

APPENDIX 19: INTERVENTIONS FOR LONG-TERM MANAGEMENT – STUDY CHARACTERISTICS

1.1 Pharmacological interventions.....2

Abbreviations

AUS	Australia	N Post	number of participants at post-treatment
AUT	Austria	NR	not reported
BEL	Belgium	N Rand	number of participants randomised
BUL	Bulgaria	NZL	New Zealand
BPI	bipolar I disorder	POL	Poland
CAN	Canada	RSA	Republic of South Africa
CZE	Czech Republic	TUR	Turkey
BRA	Brazil	TWN	Taiwan
DEN	Denmark	RUS	Russia
Dur	duration	SVK	Slovakia
ESP	Spain	SWE	Sweden
FRA	France	UKR	Ukraine
Freq	frequency	USA	United States of America
GBR	Great Britain		
GER	Germany		
GRE	Greece		
HUN	Hungary		
CRO	Croatia		
IND	India		
ITA	Italy		
MAS	Malaysia		
N/A	not applicable		
NED	the Netherlands		
NOR	Norway		

1.1 PHARMACOLOGICAL INTERVENTIONS

Study	Country	Age	% Female	% BPI	Concomitant medication	N Rand	N Post	Group	Dose	Freq	Dur
Lithium											
<i>Lithium at different doses</i>											
GELENBERG1989	USA	39	50%	100%	None	47	47	Lithium	1,400 mg	7	52
						47	47	Lithium	900 mg	7	52
JENSEN1995	DEN	59	58%	86%	Additional antipsychotics or antidepressants. Hypnotics allowed	25	25	Lithium	800 mg	7	65
						25	25	Lithium	1,200 mg	3.5	48
<i>Lithium compared with placebo</i>											
DUNNER1976	USA	51	58%	0%	Amitriptyline or imipramine for depression and chlorpromazine for mania	16	16	Lithium	0.8-1.2mEq/L	7	69
						24	24	Placebo	N/A	7	69
STALLONE1973	USA	51	52%	100%	Amitriptyline or imipramine for depression and chlorpromazine for mania	25	25	Lithium	900 mg	7	121
						27	27	Placebo	N/A	7	121
PRIEN1973	USA	44	35%	NR	None	101	NR	Lithium	1000 mg	7	104
						104	NR	Placebo	N/A	7	104
<i>Lithium compared with carbamazepine</i>											
COXHEAD1992	GBR	48	71%	NR	Temazepam only	16	NR	Lithium	400 mg	14	52
						15	NR	Carbamazepine	200 mg	14	52
HARTONG2003	NED	42	54%	76%	Benzodiazepines only	72	50	Lithium	800 mg	7	104
						72	44	Carbamazepine	400 mg	7	104
KLEINDIENST2000	GER	40	56%	100%	Psychotropic medication	58	NR	Lithium	26.8 mmol	7	130

Interventions for long-term management – study characteristics

Study	Country	Age	% Female	% BPI	Concomitant medication	N Rand	N Post	Group	Dose	Freq	Dur
						56	NR	Carbamazepine	635 mg	7	130
WOLF1997	HUN	44	64%	NR	Short-time hypnotics	84	84	Lithium	NR	7	52
						84	84	Carbamazepine	NR	7	52
<i>Lithium, carbamazepine, combined lithium and carbamazepine</i>											
DENICOFF1997	USA	41	52%	64%	None allowed	50	29	Lithium	0.5-1.2 mmol/L	7	52
						46	22	Carbamazepine	4-12 mg/L	7	52
						31	22	Lithium and carbamazepine	0.5-1.2 mmol/L/ 4-12 mg/L	7	52
<i>Lithium, valproate, combined lithium and valproate</i>											
GEDDES2010	GBR, FRA, USA, ITA	43	49%	100%	Non-investigational co-therapies allowed	110	87	Lithium	0.4-1.0 mmol/L	7	104
						110	89	Valproate	1000 mg	7	104
						110	87	Lithium and valproate	0.4-1.0 mmol/L /1000 mg	7	104
<i>Lithium, valproate and placebo</i>											
BOWDEN2000	NR	39	76%	100%	Lorazepam allowed. Haloperidol permitted during the second consecutive week of lorazepam use (first month only)	187	187	Lithium	0.8-1.2 mmol/L	7	52
						91	89	Valproate	71-125 ug/mL	7	52
						94	93	Placebo	N/A	7	52

Interventions for long-term management – study characteristics

Study	Country	Age	% Female	% BPI	Concomitant medication	N Rand	N Post	Group	Dose	Freq	Dur
<i>Lithium compared with valproate</i>											
CALABRESE2005c	USA	37	52%	40%	Lorazepam or alprazolam	32	NR	Lithium	1,400 mg	7	80
						28	NR	Valproate	1,600 mg	7	80
<i>Lithium compared with lamotrigine</i>											
LICHT2010	DEN, SWE	38	49%	100%	Antipsychotics and antidepressants allowed (≤ 6 months), benzodiazepines only (> 6 months)	78	NR	Lithium	0.69 mmol/L	7	104
						77	NR	Lamotrigine	379 mg	7	104
<i>Lamotrigine, lithium and placebo</i>											
BOWDEN2003	USA, AUS, AUT, BEL, CAN, GRE, NZL, NOR, POL, UKR	41	53%	100%	Chloral hydrate, lorazepam, temazepam or oxazepam	59	58	Lamotrigine	200 mg	7	76
						46	44	Lithium	0.8-1.1 mEq/L	7	76
						70	69	Placebo	N/A	7	76
CALABRESE2003	Multiple (not specified)	42	39%	100%	Chloral hydrate, lorazepam, temazepam, oxazepam or midazolam	121	NR	Lamotrigine	200 mg	7	72
						121	NR	Lithium	900 mg	7	72
						121	NR	Placebo	N/A	7	72
<i>Lithium, imipramine and placebo</i>											
PRIEN1973B	USA	43	23%	NR	None	18	18	Lithium	1,250 mg	7	104
						13	13	Imipramine	125 mg	7	104
						13	13	Placebo	N/A	7	104
<i>Lithium, imipramine and lithium and imipramine combined</i>											
PRIEN1984	NR	38	58%	NR	None	42	NR	Lithium	0.6-0.9 mEq/L	7	104
						36	NR	Imipramine	150 mg	7	104

Interventions for long-term management – study characteristics

Study	Country	Age	% Female	% BPI	Concomitant medication	N Rand	N Post	Group	Dose	Freq	Dur
						36	NR	Lithium and Imipramine	0.6-0.9 mEq/L/150 mg	7	104
<i>Olanzapine compared with lithium</i>											
TOHEN2005	Multiple (not specified)	42	53%	100%	Haloperidol, zuclopenthixol, benzodiazepine and anticholinergics	217	101	Olanzapine	11.9 mg	7	52
						214	70	Lithium	1,102.7 mg	7	52
<i>Quetiapine, lithium and placebo</i>											
WEISLER2011	Multiple (not specified)	40	53%	100%	None	404	404	Quetiapine	546 mg	7	104
						364	364	Lithium	900 mg	7	104
						404	404	Placebo	N/A	7	104
Antipsychotics											
<i>Aripiprazole compared with placebo</i>											
CARLSON2012	USA	39	65%	100%	Lorazepam, oxazepam, diazepam, chlorazepate and anticholinergics allowed	178	NR	Aripiprazole	17.4 mg	7	52
						173	NR	Placebo	N/A	7	52
<i>Aripiprazole compared with placebo (all on lithium or valproate)</i>											
MARCUS2011	USA, BRA, BUL, CRO, CZE, FRA, IND, RUS, RSA	39	55%	100%	All on lithium or valproate. Benzodiazepines, propranolol and anticholinergics allowed	168	162	Aripiprazole	15 mg	7	52
						169	164	Placebo	N/A	7	52
TOHEN2004	USA, CAN	41	52%	100%	All on lithium or valproate. Lorazepam and benztropine mesylate allowed	51	51	Olanzapine	8.6 mg	14	78
						48	48	Placebo	N/A	14	78

Interventions for long-term management – study characteristics

Study	Country	Age	% Female	% BPI	Concomitant medication	N Rand	N Post	Group	Dose	Freq	Dur
<i>Paliperidone, olanzapine and placebo</i>											
BERWAERTS2012	Multiple (not specified)	40	55%	100%	Lorazepam, clonazepam, or diazepam, nonbenzodiazepine hypnotics and anticholinergics	152	146	Paliperidone XR	6 mg	7	129
						83	82	Olanzapine	10 mg	7	129
						148	144	Placebo	N/A	7	129
<i>Quetiapine compared with placebo</i>											
YOUNG2012	Multiple (not specified)	40	60%	60%	Zolpidem tartrate or chloral hydrate and anticholinergics allowed	141	NR	Quetiapine	300 mg	7	52
						149	NR	Quetiapine	600 mg	7	52
						296	NR	Placebo	N/A	7	52
<i>Quetiapine compared with placebo (all on lithium or valproate)</i>											
SUPPES2009	USA, CAN	40	53%		All on lithium or valproate. Non-psychoactive medications, lorazepam, zolpidem tartrate, zopiclone, chloral hydrate and anticholinergics allowed	310	173	Quetiapine	519 mg	7	104
						313	229	Placebo	N/A	7	104
VIETA2008b	USA, AUS,	42	55%	100%	All on lithium or	336	336	Quetiapine	497 mg	7	104

Interventions for long-term management – study characteristics

Study	Country	Age	% Female	% BPI	Concomitant medication	N Rand	N Post	Group	Dose	Freq	Dur
	BEL, BUL, CZE, FRA, GER, HUN, ITA, NOR, POL, RUS, RSA, ESP, SVK, TUR, GBR				valproate. Zolpidem, zaleplon, zopiclone, chloral hydrate, lorazepam and anticholinergics allowed	367	367	Placebo	N/A	7	104
<i>Quetiapine compared with valproate</i>											
LANGOSCH2008	GER	42	60%	50%	No psychoactive medication allowed	24	21	Quetiapine	500 mg	7	52
						20	16	Valproate	1,300 mg	7	52
<i>Risperidone long-acting injectable compared with placebo</i>											
QUIROZ2010	AUT, IND, MAS, POL, RUS, SVK, ESP, TWN, UKR, USA	39	49%	100%	Nonbenzodiazepine hypnotics, benzodiazepines, propranolol, and anticholinergic medications allowed	154	135	Risperidone (injection)	25 mg	0.5	104
						149	133	Placebo (injection)	N/A	0.5	104
<i>Risperidone long-acting injectable, olanzapine and placebo</i>											
VIETA2012	Multiple (unspecified)	36	52%	100%	Non-benzodiazepine hypnotics, lorazepam, clonazepam, diazepam and anticholinergic medications allowed	137	135	Risperidone (injection)	25 mg	0.5	78
						138	137	Olanzapine	10 mg	7	78
						140	138	Placebo (injection)	N/A	0.5	78

Interventions for long-term management – study characteristics

Study	Country	Age	% Female	% BPI	Concomitant medication	N Rand	N Post	Group	Dose	Freq	Dur
<i>Risperidone long-acting injectable compared with treatment as usual</i>											
MACFADDEN2009	USA, IND	39	28%	100%	Antidepressants, mood stabilisers or anxiolytics	65	65	Risperidone (injection) + TAU	12.5 mg	0.5	52
						59	59	Placebo (injection) + TAU	N/A	0.5	52
BOBO2011b	USA	40	67%	73%	Oral antipsychotics, mood stabilisers, antidepressants, benzodiazepines and anticholinergics	25	20	Risperidone (injection) + TAU	27 mg	0.5	52
						25	25	TAU	N/A	0.5	52
Anticonvulsants											
<i>Gabapentin compared with placebo</i>											
VIETA2006	ESP	49	72%	76%	Lithium, valproate, carbamazepine or combination	12	12	Gabapentin	300 mg	7	52
						13	13	Placebo	N/A	7	52
<i>Oxcarbazepine compared with placebo</i>											
VIETA2008	ESP	44	65%	76%	All on lithium, lorazepam allowed	26	26	Oxcarbazepine	1,200 mg	7	52
						29	29	Placebo	N/A	7	52
Antidepressants											
<i>Imipramine compared with placebo (all on lithium)</i>											
QUITKIN1981	USA	37	52%	100%	Lithium only	37	37	Imipramine	125 mg	7	82
						38	38	Placebo	N/A	7	82
<i>Antidepressants compared with placebo</i>											
GHAEMI2010	USA	37	50%	50%	Lithium,	32	32	Antidepressants ¹	Variable	7	52

Interventions for long-term management – study characteristics

Study	Country	Age	% Female	% BPI	Concomitant medication	N Rand	N Post	Group	Dose	Freq	Dur
					lamotrigine and/or divalproex	38	38	Placebo	N/A	7	52

Note. ¹The most frequently employed antidepressant class was serotonin reuptake inhibitors (52%). Common specific agents were bupropion and paroxetine (22% each) and citalopram and venlafaxine (19% each). No tricyclic antidepressants were used.