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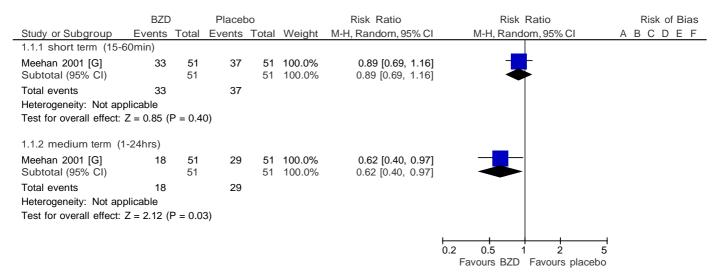
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Abbreviations

Avoreviai	ions
ABS	Aggressive Behavior Scale
ACES	Agitation and Calmness Evaluation Scale
AH	antihistamine
AP	antipsychotics
BZD	benzodiazepine
CI	confidence interval
ED	emergency department
EPS	extrapyramidal symptoms
G	general ward setting
H+P	haloperidol + promethazine
HAL	haloperidol
IM	intramuscular
IP	inpatient
IV	intravariance
M	mixed setting
M-H	Mantel-Haenzsel
OAS	Overt Aggression Scale
OLZ	olanzapine
PANSS-EC	Positive and Negative Syndrome Scale - Excited Component
PLB	placebo
QTc	corrected QT interval
SAS	Simpson-Angus Scale
SD	standard deviation

1 INTRAMUSCULAR BENZODIAZEPINE VERSUS PLACEBO [ADAPTED FROM GILLIES 2013]

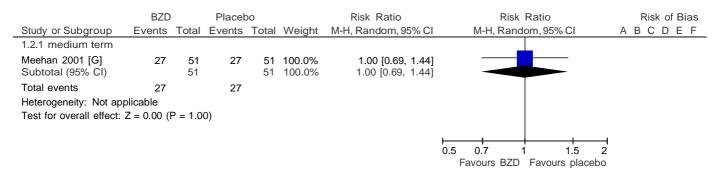
1.1 GLOBAL IMPRESSION: 1. NO IMPROVEMENT



Risk of bias legend

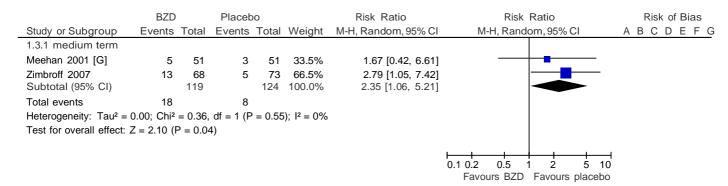
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

1.2 GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

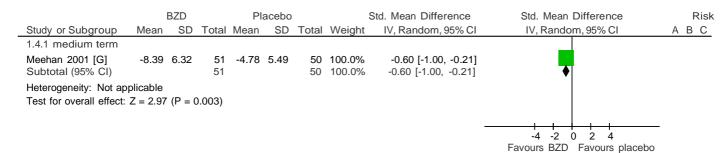
1.3 GLOBAL IMPRESSION: 3. SEDATION



Risk of bias legend

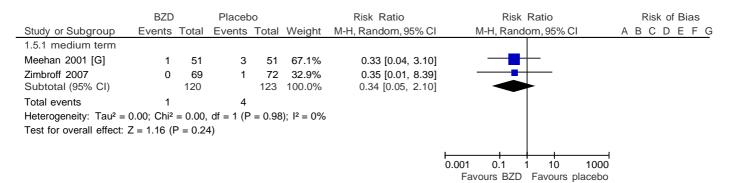
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

1.4 BEHAVIOUR: 1. AVERAGE CHANGE SCORE (ABS, HIGH = WORSE)



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

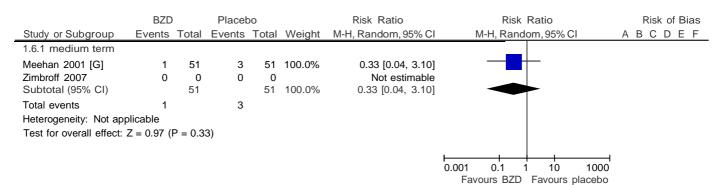
1.5 ADVERSE EFFECTS: 1. EXTRAPYRAMIDAL SYMPTOMS



Risk of bias legend

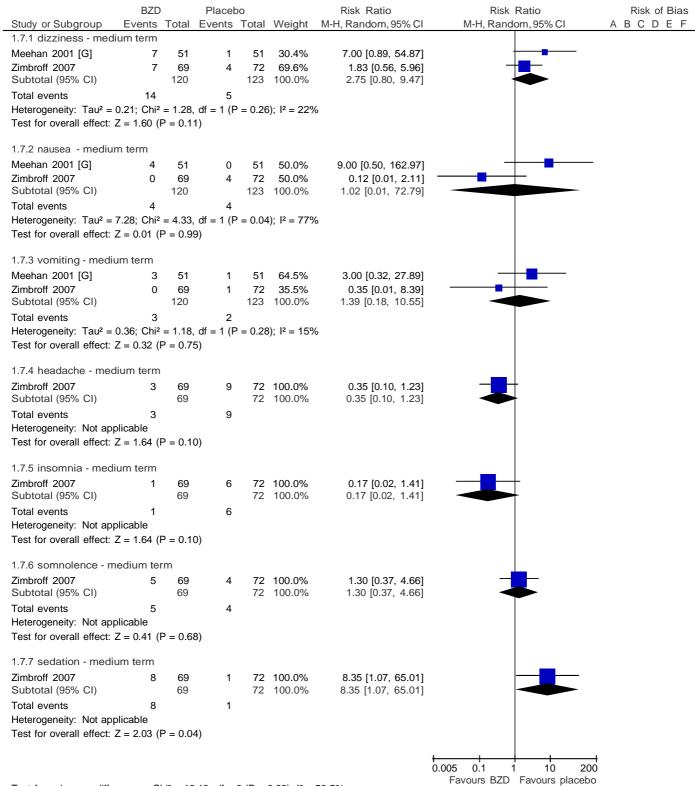
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

1.6 ADVERSE EFFECTS: 2. USE OF MEDICATION FOR EXTRAPYRAMIDAL SYMPTOMS



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

1.7 ADVERSE EFFECTS: 3. SPECIFIC

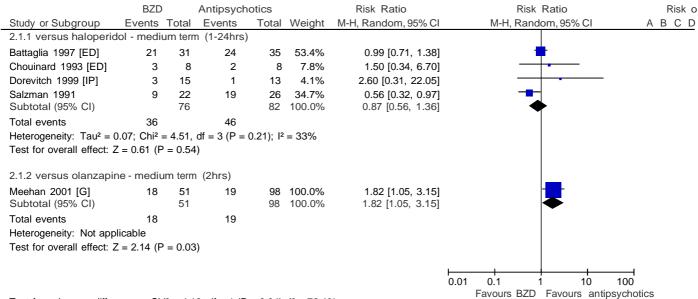


Test for subgroup differences: Chi² = 12.13, df = 6 (P = 0.06), I^2 = 50.5%

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

2 INTRAMUSCULAR BENZODIAZEPINE VERSUS ANTIPSYCHOTIC DRUG [ADAPTED FROM GILLIES 2013]

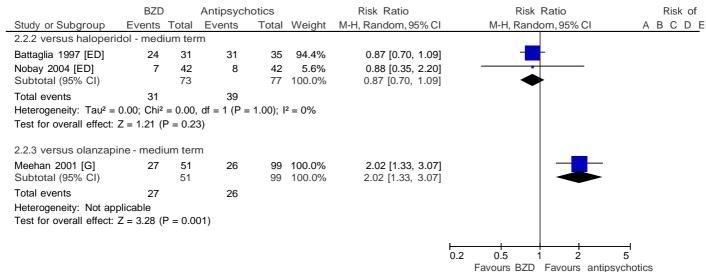
2.1 GLOBAL IMPRESSION: 1. NO IMPROVEMENT



Test for subgroup differences: $Chi^2 = 4.19$, df = 1 (P = 0.04), $I^2 = 76.1\%$

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

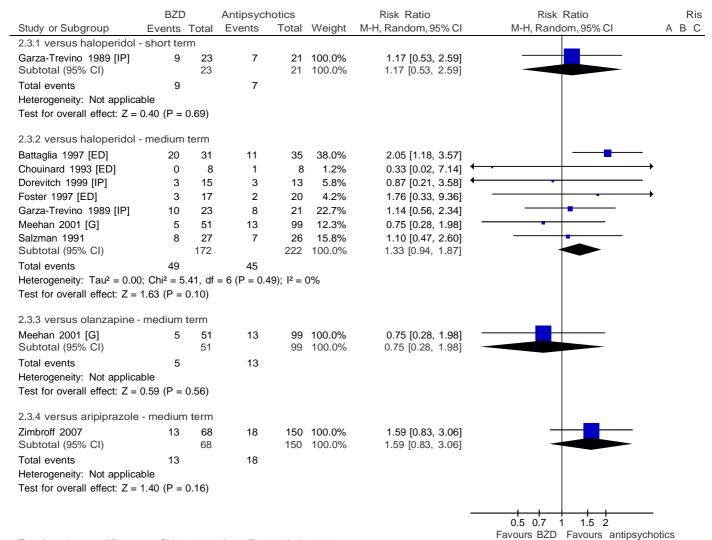
2.2 GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION



Test for subgroup differences: Chi² = 12.01, df = 1 (P = 0.0005), I^2 = 91.7%

- Risk of bias legend
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

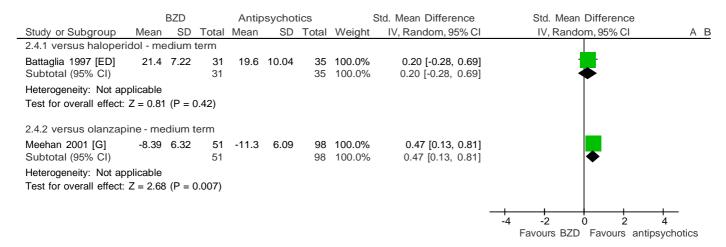
2.3 GLOBAL IMPRESSION: 3. SEDATION



Test for subgroup differences: Chi² = 1.69, df = 3 (P = 0.64), $I^2 = 0\%$

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

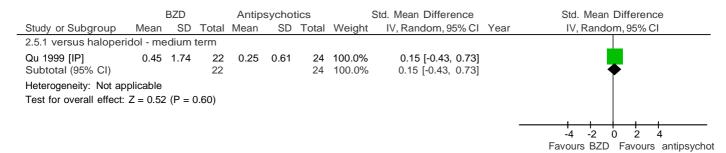
2.4 BEHAVIOUR: 1. AVERAGE CHANGE/ENDPOINT SCORE (ABS, HIGH = WORSE)



Risk of bias legend

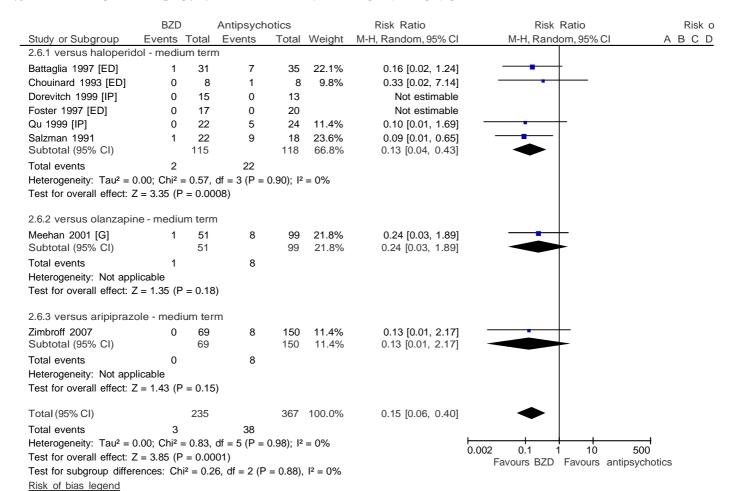
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

2.5 BEHAVIOUR: 2. AVERAGE CHANGE SCORE (OAS, HIGH = WORSE)



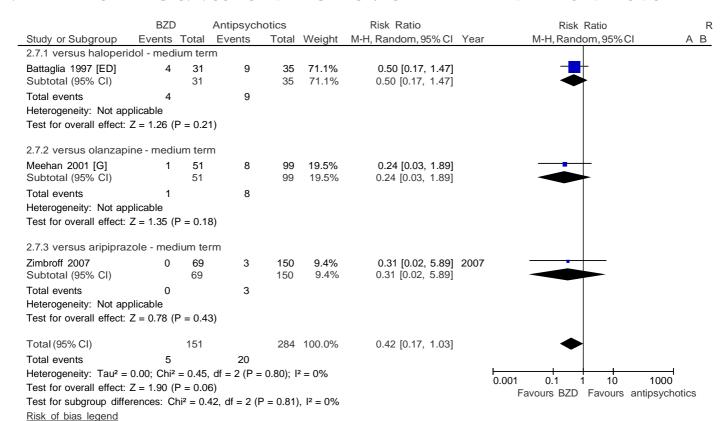
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

2.6 ADVERSE EFFECTS: 1. EXTRAPYRAMIDAL SYMPTOMS



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

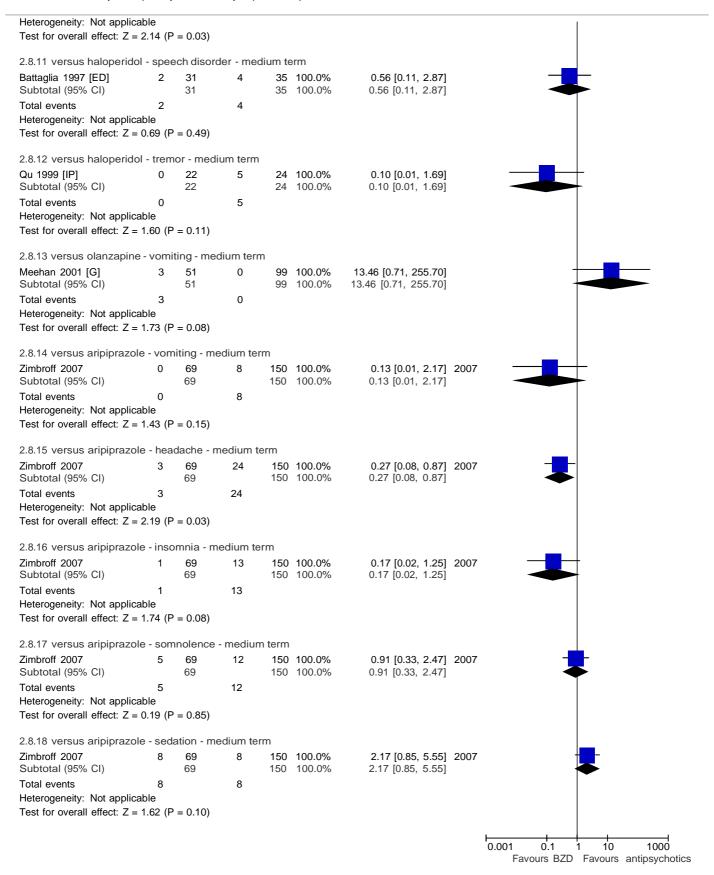
2.7 ADVERSE EFFECTS: 2. USE OF MEDICATION FOR EXTRAPYRAMIDAL SYMPTOMS



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

2.8 ADVERSE EFFECTS: 3. SPECIFIC

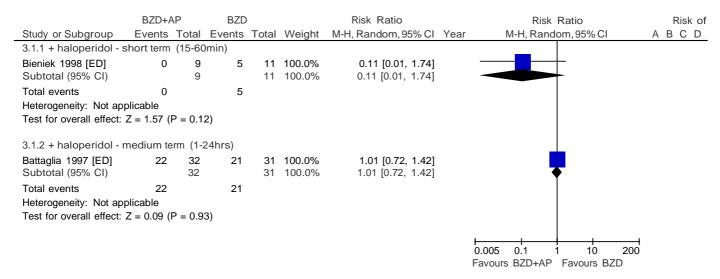
, , ,	BZD ents Tota	Antipsych al Events		Weight	Risk Ratio M-H, Random, 95% CI	Year	Risk Ratio M-H, Random, 95% CI	A B
2 8 1 versus haloperidol -	ataxia - m	nedium term				i Gai	W. F., Naridom, 30 /001	
Battaglia 1997 [ED] Subtotal (95% CI)	2 3'			100.0% 100.0%	2.26 [0.22, 23.71] 2.26 [0.22, 23.71]			
Total events Heterogeneity: Not applicab Test for overall effect: Z = 0	ole							
2.8.2 versus haloperidol -	apnoea - ı	medium term						
Nobay 2004 [ED] Subtotal (95% CI)	0 42		0 0		Not estimable Not estimable			
Total events Heterogeneity: Not applicab Test for overall effect: Not a		1						
2.8.3 versus haloperidol -	dizziness	- medium ter	m					
Battaglia 1997 [ED] Subtotal (95% CI)	3 3			100.0% 100.0%	1.13 [0.25, 5.19] 1.13 [0.25, 5.19]			
Total events Heterogeneity: Not applicab Test for overall effect: Z = 0		3 (.88)						
2.8.4 versus aripiprazole -	dizziness	s - medium te	rm					
Zimbroff 2007 Subtotal (95% CI)	7 69	9 11	150	100.0% 100.0%	1.38 [0.56, 3.42] 1.38 [0.56, 3.42]	2007	-	
Total events Heterogeneity: Not applicab	7 ole	11					•	
Test for overall effect: Z = 0	·	,						
2.8.5 versus olanzapine - o Meehan 2001 [G]	dizziness 7 5			100.0%	1.51 [0.60, 3.82]			
Subtotal (95% CI) Total events	. 5′ 7			100.0%	1.51 [0.60, 3.82]		*	
Heterogeneity: Not applicab Test for overall effect: Z = 0	ole							
2.8.6 versus haloperidol - o	dry mouth	n - medium te	rm					
Battaglia 1997 [ED] Subtotal (95% CI)	5 3°			100.0% 100.0%	1.88 [0.49, 7.24] 1.88 [0.49, 7.24]		-	
Total events Heterogeneity: Not applicab Test for overall effect: Z = 0		3						
Test for overall energy / = 0	.92 (F = 0	.30)						
2.8.7 versus haloperidol -	heart rate	_			0.22 [0.01, 4.29]		_	
2.8.7 versus haloperidol - Qu 1999 [IP] Subtotal (95% CI)	0 22	2 2	24	n 100.0% 100.0%	0.22 [0.01, 4.29] 0.22 [0.01, 4.29]			
2.8.7 versus haloperidol - Qu 1999 [IP]	0 22 0 0 ole	2 2 2 2 2	24	100.0%				
2.8.7 versus haloperidol - Qu 1999 [IP] Subtotal (95% CI) Total events Heterogeneity: Not applicab	0 22 0 ole .00 (P = 0	2 2 2 2	24 24	100.0%				
2.8.7 versus haloperidol - Qu 1999 [IP] Subtotal (95% CI) Total events Heterogeneity: Not applicab Test for overall effect: Z = 1	0 22 0 ole .00 (P = 0	2 2 2 2 .32) ive - medium 2 1	24 24	100.0%				
2.8.7 versus haloperidol - Qu 1999 [IP] Subtotal (95% CI) Total events Heterogeneity: Not applicab Test for overall effect: Z = 1 2.8.8 versus haloperidol - I Nobay 2004 [ED] Subtotal (95% CI) Total events	0 22 0 oble .00 (P = 0 hypotensi 0 42 0	2 2 2 2 .32) ive - medium 2 1	24 24 term 0	100.0%	0.22 [0.01, 4.29] Not estimable			
2.8.7 versus haloperidol - Qu 1999 [IP] Subtotal (95% CI) Total events Heterogeneity: Not applicab Test for overall effect: Z = 1 2.8.8 versus haloperidol - I Nobay 2004 [ED] Subtotal (95% CI)	0 22 0 oble .00 (P = 0 hypotensi 0 42 0 oble	2 2 2 232) ive - medium 2 1 2	24 24 term 0	100.0%	0.22 [0.01, 4.29] Not estimable			
2.8.7 versus haloperidol - Qu 1999 [IP] Subtotal (95% CI) Total events Heterogeneity: Not applicab Test for overall effect: Z = 1 2.8.8 versus haloperidol - I Nobay 2004 [ED] Subtotal (95% CI) Total events Heterogeneity: Not applicab	0 22 0 oble .00 (P = 0 hypotensi 0 42 0 oble applicable	2 2 232) ive - medium 2 1 2 1	24 24 term 0	100.0%	0.22 [0.01, 4.29] Not estimable			
2.8.7 versus haloperidol - Qu 1999 [IP] Subtotal (95% CI) Total events Heterogeneity: Not applicab Test for overall effect: Z = 1 2.8.8 versus haloperidol - I Nobay 2004 [ED] Subtotal (95% CI) Total events Heterogeneity: Not applicab Test for overall effect: Not a	0 22 0 oble .00 (P = 0 hypotensi 0 42 0 oble applicable	2 2 2 2 2	24 24 term 0 0	100.0%	0.22 [0.01, 4.29] Not estimable			
2.8.7 versus haloperidol - Qu 1999 [IP] Subtotal (95% CI) Total events Heterogeneity: Not applicab Test for overall effect: Z = 1 2.8.8 versus haloperidol - I Nobay 2004 [ED] Subtotal (95% CI) Total events Heterogeneity: Not applicab Test for overall effect: Not a 2.8.9 versus olanzapine - I Meehan 2001 [G] Subtotal (95% CI) Total events Heterogeneity: Not applicab	0 22 0 ole .00 (P = 0 hypotensi 0 42 0 ole applicable nausea - r 4 50	2 2 2 2 2.32) ive - medium 2 1 2 1 medium term 1 1	24 24 term 0 0	100.0% 100.0%	0.22 [0.01, 4.29] Not estimable Not estimable 7.76 [0.89, 67.67]			
2.8.7 versus haloperidol - Qu 1999 [IP] Subtotal (95% CI) Total events Heterogeneity: Not applicab Test for overall effect: Z = 1 2.8.8 versus haloperidol - I Nobay 2004 [ED] Subtotal (95% CI) Total events Heterogeneity: Not applicab Test for overall effect: Not a 2.8.9 versus olanzapine - I Meehan 2001 [G] Subtotal (95% CI) Total events	0 22 0 ole .00 (P = 0 hypotensi 0 42 0 ole applicable nausea - r 4 50	2 2 2 2 2.32) ive - medium 2 1 2 1 medium term 1 1	24 24 term 0 0	100.0% 100.0%	0.22 [0.01, 4.29] Not estimable Not estimable 7.76 [0.89, 67.67]			
2.8.7 versus haloperidol - Qu 1999 [IP] Subtotal (95% CI) Total events Heterogeneity: Not applicable Test for overall effect: Z = 1 2.8.8 versus haloperidol - In Nobay 2004 [ED] Subtotal (95% CI) Total events Heterogeneity: Not applicable Test for overall effect: Not an American 2001 [G] Subtotal (95% CI) Total events Heterogeneity: Not applicable Test for overall effect: Z = 1 2.8.10 versus aripiprazole	0 22 0 ole .00 (P = 0. hypotensi 0 42 0 ole applicable nausea - r 4 5: 5: 4 ole .86 (P = 0.	2 2 2 2 3.32) ive - medium 2 1 2 1 medium term 1 1 1 1 .06) - medium ter	24 24 term 0 0	100.0% 100.0%	0.22 [0.01, 4.29] Not estimable Not estimable 7.76 [0.89, 67.67] 7.76 [0.89, 67.67]			
2.8.7 versus haloperidol - Qu 1999 [IP] Subtotal (95% CI) Total events Heterogeneity: Not applicab Test for overall effect: Z = 1 2.8.8 versus haloperidol - I Nobay 2004 [ED] Subtotal (95% CI) Total events Heterogeneity: Not applicab Test for overall effect: Not a 2.8.9 versus olanzapine - I Meehan 2001 [G] Subtotal (95% CI) Total events Heterogeneity: Not applicab Test for overall effect: Z = 1	0 22 0 ole .00 (P = 0. hypotensi 0 42 0 ole applicable nausea - r 4 52 54	2 2 2 2 2 2 2 2 2	24 24 term 0 0 99 99	100.0% 100.0%	0.22 [0.01, 4.29] Not estimable Not estimable 7.76 [0.89, 67.67]	2007		



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

3 INTRAMUSCULAR BENZODIAZEPINE PLUS ANTIPSYCHOTIC DRUG SAME BENZODIAZEPINE [ADAPTED FROM GILLIES 2013]

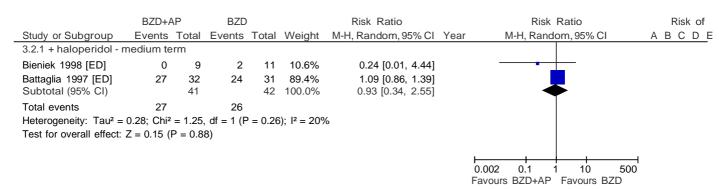
3.1 GLOBAL IMPRESSION: 1. NO IMPROVEMENT



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

3.2 GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

3.3 GLOBAL IMPRESSION: 3. SEDATION

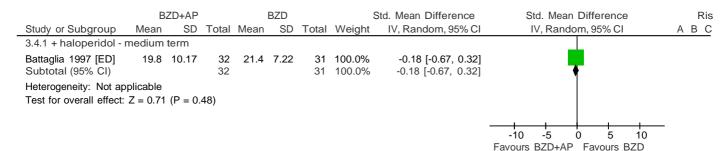
	BZD+	AP	BZC)		Risk Ratio		Risk F	Ratio	Ris
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Rando	m, 95% CI	АВС
3.3.1 +haloperidol - shor	t term									
Garza-Trevino 1989 [IP]	18	24	9	23	100.0%	1.92 [1.10, 3.35]		-		
Subtotal (95% CI)		24		23	100.0%	1.92 [1.10, 3.35]		-	•	
Total events	18		9							
Heterogeneity: Not applica	able									
Test for overall effect: Z =	2.28 (P =	0.02)								
3.3.2 +haloperidol - med	ium term									
Battaglia 1997 [ED]	20	32	20	31	74.4%	0.97 [0.67, 1.41]		-	-	
Garza-Trevino 1989 [IP]	6	24	10	23	25.6%	0.57 [0.25, 1.33]			=	
Subtotal (95% CI)		56		54	100.0%	0.85 [0.53, 1.35]		•	>	
Total events	26		30							
Heterogeneity: $Tau^2 = 0.04$	4; Chi ² = 1	.36, df	= 1 (P = 0)	0.24); l ²	$^{2} = 27\%$					
Test for overall effect: Z =	0.69 (P =	0.49)								
							-	1 1 0.05 0.2 1	 5 20	
									Favours BZD	,
Toot for cubaroup differen	ooc: Chi2	_ 1 02	df _ 1 /D	_ 0 03/	12 _ 70 2	0/		arodio BZD1/1	. avoaio DZD	

Test for subgroup differences: $Chi^2 = 4.82$, df = 1 (P = 0.03), $I^2 = 79.3\%$

Risk of bias legend

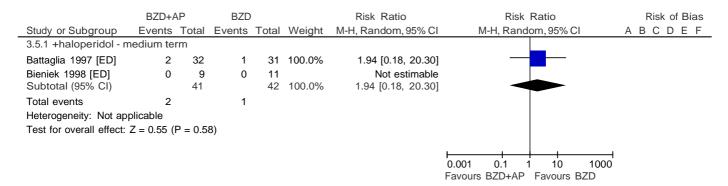
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

3.4 BEHAVIOUR: 1. AVERAGE ENDPOINT SCORE (ABS, HIGH = WORSE)



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

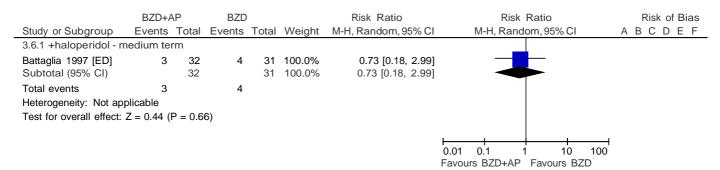
3.5 ADVERSE EFFECTS: 1. EXTRAPYRAMIDAL SYMPTOMS



Risk of bias legend

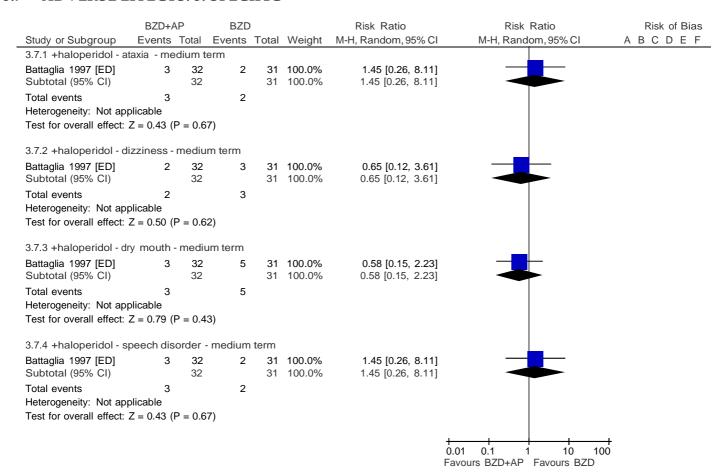
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

3.6 ADVERSE EFFECTS: 2. USE OF MEDICATION FOR EXTRAPYRAMIDAL SYMPTOMS



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

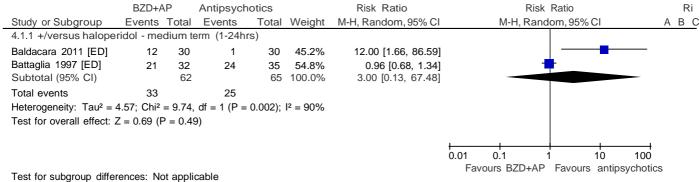
3.7 ADVERSE EFFECTS: 3. SPECIFIC



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

INTRAMUSCULAR BENZODIAZEPINE PLUS ANTIPSYCHOTIC DRUG SAME ANTIPSYCHOTIC DRUG [ADAPTED FROM GILLIES 2013]

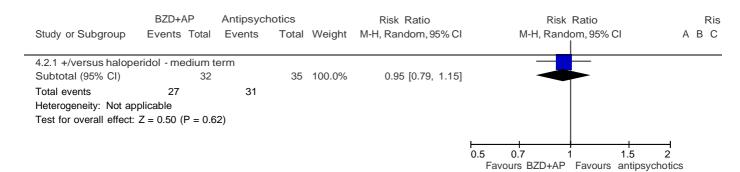
GLOBAL IMPRESSION: 1. NO IMPROVEMENT 4.1



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION 4.2



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

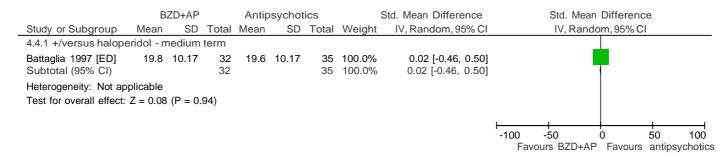
4.3 GLOBAL IMPRESSION: 3. SEDATION

	BZD+AP		Antipsychotics		Risk Ratio	Risk Ratio
Study or Subgroup	Events To	otal	Events Total	I Weight	M-H, Random, 95% CI	M-H, Random, 95% CI A
4.3.1 +/versus haloperide	ol - short teri	m				
Garza-Trevino 1989 [IP] Subtotal (95% CI)	18	24 24	7 2			
Total events Heterogeneity: Not application	18 able		7			
Test for overall effect: Z =	2.45 (P = 0.0)	01)				
4.3.2 +/versus haloperido	ol - medium	term				
Baldacara 2011 [ED]	12	30	3 3	26.8%	4.00 [1.25, 12.75]	
Battaglia 1997 [ED]	20	32	11 3	40.4%	1.99 [1.14, 3.47]	
Garza-Trevino 1989 [IP] Subtotal (95% CI)	6	24 86	8 2 80		0.66 [0.27, 1.58] 1.67 [0.67, 4.12]	
Total events	38		22			
Heterogeneity: $Tau^2 = 0.4$	5; $Chi^2 = 6.90$), df =	$= 2 (P = 0.03); I^2 =$	71%		
Test for overall effect: Z =	1.10 (P = 0.2)	27)				
						0.02 0.1 1 10 Favours BZD+AP Favours antipsyc

Risk of bias legend

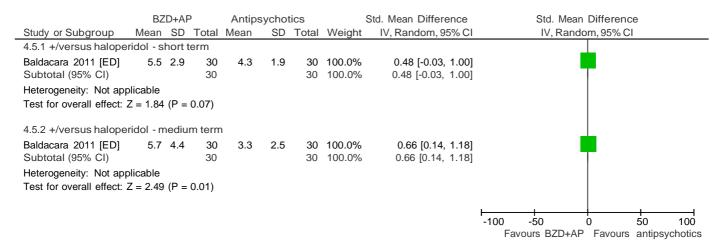
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

4.4 BEHAVIOUR: 1. AVERAGE ENDPOINT SCORE (ABS, HIGH = WORSE)



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

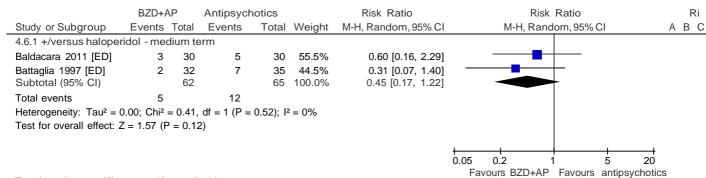
4.5 BEHAVIOUR: 2. AVERAGE ENDPOINT SCORE (OAS, HIGH = WORSE)



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

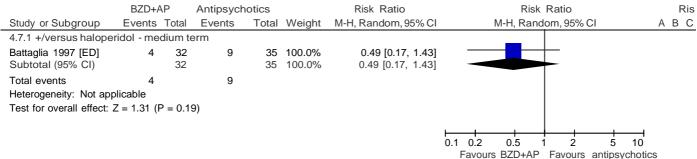
4.6 ADVERSE EFFECTS: 1. EXTRAPYRAMIDAL SYMPTOMS



Test for subgroup differences: Not applicable

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

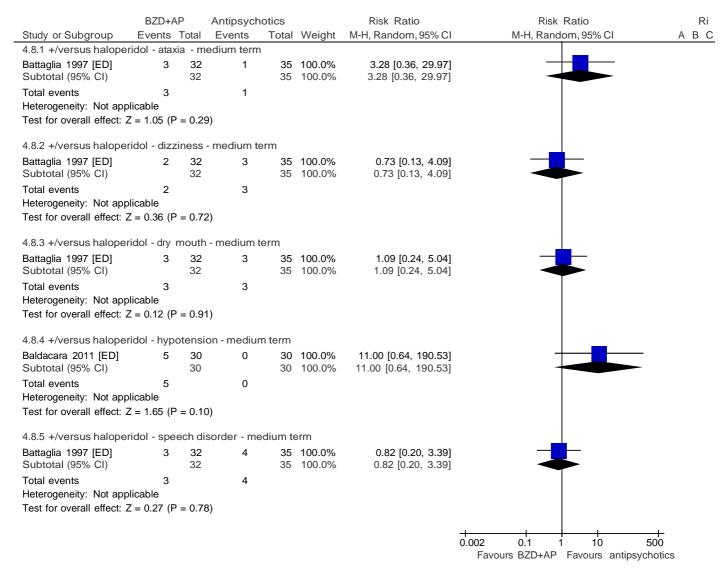
4.7 ADVERSE EFFECTS: 2. USE OF MEDICATION FOR EXTRAPYRAMIDAL SYMPTOMS



Test for subgroup differences: Not applicable

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

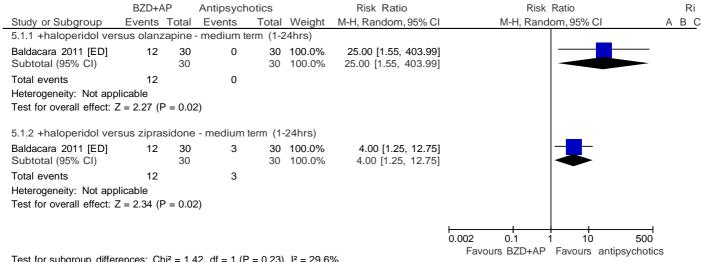
4.8 ADVERSE EFFECTS: 3. SPECIFIC



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

INTRAMUSCULAR BENZODIAZEPINE PLUS ANTIPSYCHOTIC DRUG 5 DIFFERENT ANTIPSYCHOTIC DRUG [ADAPTED FROM GILLIES 2013]

GLOBAL IMPRESSION: 1. NO IMPROVEMENT 5.1

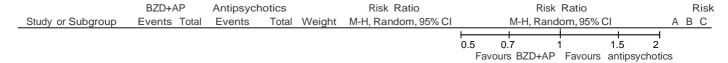


Test for subgroup differences: $Chi^2 = 1.42$, df = 1 (P = 0.23), $I^2 = 29.6\%$

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

5.2 GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

5.3 GLOBAL IMPRESSION: 3. SEDATION

	BZD+A	·P	Antipsycl	notics		Risk Ratio	Risk	Ratio	Ri
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Ranc	lom, 95% CI	АВС
5.3.1 +haloperidol vers	sus olanz	apine -	- medium t	erm					
Baldacara 2011 [ED] Subtotal (95% CI)	12	30 30	1	30 30	100.0% 100.0%	12.00 [1.66, 86.59] 12.00 [1.66, 86.59]			<u> </u>
Total events Heterogeneity: Not app	12 licable		1						
Test for overall effect: Z	z = 2.46 (P)	= 0.01	1)						
5.3.2 +haloperidol vers	sus zipras	sidone	- medium	term					
Baldacara 2011 [ED] Subtotal (95% CI)	12	30 30	3	30 30	100.0% 100.0%	4.00 [1.25, 12.75] 4.00 [1.25, 12.75]			
Total events	12		3						
Heterogeneity: Not app	licable								
Test for overall effect: Z	' = 2.34 (P	= 0.02	2)						
							0.01 0.1	1 10	100
Test for subgroup differ	onaca: Ch	:2 0 0	00 df 1/F	0 0 25\	12 00/		Favours BZD+AP	Favours antips	ychotics

Test for subgroup differences: Chi² = 0.88, df = 1 (P = 0.35), I^2 = 0%

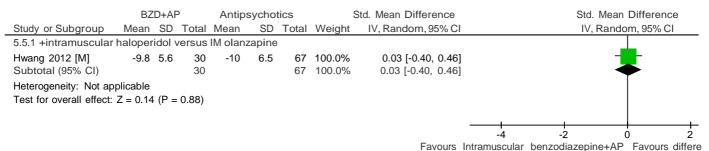
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

5.4 BEHAVIOUR: 1. AVERAGE CHANGE SCORE (OAS, HIGH = WORSE)

Study or Subgroup 5.4.1 +haloperidol ver		SD	T-4-1					Std. Mean Difference		Std. Mean Difference
						Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
	sus ola	nzapi	ine - sh	ort term	1					
Baldacara 2011 [ED] Subtotal (95% CI)	5.5	2.9	30 30	3.4	1	30 30	100.0% 100.0%	0.96 [0.42, 1.49] 0.96 [0.42, 1.49]		-
Heterogeneity: Not app Test for overall effect: 2		(P =	0.0005)						
5.4.2 +haloperidol ver	sus ola	nzapi	ine - m	edium te	erm					
Baldacara 2011 [ED] Subtotal (95% CI)	5.7	4.4	30	2.8	0.5	30 30	100.0% 100.0%	0.91 [0.38, 1.45] 0.91 [0.38, 1.45]		•
Heterogeneity: Not app Test for overall effect: 2		(P =	0.0008)						
5.4.3 +haloperidol ver	sus zipi	rasido	one - s	hort terr	n					<u>L</u>
Baldacara 2011 [ED] Subtotal (95% CI)	5.5	2.9	30 30	4.3	1		100.0% 100.0%	0.55 [0.03, 1.06] 0.55 [0.03, 1.06]		
Heterogeneity: Not app Test for overall effect: 2		(P =	0.04)							
5.4.4 +haloperidol ver	sus zipi	rasido	one - n	nedium t	term					
Baldacara 2011 [ED] Subtotal (95% CI)	5.7	4.4	30 30	2.6	0.9	30 30	100.0% 100.0%	0.96 [0.43, 1.50] 0.96 [0.43, 1.50]		
Heterogeneity: Not app Test for overall effect: 2		(P =	0.0004	.)						
										-4 -2 0 2 4 Favours BZD+AP Favours antips

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

5.5 BEHAVIOUR: 2. AVERAGE CHANGE SCORE (PANSS-EC) - 2 HOURS AFTER FIRST INJECTION

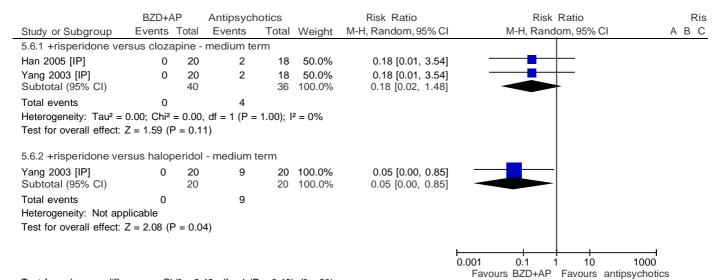


Test for subgroup differences: Not applicable

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

5.6 ADVERSE EFFECTS: 1. SIDE EFFECTS



Test for subgroup differences: $Chi^2 = 0.48$, df = 1 (P = 0.49), $I^2 = 0\%$

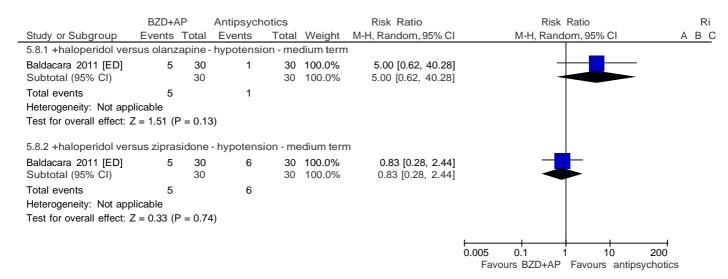
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

5.7 ADVERSE EFFECTS: 2. EXTRAPYRAMIDAL SYMPTOMS

	BZD+A	P	Antipsych	notics		Risk Ratio	Risk	Ratio	Ri
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Rand	dom, 95% CI	A B (
5.7.1 +haloperidol vei	sus olanza	apine ·	medium te	erm					
Baldacara 2011 [ED]	3	30	0	30	54.0%	7.00 [0.38, 129.93]			
Hwang 2012 [M] Subtotal (95% CI)	1	30 60	0	37 67	46.0% 100.0%	3.68 [0.16, 87.14] 5.21 [0.61, 44.54]			<u> </u>
Total events	4		0						
Test for overall effect: 2 5.7.2 +haloperidol ver Baldacara 2011 [ED]	•		,	30	100.0%	7.00 [0.38, 129.93]	_		
Subtotal (95% CI) Total events Heterogeneity: Not app Test for overall effect: 2			0	30	100.0%	7.00 [0.38, 129.93]			
							0.005 0.1 Favours BZD+AP	1 10	200

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

5.8 ADVERSE EFFECTS: 3. SPECIFIC



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

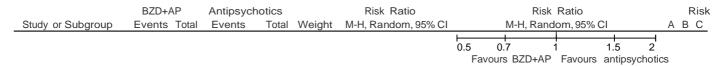
6 INTRAMUSCULAR BENZODIAZEPINE PLUS ANTIPSYCHOTIC DRUG VERSUS ANTIPSYCHOTIC DRUG PLUS ANOTHER ANTIPSYCHOTIC DRUG [ADAPTED FROM GILLIES 2013]

6.1 GLOBAL IMPRESSION: 1. NO IMPROVEMENT

	BZD+AP	Antipsychotics	;	Risk Ratio	Ris	Risk Ratio		
Study or Subgroup	Events Total	Events Tot	al Weight	M-H, Random, 95% CI	M-H, Rar	ndom, 95% CI	АВС	
					H	+ + + + + + + + + + + + + + + + + + + +		
					0.002 0.1	1 10	500	
					Favours BZD+AI	P Favours antip	sychotics	

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

6.2 GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

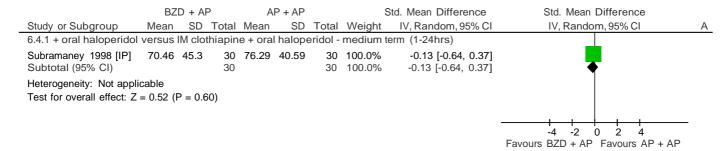
6.3 GLOBAL IMPRESSION: 3. SEDATION



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

6.4 BEHAVIOUR: 1. AVERAGE ENDPOINT SCORE (OAS, HIGH = WORSE)



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

6.5 ADVERSE EFFECTS

	BZD+AP	Antipsych	notics		Risk Ratio		Risk Ratio				Risk
Study or Subgroup	Events Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Random, 95% CI			Α	ВС
						1					
						0.01	0.1	1 10	100		
						Fav	ours BZD+AP	Favours an	tipsychotic	s	

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

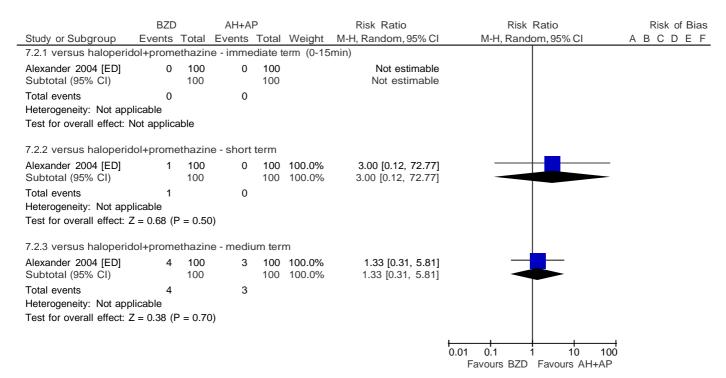
7 INTRAMUSCULAR BENZODIAZEPINE VERSUS ANTIPSYCHOTIC DRUG PLUS ANTIHISTAMINE [ADAPTED FROM GILLIES 2013]

7.1 GLOBAL IMPRESSION: 1. NO IMPROVEMENT

	BZD		AH+A	Р	Risk Ratio Risk		Ratio	Risk of Bias	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Rand	lom, 95% CI	ABCDEF
7.1.1 versus haloperio	dol+prome	ethazir	ne - imme	diate t	erm (0-15	imin)			
Alexander 2004 [ED]	70	100	39	100	100.0%	1.79 [1.36, 2.37]		- 	
Subtotal (95% CI)		100		100	100.0%	1.79 [1.36, 2.37]		•	
Total events	70		39						
Heterogeneity: Not app	licable								
Test for overall effect: 2	Z = 4.14 (F	o < 0.00	001)						
7.1.2 versus haloperio	lol+prome	ethazir	ne - short	term (15-60min)			
Alexander 2004 [ED]	42	100	17		100.0%	2.47 [1.51, 4.03]			
Subtotal (95% CI)		100		100	100.0%	2.47 [1.51, 4.03]			
Total events	42		17						
Heterogeneity: Not app									
Test for overall effect: 2	Z = 3.61 (F)	P = 0.00	003)						
7.1.3 versus haloperid	lol+prome	ethazir	ne - mediu	um terr	n (1-24hr:	s)			
Alexander 2004 [ED]	26	100	12	100	100.0%	2.17 [1.16, 4.05]			
Subtotal (95% CI)		100		100	100.0%	2.17 [1.16, 4.05]			
Total events	26		12						
Heterogeneity: Not app	licable								
Test for overall effect: 2	Z = 2.42 (F)	P = 0.02	2)						
									→
							0.1 0.2 0.5	. – .	10
							Favours BZD	Favours AH+AI	D

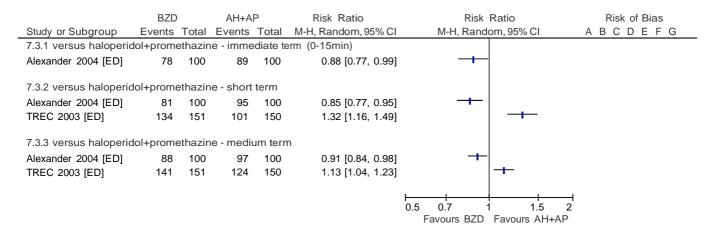
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

7.2 GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION



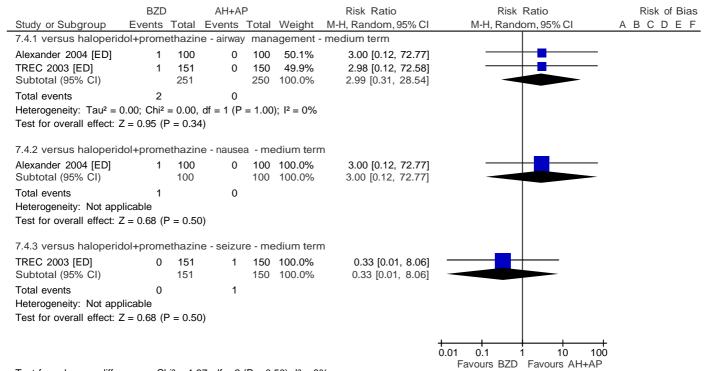
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

7.3 GLOBAL IMPRESSION: 3. SEDATION (TRANQUIL OR ASLEEP)



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

7.4 ADVERSE EFFECTS: 1. SPECIFIC

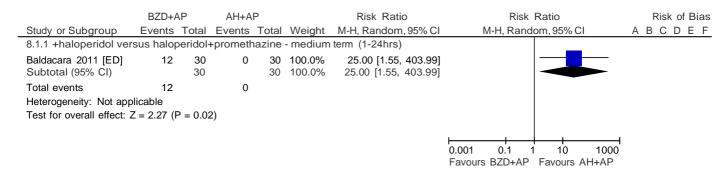


Test for subgroup differences: Chi² = 1.37, df = 2 (P = 0.50), I^2 = 0% Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

8 INTRAMUSCULAR BENZODIAZEPINE PLUS ANTIPSYCHOTIC DRUG VERSUS ANTIPSYCHOTIC DRUG PLUS ANTIHISTAMINE [ADAPTED FROM GILLIES 2013]

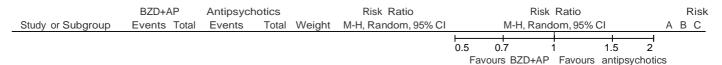
8.1 GLOBAL IMPRESSION: 1. NO IMPROVEMENT



Risk of bias legend

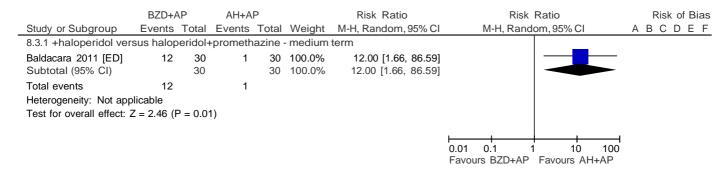
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

8.2 GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

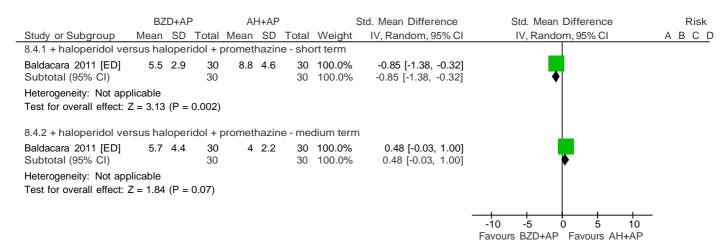
8.3 GLOBAL IMPRESSION: 3. SEDATION



Risk of bias legend

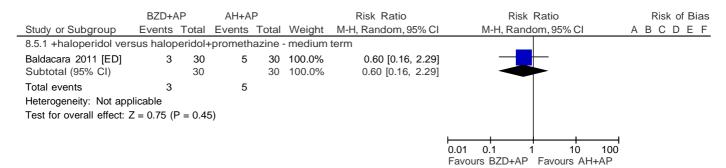
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

8.4 BEHAVIOUR: 1. AVERAGE ENDPOINT SCORE (OAS, HIGH = WORSE)



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

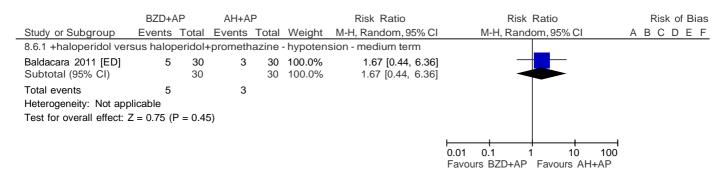
8.5 ADVERSE EFFECTS: 1. EXTRAPYRAMIDAL SYMPTOMS



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

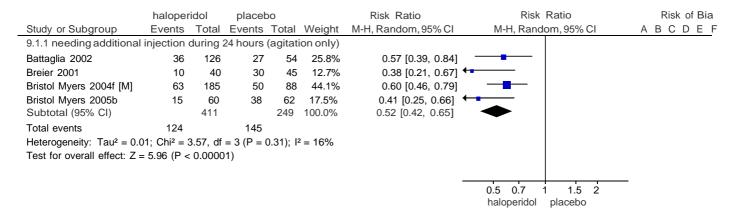
8.6 ADVERSE EFFECTS: 2. SPECIFIC



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

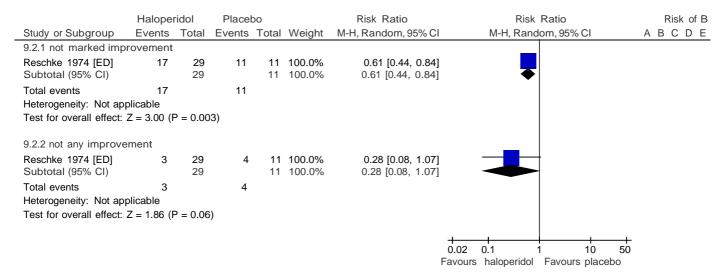
9 INTRAMUSCULAR HALOPERIDOL VERSUS PLACEBO [ADAPTED FROM POWNEY 2012]

9.1 REPEATED NEED FOR TRANQUILLISATION



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

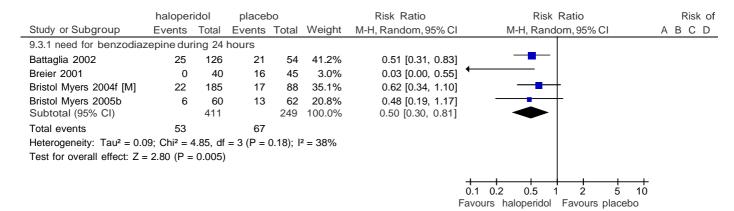
9.2 GLOBAL IMPRESSION: 1. NOT IMPROVED



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

9.3 GLOBAL IMPRESSION: 2. NEED FOR BENZODIAZEPINE DURING 24 HOURS



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

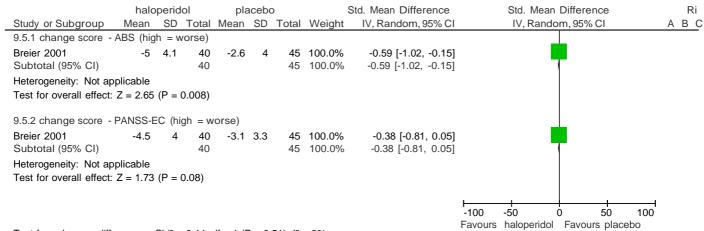
9.4 SPECIFIC BEHAVIOUR - AGITATION: 2A. AVERAGE SCORE - BY ABOUT 2 HOURS

	halo	operid	ol	pla	acebo		;	Std. Mean Difference	Std.	Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, F	Random, 95% CI	ΑI
9.4.1 change score - AB	S (high	= wor	se)								
Breier 2001	-7.7	5.2	39	-3	5	45	25.8%	-0.91 [-1.37, -0.46]	_	-	
Bristol Myers 2004f [M]	-8.28	9.55	184	-4.51	7.68	88	42.6%	-0.42 [-0.67, -0.16]			
Bristol Myers 2005b	-8.13	6.93	57	-2.95	6.93	61	31.6%	-0.74 [-1.12, -0.37]	_		
Subtotal (95% CI)			280			194	100.0%	-0.65 [-0.95, -0.35]	•	>	
Heterogeneity: Tau ² = 0.0	04; Chi ²	= 4.34	df = 2	(P = 0.1)	11); I² :	= 54%					
Test for overall effect: Z :	= 4.23 (F	o < 0.0	001)								
9.4.3 change score - PA	NSS-EC	(high	= wors	se)							
Breier 2001	-7.5	5.9	40	-2.9	4.7	45	42.1%	-0.86 [-1.31, -0.41]		-	
Bristol Myers 2004f [M]	-7.75	7.99	184	-4.78	6.53	88	57.9%	-0.39 [-0.65, -0.14]	_	<u></u>	
Subtotal (95% CI)			224			133	100.0%	-0.59 [-1.04, -0.14]	•		
Heterogeneity: Tau ² = 0.0	-			(P = 0.0)	07); I² :	= 69%					
Test for overall effect: Z	= 2.55 (F	P = 0.0	1)								
9.4.7 endpoint score - P	ANSS-E	C (higl	n = wo	rse)						_	
Battaglia 2002	10.96	4.33	106	14.75	5.38	51	100.0%	-0.80 [-1.15, -0.46]	-	-	
Subtotal (95% CI)			106			51	100.0%	-0.80 [-1.15, -0.46]	•	>	
Heterogeneity: Not applic	cable										
Test for overall effect: Z :	= 4.55 (F	o < 0.0	0001)								
											
									-2 -1	0 1	2
Test for subgroup differen	nces: Ch	$ni^2 = 0$	68. df =	2 (P =	0.71).	$I^2 = 0\%$, n		halope	ridol placebo	

Test for subgroup differences: Chi² = 0.68, df = 2 (P = 0.71), $I^2 = 0\%$

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

9.5 SPECIFIC BEHAVIOUR - AGITATION: 2B. AVERAGE SCORE - BY ABOUT 24 HOURS



Test for subgroup differences: Chi² = 0.44, df = 1 (P = 0.51), $I^2 = 0\%$

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

9.6 ADVERSE EFFECTS: 1. GENERAL

	haloperi	dol	placel	00		Risk Ratio	Risk	Ratio	Risk o
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Rand	lom, 95% CI	ABCD
9.6.1 one or more drug	related adv	verse e	effects du	ıring 24	1 hours				
Bristol Myers 2004f [M]	82	185	24	88	60.7%	1.63 [1.11, 2.37]			
Bristol Myers 2005b	29	60	18	62	39.3%	1.66 [1.04, 2.66]			
Subtotal (95% CI)		245		150	100.0%	1.64 [1.22, 2.20]		•	
Total events	111		42						
Heterogeneity: $Tau^2 = 0$. Test for overall effect: Z	,	,		0.94); I ²	2 = 0%				
9.6.2 increased severity	of advers	e effec	ts after 2	2nd inje	ection				
Bristol Myers 2004f [M]	82	185	12	88	100.0%	3.25 [1.88, 5.63]			
Subtotal (95% CI)		185		88	100.0%	3.25 [1.88, 5.63]			
Total events	82		12						
Heterogeneity: Not applie	cable								
Test for overall effect: Z	= 4.20 (P <	0.0001)						
9.6.3 overall adverse ev	ents durin	g 72 hc	ours						
Bristol Myers 2004f [M]	90	185	24	88	100.0%	1.78 [1.23, 2.59]		-	
Subtotal (95% CI)		185		88	100.0%	1.78 [1.23, 2.59]			
Total events	90		24						
Heterogeneity: Not applie	cable								
Test for overall effect: Z	= 3.05 (P =	0.002)							
								.	
							0.2 0.5	1 2 5	
							Favours haloperidol	Favours placeb	0

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

9.7 ADVERSE EFFECTS: 2. GENERAL - SERIOUS

	haloper	idol	placel	00		Risk Ratio		Risk Ratio		Risk o
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	l	M-H, Rand	om, 95% CI	ABCD
9.7.1 death										
Bristol Myers 2004f [M]	0	185	0	88		Not estimable	-			
Subtotal (95% CI)		185		88		Not estimable)			
Total events	0		0							
Heterogeneity: Not applica	ble									
Test for overall effect: Not	applicabl	е								
9.7.2 rated as serious										
Bristol Myers 2005b	0	60	1	62	100.0%	0.34 [0.01, 8.29]]			
Subtotal (95% CI)		60		62	100.0%	0.34 [0.01, 8.29]]			
Total events	0		1							
Heterogeneity: Not applica	ble									
Test for overall effect: $Z = 0$	0.66 (P =	0.51)								
9.7.3 tonic clonic seizure										
Bristol Myers 2005b	0	60	0	57		Not estimable)			
Subtotal (95% CI)		60		57		Not estimable)			
Total events	0		0							
Heterogeneity: Not applica	ble									
Test for overall effect: Not	applicabl	е								
							0.001	0.1 1	10	1000
								haloperidol	Favours place	cebo

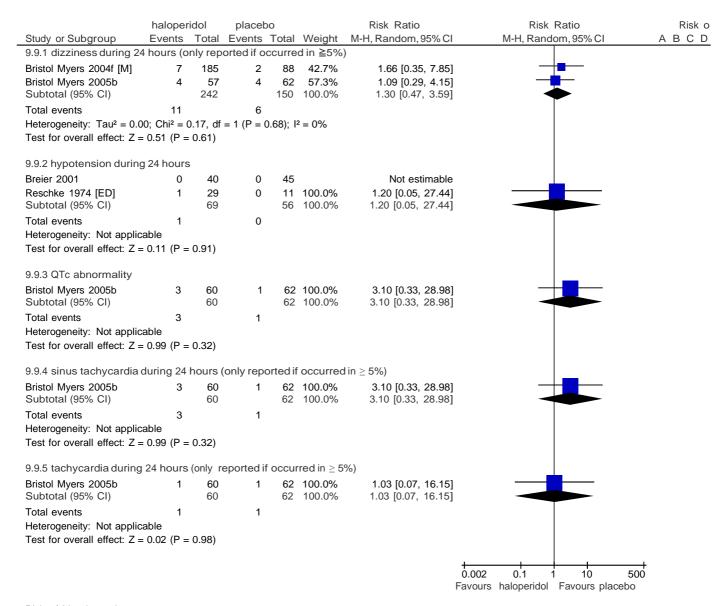
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

9.8 ADVERSE EFFECTS: 3. SPECIFIC - AROUSAL LEVEL

	haloper	idol	placeb	00		Risk Ratio	Risk Ratio	Risk o
Study or Subgroup					Weight	M-H, Random, 95% C	I M-H, Random, 95% CI	ABCD
9.8.1 insomnia during 24	4 hours (o	nly rep	orted if o	ccurre	d in ≧5%)			
Bristol Myers 2004f [M] Subtotal (95% CI)	22	185 185	8	88 88	100.0% 100.0%	1.31 [0.61, 2.82 1.31 [0.61, 2.82]	-	
Total events	22		8					
Heterogeneity: Not applic	cable							
Test for overall effect: Z =	= 0.69 (P =	0.49)						
9.8.2 "over" sedated							<u>_</u>	
Bristol Myers 2004f [M]	28	185	5	88	90.0%	2.66 [1.06, 6.66]]	
Reschke 1974 [ED]	12	29	0	11	10.0%	10.00 [0.64, 155.85]		
Subtotal (95% CI)		214		99	100.0%	3.04 [1.27, 7.26]		
Total events	40		5					
Heterogeneity: $Tau^2 = 0.0$	$00; Chi^2 = 0$	0.85, df	= 1 (P =	0.36); I	$^{2} = 0\%$			
Test for overall effect: Z =	= 2.51 (P =	0.01)						
9.8.3 somnolence during	g 24 hours	3						
Battaglia 2002	10	126	2	54	33.1%	2.14 [0.49, 9.45	ı 	
Bristol Myers 2004f [M]	6	185	1	88	16.5%	2.85 [0.35, 23.35]	i 	
Bristol Myers 2005b	7	60	3	62	42.9%	2.41 [0.65, 8.89	<u>+</u> ■	
Reschke 1974 [ED]	1	29	0	11	7.5%	1.20 [0.05, 27.44]] - • 	
Subtotal (95% CI)		400		215	100.0%	2.26 [0.96, 5.32]		
Total events	24		6					
Heterogeneity: $Tau^2 = 0.0$	00; Chi ² = 0	0.22, df	= 3 (P =	0.97); I	$^{2} = 0\%$			
Test for overall effect: Z =	= 1.87 (P =	0.06)						
							0.02 0.1 1 10 50	
							Favours haloperidol Favours placebo	

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

9.9 ADVERSE EFFECTS: 4A. SPECIFIC - CARDIAC: I. MISCELLANEOUS OUTCOMES



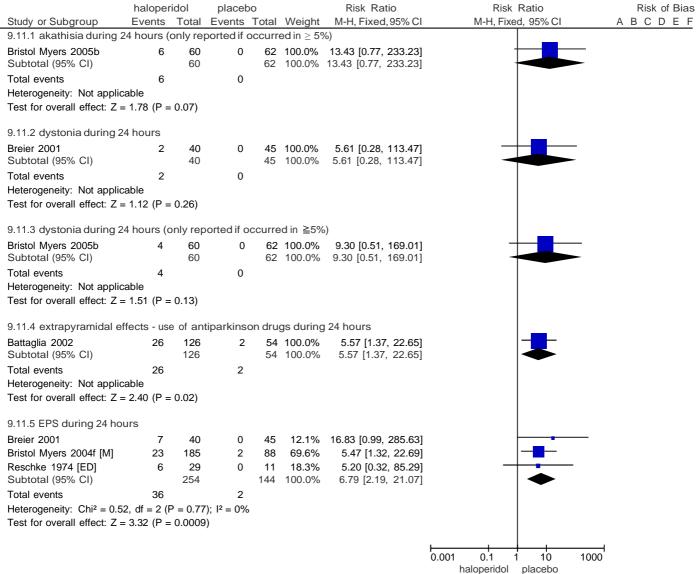
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

9.10 ADVERSE EFFECTS: 4B. SPECIFIC - CARDIAC: II. QTC INTERVAL (AVERAGE CHANGE AT 24 HOURS)

	halo	perid	ol	pla	acebo			Mean Difference	Mean Difference	Risk o
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCD
Battaglia 2002	-1.2	24.4	126	-3.7	26.1	54	59.5%	2.50 [-5.66, 10.66]	- 	
Breier 2001	6.5	24.7	40	1.2	21.5	45	40.5%	5.30 [-4.60, 15.20]	- -	
Total (95% CI)			166			99	100.0%	3.63 [-2.67, 9.93]		
Heterogeneity: Tau ² = Test for overall effect:	,		-20 -10 0 10 20							
rest for overall effect.	Z = 1.13	(P = t).26)						haloperidol placebo	

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

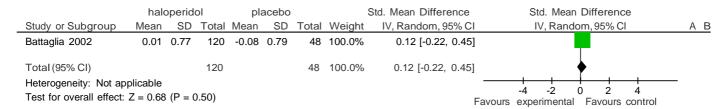
9.11 ADVERSE EFFECTS: 5A. SPECIFIC - MOVEMENT DISORDERS



Test for subgroup differences: Chi² = 0.36, df = 4 (P = 0.99), $I^2 = 0\%$

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

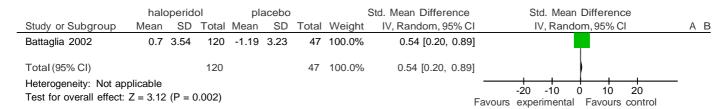
9.12 ADVERSE EFFECTS: 5B. SPECIFIC - MOVEMENT DISORDERS: I. AVERAGE CHANGE SCORE (BARNES AKATHISIA SCALE, HIGH = WORSE)



Risk of bias legend

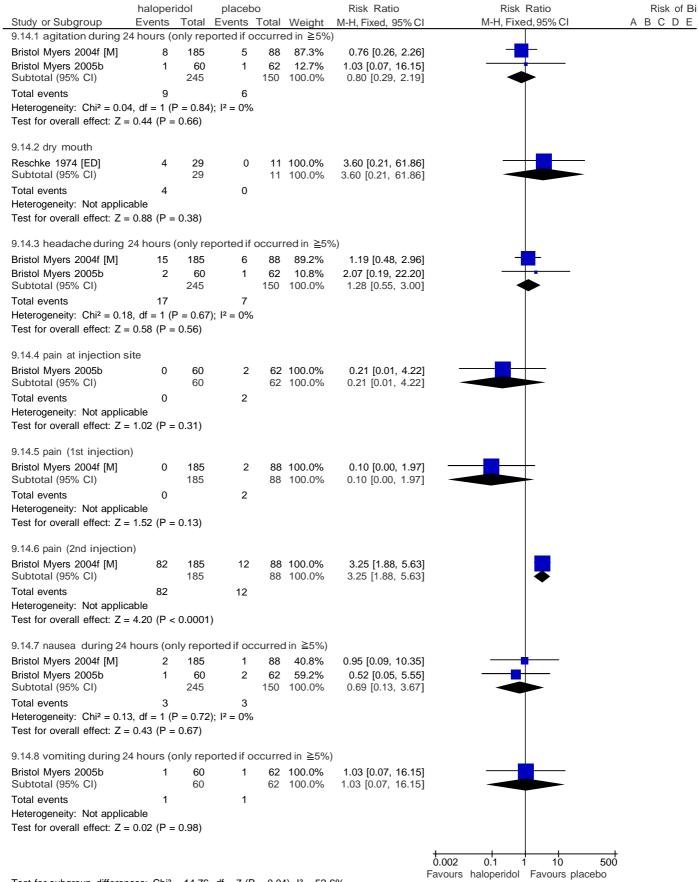
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

9.13 ADVERSE EFFECTS: 5C. SPECIFIC - MOVEMENT DISORDERS: II. AVERAGE CHANGE SCORE (SAS, HIGH = WORSE)



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

9.14 ADVERSE EFFECTS: 6. SPECIFIC - MISCELLANEOUS



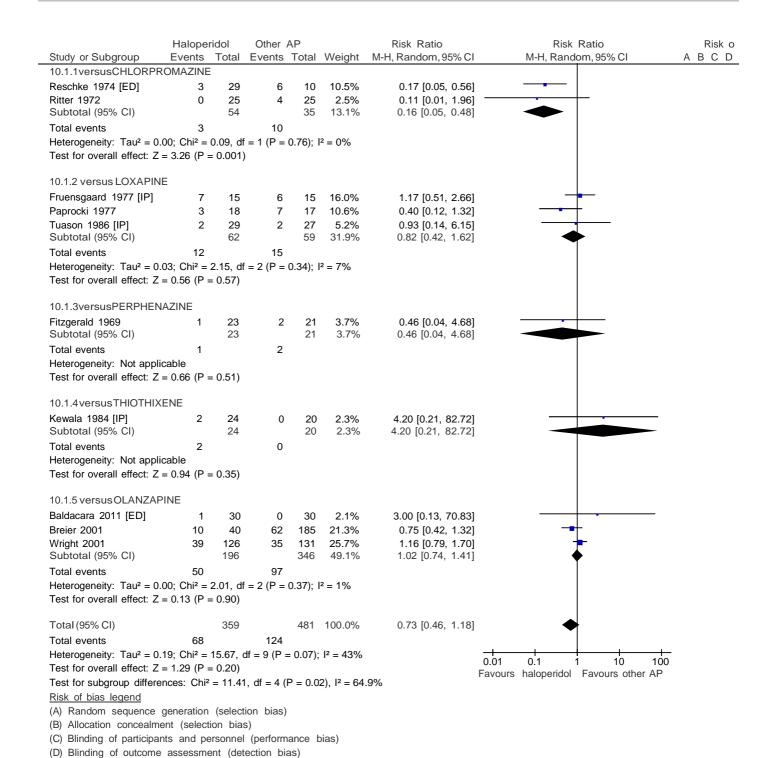
Test for subgroup differences: $Chi^2 = 14.76$, df = 7 (P = 0.04), $I^2 = 52.6\%$

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)

- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

10 INTRAMUSCULAR HALOPERIDOL VERSUS OTHER ANTIPSYCHOTIC DRUG [ADAPTED FROM POWNEY 2012]

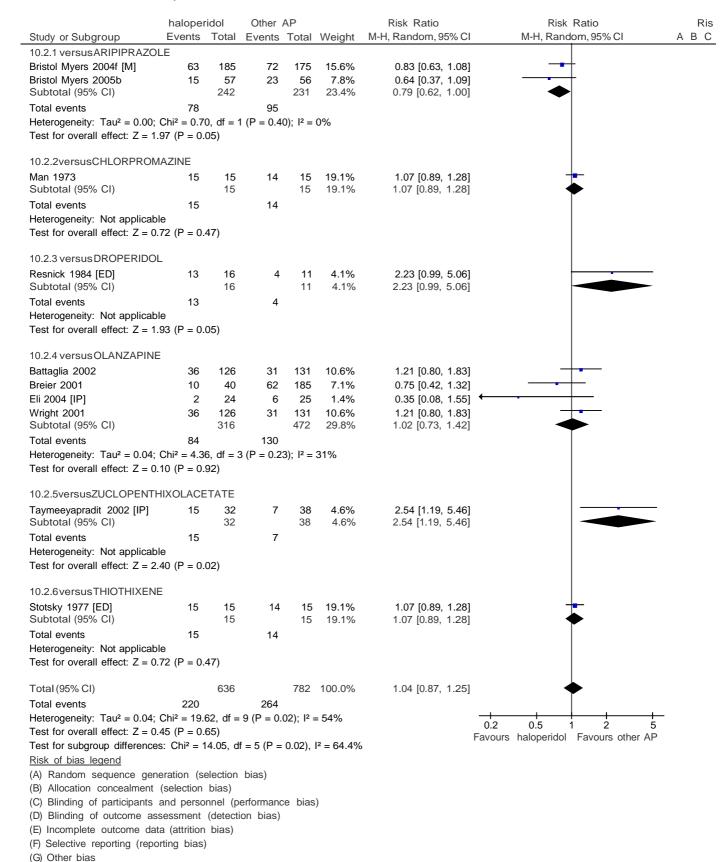
10.1 GLOBAL IMPRESSION: 1. NOT IMPROVED



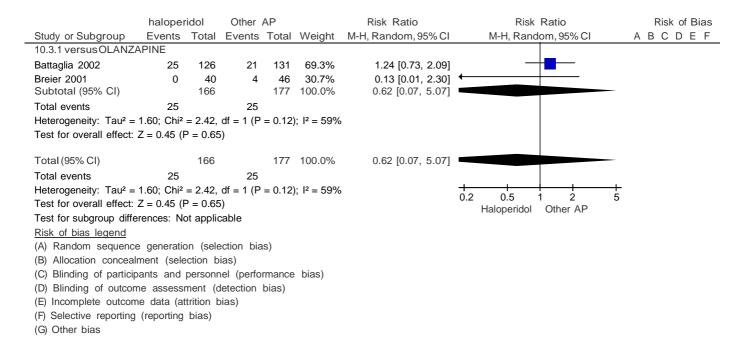
(E) Incomplete outcome data (attrition bias)(F) Selective reporting (reporting bias)

(G) Other bias

10.2 GLOBAL IMPRESSION: 2. REPEATED NEED FOR RAPID TRANQUILLISATION: NEEDING ADDITIONAL INJECTION



10.3 GLOBAL IMPRESSION: 3. NEED FOR ADDITIONAL BENZODIAZEPINE



10.4 ADVERSE EFFECTS: ONE OR MORE DRUG-RELATED ADVERSE EFFECTS

Study or Subgroup	intramuscular halo Events	peridol Total	Other A		Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% (
10.4.1 versus aripiprazo				· Otal	rro.g	,	,
Bristol Myers 2004f [M] Bristol Myers 2005b Subtotal (95% CI)	82 29	185 60 245	64 25	175 57 232	70.7% 29.3% 100.0%	1.21 [0.94, 1.56] 1.10 [0.74, 1.63] 1.18 [0.95, 1.46]	= ♦
Total events Heterogeneity: Tau ² = 0.0 Test for overall effect: Z =		(P = 0.69);	89 I ² = 0%				
10.4.2 versus chlorpron Subtotal (95% CI)	nazine	0		0		Not estimable	
Total events Heterogeneity: Not applic Test for overall effect: No			0				
Eli 2004 [IP] Subtotal (95% CI)	1	24 24	1		100.0% 100.0%	1.04 [0.07, 15.73] 1.04 [0.07, 15.73]	
Total events Heterogeneity: Not applic Test for overall effect: Z =			1				
10.4.4 versus perphena	zine						
Fitzgerald 1969 Subtotal (95% CI)	10	23 23	7	21 21	100.0% 100.0%	1.30 [0.61, 2.80] 1.30 [0.61, 2.80]	
Total events Heterogeneity: Not applic Test for overall effect: Z =			7				
10.4.5 versus ziprasidor	ne						
Brook 1998a Li 2006	21 58	42 116	28 43	90 115	26.4% 35.1%	1.61 [1.04, 2.47] 1.34 [0.99, 1.80]	
Shu 2010 Subtotal (95% CI)	116	1 87 345	54	189 394	38.4% 100.0%	2.17 [1.69, 2.79] 1.69 [1.23, 2.33]	•
Total events Heterogeneity: Tau² = 0.0 Test for overall effect: Z =		(P = 0.05);	125 l ² = 67%				
10.4.6 versus loxapine							
Fruensgaard 1977 [IP] Subtotal (95% CI)	8	15 15	10		100.0% 100.0%	0.80 [0.44, 1.45] 0.80 [0.44, 1.45]	
Total events Heterogeneity: Not applic Test for overall effect: Z =			10				
10.4.7 versus thiothixen	e						
Kewala 1984 [IP] Stotsky 1977 [ED] Subtotal (95% CI)	20 4	24 15 39	12 2	20 15	93.7% 6.3% 100.0%	1.39 [0.93, 2.07] 2.00 [0.43, 9.32] 1.42 [0.97, 2.09]	-
Total events Heterogeneity: Tau ² = 0.0 Test for overall effect: Z =			14 I ² = 0%	JU	100.070	1. -1 2 [0.81, 2.08]	
						<u> </u>	
						0.01	0.1 1 nuscular haloperidol Favours

Test for subgroup differences: Chi² = 6.16, df = 5 (P = 0.29), I^2 = 18.9%

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

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10.5 ADVERSE EFFECTS: EXTRAPYRAMIDAL SYMPTOMS

i	intramuscular halo	peridol	Other /	AΡ		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 9
10.5.1 versus aripiprazole							
Bristol Myers 2004f [M] Subtotal (95% CI)	10	185 185	1	175 175	7.8% 7.8%	9.46 [1.22, 73.13] 9.46 [1.22, 73.13]	
Fotal events Heterogeneity: Not applicable	10		1				
Test for overall effect: $Z = 2.15$	5 (P = 0.03)						
10.5.2 versus chlorpromazir			_				
Man 1973	0	15	0	15	0.00/	Not estimable	
Reschke 1974 [ED] Subtotal (95% CI)	6	29 44	1	10 25	8.2% 8.2%	2.07 [0.28, 15.15] 2.07 [0.28, 15.15]	
Fotal events Heterogeneity: Not applicable	6		1				
Test for overall effect: Z = 0.72	2 (P = 0.47)						
10.5.3 versus olanzapine							
Battaglia 2002	7	126	1	131	7.6%	7.28 [0.91, 58.31]	
Breier 2001	7	40 166	1	46 177	7.8%	8.05 [1.03, 62.66]	
Subtotal (95% CI) Total events	14	166	2	177	15.4%	7.66 [1.78, 33.02]	
Heterogeneity: Tau ² = 0.00; C Test for overall effect: Z = 2.73	$hi^2 = 0.00$, $df = 1$ (P	= 0.95); I ²					
10.5.4 versus perphenazine							
Fitzgerald 1969	6	23	2	21	14.1%	2.74 [0.62, 12.12]	+
Subtotal (95% CI)		23		21	14.1%	2.74 [0.62, 12.12]	
Total events	6		2				
Heterogeneity: Not applicable Test for overall effect: Z = 1.33	3 (P = 0.18)						
10.5.5 versus ziprasidone							
Brook 1998a	9	42	0	90	4.3%	40.21 [2.40, 674.98]	
Shu 2010	69	187	4	189	27.9%	17.43 [6.49, 46.80]	
Subtotal (95% CI) Fotal events	78	229	4	279	32.2%	19.10 [7.52, 48.51]	
Heterogeneity: $Tau^2 = 0.00$; C Test for overall effect: $Z = 6.20$	$hi^2 = 0.30$, $df = 1$ (P	= 0.58); l ²					
10.5.6 versus loxapine							
Fruensgaard 1977 [IP]	7	15	1	15	8.4%	7.00 [0.98, 50.16]	
Subtotal (95% CI)	7	15	1	15	8.4%	7.00 [0.98, 50.16]	
Total events Heterogeneity: Not applicable	/		1				
Test for overall effect: $Z = 1.94$	4 (P = 0.05)						
10.5.7 versus thiothixene							
Stotsky 1977 [ED]	0	15	0	15		Not estimable	
Subtotal (95% CI)	-	15	•	15		Not estimable	
Total events Heterogeneity: Not applicable	0		0				
Test for overall effect: Not app							
10.5.9 versus zuclopenthixo	I acetate						
Taymeeyapradit 2002 [IP]	7	32	2	38	13.9%	4.16 [0.93, 18.62]	
Subtotal (95% CI)		32		38	13.9%	4.16 [0.93, 18.62]	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 1.86			2				
Total (95% CI)		709		745	100.0%	7.45 [4.12, 13.46]	
Total events	128		13			- · ·	
Heterogeneity: Tau ² = 0.07; C	$hi^2 = 8.76$, $df = 8$ (P	= 0.36); l ²				0.01	0.1 1
Test for overall effect: $Z = 6.65$	5 (P < 0.00001)						amuscular haloperidol Favo
Test for subgroup differences:	A						

⁽A) Random sequence generation (selection bias)

⁽B) Allocation concealment (selection bias)

- (C) Blinding of participants and personnel (performance bias) (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias) (F) Selective reporting (reporting bias)
- (G) Other bias

11 INTRAMUSCULAR HALOPERIDOL PLUS ANTIHISTAMINE VERSUS HALOPERIDOL [ADAPTED FROM HUF 2011]

11.1 GLOBAL IMPRESSION: 1. NOT TRANQUIL OR ASLEEP

	Halop. + p'metl	nazine	Halope	ridol		Risk Ratio	Risk Ratio	Risk
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	АВС
11.1.1 by 20 minutes	3							
Huf 2007 [ED]	48	160	72	156	100.0%	0.65 [0.49, 0.87]		
Subtotal (95% CI)		160		156	100.0%	0.65 [0.49, 0.87]	◆	
Total events	48		72					
Heterogeneity: Not ap	oplicable							
Test for overall effect:	Z = 2.90 (P = 0.0)	04)						
44.4.0.140								
11.1.2 by 40 mins								
Huf 2007 [ED]	34	160	40		100.0%	0.83 [0.56, 1.24]		
Subtotal (95% CI)	0.4	160	40	156	100.0%	0.83 [0.56, 1.24]		
Total events	34		40					
Heterogeneity: Not ap	•	C \						
Test for overall effect:	Z = 0.92 (P = 0.3	0)						
11.1.3 by 1 hour								
Huf 2007 [ED]	24	160	31	156	100.0%	0.75 [0.46, 1.23]		
Subtotal (95% CI)		160		156	100.0%	0.75 [0.46, 1.23]		
Total events	24		31					
Heterogeneity: Not ap	oplicable							
Test for overall effect:	Z = 1.14 (P = 0.2)	6)						
11.1.4 by 2 hours								
Huf 2007 [ED]	17	160	30	156	100.0%	0.55 [0.32, 0.96]	—	
Subtotal (95% CI)		160		156	100.0%	0.55 [0.32, 0.96]		
Total events	17		30					
Heterogeneity: Not ap	oplicable							
Test for overall effect:	Z = 2.10 (P = 0.0)	4)						
							0.1 0.2 0.5 1 2 5	 10
							Favours H+P Favours HAL	. •

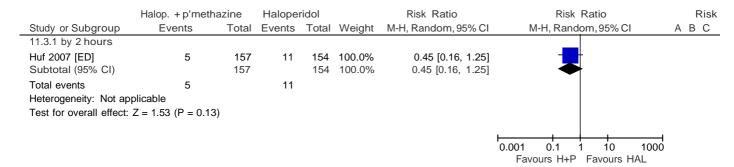
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

11.2 GLOBAL IMPRESSION: 2. NOT ASLEEP

	Halop. + p'met	hazine	Benzodiaz	epine		Risk Ratio	Risk Ratio	R
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	АВ
11.2.1 by 20 minutes								
Huf 2007 [ED]	132	160	145		100.0%	0.89 [0.82, 0.96]	=	
Subtotal (95% CI)		160		156	100.0%	0.89 [0.82, 0.96]	◆	
Total events	132		145					
Heterogeneity: Not app	licable							
Test for overall effect: 2	Z = 2.80 (P = 0.0)	05)						
11.2.2 by 40 minutes								
Huf 2007 [ED]	106	160	104	156	100.0%	0.99 [0.85, 1.16]	_	
Subtotal (95% CI)		160		156	100.0%	0.99 [0.85, 1.16]	~	
Total events	106		104					
Heterogeneity: Not app	licable							
Test for overall effect: Z	Z = 0.08 (P = 0.9)	4)						
11.2.3 by 1 hour								
Huf 2007 [ED]	86	160	81	156	100.0%	1.04 [0.84, 1.28]		
Subtotal (95% CI)		160		156	100.0%	1.04 [0.84, 1.28]		
Total events	86		81					
Heterogeneity: Not app	licable							
Test for overall effect: 2	Z = 0.33 (P = 0.7)	5)						
11.2.4 by 2 hours								
Huf 2007 [ED]	66	160	64	156	100.0%	1.01 [0.77, 1.31]		
Subtotal (95% CI)		160		156	100.0%	1.01 [0.77, 1.31]		
Total events	66		64					
Heterogeneity: Not app	licable							
Test for overall effect: Z	Z = 0.04 (P = 0.9)	7)						
							, .	
						F (0.5 0.7 1 1.5	
							Favours H+P Favours BZD	

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

11.3 GLOBAL IMPRESSION: 3. ADDITIONAL TRANQUILLISING DRUGS



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

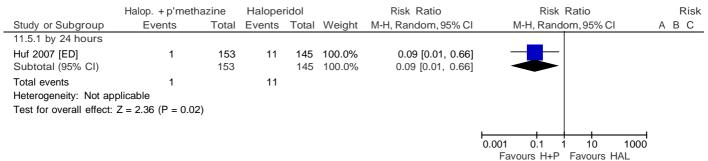
11.4 GLOBAL IMPRESSION: 4. OTHER EPISODE OF AGGRESSION - WITHIN 24 HOURS



Test for overall effect: Z = 0.56 (P = 0.57)

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

11.5 ADVERSE EFFECTS: 1. ANY SERIOUS ADVERSE EFFECT

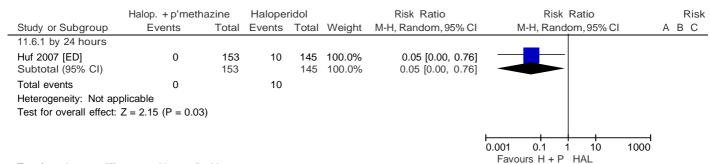


Test for subgroup differences: Not applicable

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

11.6 ADVERSE EFFECTS: 2. ACUTE DYSTONIA



Test for subgroup differences: Not applicable

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

11.7 ADVERSE EFFECTS: 3. SEIZURE

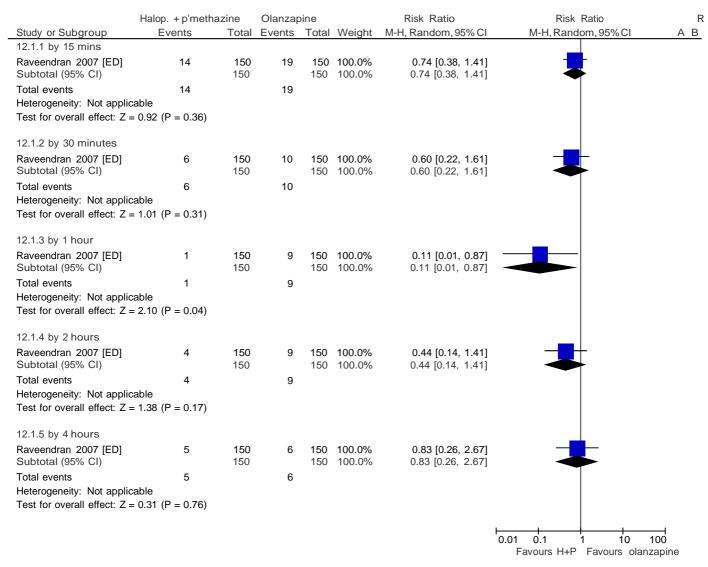
	Halop. + p'metha	Haloperidol			Risk Ratio	Risk Ratio	Risk	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	АВС
11.7.1 by 24 hours								
Huf 2007 [ED]	1	153	1	145	100.0%	0.95 [0.06, 15.01]		
Subtotal (95% CI)		153		145	100.0%	0.95 [0.06, 15.01]		
Total events	1		1					
Heterogeneity: Not app	plicable							
Test for overall effect:	Z = 0.04 (P = 0.97)							
							0.005 0.1 1 10 20	
							Favours H + P Favours HAL	U

Test for subgroup differences: Not applicable

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

12 INTRAMUSCULAR HALOPERIDOL PLUS ANTIHISTAMINE VERSUS OLANZAPINE [ADAPTED FROM HUF 2011]

12.1 GLOBAL IMPRESSION: 1. NOT TRANQUIL OR ASLEEP



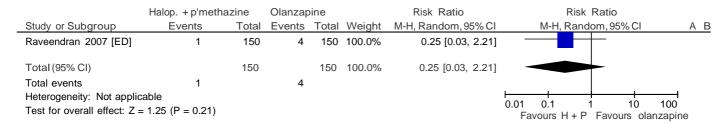
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

12.2 GLOBAL IMPRESSION: 2. NOT ASLEEP

	Halop. + p'meth	azine	Olanzap	oine		Risk Ratio	Risk Ratio	R
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	АВ
12.2.1 by 15 mins								
Raveendran 2007 [ED] Subtotal (95% CI)	64	150 150	85		100.0% 100.0%	0.75 [0.60, 0.95] 0.75 [0.60, 0.95]		
Total events	64		85					
Heterogeneity: Not applica Test for overall effect: Z =								
12.2.2 by 30 minutes								
Raveendran 2007 [ED] Subtotal (95% CI)	36	150 150	55		100.0% 100.0%	0.65 [0.46, 0.93] 0.65 [0.46, 0.93]		
Total events Heterogeneity: Not applica Test for overall effect: Z =			55					
12.2.3 by 1 hour	,							
Raveendran 2007 [ED] Subtotal (95% CI)	30	150 150	51		100.0% 100.0%	0.59 [0.40, 0.87] 0.59 [0.40, 0.87]		
Total events Heterogeneity: Not applica	30 ible		51					
Test for overall effect: Z =	2.67 (P = 0.008)							
12.2.4 by 2 hours							_	
Raveendran 2007 [ED] Subtotal (95% CI)	14	150 150	59		100.0% 100.0%	0.24 [0.14, 0.41] 0.24 [0.14, 0.41]		
Total events Heterogeneity: Not applica	14 ible		59					
Test for overall effect: Z =		1)						
12.2.5 by 4 hours							_	
Raveendran 2007 [ED] Subtotal (95% CI)	38	150 150	62		100.0% 100.0%	0.61 [0.44, 0.86] 0.61 [0.44, 0.86]		
Total events Heterogeneity: Not applica	38 Ible		62					
Test for overall effect: Z =								
							0.1 0.2 0.5 1 2 5	10
							Favours H+P Favours olan:	

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

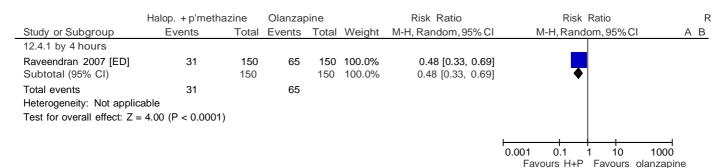
12.3 GLOBAL IMPRESSION: 3. NEVER TRANQUIL OR ASLEEP DURING FIRST 4 HOURS



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

12.4 GLOBAL IMPRESSION: 4. REQUIRING ADDITIONAL DRUGS DURING INITIAL PHASE



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

12.5 GLOBAL IMPRESSION: 5. NOT CLINICALLY IMPROVED

	Halop. + p'metha	azine	Olanzar	oine		Risk Ratio	Risk Ratio	R
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	A B
12.5.1 by 15 mins								
Raveendran 2007 [ED] Subtotal (95% CI)	41	150 150	52		100.0% 100.0%	0.79 [0.56, 1.11] 0.79 [0.56, 1.11]		
Total events	41		52					
Heterogeneity: Not applica	able							
Test for overall effect: Z =	1.37 (P = 0.17)							
12.5.2 by 30 minutes								
Raveendran 2007 [ED]	23	150	40		100.0%	0.57 [0.36, 0.91]		
Subtotal (95% CI)		150		150	100.0%	0.57 [0.36, 0.91]		
Total events	23		40					
Heterogeneity: Not applica								
Test for overall effect: Z =	2.36 (P = 0.02)							
12.5.3 by 1 hour							_	
Raveendran 2007 [ED]	12	150	30		100.0%	0.40 [0.21, 0.75]		
Subtotal (95% CI)		150		150	100.0%	0.40 [0.21, 0.75]		
Total events	12		30					
Heterogeneity: Not applica								
Test for overall effect: Z =	2.85 (P = 0.004)							
12.5.4 by 2 hours								
Raveendran 2007 [ED]	14	150	32	150	100.0%	0.44 [0.24, 0.79]		
Subtotal (95% CI)		150		150	100.0%	0.44 [0.24, 0.79]		
Total events	14		32					
Heterogeneity: Not applica								
Test for overall effect: Z =	2.77 (P = 0.006)							
12.5.5 by 4 hours								
Raveendran 2007 [ED]	9	150	19	150	100.0%	0.47 [0.22, 1.01]		
Subtotal (95% CI)		150		150	100.0%	0.47 [0.22, 1.01]		
Total events	9		19					
Heterogeneity: Not applica								
Test for overall effect: Z =	1.93 (P = 0.05)							
							0.2 0.5 1 2	5
							Favours H+P Favours olan	zapine

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

12.6 GLOBAL IMPRESSION: 6.FURTHER OBSERVATION AFTER 4 HOURS

	Halop. + p'methazine		Olanzapine			Risk Ratio	Risk Ratio	R	
Study or Subgroup	Events To		Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	АВ	
Raveendran 2007 [ED]	42	150	36	150	100.0%	1.17 [0.80, 1.71]	-		
Total (95% CI)		150		150	100.0%	1.17 [0.80, 1.71]	•		
Total events 42 Heterogeneity: Not applicable Test for overall effect: Z = 0.79 (P = 0.43)		36				0.1 0.2 0.5 1 2 5 10 Favours H+P Favours olanzap			

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

12.7 ADVERSE EFFECTS: 1. SERIOUS ADVERSE EFFECT

Halop. + p'methazine		Olanzapine			Risk Ratio	Risk Ratio	R	
Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	АВ	
1	150	3	150	100.0%	0.33 [0.04, 3.17]			
	150		150	100.0%	0.33 [0.04, 3.17]			
1		3						
able								
= 0.96 (P = 0.34)								
0	150	1	150	100.0%	0.33 [0.01, 8.12]			
	150		150	100.0%	0.33 [0.01, 8.12]			
0		1						
able								
= 0.67 (P = 0.50)								
						0.005 0.1 1 10 3	1 200	
	1 1 sable = 0.96 (P = 0.34) 0 sable	Events Total 1 150 150 1 eable = 0.96 (P = 0.34) 0 150 150 0 eable	Events Total Events 1 150 3 150 3 150 3 150 1 2able = 0.96 (P = 0.34) 0 150 1 150 0 1 able	Events Total Events Total 1 150 3 150 150 150 1 3 eable 0 150 1 150 0 150 1 150 150 150 150 1 150 150 1 150 150 1 150 150 1 150	Events Total Events Total Weight 1 150 3 150 100.0% 150 150 150 100.0% 2 able = 0.96 (P = 0.34) 0 150 1 150 100.0% 150 1 150 100.0% 150 1 150 100.0% 150 1 150 100.0%	Events Total Events Total Weight M-H, Random, 95% CI 1 150 3 150 100.0% 0.33 [0.04, 3.17] 150 150 100.0% 0.33 [0.04, 3.17] 1 3 able = 0.96 (P = 0.34) 0 150 1 150 100.0% 0.33 [0.01, 8.12] 150 150 100.0% 0.33 [0.01, 8.12] 0 1 1 150 100.0% 0.33 [0.01, 8.12] 0 1 1 150 100.0% 0.33 [0.01, 8.12]	Events Total Events Total Weight M-H, Random, 95% CI 1 150 3 150 100.0% 0.33 [0.04, 3.17] 150 150 100.0% 0.33 [0.04, 3.17] 1 3 able = 0.96 (P = 0.34) 0 150 1 150 100.0% 0.33 [0.01, 8.12] 0 1 1 150 100.0% 0.33 [0.01, 8.12] 0 1 1 150 100.0% 0.33 [0.01, 8.12] 0 1 1 150 100.0% 0.33 [0.01, 8.12] 0 1 1 150 100.0% 0.33 [0.01, 8.12] 0 1 1 150 100.0% 0.33 [0.01, 8.12]	

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

12.8 ADVERSE EFFECTS: 2. EXTRAPYRAMIDAL PROBLEMS - 0-4 HOURS

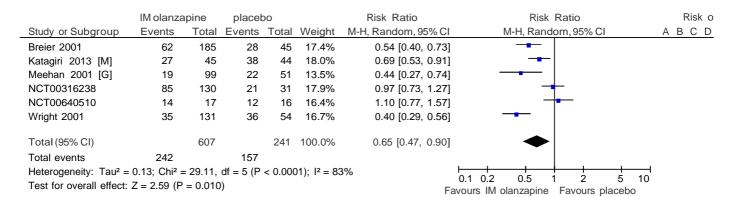
	Halop. + p'methazine		Olanzap	ine		Risk Difference	Risk I		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Rai	ndom, 95% CI	АВ
12.8.1 any change in so	ale-rated extrapyr	amidal	problems	(Simp	son & An	gus Scale)			
Raveendran 2007 [ED] Subtotal (95% CI)	0	150 150	0	150 150	100.0% 100.0%	0.00 [-0.01, 0.01] 0.00 [-0.01, 0.01]		•	
Total events	0		0						
Heterogeneity: Not applie	cable								
Test for overall effect: Z	= 0.00 (P = 1.00)								
							-0.5 -0.25 Favours H +	0 0.25 P Favours olana	0.5 zapine

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

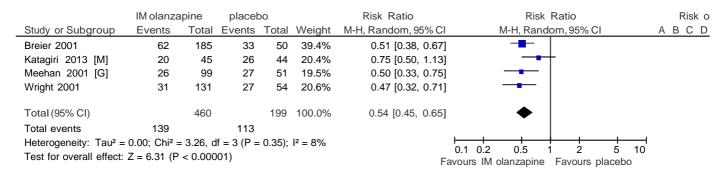
13 INTRAMUSCULAR OLAZAPINE VERSUS INTRAMUSCULAR PLACEBO [ADAPTED FROM BELGAMWAR 2009]

13.1 GLOBAL IMPRESSION: 1. DID NOT RESPOND - BY 2 HOURS



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

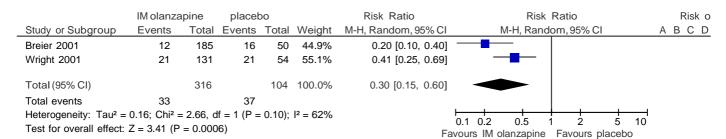
13.2 GLOBAL IMPRESSION: 2. REQUIRING FURTHER INTRAMUSCULAR INJECTION - BY 24 HOURS



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

13.3 GLOBAL IMPRESSION: 3. REQUIRING ADDITIONAL BENZODIAZEPINE - WITHIN 24 HOURS



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

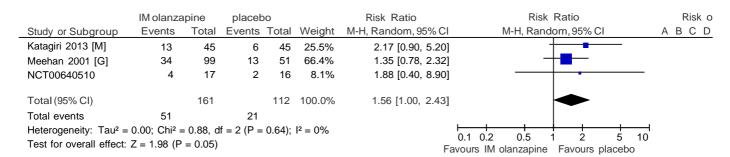
13.4 BEHAVIOUR: 1. AVERAGE CHANGE SCORE (PANSS-EC) - MEDIUM TERM (2 HOURS)

			IM olanzapine pl	lacebo		Mean Difference		Mear	n Diffe	erence	
Study or Subgroup	Mean Difference	SE	Total	Total	Weight	IV, Random, 95% C	l	IV, Ra	ndom	ı, 95% C	:1
Wright 2001	-4.19	0.8623	131	54	100.0%	-4.19 [-5.88, -2.50]					
Total (95% CI)			131	54	100.0%	-4.19 [-5.88, -2.50]		•	•		
Heterogeneity: Not ap Test for overall effect:	•	01)				ı	-20	-10 IM olanzapi	0 ne F	avours	10 placebo

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

13.5 ADVERSE EFFECTS: 1. ANY ADVERSE EVENT - IN 24 HOURS



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

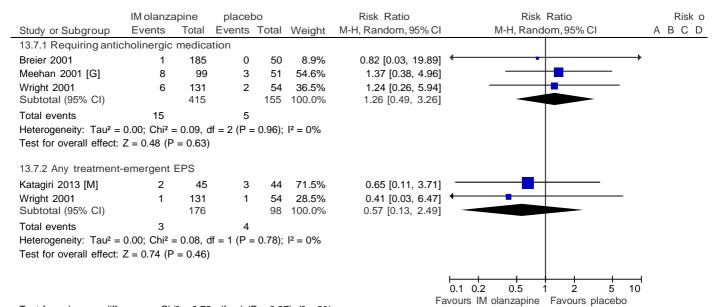
13.6 ADVERSE EFFECTS: 2. ANXIETY - BY 24 HOURS

	IM olanzapine			00		Risk Ratio		Ri		Risk	0	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Ra	andom, 95% C	1	АВС	D
Breier 2001	0	185	3	50	100.0%	0.04 [0.00, 0.75]	+		-			
Total (95% CI)		185		50	100.0%	0.04 [0.00, 0.75]			_			
Total events	0		3									
Heterogeneity: Not ap	plicable						0.005	0.1	1 10	200		
Test for overall effect:	Z = 2.15 (P	= 0.03)				F		0. i 1 olanzapii				

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

13.7 ADVERSE EFFECTS: 3. EXTRAPYRAMIDAL SYMPTOMS - BY 24 HOURS



Test for subgroup differences: Chi² = 0.79, df = 1 (P = 0.37), $I^2 = 0\%$

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

13.8 ADVERSE EFFECTS: 4. SERIOUS ADVERSE EVENT - BY 24 HOURS

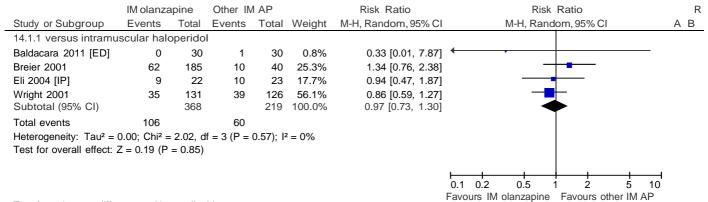
	IM olanza	apine	placeb	00		Risk Ratio	Risk Ratio	Risk o
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	ABCD
Breier 2001	1	185	0	45	50.0%	0.74 [0.03, 17.92]		
Katagiri 2013 [M]	0	45	0	45		Not estimable		
NCT00640510	0	17	0	16		Not estimable		
Wright 2001	1	131	0	54	50.0%	1.25 [0.05, 30.21]		
Total (95% CI)		378		160	100.0%	0.96 [0.10, 9.15]		
Total events	2		0					
Heterogeneity: Tau ² =	0.00; Chi ² =	= 0.05, c	lf = 1 (P =	0.82);	$I^2 = 0\%$	0.00)5 0.1 1 10	
Test for overall effect:	Z = 0.03 (P	= 0.97)				****	95 0.1 1 10 s IM olanzapine Favours placebo	200

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

14 INTRAMUSCULAR OLAZAPINE VERSUS OTHER ANTIPSYCHOTIC DRUG [ADAPTED FROM BELGAMWAR 2009]

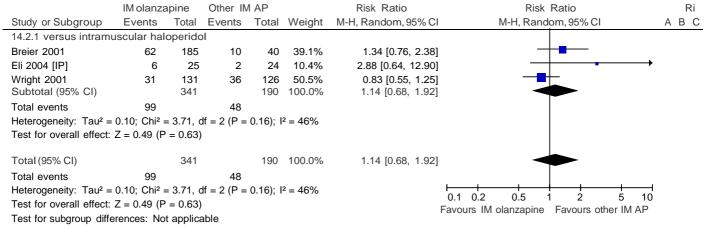
14.1 GLOBAL IMPRESSION: 1. NOT IMPROVED



Test for subgroup differences: Not applicable

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

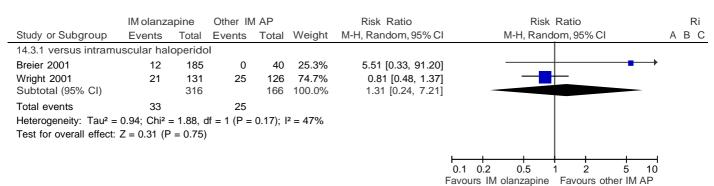
14.2 GLOBAL IMPRESSION: 2. REQUIRING ADDTIONAL INTRAMUSCULAR INJECTION - BY 24 HOURS



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

14.3 GLOBAL IMPRESSION: 3. REQUIRING ADDITIONAL BENZODIAZEPINE - BY 24 HOURS



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

14.4 BEHAVIOUR: 1A. AVERAGE CHANGE SCORE (PANSS-EC) - VERY SHORT TERM (15 MINUTES)

			IM olanzapine Oth	er AP		Mean Difference	Mean Difference
Study or Subgroup	Mean Difference	SE	Total	Total	Weight	IV, Random, 95% C	I IV, Random, 95% CI
14.4.1 versus intramus	scular haloperidol						
Hsu 2010 [IP]	-4.55	1.58	11	11	100.0%	-4.55 [-7.65, -1.45]	ı -
Subtotal (95% CI)			11	11	100.0%	-4.55 [-7.65, -1.45]	
Heterogeneity: Not app	olicable						
Test for overall effect: 2	Z = 2.88 (P = 0.004))					
14.4.2 versus oral RIS	3						
Hsu 2010 [IP]	-0.76	1.62	11	10	100.0%	-0.76 [-3.94, 2.42]] — ———
Subtotal (95% CI)			11	10	100.0%	-0.76 [-3.94, 2.42]	
Heterogeneity: Not app	olicable						
Test for overall effect: Z	Z = 0.47 (P = 0.64)						
14.4.3 versus ODT ola	nzapine						
Hsu 2010 [IP]	1.49	1.62	11	10	100.0%	1.49 [-1.69, 4.67]] -
Subtotal (95% CI)			11	10	100.0%	1.49 [-1.69, 4.67]]
Heterogeneity: Not app	licable						
Test for overall effect: Z	Z = 0.92 (P = 0.36)						
							
							-20 -10 0 10
Took for authorizing differ	Obia 7.04	-If 0	(D 000) 12 70 (20/			Favours IM olanzapine Favours Otl

Test for subgroup differences: $Chi^2 = 7.31$, df = 2 (P = 0.03), $I^2 = 72.6\%$

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

14.5 BEHAVIOUR: 1B. AVERAGE CHANGE SCORE (PANSS-EC) - SHORT TERM (60 MINUTES)

			IM olanzapine C	Other AP		Mean Difference	Mean Difference
Study or Subgroup	Mean Difference	SE	Total	Total	Weight	IV, Random, 95% C	I IV, Random, 95% CI
14.5.1 versus intramus	scular haloperidol						
Hsu 2010 [IP]	-4.55	1.58	11	11	100.0%	-4.55 [-7.65, -1.45] -
Subtotal (95% CI)			11	11	100.0%	-4.55 [-7.65, -1.45]]
Heterogeneity: Not appl	licable						
Test for overall effect: Z	Z = 2.88 (P = 0.004)						
14.5.2 versus oral RIS							
Hsu 2010 [IP]	-1.05	1.62	11	10	100.0%	-1.05 [-4.23, 2.13	ı ———
Subtotal (95% CI)			11	10	100.0%	-1.05 [-4.23, 2.13	j 🔷
Heterogeneity: Not appl	licable						
Test for overall effect: Z	Z = 0.65 (P = 0.52)						
14.5.3 versus ODT olai	nzapine						
Hsu 2010 [IP]	0.81	1.62	11	10	100.0%	0.81 [-2.37, 3.99	ı ————
Subtotal (95% CI)			11	10	100.0%	0.81 [-2.37, 3.99	j 🗪
Heterogeneity: Not appl	licable						
Test for overall effect: Z	Z = 0.50 (P = 0.62)						
							-20 -10 0 10
Toot for subgroup, diffor	Chi2 F 04	طد o	(D 0.0E) 13 C	E C0/			Favours IM olanzapine Favours Other

Test for subgroup differences: $Chi^2 = 5.81$, df = 2 (P = 0.05), $I^2 = 65.6\%$

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

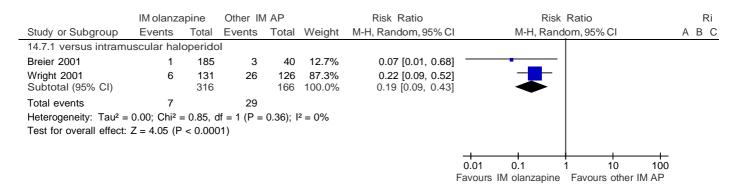
14.6 BEHAVIOUR: 1C. AVERAGE CHANGE SCORE (PANSS-EC) - MEDIUM TERM (1 HOURS)

			IM olanzapine	Other AP		Mean Difference	Mean Difference
Study or Subgroup	Mean Difference	SE	Tota	l Total	Weight	IV, Random, 95% C	I IV, Random, 95% CI
14.6.1 versus intram	uscular haloperido						
Eli 2004 [IP]	-1.1	2.1429	22	23	19.7%	-1.10 [-5.30, 3.10]]
Hsu 2010 [IP]	-3.6	1.47	11	11	30.6%	-3.60 [-6.48, -0.72]]
Wright 2001	-0.18	0.6939		_	49.6%	-0.18 [-1.54, 1.18]	
Subtotal (95% CI)			164	160	100.0%	-1.41 [-3.68, 0.86]	· •
Heterogeneity: Tau ² =	= 2.23; Chi ² = 4.44, d	f = 2 (P =	$= 0.11$); $I^2 = 55\%$	•			
Test for overall effect:	Z = 1.22 (P = 0.22)						
14.6.2 versus oral R	IS						
Hsu 2010 [IP]	-1.15	1.51	11	10	100.0%	-1.15 [-4.11, 1.81]	ı -
Subtotal (95% CI)			11	10	100.0%	-1.15 [-4.11, 1.81]	
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 0.76 (P = 0.45)						
14.6.3 versus ODT o	lanzapine						
Hsu 2010 [IP]	-0.5	1.51	11	10	100.0%	-0.50 [-3.46, 2.46]	ı —
Subtotal (95% CI)			11	10	100.0%	-0.50 [-3.46, 2.46]	-
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 0.33 (P = 0.74)						
							-20 -10 0 1
Test for subaroup diff	oroncos: Chi2 - 0.23	df = 2 (D = 0.80\ 12 = 00	0/_			Favours IM olanzapine Favours C

Test for subgroup differences: Chi² = 0.23, df = 2 (P = 0.89), $I^2 = 0\%$

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

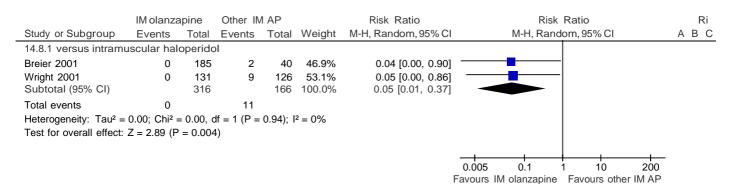
14.7 ADVERSE EFFECTS: 1B. EXTRAPYRAMIDAL SYMPTOMS - REQUIRING ANTICHOLINERGIC MEDICATION - BY 24 HOURS



Risk of bias legend

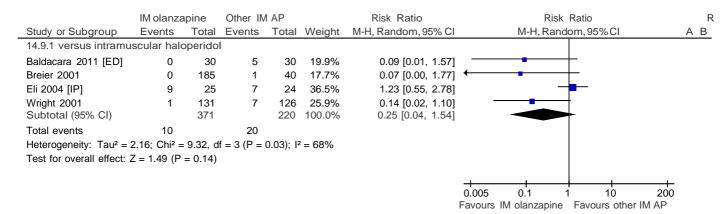
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

14.8 ADVERSE EFFECTS: 1C. EXTRAPYRAMIDAL SYMPTOMS - DYSTONIA - BY 24 HOURS



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

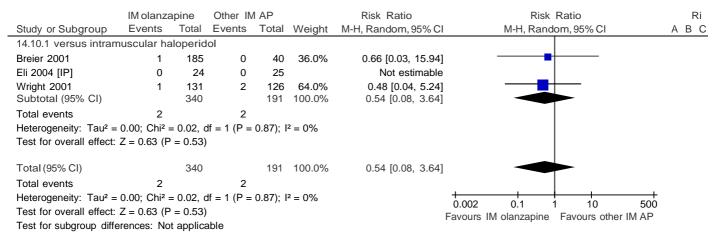
14.9 ADVERSE EFFECTS: 1D. EXTRAPYRAMIDAL SYMPTOMS/EXTRAPYRAMIDAL SYNDROME



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

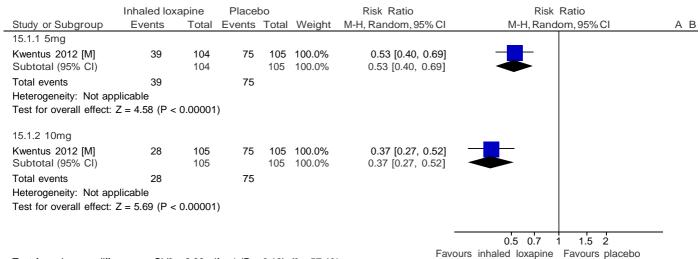
14.10 ADVERSE EFFECTS: 2. SERIOUS ADVERSE EVENT



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

15 INHALED LOXAPINE VERSUS PLACEBO [NCCMH]

15.1 GLOBAL IMPRESSION: 1. MILD TO MARKED AGITATION AT 2 HOURS POST-DOSE (ACES)



Test for subgroup differences: $Chi^2 = 2.33$, df = 1 (P = 0.13), $I^2 = 57.1\%$

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

15.2 GLOBAL IMPRESSION: 2. NON-RESPONSE (CLINICAL GLOBAL IMPRESSIONS - IMPROVEMENT SCALE)

	Inhaled lox	apine	Placel	00		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	Α
15.2.1 5mg								
Allen 2011b [M]	23	45	34	43	29.2%	0.65 [0.47, 0.89]		
Kwentus 2012 [M]	35	104	76	105	32.5%	0.46 [0.35, 0.62]		
Lesem 2011 [M]	50	116	74	115	38.3%	0.67 [0.52, 0.86]	_	
Subtotal (95% CI)		265		263	100.0%	0.59 [0.47, 0.74]	•	
Total events	108		184					
Heterogeneity: Tau ² =	0.02 ; $Chi^2 = 3$	3.86, df =	2 (P = 0.	15); l² =	= 48%			
Test for overall effect:	Z = 4.50 (P <	0.00001)					
15.2.2 10mg								
Allen 2011b [M]	15	40	34	43	24.0%	0.47 [0.31, 0.73]		
Kwentus 2012 [M]	27	105	76	105	33.8%	0.36 [0.25, 0.50]		
Lesem 2011 [M]	37	112	74	115	42.2%	0.51 [0.38, 0.69]	-	
Subtotal (95% CI)		257		263	100.0%	0.44 [0.35, 0.56]	•	
Total events	79		184					
Heterogeneity: Tau ² =	0.01 ; $Chi^2 = 2$.62, df =	2 (P = 0.	27); l² =	= 24%			
Test for overall effect:	Z = 6.86 (P <	0.00001)					
						0.1	0.2 0.5 1 2 5	10
							0.2 0.5 1 2 5 inhaled loxapine Favours placebo	

Test for subgroup differences: Chi² = 2.83, df = 1 (P = 0.09), I^2 = 64.6% Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

15.3 GLOBAL IMPRESSION: 3. DEEP SLEEP (ACES)

	Inhaled loxapine Placebo			00		Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year	M-H, Fixe	d, 95% CI	Α
15.3.1 5mg										-
Kwentus 2012 [M]	10	104	2	105	100.0%	5.05 [1.13, 22.48]	2012		_	
Subtotal (95% CI)		104		105	100.0%	5.05 [1.13, 22.48]				
Total events	10		2							
Heterogeneity: Not ap	plicable									
Test for overall effect:	Z = 2.12 (P =	0.03)								
15.3.2 10mg										
Kwentus 2012 [M]	13	105	2	105	100.0%	6.50 [1.50, 28.10]	2012			
Subtotal (95% CI)		105		105	100.0%	6.50 [1.50, 28.10]				
Total events	13		2							
Heterogeneity: Not ap	plicable									
Test for overall effect:	Z = 2.51 (P =	0.01)								
								0.005 0.1	1 10	200
							Fav	ours inhaled loxapine	Favours place	
									o p.a.oo	

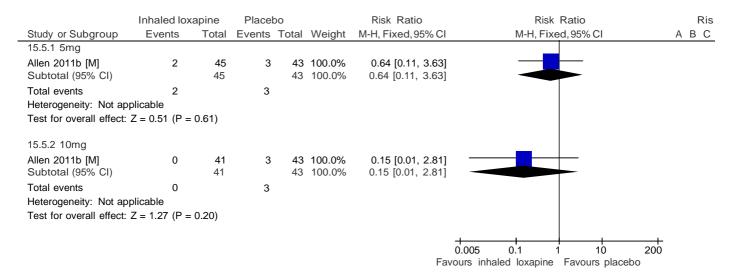
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

15.4 GLOBAL IMPRESSION: 4. UNAROUSABLE (ACES)

	Inhaled lox	apine	Placeb	00	Risk Ratio	Risk Ratio	Ris
Study or Subgroup	Events	Total	Events	Total Weigh	t M-H, Fixed, 95% CI	M-H, Fixed, 95% CI	АВ (
15.4.1 5mg							
Kwentus 2012 [M]	0	104	0	105	Not estimable		
Lesem 2011 [M]	0	116	0	115	Not estimable		
Subtotal (95% CI)		220		220	Not estimable		
Total events	0		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Not applicable	;					
15.4.2 10mg							
Kwentus 2012 [M]	0	105	0	105	Not estimable		
Lesem 2011 [M]	0	112	0	115	Not estimable		
Subtotal (95% CI)		217		220	Not estimable		
Total events	0		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Not applicable)					
					+	1 1	
						005 0.1 1 10 rs inhaled loxapine Favours placebo	200
					ravou	is illiaied luxapille Favouis placebo	

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

15.5 GLOBAL IMPRESSION: 5. NEED FOR RESCUE MEDICATION AT 4 HOURS



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

15.6 GLOBAL IMPRESSION: 5. NEED FOR RESCUE MEDICATION AT 24 HOURS

1	Inhaled lox	apine	Placel	00		Risk Ratio	F	Risk Ratio	Ris
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H,	Fixed, 95% CI	АВС
15.6.1 5mg							_	_	
Allen 2011b [M]	5	45	14	43	100.0%	0.34 [0.13, 0.87]	_	<u>-</u>	
Subtotal (95% CI)		45		43	100.0%	0.34 [0.13, 0.87]	◀	>	
Total events	5		14						
Heterogeneity: Not applie	cable								
Test for overall effect: Z	= 2.26 (P =	0.02)							
15.6.2 10mg									
Allen 2011b [M]	6	41	14	43	100.0%	0.45 [0.19, 1.06]	_	-	
Subtotal (95% CI)		41		43	100.0%	0.45 [0.19, 1.06]	•		
Total events	6		14						
Heterogeneity: Not applie	cable								
Test for overall effect: Z	= 1.83 (P =	0.07)							
							0.005 0.1	1 10	200
						Fav	ours inhaled loxap	ine Favours place	

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

15.7 BEHAVIOUR: 1A. AVERAGE CHANGE SCORE (PANSS-EC) - MEDIUM TERM (2 HOURS)

	Inhaled	loxap	ine	Pla	cebo)		Std. Mean Difference	Std. I	Mean Diffe	rence	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total V	Veight	IV, Random, 95% CI	IV, F	Random, 95	% CI	
15.7.1 5mg												
Allen 2011b [M]	0	0	0	0	0	0		Not estimable				
Subtotal (95% CI)			0			0		Not estimable				
Heterogeneity: Not app	olicable											
Test for overall effect: I	Not applic	able										
Total (95% CI)			0			0		Not estimable				
Heterogeneity: Not app	olicable							F	100 50			100
Test for overall effect: I	Not applic	able							100 -50 ours [experime	untall Fav	50 ours [cont	100
Test for subgroup differ	rences: N	ot appl	icable					Tav	ours fexberning	iitaij Lavi	Juis [COIII	uoij

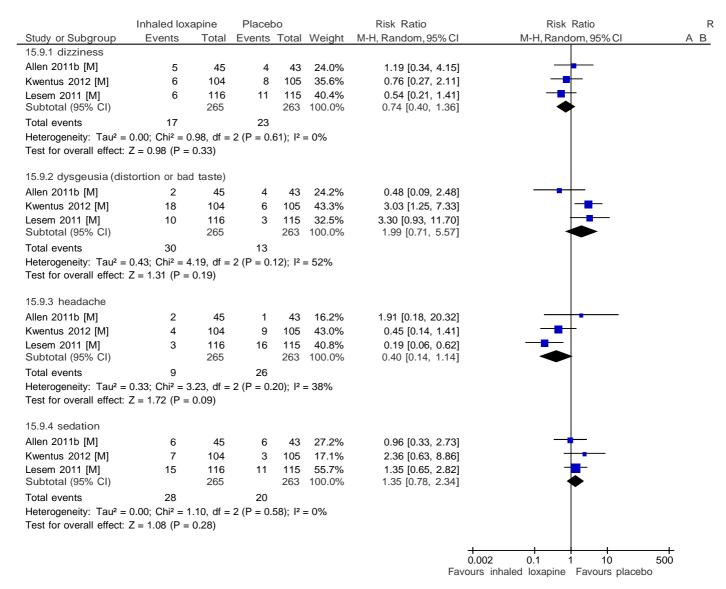
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

15.8 ADVERSE EFFECTS: 1. AT LEAST ONE ADVERSE EFFECT

	Inhaled lox	apine	Placel	bo		Risk Ratio	Risk Ratio	R
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	АВ
15.8.1 5mg Allen								
2011b [M]	14	45	14	43	22.4%	0.96 [0.52, 1.76]	-	
Kwentus 2012 [M]	36	104	24	105	34.0%	1.51 [0.98, 2.35]	 	
Lesem 2011 [M] Subtotal (95% CI)	40	116 265	44	115 263	43.6% 100.0%	0.90 [0.64, 1.27] 1.09 [0.77, 1.54]	•	
Total events	90		82					
Heterogeneity: Tau ² =	0.04; Chi ² = 3	3.51, df =	2 (P = 0.	17); l ² :	= 43%			
Test for overall effect:	Z = 0.49 (P =	0.62)						
15.8.2 10mg								
Allen 2011b [M]	16	41	14	43	17.9%	1.20 [0.67, 2.13]	- 	
Kwentus 2012 [M]	30	105	24	105	27.7%	1.25 [0.79, 1.99]	 -	
Lesem 2011 [M] Subtotal (95% CI)	43	113 259	44	115 263	54.4% 100.0%	0.99 [0.71, 1.38] 1.10 [0.86, 1.40]	*	
Total events	89		82					
Heterogeneity: Tau ² =	: 0.00; Chi ² = 0).74, df =	2 (P = 0.	.69); I ² :	= 0%			
Test for overall effect:	-	-	`	,,				
							0.01 0.1 1 10	100
						Favo	ours inhaled loxapine Favours placebo	D

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

15.9 ADVERSE EFFECTS: 2. TREATMENT-EMERGENT ADVERSE EFFECTS IN ≥ 5% OF PATIENTS -5 MG VERSUS PLACEBO



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

15.10 ADVERSE EFFECTS: 2. TREATMENT-EMERGENT ADVERSE EFFECTS IN $\geq 5\%$ OF PATIENTS –10 MG VERSUS PLACEBO

	Inhaled lox	•	Placeb			Risk Ratio	Risk Ratio	F
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	A E
15.10.1 dizziness								
Allen 2011b [M]	2	41	4	43	12.9%	0.52 [0.10, 2.71]	-	
Kwentus 2012 [M]	5	105	8	105	29.5%	0.63 [0.21, 1.85]		
Lesem 2011 [M]	12	113	11	115	57.6%	1.11 [0.51, 2.41]		
Subtotal (95% CI)		259		263	100.0%	0.85 [0.47, 1.53]	•	
Total events	19		23					
Heterogeneity: Tau ² = Test for overall effect:			2 (P = 0.	58); I²:	= 0%			
15.10.2 dysgeusia (d	listortion or b	ad taste)					
Allen 2011b [M]	7	41	4	43	28.1%	1.84 [0.58, 5.81]	 	
Kwentus 2012 [M]	18	105	6	105	47.7%	3.00 [1.24, 7.26]		
Lesem 2011 [M] Subtotal (95% CI)	12	113 259	3	115 263	24.3% 100.0%	4.07 [1.18, 14.04] 2.81 [1.53, 5.18]	•	
Total events	37		13					
Test for overall effect:	Z = 3.32 (P =	0.0009)	·	,.				
15.10.3 headache								
Allen 2011b [M]	2	41	1	43	19.3%	2.10 [0.20, 22.26]		
Kwentus 2012 [M]	2	105	9	105	35.6%	0.22 [0.05, 1.00]		
Lesem 2011 [M] Subtotal (95% CI)	3	113 259	16	115 263	45.1% 100.0%	0.19 [0.06, 0.64] 0.32 [0.10, 1.04]		
Total events	7		26					
Heterogeneity: Tau ² = Test for overall effect:			2 (P = 0.	19); I²:	= 39%			
15.10.4 sedation								
Allen 2011b [M]	9	41	6	43	33.9%	1.57 [0.61, 4.03]	 	
Kwentus 2012 [M]	6	105	3	105	16.2%	2.00 [0.51, 7.79]	 •	
Lesem 2011 [M] Subtotal (95% CI)	12	113 259	11	115 263	49.8% 100.0%	1.11 [0.51, 2.41] 1.37 [0.80, 2.38]		
Total events	27		20					
Heterogeneity: Tau ² = Test for overall effect:			2 (P = 0.	72); l²:	= 0%			
							1 1	+
								100 ırs placeb

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

16 INTRAVENEOUS BENZODIAZEPINE VERSUS INTRAVENEOUS HALOPERIDOL (FOR ACUTE BEHAVIOUR DUE TO PSYCHOSIS)

16.1 GLOBAL IMPRESSION: 1. NO IMPROVEMENT



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

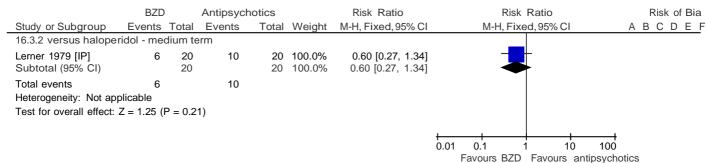
16.2 GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

16.3 GLOBAL IMPRESSION: 3. SEDATION



Test for subgroup differences: Not applicable

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

16.4 ADVERSE EFFECTS

	BZD+AP	Antipsych	notics	Risk Ratio			Risk		Risk	
Study or Subgroup	Events Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Rand	om, 95% CI		ABC
							1			
						0.01	0.1	1 10	100	
						Fav	ours BZD+AP	Favours a	ntipsychot	ics

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

17 INTRAVENEOUS OLANZAPINE PLUS MIDAZOLAM VERSUS PLACEBO PLUS MIDAZOLAM [NCCMH]

17.1 GLOBAL IMPRESSION: 1. NOT ADEQUATELY SEDATED

	IV olanzapine + midaz	olam	Placebo + midaz	olam		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	M-H, Random, 95% C
17.1.1 at 5 min							
Chan 2013 [ED]	70	109	84	115	100.0%	0.88 [0.74, 1.05]
Subtotal (95% CI)		109		115	100.0%	0.88 [0.74, 1.05]	1 ◆
Total events	70		84				
Heterogeneity: Not app	olicable						
Test for overall effect: 2	Z = 1.41 (P = 0.16)						
17.1.2 at 5 min							
Chan 2013 [ED]	35	109	59	115	100.0%	0.63 [0.45, 0.87]	ı -
Subtotal (95% CI)		109		115	100.0%	0.63 [0.45, 0.87]	ı
Total events	35		59				
Heterogeneity: Not app	olicable						
Test for overall effect: 2	Z = 2.82 (P = 0.005)						
17.1.3 at 30 min							
Chan 2013 [ED]	11	109	25	_	100.0%	0.46 [0.24, 0.90	
Subtotal (95% CI)		109		115	100.0%	0.46 [0.24, 0.90]	
Total events	11		25				
Heterogeneity: Not app							
Test for overall effect: 2	Z = 2.28 (P = 0.02)						
17.1.4 at 60 min							
Chan 2013 [ED]	5	109	15	115	100.0%	0.35 [0.13, 0.93]]
Subtotal (95% CI)		109		115	100.0%	0.35 [0.13, 0.93]	
Total events	5		15				
Heterogeneity: Not app							
Test for overall effect: 2	Z = 2.10 (P = 0.04)						
							0.1 0.2 0.5 1 2
							Favours IV olanzapine Favours p

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

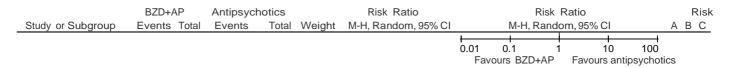
17.2 GLOBAL IMPRESSION: 2. REQUIRING ADDITIONAL INTRAMUSCULAR INJECTION

	IV olanzapine + midaze	olam	Placebo + midaz	olam		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95	% C
17.2.1 to reach initial	adquate sedation							
Chan 2013 [ED] Subtotal (95% CI)	20	109 109	29		100.0% 100.0%	0.73 [0.44, 1.21] 0.73 [0.44, 1.21]		
Total events	20		29					
Heterogeneity: Not app	plicable							
Test for overall effect:	Z = 1.23 (P = 0.22)							
17.2.2 resedation in the	he 60min after initial add	equate s	sedation					
Chan 2013 [ED] Subtotal (95% CI)	25	109 109	42		100.0% 100.0%	0.63 [0.41, 0.96] 0.63 [0.41, 0.96]		
Total events	25		42					
Heterogeneity: Not app	plicable							
Test for overall effect:	Z = 2.17 (P = 0.03)							
17.2.3 resedation from	n 60 min after initial ade	quate s	edation until ED	discharg	je			
Chan 2013 [ED]	35	109	37		100.0%	1.00 [0.68, 1.46]	-	
Subtotal (95% CI)		109		115	100.0%	1.00 [0.68, 1.46]	•	
Total events	35		37					
Heterogeneity: Not app	plicable							
Test for overall effect:	Z = 0.01 (P = 0.99)							
							0.1 0.2 0.5 1	—— 2
						Favours		vours
							pla	cebo

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

17.3 GLOBAL IMPRESSION: 3. SEDATION



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

17.4 ADVERSE EFFECTS: 1. NO. WITH REPORTED ADVERSE EVENT

	IV olanzapine + mida	zolam	Placebo + mida	azolam		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% C
Chan 2013 [ED]	9	109	18	115	100.0%	0.53 [0.25, 1.12]	_
Total (95% CI)		109		115	100.0%	0.53 [0.25, 1.12]	
Total events	9		18				
Heterogeneity: Not app	olicable						
Test for overall effect:	Z = 1.66 (P = 0.10)					Fa	0.1 0.2 0.5 1 2 vours IV olanzapine Favours placebo

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

17.5 ADVERSE EFFECTS: 2. OTHER - BY 24 HOURS

	IV olanzapine + midaze	olam	Placebo + midazo	olam		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% (
17.5.1 airway obstruc	tion						
Chan 2013 [ED] Subtotal (95% CI)	3	109 109	5		100.0% 100.0%	0.63 [0.15, 2.59] 0.63 [0.15, 2.59]	
Total events Heterogeneity: Not app			5				
Test for overall effect:	$Z = 0.04 \ (P = 0.52)$						
17.5.2 oxyen desatura	ation						_
Chan 2013 [ED] Subtotal (95% CI)	5	109 109	9		100.0% 100.0%	0.59 [0.20, 1.69] 0.59 [0.20, 1.69]	
Total events	5		9				
Heterogeneity: Not approved for overall effect:							
17.5.3 hypotension							
Chan 2013 [ED] Subtotal (95% CI)	3	109 109	6		100.0% 100.0%	0.53 [0.14, 2.06] 0.53 [0.14, 2.06]	
Total events Heterogeneity: Not appress for overall effect:			6				
17.5.4 arrhythmia							
Chan 2013 [ED] Subtotal (95% CI)	1	109 109	1		100.0% 100.0%	1.06 [0.07, 16.66] 1.06 [0.07, 16.66]	
Total events Heterogeneity: Not appress for overall effect:			1				
17.5.5 decreased Gla	sgow Coma Scale (scor	o of 6)					
Chan 2013 [ED]	sgow coma scale (scor	109	1	115	100.0%	0.35 [0.01, 8.54]	
Subtotal (95% CI)	U	109	1		100.0%	0.35 [0.01, 8.54]	
Total events	0		1				
Heterogeneity: Not app							
Test for overall effect:	Z = 0.64 (P = 0.52)						
							+ + + + + + + + + + + + + + + + + + + +
						-	0.01 0.1 1
						Favours	intravenous olanzapine Favou placeb

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias