong term fo	llow-up						
5	randomise	serious	serious ²	no serious	no serious	none	18/247	69/228	RR 0.27	221		CRITICAL
	d trials	1		indirectness	imprecision		(7.3%)	(30.3%)	(0.11 to	fewer	LOW	
									0.66)	per 1000		
										(from		
										103		
										fewer to		
										269		
										fewer)		
								0%	-	_		
Notre			ر المانية الم		Fa4e1			0 70		_		
not rer	itaining in C		vith psychiatr	ic services- 1	otai							
9	randomise	very	serious ²	no serious	no serious	none	93/822	219/811	RR 0.43	154		CRITICAL
	d trials	serious		indirectness	imprecision		(11.3%	(27%)	(0.3 to	fewer	VERY LOW	
		3)		0.61)	per 1000		
										(from		

											Appenaix 1	/
										105		
										fewer to		
										189		
										fewer)		
								0%		-		
Qualit	y of Life - by	y short t	erm follow-uj	p (Better ind:	icated by lo	wer values)						
			<u>, </u>	· ·	<u>-</u>	,						
1	randomise	serious	no serious	no serious	serious ⁴	none	67	58	-	MD 0.53		CRITICAL
	d trials	3	inconsistency	indirectness						lower	LOW	
										(0.97 to		
										0.09		
										lower)		
										,		
Qualit	y of Life - by	y mediu	m term follov	v-up (LQoLP) (Better inc	licated by lowe	r value	s)				
1	randomise	serious	no serious	no serious	serious ⁴	none	26	26	-	MD 0.09		CRITICAL
	d trials	3	inconsistency	indirectness						lower	LOW	
			-							(0.78		
										lower to		
										0.6		
										higher)		
										0 - /		
Qualit	y of Life - by	y mediu	m term follov	v-up (MANS	A) (Better i	ndicated by low	er valu	es)				
1	randomise	no	no serious	no serious	serious ⁴	none	45	36	-	MD 0.2		CRITICAL
	d trials	serious	inconsistency	indirectness						lower	MODERAT	
		risk of								(0.69	Е	
										lower to		
										1361 10		

											прреник 1	<u> </u>		
		bias								0.29				
										higher)				
Quality	Quality of Life - by long term follow-up (LQoLP) (Better indicated by lower values)													
	ı	1	T		1	T						ı		
	randomise				serious ⁴	none	54	59	-	MD 0.23		CRITICAL		
	d trials	1	inconsistency	indirectness						higher	LOW			
										(0.08)				
										lower to				
										0.55				
										higher)				
										,				
Quality	y of Life - by	y long te	erm follow-up	(QOLI) (Be	tter indicate	d by lower valu	ıes)							
	1	ı	T			T						1		
	randomise				serious ⁴	none	67	65	-	MD 0.09		CRITICAL		
	d trials	1	inconsistency	indirectness						lower	LOW			
										(0.42)				
										lower to				
										0.24				
										higher)				
										,				
Partici _]	pant Satisfa	ction - b	y short term f	follow-up (B	etter indicat	ed by lower va	lues)							
1	randomise	serious	no serious	serious ⁵	serious ⁶	none	31	30	-	MD 6.2		CRITICAL		
	d trials	3	inconsistency							lower	VERY LOW			
										(9.8 to				
										2.6				
										lower)				
										10 (()				
	l	1	1	l .	l .	1								

											Appenuix 17	'
Partici	pant Satisfa	ction - b	y medium ter	m follow-up	(Better ind	icated by lower	values)				
2	randomise d trials		no serious inconsistency		no serious imprecision	none	272	228	-	MD 1.93 lower (3.01 to 0.86 lower)	HIGH	CRITICAI
Partici	pant Satisfa	ction - b	y long term f	ollow-up (Be	tter indicate	ed by lower val	ues)					
2	randomise d trials		no serious inconsistency		serious ⁶	none	233	190	-	MD 3.23 lower (4.14 to 2.31 lower)	MODERAT E	CRITICAI
Global	Functionin	g (GAF)	- by short teri	n follow-up	(Better indi	cated by higher	r values)				
4	randomise d trials		no serious inconsistency		no serious imprecision	none	437	360	-	MD 2.07 lower (3.86 to 0.28 lower)	MODERAT E	CRITICAI
Global	Functionin	g (GAF)	- by medium	term follow-	up (Better i	ndicated by hig	ther val	ues)				
3	randomise d trials	serious	serious²	no serious indirectness	serious ⁴	none	404	318	-	MD 0.09 lower (3.28	VERY LOW	CRITICAL

										lower to	110000000000000000000000000000000000000				
										3.11					
										higher)					
Global	Global Functioning (GAF)- by long term follow-up (Better indicated by lower values)														
5	randomise	serious	no serious	no serious	no serious	none	433	385	-	MD 3.41		CRITICAL			
	d trials	1	inconsistency	indirectness	imprecision					lower	MODERAT				
			-		_					(5.16 to	Е				
										1.66					
										lower)					

¹ Most information is from studies at moderate risk of bias

1.7.4 ICM versus any alternative management strategy- health economic profile

ICM versus standard care											
Study & country	Limitations	Applicability	Other comments	Incremental cost (£)1	Incremental effect	ICER (£/effect)	Uncertainty				
Harrison-Read et al, 2002 UK	Minor limitations ²	Directly applicable ³	Cost minimisation analysis Time horizon 1 and 2 years	£761 year 1 -£599 year 2	Simillar effects	NA	NA				

² Evidence of serious heterogeneity of study effect size

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

⁴ CI crosses clinical decision threshold

⁵ Concerns as to the directness of sample

⁶ OIS not met

Appendix 17

Karow et al, 2012 Germany	Minor limitations ⁴	Partially applicable ⁵	Outcome measure: QALYs Time horizon 1 year	-£2,274	0.1	ACT dominant	Probability ICM cost effective at WTP of €50,000 per QALY is 0.995
McCrone et al, 2009 UK	Minor limitations ⁶	Partially applicable ⁷	Outcome measure: change in satisfaction score on Gerber and Prince's scale Time horizon 18 months	£4,859	7.6	£639/extra satisfaction score	Probability ACT cost effective at WTP: £0 per additional satisfaction score 0.21; £1,000 per additional satisfaction score 0.78; £2,500 per additional satisfaction score 0.95
Slade et al, 2013 US	Minor limitations ⁸	Partially applicable ⁹	Cost analysis Time horizon 1 year	£1,165	NA	NA	Living near hospital with ACT programme had no significant effect on health care utilisation and costs; varying year of entry into ACT programme had no significant effect on costs
Udechuku et al, 2005 Australia	Potentially serious limitations ¹⁰	Partially applicable ¹¹	Cost analysis Time horizon 1 year	-£8,775	NA	NA	SA not performed

^{1.} In non-UK studies costs converted to UK pounds using purchasing power parities (PPP) exchange rates (http://www.oecd.org/std/ppp); all costs uplifted to 2011/2012 UK pounds using the UK HCHS inflation index

^{2.} Study based on one RCT (n=193); unit costs based on local and national sources

^{3.} NHS and PSS perspective adopted; comparator is routinely used service in the NHS

- 4. Study based on small prospective cohort study (n=120); time horizon may not be sufficiently long to reflect all important differences in costs and outcomes
- 5. Cost-utility analysis with QALYs based on EQ-5D, UK valuations; German public sector payer perspective; unclear if all costs relevant to NHS and PSS perspective were included; standard care may not be representative of routine and best practice in the NHS
- 6. Effectiveness data and resource use based on one RCT (n=251)
- 7. Societal perspective however NHS and PSS costs reported separately; outcome measure other than QALY was used
- 8. Based on pre-, post-observational study (n=6,030); cost year unclear (costs converted to UK pounds using purchasing power parities (PPP) exchange rates for 2008)
- 9. US mental health service payer perspective
- 10. Based on small pre-, post-observational study (n=31); local unit costs; time horizon may not be sufficiently long to reflect all important differences in costs
- 11. Australian mental health service payer perspective

1.7.5 ICM versus Non-ICM- clinical evidence profile

	Quality assessment								Ef	fect	المالية	Too as out on a co	
No of studies	l Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ICM	Non- ICM	Relative (95% CI)	Absolute	Quality	Importance	
Service	Service use: Average number of days in hospital per month - by about 24 months (Better indicated by lower values)												
	randomised trials			no serious indirectness	serious ²	none	1128	1092	-	MD 0.08 lower (0.37 lower to 0.21 higher)	LOW	CRITICAL	
Not ren	naining in co	ontact w	ith psychiatric	services- me	dium term fo	ollow-up							
	randomised trials			no serious indirectness	serious ²	none	3/37 (8.1%)	•	RR 0.27 (0.08 to 0.87)	223 fewer per 1000 (from 40 fewer to 281 fewer)	LOW	CRITICAL	

Not re	maining in co	ontact w	ith psychiatric	services- lon	g term follo	ow-up					, ,	
3	randomised trials	serious ¹	very serious ⁴	no serious indirectness	serious ²	none		-	RR 0.82 (0.34 to 1.98)	20 fewer per 1000 (from 73 fewer to 109 more)		CRITICAL
Not re	maining in co	ontact w	ith psychiatric	services- To	tal							
4	trials		very serious ⁴	no serious indirectness	serious ²	none		•	RR 0.63 (0.27 to 1.49)	45 fewer per 1000 (from 89 fewer to 60 more)	VERY LOW	CRITICAL
1	randomised trials	serious ³	inconsistency	no serious indirectness	serious ²	none	105	98	-	MD 0.02 higher (0.39 lower to 0.43 higher)	LOW	CRITICAL
Qualit	y of Life - by	mediun	n term follow-	up (Better in	dicated by 1	ower values)						

	1 . 1						40-			1.50 0.04	1100000001	
1	randomised	serious ³	no serious	no serious	serious ²	none	105	98	-	MD 0.04		CRITICAL
f	trials		inconsistency	indirectness						higher	LOW	
			_							(0.35		
										lower to		
										0.43		
										higher)		
Ouglitz	of Life by	long ton	m follow up ()	Ool) (Rotto	indicated by	v lovos voluce)						
Quanty	of Life - by	iong ter	iii ioiiow-up (i	LQOL) (Better	i iliulcateu b	y lower values)						
1 :	randomised	serious ³	no serious	no serious	no serious	none	274	252	-	MD 0.03		CRITICAL
1	trials		inconsistency	indirectness	imprecision					lower	MODERATE	
			, and the second		1					(0.16		
										lower to		
										0.1		
										higher)		
Quality	of Life - by	long ter	m follow-up (I	MANSA) (Be	tter indicate	d by lower value	es)					
	· ·	_			I	,						
1	randomised	no	no serious	no serious	serious ⁵	none	91	75	-	MD 0.1		CRITICAL
f	trials	serious	inconsistency	indirectness						lower	MODERATE	
		risk of								(0.39		
		bias								lower to		
										0.19		
										higher)		
										mgner)		
Quality	of Life - by	long ter	m follow-up -	overall life s	atisfaction (C	QOLI) (Better in	dicated	by low	er values	5)		
~ 7	,	0	1			, (<i>y</i>		,		
1	randomised	serious ³	no serious	no serious	serious ²	none	105	98	-	MD 0.1		CRITICAL
Į.			l	. 1						1	TOTAL	
	trials		inconsistency	indirectness						lower	LOW	

											Аррепаіх 1	
										(0.45		
										lower to		
										0.25		
										higher)		
Danti ain	ant Cations	tion be	langtaun fall	Dati	ont mood (CA	NI) (Dattagin di		- 10				
rartici	ani Sausiac	11011 - by	iong term fon	low-up - ratio	ent need (CA	N) (Better indic	cated by	lower	varuesj			
1	randomised	serious ³	no serious	no serious	serious ²	none	306	279	-	MD 0.29		CRITICAL
	trials		inconsistency	indirectness						lower	LOW	
										(0.69		
										lower to		
										0.11		
										higher)		
Global	Functioning	(HoNO	S)- short term	follow-up (B	etter indicato	ed by lower val	ues)					
1	randomised	serious ³	no serious	no serious	serious ²	none	54	64	-	MD 0.60		CRITICAL
	trials		inconsistency	indirectness						higher	LOW	
										(1.8 lower		
										to 3		
										higher)		
Global	functioning	(HoNO:	 S)- long term f	ollow-up (Re	tter indicate	d by lower valu	es)					
Global	ranctioning	(110110)	o, long term i	onow up (be	tter marcute	a by lower vara	C 5,					
1	randomised	serious ³	no serious	no serious	serious ²	none	124	115	-	MD 0.40		CRITICAL
	trials		inconsistency	indirectness						lower	LOW	
										(1.77		
										lower to		
										0.97		
	•		•			•						

						Tipperions 11		
					higher)			
							1	

¹ Most information is from studies at moderate risk of bias

² Confidence interval (CI) cross the clinical decision threshold

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

 $^{^{4}}$ Evidence of very serious heterogeneity of study effect size

⁵ Optimal information size not met

1.7.6 Crisis resolution/ home intervention teams versus standard care- clinical evidence profile

			Quality as	sessment		No of pat	ients	Ef	fect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Crisis Resolution/ Home intervention teams	Control	Relative (95% CI)	Absolute		Importance
Service	use: Admitt	ted to ac	ute care - by 3	months								
	randomised trials	serious ¹	serious ²	no serious indirectness	serious ³	none	31/109 (28.4%)	82/96 (85.4%)	(0.11 to	555 fewer per 1000 (from 760 fewer to 154 more)	VERY	CRITICAL
								83.3%		541 fewer per 1000 (from 741 fewer to 150 more)		
Service	use: Admitt	ted to ac	ute care - by 6	months								
3	randomised	serious ¹	very serious ²	no serious	serious ³	none	46/169	141/156	RR 0.28	651 fewer		CRITICAL

	ı				1	,		, ,			ochuix 17	
	trials			indirectness			(27.2%)	(90.4%)	(0.09 to)	per 1000	VERY	
									0.88)	(from 108	LOW	
										fewer to		
										822		
										fewer)		
										(10 f		
										648 fewer		
										per 1000		
								90%		(from 108		
										fewer to		
										819		
										fewer)		
Service	use: Admitt	ed to ac	ute care - by 12	2 months								
0	1 , 1	• 1	• 4	•		 	70 /202	106 /100	DD 0.4	E04.6		CDITICAL
3	randomised	serious				none						CRITICAL
	trials			indirectness	imprecision		(38.6%)	(99%)	•	1		
									0.51)	(from 485		
										fewer to		
										683		
										fewer)		
										600 fewer		
										per 1000		
										(from 490		
								100%		fewer to		
										690		
										fewer)		

Servic	Service use: Admitted to acute care - by 24 months													
1	randomised	serious ⁵	no serious	no serious	serious ⁶	none	20/64	54/54	RR 0.32	680 fewer		CRITICAL		
	trials		inconsistency				(31.3%)	-		per 1000				
			-						0.46)	(from 540				
										fewer to				
										780				
										fewer)				
										680 fewer				
										per 1000				
								100%		(from 540				
								100 /6		fewer to				
										780				
										fewer)				
Servic	e use: Readm	itted to	acute care - by	12 months										
4	randomised	serious ¹	very serious ²	no serious	serious ³	none	64/295	123/306	RR 0.51	197 fewer		CRITICAL		
	trials			indirectness			(21.7%)	(40.2%)	(0.21 to	per 1000	VERY			
									1.2)	(from 318	LOW			
										fewer to				
										80 more)				
										221 fewer				
										per 1000				
								45.1%		(from 356				
										fewer to				
										90 more)				

	Service use: Readmitted to acute care - by 24 months													
Service	use: Readm	itted to	acute care - by	24 months										
2	randomised	serious1	very serious ²	no serious	serious³	none	50/155	59/151	RR 0.76	94 fewer		CRITICAL		
	trials		, and the second	indirectness			(32.3%)	(39.1%)	(0.36 to	per 1000	VERY			
							()	()	•	(from 250				
									1.00)	fewer to	20,,			
										246				
										more)				
										more)				
										98 fewer				
										per 1000				
								10 =0/		(from 260				
								40.7%		fewer to				
										256				
										more)				
Service	use: Davs o	f acute i	nnatient care :	by 3 months	Better indi	cated by lower	values)			,				
Service	use. Duys o	i ucute i	inputite it cure	by a month	(Better mar	cuted by lower	uruesj							
1	randomised	serious ⁵	no serious	no serious	serious³	none	43	42	-	SMD 0.52		CRITICAL		
	trials		inconsistency	indirectness						lower	LOW			
										(0.95 to				
										0.09				
										lower)				
Service	use: Days o	f acute i	npatient care -	· by 6 months	(Better indi	cated by lower	values)							
3	randomised	serious ¹	very serious ²	no serious	serious ³	none	143	193	-	SMD 0.81		CRITICAL		
	trials			indirectness						lower	VERY			
										(1.73	LOW			
										lower to				
		I	I	I.	I	1								

										IIp	venuix 17	<u> </u>
										0.11		
										higher)		
										mgner)		
Service	e use: Davs o	f acute i	npatient care -	by 12 month	s (Better inc	dicated by lower	r values)					
001110	2	_ 0.00.00 _	P	~ <i>y</i> == =======	-5 (2 50002 222)							
${1}$	randomised	serious ⁵	no serious	no serious	serious ⁶	none	76	79	-	SMD 0.62		CRITICAL
	trials		inconsistency	indirectness						lower	LOW	
										(0.94 to		
										0.3		
										lower)		
Coursia)			la 20 o 41a	o (Dallanin d	Lastad lass lassace						
Service	e use: Days o	i acute i	npatient care -	by Zomonth	s (better mo	licated by lower	varues)					
1	randomised	serious ⁵	no serious	no serious	serious ⁶	none	92	97	_	SMD 1.01		CRITICAL
	trials		inconsistency	indirectness						lower	LOW	
										(1.31 to	20,,	
										0.71		
										lower)		
Manta	1 11001410 A 04	A denicai	h 2 o	1 16 a								
Menta	i Health Act	Aumissi	on - by 3 mon	tns								
1	randomised	serious ⁵	no serious	no serious	serious ³	none	9/45	13/42	RR 0.65	108 fewer		CRITICAL
	trials		inconsistency	indirectness			(20%)	(31%)				
							(=0 /0)	(0270)	,	(from 214	20,,	
									1.55)	`		
										fewer to		
										108		
										more)		
								24.0/		100 (
								31%		109 fewer		

										I1p	penaix 17	<u></u>
										per 1000		
										(from 214		
										fewer to		
										109		
										more)		
Satisfa	⊥ ction -Patien	t satisfie	ed with care: S	atisfaction S	cale - by 6 m	onths (Better in	dicated by his	gher val	11es)	/		
344314					cure 2 y 0 m	011113 (20101 111		B-101 141				
1	randomised	serious ⁵	no serious	no serious	serious ⁶	none	61	54	-	SMD 0.95		CRITICAL
	trials		inconsistency	indirectness						higher	LOW	
										(0.57 to		
										1.34		
										higher)		
Satisfa	ction -Patien	t satisfie	ed with care: S	atisfaction S	cale - by 12 n	nonths (Better i	ndicated by h	igher va	ılues)			
1	randomised	serious ⁵	no serious	no serious	serious ⁶	none	62	59	-	SMD 1.02		CRITICAL
	trials		inconsistency	indirectness						higher	LOW	
										(0.64 to		
										1.4		
										higher)		
Satisfa	ction -Patien	t satisfie	ed with care: S	atisfaction S	cale - by 20 n	nonths (Better i	ndicated by h	igher va	ılues)			
1	randomised	serious ⁵	no serious	no serious	serious ⁶	none	69	68	-	SMD 1.21		CRITICAL
	trials		inconsistency	indirectness						higher	LOW	
										(0.85 to		
										1.58		
										higher)		
										0 /		

Satisfac	ction- patien	t (CSQ)	- by 3 months	(not satisfied	l with care)							
1	randomised	serious ⁵	no serious	no serious	serious ³	none	19/45	17/42	RR 1.04	16 more		CRITICAL
	trials		inconsistency	indirectness			(42.2%)	(40.5%)	(0.63 to	per 1000	LOW	
									1.72)	(from 150		
										fewer to		
										291		
										more)		
										11 more		
										per 1000		
								28.6%		(from 106		
								20.0 /0		fewer to		
										206		
										more)		

¹ Most information is from studies at moderate risk of bias

² Evidence of very serious heterogeneity of study effect size

³ Confidence interval (CI) cross the clinical decision threshold

⁴ Evidence of serious heterogeneity of study effect size

⁵ Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect

⁶ Criteria for an optimal information size not met

1.7.7 Crisis resolution/ home intervention teams versus standard care- health economic profile

CRHTTs versus	s standard car	e					
Study & country	Limitations	Applicability	Other comments	Incremental cost (£)1	Incremental effect	ICER (£/effect)	Uncertainty
McCrone et al, 2009 UK	Minor limitations ²	Partially applicable ³	Cost analysis Time horizon 6 months	-£2,444	NA	NA	If CRHTT contact unit cost was £40, cost difference would be £1,807
McCrone et al, 2009 UK	Minor limitations ⁴	Directly applicable ⁵	Outcome measure: days on psychiatric ward avoided Time horizon 6 months	£976	3.1	£315/avoided inpatient day	Probability CRHTT cost effective at WTP £0 for avoided inpatient day <0.10; WTP £25 for avoided inpatient day 0.41; WTP £100 for avoided inpatient day 1.00

- 1. All costs uplifted to 2011/2012 UK pounds using the UK HCHS inflation index
- 2. Based on pre-, post-observational study (n=200); local, national and published sources for unit costs; limited sensitivity analysis; time horizon may not be sufficiently long to reflect all important differences in costs
- 3. Includes costs not relevant to NHS and PSS perspective
- 4. Time horizon may not be sufficiently long to reflect all important differences in costs
- 5. Perspective of NHS and PSS and criminal justice sector, however costs not relevant to NHS and PSS accounted only for a small proportion of costs

1.7.8 Crisis houses versus standard care- clinical evidence profile

			Quality as	sessment			No of pa	ntients	Ef	fect		
No of studies	l Jesion	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Crisis houses (recovery houses)	Control	Relative (95% CI)	Absolute	Quality	Importance
Service	use: Admitt	ed to acı	ite care - by 6 i	nonths follov	v-up							
	randomised trials			no serious indirectness	serious ¹	none	93/93 (100%)	92/92 (100%) 100%	RR 1 (0.98 to 1.02)	0 fewer per 1000 (from 20 fewer to 20 more) 0 fewer per 1000 (from 20 fewer to 20 more)	LOW	CRITICAL
Service	use: Readm	itted to a	icute care - by	6 months foll	ow-up							
	randomised trials			no serious indirectness	serious ³	none	67/93 (72%)	74/92 (80.4%)	RR 0.9 (0.76 to 1.05)	80 fewer per 1000 (from 193 fewer to	LOW	CRITICAL

										0.36 higher)		
										0.36		
	litais		liteorisistericy	munectness						lower to	LOW	
	randomised trials		inconsistency		serious ³	none	61	47	-	lower (0.4		CRITICAL
	,		_		- `	T	1	·		CMD 0 02		CDITICAL
Service	use: Days of	acute in	npatient care -	by 6 months	 follow-up (B	Setter indicated	by lower v	alues)		10 111010)		
										40 more)		
								00.4 /0		fewer to		
								80.4%		per 1000 (from 193		
										80 fewer		
										00.6		
										40 more)		

¹ Criteria for an optimal information size not met

1.7.9 Acute day hospital care versus inpatient admission-clinical evidence profile

Quality assessment	No of patients	Effect	Quality	Importanc

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

³ Confidence interval (CI) cross the clinical decision threshold

											пррениіх 1	<u>'</u>
				ī								e
No of studie	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Acute day hospita 1 care	Inpatient admissio n	Relativ e (95% CI)	Absolut e		
Type 1	studies: Fea	sibility	and engageme	ent: lost to fo	llow up - en	d of study (by	3 months	s)				
1	randomise	no	no serious	no serious	no serious	none	163/596	147/521	RR 0.97	8 fewer		CRITICAL
	d trials	serious	inconsistency	indirectness	imprecision		(27.3%)	(28.2%)	(0.8 to	per 1000	HIGH	
		risk of							1.17)	(from 56		
		bias								fewer to		
										48 more)		
								0%		_		
Type 1	studies: Fea	sibility	and engageme	ent: lost to fo	ollow up - en	d of study (by	2-6 mont	ths)				
2	randomise	serious	serious²	no serious	no serious	none	37/144	53/168	RR 0.83	54 fewer		CRITICAL
	d trials	1		indirectness	imprecision		(25.7%)	(31.5%)	(0.58 to	per 1000	LOW	
									1.19)	(from		
										133		
										fewer to		
										60 more)		
								0%		-		
Type 1	studies: Fea	sibility	and engageme	ent: lost to fo	llow up - en	d of study (by	1 year)					
5	randomise	no	serious ²	no serious	no serious	none	274/887	267/817	RR 0.94	20 fewer		CRITICAL
		serious							(0.82 to	per 1000	MODERAT	

			I	I	<u></u>	T					<u> 11ррениіх 1</u>	,
	d trials	risk of		indirectness	imprecision		(30.9%)	(32.7%)	1.08)	(from 59	E	
		bias								fewer to		
										26 more)		
										·		
								0%		-		
Type 1	studies: Du	ration o	f index admiss	sion (days/m	onth) (Better	indicated by 1	ower val	ues)				
4	randomise	no	serious ²	no serious	no serious	none	820	762	-	MD		CRITICAL
	d trials	serious		indirectness	imprecision					27.47	MODERAT	
		risk of			-					higher	E	
		bias								(3.96 to		
										50.98		
										higher)		
										11181101)		
Type 1	studies: Du	ration o	f all hospital c	are (days/mo	onth) (Better	indicated by lo	wer valu	ies)				
3	randomise	serious	no serious	no serious	serious³	none	224	241	-	MD 0.38		CRITICAL
	d trials	1	inconsistency	indirectness						lower	LOW	
										(1.32		
										lower to		
										0.55		
										higher)		
										0 - /		
Type 1	studies: Du	ration o	f stay in hospi	tal (days/mo	nth) (Better	indicated by lo	wer valu	ies)				
3	randomise	serious	no serious	no serious	serious ³	none	224	241	-	MD 2.75		CRITICAL
	d trials	1	inconsistency	indirectness						lower	LOW	
										(3.63 to		
										1.87		
	1	1		l								

											Аррепиіх 1	<u>'</u>
										lower)		
Type 1	studies: Du	ration of	f all day patie	nt care (days,	/month) (Bet	tter indicated b	y lower v	alues)				
3	randomise	serious	serious²	no serious	no serious	none	224	241	_	MD 2.34		CRITICAL
	d trials	1		indirectness	imprecision					higher	LOW	
										(1.97 to		
										2.7		
										higher)		
ype 1	studies: re-a	admitted	l to in/day pat	ient care afte	er discharge	(days/month)						
	randomise	serious	no serious	no serious	serious ³	none	92/326	106/341	_	311		CRITICAL
	d trials	1	inconsistency	indirectness			(28.2%)	(31.1%)		fewer	LOW	
										per 1000		
										(from		
										311		
										fewer to		
										311		
										fewer)		
								0%	-	-		
ype 1	studies: Sat	isfaction	with services	s: not satisfie	d with care	received						
	randomise	no	no serious	no serious	serious ³	none	12/43	29/48	RR 0.46	326		CRITICAL
	d trials	serious	inconsistency	indirectness			(27.9%)	(60.4%)	(0.27 to	fewer	MODERAT	
		risk of							0.79)	per 1000	E	
		bias ¹								(from		
										127		

		•									Аррениіх 1	,			
										fewer to					
										441					
										fewer)					
									-						
								0%		-					
Type 2	studies – Fe	asibility	and engagen	nent: lost to f	follow up (at	2 years)									
1	randomise serious no serious no serious serious³ none 36/103 29/57 RR 0.69 158 ☐☐☐ CRITICAL														
	d trials	1	inconsistency	indirectness			(35%)	(50.9%)	(0.48 to	fewer	LOW				
									0.99)	per 1000					
										(from 5					
										fewer to					
										265					
										fewer)					
									_	·					
								0%		-					
Type 2	studies – D	uration (of all hospital	care (days/m	onths, IPD	- "nights in" &	"nights	out") (Bett	er indica	ited by lo	wer values)				
1	randomise	serious	no serious	no serious	serious ³	none	103	57	_	MD 1.10		CRITICAL			
	d trials	1	inconsistency	indirectness						higher	LOW				
										(1.58					
										lower to					
										3.78					
										higher)					
Type 2	studies: re-a	dmitted	l to in/day pat	ient care afte	er discharge	(days/month)									
1	randomise	serious	no serious	no serious	serious ³	none	42/103	25/57	RR 0.93	31 fewer		CRITICAL			
									(0.64 to	per 1000					
				1		ı			1			ı			

									Tipperions I	
d trials	1	inconsistency	indirectness		(40.8%)	(43.9%)	1.35)	(from	LOW	
								158		
								fewer to		
								154		
								more)		
						0%		-		

¹ Most information is from studies at moderate risk of bias

² Evidence of serious heterogeneity of study effect size ³ CI crosses clinical decision threshold

1.8 VOCATIONAL REHABILITATION - CRITICAL OUTCOMES

1.8.1 Supported employment (standard or modified) versus pre-vocational training (standard or modified) - clinical evidence profile

			Quality as	sessment			No of pa	atients	Ef	fect		
No of studie s	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	t (Standard OR Modified)	1 1 2 2 1 2 1 2 2	e (95% CI)	Absolut e	Quality	Importanc e
Emplo	yment (com	petitive) - End of trea	tment - NO	T in compet	itive employm	ent					
	randomise d trials	serious risk of bias		indirectness	imprecisio n	none	963/1840 (52.3%)	0%	RR 0.63 (0.56 to 0.72)		MODERAT E	CRITICAL
Employ	yment, com	petitive	- End of treat	ment - Earn	ings (Better	indicated by h	igher values	5)		<u> </u>		
12	randomise	serious	very serious ³	no serious	no serious	none	1267	1208	-	SMD		CRITICAL

											πρρίπαιλ 17	
	d trials	2		indirectness	imprecisio					0.74	VERY LOW	
					n					higher		
										(0.38 to		
										1.10		
										higher)		
Emplo	yment (com	petitive	e) - End of trea	atment - Dur	ation (Bette	r indicated by	higher value	s)				
2	randomise	serious	serious ¹	no serious	no serious	none	205	201	_	SMD		CRITICAL
	d trials	2		indirectness	imprecisio					0.17	LOW	
					n					higher		
										(0.26		
										lower to		
										0.60		
										higher)		
Emplo	yment (com	petitive	e) - End of trea	atment - Lon	gest job wo	rked (Better in	dicated by h	igher value	es)			
5	randomise	no	serious ¹	no serious	serious ⁴	none	302	359	-	SMD		CRITICAL
	d trials	serious		indirectness						0.45	LOW	
		risk of								higher		
		bias								(0.07 to		
										0.83		
										higher)		
Emplo	yment (com	petitive	e) - End of trea	atment - Tim	e to first jol	Better indica	ited by lower	values)				
7	randomise	no	no serious	no serious	no serious	none	355	372	-	SMD		CRITICAL
	d trials	serious	inconsistenc	indirectness	imprecisio					0.48	HIGH	
L	I	i .	1	I	l	1	1			İ	l	

											71ppenuix 17				
		risk of	у		n					lower					
		bias								(0.65 to					
										0.31					
										lower)					
										,					
Emplo	yment (com	petitive	e) - End of trea	atment - Nur	nber of jobs	(Better indica	ted by highe	r values)							
2	randomise	no	serious ¹	no serious	no serious	none	108	113	-	SMD		CRITICAL			
	d trials	serious		indirectness	imprecisio					0.54	MODERAT				
		risk of			n					higher	E				
		bias								(0.25 to					
										0.84					
										higher)					
Emplo	Employment, competitive - End of treatment - Hours worked (Better indicated by higher values)														
9	randomise	serious	very serious ³	no serious	no serious	none	1193	1211	-	SMD		CRITICAL			
	d trials	2		indirectness	imprecisio					0.67	VERY LOW				
					n					higher					
										(0.35 to					
										0.98					
										higher)					
Emplo	yment (com	petitive	e) - End of trea	ntment - Day	s/weeks wo	rked (Better ir	idicated by h	igher valu	es)						
7	randomise	serious	serious ¹	no serious	no serious	none	464	530	-	SMD		CRITICAL			
	d trials	2		indirectness	imprecisio					0.72	LOW				
					n					higher					
										(0.46 to					
L	1	1	I	I .	I	ı	l	I	l .		l	1			

			•								Appenaix 17	
]										0.87		
										higher)		
										0 /		
Emplo	yment (com	petitive	e) -up to 12 m	onth FU - NO	OT in comp	etitive employı	ment					
	`	<u>-</u>	· -		_							
1	randomise	no	no serious	no serious	serious ⁴	reporting	90/109	99/110	RR 0.92	72 fewer		CRITICAL
	d trials	serious	inconsistenc	indirectness		bias ⁵	(82.6%)	(90%)	(0.82 to	per 1000	LOW	
		risk of	v						1.02)	(from		
		bias							,	162		
										fewer to		
										18 more)		
										10 111016)		
								0%		_		
Fmplo	vment (com	netitive) - >12 month	s FU - Hour	s worked (R	etter indicated	hy higher va					
Linpio	y mem (com	реши	., - 12 11101101	1510 11041	, worken (B	citer indicated	by migner ve	iracs,				
2	randomise	no	no serious	no serious	serious ⁶	none	90	85	_	SMD		CRITICAL
	d trials	serious	inconsistenc	indirectness						0.42	MODERAT	
		risk of	V							higher	E	
		bias								(0.06	_	
		Dias								lower to		
										0.91		
										higher)		
Emala	Imont loom	notiti	\ \12 manth	C EII Eanni	na (Rottor:	l Indicated by high	ther walnes					
Emplo	yment (com	pennve	:) - ~12 monti	is PU - Eaffill	ng (bener n	idicated by file	gner varues)					
2	randomise	serious	serious ³	no serious	serious ⁴	none	90	85	_	SMD		CRITICAL
_	d trials	2		indirectness						0.37	VERY LOW	
	a arais	1	1	midii ccuicss					1	0.07	A LIVI LOVA	1
										highor		
										higher (0.09		

											тррении 17	
]										lower to		
										0.84		
										higher)		
										0 - 7		
Emplo	yment (com	petitive) - >12 month	ns FU - Numl	er of jobs (Better indicate	d by higher	values)				
1	randomise	no	no serious	no serious	serious ⁴	none	17	18	-	SMD		CRITICAL
	d trials	serious	inconsistenc	indirectness						0.07	MODERAT	
		risk of	у							higher	E	
		bias								(0.59		
										lower to		
										0.73		
										higher)		
										0 /		
Emplo	yment (com	petitive) - >12 month	ns FU - Days/	weeks worl	ced (Better ind	icated by hig	her values	5)			
1	randomise	no	no serious	no serious	serious ⁴	none	17	18	-	SMD		CRITICAL
	d trials	serious	inconsistenc	indirectness						0.22	MODERAT	
		risk of	у							higher	E	
		bias								(0.44		
										lower to		
										0.88		
										higher)		
										,		
Occup	ation (any)-	End of	treatment - N	OT in any o	ccupation (p	oaid/unpaid/co	mpetitive/un	competitiv	ve)			
7	randomise	serious	serious ¹	no serious	very	none	184/500	288/543	RR 0.70	159		CRITICAL
	d trials	2		indirectness	serious ⁴		(36.8%)	(53%)	(0.56 to	fewer	VERY LOW	
										per 1000		
	I		1	1	I	1			1	l		

											түрениіх 17	
									0.87)	(from 69		
										fewer to		
										233		
										fewer)		
										,		
										159		
										fewer		
										per 1000		
								53.1%		(from 69		
										fewer to		
										234 fewer)		
	1: ()	F 1 6		OT: 1						iewei)		
Occup	ation (any)-	End of	treatment - N	O1 in volun	teer employ	ment						
2	randomise	serious		no serious		none	122/129	118/127				CRITICAL
	d trials	2		indirectness	imprecisio		(94.6%)	(92.9%)	(0.84 to	per 1000	LOW	
					n				1.28)	(from		
										149		
										fewer to		
										260		
										more)		
										/		
										35 more		
										per 1000		
										(from		
								87%		139		
										fewer to		
										244		
										more)		

	randomise	corious	corious1	no serious	serious ⁴	none	239	255		SMD	ППП	CRITICA
		serious	serious			none	239	233	-			CKITICA
	d trials	_		indirectness						0.23	VERY LOW	
										lower		
										(0.42 to		
										0.05		
										lower)		
200111	astion (any)	End of	traatmant	- Weeks worke	d (Rotton in	l disated by big	rhor walnes)					
ccu	ation (any)	- Ella ol	treatment.	- weeks worke	a (better in	dicated by fife	giter varues)					
	randomise	serious	serious ¹	no serious	serious ⁴	none	332	399	_	SMD		CRITICA
	d trials	2		indirectness						0.32	VERY LOW	
										higher		
										(0.17 to		
										0.46		
										higher)		
										0 /		
Occup	oation (any)	- End of	treatment -	- Hours worked	d (Better inc	dicated by hig	her values)					
<u> </u>	randomise	serious	serious ¹	no serious	no serious	none	312	371	_	SMD		CRITICA
	d trials	2		indirectness						0.24	LOW	
					n					higher		
										(0.08 to		
										0.40		
										higher)		
				1		1	1		1	THEILELI	ı	1

											тррспик т	
4	randomise	serious	serious ¹			none	285	353	-	SMD		CRITICAL
	d trials	2		indirectness	imprecisio					0.23	LOW	
					11					higher (0.08 to		
										0.39		
										higher)		
Occup	ation (any)	Fnd of	treatment - N	Jumber of io	hs (Retter i	 ndicated by hig	oher values)					
Occup	ation (any)	Liid Oi	treatment - 1	dumber of jo	bs (better in	idicated by ing	Silci values)					
1	randomise		no serious		no serious	none	91	95	-	SMD		CRITICAL
				indirectness	imprecisio					0.06	HIGH	
		risk of	У		n					higher		
		bias								(0.23		
										lower to 0.34		
										higher)		
Occup	ation (any)	- End of	treatment - E	arnings (Bet	ter indicate	d by higher va	lues)					
4	randomise	no	serious ¹	no serious	serious ⁴	none	249	303	-	SMD		CRITICAL
	d trials	serious		indirectness						0.37	LOW	
		risk of								higher		
		bias								(0.2 to		
										0.54		
										higher)		
Globa	l state - fund	ctional d	lisability - En	d of treatme	nt (Better in	dicated by lov	ver values)					
4	randomise	serious	no serious	no serious	no serious	none	350	349	-	SMD		CRITICAL
]						<u> </u>

											Appenuix 17	
	d trials	2	inconsistenc	indirectness	imprecisio					0.02	MODERAT	
			у		n					higher	E	
										(0.13		
										lower to		
										0.17		
										higher)		
Global	state - func	tional d	lisability - up	to 12 month	FU (Better	indicated by lo	ower values)					
1	randomise	serious	no serious	no serious	no serious	none	93	95	-	SMD		CRITICAL
	d trials		inconsistenc		imprecisio					0.04	MODERAT	
			y		n					higher	Е	
										(0.25		
										lower to		
										0.33		
										higher)		
Quality	y of Life - E	nd of tr	eatment (Bett	er indicated	by lower va	lues)						
4	randomise	no	no serious	no serious	no serious	none	344	339	-	SMD		CRITICAL
	d trials	serious	inconsistenc	indirectness	imprecisio					0.00	HIGH	
		risk of			n					higher		
		bias								(0.15		
										lower to		
										0.15		
										higher)		

- ¹ Evidence of serious heterogeneity of study effect size
- ² Most information is from studies at moderate risk of bias
- ³ Evidence of very serious heterogeneity of study effect size
- ⁴ Confidence interval (CI) cross the clinical decision threshold
- ⁵ Lack of follow-up data suggests likely publication bias
- ⁶ Optimal information size not met

1.8.2 Supported employment (standard or modified) versus pre-vocational training (standard or modified) - health economic profile

Supported emp	Supported employment (standard or modified) versus prevocational training (standard or modified)													
Study & country	Limitations	Applicability	Other comments	Incremental cost (£)1	Incremental effect	ICER (£/effect)	Uncertainty							
Howard et al, 2010 Heslin et al, 2011 UK	Potentially serious limitations ²	Directly applicable ³	Outcome measure: % in competitive employment Time horizon 1 and 2 years	-£2,489 year 1 -£2,700 year 2	6% year 1 11% year 2	IPS dominant	Probability IPS cost effective at WTP £0 for extra person gaining employment is 0.90 at year 2							

- 1. All costs uplifted to 2011/2012 UK pounds using the UK HCHS inflation index
- 2. Effectiveness and resource use based on one RCT (n=219); intervention not delivered at optimum
- 3. Includes costs not relevant to NHS and PSS perspective, however these accounted only for a small proportion of total costs

Appendix 17

1.8.3 Supported employment (standard or modified) versus TAU/control (non-vocational comparison group) - clinical evidence profile

			Quality as	sessment			No of p	oatients	Ef	fect		
No of studie s	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	(Standard	I I A U/C Onfr	Relativ e (95%	Absolut e	Quality	Importanc e
Employ	yment (com	petitive	e) - End of int	ervention - 1	NOT in com	petitive empl	oyment					
3	randomise	serious	serious ²	no serious	serious ³	none	511/1119	796/1158	RR 0.46	371		CRITICAL
	d trials	1		indirectnes			(45.7%)	(68.7%)	(0.25 to	fewer	VERY LOW	
				s					0.85)	per 1000		
										(from		
										103		
										fewer to		
										516		
										fewer)		
										458		
										fewer		
								84.9%		per 1000		
										from		
										127		

											Appenaix 17	
									-	fewer to		
										637		
										fewer)		
Emplo	ovment (com	petitive	e) - End of int	ervention - 1	Davs/Week	s/Months Wor	ked (Better i	ndicated by h	nigher va	lues)		
•	J (•	<u>'</u>		<i>y</i> ,	,	`	,	0	,		
1	randomise	no	no serious	no serious	serious ³	none	20	21	-	SMD		CRITICAL
	d trials	serious	inconsistenc	indirectnes						0.49	MODERAT	
		risk of	y	s						higher	E	
		bias								(1.11		
									-	lower to		
										0.13		
										higher)		
										,		
Emplo	yment (com	npetitive	e) - End of int	ervention - 1	Hours work	ed (Better ind	cated by hig	her values)				
1	1 .				• 4		20	21		C) (I)		CDITICAL
1	randomise				serious ⁴	none	20	21	-	SMD		CRITICAL
	d trials		inconsistenc	indirectnes							MODERAT	
		risk of	У	S						higher	E	
		bias								(0.20 to		
										1.49		
										higher)		
Emp1	Time and leave) Endofine	ownontion 1	Laurings (P	 etter indicated	hr highour	2144.00)				
Empio	Jymeni (con	ipetitive	e) - End of mi	ervention -	Lamings (D	etter murcateu	by mgner va	aruesj				
1	randomise	no	no serious	no serious	serious ³	none	20	21	-	SMD		CRITICAL
	d trials	serious	inconsistenc	indirectnes						0.09	MODERAT	
		risk of		s						higher	Е	
		bias	Ĭ							(0.53		
										lower to		
										- 11 32 00		

										Appenaix 17		
										0.70		
										higher)		
										0 /		
Employment (competitive) - End of intervention - Time to first job (Better indicated by lower values)												
1	randomise	no	no serious	no serious	no serious	none	526	347	-	SMD		CRITICAL
	d trials	serious	inconsistenc	indirectnes	imprecisio					0.09	HIGH	
		risk of	у	s	n					lower		
		bias								(0.22)		
									-	lower to		
										0.05		
										higher)		
										0 /		
Employment (competitive) - > 12 month follow-up - NOT in Competitive employment												
	randomise	serious	no serious	serious ⁶	serious ³	reporting bias		51/79	RR 0.76	155		CRITICAL
	d trials	5	inconsistenc				(49.3%)	(64.6%)	(0.57 to	fewer	VERY LOW	
			у						1.02)	per 1000		
										(from		
										278		
										fewer to		
										13		
										more)		
									1	155		
										fewer		
								64.6%		per 1000		
										(from		
										278		

_	1	1	T			1			1	1	пррении 1	
										fewer to		
										13		
										more)		
Occup	ation (any)	- End of	intervention	NOT in a	ny occupatio) nn						
occup	action (unity)	Liid oi	intervention		ny occupativ	711						
1	randomise	no	no serious	no serious	no serious	none	399/1004	628/1051	RR 0.67	197		CRITICAL
	d trials	serious	inconsistenc	indirectnes	imprecisio		(39.7%)	(59.8%)	(0.61 to	fewer	HIGH	
		risk of		s	n		,	, ,	`	per 1000		
		bias							,	(from		
										161		
										fewer to		
										233		
										fewer)		
										197		
										fewer		
										per 1000		
										(from		
								59.8%		161		
										fewer to		
										233		
										fewer)		
Occur	ation (any)	End of	intorvantion	_ Time to fi	retion (Rett	er indicated b	v 10mos mals	oe)		10.761)		
Occup	ation (any)	- Ena or	intervention	- Time to H	rat Jon (nett	er murcated b	y lower valu	C 5)				
1	randomise	no	no serious	no serious	no serious	none	605	423	_	SMD		CRITICAL
	d trials			indirectnes						0.11	HIGH	
		risk of		s	n					lower	_	
										(0.24		
					1				<u> </u>	(0.21		

		bias								lower to 0.01 higher)	пррении 17	
Occup	ation (any)	- End of	intervention	- Days/Wee	ks/Months	worked (Bette	r indicated b	y higher val	ues)			
1	randomise d trials		inconsistenc			none	1004	1051	-	SMD 0.37 higher (0.28 to 0.46 higher)	HIGH	CRITICAL
Occup	ation (any)	- End of	intervention	- Weekly E	arnings (Be	tter indicated l	y higher val	lues)				
1			inconsistenc			none	1004	1051	-	SMD 0.29 higher (0.20 to 0.38 higher)	HIGH	CRITICAL
Occup	ation (any)	- End of	intervention	- Past 3 mo	nths earning	gs (Better indi	cated by high	ner values)				
1	randomise d trials		inconsistenc			none	1004	1051	-	SMD 0.22 higher (0.13 to 0.31	HIGH	CRITICAL

											Appendix 17	/
										higher)		
Occup	ation (any)	- End of	intervention	- Hours per	week (Bett	er indicated by	higher valu	ies)		<u> </u>		
1			inconsistenc			none	1004	1051	-	SMD 0.36 higher (0.28 to 0.45 higher)	HIGH	CRITICAI
Occup	ation (any)	- End of	intervention	- Highest h	ourly wage	(Better indicat	ed by higher	r values)		<u> </u>		
1			inconsistenc			none	1004	1051	-	SMD 0.3 higher (0.22 to 0.39 higher)	HIGH	CRITICAI
Qualit	y of Life - E	nd of ir	ntervention (E	Better indica	ted by high	er values)						
1			inconsistenc	no serious indirectnes s		none	1004	1051	-	SMD 0.14 lower (0.22 to 0.05 lower)	HIGH	CRITICAL

¹ Most information is from studies at moderate risk of bias

² Evidence of very serious heterogeneity of study effect size

1.8.4 Supported employment (standard or modified) versus TAU/control (non-vocational comparison group) - health economic profile

Supported emp	ployment (star	ndard or modif	ied) versus control (non-vo	cational)			
Study & country	Limitations	Applicability	Other comments	Incremental cost (£)1	Incremental effect	ICER (£/ effect)	Uncertainty
Dixon et al, 2002 US	Minor limitations ²	Partially applicable ³	Outcome measure: number of hours/weeks of competitve work and combined earnings Time horizon 18 months	£4,415	298 hours 14 weeks	£15/ hour £315/ week	IPS costs more and provides more competitive work in 91% cases; IPS dominated by SC when combined earnings used as an outcome measure
Knapp et al, 2013 UK	Minor limitations ⁴	Directly applicable ⁵	Outcome measure: number of days worked in competitive settings; percent of sample members who worked at least 1 day Time horizon 18 months	-£4,774	27% worked at least 1 day	IPS dominant using both outcomes	Probability IPS cost effective at WTP £0-1,000 for additional 1% of clients working for at least 1 day or for additional day of work is 1.00
Economic analysis for this guideline	Minor limitations ⁶	Directly applicable ⁷	Cost utility Time horizon 10 years	£241	0.22 QALYs	£1,082/QALY	Probability supported employment cost effective at WTP £20,000-30,000/QALY is 0.85-0.91;

³ Confidence interval (CI) cross the clinical decision threshold

⁴ Optimal information size not met

⁵ Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect

⁶ Intervention and sample may not be representative

			11
			as risk ratio is varied accross its range supported emplyment ranges from being dominant to
			£14,985/QALY gained; as
			intervention cost varied
			±50%, ICER ranged from
			£15,080/QALY to
			supported employment
			being dominant; as cost of
			TAU varied by ±50%, ICER
			ranged from supported
			employment programme
			being dominant to £12,444/
			QALY gained

- 1. In non-UK studies costs converted to UK pounds using purchasing power parities (PPP) exchange rates (http://www.oecd.org/std/ppp); all costs uplifted to 2011/2012 UK pounds using the UK HCHS inflation index
- 2. Effectiveness and resources use based on one RCT (n=152) and service logs; local and national unit costs; time horizon may not be sufficiently long to reflect all important differences in costs
- 3. US public sector payer perspective; standard care may not be representative of routine and best practice in the NHS
- 4. Effectiveness and resource use based on one RCT (n=312); outcome measure of percent of sample who worked at least 1 day potentially biased in favour of intervention; international study with small proportion of sample (n=50) based in the UK
- 5. Included costs relevant to NHS and PSS perspective
- 6. Lack of data on the long-term benefits associated with provision of supported employment programmes; lack of data pertaining to standard care in the UK; clinical evidence from non-UK based RCTs
- 7. NHS and PSS perspective; health effects expressed in QALYs

Appendix 17

1.8.5 Pre-vocational training (standard or modified) versus TAU/active control (non-vocational comparison group) - clinical evidence profile

			Quality as	sessment			No of	patients	Ef	fect		
No of studie s	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Pre- vocationa 1 training (Standard OR Modified)	e control (non- vocational	Relativ e	Absolut e	Quality	Importanc e
Employ	yment (com	petitive	- End of inte	rvention - N	OT in Com	yment						
	randomise					none	140/207	164/214	RR 0.87			CRITICAL
	d trials	1	inconsistency	indirectness			(67.6%)	(76.6%)	(0.76 to 1.01)	fewer per 1000	LOW	
									1.01)	(from		
										184		
										fewer to		
										8 more)		
										89 fewer		
								(0.00/		per 1000		
								68.8%		(from 165		
										fewer to		

-					•		-				Appenaix 17	
										7 more)		
Emplo	yment (com	petitive) - End of inte	rvention - E	arnings (Bet	ter indicated b	y higher v	alues)				
_		1 -	Г .	_		T						
1	randomise					none	41	48	-	SMD		CRITICAL
	d trials	3	inconsistency	indirectness	imprecision					0.26	MODERAT	ļ
										higher	Е	
										(0.16		
										lower to		
										0.68		
										higher)		
Emplo	ymont (com	notitivo)- up to 12 mo	nth follow_1	110							
Emplo	yment (com	petitive)- up to 12 mo	11t11 10110W-t					_			
1	randomise	serious	no serious	no serious	no serious	reporting	13/14	11/14	RR 1.18	141		CRITICAL
	d trials	3	inconsistency	indirectness	imprecision	bias ⁴	(92.9%)	(78.6%)	(0.87 to	more	LOW	
									1.61)	per 1000		
										(from		
										102		
										fewer to		
										479		
										more)		
										141		
										more		
										per 1000		
								78.6%		(from		
										102		
										fewer to		

						,					търсник т	
										479		
										more)		
Occupa	ation (any) -	End of	intervention -	Hours worl	ked (Better i	ndicated by lo	wer values	5)	1			
		_	ı						T	_		T
1	randomise					none	14	14	-	SMD 0.8		CRITICAL
	d trials	3	inconsistency	indirectness						higher	LOW	
										(0.03 to		
										1.58		
										lower)		
Occum	tion (any) -	End of	intervention -	NOT in any	z occupation							
Occupa	ation (any) -	Elia oi	intervention -	TNOT III ally	occupation	_						
5	randomise	serious	serious ⁵	no serious	serious ²	none	274/415	185/226	RR 0.73	221		CRITICAL
	d trials	1		indirectness			(66%)	(81.9%)	(0.58 to	fewer	VERY LOW	
									0.93)	per 1000		
										(from 57		
										fewer to		
										344		
										fewer)		
									1	212		
										212		
										fewer		
										per 1000		
								78.6%		(from 55		
								70.0 /0		fewer to		
										330		
										fewer)		
									1			

Occupa	Occupation (any) - up to 6 month follow-up													
2	randomise	serious	serious ⁵	no serious	serious ²	reporting	133/197	57/71	RR 0.78	177		CRITICAL		
	d trials	1		indirectness		bias ⁴	(67.5%)	(80.3%)	(0.53 to		VERY LOW			
							, ,	,	1.14)	per 1000				
									,	(from				
										377				
										fewer to				
										112				
										more)				
										185				
										fewer				
										per 1000				
								84.3%		(from				
										396				
										fewer to				
										118				
										more)				
Occupa	ation (any) -	7-12 m	onth follow-u	p - NOT em _l	ployed									
1	randomise	serious	no serious	no serious	serious ²	reporting	107/163	39/52	RR 0.88	90 fewer		CRITICAL		
	d trials	3	inconsistency	indirectness		bias ⁴	(65.6%)	(75%)	(0.72 to	per 1000	VERY LOW			
									1.06)	(from				
										210				
										fewer to				
										45 more)				

											түрениіх т	
										90 fewer		
										per 1000		
								75.0/		(from		
								75%		210		
										fewer to		
										45 more)		
Educat	ion, attenda	nce - En	d of interven	tion - NOT a	ıttending					<u> </u>		
	,											
2	randomise	serious	no serious	no serious	no serious	none	91/102	102/109	RR 0.94	56 fewer		CRITICAL
	d trials	1	inconsistency	indirectness	imprecision		(89.2%)	(93.6%)	(0.88 to	per 1000	MODERAT	
									1.01)	(from	E	
										112		
										fewer to		
										9 more)		
									-			
										56 fewer		
										per 1000		
								92.7%		(from		
								72.7 /0		111		
										fewer to		
										9 more)		
Qualit	y of Life - E	nd of in	tervention (Be	etter indicate	ed by lower	values)						
	1 .	1				1			1	1		
1	randomise					none	47	44	_	SMD 0.6		
	d trials	3	inconsistency	indirectness	imprecision					lower	MODERAT	
										(1.02 to	E	
										0.18		

						Tipperions IT	
					lower)		

¹ Most information is from studies at moderate risk of bias

² Confidence interval (CI) cross the clinical decision threshold

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

⁴ Suspicion of publication bias

⁵ Evidence of serious heterogeneity of study effect size

1.8.6 Modified pre-vocational training versus standard pre-vocational training- clinical evidence profile

			Quality as	sessment			No of p	oatients	Ef	fect		-		
No of studie s	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Pre- vocationa	Standard Pre- vocationa I training	e (95%	Absolut e	Quality	Importanc e		
Employ	mployment (competitive) - End of intervention - NOT in Competitive employment													
	randomise d trials		no serious inconsistency		serious ²	none	50/69 (72.5%)	55/67 (82.1%) 54.4%	(0.73 to 1.06)	99 fewer per 1000 (from 222 fewer to 49 more) 65 fewer per 1000 (from 147 fewer to	LOW	CRITICAL		
Employ	ment (com	 petitive)	 - End of inter	vention - Ear	rnings (Bette	 er indicated by	higher val	lues)		33 more)				
1	randomise	serious	no serious	no serious	no serious	none	69	67	-	SMD 0.25	MODERAT	CRITICAL		

Employment (competitive)- End of intervention - Weeks worked (Better indicated by higher values) 1 randomise serious no serious no serious no serious none 69 67 - SMD	
Employment (competitive)- End of intervention - Weeks worked (Better indicated by higher values) 1 randomise serious no serious no serious no no serious no no serious no serio	
Employment (competitive)- End of intervention - Weeks worked (Better indicated by higher values) 1 randomise serious no serious no serious no no serious	
Employment (competitive)- End of intervention - Weeks worked (Better indicated by higher values) 1 randomise serious no serious no serious no serious none 69 67 - SMD	
Employment (competitive)- End of intervention - Weeks worked (Better indicated by higher values) 1 randomise serious no serious no serious no no serious no no serious no serio	
1 randomise serious no serious no serious no no serious no no serious no no serious no s	
	CRITICAL
d trials inconsistency indirectness imprecision 3.37 MODERAT	
higher E	
(3.04 to	
higher)	
Employment (competitive)- End of intervention - Hours worked (Better indicated by higher values)	
1 randomise serious no serious no serious serious ² none 69 67 - SMD III C	CRITICAL
production periods are believed periods provided provided periods provided periods period	
d trials inconsistency indirectness 0.24 LOW	
d trials inconsistency indirectness 0.24 LOW	
d trials inconsistency indirectness 0.24 LOW higher	
d trials ¹ inconsistency indirectness 0.24 higher (0.09	
d trials ¹ inconsistency indirectness 0.24 LOW higher (0.09 lower to 0.57	
d trials 1 inconsistency indirectness 0.24 LOW higher (0.09 lower to	
d trials ¹ inconsistency indirectness 0.24 LOW higher (0.09 lower to 0.57	
d trials 1 inconsistency indirectness 0.24 higher (0.09 lower to 0.57 higher)	CRITICAL
d trials 1 inconsistency indirectness 0.24 higher (0.09 lower to 0.57 higher)	CRITICAL

											Аррениіх 1.	<u>'</u>
										higher		
										(0.16		
										lower to		
										0.5		
										higher)		
										,		
Emplo	yment (com	petitive))- End of inter	vention - Tii	me to first jo	b (Better indicate)	ated by lo	wer values	5)			
1	randomise	serious	no serious	no serious	no serious	none	69	67	-	SMD		CRITICAL
	d trials	1	inconsistency	indirectness	imprecision					0.76	MODERAT	
										lower	Е	
										(1.1 to		
										0.42		
										lower)		
Occupa	ation (any)-	End of i	ntervention -	NOT in any	paid (compe	etitive or uncor	npetitive)	employme	ent			
2	randomise	serious	serious ³	no serious	serious ²	none	56/149	97/137	RR 0.53	333		CRITICAL
	d trials	1		indirectness			(37.6%)	(70.8%)	(0.3 to	fewer	VERY LOW	
									0.94)	per 1000		
										(from 42		
										fewer to		
										496		
										fewer)		
									<u> </u> -			
										141		
								30%		fewer		
										per 1000		
1										(from 18		

			1							1	Appenaix 17	,
										fewer to		
										210		
										fewer)		
Occupa	ation (any)-	End of i	ntervention -	Earnings (Be	etter indicate	ed by higher va	ılues)		L			
	I	T		ı	ı				T		T	
		serious	very serious ⁴			none	149	131	-	SMD		CRITICAL
	d trials	1		indirectness	imprecision					0.70	VERY LOW	
										higher		
										(0.46 to		
										0.95		
										higher)		
Occup	ation (any)-	End of i	ntervention -	Mooks work	ad (Rottor ir	dicated by hig	hor values)				
Occupa	ation (any)-	Liid oi i	intervention -	VVCCR5 WOIN	ica (Detter II	idicated by mg	iici vaiucs	,				
1	randomise	serious	no serious	no serious	serious ²	none	69	67	-	SMD		CRITICAL
	d trials	1	inconsistency	indirectness						0.29	LOW	
										higher		
										(0.05		
										lower to		
										0.63		
										higher)		
Occur	tion (any)	End of :	ntorwontion	House work	od (Bottor in	dicated by hig	hor values					
Occupa	ation (any)-	Enu of 1	ineiveinion -	110ul5 WUIK	eu (Denei III	dicated by filg	nei vaiues)					
2	randomise	serious	no serious	no serious	no serious	none	149	131	-	SMD		CRITICAL
	d trials	1	inconsistency	indirectness	imprecision					0.90	MODERAT	
										higher	Е	
										(0.58 to		
										1.21		

											пррении 1	<u> </u>
										lower)		
)ccupa	ition (any)-	End of i	ntervention -	Longest job	worked (Be	tter indicated b	y higher v	alues)				
	randomise	serious	no serious	no serious	serious ²	none	69	67	-	SMD		CRITICAL
	d trials	1	inconsistency	indirectness						0.29	LOW	
										higher		
										(0.04		
										lower to		
										0.62		
										higher)		
Occupa	ition (any)-	End of i	ntervention -	Time to first	job (Better	indicated by lo	wer value	s)				1
	randomise	serious	no serious	no serious	serious ²	none	69	67	-	SMD		CRITICAL
	d trials	1	inconsistency	indirectness						0.60	LOW	
										lower		
										(0.95 to		
										0.25		
										lower)		

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

² Confidence interval (CI) cross the clinical decision threshold

³ Evidence of serious heterogeneity of study effect size

⁴ Evidence of very serious heterogeneity of study effect size

Appendix 17

1.8.7 Modified pre-vocational training (paid + psych) versus modified pre-vocational training (+paid) - clinical evidence profile

			Quality as	sessment			No of p	oatients	Ef	fect		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Pre- vocational	Modified Pre-	Relative (95% CI)	Absolute		Importance
Occupa	ition (any)- I	End of ir	ntervention - W	Veeks worked	d (Better ind	icated by highe	r values)					
2	randomised	serious ¹	no serious	no serious	serious ²	none	73	74	-	SMD		CRITICAL
	trials		inconsistency	indirectness						0.51	LOW	
			_							higher		
										(0.18 to		
										0.84		
										higher)		
Occupa	 ntion (any)- I	 End of ir	l ntervention - H	lours worked	l (Better indi	cated by higher	r values)					
2	randomised	serious	no serious	no serious	serious ²	none	73	74	-	SMD		CRITICAL
	trials		inconsistency	indirectness						0.63	LOW	
										higher		
										(0.3 to		
										0.96		
										higher)		

_															
	Functional disability - End of intervention (Better indicated by lower values)														
	3	randomised	serious	no serious	no serious	serious ³	none	103	107	-	SMD		CRITICAL		
		trials		inconsistency	indirectness						0.61	LOW			
											lower				
											(0.89 to				
											0.33				
											lower)				

¹ Most of the information is from studies at moderate risk of bias

² Optimal information size not met ³ Confidence interval (CI) cross the clinical decision threshold

1.8.8 Supported employment plus pre-vocational training versus pre-vocational training- clinical evidence profile

			Quality as	sessment			No of pa	tients	Ef	fect		
No of studie	Design	Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Supported Employmen t PLUS Pre- vocational Training	Pre- vocationa 1 Training	(95%	Absolut e	Quality	Importanc e
Emplo	yment (com	petitive	e) - End of into	ervention								
1	randomise	no	no serious	no serious	serious ¹	none	11/52	51/55	RR 0.23	714		CRITICAL
	d trials	seriou	inconsistency	indirectness			(21.2%)	(92.7%)	(0.13 to	fewer	MODERAT	
		s risk							0.39)	per 1000	E	
		of bias								(from		
										566		
										fewer to		
										807		
										fewer)		
								0%		-		
Emplo	yment, com	petitive	e - Earnings - I	End of interv	vention (Bet	ter indicated b	y higher valı	ies)				
1	randomise	no	no serious	no serious	serious ¹	none	52	55	_	SMD		CRITICAL
	d trials	seriou	inconsistency	indirectness						3.86	MODERAT	
		s risk								higher	E	

							1 17 7 0,00000 17	
	of	bias				(3.21 to		
						4.51		
						higher)		

¹ Optimal information size not met

1.8.9 Supported employment plus pre-vocational training versus supported employment-clinical evidence profile

			Quality as	sessment			No of p	oatients	Ef:	fect		
No of studie s		Risk of bias	Inconsistenc y	Indirectnes s	Imprecisio n	Other consideration s	Supported Employme nt PLUS Pre- vocational Training		Relativ e (95% CI)	Absolut e	Quality	Importanc e
Emplo	yment (com	petitiv	e) - End of in	tervention								
1	randomise	no	no serious	no serious	serious ¹	none	11/52	26/56	RR 0.46	251		CRITICAL
	d trials	seriou	inconsistenc	indirectnes			(21.2%)	(46.4%)	(0.25 to	fewer	MODERAT	
		s risk	y	s					0.83)	per 1000	E	
		of bias								(from 79		
										fewer to		
										348		
										fewer)		
								0%		-		
Emplo	yment, com	petitiv	e - Earnings -	End of inter	evention (Be	tter indicated	by higher va	lues)				
1	randomise	no	no serious	no serious	serious ²	none	52	56	-	SMD		CRITICAL
	d trials	seriou	inconsistenc	indirectnes						0.34	MODERAT	
		s risk	у	s						higher	E	
		of bias								(0.04		

						11pperious 17	
					lower to		
					0.72		
					higher)		

¹ Optimal information size not met ² Confidence interval (CI) cross the clinical decision threshold

1.8.10 Cognitive remediation plus vocational rehabilitation versus vocational rehabilitation- clinical evidence profile

			Quality as	sessment			No of p	oatients	Ef	fect		
No of studie	Design	Risk of bias	Inconsistenc y	Indirectne ss	Imprecisio n	Other consideratio ns	Cognitive Remediation + Vocational Rehabilitatio n	Rehabilitati	Relativ e (95% CI)	Absolut e	Quality	Importanc e
Emplo	yment (con	petitiv	e) - End of in	tervention -	NOT in co	mpetitive emp	oloyment					
	randomise d trials	1		indirectnes s		none	22/61 (36.1%)	41/55 (74.5%)	,		VERY LOW	CRITICAL
Emplo	yment (con	ıpetitiv	e) - End of in	tervention -	Hours wor	ked (Better in	dicated by hig	gher values)				
	randomise d trials	serious 1		no serious indirectnes s	serious ³	none	79	71	-	SMD 0.38 higher (0.31 lower to	VERY LOW	CRITICAL

											Appenaix 17	
										1.26		
										higher)		
										0 /		
Emplo	yment (con	petitiv	e) - End of in	tervention -	Number of	f jobs (Better i	ndicated by h	igher values)				
				1								-
2	randomise	serious	serious ²	no serious	serious ³	none	61	55	-	SMD		CRITICAL
	d trials	1		indirectnes						0.57	VERY	
				s						higher	LOW	
										(1.13		
										lower to		
										2.28		
										higher)		
										ingrici)		
Emplo	vment (con	petitiv	e) - End of in	tervention -	Weeks wo	rked (Better in	dicated by his	gher values)		L		
•		•	,			`	,	,				
2	randomise	serious	no serious	no serious	serious ³	none	56	50	-	SMD		CRITICAL
	d trials	1	inconsistenc	indirectnes						0.05	LOW	
			V	s						lower		
										(0.43		
										lower to		
										0.33		
										higher)		
										ingrier)		
Emplo	vment (con	npetitiv	e) - End of in	tervention -	Earnings (Better indicate	d by higher v	alues)				
F 10) ====== (3 011	-F	-, or									
2	randomise	serious	serious ²	no serious	serious ³	none	41	37	-	SMD		CRITICAL
	d trials	1		indirectnes						0.54	VERY	
				s						higher	LOW	
										(0.08		
										(0.00		

		1	1	,				1		<u> 1</u> ррениіх 17	•
									lower to		
									1.16		
									higher)		
									,		
yment (com	petitiv	e) - up to 6 m	onth follow	-up - NOT	in competitive	employment					
randomise	serious	no serious	no serious	serious ⁵	none	41/60	51/67	RR 0.90	76 fewer		CRITICAL
d trials	4	inconsistenc	indirectnes			(68.3%)	(76.1%)	(0.72 to	per 1000	LOW	
		у	s					1.12)	(from		
									213		
									fewer to		
									91		
									more)		
									,		
							0%		-		
yment (com	petitiv	e) - up to 12 n	nonth follov	w-up - NOT	in competitiv	e employmen	t				
randomise	serious	no serious	no serious	serious ³	none	13/37	16/28	RR 0.61	223		CRITICAL
d trials	4	inconsistenc	indirectnes			(35.1%)	(57.1%)	(0.36 to	fewer	LOW	
		y	S			,	,	1.06)	per 1000		
								,	(from		
									366		
									fewer to		
									34		
									more)		
									-		
							0%				
	randomise d trials yment (com	randomise serious d trials 4 yment (competitiv randomise serious	randomise serious no serious d trials 4 inconsistenc y yment (competitive) - up to 12 re randomise serious no serious	randomise serious no serious inconsistenc indirectnes y yment (competitive) - up to 12 month follow randomise serious no serious no serious no serious	randomise serious no serious no serious serious ⁵ d trials ⁴ inconsistenc indirectnes s y yment (competitive) - up to 12 month follow-up - NOT randomise serious no serious no serious serious ³	randomise serious no serious no serious serious none inconsistenc indirectnes s y yment (competitive) - up to 12 month follow-up - NOT in competitive randomise serious no serious no serious serious none	randomise serious no serious inconsistenc indirectnes serious serious no serious indirectnes y yment (competitive) - up to 12 month follow-up - NOT in competitive employment randomise serious no serious no serious serious no serious serious no serious	d trials 4 inconsistenc y y s s s (76.1%) yment (competitive) - up to 12 month follow-up - NOT in competitive employment randomise serious no serious inconsistenc y s s none (35.1%) (57.1%) y	yment (competitive) - up to 6 month follow-up - NOT in competitive employment randomise serious inconsistenc y no serious indirectnes s y no serious serious serious indirectnes s none 41/60 (68.3%) (76.1%) (0.72 to 1.12) 1.12) yment (competitive) - up to 12 month follow-up - NOT in competitive employment randomise serious no serious inconsistenc y no serious serious serious indirectnes s none 13/37 (35.1%) (57.1%) (0.36 to 1.06)	yment (competitive) - up to 6 month follow-up - NOT in competitive employment randomise serious no serious inconsistency y	yment (competitive) - up to 6 month follow-up - NOT in competitive employment randomise serious no serious indirectnes y y y y more 4 1/60 51/67 (RR 0.90) 76 fewer (0.72 to pper 1000 1.12) (from 213 fewer to 91 more) yment (competitive) - up to 12 month follow-up - NOT in competitive employment randomise serious no serious d trials 4 inconsistenc y no serious indirectnes sindirectnes serious no serious indirectnes sindirectnes sindirectnes sindirectnes serious no serious indirectnes sindirectnes serious no serious indirectnes sindirectnes sindirect

Occup	ation (any)	- End o	f interventio	n - Hours wo	orked (Bette	er indicated by	higher value	s)			трреник 17	
3	randomise d trials	serious 1	serious ²	no serious indirectnes s	serious ³	none	116	117	1	SMD 0.02 lower (0.59 lower to 0.55 higher)	VERY LOW	CRITICAL
Occup	ation (any)	- End o	f intervention	n - Earnings	(Better ind	icated by high	er values)					
2	randomise d trials	serious 1	serious ²	no serious indirectnes s	serious ³	none	78	83	1	SMD 0.23 higher (0.70 lower to 1.16 higher)	VERY LOW	CRITICAL
Occup	ation (any)	- End o	f intervention	n - Weeks w	orked (Bett	er indicated by	y higher value	es)				
1	randomise d trials	serious 4	no serious inconsistenc y		serious ³	none	18	16	1	SMD 0.89 higher (0.18 to 1.6 higher)	LOW	CRITICAL

	1		T	,	1		T	T	1	·	Appenaix 17	,
Occup	ation (any)	-up to 6	month follo	w-up - Hou	rs worked (Better indicate	ed by higher v	values)	1			
	randomise d trials ation (any)	4	inconsistenc y	indirectnes s	serious ³ ings (Better	none	60 higher values	67	-	SMD 0.45 higher (0.1 to 0.8 higher)	LOW	CRITICAL
	randomise d trials	4	inconsistenc y	indirectnes s		none	60	67	-	SMD 0.14 higher (0.21 lower to 0.48 higher)	LOW	CRITICAL
Occup	ation (any)	- up to 1	12 month fol	low-up - Dio	d not obtair	n work						
			inconsistenc		serious ³	none	18/37 (48.6%)	20/31 (64.5%)	,		MODERAT E	CRITICAL

											тррениих 17	
										97		
										more)		
										,		
								0%		_		
ccupa	tion (any)-	up to 1	2 month foll	ow-up - Ho	urs worked	(Better indicat	ted by higher	values)				
r	randomise	no	no serious	no serious	serious ³	none	37	31	-	SMD		CRITICA
Ċ	d trials	serious	inconsistenc	indirectnes						0.43	MODERAT	
		risk of	v	S						higher	Е	
		bias								(0.06		
										lower to		
										0.91		
										higher)		
										11161161)		
ccupa	tion (any)-	up to 1	2 month foll	ow-up - We	eks worked	l (Better indica	ted by higher	values)				
	tion (any)-	_	2 month foll	_	eks worked	l (Better indica	ted by higher	values)	-	SMD		CRITICA
r	randomise	no		no serious	serious ³	·	, ,	,	-		MODERAT	
r	randomise d trials	no	no serious inconsistenc	no serious	serious ³	·	, ,	,	-			
r	randomise d trials	no serious	no serious inconsistenc	no serious	serious ³	·	, ,	,	-	0.49	MODERAT	
r	randomise d trials	no serious risk of	no serious inconsistenc	no serious	serious ³	·	, ,	,	-	0.49 higher	MODERAT E	
r	randomise d trials	no serious risk of	no serious inconsistenc	no serious	serious ³	·	, ,	,	-	0.49 higher (0.00	MODERAT E	
r	randomise d trials	no serious risk of	no serious inconsistenc	no serious	serious ³	·	, ,	,	-	0.49 higher (0.00 lower to 0.97	MODERAT E	
r	randomise d trials	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	serious ³	none	37	31	-	0.49 higher (0.00 lower to	MODERAT E	
r	randomise d trials	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	serious ³	·	37	31	-	0.49 higher (0.00 lower to 0.97	MODERAT E	
ccupa	randomise d trials	no serious risk of bias	no serious inconsistenc y	no serious indirectnes s	serious ³	none	37	31	-	0.49 higher (0.00 lower to 0.97	MODERAT E	
ccupa	randomise d trials ttion (any)-	no serious risk of bias • up to 1	no serious inconsistenc y 2 month foll	no serious indirectnes s ow-up - Ear	serious ³ nings (Bett	none er indicated by	37 higher value	31 s)	-	0.49 higher (0.00 lower to 0.97 higher)	MODERAT E	CRITICAI
ccupa	randomise d trials ation (any)-	no serious risk of bias	no serious inconsistenc y 2 month foll	no serious indirectnes s	serious ³	none er indicated by	37 higher value	31 s)	-	0.49 higher (0.00 lower to 0.97 higher)	MODERAT	

_								1100000000	
		bias	У	s			(0.09	Е	
							lower to		
							0.87		
							higher)		

¹ Most information is from studies at moderate risk of bias

 $^{^{2}}$ Evidence of serious heterogeneity of study effect size

³ Confidence interval (CI) cross the clinical decision threshold

⁴ Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect

⁵ Optimal information size not met