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#### Abbreviations

ABS Agitated Behavior Scale

ACES Agitation and Calmness Evaluation Scale

AD antidepressant AP antipsychotic BZD benzodiazepine

CES Coercion Experience Scale

CI confidence interval

EPS extrapyramidal symptoms

HAL haloperidol IM intramuscular MD mean difference

NE non-emergency situations
OAS Overt Aggression Scale
OIS optimal information size

OR odds ratio

PANSS-EC Positive and Negative Syndrome Scale – Excited Component

ROB risk of bias

RR relative risk/risk ratio

SMD standardised mean difference

TAU treatment as usual

TEAE treatment emergent adverse events
WAIC Working Alliance Inventory – client form

WAIT Working Alliance Inventory – therapist form

### 1.1 NON-PHARMACOLOGICAL INTERVENTIONS

## 1.1.1 Pre- and immediately pre-event: inpatient settings – adults

### **1.1.1.1** Modifications to the environment versus an alternative management strategy

			Quality asse	ssment			Number o	f patients		Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Modifications to the environment	An alternative management strategy	Relative (95% CI)	Absolute	Quanty
Verbal aggr	ession (assessed	with: Mo	dified Overt Agg	ression Scale)							ļ.
	observational studies	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious²	none	0/99 (0%)	0/107 (0%)	OR 0.49 (0.26 to 0.91)	-	VERY LOW
Aggression	towards others (	(assessed v	with: Modified O	vert Aggression	Scale)						
	observational studies	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious²	none	0/99 (0%)	0/107 (0%)	OR 0.51 (0.09 to 2.78)	-	VERY LOW
Risk of aggr	ession (measure	ed with: B	røset Violence Ch	necklist; better ir	ndicated by lowe	er values)					L
	observational studies	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	31	25	-	SMD 0.11 lower (0.64 lower to 0.42 higher)	VERY LOW
Rates of sec	lusion – total pr	ivate spac	e per patient (m²)								
	observational studies <sup>4</sup>	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	none	-		OR 0.88 (0.82 to 0.94)	-	VERY LOW
Rates of sec	lusion – observa	ition bedr	ooms	1	<u> </u>						

1	observational studies <sup>4</sup>	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	-	OR 0.78 (0.5 to 1.22)	VERY LOW
Rates o	of seclusion – numbe	r of patier	nts in the buildin	ng					
1	observational studies <sup>4</sup>	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	OR 1.01 (1 to - 1.02)	VERY LOW
Rates o	of seclusion – present	ce of outd	oor space or gard	len (yes versus 1	10)				
1	observational studies <sup>4</sup>	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	OR 9.09 - (2.31 to 35.77)	VERY LOW
Rates o	of seclusion – comfor	t		•					
1	observational studies <sup>4</sup>	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	OR 0.77 - (0.61 to 0.97)	VERY LOW
Rates o	of seclusion – person	al furnitui	re (yes versus no					I	
1	observational studies <sup>4</sup>	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	-	OR 0.81 - (0.51 to 1.29)	VERY LOW
Rates o	of seclusion – type of	ventilatio	on					I	
1	observational studies <sup>4</sup>	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	-	OR 0.84 - (0.49 to 1.44)	VERY LOW
Rates o	of seclusion – presen	ce of nursi	ing station (yes v	versus no)					
1	observational studies <sup>4</sup>	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	-	OR 1.03 - (0.63 to 1.68)	VERY LOW

	observational	serious3	no serious	no serious	no serious	none	-	OR 1.6 (1.09	-	
	studies4		inconsistency	indirectness	imprecision			to 2.35)		VERY
										LOW
es (	of seclusion - visibil	ity on war	d							
	observational	serious <sup>3</sup>	no serious	no serious	no serious	none	=	OR 0.69	-	
	studies <sup>4</sup>		inconsistency	indirectness	imprecision		F	(0.49 to 0.97)		VER
										LOW
s (	of seclusion – violen	ce-proof fi	nish							
			•	T .	1			OP 4 2 /0 50		
	observational studies <sup>4</sup>	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>5</sup>	none	-	OR 1.3 (0.59 to 2.86)	-	VER
	staties		inconsistency	marecticss				10 2.00)		LOV
es (	of seclusion - number	er of seclus	sion rooms (ward	i)						
	observational	serious <sup>3</sup>	no serious	no serious	no serious	none	-	OR 1.12	-	
	observational studies <sup>4</sup>	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	no serious imprecision	none	- -	OR 1.12 (0.89 to 1.41)	-	
		serious <sup>3</sup>				none	-		-	
es (			inconsistency	indirectness		none	-		-	VER'
es (	studies <sup>4</sup> of seclusion – number	er of seclus	inconsistency sion rooms (buil	indirectness ding)	imprecision		-	(0.89 to 1.41)	-	
28 (	studies <sup>4</sup>		inconsistency	indirectness		none				LOV
es (	studies <sup>4</sup> of seclusion – number observational	er of seclus	inconsistency sion rooms (build	indirectness  ding)  no serious	imprecision			(0.89 to 1.41) OR 1.24 (0.9)		LOV
	observational studies <sup>4</sup>	serious <sup>3</sup>	inconsistency sion rooms (build no serious inconsistency	indirectness  ding)  no serious indirectness	imprecision			(0.89 to 1.41) OR 1.24 (0.9)		
	studies <sup>4</sup> of seclusion – number observational	serious <sup>3</sup>	inconsistency sion rooms (build no serious inconsistency	indirectness  ding)  no serious indirectness	imprecision			(0.89 to 1.41) OR 1.24 (0.9)		LOV
	observational studies <sup>4</sup> of seclusion – number observational observational observational	serious <sup>3</sup>	inconsistency sion rooms (build no serious inconsistency	indirectness  ding)  no serious indirectness	imprecision			OR 1.24 (0.9 to 1.71)  OR 1.25		VER LOV
	of seclusion – number observational studies <sup>4</sup>	serious <sup>3</sup>	inconsistency sion rooms (build no serious inconsistency ooms that can be	indirectness  ding)  no serious indirectness  locked	imprecision serious <sup>5</sup>	none	-	OR 1.24 (0.9 to 1.71)	-	VER LOV
	observational studies <sup>4</sup> of seclusion – number observational observational observational	serious <sup>3</sup>	inconsistency  sion rooms (build no serious inconsistency)  oms that can be no serious	indirectness  ding)  no serious indirectness  locked  no serious	imprecision serious <sup>5</sup>	none	-	OR 1.24 (0.9 to 1.71)  OR 1.25	-	VER LOV
s	observational studies <sup>4</sup> of seclusion – number observational observational observational	serious <sup>3</sup> serious <sup>3</sup> serious <sup>3</sup>	no serious inconsistency  oms that can be no serious inconsistency	indirectness  ding)  no serious indirectness  locked  no serious indirectness	serious <sup>5</sup>	none	-	OR 1.24 (0.9 to 1.71)  OR 1.25	-	LOV
es (	observational studies <sup>4</sup> observational studies <sup>4</sup> observational studies <sup>4</sup>	serious <sup>3</sup> serious <sup>3</sup> serious <sup>3</sup>	no serious inconsistency  oms that can be no serious inconsistency	indirectness  ding)  no serious indirectness  locked  no serious indirectness	serious <sup>5</sup>	none	-	OR 1.24 (0.9 to 1.71)  OR 1.25	-	VER LOV

	studies		inconsistency	indirectness						(0.95 to 5.89 higher)	LOW
erienc	re of seclusion – to	reatment s	atisfaction (male	es) (better indica	ted by lower va	lues)					
	observational studies	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	6	9	-	MD 1.55 higher (2.42 lower to 5.52 higher)	VERY LOW
perieno	e of seclusion - to	eatment s	atisfaction (fema	les) (better indi	cated by lower	values)		,	-		
	observational studies	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	9	7	-	MD 5.6 higher (2.56 to 8.64 higher)	VERY LOW
perienc	re of seclusion – in	nfluence o	f interior on beh	aviour (total) (be	etter indicated	by lower values)					
	observational studies	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	15	16	-	MD 3.26 higher (0.98 to 5.54 higher)	VERY LOW
perienc	e of seclusion – in	nfluence o	f interior on beh	aviour (males) (	petter indicated	l by lower values)		1			
	1 1	serious <sup>3</sup>	no serious	no serious	serious <sup>2</sup>	none	6	9		MD 0.83 higher	
	observational studies	serious	inconsistency	indirectness	scrious	Horic	O	9		(2.93 lower to 4.59 higher)	VERY LOW
operieno	studies		inconsistency	indirectness		ed by lower values)	0	,		(2.93 lower to 4.59	

<sup>&</sup>lt;sup>1</sup> High risk of bias across all domains.

<sup>&</sup>lt;sup>2</sup> Sample size did not reach optimal information size.

<sup>&</sup>lt;sup>3</sup> Participants/care administrators/raters non-blind.

<sup>&</sup>lt;sup>4</sup> Case-control.

<sup>&</sup>lt;sup>5</sup> 95% CI includes both important effect and no effect; OIS met.

### 1.1.1.2 Management strategies/training programmes versus an alternative management strategy

			Quality assess	sment			Number of p	atients		Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Management strategies/training programmes	Alternative management strategy	Relative (95% CI)	Absolute	Quarty
Rate of sec	lusion, restrai	nt or room o	bservation (bette	r indicated by l	ower values)						
1	randomised trials	serious¹	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	0	-	-	MD 0.09 lower (0.13 to 0.05 lower)	LOW
Duration of	f seclusion-re	straint (bette	er indicated by lo	wer values)							<u> </u>
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>2,3</sup>	none	50	38	-	MD 0.24 lower (0.4 to 0.08 lower)	VERY LOW
violence an	d aggression:	physical vio	olence (self, other	) (better indicat	ed by lower v	values)					
1	randomised trials	serious¹	no serious inconsistency	no serious indirectness	very serious <sup>2,3</sup>	none	0	-	-	MD 0.03 higher (0.39 lower to 0.45 higher)	VERY LOW
Rates of res	strictive interv	ention 'con	tainment'								
1	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	-	-	RD 0.23 (0.09 to 0.37)	-	MODERATE
Rates of vio	olence and agg	gression 'cor	nflict'	<u> </u>							
1	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	-	-	RD 0.15 (0.05 to 0.25)	-	MODERATE

<sup>&</sup>lt;sup>1</sup> Unclear ROB across multiple, from: sequence/ allocation/ blinding/ outcome/ reporting/ other.

<sup>&</sup>lt;sup>2</sup> Sample size did not reach optimal information size.

<sup>&</sup>lt;sup>3</sup> 95% CI included line of no effect, OIS met.

# 1.1.2 Pre- and immediately pre-event: community settings – adults

### **1.1.2.1** Advance decisions and statements versus an alternative management strategy

			Quality assessi	nent			Number	of patients		Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Advance decisions and statements	An alternative management strategy	Relative (95% CI)	Absolute	Quanty
sychiatric	admission – vo	luntary admi	ssions [15 month	s UK] (follow-u	p 15 months)						
	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>1,2</sup>	none	27/159 (17%)	26/157 (16.6%)	RR 1.03 (0.63 to 1.68)	5 more per 1000 (from 61 fewer to 113 more)	LOW
'sychiatric	admission - co	mpulsory adı	mission under M	ental Health Act	t (follow-up n	nean 15 months)					
	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>1</sup>	none	3/80 (3.8%)	11/80 (13.8%)	RR 0.27 (0.08 to 0.94)	100 fewer per 1000 (from 8 fewer to 126 fewer)	MODERATE
Psychiatric a	admission – all	admissions	[UK] (follow-up 1	15-18 months)							
	randomised trials	no serious risk of bias	serious³	no serious indirectness	very serious <sup>1,2</sup>	none	101/347 (29.1%)	116/360 (32.2%)	OR 0.86 (0.62 to 1.19)	32 fewer per 1000 (from 95 fewer to 39 more)	VERY LOW
Psychiatric a	  admission	oluntary adı	missions [UK] (fo	llow-up 15-18 n	nonths)						
	randomised trials	no serious risk of bias	serious <sup>3</sup>	no serious indirectness	very serious <sup>1,2</sup>	none	74/426 (17.4%)	93/437 (21.3%)	OR 0.78 (0.55 to 1.09)	39 fewer per 1000 (from 83 fewer to 15 more)	VERY LOW
Psychiatric a	admission – wi	thin 18 mont	hs – compulsory	admission [18 m	nonths: white]	(follow-up mean	18 months)				ı
l	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>1,2</sup>	none	-	-	Not estimable	-	LOW

11atr	ic admission – W	itnin 18 mont	ins – compulsory	y admission [18]	months: black	ybiack Britisnj	(follow-up mean 18 m	iontns)			
	randomised	no serious	no serious	no serious	very	none	-	-	Not	-	
	trials	risk of bias	inconsistency	indirectness	serious <sup>1,2</sup>				estimable		LOW
niatr	ic admission – w	ithin 18 mont	ths - compulsory	y admission [18	months: Asia	n/Asian British	] (follow-up mean 18 r	nonths)			
	randomised	no serious	no serious	no serious	very	none	- 1	-	Not	-	
	trials	risk of bias	inconsistency	indirectness	serious <sup>1,2</sup>				estimable		LOW
niatr	ic admission – w	ithin 18 mont	ths – compulsory	y admission [18	months: total]	(follow-up me	ean 18 months)				
	randomised	no serious	no serious	no serious	very	none		-	OR 0.9 (0.59	-	
	trials		inconsistency	indirectness	serious <sup>1,2</sup>				to 1.37)		LOW
iatr	ic admissions – v	vithin 18 mor	 nths [clinician ve	ersus advocate] -	- total admiss	ions [18 month	s NE] (follow-up medi	an 18 months)			
	randomised	no serious	no serious	no serious	very	none	33/69	24/70	See	134 more per 1000	
	trials		inconsistency	indirectness	serious <sup>1,2</sup>	none	(47.8%)	(34.3%)	comment	(from 31 fewer to 302 more)	LOW
hiatr	ic admissions – v	vithin 18 mor	 nths [clinician ve	ersus advocate] -	- voluntary ad	  missions [18 m	nonths NE] (follow-up	mean 18 months)			
	randomised	no serious	no serious	no serious	verv	none	16/69	14/70	See	32 more per 1000	
	trials		inconsistency	indirectness	serious <sup>1,2</sup>		(23.2%)	(20%)	comment	(from 100 fewer to 170 more)	LOW
hiatr	ic admissions – v	vithin 18 mor	 nths [clinician ve	ersus advocate] -	- emergency a	dmissions [18]	months NE] (follow-up	p mean 18 months			
	randomised	no serious	no serious	no serious	very	none	12/69	7/70	See	74 more per 1000	
	trials	risk of bias	inconsistency	indirectness	serious <sup>1,2</sup>		(17.4%)	(10%)	comment	(from 40 fewer to 190 more)	LOW
	ic admissions – v	vithin 18 mor	ths [clinician ve	ersus advocate] -	- court order a	dmission [18 n	nonths NE]				
hiatr	1	no serious	no serious	no serious	very	none	11/69	7/70	See	59 more per 1000	
hiatr	randomised		1	1	serious <sup>1,2</sup>	1	(15.9%)	(10%)		(from 50 fewer to	LOW

ychia	tric admissions – v	within 18 mor	nths [clinician ve	ersus advocate] -	- emergency v	visits [18 month	s NE] (follow-up mear	n 18 months)			
	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious <sup>1,2</sup>	none	22/69 (31.9%)	22/70 (31.4%)	See comment	3 more per 1000 (from 151 fewer to 160 more)	LOW
chia	tric admission – w	rithin 18 mont	ths [ADs versus	TAU] – total adı	missions [18 1	nonths NE] (fol	llow-up mean 18 mont	hs)			1
	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious <sup>1,2</sup>	none	57/139 (41%)	33/73 (45.2%)	OR 0.84 (0.48 to 1.49)	43 fewer per 1000 (from 168 fewer to 99 more)	LOW
ychia	tric admission - w	rithin 18 mont	ths [ADs versus	TAU] - volunta	ry admissions	s [18 months NI	E] (follow-up mean 18	months)			
	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious <sup>1,2</sup>	none	30/139 (21.6%)	12/73 (16.4%)	OR 1.4 (0.67 to 2.93)	52 more per 1000 (from 48 fewer to 201 more)	LOW
ychia	tric admission – w	rithin 18 mont	ths [ADs versus	TAU] - emerger	ncy admission	ns [18 months N	IE] (follow-up mean 18	3 months)			
	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious <sup>1,2</sup>	none	19/139 (13.7%)	14/73 (19.2%)	OR 0.67 (0.31 to 1.42)	55 fewer per 1000 (from 123 fewer to 60 more)	LOW
ychia	tric admission – w	rithin 18 mont	ths [ADs versus	TAU] - court or	der [18 month	ns NE] (follow-	up mean 18 months)				
	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>1</sup>	none	18/139 (12.9%)	19/73 (26%)	OR 0.42 (0.21 to 0.87)	132 fewer per 1000 (from 26 fewer to 191 fewer)	MODERATI
ychia	tric admission – w	rithin 18 mont	ths [ADs versus	TAU] – emerger	ncy visit [18 n	nonths NE] (fol	low-up mean 18 month	ns)			
	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious <sup>1,2</sup>	none	44/139 (31.7%)	19/73 (26%)	OR 1.32 (0.7 to 2.48)	57 more per 1000 (from 63 fewer to 206 more)	LOW
ychia	tric admissions 'd	uration' – wit	hin 18 months –	total number of	admissions (	follow-up mea	n 18 months; better inc	licated by lower v	values)		
	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious <sup>1,2</sup>	none	267	280		MD 0.03 higher (0.13 lower to 0.19 higher)	

	randomised trials	no serious	no serious inconsistency	no serious indirectness	very serious <sup>1,2</sup>	none	267	280	-	MD 1.7 higher (10.49 lower to 13.89	LOW
	triais	iisk of blas	niconsistency	maneciness	SCITOUS *					higher)	LOW
chia	tric admissions 'du	ıration' – wit	hin 18 months –	mean days' adn	nission [18 m	onths UK] (follo	ow-up mean 18 month	s; better indicated	l by lower value	es)	
	randomised	no serious	no serious	no serious	very	none	267	280	-	MD 3.1 higher (9.63	
	trials	risk of bias	inconsistency	indirectness	serious <sup>1,2</sup>					lower to 15.83 higher)	LOW
erciv	e intervention – w	ithin 24 mont	hs (follow-up m	ean 24 months)							
_	observational	very	no serious	no serious	serious <sup>5</sup>	none	-	-	-	-	
	studies	serious <sup>4</sup>	inconsistency	indirectness							VERY LOW
rkin	g alliance (1 montl	n) – complete	d PADs with im	proved working	g alliance (fol	low-up mean 1	months)				
	randomised	no serious	no serious	no serious	serious1	none	-	-	Not	-	
	trials	risk of bias	inconsistency	indirectness					estimable		MODERAT
rkin	g alliance (1 month	n) – not comp	leted PADs with	improved wor	king alliance	(follow-up mea	n 1 months)		<u> </u>		
	randomised	no serious	no serious	no serious	very	none	-	-	Not	-	
	trials	risk of bias	inconsistency	indirectness	serious <sup>1,2</sup>				estimable		LOW
kin	g alliance (1 month	n) – complete	d PADs with no	improvement i	n working all	iance (follow-u	p mean 1 months)				
	randomised		no serious	no serious	very	none	-	-	Not	-	
	trials	risk of bias	inconsistency	indirectness	serious <sup>1,2</sup>				estimable		LOW
		18 months) -	WAIT (therapis	t) (follow-up me	ean 18 month	s; better indicat	ed by lower values)				
rkin	g alliance (within					none	267	280	-	MD 4.6 lower (13.24	
rkin	randomised	no serious	no serious	no serious	very						T OTAT
rkin			no serious inconsistency	no serious indirectness	very serious <sup>1,2</sup>					lower to 4.04 higher)	LOW
	randomised	risk of bias	inconsistency	indirectness	serious <sup>1,2</sup>		by lower values)			lower to 4.04 higher)	LOW
	randomised trials	risk of bias	inconsistency	indirectness	serious <sup>1,2</sup>		by lower values)	280	-	MD 3.1 higher (9.63	LOW

Working all	liance (within 18	3 months) - 5	Service Engageme	ent Scale (follow	-up mean 18	months; better in	dicated by lower v	alues)			
					very serious <sup>1,2</sup>	none	202	228		MD 0.31 higher (1.05 lower to 1.67 higher)	
Working all	liance (within 18	3 months) - 1	perceived coercion	n (follow-up me	an 18 months	s; better indicated	by lower values)				
					very serious <sup>1,2</sup>	none	213	245	-	MD 0.23 lower (0.55 lower to 0.09 higher)	

<sup>&</sup>lt;sup>1</sup> Sample size did not reach optimal information size.

<sup>&</sup>lt;sup>2</sup> 95% CI included line of no effect, OIS met.

<sup>&</sup>lt;sup>3</sup> Moderate heterogeneity ( $I^2 = 30-60\%$ ). <sup>4</sup> Unclear/ serious ROB across multiple, from: selection/ performance/ attrition/ detection.

<sup>&</sup>lt;sup>5</sup> No explanation was provided.

# 1.1.3 During event: inpatient settings – adults

### **1.1.3.1** Seclusion and restraint versus an alternative management strategy: effectiveness

			Quality asse	essment			Numb	per of patients		Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Seclusion and restraint	An alternative management strategy	Relative (95% CI)	Absolute	
iolence an	nd aggression (l	PANSS sco	ore) - randomly a	ssigned (better in	dicated by lov	wer values)	,		<u>'</u>		1
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>2,3</sup>	none	12	14	-	SMD 0.31 higher (0.47 lower to 1.08 higher)	VERY LOW
iolence an	nd aggression (l	PANSS sco	ore) – non-randon	nly assigned (bet	ter indicated b	y lower values)			L		
	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>2,3</sup>	none	48	28	-	SMD 0.42 higher (0.06 lower to 0.89 higher)	VERY LOW
											LOW
Change of i	intervention: se	clusion ve	ersus restraint – n	eed to change int	ervention earl	y – within 1 hour					LOW
Change of i	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	y - within 1 hour	18/54 (33.3%)	7/51 (13.7%)	RR 2.43 (1.11 to 5.32)	196 more per 1000 (from 15 more to 593 more)	
	randomised trials	serious <sup>1</sup>	no serious	no serious indirectness	serious <sup>2</sup>		,		,	- '	L
	randomised trials	serious <sup>1</sup> clusion ve	no serious inconsistency	no serious indirectness	serious <sup>2</sup>		,		,	15 more to 593 more)	LOW
hange of i	randomised trials intervention: se randomised trials	serious <sup>1</sup> clusion ve	no serious inconsistency ersus restraint - st	no serious indirectness  ill restricted by 4  no serious indirectness	hours  very serious <sup>2,3</sup>	none	(33.3%)	(13.7%)	to 5.32)	15 more to 593 more) 44 fewer per 1000 (from	LOW

	randomised	serious1	no serious	no serious	serious <sup>2</sup>	none	18/54	0/51	RR 34.98 (2.16	-	
	trials		inconsistency	indirectness			(33.3%)	(0%)	to 565.75)		LOW
	1										<u> </u>
nge of	intervention: se	clusion ve	ersus restraint – r	not discharged by	14 days						
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>2,3</sup>	none	39/54 (72.2%)	39/51 (76.5%)	RR 0.94 (0.75 to 1.18)	46 fewer per 1000 (from 191 fewer to 138 more)	VERY LOW
pliano	e – need to call	doctor – ii	n first 24 hours								
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>2,4</sup>	none	21/54 (38.9%)	26/51 (51%)	RR 0.76 (0.5 to 1.17)	122 fewer per 1000 (from 255 fewer to 87 more)	VER'S
pliano	randomised	pt oral me	no serious	no serious	very serious <sup>2,3</sup>	none	2/54	3/51	RR 0.63 (0.11	22 fewer per 1000 (from 52 fewer to 154 more)	VER'
		tranquil	inconsistency ising drugs - in f	indirectness	serious		(3.7%)	(5.9%)	to 3.62)	52 fewer to 154 more)	LOW
грпанс											
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>2,3</sup>	none	21/54 (38.9%)	22/51 (43.1%)	RR 0.9 (0.57 to 1.43)	43 fewer per 1000 (from 185 fewer to 185 more)	VERY LOW
	fects - hyperten	sion (24 h	ours)								
erse ef		1 . 1	no serious	no serious indirectness	very serious <sup>2,3</sup>	none	1/54 (1.9%)	2/51 (3.9%)	RR 0.47 (0.04 to 5.05)	21 fewer per 1000 (from 38 fewer to 159 more)	VER
erse ef	randomised trials	serious <sup>1</sup>	inconsistency	manechess							LOW
		serious	inconsistency	munectiess							LOW

											LOW
Adverse effe	cts – pain in sl	noulder									
1	randomised	serious1	no serious	no serious	very	none	1/54	0/51	RR 2.84 (0.12	-	
	trials		inconsistency	indirectness	serious <sup>2,3</sup>		(1.9%)	(0%)	to 68.07)		VERY
											LOW

<sup>&</sup>lt;sup>1</sup> Low/unclear ROB across multiple, from: selection/ performance/ attrition/ detection. <sup>2</sup> Sample size did not reach optimal information size.

<sup>&</sup>lt;sup>3</sup> 95% CI included line of no effect, OIS met.

<sup>&</sup>lt;sup>4</sup> Unclear/ serious ROB across multiple, from: selection/ performance/ attrition/ detection.

## **1.1.3.2** Restrictive intervention versus alternative: experience

			Quality asse	essment			Number	of patients		Effect	Ozalita
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Restrictive interventions	An alternative management strategy	Relative (95% CI)	Absolute	Quality
Perceived o	coercion (CES	seclusion	on versus mecha	nical restraint –	· CES (restrict	tion of freedom to	o move) (better i	ndicated by lower	alues)		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	60	48	-	MD 1.1 lower (1.65 to 0.55 lower)	LOW
Perceived o	coercion (CES	seclusion)	on versus mecha	nical restraint –	CES (experie	ence of restriction	n of freedom to n	nove) (better indica	ted by low	er values)	
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>2,3</sup>	none	60	48	-	MD 0.5 lower (1.09 lower to 0.09 higher)	VERY LOW
Perceived of	coercion (CES	s) seclusio	on versus mecha	nical restraint –	· CES (restrict	tion of autonomy	) (better indicate	ed by lower values)		L	
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>2,3</sup>	none	60	48	-	MD 0.5 lower (0.99 to 0.01 lower)	VERY LOW
Perceived of	coercion (CES	seclusion	on versus mecha	nical restraint –	· CES (experie	ence of restriction	n of autonomy) (	better indicated by	lower valu	es)	
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>2,3</sup>	none	60	48	-	MD 0.4 lower (0.93 lower to 0.13 higher)	VERY LOW
Perceived of	coercion (CES	seclusio	on versus mecha	nical restraint –	· CES (coercio	on at beginning o	f measure) (bette	er indicated by low	er values)		
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>2,3</sup>	none	60	48	-	MD 0.4 lower (0.95 lower to 0.15 higher)	VERY LOW

rceiv	red coercion (CES	6) seclusio	on versus mech	anical restraint	- CES (expe	rience of coercion	at the beginning	of measure) (bett	er indicated	by lower values)	
	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>1,2</sup>	none	60	48	-	MD 0.4 higher (0.17 lower to 0.97 higher)	VERY LOW
rceiv	red coercion (CES	6) seclusio	on versus mech	anical restraint	- CES (restri	ction of interper	sonal contact) (bet	ter indicated by le	ower values)		
	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>2,3</sup>	none	60	48	-	MD 0.2 higher (0.39 lower to 0.79	VERY
										higher)	LOW
rceiv	red coercion (CES	s) seclusio	on versus mech	anical restraint	- CES (expe	rience of restricti	on of interpersona	l contact) (better	indicated by	lower values)	
	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>2,3</sup>	none	60	48	-	MD 0 higher (0.54 lower to 0.54 higher)	VERY LOW
tient	rated satisfaction	n: seclusi	on versus restra	int							
	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>2,3</sup>	none	47/216 (21.8%)	45/204 (22.1%)	RR 0.65 (0.36 to 1.17)	77 fewer per 1000 (from 141 fewer to 37 more)	VERY LOW
ient	rated satisfaction	n: seclusi	on versus restra	int - Not satisf	ied						
	randomised trials		no serious inconsistency	no serious indirectness	very serious <sup>2,3</sup>	none	13/54 (24.1%)	19/51 (37.3%)	RR 0.65 (0.36 to 1.17)	130 fewer per 1000 (from 238 fewer to 63 more)	VERY LOW
		ni coelinci	on versus restra	int – Unclear	,	•	•		•		1
tient	rated satisfaction	ii. seciusii									

Patient rate	ed satisfaction	n: seclusio	on versus restrai	nt - Satisfied							
	randomised trials				very serious <sup>2,3</sup>	none	8/54 (14.8%)	5/51 (9.8%)	RR 1.51 (0.53 to 4.32)	50 more per 1000 (from 46 fewer to 325 more)	
Patient rate	ed satisfaction	ı: seclusio	on versus restrai	nt – Refused/ur	nable to ansv	ver					
	randomised trials				very serious <sup>2,3</sup>	none	13/54 (24.1%)	9/51 (17.6%)	RR 1.36 (0.64 to 2.91)	64 more per 1000 (from 64 fewer to 337 more)	

<sup>&</sup>lt;sup>1</sup> Unclear/ serious ROB across multiple, from: selection/ performance/ attrition/ detection.

<sup>&</sup>lt;sup>2</sup> Sample size did not reach optimal information size. <sup>3</sup> 95% CI included line of no effect, OIS met.

## 1.1.4 Post-event: inpatient settings – adults

#### **1.1.4.1** Post-incident management versus treatment as usual

			Quality assess	ment			Number of patie	nts		Effect	Quality	
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Post-incident (seclusion) review	TAU	Relative (95% CI)	Absolute	Quanty	
Trauma exp	erienced by serv	ice user (I	mpact of Event Sc	ale - Revised) -	total (better i	ndicated by lower	values)					
	observational studies				very serious <sup>2,3</sup>	none	0	-	-	SMD 0.12 higher (0.59 lower to 0.83 higher)	VERY LOW	

<sup>&</sup>lt;sup>1</sup> Low/unclear ROB across multiple, from: selection/ performance/ attrition/ detection.

<sup>&</sup>lt;sup>2</sup> Sample size did not reach optimal information size.

<sup>&</sup>lt;sup>3</sup> 95% CI included line of no effect, OIS met.

## 1.2 RAPID TRANQUILLISATION

# 1.2.1 During event: inpatient and emergency settings – adults

### **1.2.1.1** Intramuscular (IM) BZD versus placebo

			Quality asses	sment				ber of ients		Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IM BZD	Placebo	Relative (95% CI)	Absolute	
Global impr	ession: 1. No i	mproveme	ent – short term (fo	ollow-up 15-60 m	inutes)						
1	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	33/51 (64.7%)	37/51 (72.5%)	RR 0.89 (0.69 to 1.16)	80 fewer per 1000 (from 225 fewer to 116 more)	LOW
Global impr	ession: 1. No i	mproveme	ent – medium term	(follow-up 1-24	hours)						
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	18/51 (35.3%)	29/51 (56.9%)	RR 0.62 (0.4 to 0.97)	216 fewer per 1000 (from 17 fewer to 341 fewer)	LOW
Global impr	ression: 2. Nee	d for addit	ional medication -	- medium term (1	follow-up me	an 1-24 hours)					
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	27/51 (52.9%)	27/51 (52.9%)	RR 1 (0.69 to 1.44)	0 fewer per 1000 (from 164 fewer to 233 more)	LOW
Global impr	ression: 3. Seda	ation – me	dium term (follow	-up mean 1-24 ho	ours)	L	1	1	<u> </u>		
2	randomised trials	serious <sup>2</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	18/119 (15.1%)	8/124 (6.5%)	RR 2.16 (1.06 to 4.09)	75 more per 1000 (from 4 more to 199 more)	LOW
Behaviour: 1	. Average cha	nge score (	ABS, high = worse	e) – medium tern	(follow-up	mean 1-24 hours;	better inc	dicated by	y lower values	;)	
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	51	50	-	SMD 0.60 lower (1 to 0.21 lower)	LOW

dverse	e effects: 1. Extrapy	ramidal s	ymptoms - medi	um term (follow-	-up mean 1-24	4 hours)					
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	1/120 (0.83%)	4/123 (3.3%)	RR 0.34 (0.05 to 2.1)	21 fewer per 1000 (from 31 fewer to 36 more)	LOW
dverse	e effects: 2. Use of	medication	n for EPS - medi	um term (follow-	up mean 1-24	l hours)					
2	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	1/51 (2%)	3/51 (5.9%)	RR 0.33 (0.04 to 3.1)	39 fewer per 1000 (from 56 fewer to 124 more)	LOW
Adverso	e effects: 3. Specifi	c – dizzine	ess – medium teri	m (follow-up mea	an 1-24 hours	)					
2	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	14/120 (11.7%)	5/123 (4.1%)	RR 2.75 (0.8 to 9.47)	71 more per 1000 (from 8 fewer to 344 more)	LOW
Adverse	e effects: 3. Specifi	c – nausea	- medium term (	(follow-up mean	1-24 hours)						
2	randomised trials	serious <sup>1</sup>	serious <sup>3</sup>	no serious indirectness	serious <sup>2</sup>	none	4/120 (3.3%)	4/123 (3.3%)	RR 1.02 (0.01 to 72.79)	1 more per 1000 (from 32 fewer to 1000 more)	VERY LOW
Adverse	e effects: 3. Specifi	c – vomitii	ng – medium terr	n (follow-up mea	an 1-24 hours	)					
<u> </u>	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	3/120 (2.5%)	2/123 (1.6%)	RR 1.39 (0.18 to 10.55)	6 more per 1000 (from 13 fewer to 155 more)	LOW
Adverse	e effects: 3. Specifi	c – headac	he – medium teri	m (follow-up mea	an 1-24 hours	)					
L	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	3/69 (4.3%)	9/72 (12.5%)	RR 0.35 (0.1 to 1.23)	81 fewer per 1000 (from 112 fewer to 29 more)	LOW
Adverse	e effects: 3. Specifi	c – insomr	nia – medium teri	m (follow-up mea	an 1-24 hours	)					
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	1/69 (1.4%)	6/72 (8.3%)	RR 0.17 (0.02 to 1.41)	69 fewer per 1000 (from 82 fewer to 34 more)	LOW
Adverse	e effects: 3. Specifi	c – somno	lence – medium t	erm (follow-up r	mean 1-24 ho	urs)			1		
<u> </u>	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	5/69	4/72	RR 1.3 (0.37	17 more per 1000 (from	

	trials		inconsistency	indirectness			(7.2%)	(5.6%)	to 4.66)	35 fewer to 203 more)	LOW	
Adverse effe	ects: 3. Specific	- sedation	n – medium term (	follow-up mean 1	1-24 hours)							
1	randomised trials			no serious indirectness	serious <sup>2</sup>	none	8/69 (11.6%)	1/72 (1.4%)	RR 8.35 (1.07 to 65.01)	102 more per 1000 (from 1 more to 889 more)	LOW	

<sup>&</sup>lt;sup>1</sup> Generally unclear risk of bias and funded by manufacturer.

### **1.2.1.2** IM BZD versus IM antipsychotic (AP)

			Quality assess	sment			Numl patio			Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IM BZD	IM AP	Relative (95% CI)	Absolute	
Global impre	ession: 1. No ii	mproveme	nt – versus halope	ridol - medium t	erm (follow-	up 1-24 hours)					
4	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	36/76 (47.4%)	46/82 (56.1%)	RR 0.87 (0.56 to 1.36)	73 fewer per 1000 (from 247 fewer to 202 more)	LOW
Global impr	ession: 2. Need	l for addit	ional medication –	versus haloperio	dol – mediun	n term (follow-up	mean 1-2	4 hours)			
2	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	31/73 (42.5%)	39/77 (50.6%)	RR 0.87 (0.7 to 1.09)	66 fewer per 1000 (from 152 fewer to 46 more)	LOW
Global impr	ession: 2. Need	l for addit	ional medication –	versus olanzapi	ne – medium	term (follow-up	mean 1-24	hours)			<b> </b>
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	27/51 (52.9%)	26/99 (26.3%)	RR 2.02 (1.33 to 3.07)	268 more per 1000 (from 87 more to 544 more)	LOW
Global impre	ession: 3. Seda	tion – vers	sus haloperidol - s	hort term (follow	-up mean 15	-60 minutes)					<b>-</b>
1	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	9/23	7/21	RR 1.17 (0.53	57 more per 1000 (from	

<sup>&</sup>lt;sup>2</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

<sup>&</sup>lt;sup>3</sup> One study shows positive effect and one study shows negative effect and I squared value significant.

	trials		inconsistency	indirectness			(39.1%)	(33.3%)	to 2.59)	157 fewer to 530 more)	LOW
lobal in	npression: 3. Seda	ition – ver	sus haloperidol -	medium term (fo	ollow-up 1-2	l hours)					
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none		45/222 (20.3%)	RR 1.33 (0.94 to 1.87)	67 more per 1000 (from 12 fewer to 176 more)	LOW
lobal in	pression: 3. Seda	ition – ver	sus olanzapine - 1	medium term (fo	llow-up 1-24	hours)					•
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	5/51 (9.8%)	13/99 (13.1%)	RR 0.75 (0.28 to 1.98)	33 fewer per 1000 (from 95 fewer to 129 more)	LOW
Global in	pression: 3. Seda	ition – ver	sus aripiprazole –	medium term (f	ollow-up 1-2	4 hours)					1
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	13/68 (19.1%)	18/150 (12%)	RR 1.59 (0.83 to 3.06)	71 more per 1000 (from 20 fewer to 247 more)	LOW
ehaviou	r: 1. Average chai	nge/endpo	int score (ABS, hi	gh = worse) - ve	rsus haloper	idol – medium teri	n (follow-	up 1-24 l	nours; better in	dicated by lower values)	l
	randomised	serious1	no serious	no serious	serious <sup>2</sup>	none	31	35	_	SMD 0.20 higher (0.28	
	trials		inconsistency	indirectness						lower to 0.69 higher)	LOW
Sehaviou		nge/endpo	Ĭ		rsus olanzap			ıp 1-24 h	ours; better inc	Č ,	LOW
Sehaviou		serious <sup>1</sup>	Ĭ		rsus olanzap			1 <b>p 1-24 h</b>	-	lower to 0.69 higher)	LOW
	r: 1. Average char randomised trials	serious <sup>1</sup>	int score (ABS, hi	gh = worse) - ve no serious indirectness	serious <sup>2</sup>	ine – medium tern	1 <b>(follow-1</b>	98	-	lower to 0.69 higher) dicated by lower values) SMD 0.47 higher (0.13 to 0.81 higher)	
	r: 1. Average char randomised trials	serious <sup>1</sup>	int score (ABS, hi	gh = worse) - ve no serious indirectness	serious <sup>2</sup>	ine – medium tern	1 <b>(follow-1</b>	98	-	lower to 0.69 higher) dicated by lower values) SMD 0.47 higher (0.13 to 0.81 higher)	
Behaviou	r: 1. Average char randomised trials r: 2. Average char randomised trials	serious <sup>1</sup> nge score ( serious <sup>3</sup>	int score (ABS, hi no serious inconsistency  OAS, high = wors	no serious indirectness se) – versus halo no serious indirectness	serious <sup>2</sup>	none	51 -up 1-24 h	98 ours; bet	-	lower to 0.69 higher) dicated by lower values) SMD 0.47 higher (0.13 to 0.81 higher) y lower values) SMD 0.15 higher (0.43	LOW

	randomised	serious1	no serious	no serious	serious <sup>2</sup>	none	2/115	22/118	RR 0.13 (0.04	162 fewer per 1000 (from	
	trials		inconsistency	indirectness			(1.7%)	(18.6%)	to 0.43)	106 fewer to 179 fewer)	LOW
vers	e effects: 1. Extrapy	ramidal sy	mptoms - versus	s olanzapine – m	edium term (	follow-up 1-24	hours)				
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	1/51	8/99	RR 0.24 (0.03	61 fewer per 1000 (from	
	trials		inconsistency	indirectness			(2%)	(8.1%)	to 1.89)	78 fewer to 72 more)	LOW
lvers	e effects: 1. Extrapy	ramidal sy	mptoms - versus	s aripiprazole – n	nedium term	(follow-up 1-24	4 hours)				
	randomised	serious1	no serious	no serious	serious <sup>2</sup>	none	0/69	8/150	RR 0.13 (0.01	46 fewer per 1000 (from	
	trials		inconsistency	indirectness			(0%)	(5.3%)	to 2.17)	53 fewer to 62 more)	LOW
lvers	e effects: 2. Use of 1	medication	ı for extrapyrami	dal symptoms (fo	ollow-up 24 h	iours)					
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	5/151	20/284	RR 0.42 (0.17	41 fewer per 1000 (from	
	trials		inconsistency	indirectness			(3.3%)	(7%)	to 1.03)	58 fewer to 2 more)	LOW
dvers	trials e effects: 2. Use of 1	medication			versus halope	eridol – mediun		, ,	,	58 fewer to 2 more)	LOW
dvers		medication serious <sup>1</sup>			versus halope	eridol – medium		v-up 1-24	hours)	,	LOW
lvers	e effects: 2. Use of 1	_	for extrapyrami	dal symptoms – v			n term (follow	v-up 1-24	hours)	,	
	e effects: 2. Use of 1	serious <sup>1</sup>	n for extrapyrami no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	n term (follow 4/31 (12.9%)	y-up 1-24 9/35 (25.7%)	RR 0.5 (0.17 to 1.47)	129 fewer per 1000 (from	LOW
	e effects: 2. Use of a	serious <sup>1</sup>	n for extrapyrami no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	n term (follow 4/31 (12.9%)	y-up 1-24 9/35 (25.7%)	RR 0.5 (0.17 to 1.47)	129 fewer per 1000 (from	
	randomised trials e effects: 2. Use of 1	serious <sup>1</sup>	n for extrapyrami no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	4/31 (12.9%)	9/35 (25.7%)	RR 0.5 (0.17 to 1.47)	129 fewer per 1000 (from 213 fewer to 121 more)	
lvers	randomised trials  e effects: 2. Use of 1  randomised  randomised	serious <sup>1</sup> medication serious <sup>2</sup>	n for extrapyrami no serious inconsistency n for extrapyrami no serious inconsistency	no serious indirectness  no serious indirectness	serious <sup>2</sup> serious <sup>2</sup>	none  pine – medium	4/31 (12.9%) n term (follow 1/51 (2%)	9/35 (25.7%) -up 1-24 8/99 (8.1%)	RR 0.5 (0.17 to 1.47)  hours)  RR 0.24 (0.03 to 1.89)	129 fewer per 1000 (from 213 fewer to 121 more) 61 fewer per 1000 (from	LOW
lvers	randomised trials  e effects: 2. Use of randomised trials	serious <sup>1</sup> medication serious <sup>2</sup>	n for extrapyrami no serious inconsistency n for extrapyrami no serious inconsistency	no serious indirectness  no serious indirectness	serious <sup>2</sup> serious <sup>2</sup>	none  pine – medium	4/31 (12.9%) n term (follow 1/51 (2%)	9/35 (25.7%) -up 1-24 8/99 (8.1%)	RR 0.5 (0.17 to 1.47)  hours)  RR 0.24 (0.03 to 1.89)	129 fewer per 1000 (from 213 fewer to 121 more) 61 fewer per 1000 (from	LOW
lvers	randomised trials  e effects: 2. Use of 1  randomised trials  randomised trials  e effects: 2. Use of 1	serious <sup>1</sup> medication serious <sup>2</sup> medication	n for extrapyrami no serious inconsistency no serious inconsistency no serious inconsistency	no serious indirectness  dal symptoms - volume indirectness  dal symptoms - volume indirectness  dal symptoms - volume indirectness	serious <sup>2</sup> serious <sup>2</sup> serious <sup>2</sup> rersus aripip	none none none razole - medium	1/51 (2%) m term (follow	9/35 (25.7%) -up 1-24 8/99 (8.1%) w-up 1-24	RR 0.5 (0.17 to 1.47)  hours)  RR 0.24 (0.03 to 1.89)  4 hours)	129 fewer per 1000 (from 213 fewer to 121 more) 61 fewer per 1000 (from 78 fewer to 72 more)	LOW
vers	randomised trials  e effects: 2. Use of 1  randomised trials  e effects: 2. Use of 1  randomised trials  e effects: 2. Use of 1	serious <sup>1</sup> medication  serious <sup>2</sup> medication  serious <sup>1</sup>	n for extrapyrami no serious inconsistency no serious inconsistency no serious inconsistency no serious inconsistency inconsistency	no serious indirectness  dal symptoms - v  no serious indirectness  dal symptoms - v  no serious indirectness  indirectness	serious <sup>2</sup> serious <sup>2</sup> serious <sup>2</sup> versus aripip	none none none none	1/51 (2%) m term (follow follow follo	9/35 (25.7%) up 1-24 8/99 (8.1%) wup 1-2-	RR 0.5 (0.17 to 1.47)  hours)  RR 0.24 (0.03 to 1.89)  4 hours)  RR 0.31 (0.02	129 fewer per 1000 (from 213 fewer to 121 more) 61 fewer per 1000 (from 78 fewer to 72 more) 14 fewer per 1000 (from	LOW
dvers	randomised trials  e effects: 2. Use of 1  randomised trials  e effects: 2. Use of 1  randomised trials  e effects: 2. Use of 1	serious <sup>1</sup> medication  serious <sup>2</sup> medication  serious <sup>1</sup>	n for extrapyrami no serious inconsistency no serious inconsistency no serious inconsistency no serious inconsistency inconsistency	no serious indirectness  dal symptoms - v  no serious indirectness  dal symptoms - v  no serious indirectness  indirectness	serious <sup>2</sup> serious <sup>2</sup> serious <sup>2</sup> versus aripip	none none none none	1/51 (2%) m term (follow follow follo	9/35 (25.7%) up 1-24 8/99 (8.1%) wup 1-2-	RR 0.5 (0.17 to 1.47)  hours)  RR 0.24 (0.03 to 1.89)  4 hours)  RR 0.31 (0.02	129 fewer per 1000 (from 213 fewer to 121 more) 61 fewer per 1000 (from 78 fewer to 72 more) 14 fewer per 1000 (from	LOW

	randomised	serious1	no serious	no serious	serious <sup>2</sup>	none	0/42	1/42	RR 0.33 (0.01	16 fewer per 1000 (from	
	trials		inconsistency	indirectness			(0%)	(2.4%)	to 7.96)	24 fewer to 166 more)	LOW
lvers	e effects: 3. Specifi	c – versus	haloperidol – diz	ziness – medium	term (follow	-up 1-24 hours	s)				
	randomised	serious1	no serious	no serious	serious <sup>2</sup>	none	3/31	3/35	RR 1.13 (0.25	11 more per 1000 (from	
	trials		inconsistency	indirectness			(9.7%)	(8.6%)	to 5.19)	64 fewer to 359 more)	LOW
dvers	e effects: 3. Specifi	c – versus	aripiprazole - diz	zziness – medium	term (follov	v-up 1-24 hours	s)				
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	7/69	11/150	RR 1.38 (0.56	28 more per 1000 (from	
	trials		inconsistency	indirectness			(10.1%)	(7.3%)	to 3.42)	32 fewer to 177 more)	LOW
lvers	e effects: 3. Specifi	c – versus	l olanzapine – dizz	ziness – medium	term (follow	-up 1-24 hours)					
	randomised	serious1	no serious	no serious	serious <sup>2</sup>	none	7/51	9/99	RR 1.51 (0.6 to	46 more per 1000 (from	
	randomised	Serious.	no senous	no scrious	SCIIOUS	TIOTIC					
	trials	serious	inconsistency	indirectness	Scrious	riorie	(13.7%)	(9.1%)	3.82)	36 fewer to 256 more)	LOW
lvers			inconsistency	indirectness			(13.7%)				LOW
lvers	trials		inconsistency	mouth - medium			(13.7%) rs) 5/31	(9.1%)	3.82) RR 1.88 (0.49	36 fewer to 256 more)  75 more per 1000 (from	
vers	trials e effects: 3. Specific	c – versus	inconsistency haloperidol – dry	indirectness mouth - medium	n term (follo	w-up 1-24 hour	(13.7%)	(9.1%)	3.82)	36 fewer to 256 more)	
	trials e effects: 3. Specific	c - versus l	inconsistency haloperidol - dry no serious inconsistency	mouth - medium no serious indirectness	n term (follo	w-up 1-24 hour	(13.7%) rs) 5/31 (16.1%)	(9.1%)	3.82) RR 1.88 (0.49	36 fewer to 256 more)  75 more per 1000 (from	
	e effects: 3. Specific randomised trials	c - versus l	inconsistency haloperidol - dry no serious inconsistency	mouth - medium no serious indirectness	n term (follo	w-up 1-24 hour	(13.7%) rs) 5/31 (16.1%)	(9.1%)	3.82) RR 1.88 (0.49	36 fewer to 256 more)  75 more per 1000 (from	
	randomised trials  e effects: 3. Specific	serious <sup>1</sup>	inconsistency haloperidol – dry no serious inconsistency haloperidol – hea	no serious indirectness  rt rate – high – m	n term (follo serious <sup>2</sup>	none (follow-up 1-24	(13.7%) rs) 5/31 (16.1%) 4 hours)	(9.1%) 3/35 (8.6%)	3.82)  RR 1.88 (0.49 to 7.24)	36 fewer to 256 more)  75 more per 1000 (from 44 fewer to 535 more)	LOW
vers	randomised trials  e effects: 3. Specific randomised randomised	serious <sup>1</sup> c - versus  serious <sup>3</sup>	no serious inconsistency haloperidol - dry haloperidol - hea no serious inconsistency	no serious indirectness  rt rate - high - m  no serious indirectness	serious <sup>2</sup> serious <sup>2</sup> serious <sup>2</sup>	none  (follow-up 1-24  none	(13.7%)  5/31 (16.1%)  4 hours)  0/22 (0%)	(9.1%) 3/35 (8.6%)	RR 1.88 (0.49 to 7.24)	75 more per 1000 (from 44 fewer to 535 more)  65 fewer per 1000 (from	LOW
lvers	randomised trials  e effects: 3. Specific randomised trials	serious <sup>1</sup> c - versus  serious <sup>3</sup>	no serious inconsistency haloperidol - dry haloperidol - hea no serious inconsistency	no serious indirectness  rt rate - high - m  no serious indirectness	serious <sup>2</sup> serious <sup>2</sup> serious <sup>2</sup>	none  (follow-up 1-24  none	(13.7%)  5/31 (16.1%)  4 hours)  0/22 (0%)	(9.1%) 3/35 (8.6%)	RR 1.88 (0.49 to 7.24)	75 more per 1000 (from 44 fewer to 535 more)  65 fewer per 1000 (from	LOW
vers	randomised trials  e effects: 3. Specific randomised trials  randomised trials  e effects: 3. Specific randomised trials	serious <sup>1</sup> c - versus  serious <sup>3</sup> c - versus	no serious inconsistency haloperidol - dry haloperidol - hea no serious inconsistency haloperidol - hyp	no serious indirectness  rt rate - high - m  no serious indirectness  otensive - media	serious <sup>2</sup> medium term  serious <sup>2</sup> um term (follo	none  (follow-up 1-24 hour none	(13.7%) rs)  5/31 (16.1%) 4 hours)  0/22 (0%) urs)	(9.1%) 3/35 (8.6%) 2/24 (8.3%)	RR 1.88 (0.49 to 7.24)  RR 0.22 (0.01 to 4.29)	36 fewer to 256 more)  75 more per 1000 (from 44 fewer to 535 more)  65 fewer per 1000 (from 82 fewer to 274 more)	LOW
vers	randomised trials  e effects: 3. Specific randomised trials  e effects: 3. Specific randomised trials  e effects: 3. Specific randomised	serious <sup>1</sup> c - versus l serious <sup>3</sup> c - versus l serious <sup>3</sup> c - versus l serious <sup>1</sup>	inconsistency  haloperidol – dry  no serious inconsistency  haloperidol – hea  no serious inconsistency  haloperidol – hyp  no serious inconsistency	no serious indirectness  rt rate - high - re no serious indirectness  ootensive - media	serious <sup>2</sup> medium term serious <sup>2</sup> um term (following serious <sup>2</sup> )	none  (follow-up 1-24 hour none  none  none	(13.7%) rs)  5/31 (16.1%) 4 hours)  0/22 (0%) urs)	(9.1%) 3/35 (8.6%) 2/24 (8.3%)	RR 1.88 (0.49 to 7.24)  RR 0.22 (0.01 to 4.29)  RR 0.33 (0.01	36 fewer to 256 more)  75 more per 1000 (from 44 fewer to 535 more)  65 fewer per 1000 (from 82 fewer to 274 more)	LOW
lvers	randomised trials  e effects: 3. Specific randomised trials  e effects: 3. Specific randomised trials  e effects: 3. Specific randomised trials	serious <sup>1</sup> c - versus l serious <sup>3</sup> c - versus l serious <sup>3</sup> c - versus l serious <sup>1</sup>	inconsistency  haloperidol – dry  no serious inconsistency  haloperidol – hea  no serious inconsistency  haloperidol – hyp  no serious inconsistency	no serious indirectness  rt rate - high - re no serious indirectness  ootensive - media	serious <sup>2</sup> medium term serious <sup>2</sup> um term (following serious <sup>2</sup> )	none  (follow-up 1-24 hour none  none  none	(13.7%) rs)  5/31 (16.1%) 4 hours)  0/22 (0%) urs)	(9.1%) 3/35 (8.6%) 2/24 (8.3%)	RR 1.88 (0.49 to 7.24)  RR 0.22 (0.01 to 4.29)  RR 0.33 (0.01 to 7.96)	36 fewer to 256 more)  75 more per 1000 (from 44 fewer to 535 more)  65 fewer per 1000 (from 82 fewer to 274 more)	LOW

Adverse ef	fects: 3. Specific	- versus a	aripiprazole - nau	ısea - medium te	erm (follow-u	p 1-24 hours)					
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	0/69 (0%)	22/150 (14.7%)	RR 0.05 (0 to 0.78)	139 fewer per 1000 (from 32 fewer to 147 fewer)	LOW
Adverse ef	fects: 3. Specific	- versus l	haloperidol - spe	ech disorder – m	edium term (	follow-up 1-24 ho	ours)				
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	2/31 (6.5%)	4/35 (11.4%)	RR 0.56 (0.11 to 2.87)	50 fewer per 1000 (from 102 fewer to 214 more)	LOW
Adverse ef	fects: 3. Specific	- versus l	haloperidol – tren	nor – medium te	rm (follow-u <sub>]</sub>	o 1-24 hours)					
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	0/22 (0%)	5/24 (20.8%)	RR 0.1 (0.01 to 1.69)	187 fewer per 1000 (from 206 fewer to 144 more)	LOW
Adverse ef	fects: 3. Specific	- versus	olanzapine – vom	iting - medium	term (follow-	up 1-24 hours)	<u> </u>		<b>,</b>		
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	3/51 (5.9%)	0/99 (0%)	RR 13.46 (0.71 to 255.7)	-	LOW
Adverse ef	fects: 3. Specific	- versus a	 aripiprazole – vor	niting - medium	term (follow	r-up 1-24 hours)					
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	0/69 (0%)	8/150 (5.3%)	RR 0.13 (0.01 to 2.17)	46 fewer per 1000 (from 53 fewer to 62 more)	LOW
Adverse ef	fects: 3. Specific	- versus a	aripiprazole – hea	dache – mediun	n term (follow	7-up 1-24 hours)					
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	3/69 (4.3%)	24/150 (16%)	RR 0.27 (0.08 to 0.87)	117 fewer per 1000 (from 21 fewer to 147 fewer)	LOW
Adverse ef	fects: 3. Specific	- versus a	aripiprazole - ins	omnia – mediun	n term (follow	7-up 1-24 hours)		L		l	L
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	1/69 (1.4%)	13/150 (8.7%)	RR 0.17 (0.02 to 1.25)	72 fewer per 1000 (from 85 fewer to 22 more)	LOW
Adverse ef	fects: 3. Specific	- versus a	aripiprazole – son	nnolence – medi	um term (foll	ow-up 1-24 hours	s)	1			
1	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	5/69	12/150	RR 0.91 (0.33	7 fewer per 1000 (from 54	

	trials		inconsistency	indirectness			(7.2%)	(8%)	to 2.47)	fewer to 118 more)	LOW
Adverse effe	ects: 3. Specific	- versus a	ripiprazole – seda	tion – medium to	erm (follow-u	ip 1-24 hours)					
1	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	8/69 (11.6%)		RR 2.17 (0.85 to 5.55)	62 more per 1000 (from 8 fewer to 243 more)	LOW

<sup>&</sup>lt;sup>1</sup> Generally unclear risk of bias and funded by manufacturer.

<sup>&</sup>lt;sup>2</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

<sup>&</sup>lt;sup>3</sup> Generally unclear risk of bias and funding not reported.

### **1.2.1.3** IM BZD + AP versus same BZD

			Quality asses	sment			Numb patie			Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IM BZD + AP	Same BZD	Relative (95% CI)	Absolute	
Global impr	ession: 1. No	mprovem	ent – + haloperido	l – short term (15	5-60 minutes)	(follow-up 15-60	minutes)				
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	very serious <sup>2</sup>	none	0/9 (0%)	5/11 (45.5%)	RR 0.11 (0.01 to 1.74)	405 fewer per 1000 (from 450 fewer to 336 more)	VERY LOW
Global impr	ession: 1. No	improvem	ent - + haloperido	l – medium term	(1-24 hours)	(follow-up 1-24 h	ours)				
2	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	27/42 (64.3%)	28/41 (68.3%)	RR 0.96 (0.7 to 1.3)	27 fewer per 1000 (from 205 fewer to 205 more)	LOW
Global impr	ession: 2. Nee	d for addi	tional medication	- + haloperidol -	- medium ter	m (follow-up 1-24	hours)				
2	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	27/41 (65.9%)	26/42 (61.9%)	RR 0.93 (0.34 to 2.55)	43 fewer per 1000 (from 409 fewer to 960 more)	LOW
Global impr	ession: 3. Sed	ation - + h	aloperidol – short	term (follow-up	15-60 minute	es)					
1	randomised trials	serious <sup>4</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	18/24 (75%)	9/23 (39.1%)	RR 1.92 (1.1 to 3.35)	360 more per 1000 (from 39 more to 920 more)	LOW
Global impr	ession: 3. Sed	ation - + h	aloperidol – medi	um term (follow	-up 1-24 hour	rs)					
2	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	26/56 (46.4%)	30/54 (55.6%)	RR 0.85 (0.53 to 1.35)	83 fewer per 1000 (from 261 fewer to 194 more)	LOW
Behaviour: 1	. Average end	point scor	re (ABS, high = wo	orse) - + haloperi	dol – mediun	n term (follow-up	1-24 hours	; better i	ndicated by lo	ower values)	
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	32	31	-	SMD 0.18 lower (0.67 lower to 0.32 higher)	LOW

dverse	effects: 1. Extrapy	yramidal s	ymptoms - + hal	operidol – mediu	ım term (foll	ow-up 1-24 hour	s)				
	randomised	serious1	no serious	no serious	serious <sup>3</sup>	none	2/41	1/42	RR 1.94 (0.18	22 more per 1000 (from	
	trials		inconsistency	indirectness			(4.9%)	(2.4%)	to 20.3)	20 fewer to 460 more)	LOW
dverse	effects: 2. Use of	medicatio	n for EPS - + halo	operidol – mediu	ım term (foll	ow-up 1-24 hours	5)				
	randomised	serious1	no serious	no serious	serious <sup>3</sup>	none	3/32	4/31	RR 0.73 (0.18	35 fewer per 1000 (from	
	trials		inconsistency	indirectness			(9.4%)	(12.9%)	to 2.99)	106 fewer to 257 more)	LOW
dverse	effects: 3. Specifi	ic – + haloj	peridol – ataxia –	medium term (fo	ollow-up 1-2	4 hours)			l		
	randomised	serious1	no serious	no serious	serious <sup>3</sup>	none	3/32	2/31	RR 1.45 (0.26	29 more per 1000 (from	
	trials		inconsistency	indirectness			(9.4%)	(6.5%)	to 8.11)	48 fewer to 459 more)	LOW
dverse	effects: 3. Specifi	ic – + haloj	peridol – dizzines	ss – medium tern	n (follow-up	1-24 hours)		ļ	1		
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>3</sup>	none	2/32	3/31	RR 0.65 (0.12	34 fewer per 1000 (from	
	trials		inconsistency	indirectness			(6.3%)	(9.7%)	to 3.61)	85 fewer to 253 more)	LOW
dverse	effects: 3. Specifi	ic – + haloj	peridol – dry mou	ıth – medium ter	m (follow-u	p 1-24 hours)			ļ		
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>3</sup>	none	3/32	5/31	RR 0.58 (0.15	68 fewer per 1000 (from	
	trials		inconsistency	indirectness			(9.4%)	(16.1%)	to 2.23)	137 fewer to 198 more)	LOW
Adverse	effects: 3. Specifi	ic – + haloj	peridol - speech	lisorder – mediu	m term (foll	ow-up 1-24 hours	s)	1	1		
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>3</sup>	none	3/32	2/31	RR 1.45 (0.26	29 more per 1000 (from	
	trials		inconsistency	indirectness			(9.4%)	(6.5%)	to 8.11)	48 fewer to 459 more)	LOW
	11 1 1 1	(1)	16 1 11				I	1			

 $<sup>^{\</sup>mathrm{1}}$  Generally unclear risk of bias and funded by manufacturer.

<sup>&</sup>lt;sup>2</sup> Very small sample with wide CIs crossing the line of no effect.

<sup>&</sup>lt;sup>3</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

<sup>&</sup>lt;sup>4</sup> Generally unclear risk of bias and funding not reported.

### **1.2.1.4** IM BZD + AP versus same AP

			Quality assessm	ient			Numb patio			Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IM BZD + AP	SAME AP	Relative (95% CI)	Absolute	
Global impi	ression: 1. no im	provement -	+/versus haloperi	idol – medium t	erm (1-24 hou	ırs) (follow-up 1-2	24 hours)				
	randomised trials	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	serious <sup>2</sup>	none	33/62 (53.2%)	25/65 (38.5%)	RR 3 (0.13 to 67.48)	769 more per 1000 (from 335 fewer to 1000 more)	LOW
Global impi	ression: 2. need t	for additional	l medication – +/v	ersus haloperid	lol – medium	term (follow-up	1-24 hours	5)			
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	27/32 (84.4%)	31/35 (88.6%)	RR 0.95 (0.79 to 1.15)	44 fewer per 1000 (from 186 fewer to 133 more)	LOW
Global impi	ression: 3. sedati	on – +/versus	s haloperidol – sh	ort term (follow	r-up 15-60 mi	nutes)	ļ			l .	
	randomised trials	serious <sup>4</sup>		no serious indirectness	serious <sup>2</sup>	none	18/24 (75%)	7/21 (33.3%)	RR 2.25 (1.18 to 4.3)	417 more per 1000 (from 60 more to 1000 more)	LOW
Global impi	ression: 3. sedati	on – +/versus	s haloperidol – me	edium term (fol	low-up 1-24 h	nours)					
	randomised trials	serious <sup>3</sup>	serious <sup>1</sup>	no serious indirectness	serious <sup>2</sup>	none	38/86 (44.2%)	22/86 (25.6%)	RR 1.67 (0.67 to 4.12)	171 more per 1000 (from 84 fewer to 798 more)	VERY LOW
Behaviour: 1	1. average endpo	oint score (AB	S, high = worse)	- +/versus halop	peridol – med	lium term (follow	-up 1-24 h	ours; be	tter indicated	by lower values)	
	randomised trials	serious³		no serious indirectness	serious <sup>2</sup>	none	32	35	-	SMD 0.02 higher (0.46 lower to 0.5 higher)	LOW

Behavi	our: 2. average endp	oint score (	OAS, high = worse	e) - +/versus hal	operidol - sh	ort term (follo	ow-up 15-60 mi	nutes; be	etter indicated	l by lower values)	
	randomised trials	serious <sup>5</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	30	30	-	SMD 0.48 higher (0.03 lower to 1 higher)	LOW
ehavi	our: 2. average endp	oint score (	OAS, high = worse	e) – +/versus hal	operidol – m	edium term (f	ollow-up 1-24 l	nours; be	tter indicated	by lower values)	
	randomised trials	serious <sup>5</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	30	30	-	SMD 0.66 higher (0.14 to 1.18 higher)	LOW
dvers	e effects: 1. extrapyı	ramidal sym	nptoms - +/versus l	haloperidol - me	edium term (	follow-up 1-24	4 hours)				
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	5/62 (8.1%)	12/65 (18.5%)	RR 0.45 (0.17 to 1.22)	102 fewer per 1000 (from 153 fewer to 41 more)	LOW
dvers	e effects: 2. use of m	nedication fo	or EPS - +/versus h	naloperidol - me	edium term (	follow-up 1-24	l hours)				
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	4/32 (12.5%)	9/35 (25.7%)	RR 0.49 (0.17 to 1.43)	131 fewer per 1000 (from 213 fewer to 111 more)	LOW
dvers	e effects: 3. specific	- +/versus l	naloperidol – ataxia	a – medium tern	n (follow-up	mean 1-24 hou	urs)	ļ			
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	3/32 (9.4%)	1/35 (2.9%)	RR 3.28 (0.36 to 29.97)	65 more per 1000 (from 18 fewer to 828 more)	LOW
dvers	e effects: 3. specific	- +/versus l	naloperidol - dizzi	ness – medium	term (follow	-up 1-24 hours	)	<b>!</b>			
	observational	serious <sup>3</sup>	no serious	no serious	serious <sup>2</sup>	none	2/32 (6.3%)	3/35 (8.6%)	RR 0.73 (0.13 to 4.09)	23 fewer per 1000 (from 75 fewer to 265	LOW
	studies		inconsistency	indirectness			(6.3%)	(8.0%)	10 4.09)	more)	2011
dvers	studies e effects: 3. specific	- +/versus l			term (follov	v-up 1-24 hour	, ,	(8.6%)	10 4.09)		2011

Adverse eff	fects: 3. specific -	+/versus ha	loperidol - hypot	ension – mediui	n term (follo	w-up 1-24 hours)					
1	randomised	serious <sup>5</sup>	no serious	no serious	serious <sup>2</sup>	none	5/30	0/30	RR 11 (0.64	-	
	trials		inconsistency	indirectness			(16.7%)	(0%)	to 190.53)		LOW
Adverse eff	fects: 3. specific -	+/versus ha	loperidol – speech	n disorder – med	lium term (fo	ollow-up 1-24 hour	rs)				
1	randomised	serious <sup>3</sup>	no serious	no serious	serious <sup>2</sup>	none	3/32	4/35	RR 0.82 (0.2	21 fewer per 1000	
	trials		inconsistency	indirectness			(9.4%)	(11.4%)	to 3.39)	(from 91 fewer to 273	LOW
			1					, ,		more)	

<sup>&</sup>lt;sup>1</sup> Studies found contrasting results. High, significant *I*<sup>2</sup> value.

#### **1.2.1.5** IM BZD + AP versus different IM AP

			Quality asses	sment			Numbe	er of patients		Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IM BZD + AP	DIFFERENT IM AP	Relative (95% CI)	Absolute	
Global impr	ession: 1. no i	mprovem	ent - +haloperido	l versus olanzap	oine – mediui	n term (1-24 hour	s) (follow-	-up 1-24 hours)			
	randomised trials			no serious indirectness	serious <sup>2</sup>	none	12/30 (40%)	0/30 (0%)	RR 25 (1.55 to 403.99)	-	LOW
Global impr	ession: 1. no i	mprovem	ent - +haloperido	l versus ziprasio	done – mediu	m term (1-24 hou	rs) (follow	7-up 1-24 hours)			
	randomised trials			no serious indirectness	serious <sup>2</sup>	none	12/30 (40%)	3/30 (10%)	RR 4 (1.25 to 12.75)	300 more per 1000 (from 25 more to 1000 more)	LOW

<sup>&</sup>lt;sup>2</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

<sup>&</sup>lt;sup>3</sup> Generally unclear risk of bias and funded by manufacturer.

<sup>&</sup>lt;sup>4</sup> Generally unclear or high risk of bias and funding not reported.

<sup>&</sup>lt;sup>5</sup> Generally unclear risk of bias and funding not reported.

	mpression: 2. nee	ed for add	itional medicatio	on – not reported	I						
	-	_3	-	-	_2	none	27/41 (65.9%)	26/42 (61.9%)	-	-	
obal i	mpression: 3. sed	lation – +1	naloperidol versu	ıs olanzapine – ı	medium term	ı (follow-up 1	-24 hours)				
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	12/30 (40%)	1/30 (3.3%)	RR 12 (1.66 to 86.59)	367 more per 1000 (from 22 more to 1000 more)	LOW
obal i	mpression: 3. sed	lation - +l	naloperidol versu	ıs ziprasidone –	medium terr	n (follow-up 1	1-24 hours)				
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	12/30 (40%)	3/30 (10%)	RR 4 (1.25 to 12.75)	300 more per 1000 (from 25 more to 1000 more)	LOW
ehavio	ur: 1. average cha	nge score	(OAS, high = wo	orse) – +haloperi	idol versus o	lanzapine - sł	nort term (follow	v-up 15-60 mir	nutes; better ir	dicated by lower value	es)
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	30	30	-	SMD 0.96 higher (0.42 to 1.49 higher)	LOW
ehavio	ur: 1. average cha	nge score	(OAS, high = we	orse) – +haloperi	idol versus o	lanzapine - m	edium term (fol	low-up 1-24 h	ours; better in	dicated by lower value	es)
	randomised	serious <sup>1</sup>	no serious	no serious indirectness	serious <sup>2</sup>	none	30	30	-	SMD 0.91 higher (0.38	
	trials		inconsistency	manecticss						to 1.45 higher)	LOW
ehavio		nge score	,		idol versus z	iprasidone – s	hort term (follow	w-up 15-60 mi	nutes; better i	ndicated by lower valu	
<b>S</b> ehavio		serious <sup>1</sup>	,		serious <sup>2</sup>	iprasidone - s	hort term (follow	30 30	nutes; better i	,	
	randomised	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	30	30	-	ndicated by lower valu	LOW

	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	0/40 (0%)	4/36 (11.1%)	RR 0.18 (0.02 to 1.48)	91 fewer per 1000 (from 109 fewer to 53 more)	LOW
Adverse e	ffects: 1. side ef	fects - +ri	isperidone versu	s haloperidol – 1	nedium term	(follow-up 1-	24 hours)		-		
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	0/20 (0%)	9/20 (45%)	RR 0.05 (0 to 0.85)	427 fewer per 1000 (from 67 fewer to 450 fewer)	LOW
Adverse e	ffects: 2. extrap	yramidal :	symptoms - +hal	operidol versus	olanzapine -	· medium tern	n (follow-up 1-2	4 hours)		l	
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	3/30 (10%)	0/30 (0%)	RR 7 (0.38 to 129.93)	-	LOW
Adverse e	effects: 2. extrap	 yramidal :	 symptoms - +hal	operidol versus	ziprasidone	– medium teri	m (follow-up 1-2	24 hours)			
Adverse e	randomised trials	yramidal s	no serious inconsistency	no serious indirectness	ziprasidone serious <sup>2</sup>	none	3/30 (10%)	0/30 (0%)	RR 7 (0.38 to 129.93)	-	LOW
1	randomised trials	serious <sup>1</sup>	no serious	no serious indirectness	serious <sup>2</sup>	none	3/30 (10%)	0/30 (0%)	,	-	LOW
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	3/30 (10%)	0/30 (0%)	,		
1 <b>Adverse e</b> 1	randomised trials effects: 3. specifi randomised trials	serious <sup>1</sup> serious <sup>1</sup>	no serious inconsistency peridol versus ol	no serious indirectness  anzapine - hypo  no serious indirectness	serious <sup>2</sup> otension – me	none dium term (fo	3/30 (10%) ollow-up 1-24 ho 5/30 (16.7%)	0/30 (0%) Durs) 1/30 (3.3%)	129,93)  RR 5 (0.62 to	133 more per 1000 (from 13 fewer to 1000	

<sup>&</sup>lt;sup>1</sup> Generally unclear risk of bias and funding not reported.

<sup>&</sup>lt;sup>2</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

#### **1.2.1.6** IM BZD + AP versus IM AP + AP

			Quality assess	ment			Numb patie			Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IM BZD + AP	IM AP + AP	Relative (95% CI)	Absolute	Quanty
Global impres	ssion: 1. no imp	provement	- not reported								<u> </u>
0	-	-	-	-	-	none	-	-	-	-	
Global impres	ssion: 2. need f	or addition	nal medication – not	reported							
0	-	-	-	-	-	none	-	-	-	-	
Behaviour: 1. indicated by l		int score (C	DAS, high = worse)	- + haloperidol v	ersus clothia	pine + haloperidol	- mediun	n term (1	-24 hours	) (follow-up 1-24 hours; b	etter
	randomised trials	Serious <sup>1</sup>		no serious indirectness	serious <sup>2</sup>	none	30	30	-	SMD 0.13 lower (0.64 lower to 0.37 higher)	LOW
Adverse effec	ts – not reporte	d			•						
0	-	-	-	-	-	none	-	-	-	-	

<sup>&</sup>lt;sup>1</sup> Generally unclear risk of bias and funding not reported.

<sup>&</sup>lt;sup>2</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

## **1.2.1.7** IM BZD versus IM AP + IM antihistamine (promethazine)

Quality assessment							Number of patients		Effect		Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IM BZD	IM AP + antihistamines	Relative (95% CI)	Absolute	
Global imp	ression: 1. No	improven	nent – versus halo	peridol + prome	ethazine – in	nmediate term (0-	15 minut	es) (follow-up 0-15	5 minutes)		
1	randomised trials		no serious inconsistency	no serious indirectness	serious²	none	70/100 (70%)	39/100 (39%)	RR 1.79 (1.36 to 2.37)	308 more per 1000 (from 140 more to 534 more)	LOW
Global imp	ression: 1. No	improven	nent – versus halo	pperidol + prome	ethazine – sh	ort term (15-60 m	inutes) (f	follow-up 15-60 m	inutes)		
1	randomised trials		no serious inconsistency	no serious indirectness	serious²	none	42/100 (42%)	17/100 (17%)	RR 2.47 (1.51 to 4.03)	250 more per 1000 (from 87 more to 515 more)	LOW
Global imp	ression: 1. No	improven	nent – versus halo	pperidol + prome	ethazine - m	edium term (1-24	hours) (f	ollow-up 1-24 hou	irs)		
1	randomised trials		no serious inconsistency	no serious indirectness	serious²	none	26/100 (26%)	12/100 (12%)	RR 2.17 (1.16 to 4.05)	140 more per 1000 (from 19 more to 366 more)	LOW
Global imp	ression: 2. Ne	ed for add	itional medicatio	n – versus halop	eridol + pro	methazine – imm	ediate ter	rm (follow-up 0-15	minutes)		
1	-	-	-	-	-	-	-	-	not pooled	not pooled	-
Global imp	ression: 2. Ne	ed for add	itional medicatio	n – versus halop	eridol + pro	methazine – short	term (fo	llow-up 15-60 min	utes)		
1	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	1/100 (1%)	0/100 (0%)	RR 3 (0.12 to 72.77)	-	LOW
Global impression: 2. Need for additional medication – versus haloperidol + promethazine – medium term (follow-up 1-24 hours)											
1	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	4/100	3/100	RR 1.33 (0.31	10 more per 1000 (from 21 fewer to 144	

	trials		inconsistency	indirectness			(4%)	(3%)	to 5.81)	more)	LOW
lobal in	pression: 3. Sec	lation (tra	nquil or asleep)	- versus haloper	ridol + prom	ethazine – im	mediate term (fo	ollow-up 0-15	minutes)		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	78/100 (78%)	89/100 (89%)	RR 0.88 (0.77 to 0.99)	107 fewer per 1000 (from 9 fewer to 205 fewer)	LOW
lobal in	pression: 3. Sec	lation (tra	nquil or asleep)	- versus haloper	ridol + prom	ethazine – sh	ort term (follow-	-up 15-60 min	utes)		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	81/100 (81%)	95/100 (95%)	RR 0.85 (0.77 to 0.95)	142 fewer per 1000 (from 48 fewer to 219 fewer)	LOW
Global in	pression: 3. Sed	lation (tra	nquil or asleep)	- versus haloper	ridol + prom	ethazine - m	edium term (foll	ow-up 1-24 ho	ours)		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	88/100 (88%)	97/100 (97%)	RR 0.91 (0.84 to 0.98)	87 fewer per 1000 (from 19 fewer to 155 fewer)	LOW
Global in	pression: 3. Sed	lation (tra	nquil or asleep)	- versus haloper	ridol + prom	ethazine – sh	ort term (follow-	-up 15-60 min	utes)		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	134/151 (88.7%)	101/150 (67.3%)	RR 1.32 (1.16 to 1.49)	215 more per 1000 (from 108 more to 330 more)	LOW
Global in	pression: 3. Sec	lation (tra	nquil or asleep)	- versus haloper	ridol + prom	ethazine – m	edium term (foll	ow-up 1-24 ho	ours)		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	141/151 (93.4%)	124/150 (82.7%)	RR 1.13 (1.04 to 1.23)	107 more per 1000 (from 33 more to 190 more)	LOW
Adverse e	ffects: 1. Specif	ic – versus	s haloperidol + p	promethazine – a	irway mana	gement - med	lium term (follo	w-up 1-24 hou	ırs)		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	2/251 (0.8%)	0/250 (0%)	RR 2.99 (0.31 to 28.54)	-	LOW

Adverse ef	fects: 1. Specifi	ic – versus	s haloperidol + pı	omethazine – na	nusea – medi	um term (follow-	ıp 1-24 h	ours)			
1	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	1/100 (1%)	0/100 (0%)	RR 3 (0.12 to 72.77)	-	LOW
Adverse ef	fects: 1. Specifi	c – versus	s haloperidol + pr	omethazine – se	izure – med	ium term (follow-	up 1-24 h	ours)			
1	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	0/151 (0%)	1/150 (0.67%)	RR 0.33 (0.01 to 8.06)	4 fewer per 1000 (from 7 fewer to 47 more)	LOW

<sup>&</sup>lt;sup>1</sup> Participants and outcome assessors were non-blinded.

### **1.2.1.8** IM BZD + AP versus IM AP + IM antihistamine (promethazine)

			Quality asses	sment			Nu	umber of patients		Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IM BZD + AP	IM AP + ANTIHISTAMINES	Relative (95% CI)	Absolute	
Global imp	pression: 1. no	improve	ment – +haloperi	dol versus halo	peridol + pro	methazine - med	lium term	n (1-24 hours) (follow-u	p 1-24 hours)		
	randomised trials	serious <sup>1</sup>		no serious indirectness	serious <sup>2</sup>	none	12/30 (40%)	0/30 (0%)	RR 25 (1.55 to 403.99)	-	LOW
Global imp	pression: 2. ne	ed for add	litional medication	on – not reporte	ed.						
0	-	-	-	-	-		27/41 (65.9%)	26/42 (61.9%)	-	-	
Global imp	pression: 3. sec	lation - +	haloperidol vers	us haloperidol	+ promethazi	ne – medium ter	m (follow	r-up 1-24 hours)			
	randomised trials	serious <sup>1</sup>		no serious indirectness	serious <sup>2</sup>	none	12/30 (40%)	1/30 (3.3%)	RR 12 (1.66 to 86.59)	367 more per 1000 (from 22 more to 1000 more)	LOW

<sup>&</sup>lt;sup>2</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

Behaviour: lower value	U	dpoint sc	ore (OAS, high =	worse) – + halo	peridol vers	us haloperidol +	prometha	zine – short term (follo	w-up 15-60 r	ninutes; better indic	cated by
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	30	30	-	SMD 0.85 lower (1.38 to 0.32 lower)	LOW
Behaviour: lower value	_	dpoint sc	ore (OAS, high =	worse) - + halo	peridol vers	us haloperidol +	prometha	zine – medium term (fo	llow-up 1-2	4 hours; better indic	ated by
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	30	30	-	SMD 0.48 higher (0.03 lower to 1 higher)	LOW
Adverse eff	fects: 1. extrap	yramidal	symptoms - +ha	loperidol versu	s haloperido	ol + promethazine	- mediu	m term (follow-up 1-24	hours)		<u> </u>
1	randomised trials	serious¹	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	3/30 (10%)	5/30 (16.7%)	RR 0.6 (0.16 to 2.29)	67 fewer per 1000 (from 140 fewer to 215 more)	LOW
Adverse eff	fects: 2. specif	ic – +halo	peridol versus h	aloperidol + pro	omethazine -	- hypotension - n	nedium te	erm (follow-up 1-24 hou	rs)		
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	5/30 (16.7%)	3/30 (10%)	RR 1.67 (0.44 to 6.36)	67 more per 1000 (from 56 fewer to 536 more)	LOW

<sup>&</sup>lt;sup>1</sup> Participants and outcome assessors were non-blinded.

<sup>&</sup>lt;sup>2</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

# **1.2.1.9** IM HAL versus placebo

			Quality ass	sessment			Num pati	ber of ents		Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IM HAL	Placebo	Relative (95% CI)	Absolute	
Repeated n	eed for tranqu	illisation	- needing addition	onal injection du	ring 24 hours (a	gitation only)					
4	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	124/411 (30.2%)	-	RR 0.52 (0.42 to 0.65)	280 fewer per 1000 (from 204 fewer to 338 fewer)	LOW
Global outo	come: 1. not in	nproved -	not marked impr	ovement							<u> </u>
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	17/29 (58.6%)	11/11 (100%)	RR 0.61 (0.44 to 0.84)	390 fewer per 1000 (from 160 fewer to 560 fewer)	LOW
Global outo	come: 1. not in	nproved -	not any improve	ment			ı				
1	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	3/29 (10.3%)	4/11 (36.4%)	RR 0.28 (0.08 to 1.07)	262 fewer per 1000 (from 335 fewer to 25 more)	LOW
Global outo	come: 2. need i	for benzoo	diazepine during	24 hours - need	for benzodiazep	ine during 24 hou	urs				
4	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	53/411 (12.9%)	67/249 (26.9%)	RR 0.5 (0.3 to 0.81)	135 fewer per 1000 (from 51 fewer to 188 fewer)	LOW
Specific bel	haviour - agita	ation: 2a. A	Average score - b	y about 2 hours -	- change score -	ABS (high = wors	se) (bette	r indicate	ed by lower v	alues)	
3	randomised trials		no serious inconsistency	no serious indirectness	no serious imprecision	none	280	194	-	SMD 0.65 lower (0.95 to 0.35 lower)	MODERATE

Specific	behaviour – agita	ation: 2a.	Average score -	by about 2 hours	- change score	- PANSS-EC (	high = worse)	(better i	ndicated by l	ower values)	
2	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	224	133	-	SMD 0.59 lower (1.04 to 0.14 lower)	LOW
pecific	behaviour - agita	ation: 2b.	Average score -	by about 24 hour	rs - change score	e - ABS (high	= worse) (bett	er indica	ited by lower	values)	
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	40	45	-	SMD 0.59 lower (1.02 to 0.15 lower)	LOW
pecific	behaviour – agit	ation: 2b.	Average score -	by about 24 hour	rs – change score	e – PANSS-EC	(high = worse	e) (better	indicated by	lower values)	
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	40	45	-	SMD 0.38 lower (0.81 lower to 0.05 higher)	LOW
Adverse	e effects: 1. Gener	al – one o	r more drug-rela	ted adverse effec	cts during 24 ho	urs					
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	no serious imprecision <sup>2</sup>	none	111/245 (45.3%)	42/150 (28%)	RR 1.64 (1.22 to 2.2)	179 more per 1000 (from 62 more to 336 more)	MODERATE
Adverse	e effects: 1. Gener	al – increa	sed severity of a	dverse effects af	ter second injec	tion			1		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	82/185 (44.3%)	12/88 (13.6%)	RR 3.25 (1.88 to 5.63)	307 more per 1000 (from 120 more to 631 more)	LOW
Adverse	e effects: 1. Gener	al – overa	ll adverse events	during 72 hours	3						
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	90/185 (48.6%)	24/88 (27.3%)	RR 1.78 (1.23 to 2.59)	213 more per 1000 (from 63 more to 434 more)	LOW
dverse	e effects: 2. Gener	al – seriou	is – death								
	randomised trials					none	0/185 (0%)	0/88 (0%)	not pooled	not pooled	

lverse	effects: 2. Genera	al – seriou	ıs – rated as seri	ous							
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	0/60 (0%)	1/62 (1.6%)	RR 0.34 (0.01 to 8.29)	11 fewer per 1000 (from 16 fewer to 118 more)	LOW
verse	effects: 2. Genera	al – seriou	ıs – tonic clonic	seizure							
	randomised trials					none	0/60 (0%)	0/57 (0%)	not pooled	not pooled	
verse	effects: 3. Specif	ic – arous	al level - insomi	nia during 24 ho	urs (only repo	rted if occurred	in ≥ 5%)				
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	22/185 (11.9%)	8/88 (9.1%)	RR 1.31 (0.61 to 2.82)	28 more per 1000 (from 35 fewer to 165 more)	LOW
verse	effects: 3. Specif	ic – arous	al level - 'over'	sedated						1	
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	40/214 (18.7%)	5/99 (5.1%)	RR 3.04 (1.27 to 7.26)	103 more per 1000 (from 14 more to 316 more)	LOW
lverse	effects: 3. Specif	ic – arous	al level – somno	lence during 24	hours						
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	24/400 (6%)	6/215 (2.8%)	RR 2.26 (0.96 to 5.32)	35 more per 1000 (from 1 fewer to 121 more)	LOW
dverse	effects: 4a. Speci	fic – cardi	iac: i. Miscellane	eous outcomes -	dizziness dur	ing 24 hours (on	ly reported if	occurred	in ≥ 5%)		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	11/242 (4.5%)	6/150 (4%)	RR 1.3 (0.47 to 3.59)	12 more per 1000 (from 21 fewer to 104 more)	LOW
lverse	effects: 4a. Speci	fic – cardi	iac: i. Miscellane	eous outcomes -	hypotension o	during 24 hours	,		1		
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	1/69	0/56	RR 1.2 (0.05	-	

	trials		inconsistency	indirectness			(1.4%)	(0%)	to 27.44)		LOW
verse	e effects: 4a. Speci	fic - card	iac: i. Miscellane	eous outcomes -	QTc <sup>4</sup> abnorma	ality					
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	3/60 (5%)	1/62 (1.6%)	RR 3.1 (0.33 to 28.98)	34 more per 1000 (from 11 fewer to 451 more)	LOW
lverse	e effects: 4a. Speci	fic – card	iac: i. Miscellane	eous outcomes -	sinus tachycar	dia during 24 ho	ours (only rep	orted if o	occurred in ≥ 5	5%)	
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	3/60 (5%)	1/62 (1.6%)	RR 3.1 (0.33 to 28.98)	34 more per 1000 (from 11 fewer to 451 more)	LOW
dverse	e effects: 4a. Speci	  fic – card	iac: i. Miscellane	eous outcomes -	tachycardia dı	uring 24 hours (o	nly reported i	if occurre	ed in ≥ 5%)		
dverse	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	1/60 (1.7%)		RR 1.03 (0.07	0 more per 1000 (from 15 fewer to 244 more)	LOW
	randomised	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	1/60 (1.7%)	1/62 (1.6%)	RR 1.03 (0.07 to 16.15)	15 fewer to 244 more)	LOW
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	1/60 (1.7%)	1/62 (1.6%)	RR 1.03 (0.07 to 16.15)	15 fewer to 244 more)	LOW
dverse	randomised trials e effects: 5b. Spectrandomised	serious <sup>1</sup> ific - mov	no serious inconsistency ement disorders no serious inconsistency	no serious indirectness  i. Average char  no serious indirectness	serious <sup>2</sup> nge score (Barr  serious <sup>2</sup>	none nes Akathisia Sca	1/60 (1.7%) ale, high = wo	1/62 (1.6%) orse) (bet	RR 1.03 (0.07 to 16.15) ter indicated	by lower values)  SMD 0.12 higher (0.22 lower to 0.45 higher)	

<sup>&</sup>lt;sup>1</sup> Risk of bias generally unclear and funding not reported.

<sup>&</sup>lt;sup>2</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

<sup>&</sup>lt;sup>3</sup> Risk of bias generally unclear and trial funded by manufacturer.

<sup>&</sup>lt;sup>4</sup> The corrected QT interval (the period from the start of the Q wave to the end of the T wave; duration of ventricular electrical activity).

# **1.2.1.10** IM HAL versus other IM AP

			Quality asse	ssment				iber of ients		Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IM HAL	Other IM AP	Relative (95% CI)	Absolute	
Repeated no	eed for rapid tra	inquillisat	ion: needing addi	tional injection			I				
9	randomised trials	serious <sup>1</sup>	serious <sup>2</sup>	no serious indirectness	no serious imprecision	none	220/636 (34.6%)	264/782 (33.8%)	RR 1.04 (0.87 to 1.25)	14 more per 1000 (from 44 fewer to 84 more)	LOW
Repeated no	eed for rapid tra	ınquillisat	ion: needing addi	tional injection	- versus aripipr	azole					
2	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	78/242 (32.2%)	95/231 (41.1%)	RR 0.79 (0.62 to 1)	86 fewer per 1000 (from 156 fewer to 0 more)	LOW
Repeated no	eed for rapid tra	inquillisat	ion: needing addi	tional injection	- versus chlorp	romazine					
1	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	none	15/15 (100%)	14/15 (93.3%)	RR 1.07 (0.89 to 1.28)	65 more per 1000 (from 103 fewer to 261 more)	VERY LOW
Repeated no	eed for rapid tra	ınquillisat	ion: needing addi	tional injection	- versus droper	idol					L
1	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	13/16 (81.3%)	4/11 (36.4%)	RR 2.23 (0.99 to 5.06)	447 more per 1000 (from 4 fewer to 1000 more)	LOW
Repeated no	eed for rapid tra	ınquillisat	ion: needing addi	tional injection	- versus olanza	pine			1		<u> </u>
4	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	84/316 (26.6%)	130/472 (27.5%)	RR 1.02 (0.73 to 1.42)	6 more per 1000 (from 74 fewer to 116 more)	LOW

	randomised	serious <sup>3</sup>	no serious	no serious	serious4	none	15/32	7/38	RR 2.54 (1.19	284 more per 1000	
	trials	serious	inconsistency	indirectness	Serious.	none	(46.9%)	(18.4%)	to 5.46)	(from 35 more to 822	LOW
	urais		inconsistency	munectiess			(40.9%)	(10.4 /0)	10 5.40)	`	LOW
										more)	
eat	ed need for rapid tr	ranquillisa	tion: needing add	ditional injection	n – versus thio	thixene	·				
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>4</sup>	none	15/15	14/15	RR 1.07 (0.89		
	trials		inconsistency	indirectness			(100%)	(93.3%)	to 1.28)	(from 103 fewer to 261	LOW
										more)	
oal	outcome: 1. need fo	or addition	 al benzodiazepi	ne – versus olanz	zapine						
	randomised	serious <sup>3</sup>	no serious	no serious	serious <sup>4</sup>	none	25/166	25/177	RR 0.62 (0.07	54 fewer per 1000	
	trials		inconsistency	indirectness			(15.1%)	(14.1%)	to 5.07)	(from 131 fewer to 575	LOW
			,				` ′	, ,	1	` ,	
hal	outcome: not impr	oved								more)	
bal	outcome: not impro	oved serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	68/359 (18.9%)	124/481 (25.8%)	RR 0.73 (0.46 to 1.18)	,	LOW
bal	randomised	1			serious <sup>4</sup>	none	, ,	•	`	70 fewer per 1000	LOW
	randomised	serious <sup>3</sup>	inconsistency	indirectness	serious <sup>4</sup>	none	, ,	•	`	70 fewer per 1000 (from 139 fewer to 46	LOW
	randomised trials  outcome: not impro	serious <sup>3</sup>	inconsistency	indirectness	serious <sup>4</sup>	none	, ,	•	`	70 fewer per 1000 (from 139 fewer to 46 more)	LOW
	randomised trials outcome: not impro	serious <sup>3</sup>	inconsistency sus chlorpromazi	indirectness			(18.9%)	(25.8%)	to 1.18)	70 fewer per 1000 (from 139 fewer to 46 more)	
bal	randomised trials  outcome: not impro	serious <sup>3</sup> oved – vers  serious <sup>3</sup>	inconsistency sus chlorpromazi no serious inconsistency	indirectness ine no serious			(18.9%)	(25.8%)	to 1.18)	70 fewer per 1000 (from 139 fewer to 46 more) 240 fewer per 1000 (from 149 fewer to 271	LOW
bal	randomised trials  outcome: not improrandomised trials	serious <sup>3</sup> oved – vers  serious <sup>3</sup>	inconsistency sus chlorpromazi no serious inconsistency	indirectness ine no serious			(18.9%)	(25.8%)	to 1.18)	70 fewer per 1000 (from 139 fewer to 46 more)  240 fewer per 1000 (from 149 fewer to 271 fewer)	

Global	outcome: not impre	oved - vers	us perphenazin	e							
-	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	1/23 (4.3%)	2/21 (9.5%)	RR 0.46 (0.04 to 4.68)	51 fewer per 1000 (from 91 fewer to 350 more)	LOW
Global	outcome: not impre	oved - vers	us thiothixene								
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	2/24 (8.3%)	0/20 (0%)	RR 4.2 (0.21 to 82.72)	-	LOW
Global	outcome: not impro	oved – vers	sus olanzapine								
3	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	50/196 (25.5%)	97/346 (28%)	RR 1.04 (0.74 to 1.42)	11 more per 1000 (from 73 fewer to 118 more)	LOW
Advers	se effects: 1a. Gener	al (aripipra	zole) – one or m	ore drug-related	adverse effect	s during 24 hou	ırs		,		
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	111/245 (45.3%)	89/232 (38.4%)	RR 1.18 (0.95 to 1.46)	69 more per 1000 (from 19 fewer to 176 more)	LOW
dvers	se effects: 1a. Gener	al (aripipra	zole) – increased	d severity of adv	erse effects aft	er second injec	tion				
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	82/185 (44.3%)	58/175 (33.1%)	RR 1.34 (1.03 to 1.74)	113 more per 1000 (from 10 more to 245 more)	LOW
dvers	se effects: 1a. Gener	al (aripipra	zole) – overall a	dverse events du	ring 72 hours						
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	90/185 (48.6%)	64/175 (36.6%)	RR 1.33 (1.04 to 1.7)	121 more per 1000 (from 15 more to 256 more)	LOW
Advers	se effects: 1b. 'Serio	us' (aripipr	razole) – any	_	1				1		
	observational	serious <sup>3</sup>	no serious	no serious	serious <sup>4</sup>	none	4/245	7/232	RR 0.55 (0.1	14 fewer per 1000 (from 27 fewer to 65	

	studies		inconsistency	indirectness			(1.6%)	(3%)	to 3.16)	more)	
vers	se effects: 1b. 'Serio	us' (aripipı	 cazole) – tonic clo	nic seizure							
		`	,						T		
	randomised	serious <sup>3</sup>	no serious	no serious	serious <sup>4</sup>	none	0/60	1/57	RR 0.32 (0.01	-	
	trials		inconsistency	indirectness			(0%)	(1.8%)	to 7.62)	(from 17 fewer to 116	LOW
										more)	
lver	se effects: 1b. 'Serio	us' (aripipi	azole) – death								
	randomised		T	T	T	none	0/185	0/175	not pooled	not pooled	
	trials					Tioric	(0%)	(0%)	not pooled	not pooled	
	triais						(0 /0)	(070)			
vers	se effects: any seriou	ıs or specif	ic antiepileptics	(chlorpromazine	e) – allergy – hae	matological - le	eukopenia -	mild			
	-										
	randomised	serious <sup>3</sup>	no serious	no serious	serious <sup>4</sup>	none	1/25	0/25	RR 3 (0.13 to	-	
	trials		inconsistency	indirectness			(4%)	(0%)	70.3)		LOW
						1			1		
1		• •		/ 1 1	\ 11 1		• •				
dvers	se effects: any seriou	ıs or specif	ic antiepileptics	(chlorpromazine	e) – allergy – hep	atic – glutamic	pyruvic trar	isaminas	e elevated		
dvers	randomised	serious <sup>3</sup>	no serious	no serious	e) - allergy - hep	none	pyruvic trar	1/25	RR 0.33 (0.01	27 fewer per 1000	
dvers						1				27 fewer per 1000 (from 40 fewer to 272	LOW
dvers	randomised		no serious	no serious		1	0/25	1/25	RR 0.33 (0.01	-	LOW
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	0/25 (0%)	1/25	RR 0.33 (0.01	(from 40 fewer to 272	LOW
	randomised	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	0/25 (0%)	1/25	RR 0.33 (0.01	(from 40 fewer to 272	LOW
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	0/25 (0%)	1/25 (4%)	RR 0.33 (0.01 to 7.81)	(from 40 fewer to 272 more)	LOW
	randomised trials se effects: any seriou	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	0/25 (0%)	1/25 (4%)	RR 0.33 (0.01	(from 40 fewer to 272	LOW
	randomised trials se effects: any seriou	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	0/25 (0%)	1/25 (4%)	RR 0.33 (0.01 to 7.81)	(from 40 fewer to 272 more)	LOW
dvers	randomised trials se effects: any seriou	serious <sup>3</sup>	no serious inconsistency fic antiepileptics	no serious indirectness (chlorpromazine	serious <sup>4</sup>	none n irritation - loc	0/25 (0%) cal	1/25 (4%)	RR 0.33 (0.01 to 7.81)	(from 40 fewer to 272 more)	LOW
lvers	randomised trials  se effects: any seriou randomised trials	serious <sup>3</sup>	no serious inconsistency fic antiepileptics	no serious indirectness (chlorpromazine	serious <sup>4</sup> e) – allergy – skir  e) – anticholiners	none n irritation - loc	0/25 (0%) ccal 0/15 (0%)	1/25 (4%) 0/15 (0%)	RR 0.33 (0.01 to 7.81)	(from 40 fewer to 272 more)	LOW
dvers	randomised trials  se effects: any seriou randomised trials  se effects: any seriou randomised	serious <sup>3</sup> as or specif	no serious inconsistency  ic antiepileptics  ic antiepileptics  no serious	no serious indirectness  (chlorpromazine) (chlorpromazine) no serious	serious <sup>4</sup>	none n irritation - loc none gic - dry mouth	0/25 (0%) cal 0/15 (0%)	1/25 (4%) 0/15 (0%)	RR 0.33 (0.01 to 7.81)  not pooled  RR 1.38 (0.17	(from 40 fewer to 272 more)  not pooled  38 more per 1000	
dvers	randomised trials  se effects: any seriou randomised trials  se effects: any seriou	serious <sup>3</sup> as or specif	no serious inconsistency  fic antiepileptics  fic antiepileptics	no serious indirectness  (chlorpromazine)	serious <sup>4</sup> e) – allergy – skir  e) – anticholiners	none n irritation - loc none gic - dry mouth	0/25 (0%) ccal 0/15 (0%)	1/25 (4%) 0/15 (0%)	RR 0.33 (0.01 to 7.81)	(from 40 fewer to 272 more)  not pooled  38 more per 1000 (from 83 fewer to 993	VERY
dvers	randomised trials  se effects: any seriou randomised trials  se effects: any seriou randomised	serious <sup>3</sup> as or specif	no serious inconsistency  ic antiepileptics  ic antiepileptics  no serious	no serious indirectness  (chlorpromazine) (chlorpromazine) no serious	serious <sup>4</sup> e) – allergy – skir  e) – anticholiners	none n irritation - loc none gic - dry mouth	0/25 (0%) cal 0/15 (0%)	1/25 (4%) 0/15 (0%)	RR 0.33 (0.01 to 7.81)  not pooled  RR 1.38 (0.17	(from 40 fewer to 272 more)  not pooled  38 more per 1000	
dvers	randomised trials  se effects: any seriou randomised trials  se effects: any seriou randomised	serious <sup>3</sup> us or specifications or specificatio	no serious inconsistency  ic antiepileptics  ic antiepileptics  no serious inconsistency	no serious indirectness  (chlorpromazine no serious indirectness	serious <sup>4</sup> e) – allergy – skin  e) – anticholinerg  very serious <sup>5</sup>	none n irritation - loc none gic - dry mouth none	0/25 (0%) cal 0/15 (0%) 1 4/29 (13.8%)	1/25 (4%) 0/15 (0%)	RR 0.33 (0.01 to 7.81)  not pooled  RR 1.38 (0.17	(from 40 fewer to 272 more)  not pooled  38 more per 1000 (from 83 fewer to 993	VERY
dvers	randomised trials  se effects: any seriou randomised trials  se effects: any seriou randomised trials	serious <sup>3</sup> us or specifications or specificatio	no serious inconsistency  ic antiepileptics  ic antiepileptics  no serious inconsistency	no serious indirectness  (chlorpromazine no serious indirectness	serious <sup>4</sup> e) – allergy – skin  e) – anticholinerg  very serious <sup>5</sup>	none n irritation - loc none gic - dry mouth none	0/25 (0%) cal 0/15 (0%) 4/29 (13.8%)	1/25 (4%) 0/15 (0%) 1/10 (10%)	RR 0.33 (0.01 to 7.81)  not pooled  RR 1.38 (0.17 to 10.93)	(from 40 fewer to 272 more)  not pooled  38 more per 1000 (from 83 fewer to 993 more)	VERY
dvers	randomised trials  se effects: any seriou randomised trials  se effects: any seriou randomised trials  se effects: any seriou randomised trials	serious <sup>3</sup> as or specif  serious <sup>3</sup> serious <sup>3</sup>	no serious inconsistency  ic antiepileptics  ic antiepileptics  no serious inconsistency	no serious indirectness  (chlorpromazine no serious indirectness  (chlorpromazine chlorpromazine	serious <sup>4</sup> 2) - allergy - skin  2) - anticholinerg  very serious <sup>5</sup> 2) - arousal - dro	none none none powsy but asleep	0/25 (0%) cal 0/15 (0%) 1 4/29 (13.8%)	1/25 (4%) 0/15 (0%)	RR 0.33 (0.01 to 7.81)  not pooled  RR 1.38 (0.17	(from 40 fewer to 272 more)  not pooled  38 more per 1000 (from 83 fewer to 993	VERY

										fewer)	
verse	effects: any seriou	s or specif	ic antiepileptics	(chlorpromazino	e) – arousal – dro	wsy but awal	ke				
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	none	12/29 (41.4%)	0/10 (0%)	RR 9.17 (0.59 to 142.1)	-	VERY LOW
verse	effects: any seriou	s or specif	ic antiepileptics	  (chlorpromazin	e) – cardiovascul	ar – hypotens	ion				
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	3/44 (6.8%)	3/25 (12%)	RR 0.59 (0.1 to 3.33)	49 fewer per 1000 (from 108 fewer to 280 more)	LOW
erse	effects: any seriou	s or specif	ic antiepileptics	(chlorpromazino	e) – central nervo	ous system – s	seizures		1		
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	very serious <sup>5</sup>	none	0/15 (0%)	1/15 (6.7%)	RR 0.33 (0.01 to 7.58)	45 fewer per 1000 (from 66 fewer to 439 more)	VERY LOW
erse (	effects: any seriou	s or specif	ic antiepileptics	(chlorpromazin	e) – movement di	isorders – ext	rapyramidal a	dverse ef	fects		
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	6/44 (13.6%)	1/25 (4%)	RR 2.07 (0.28 to 15.15)	43 more per 1000 (from 29 fewer to 566 more)	LOW
verse	effects: 1. General	and serio	us (olanzapine) –	one or more dru	g-related advers	se effects					
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	1/24 (4.2%)	1/25 (4%)	RR 1.04 (0.07 to 15.73)	2 more per 1000 (from 37 fewer to 589 more)	LOW
verse	effects: 1. General	and serio	us (olanzapine) –	treatment emer	gent adverse eve	nts – all					
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	7/24 (29.2%)	9/25 (36%)	RR 0.81 (0.36 to 1.83)	68 fewer per 1000 (from 230 fewer to 299	LOW

	effects: 1. General	and serio	us (olanzapine) -	overall serious a	dverse effects						
	randomised trials					none	0/25 (0%)	0/24 (0%)	not pooled	not pooled	
verse	effects: 1. General	and serio	us (olanzapine) -	death							
	randomised trials					none	0/24 (0%)	0/25 (0%)	not pooled	not pooled	
lverse	effects: 1. General	(perphena	azine) - one or m	ore adverse effec	et						
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>4</sup>	none	10/23 (43.5%)	7/21 (33.3%)	RR 1.3 (0.61 to 2.8)	100 more per 1000 (from 130 fewer to 600 more)	LOW
lverse	effects: 1. General	(perphena	azine) – clinically	significant labo	ratory changes	S					
	randomised trials					none	0/23 (0%)	0/21 (0%)	not pooled	not pooled	
lverse	effects: 1. General	(ziprasido	one) – one or mor	e drug-related a	lverse effects -	- by 72 hours					
		serious <sup>1</sup>	serious <sup>2</sup>	no serious	serious <sup>4</sup>	none	1	12E /204	RR 1.69 (1.23	219 more per 1000	
	randomised trials	serious	serious	indirectness	Scrious	none	(56.5%)	(31.7%)	to 2.33)	(from 73 more to 422 more)	VERY LOW
lverse				indirectness		none	1 -		,	(from 73 more to 422	
dverse	trials			indirectness		none	1 -		,	(from 73 more to 422	
	effects: 1. General	(ziprasido	one) – severe advo	indirectness erse effect - by 7	2 hours	none	0/187	(31.7%)	to 2.33)	(from 73 more to 422 more)	

Adverse effe	ects: 1. General	(loxapine)	- one or more dr	ug-related adver	se effect							
	randomised trials			no serious indirectness	serious <sup>4</sup>	none	8/15 (53.3%)	10/15 (66.7%)	RR 0.8 (0.44 to 1.45)	133 fewer per 1000 (from 373 fewer to 300 more)	LOW	
Adverse eff	ects: 1. General	one or m	ore adverse effec	ts (thiothixene)								
	randomised trials			no serious indirectness	serious <sup>4</sup>	none	24/39 (61.5%)	14/35 (40%)	RR 1.42 (0.97 to 2.09)	168 more per 1000 (from 12 fewer to 436 more)	LOW	

<sup>&</sup>lt;sup>1</sup> Risk of bias generally unclear and funded by manufacturer.

# 1.2.1.11 IM HAL + IM antihistamine (promethazine) versus HAL

			Quality asses	sment			Number of pat	ients		Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IM HAL + antihistamine	HAL	Relative (95% CI)	Absolute	
Tranquil or	asleep: 1. Not	tranquil (	or asleep - by 20 n	ninutes							
	randomised trials			no serious indirectness	serious <sup>2</sup>	none	48/160 (30%)	72/156 (46.2%)	RR 0.65 (0.49 to 0.87)	162 fewer per 1000 (from 60 fewer to 235 fewer)	LOW
Tranquil or	asleep: 1. Not	tranquil o	or asleep - by 40 n	ninutes							
	randomised trials			no serious indirectness	serious <sup>2</sup>	none	34/160 (21.3%)	40/156 (25.6%)	RR 0.83 (0.56 to 1.24)	44 fewer per 1000 (from 113 fewer to 62 more)	LOW

<sup>&</sup>lt;sup>2</sup> High and significant I squared value.

<sup>&</sup>lt;sup>3</sup> Risk of bias generally unclear and funding not reported.

<sup>&</sup>lt;sup>4</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

<sup>&</sup>lt;sup>5</sup> Very small sample with wide CIs crossing the line of no effect.

anqu	il or asleep: 1. Not	tranquil	or asleep - by 1	hour							
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	24/160 (15%)	31/156 (19.9%)	RR 0.75 (0.46 to 1.23)	50 fewer per 1000 (from 107 fewer to 46 more)	LOW
ınqu	il or asleep: 1. Not	tranquil	or asleep - by 2	hours							
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	17/160 (10.6%)	30/156 (19.2%)	RR 0.55 (0.32 to 0.96)	87 fewer per 1000 (from 8 fewer to 131 fewer)	LOW
nqu	il or asleep: 3. Not	asleep -	by 20 minutes								
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	132/160 (82.5%)	145/156 (92.9%)	RR 0.89 (0.82 to 0.96)	102 fewer per 1000 (from 37 fewer to 167 fewer)	LOW
nqu	il or asleep: 3. Not	asleep -	by 40 minutes								
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	106/160 (66.3%)	104/156 (66.7%)	RR 0.99 (0.85 to 1.16)	7 fewer per 1000 (from 100 fewer to 107 more)	LOW
nqu	il or asleep: 3. Not	asleep -	by 1 hour								
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	86/160 (53.8%)	81/156 (51.9%)	RR 1.04 (0.84 to 1.28)	21 more per 1000 (from 83 fewer to 145 more)	LOW
nqu	il or asleep: 3. Not	asleep -	by 2 hours			_					
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	66/160 (41.3%)	64/156 (41%)	`	4 more per 1000 (from 94 fewer to 127 more)	
vers	e effects: 1. Any se	erious adv	rerse effect - by 2	24 hours	·			•			
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	1/153	11/145	RR 0.09 (0.01	69 fewer per 1000 (from 26 fewer to 75	

	trials		inconsistency	indirectness			(0.65%)	(7.6%)	to 0.66)	fewer)	LOW
dverse e	ffects: 2. Acute	dystonia -	- by 24 hours								
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	0/153 (0%)	10/145 (6.9%)	RR 0.05 (0 to 0.76)	66 fewer per 1000 (from 17 fewer to 69 fewer)	LOW
dverse e	ffects: 3. Seizur	e – by 24	hours	1	_	<u>'</u>					
l	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	1/153 (0.65%)	1/145 (0.69%)	RR 0.95 (0.06 to 15.01)	(from 6 fewer to 97	LOW
										more)	
Global ef	fect: 1. Addition	al tranqu	illising drugs - b	by 2 hours						more)	
Global eff	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	5/157 (3.2%)	11/154 (7.1%)	RR 0.45 (0.16 to 1.25)	·	LOW
	randomised trials	serious <sup>1</sup>	no serious	no serious indirectness	serious <sup>2</sup>	none		-	,	39 fewer per 1000 (from 60 fewer to 18	LOW

<sup>&</sup>lt;sup>1</sup> Risk of bias generally unclear and funding not reported.
<sup>2</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

# **1.2.1.12** IM HAL + IM antihistamine (promethazine) versus IM olanzapine

			Quality asses	ssment			Number of	patients		Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IM HAL + antihistamine	IM olanzapine	Relative (95% CI)	Absolute	
Tranquil or	r asleep: 1. No	t tranquil	or asleep - by 15	minutes							
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2,3</sup>	none	14/150 (9.3%)	19/150 (12.7%)	RR 0.74 (0.38 to 1.41)	33 fewer per 1000 (from 79 fewer to 52 more)	LOW
Tranquil or	r asleep: 1. No	t tranquil	or asleep - by 30	minutes							
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	6/150 (4%)	10/150 (6.7%)	RR 0.6 (0.22 to 1.61)	27 fewer per 1000 (from 52 fewer to 41 more)	LOW
Tranquil o	r asleep: 1. No	t tranquil	or asleep - by 1	hour							
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	1/150 (0.67%)	9/150 (6%)	RR 0.11 (0.01 to 0.87)	53 fewer per 1000 (from 8 fewer to 59 fewer)	LOW
Tranquil or	r asleep: 1. No	t tranquil	or asleep - by 2	hours							
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	4/150 (2.7%)	9/150 (6%)	RR 0.44 (0.14 to 1.41)	34 fewer per 1000 (from 52 fewer to 25 more)	LOW
Tranquil or	r asleep: 1. No	t tranquil	or asleep - by 4	hours				1	I		<u>.                                    </u>
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	5/150 (3.3%)	6/150 (4%)	RR 0.83 (0.26 to 2.67)	7 fewer per 1000 (from 30 fewer to 67 more)	LOW

ranqui	l or asleep: 3. No	t asleep –	by 15 minutes								
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	64/150 (42.7%)	85/150 (56.7%)	RR 0.75 (0.6 to 0.95)	142 fewer per 1000 (from 28 fewer to 227 fewer)	LOW
anqui	l or asleep: 3. No	t asleep –	by 30 minutes								
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	36/150 (24%)	55/150 (36.7%)	RR 0.65 (0.46 to 0.93)	128 fewer per 1000 (from 26 fewer to 198 fewer)	LOW
ranqui	l or asleep: 3. No	t asleep –	by 1 hour				<b>'</b>	l			
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	30/150 (20%)	51/150 (34%)	RR 0.59 (0.4 to 0.87)	139 fewer per 1000 (from 44 fewer to 204 fewer)	LOW
ranqui	l or asleep: 3. No	t asleep –	by 2 hours					L			
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	14/150 (9.3%)	59/150 (39.3%)	RR 0.24 (0.14 to 0.41)	299 fewer per 1000 (from 232 fewer to 338 fewer)	LOW
ranqui	l or asleep: 3. No	t asleep –	by 4 hours								
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	38/150 (25.3%)	62/150 (41.3%)	RR 0.61 (0.44 to 0.86)	161 fewer per 1000 (from 58 fewer to 231 fewer)	LOW
ranqui	l or asleep: 5. Ne	ver tranq	uil or asleep dui	ring first 4 hours	s						
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	1/150 (0.67%)	4/150 (2.7%)	RR 0.25 (0.03 to 2.21)	20 fewer per 1000 (from 26 fewer to 32 more)	LOW

erse	e effects: 1. Seriou	ıs adverse	e effect - by 4 ho	urs							
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	1/150 (0.67%)	3/150 (2%)	RR 0.33 (0.04 to 3.17)	13 fewer per 1000 (from 19 fewer to 43 more)	LOW
erse	e effects: 1. Seriou	ıs adverse	e effect – at 2 we	eks				l			
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	0/150 (0%)	1/150 (0.67%)	RR 0.33 (0.01 to 8.12)	4 fewer per 1000 (from 7 fewer to 47 more)	LOW
erse	e effects: 2. Extrap	yramidal	problems - 0-4	hours – any cha	nge in scale	-rated extrapy	amidal problems (Sin	npson-Angu	s Scale)		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	0/150 (0%)	0/150 (0%)	See comment	-	LOW
bal (	effect: 1. Requirii	ng additio	onal drugs durin	g initial phase -	- by 4 hours		<u> </u>	1			
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	31/150 (20.7%)	65/150 (43.3%)	RR 0.48 (0.33 to 0.69)	225 fewer per 1000 (from 134 fewer to 290 fewer)	LOW
bal (	effect: 2. Not clin	ically imp	proved - by 15 m	inutes				1			
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	41/150 (27.3%)	52/150 (34.7%)	RR 0.79 (0.56 to 1.11)	73 fewer per 1000 (from 153 fewer to 38 more)	LOW
bal (	effect: 2. Not clin	ically imp	proved - by 30 m	inutes			<u> </u>				
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	23/150 (15.3%)	40/150 (26.7%)	RR 0.57 (0.36 to 0.91)	115 fewer per 1000 (from 24 fewer to 171 fewer)	LOW
bal (	effect: 2. Not clin	ically imp	proved - by 1 ho	ur							ļ
	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>3</sup>	none	12/150	30/150	RR 0.4 (0.21	120 fewer per 1000 (from 50 fewer to	

	trials		inconsistency	indirectness			(8%)	(20%)	to 0.75)	158 fewer)	LOW
Global eff	ect: 2. Not clin	ically imp	proved - by 2 hou	ırs	_						
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	14/150 (9.3%)	32/150 (21.3%)	RR 0.44 (0.24 to 0.79)	119 fewer per 1000 (from 45 fewer to 162 fewer)	LOW
Global eff	ect: 2. Not clin	ically imp	proved - by 4 hou	ırs							
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	9/150 (6%)	19/150 (12.7%)	RR 0.47 (0.22 to 1.01)	67 fewer per 1000 (from 99 fewer to 1 more)	LOW
Global eff	ect: 5. Further	observatio	on after 4 hours		_						
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>3</sup>	none	42/150 (28%)	36/150 (24%)	RR 1.17 (0.8 to 1.71)	41 more per 1000 (from 48 fewer to 170 more)	LOW

<sup>&</sup>lt;sup>1</sup> Risk of bias generally high or unclear and funding not reported.

#### **1.2.1.13** IM olanzapine versus IM placebo

			Quality ass	essment			Number of	patients		Effect	Quality	
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IM olanzapine	IM placebo	Relative (95% CI)	Absolute		
Global effe	ct: 1. Did not	respond -	by 2 hours									
6	randomised trials				no serious imprecision	none	242/607 (39.9%)	157/241 (65.1%)	RR 0.65 (0.47 to 0.9)	228 fewer per 1000 (from 65 fewer to 345 fewer)	MODERATE	

<sup>&</sup>lt;sup>2</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) met but CIs cross line of no effect.

<sup>&</sup>lt;sup>3</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

navi	our: 2. Requiring	further IN	M injection – by 2	24 hours							
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	139/460 (30.2%)	113/199 (56.8%)	RR 0.54 (0.45 to 0.65)	261 fewer per 1000 (from 199 fewer to 312 fewer)	LOW
havi	our: 3. Requiring	additiona	l benzodiazepin	es – within 24 h	ours				L		
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	33/316 (10.4%)	37/104 (35.6%)	RR 0.3 (0.15 to 0.6)	249 fewer per 1000 (from 142 fewer to 302 fewer)	LOW
dvers	e event: 1. Any ad	lverse eve	ent – in 24 hours			1	1				
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	51/161 (31.7%)	21/112 (18.8%)	RR 1.56 (1 to 2.43)	105 more per 1000 (from 0 more to 268 more)	LOW
dvers	se event: 2. Anxiet	y - by 24	hours								
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	0/185 (0%)	3/50 (6%)	RR 0.04 (0 to 0.75)	58 fewer per 1000 (from 15 fewer to 60 fewer)	LOW
dvers	se event: 3. EPS – 1	equiring	anticholinergic 1	nedication - by	24 hours				L	<u> </u>	
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	15/415 (3.6%)	5/155 (3.2%)	RR 1.26 (0.49 to 3.26)	8 more per 1000 (from 16 fewer to 73 more)	LOW
dvers	se event: 4. Serious	s adverse	event - by 24 ho	urs							
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	2/378 (0.53%)	0/160 (0%)	RR 0.96 (0.1 to 9.15)	-	LOW
D: 1	(1: 11	<del></del>	16 1 11					1	l .		

<sup>&</sup>lt;sup>1</sup> Risk of bias generally unclear and funded by manufacturer.

<sup>&</sup>lt;sup>2</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

<sup>&</sup>lt;sup>3</sup> Risk of bias generally unclear and funding not reported.

# **1.2.1.14** IM olanzapine versus IM AP

			Quality asses	Number of 1	patients	Effect		Quality			
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IM olanzapine	IM AP	Relative (95% CI)	Absolute	
Global effec	ct: Did not resp	ond - by	2 hours (≥40% cha	nge on PANSS-I	EC)		1				1
2	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	97/316 (30.7%)	49/166 (29.5%)	RR 1.02 (0.67 to 1.55)	6 more per 1000 (from 97 fewer to 162 more)	LOW
Behaviour: 1	l. Leaving the	study - by	24 hours					1			
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	9/131 (6.9%)	10/126 (7.9%)	RR 0.87 (0.36 to 2.06)	10 fewer per 1000 (from 51 fewer to 84 more)	LOW
Behaviour: 2	2. Requiring ac	dditional I	M injection - by 2	4 hours			1				
2	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	93/316 (29.4%)	46/166 (27.7%)	RR 1.01 (0.63 to 1.61)	3 more per 1000 (from 103 fewer to 169 more)	LOW
Behaviour: 3	3. Requiring ac	dditional b	enzodiazepines –	by 24 hours							<u> </u>
2	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	33/316 (10.4%)	25/166 (15.1%)	RR 1.31 (0.24 to 7.21)	47 more per 1000 (from 114 fewer to 935 more)	LOW
Adverse eve	ent: 1b. EPS – r	equiring a	nticholinergic me	dication – by 24	hours						
2	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	7/316 (2.2%)	29/166 (17.5%)	`	142 fewer per 1000 (from 100 fewer to 159 fewer)	LOW
Adverse eve	ent: 1c. EPS - d	ystonia – 1	by 24 hours								
2	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	0/316 (0%)	11/166 (6.6%)	RR 0.05 (0.01 to 0.37)	63 fewer per 1000 (from 42 fewer to 66 fewer)	LOW

Adverse eve	ent: 1d. EPS – g	eneral EPS	S – extrapyramidal	syndrome								
1	randomised trials	serious <sup>1</sup>		no serious indirectness	serious <sup>2</sup>	none	1/131 (0.76%)	7/126 (5.6%)		48 fewer per 1000 (from 54 fewer to 6 more)	LOW	
Adverse eve	ent: 2. Serious a	dverse ev	ent									
3	randomised trials	serious <sup>1</sup>		no serious indirectness	serious <sup>2</sup>	none	2/340 (0.59%)	2/191 (1%)	RR 0.54 (0.08 to 3.64)	5 fewer per 1000 (from 10 fewer to 28 more)	LOW	

<sup>&</sup>lt;sup>1</sup> Risk of bias generally unclear and funded by manufacturer.

# 1.2.1.15 Inhaled loxapine versus placebo

			Quality assess	Number of	patients		Quality				
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Inhaled loxapine	Placebo	Relative (95% CI)	Absolute	
Global impi	ression: 1. Milo	d to marke	d agitation at 2 ho	urs post dose (A	CES) - 5 mg						
1	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	39/104 (37.5%)	75/105 (71.4%)	RR 0.52 (0.4 to 0.69)	343 fewer per 1000 (from 221 fewer to 429 fewer)	LOW
Global impi	ression: 1. Milo	d to marke	d agitation at 2 ho	urs post dose (A	CES) - 10 mg	5					
1	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	28/105 (26.7%)	75/105 (71.4%)	RR 0.37 (0.27 to 0.52)	450 fewer per 1000 (from 343 fewer to 521 fewer)	LOW
Global impi	ression: 2. Non	-response	(Clinical Global I	mpressions - Im	provement) -	- 5 mg					
3	randomised trials		no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	108/265 (40.8%)	184/263 (70%)	RR 0.59 (0.47 to 0.74)	287 fewer per 1000 (from 182 fewer to 371	LOW

<sup>&</sup>lt;sup>2</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

										fewer)	
Global	impression: 2. Nor	 1-response	(Clinical Globa	l Impressions – I	mprovement	) - 10 mg					
	-		`	•	<u>-</u>	, 3			ı		
3	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	79/257		RR 0.44 (0.35	*	
	trials		inconsistency	indirectness			(30.7%)	(70%)	to 0.56)	(from 308 fewer to 455	LOW
										fewer)	
Global	impression: 3. Dee	p sleep (A	CES) - 5 mg								
1	randomised	serious <sup>1</sup>	no serious	no serious	serious <sup>2</sup>	none	10/104	2/105	RR 5.05 (1.13	77 more per 1000 (from	
	trials		inconsistency	indirectness			(9.6%)	(1.9%)	to 22.48)	2 more to 409 more)	LOW
Clobal	impression: 3. Dee	m sloom (A	CEC) 10 ma								
GIUDAI	impression, 5. Dee	p sieep (A	(CE3) - 10 mg								
1	randomised	serious1	no serious	no serious	serious <sup>2</sup>	none	13/105	2/105	RR 6.5 (1.5 to	105 more per 1000 (from	
	trials		inconsistency	indirectness			(12.4%)	(1.9%)	28.1)	10 more to 516 more)	LOW
Global	impression: 4. Una	rousable (	(ACFS) = 5 mg								
GIODUI			(11023) 0 mg								
2	randomised					none	0/220	0/220	not pooled	not pooled	
	trials						(0%)	(0%)			
Global	impression: 4. Una	rousable	(ACES) - 10 mg					1			
<u>,</u>	randomised	Ī			T	none	0/217	0/220	not pooled	not pooled	
	trials						(0%)	(0%)	1	1	
ilobal	impression: 5. Nee	d for resci	ue medication at	4 hours – 5 mg							
1	randomised	serious <sup>3</sup>	no serious	no serious	serious <sup>2</sup>	none	2/45	3/43	RR 0.64 (0.11	25 fewer per 1000 (from	
	trials		inconsistency	indirectness			(4.4%)	(7%)	to 3.63)	62 fewer to 183 more)	LOW
Global	impression: 5. Nee	d for resci	 ue medication at	4 hours - 10 mg							
	man dancia. 1	la ami a 2	ma sawisara	ma aari	lagui a 2	la cano	0 / 41	2/42	DD 0.15 /0.01	E0 forecast mar 1000 (free se	
L	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	0/41 (0%)	3/43 (7%)	to 2.81)	59 fewer per 1000 (from 69 fewer to 126 more)	LOW

lobal in	npression: 5. Nee	ed for resc	ue medication at	24 hours - 5 mg							
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	5/45 (11.1%)	14/43 (32.6%)	RR 0.34 (0.13 to 0.87)	215 fewer per 1000 (from 42 fewer to 283 fewer)	LOW
lobal ii	npression: 5. Nee	ed for resc	ue medication at	24 hours - 10 mg	5			L		l	
	randomised trials	serious <sup>3</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	6/41 (14.6%)	14/43 (32.6%)	RR 0.45 (0.19 to 1.06)	179 fewer per 1000 (from 264 fewer to 20 more)	LOW
Adverse	event: 1. At least	1 antiepile	eptic – 5 mg				<b>-</b>	1			
,	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	90/265 (34%)	82/263 (31.2%)	RR 1.09 (0.77 to 1.54)	28 more per 1000 (from 72 fewer to 168 more)	LOW
dverse	event: 1. At least	1 antiepile	eptic – 10 mg								
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	89/259 (34.4%)	82/263 (31.2%)	RR 1.1 (0.86 to 1.4)	31 more per 1000 (from 44 fewer to 125 more)	LOW
dverse	event: 2. TEAE ir	$1 \ge 5\%$ of p	patients – 5 mg ve	ersus placebo – d	izziness						
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	17/265 (6.4%)	23/263 (8.7%)	RR 0.74 (0.4 to 1.36)	23 fewer per 1000 (from 52 fewer to 31 more)	LOW
Adverse	event: 2. TEAE ir	$1 \ge 5\%$ of p	oatients – 5 mg ve	ersus placebo – d	ysgeusia (dis	stortion or bad	taste)				
	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	30/265 (11.3%)	13/263 (4.9%)	RR 1.99 (0.71 to 5.57)	49 more per 1000 (from 14 fewer to 226 more)	LOW
Adverse	event: 2. TEAE ir	$1 \ge 5\%$ of p	patients – 5 mg ve	ersus placebo – h	eadache						
<u> </u>	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	9/265 (3.4%)	26/263 (9.9%)	RR 0.4 (0.14 to 1.14)	59 fewer per 1000 (from 85 fewer to 14 more)	LOW

Adverse e	vent: 2. TEAE in	$\geq 5\%$ of p	atients - 5 mg ve	rsus placebo - sec	dation						
3	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	28/265 (10.6%)	20/263 (7.6%)	RR 1.35 (0.78 to 2.34)	27 more per 1000 (from 17 fewer to 102 more)	LOW
Adverse e	vent: 2. TEAE in	$\geq$ 5% of p	atients – 10 mg v	ersus placebo - d	izziness						
3	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	19/259 (7.3%)	23/263 (8.7%)	RR 0.85 (0.47 to 1.53)	13 fewer per 1000 (from 46 fewer to 46 more)	LOW
Adverse e	vent: 2. TEAE in	$\geq$ 5% of p	atients - 10 mg v	ersus placebo - d	ysgeusia (dis	tortion or bad tast	e)	1			
3	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	37/259 (14.3%)	13/263 (4.9%)	RR 2.81 (1.53 to 5.18)	89 more per 1000 (from 26 more to 207 more)	LOW
Adverse e	vent: 2. TEAE in	$\geq$ 5% of p	atients – 10 mg v	ersus placebo – h	eadache						
3	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	7/259 (2.7%)	26/263 (9.9%)	RR 0.32 (0.1 to 1.04)	67 fewer per 1000 (from 89 fewer to 4 more)	LOW
Adverse e	vent: 2. TEAE in	$\geq 5\%$ of p	atients - 10 mg v	ersus placebo - se	edation						
3	randomised trials	serious <sup>1</sup>	no serious inconsistency	no serious indirectness	serious <sup>2</sup>	none	27/259 (10.4%)	20/263 (7.6%)	RR 1.37 (0.8 to 2.38)	28 more per 1000 (from 15 fewer to 105 more)	LOW

<sup>&</sup>lt;sup>1</sup> Risk of bias generally unclear and funding not reported.

<sup>&</sup>lt;sup>2</sup> Optimal information size (for dichotomous outcomes, OIS = 300 events; for continuous outcomes, OIS = 400 participants) not met.

<sup>&</sup>lt;sup>3</sup> Risk of bias generally unclear or high and funded by manufacturer.