1. Episodio maniacale

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Question: Should aripiprazole vs placebo be used for acute mania?

Bibliography: Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, Purgato M, Spineli LM, Goodwin GM, Geddes JR. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. Lancet 2011;378:1306-15.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Aripiprazole	Placebo	Relative (95% CI)	Absolute		
Response (follow-up mean 3 weeks; measured with: Mania rating scale score (mean change or endpoint score); Better indicated by lower values)												
6	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	984	972	-	SMD 0.308 higher (0.197 to 0.419 higher)	⊕⊕⊕O MODERATE	CRITICAL
Dropout rate												
6	randomised trials	serious[1]	serious[2]	no serious indirectness	no serious imprecision	none	-	0%	OR 1.16 (0.84 to 1.61)	-	⊕⊕OO LOW	CRITICAL

[1] High dropout rate in 10-30% of included studies
[2] I squared=62%

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Question: Should lithium vs placebo be used for acute mania?

Bibliography: Brown R, Stockton S, Purgato M, Spineli LM, Goodwin GM, Geddes JR. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. Lancet 2011;378:1306-15.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Lithium	Placebo	Relative (95% CI)	Absolute		
Response (follow-up mean 3 weeks; measured with: Mania rating scale score (mean change or endpoint score); Better indicated by lower values)												
7	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	695	671	-	SMD 0.4 higher (0.263 to 0.537 higher)	⊕⊕⊕O MODERATE	CRITICAL
Dropout rate (follow-up mean 3 weeks)												
7	randomised trials	serious[1]	serious[2]	no serious indirectness	no serious imprecision	none	-	0%	OR 1.099 (0.739 to 1.634)	-	⊕⊕OO LOW	CRITICAL

[1] High dropout rate in 10-30% of included studies

[2] I squared=60%

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Question: Should haloperidol vs placebo be used for acute mania?

Bibliography: Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, Purgato M, Spineli LM, Goodwin GM, Geddes JR. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. Lancet 2011;378:1306-15.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Haloperidol	Placebo	Relative (95% CI)	Absolute		
Response (follow-up mean 3 weeks; measured with: Mania rating scale score (mean change or endpoint score); Better indicated by lower values)												
6	randomised trials	serious[1]	serious[2]	no serious indirectness	no serious imprecision	very strong association[3]	652	633	-	SMD 0.581 higher (0.393 to 0.77 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Dropout rate												
6	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	0%	OR 1.378 (0.943 to 2.014)	-	⊕⊕⊕O MODERATE	CRITICAL

[1] High dropout rate in more than 30% of included studies
[2] I squared=58.6%
[3] Large effect size

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Question: Should quetiapine vs placebo be used for acute mania?

Bibliography: Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, Purgato M, Spineli LM, Goodwin GM, Geddes JR. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. Lancet 2011;378:1306-15.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quetiapine	Placebo	Relative (95% CI)	Absolute		
Response (measured with: Mania rating scale score (mean change or endpoint score); Better indicated by lower values)												
6	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	728	695	-	SMD 0.373 higher (0.237 to 0.509 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Dropout rate (follow-up mean 3 weeks)												
6	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	0%	OR 1.670 (1.136 to 2.454)	-	⊕⊕⊕⊕ HIGH	CRITICAL

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Question: Should ziprasidone vs placebo be used for acute mania?

Bibliography: Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, Purgato M, Spineli LM, Goodwin GM, Geddes JR. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. Lancet 2011;378:1306-15.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ziprasidone	Placebo	Relative (95% CI)	Absolute		
Response (measured with: Mania rating scale score (mean change or endpoint score); Better indicated by lower values)												
5	randomised trials	serious[1]	very serious[2]	no serious indirectness	no serious imprecision	none	798	769	-	SMD 0.245 higher (0.004 to 0.486 higher)	⊕OOO VERY LOW	CRITICAL
Dropout rate (follow-up mean 3 weeks)												
5	randomised trials	serious[1]	serious[3]	no serious indirectness	no serious imprecision	none	-	0%	OR 1.082 (0.711 to 1.646)	-	⊕⊕OO LOW	CRITICAL

[1] High dropout rate in 10-30% of included studies
[2] I squared=76.6%
[3] I squared=60%

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Question: Should olanzapine vs placebo be used for acute mania?

Bibliography: Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, Purgato M, Spineli LM, Goodwin GM, Geddes JR. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. Lancet 2011;378:1306-15.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Olanzapine**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Response (follow-up mean 3 weeks; measured with: Mania rating scale score (mean change or endpoint score); Better indicated by lower values)												
9	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1053	987	-	SMD 0.439 higher (0.318 to 0.56 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Dropout rate (follow-up mean 3 weeks)												
9	randomised trials	no serious risk of bias	serious[1]	no serious indirectness	no serious imprecision	none	-	0%	OR 1.672 (1.223 to 2.288)	-	⊕⊕⊕O MODERATE	CRITICAL

[1] I squared=60%

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Question: Should lamotrigine vs placebo be used for acute mania?

Bibliography: Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, Purgato M, Spineli LM, Goodwin GM, Geddes JR. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. Lancet 2011;378:1306-15.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Lamotrigine**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Response (follow-up mean 3 weeks; measured with: Mania rating scale score (mean change or endpoint score); Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	183	148	-	SMD 0.003 lower (0.219 lower to 0.213 higher)	⊕OOO VERY LOW	CRITICAL
Dropout rate (follow-up mean 3 weeks)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	-	0%	OR 0.796 (0.512 to 1.238)	-	⊕OOO VERY LOW	CRITICAL

[1] High dropout rate in more than 30% of included studies
[2] 95% CI ranges from substantial benefit with lamotrigine to substantial benefit with placebo

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Question: Should divalproex (or sodium valproate) vs placebo be used for acute mania?

Bibliography: Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, Purgato M, Spineli LM, Goodwin GM, Geddes JR. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. Lancet 2011;378:1306-15.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Divalproex (or sodium valproate)	Placebo	Relative (95% CI)	Absolute		
Response (follow-up mean 3 weeks; measured with: Mania rating scale score (mean change or endpoint score); Better indicated by lower values)												
6	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	643	586	-	SMD 0.162 higher (0.026 to 0.299 higher)	⊕⊕⊕O MODERATE	CRITICAL
Dropout rate (follow-up mean 3 weeks)												
6	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	-	0%	OR 1.259 (0.975 to 1.626)	-	⊕⊕OO LOW	CRITICAL

[1] High dropout rate in 10-30% of included studies
[2] 95% CI ranges from substantial benefit with divalproex to substantial benefit with placebo

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Question: Should risperidone (or paliperidone) vs placebo be used for acute mania?

Bibliography: Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, Purgato M, Spineli LM, Goodwin GM, Geddes JR. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. Lancet 2011;378:1306-15.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Risperidone (or paliperidone)**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Response (follow-up mean 3 weeks; measured with: Mania rating scale score (mean change or endpoint score); Better indicated by lower values)												
8	randomised trials	no serious risk of bias	serious[1]	no serious indirectness	no serious imprecision	strong association[2]	1173	994	-	SMD 0.50 higher (0.331 to 0.669 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Dropout rate (follow-up mean 3 weeks)												
7	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	0%	OR 1.85 (1.382 to 2.478)	-	⊕⊕⊕⊕ HIGH	CRITICAL

[1] I squared=69.0%
[2] Large effect size

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Question: Should asenapine vs placebo be used for acute mania?

Bibliography: Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, Purgato M, Spineli LM, Goodwin GM, Geddes JR. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. Lancet 2011;378:1306-15.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Asenapine	Placebo	Relative (95% CI)	Absolute		
Response (follow-up mean 3 weeks; measured with: Mania rating scale score (mean change or endpoint score); Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	320	262	-	SMD 0.42 higher (0.245 to 0.594 higher)	⊕⊕OO LOW	CRITICAL
Dropout rate (follow-up mean 3 weeks)												
2	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	-	0%	OR 1.254 (0.882 to 1.781)	-	⊕OOO VERY LOW	CRITICAL

[1] High dropout rate in 10-30% of included studies
[2] Only two direct comparisons (olanzapine and placebo)
[3] 95% CI ranges from no difference to substantial harm with asenapine

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Question: Should carbamazepine vs placebo be used for acute mania?

Bibliography: Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, Purgato M, Spineli LM, Goodwin GM, Geddes JR. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. Lancet 2011;378:1306-15.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Carbamazepine**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Response (follow-up mean 3 weeks; measured with: Mania rating scale score (mean change or endpoint score); Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	228	215	-	SMD 0.497 higher (0.304 to 0.69 higher)	⊕⊕⊕O MODERATE	CRITICAL
Dropout rate (follow-up mean 3 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	-	0%	OR 1.398 (0.961 to 2.034)	-	⊕⊕OO LOW	CRITICAL

[1] High dropout rate

[2] 95% CI ranges from no effect to substantial harm with carbamazepine

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Question: Should topiramate vs placebo be used for acute mania?

Bibliography: Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, Purgato M, Spineli LM, Goodwin GM, Geddes JR. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. Lancet 2011;378:1306-15.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Topiramate**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Response (follow-up mean 3 weeks; measured with: Mania rating scale score (mean change or endpoint score); Better indicated by lower values)												
5	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	686	680	-	SMD 0.056 lower (0.173 lower to 0.06 higher)	⊕⊕OO LOW	CRITICAL
Dropout rate (follow-up mean 3 weeks)												
5	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	-	0%	OR 0.62 (0.472 to 0.815)	-	⊕⊕OO LOW	CRITICAL

[1] High dropout rate
[2] Only two direct comparisons (placebo and lithium)

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Question: Should gabapentin vs placebo be used for acute mania?

Bibliography: Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, Purgato M, Spineli LM, Goodwin GM, Geddes JR. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. Lancet 2011;378:1306-15.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Gabapentin**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Response (follow-up mean 3 weeks; measured with: Mania rating scale score (mean change or endpoint score); Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	60	58	-	SMD 0.323 lower (0.727 lower to 0.081 higher)	⊕OOO VERY LOW	CRITICAL
Dropout rate (follow-up mean 3 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3,4]	none	-	0%	OR 0.572 (0.273 to 1.196)	-	⊕OOO VERY LOW	CRITICAL

[1] High dropout rate
[2] Only one direct comparison (placebo)
[3] 95% CI ranges from no difference to substantial benefit with gabapentin; number of participants is less than 200
[4] 95% CI ranges from substantial benefit with gabapentin to substantial benefit with placebo; number of participants is less than 200

Bibliografia

Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, Purgato M, Spineli LM, Goodwin GM, Geddes JR. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. Lancet 2011; 378: 1306-15.

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