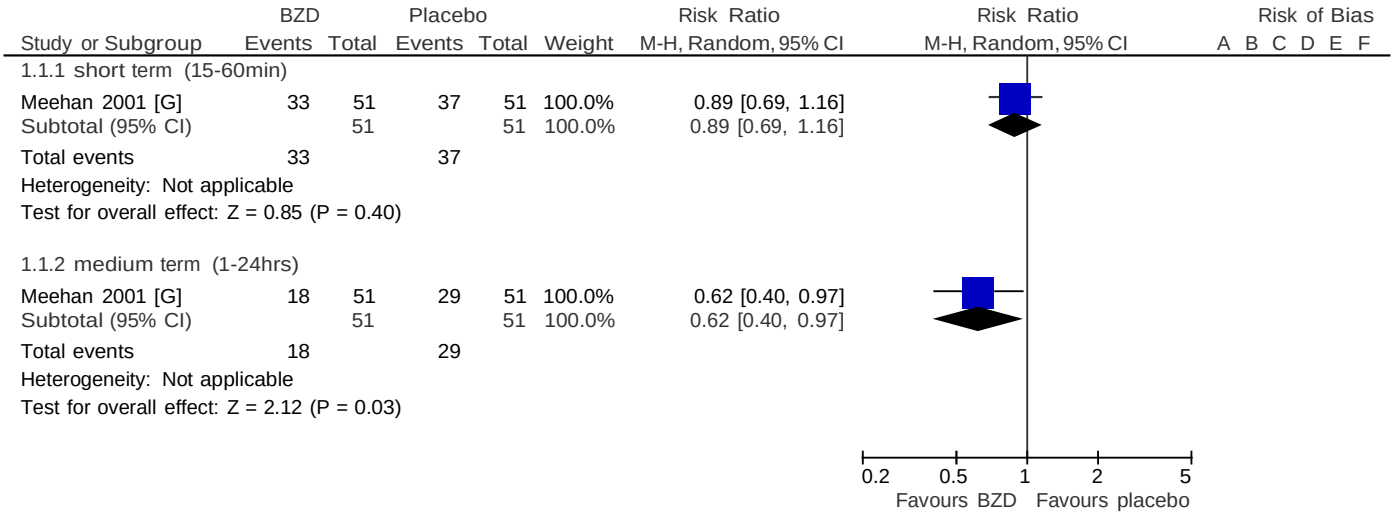
APPENDIX 15B: CLINICAL EVIDENCE – FOREST PLOTS FOR REVIEW OF RAPID TRANQUILLISATION

Abbreviations

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

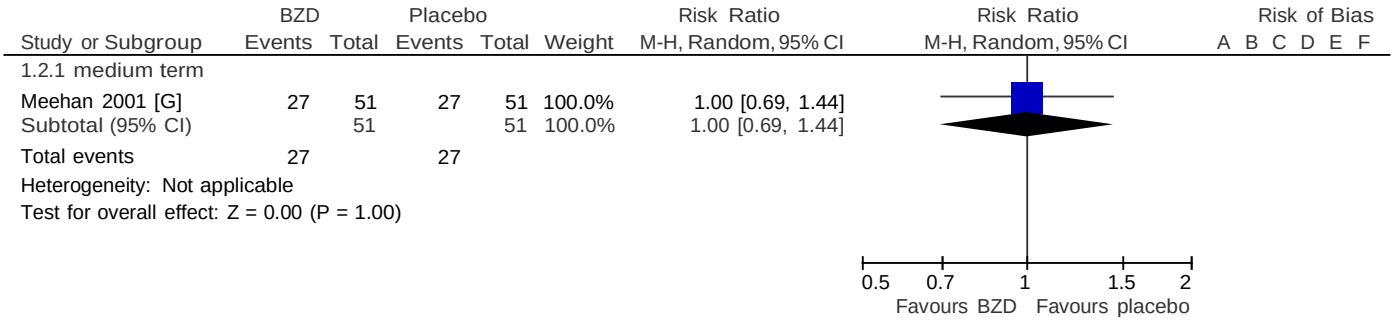
1 INTRAMUSCULAR BENZODIAZEPINE VERSUS PLACEBO [ADAPTED FROM GILLIES 2013]

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



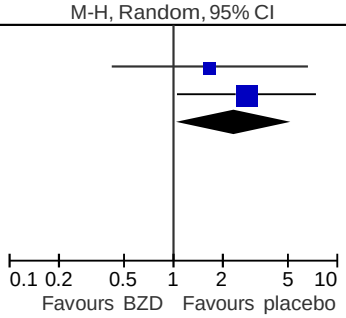
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

1.3 GLOBAL IMPRESSION: 3. SEDATION

Study or Subgroup	BZD Events	BZD Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.3.1 medium term						
Meehan 2001 [G]	5	51	3	51	33.5%	1.67 [0.42, 6.61]
Zimbroff 2007	13	68	5	73	66.5%	2.79 [1.05, 7.42]
Subtotal (95% CI)		119		124	100.0%	2.35 [1.06, 5.21]
Total events	18		8			

Heterogeneity: Tau² = 0.00; Chi² = 0.36, df = 1 (P = 0.55); I² = 0%

Test for overall effect: Z = 2.10 (P = 0.04)



Risk of bias legend

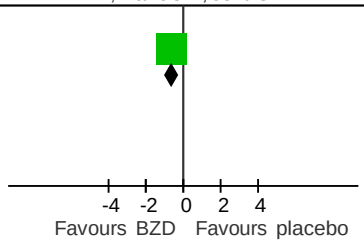
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other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

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

Study or Subgroup	BZD Mean	BZD SD	BZD Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.4.1 medium term								
Meehan 2001 [G]	-8.39	6.32	51	-4.78	5.49	50	100.0%	-0.60 [-1.00, -0.21]
Subtotal (95% CI)			51			50	100.0%	-0.60 [-1.00, -0.21]

Heterogeneity: Not applicable

Test for overall effect: Z = 2.97 (P = 0.003)



Risk of bias legend

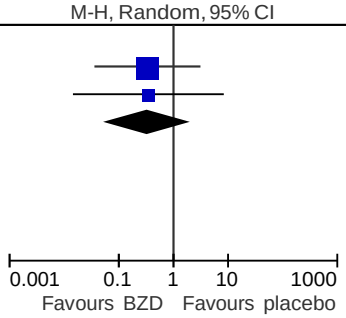
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other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

1.5 ADVERSE EFFECTS: 1. EXTRAPYRAMIDAL SYMPTOMS

Study or Subgroup	BZD Events	BZD Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.5.1 medium term						
Meehan 2001 [G]	1	51	3	51	67.1%	0.33 [0.04, 3.10]
Zimbroff 2007	0	69	1	72	32.9%	0.35 [0.01, 8.39]
Subtotal (95% CI)		120		123	100.0%	0.34 [0.05, 2.10]
Total events	1		4			

Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.98); I² = 0%

Test for overall effect: Z = 1.16 (P = 0.24)



Risk of Bias: A B C D E F G

Risk of bias legend

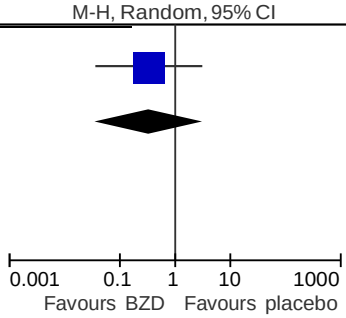
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other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

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

Study or Subgroup	BZD Events	BZD Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.6.1 medium term						
Meehan 2001 [G]	1	51	3	51	100.0%	0.33 [0.04, 3.10]
Zimbroff 2007	0	0	0	0		Not estimable
Subtotal (95% CI)		51		51	100.0%	0.33 [0.04, 3.10]
Total events	1		3			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.97 (P = 0.33)

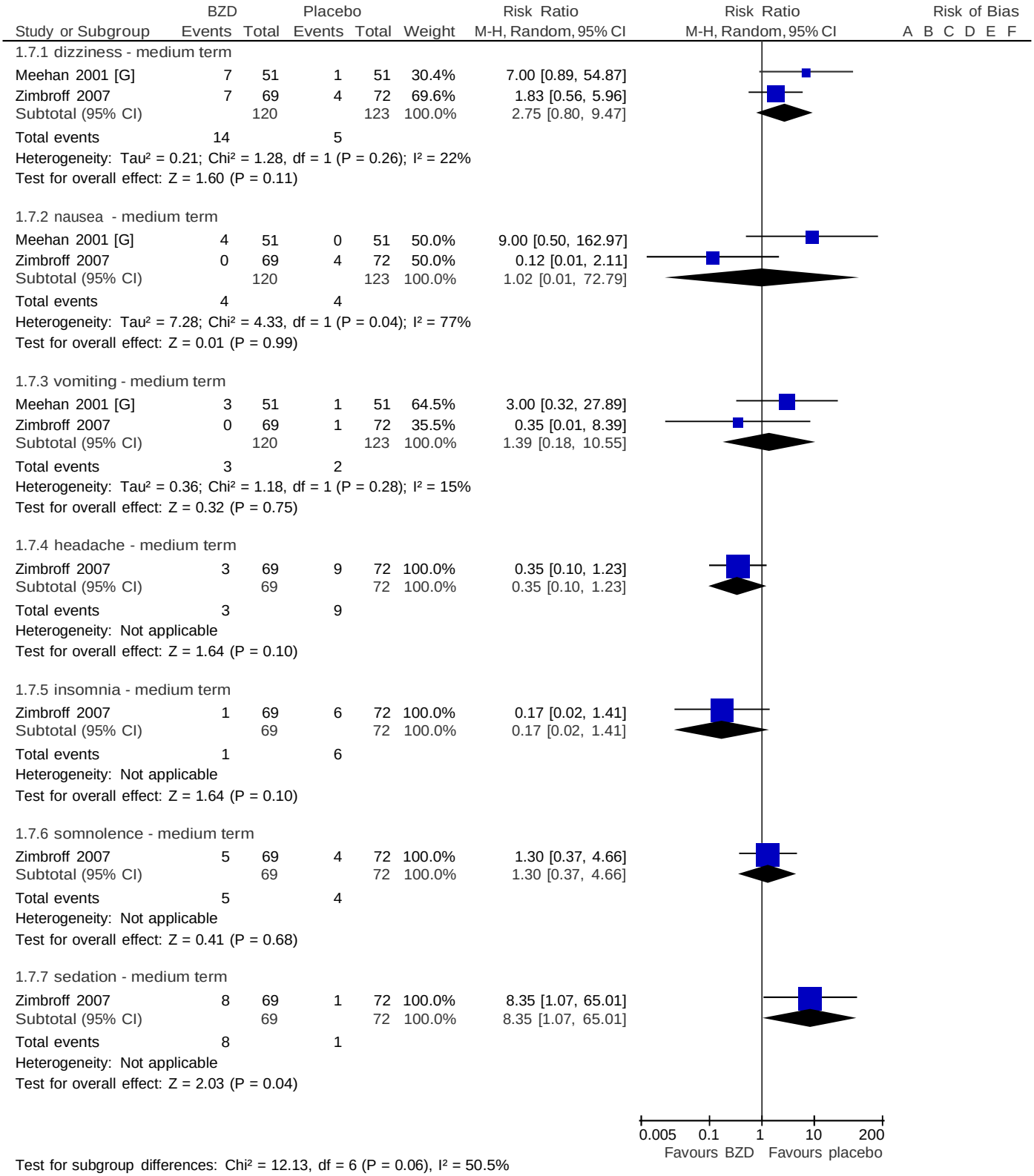


Risk of Bias: A B C D E F

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

1.7 ADVERSE EFFECTS: 3. SPECIFIC



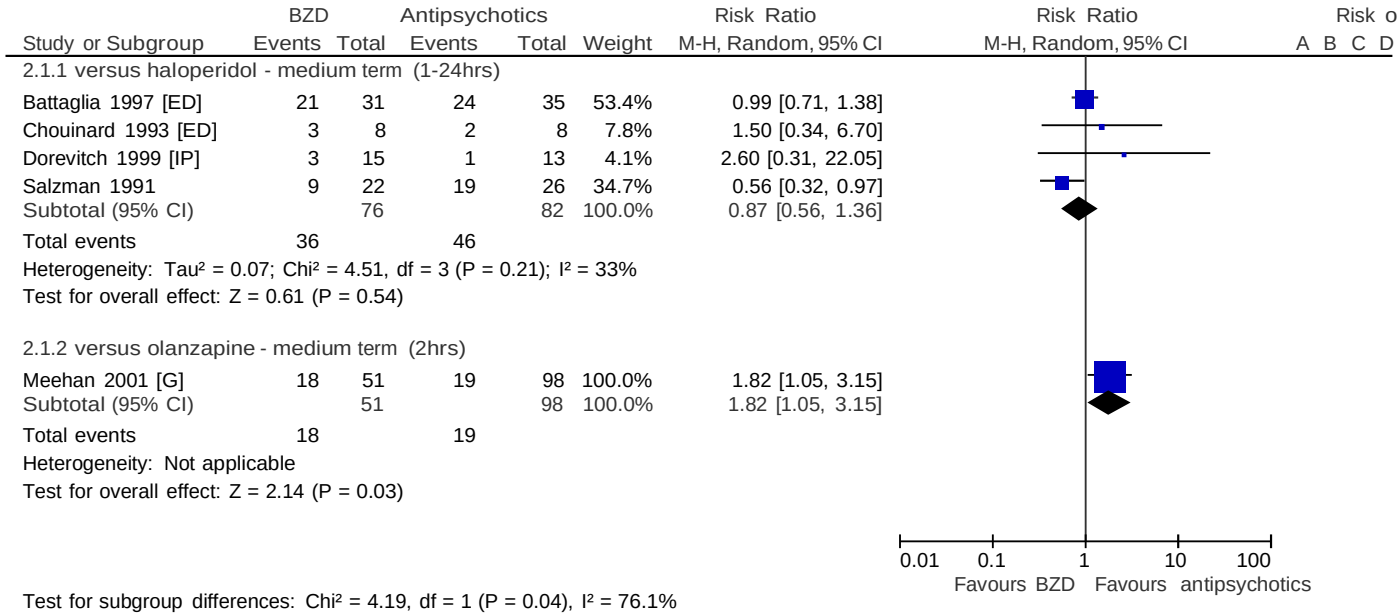
Test for subgroup differences: Chi² = 12.13, df = 6 (P = 0.06), I² = 50.5%

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 INTRAMUSCULAR BENZODIAZEPINE VERSUS ANTIPSYCHOTIC DRUG [ADAPTED FROM GILLIES 2013]

2.1 GLOBAL IMPRESSION: 1. NO IMPROVEMENT

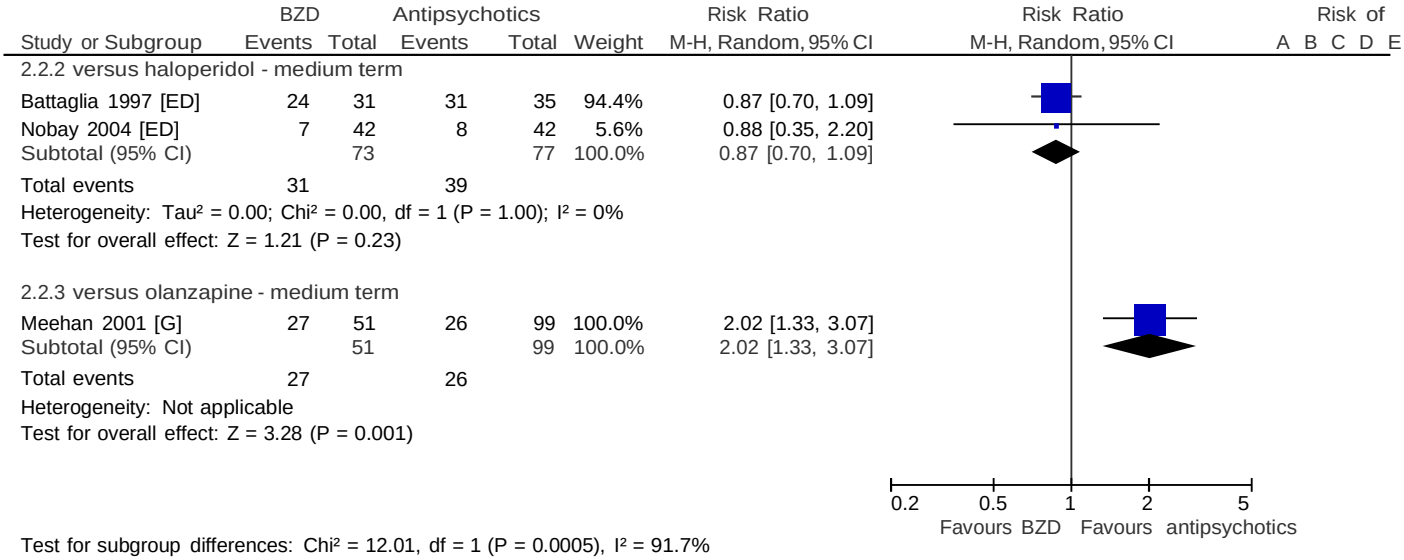


Test for subgroup differences: Chi² = 4.19, df = 1 (P = 0.04), I² = 76.1%

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

2.2 GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION

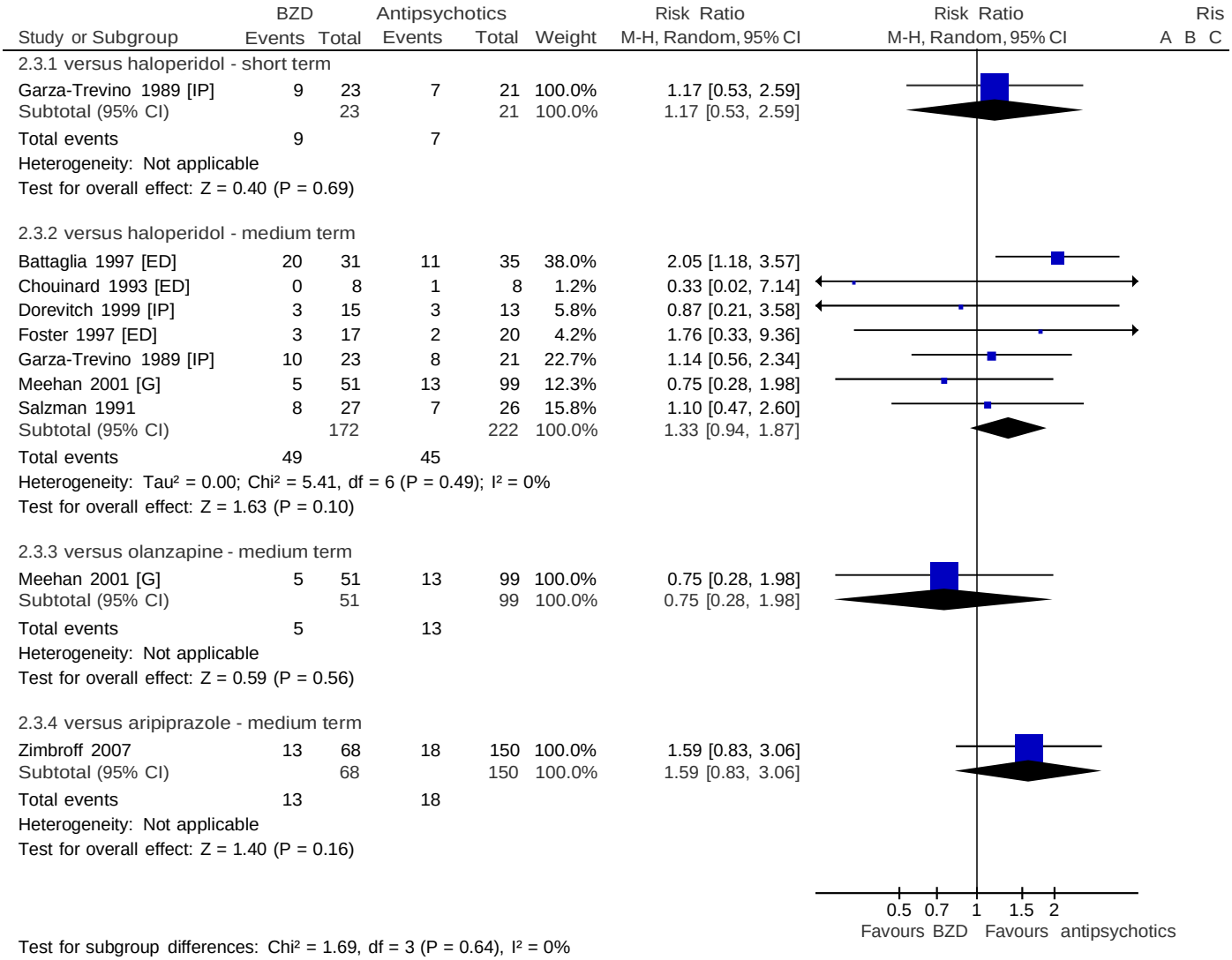


Test for subgroup differences: Chi² = 12.01, df = 1 (P = 0.0005), I² = 91.7%

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



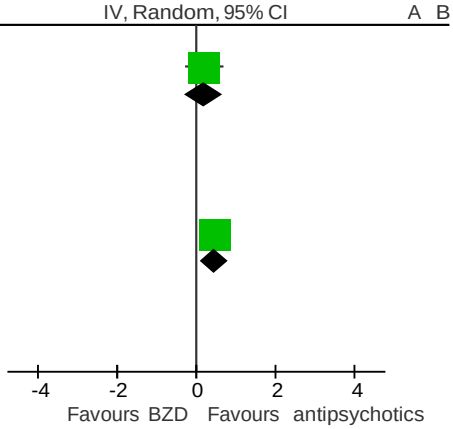
Test for subgroup differences: Chi² = 1.69, df = 3 (P = 0.64), I² = 0%

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

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

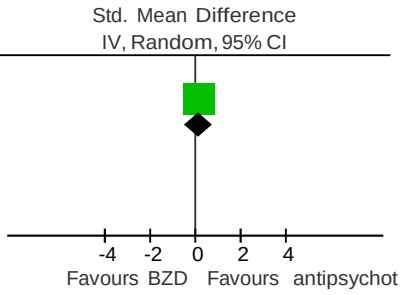
Study or Subgroup	BZD Mean	BZD SD	BZD Total	Antipsychotics Mean	Antipsychotics SD	Antipsychotics Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.4.1 versus haloperidol - medium term								
Battaglia 1997 [ED]	21.4	7.22	31	19.6	10.04	35	100.0%	0.20 [-0.28, 0.69]
Subtotal (95% CI)			31			35	100.0%	0.20 [-0.28, 0.69]
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.81 (P = 0.42)								
2.4.2 versus olanzapine - medium term								
Meehan 2001 [G]	-8.39	6.32	51	-11.3	6.09	98	100.0%	0.47 [0.13, 0.81]
Subtotal (95% CI)			51			98	100.0%	0.47 [0.13, 0.81]
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.68 (P = 0.007)								



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

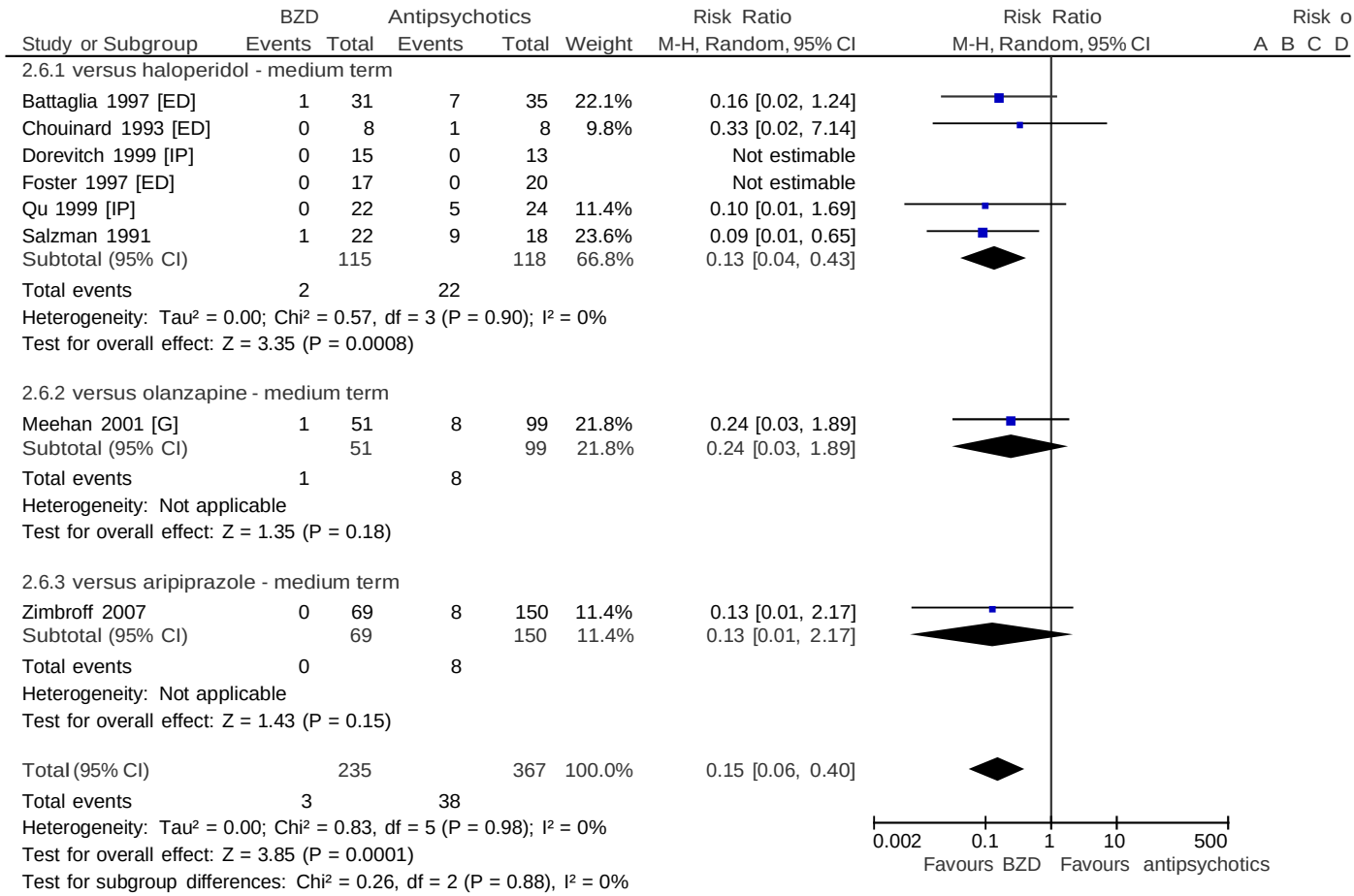
2.5 BEHAVIOUR: 2. AVERAGE CHANGE SCORE (OAS, HIGH = WORSE)

Study or Subgroup	BZD Mean	BZD SD	BZD Total	Antipsychotics Mean	Antipsychotics SD	Antipsychotics Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
2.5.1 versus haloperidol - medium term									
Qu 1999 [IP]	0.45	1.74	22	0.25	0.61	24	100.0%	0.15 [-0.43, 0.73]	
Subtotal (95% CI)			22			24	100.0%	0.15 [-0.43, 0.73]	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.52 (P = 0.60)									



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

2.6 ADVERSE EFFECTS: 1. EXTRAPYRAMIDAL SYMPTOMS



Risk of bias legend

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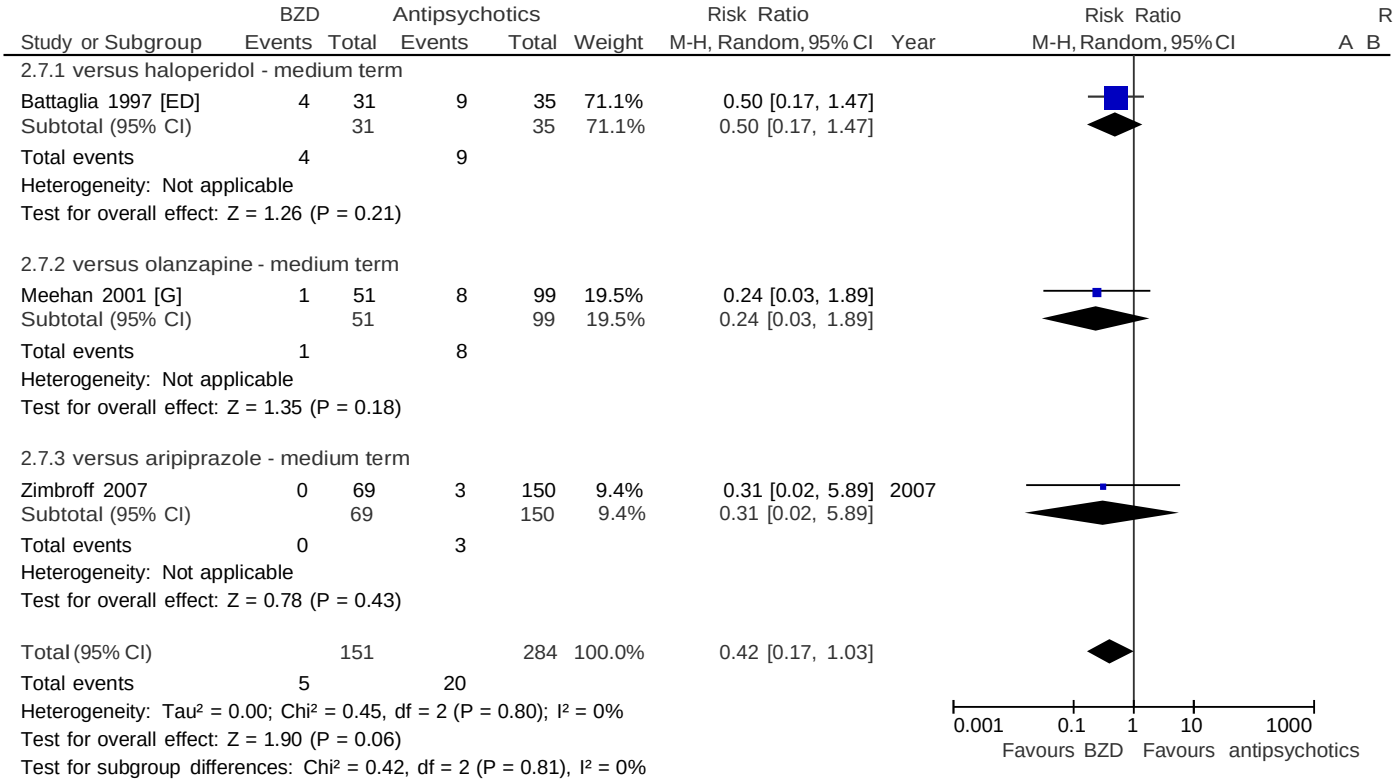
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

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



Risk of bias legend

(A) Random sequence generation (selection bias)
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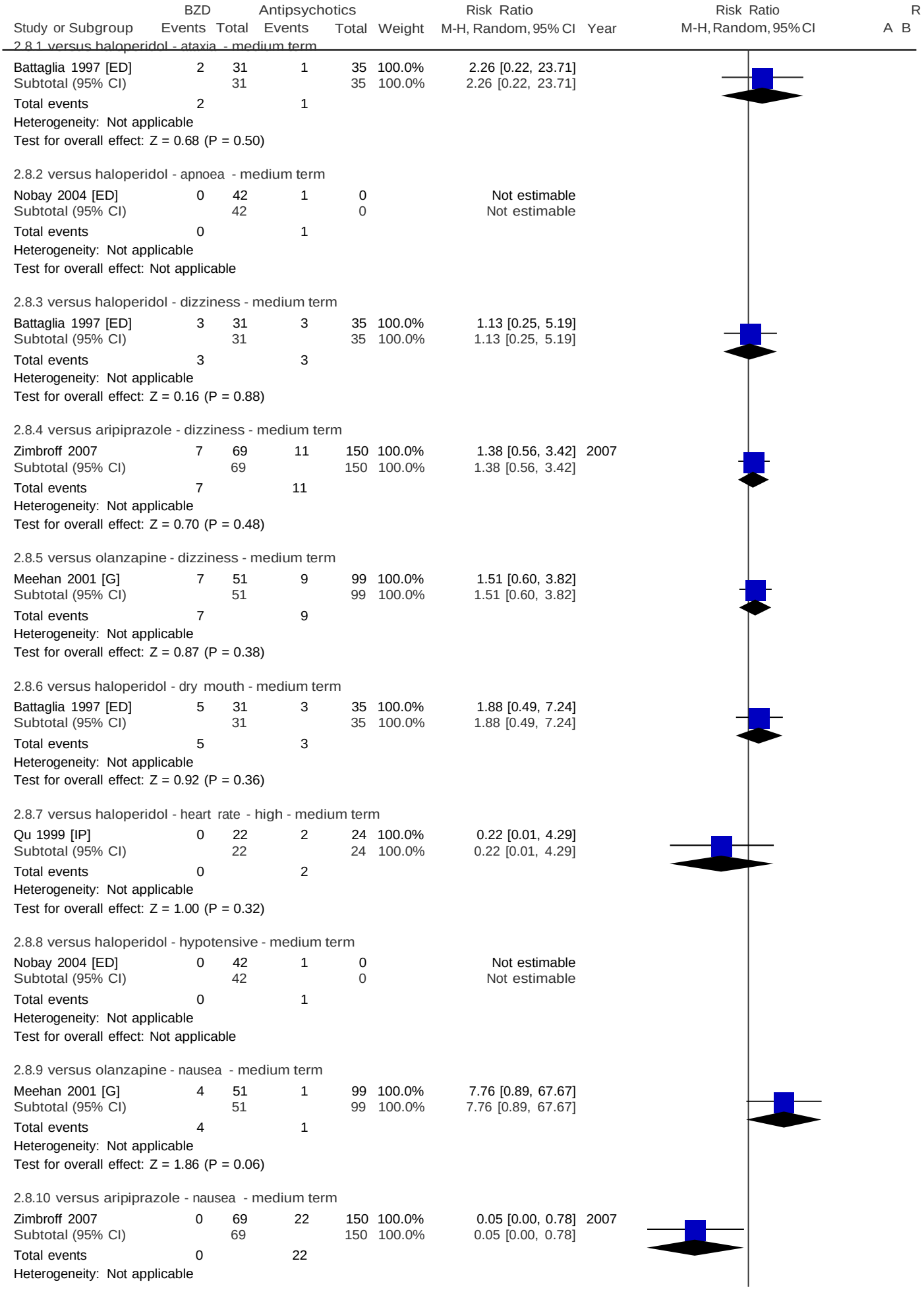
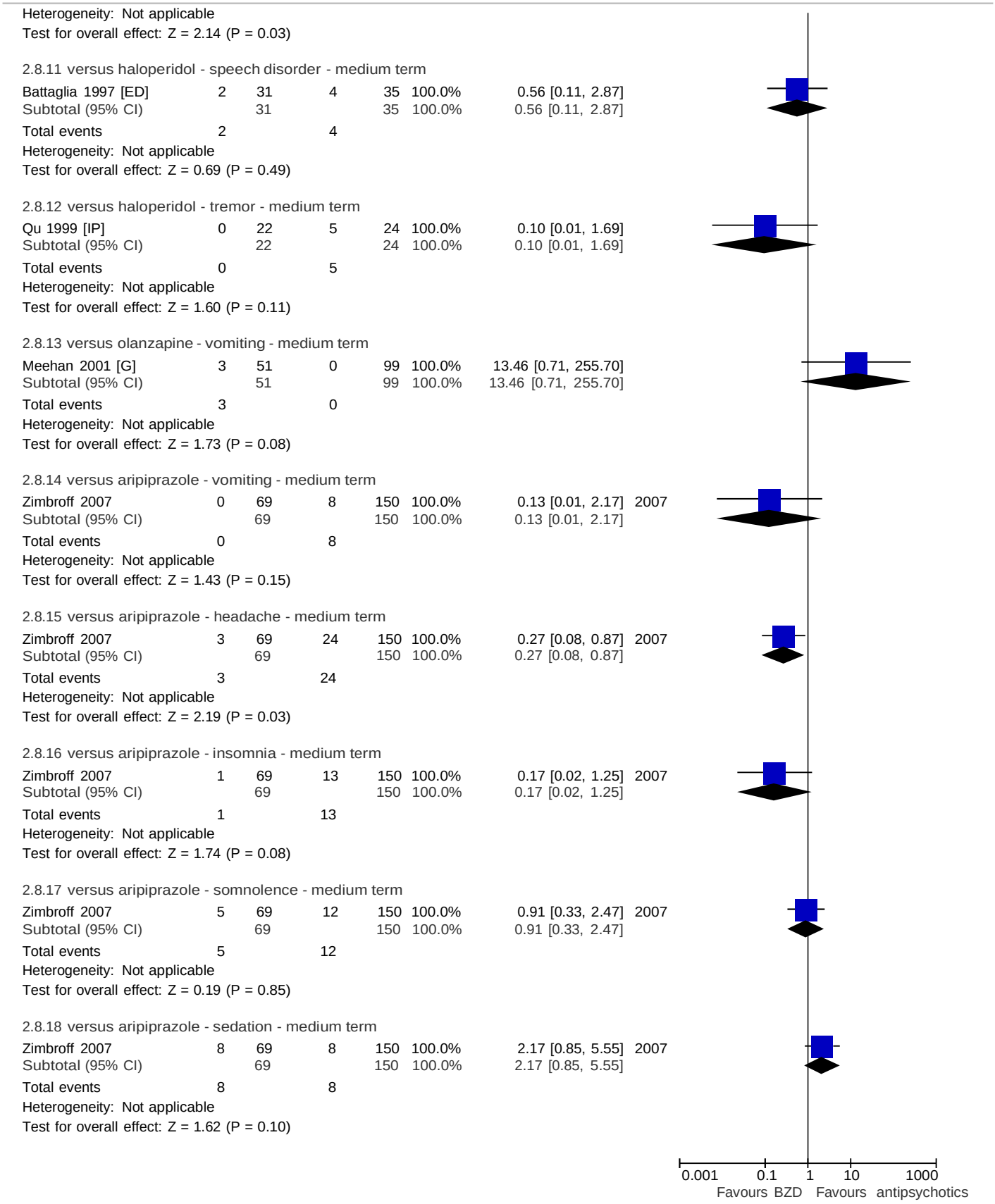
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

2.8 ADVERSE EFFECTS: 3. SPECIFIC





Risk of bias legend

(A) Random sequence generation (selection bias)
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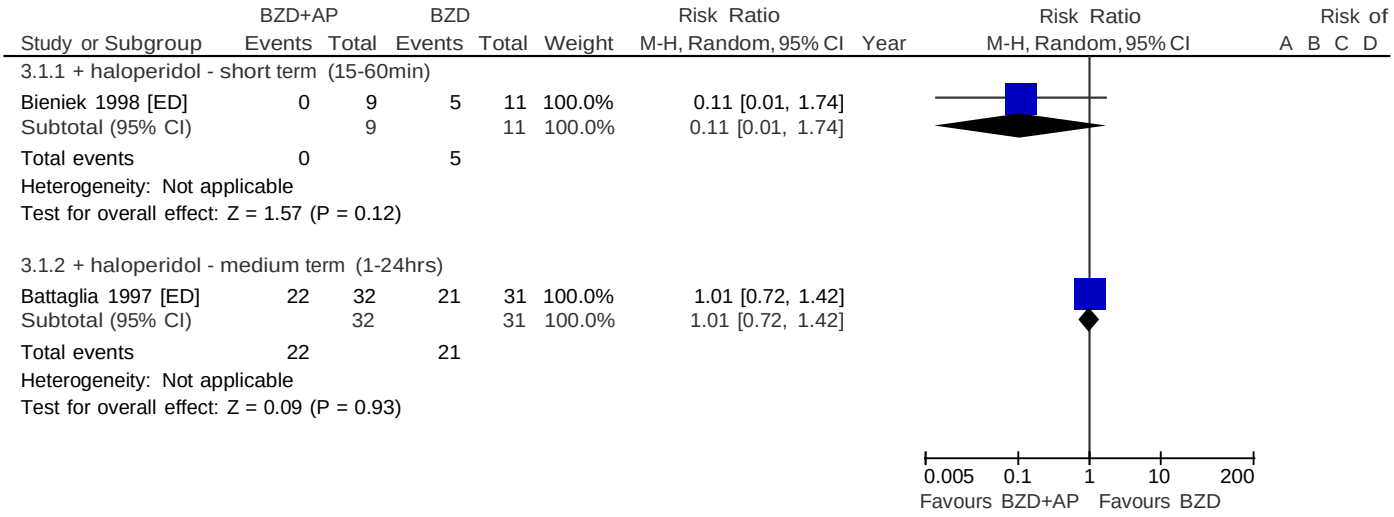
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

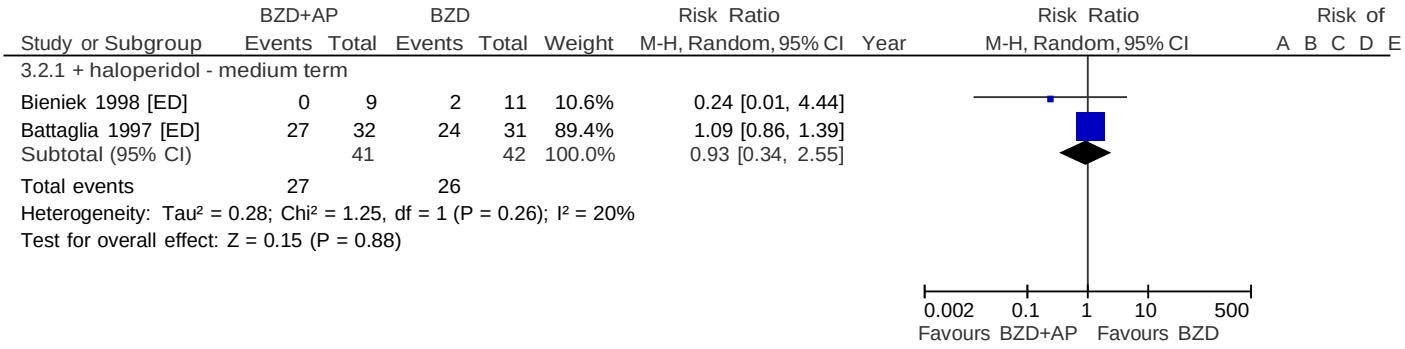
3 INTRAMUSCULAR BENZODIAZEPINE PLUS ANTIPSYCHOTIC DRUG SAME BENZODIAZEPINE [ADAPTED FROM GILLIES 2013]

3.1 GLOBAL IMPRESSION: 1. NO IMPROVEMENT



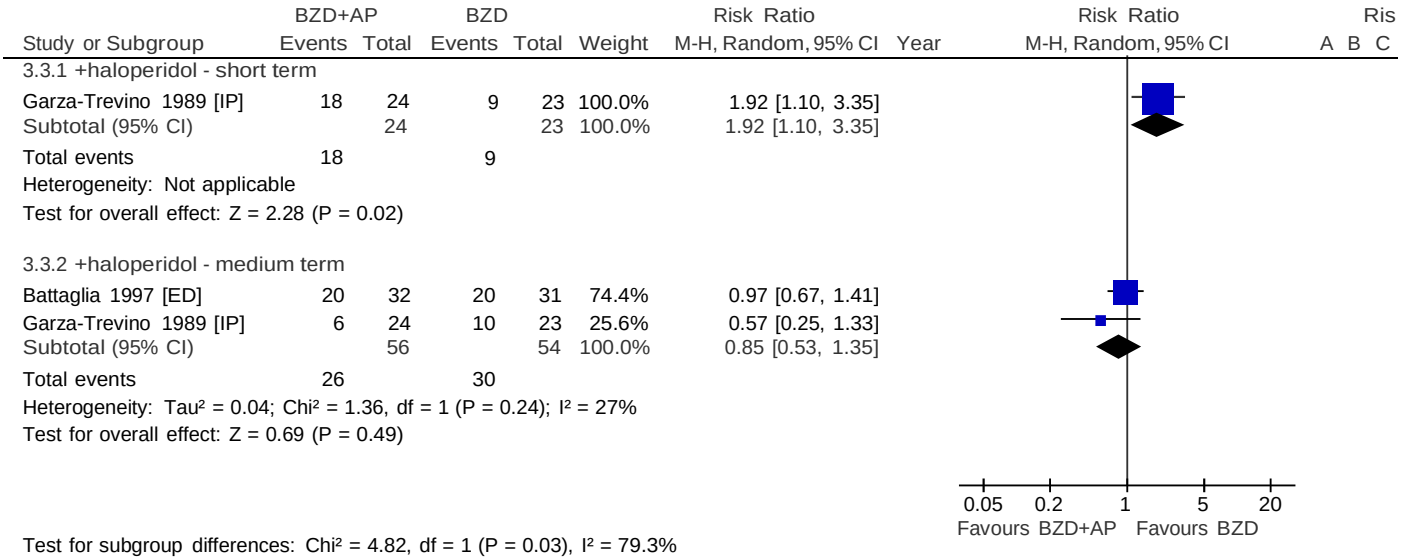
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

3.2 GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION



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

3.3 GLOBAL IMPRESSION: 3. SEDATION

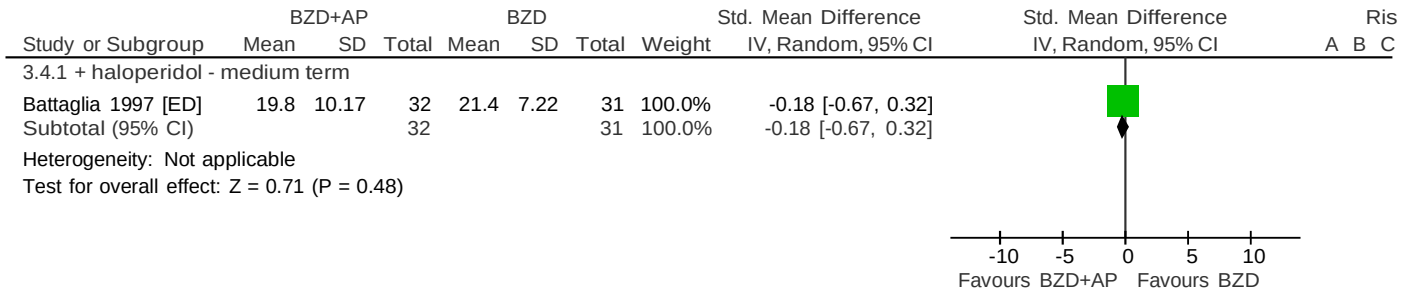


Test for subgroup differences: Chi² = 4.82, df = 1 (P = 0.03), I² = 79.3%

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

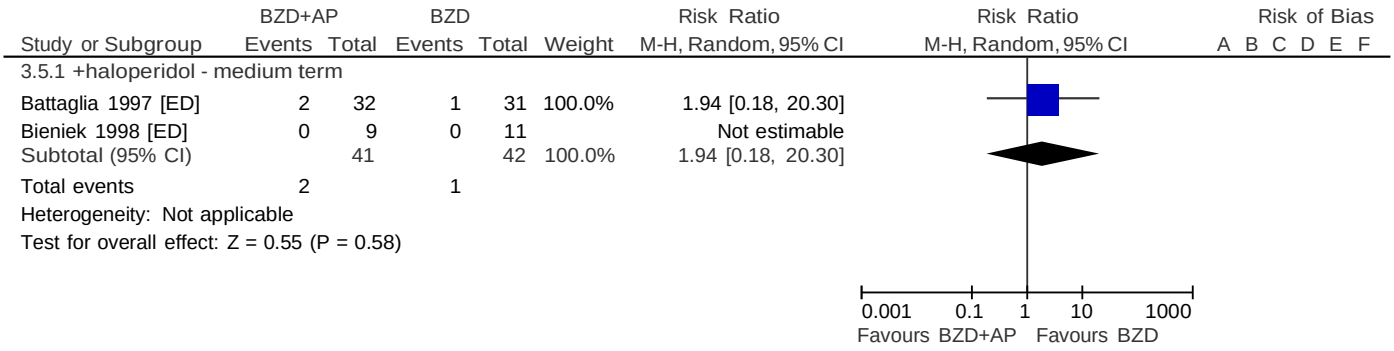
3.4 BEHAVIOUR: 1. AVERAGE ENDPOINT SCORE (ABS, HIGH = WORSE)



Risk of bias legend

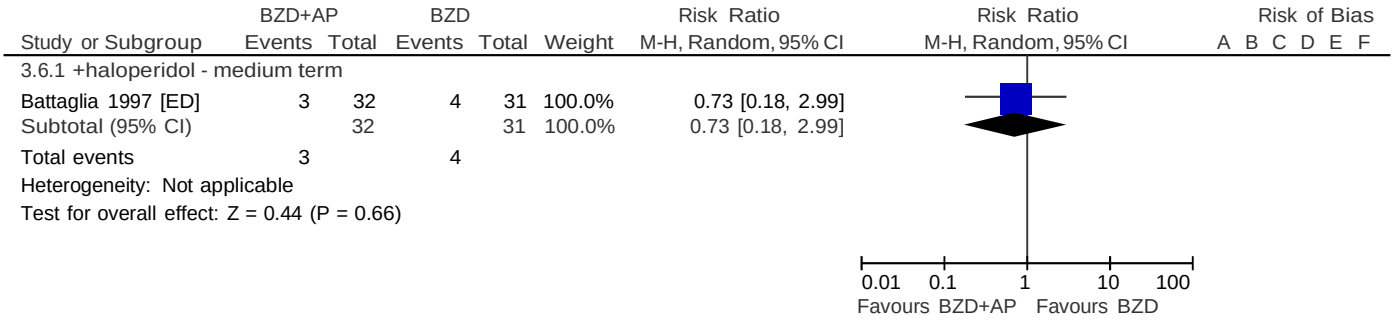
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other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

3.5 ADVERSE EFFECTS: 1. EXTRAPYRAMIDAL SYMPTOMS



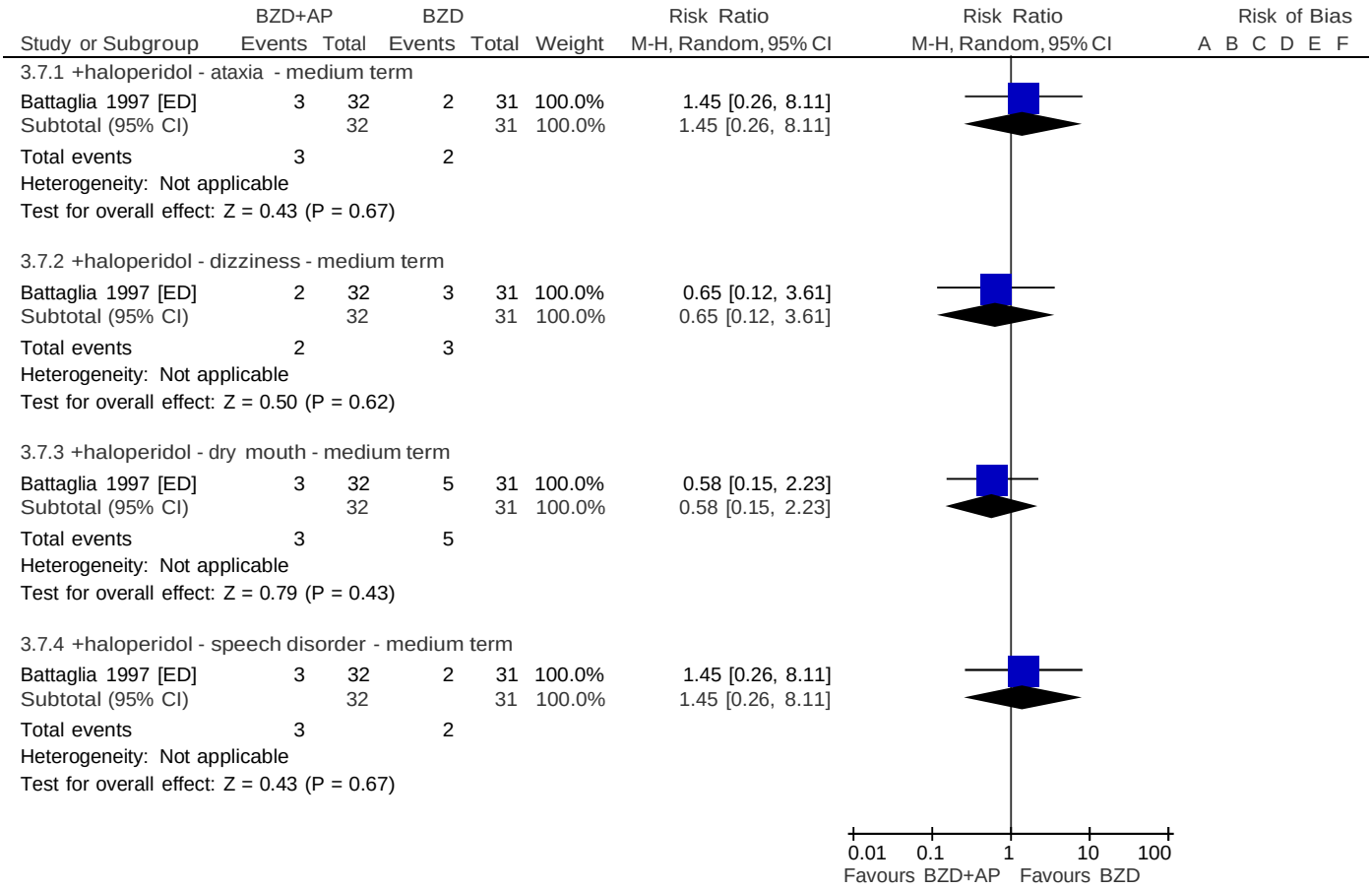
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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



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

3.7 ADVERSE EFFECTS: 3. SPECIFIC

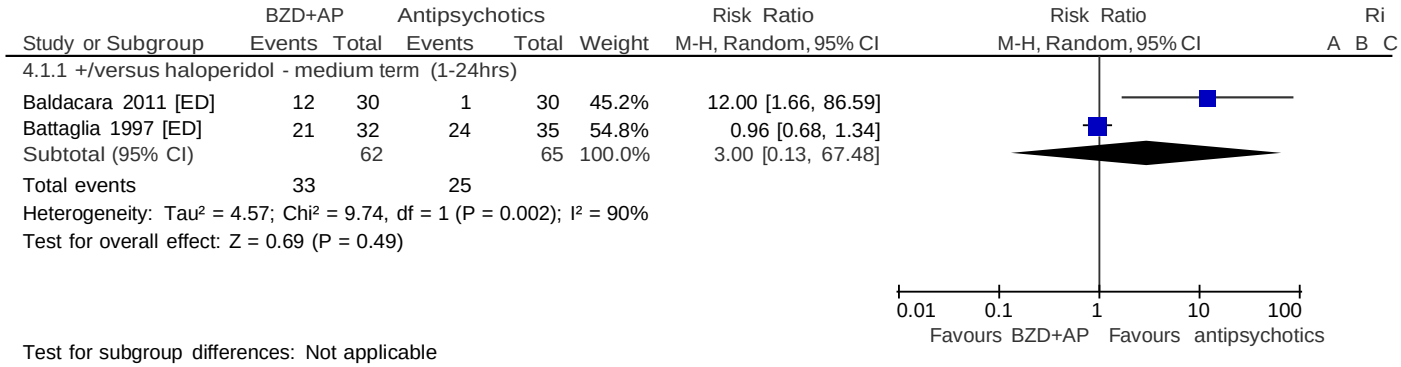


Risk of bias legend

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

4.1 GLOBAL IMPRESSION: 1. NO IMPROVEMENT

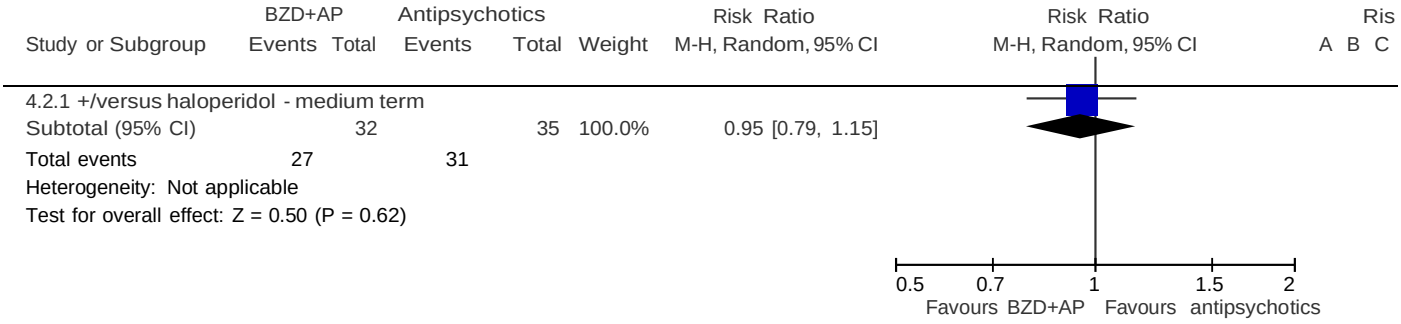


Test for subgroup differences: Not applicable

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

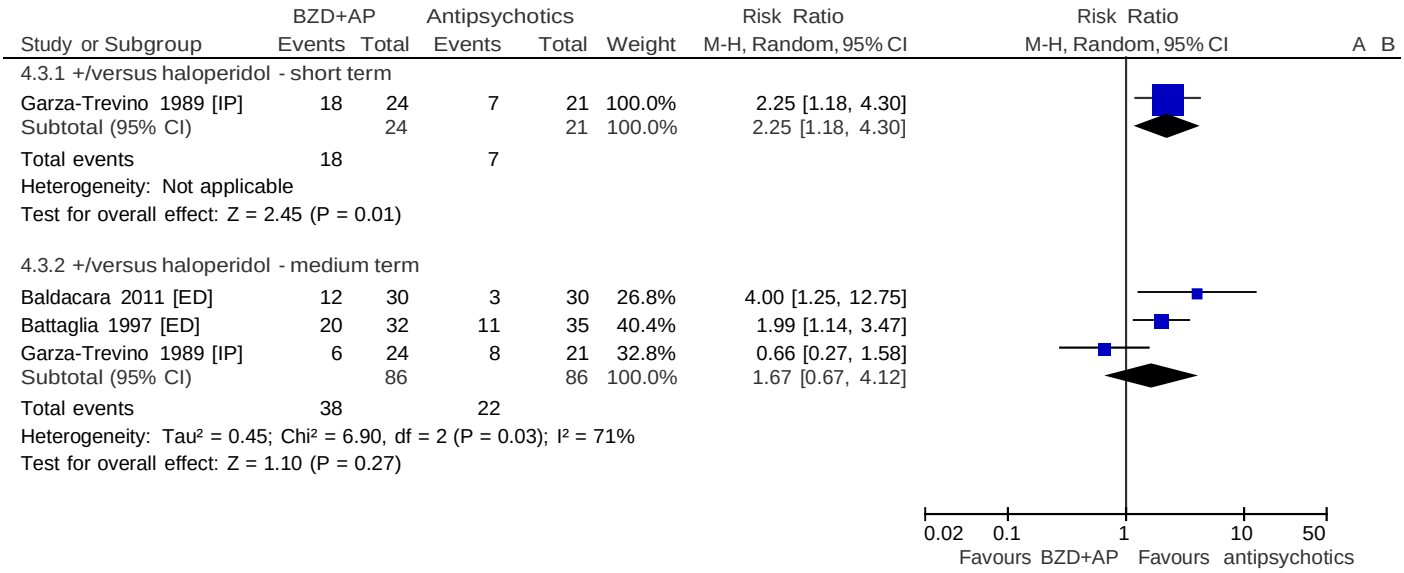
4.2 GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION



Risk of bias legend

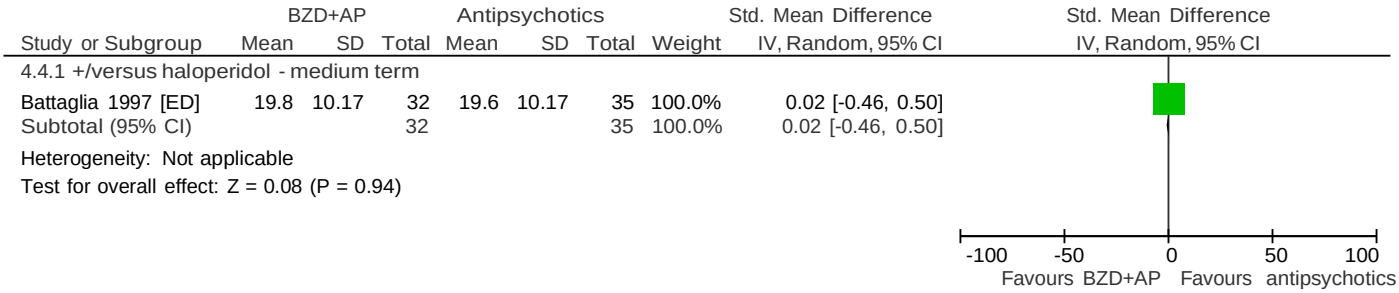
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other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

4.3 GLOBAL IMPRESSION: 3. SEDATION



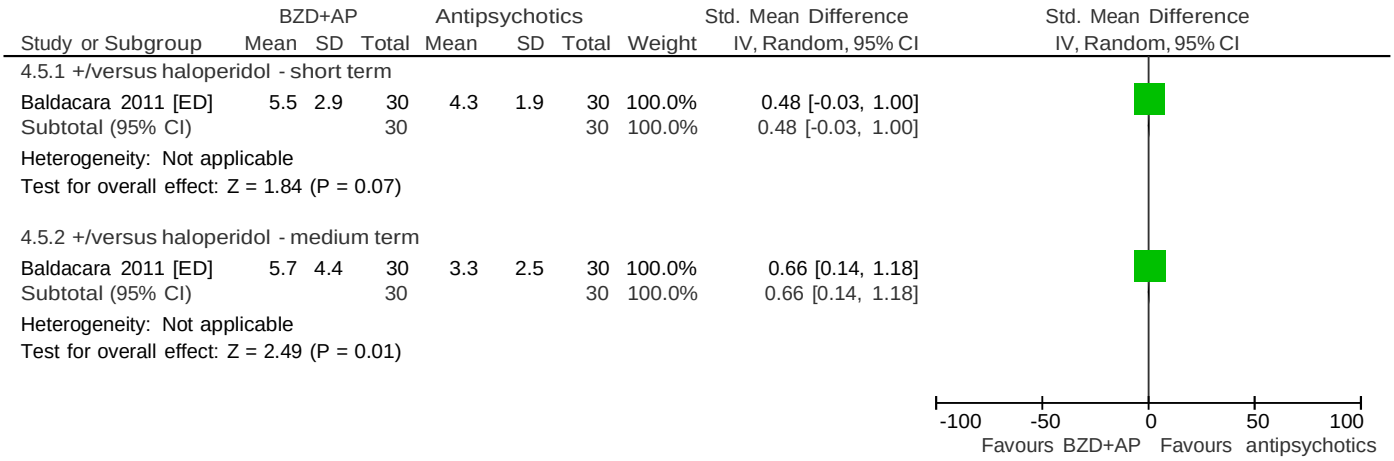
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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



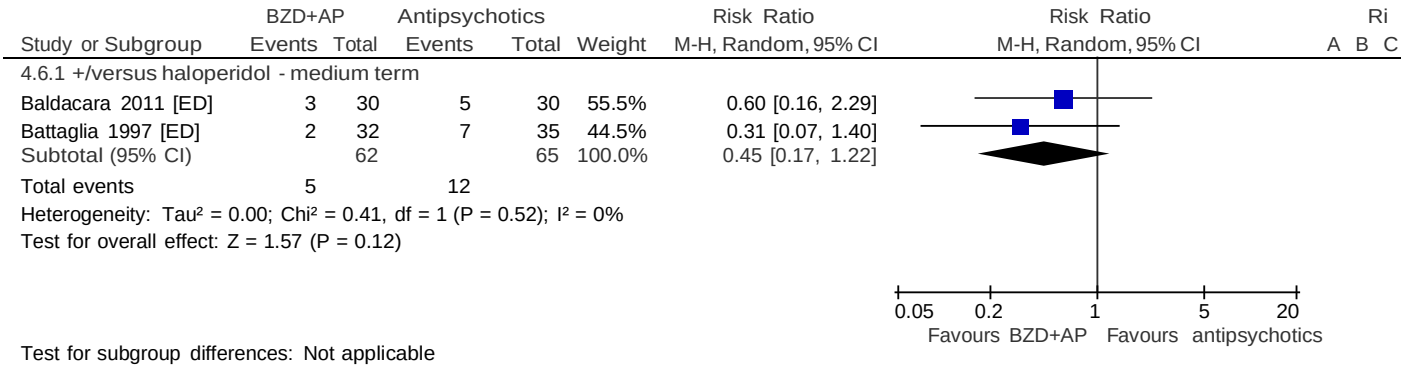
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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

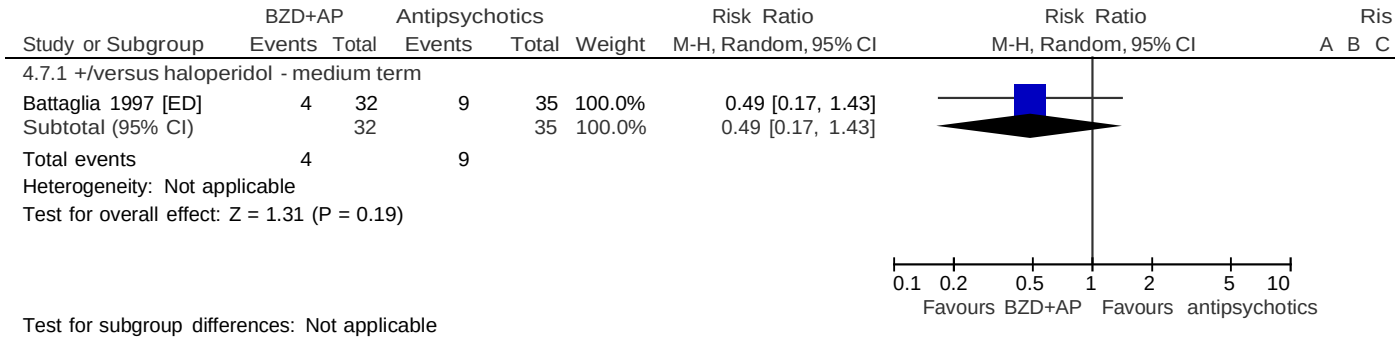
4.6 ADVERSE EFFECTS: 1. EXTRAPYRAMIDAL SYMPTOMS



Test for subgroup differences: Not applicable

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

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

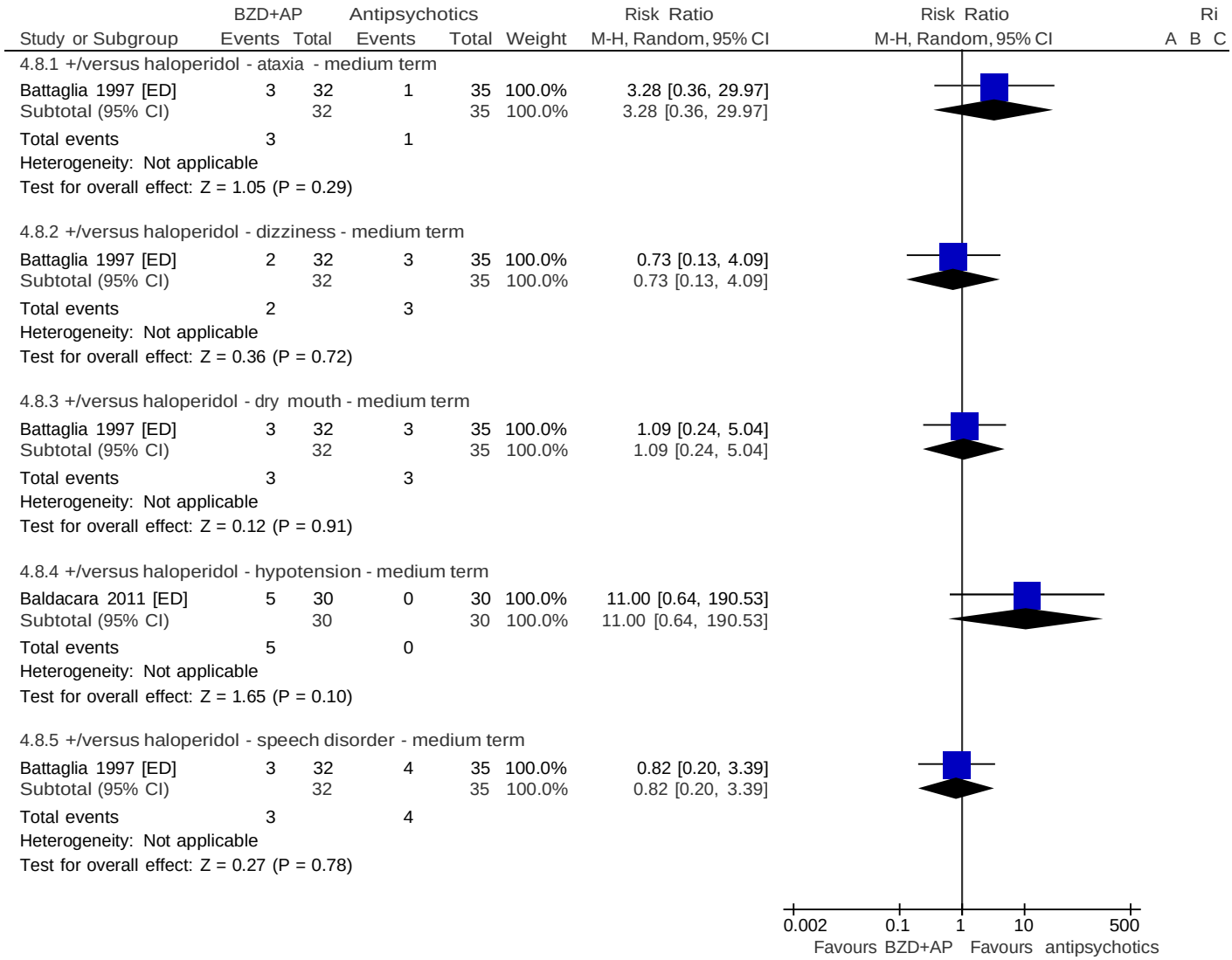


Test for subgroup differences: Not applicable

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

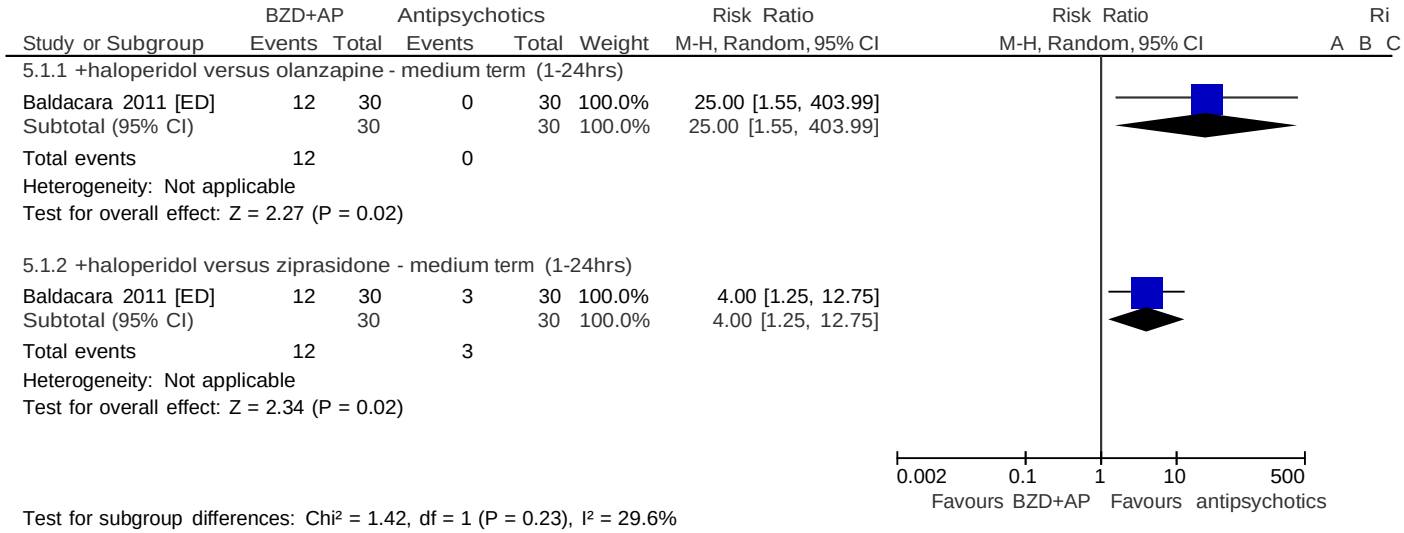
4.8 ADVERSE EFFECTS: 3. SPECIFIC



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

5.1 GLOBAL IMPRESSION: 1. NO IMPROVEMENT

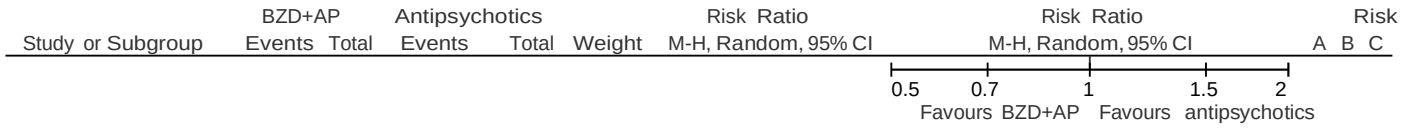


Test for subgroup differences: Chi² = 1.42, df = 1 (P = 0.23), I² = 29.6%

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

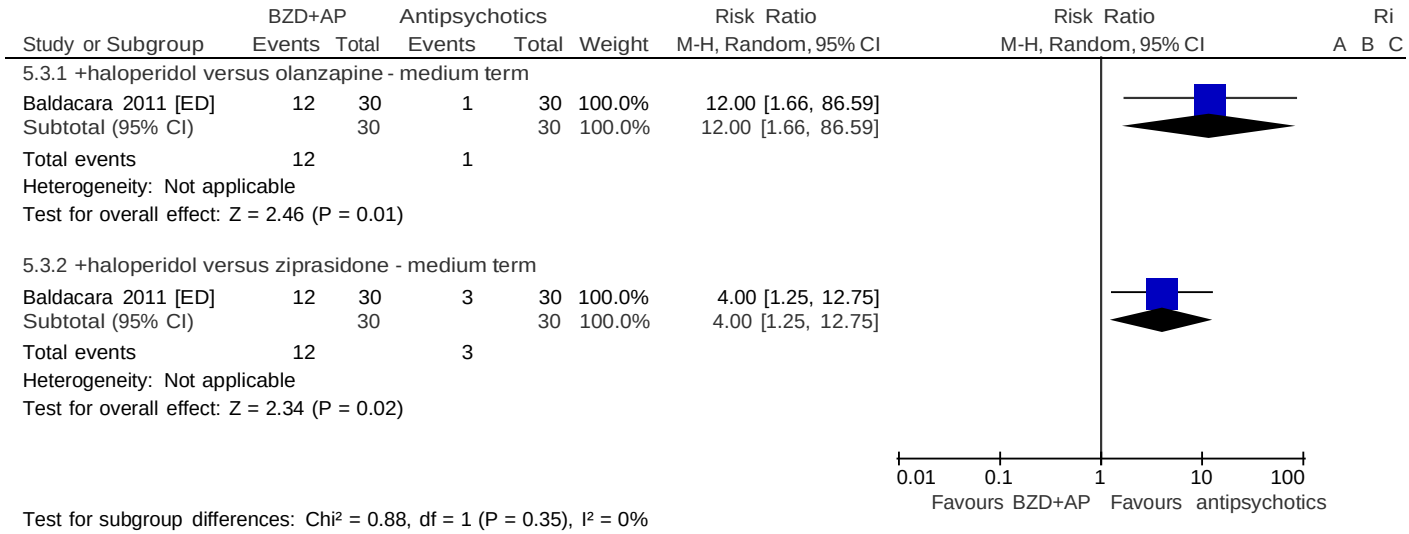
5.2 GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION



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

5.3 GLOBAL IMPRESSION: 3. SEDATION

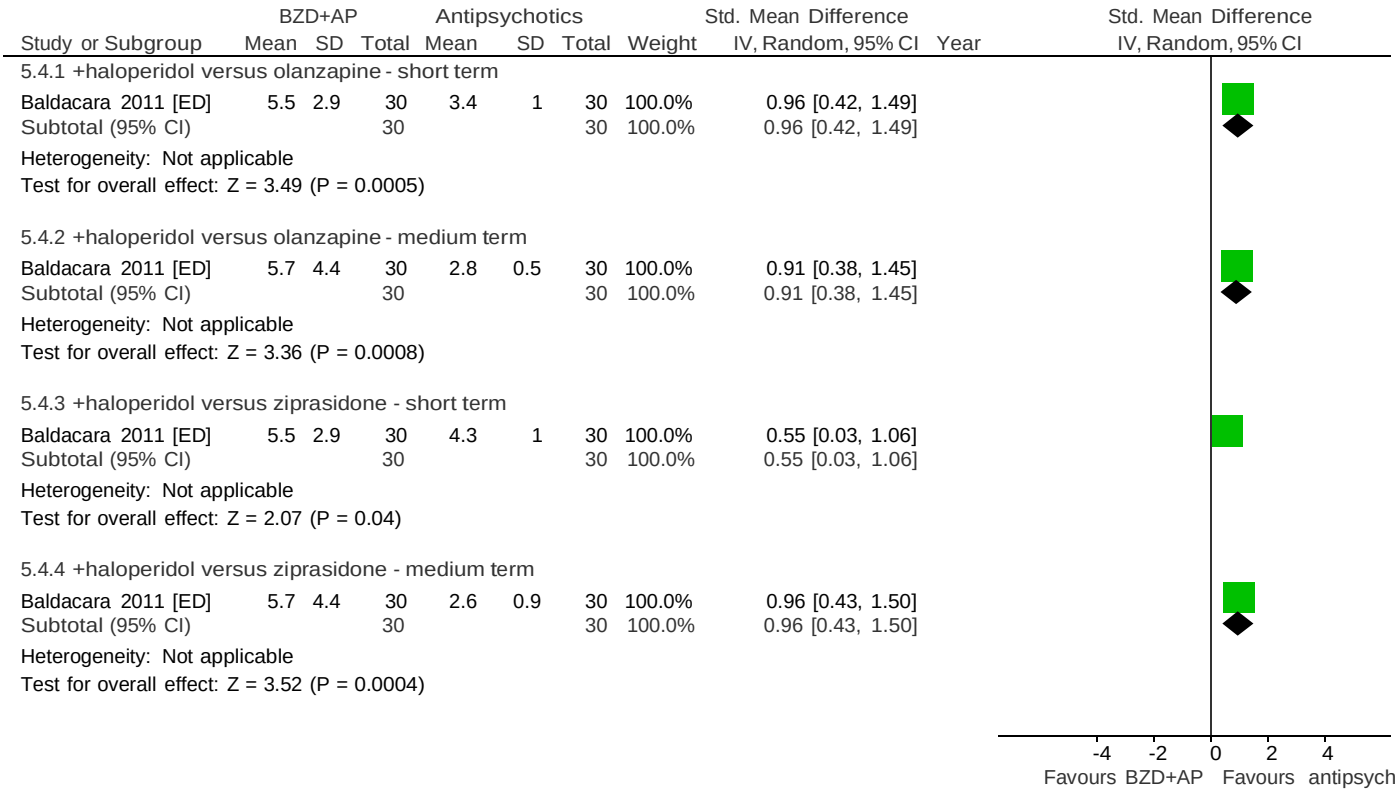


Test for subgroup differences: Chi² = 0.88, df = 1 (P = 0.35), I² = 0%

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

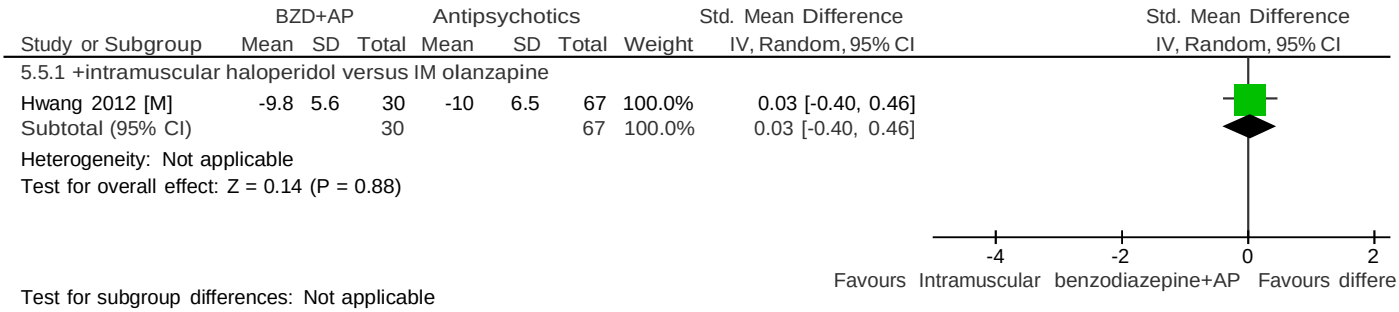
5.4 BEHAVIOUR: 1. AVERAGE CHANGE SCORE (OAS, HIGH = WORSE)



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

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

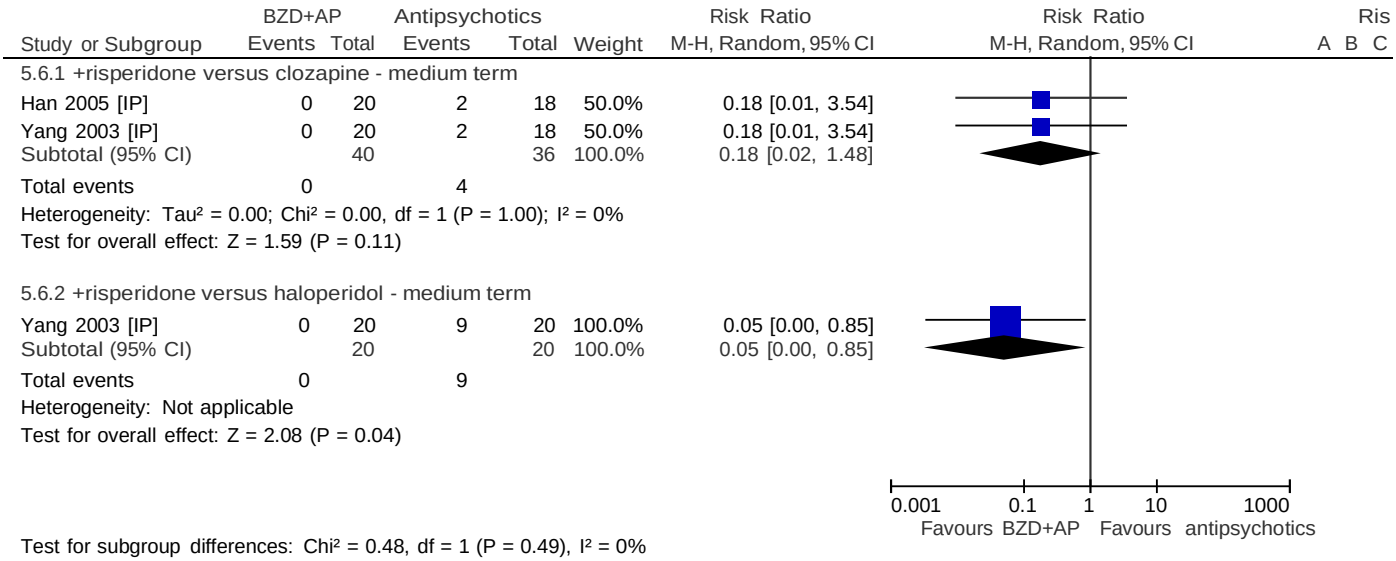


Test for subgroup differences: Not applicable

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

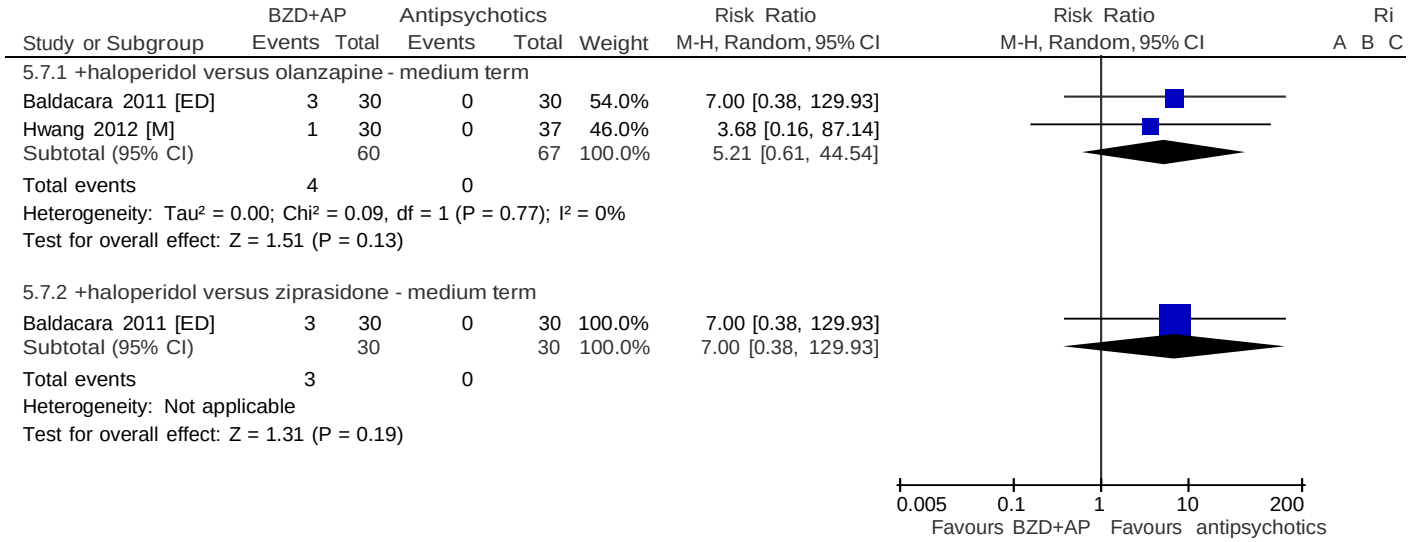


Test for subgroup differences: Chi² = 0.48, df = 1 (P = 0.49), I² = 0%

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

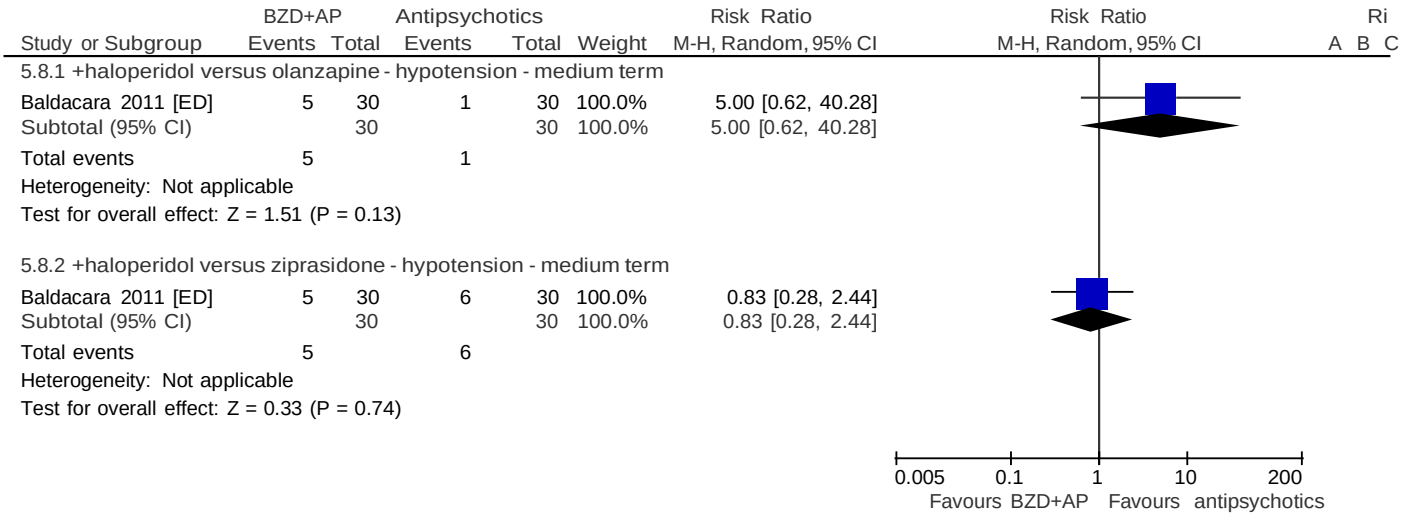
5.7 ADVERSE EFFECTS: 2. EXTRAPYRAMIDAL SYMPTOMS



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

5.8 ADVERSE EFFECTS: 3. SPECIFIC

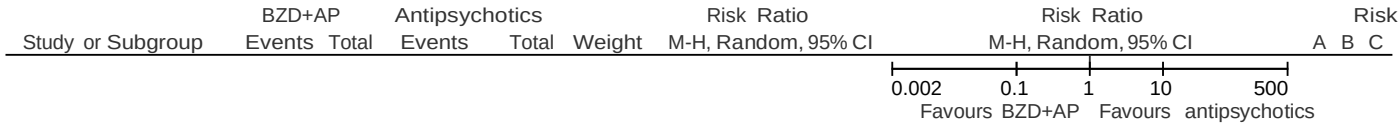


Risk of bias legend

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

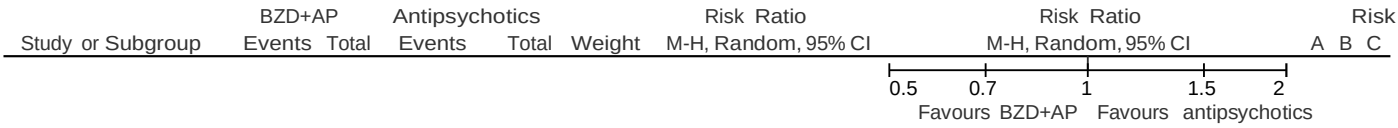
6.1 GLOBAL IMPRESSION: 1. NO IMPROVEMENT



Risk of bias legend

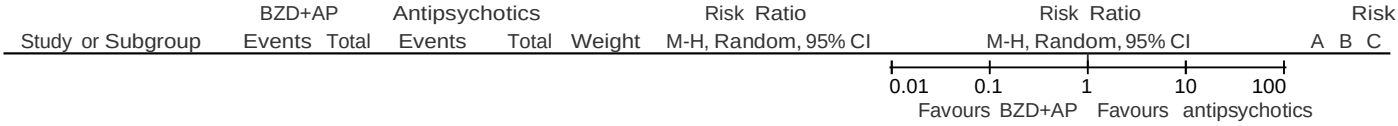
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other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

6.2 GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION



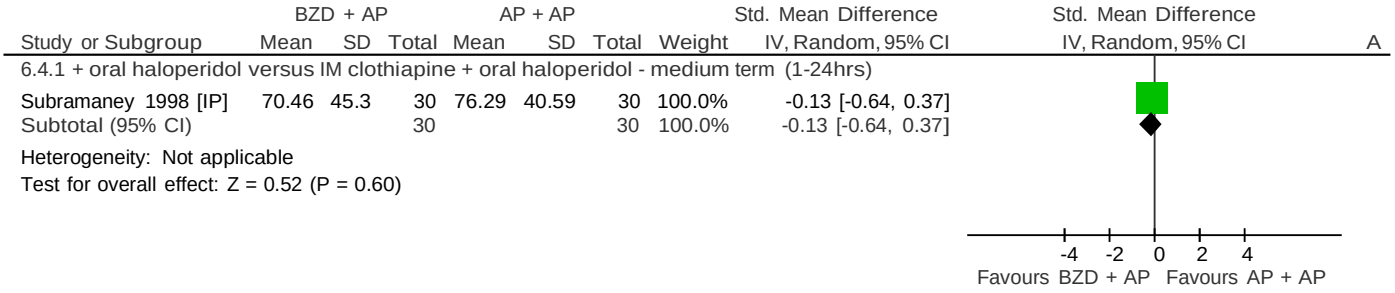
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

6.3 GLOBAL IMPRESSION: 3. SEDATION



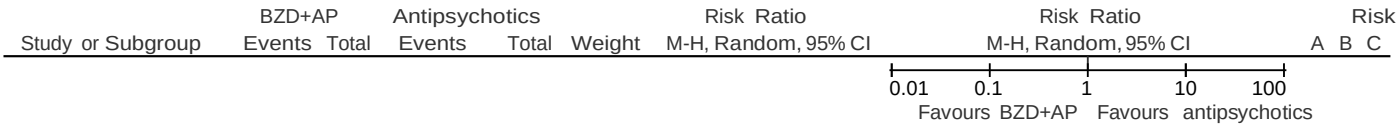
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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



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

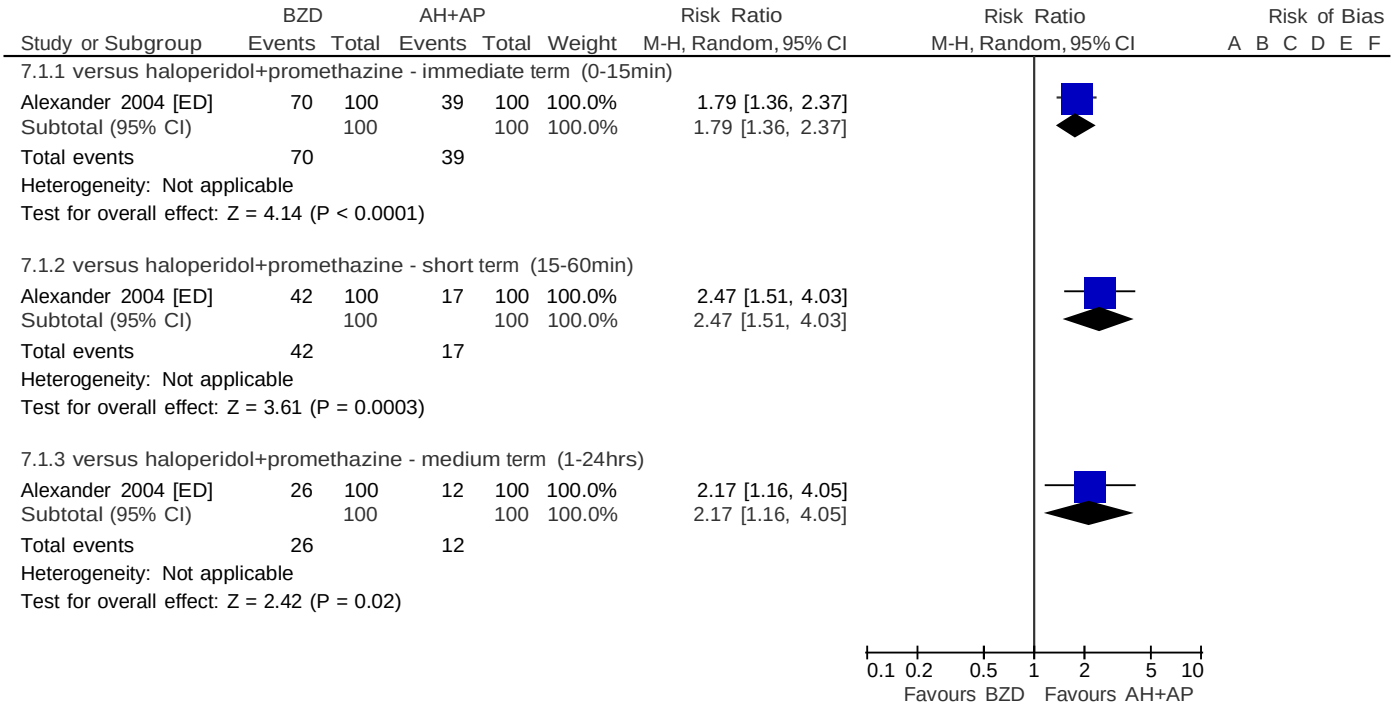
6.5 ADVERSE EFFECTS



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

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

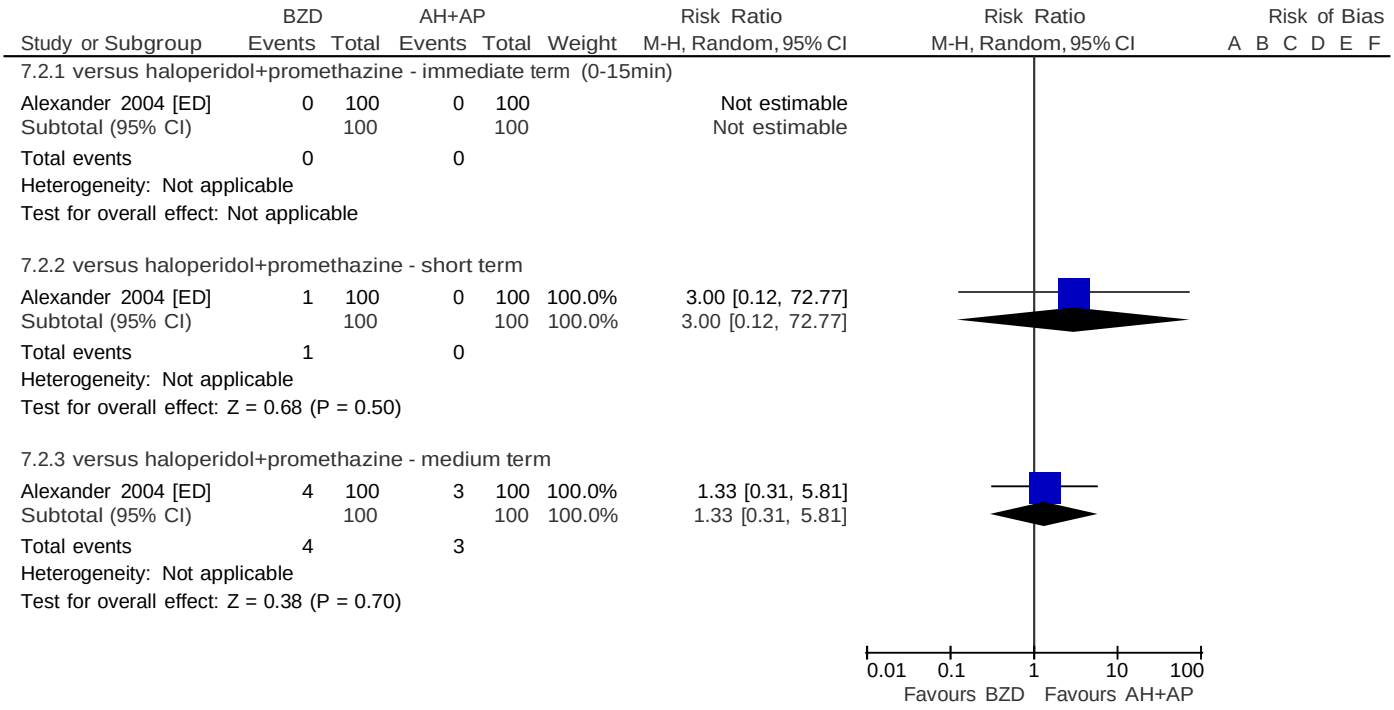
7.1 GLOBAL IMPRESSION: 1. NO IMPROVEMENT



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

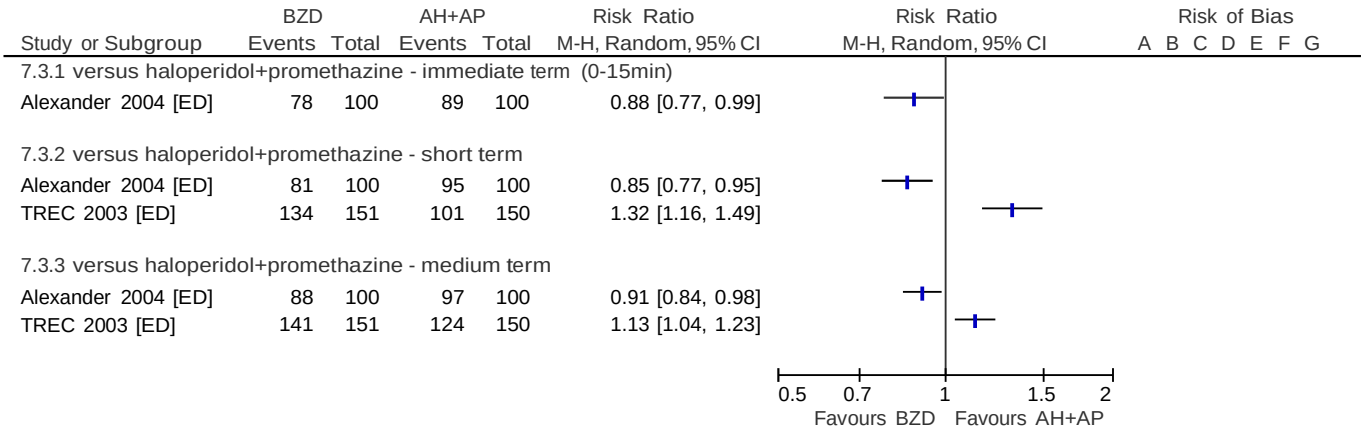
7.2 GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION



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

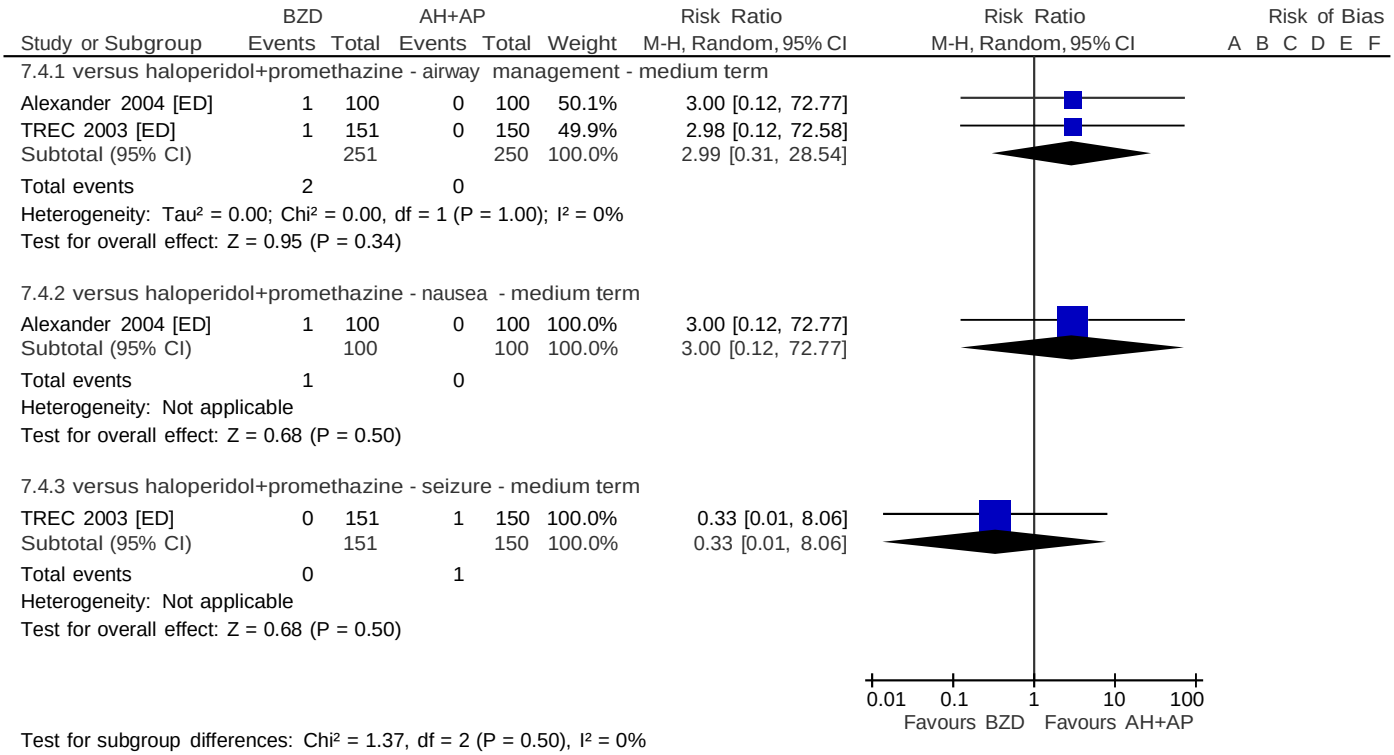
7.3 GLOBAL IMPRESSION: 3. SEDATION (TRANQUIL OR ASLEEP)



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

7.4 ADVERSE EFFECTS: 1. SPECIFIC



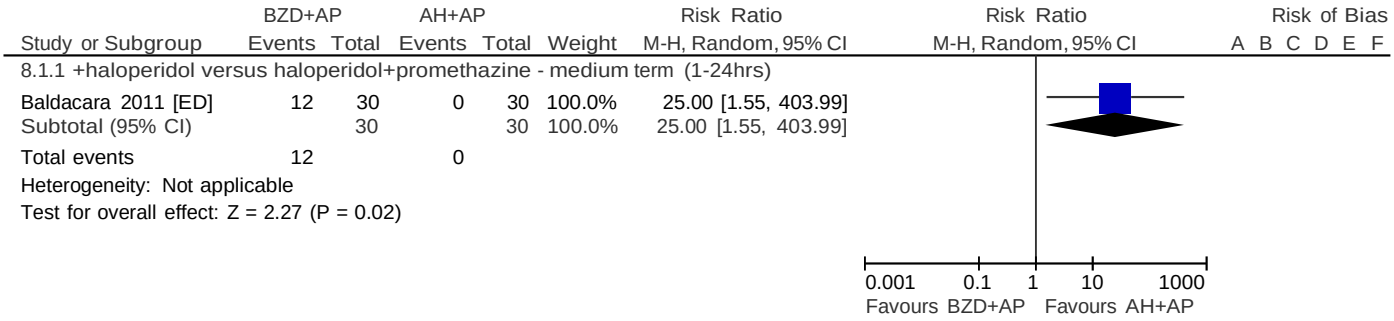
Test for subgroup differences: Chi² = 1.37, df = 2 (P = 0.50), I² = 0%

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

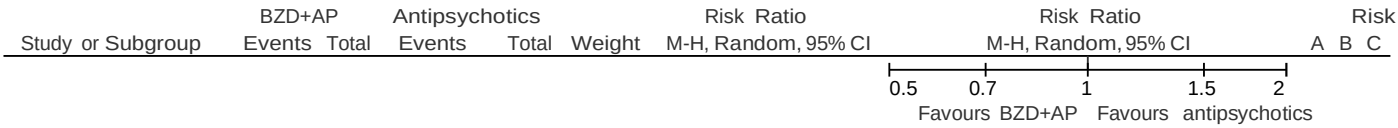
8 INTRAMUSCULAR BENZODIAZEPINE PLUS ANTIPSYCHOTIC DRUG VERSUS ANTIPSYCHOTIC DRUG PLUS ANTIHISTAMINE [ADAPTED FROM GILLIES 2013]

8.1 GLOBAL IMPRESSION: 1. NO IMPROVEMENT



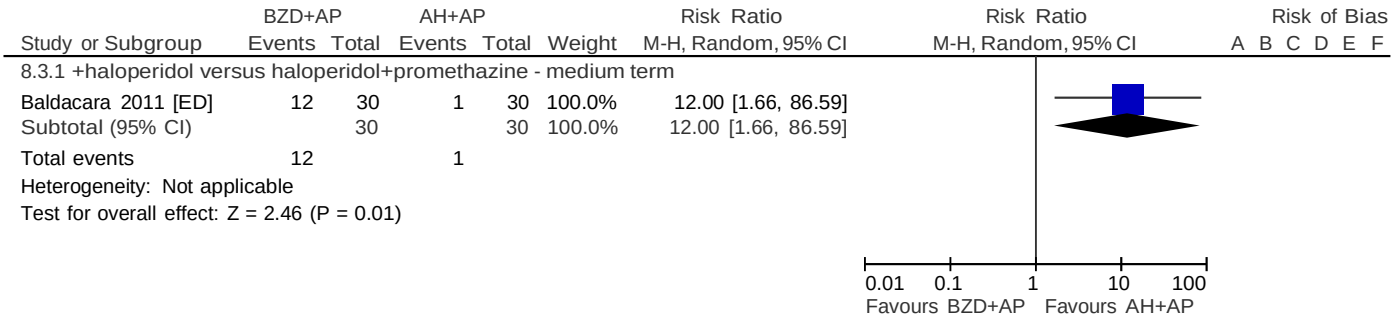
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

8.2 GLOBAL IMPRESSION: 2. NEED FOR ADDITIONAL MEDICATION



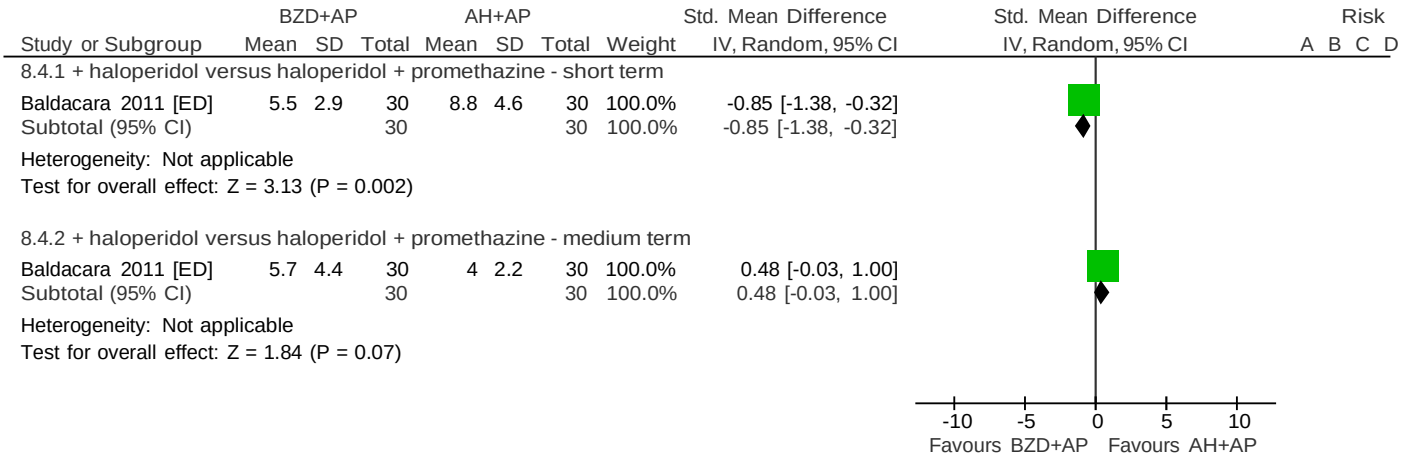
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

8.3 GLOBAL IMPRESSION: 3. SEDATION



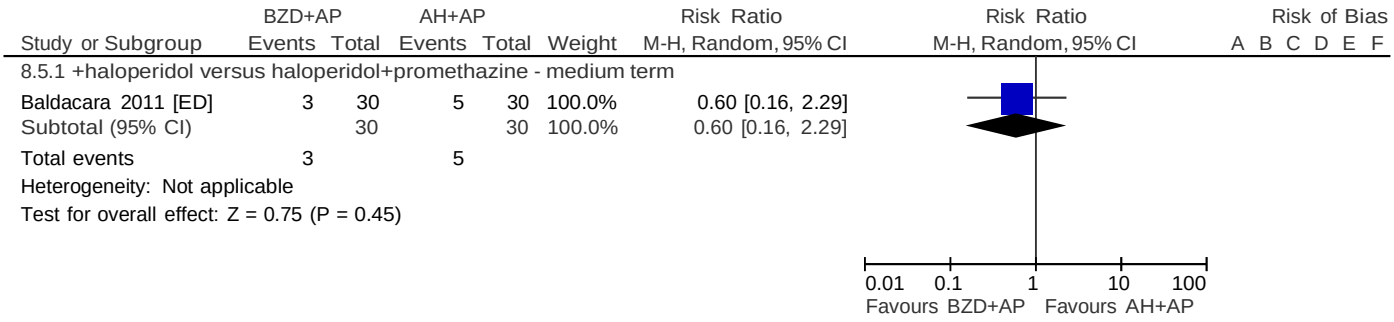
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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



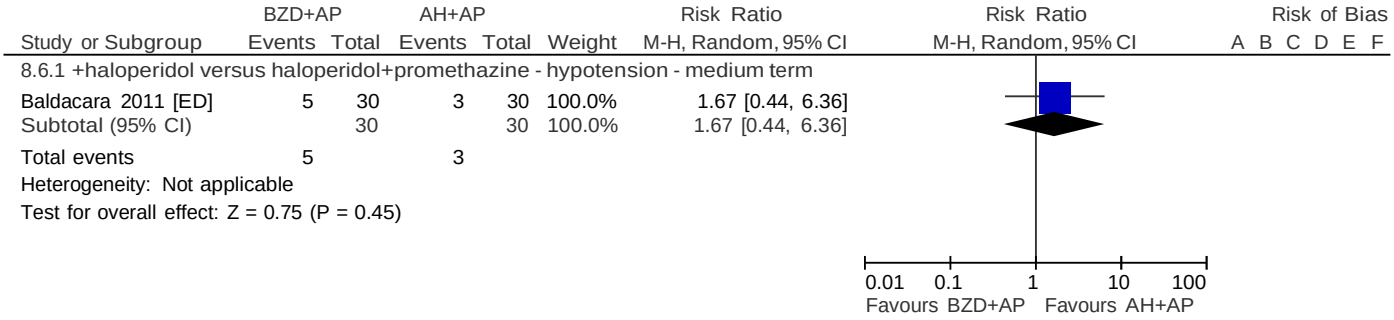
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

8.5 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

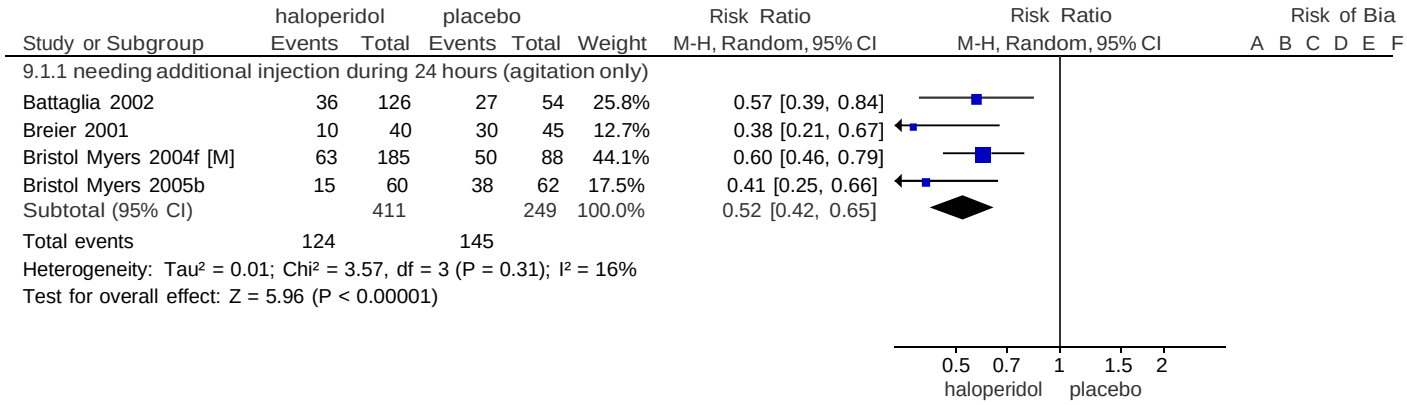
8.6 ADVERSE EFFECTS: 2. SPECIFIC



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 INTRAMUSCULAR HALOPERIDOL VERSUS PLACEBO [ADAPTED FROM POWNEY 2012]

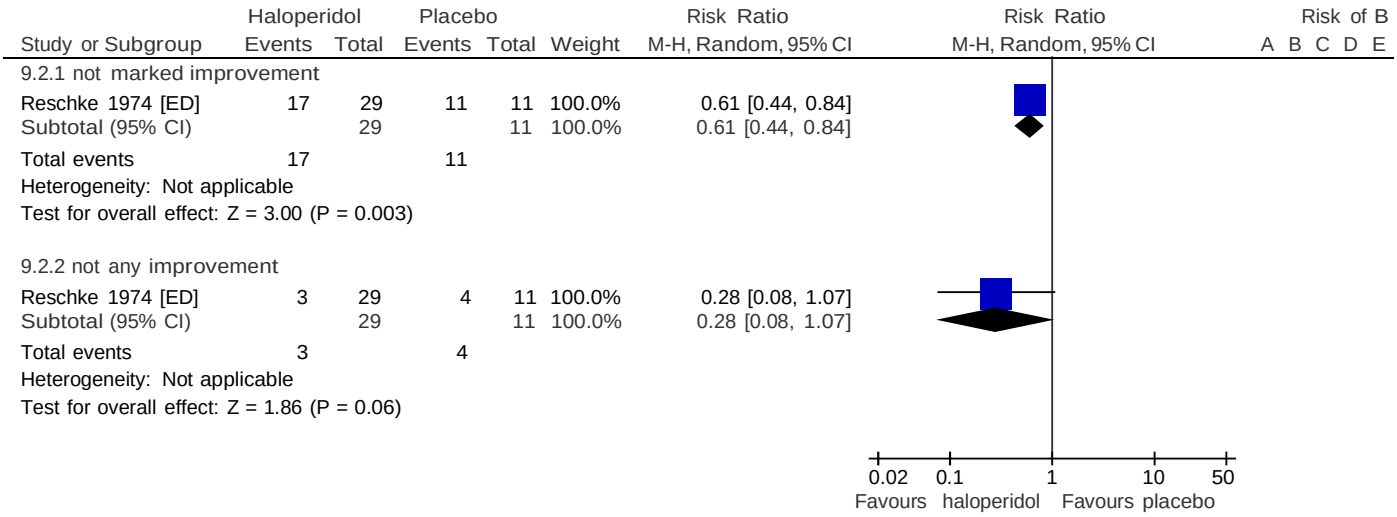
9.1 REPEATED NEED FOR TRANQUILLISATION



Risk of bias legend

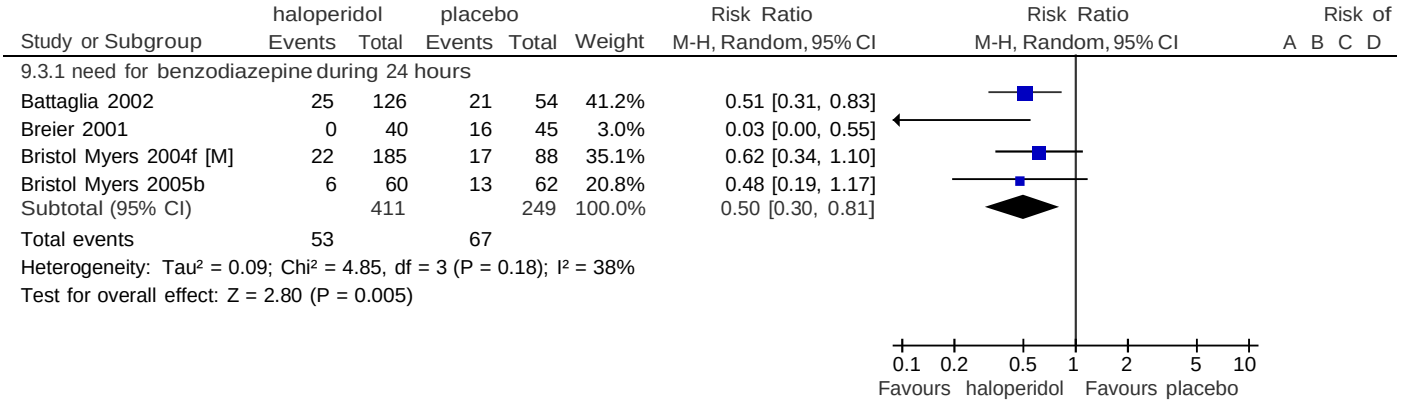
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other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

9.2 GLOBAL IMPRESSION: 1. NOT IMPROVED



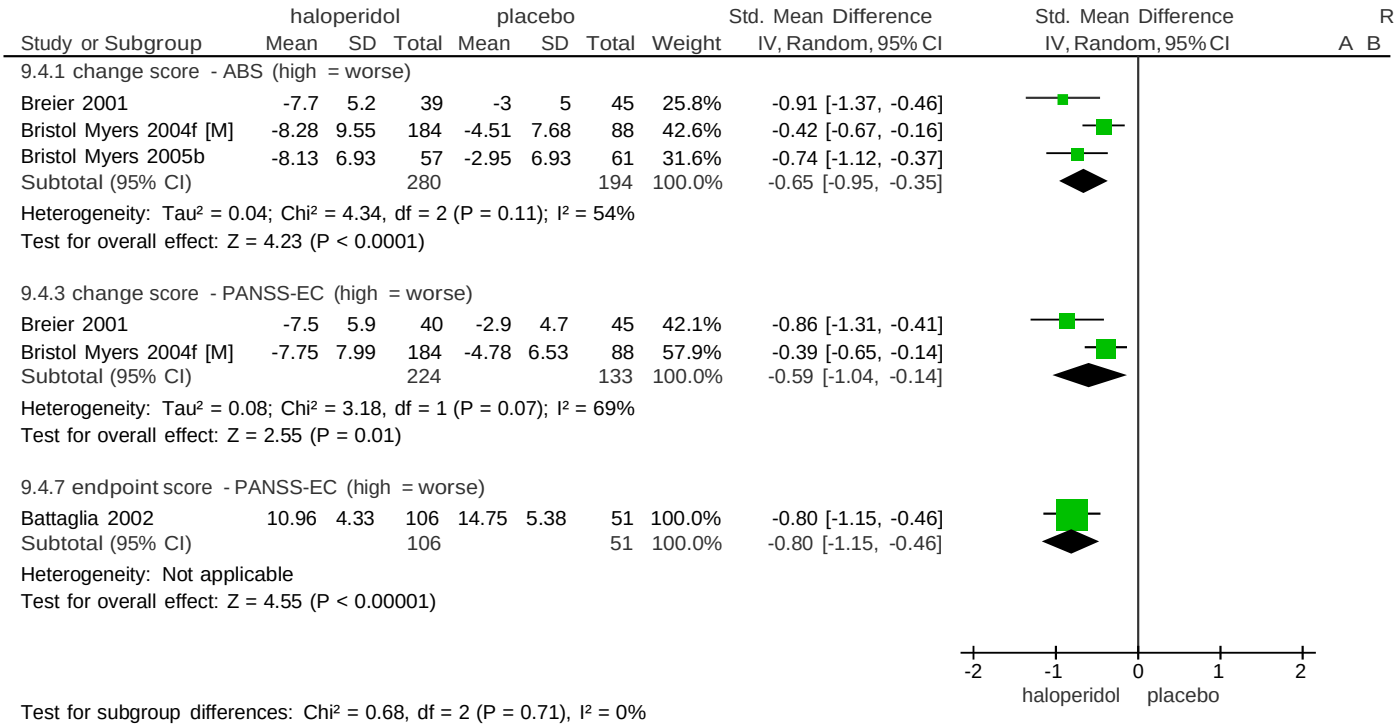
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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



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

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

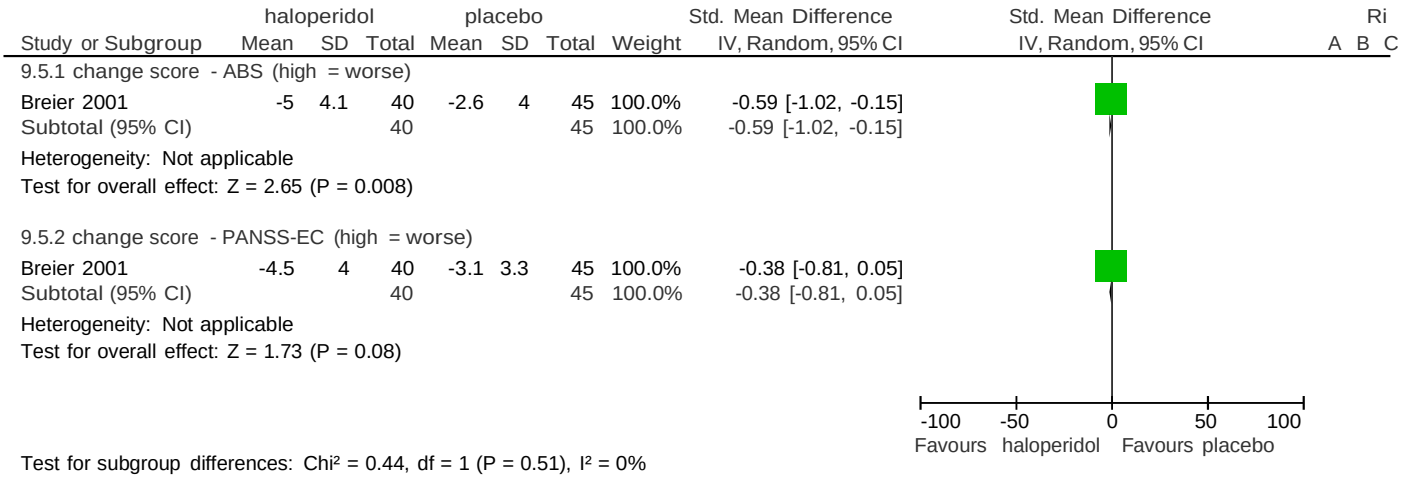


Test for subgroup differences: Chi² = 0.68, df = 2 (P = 0.71), I² = 0%

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

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

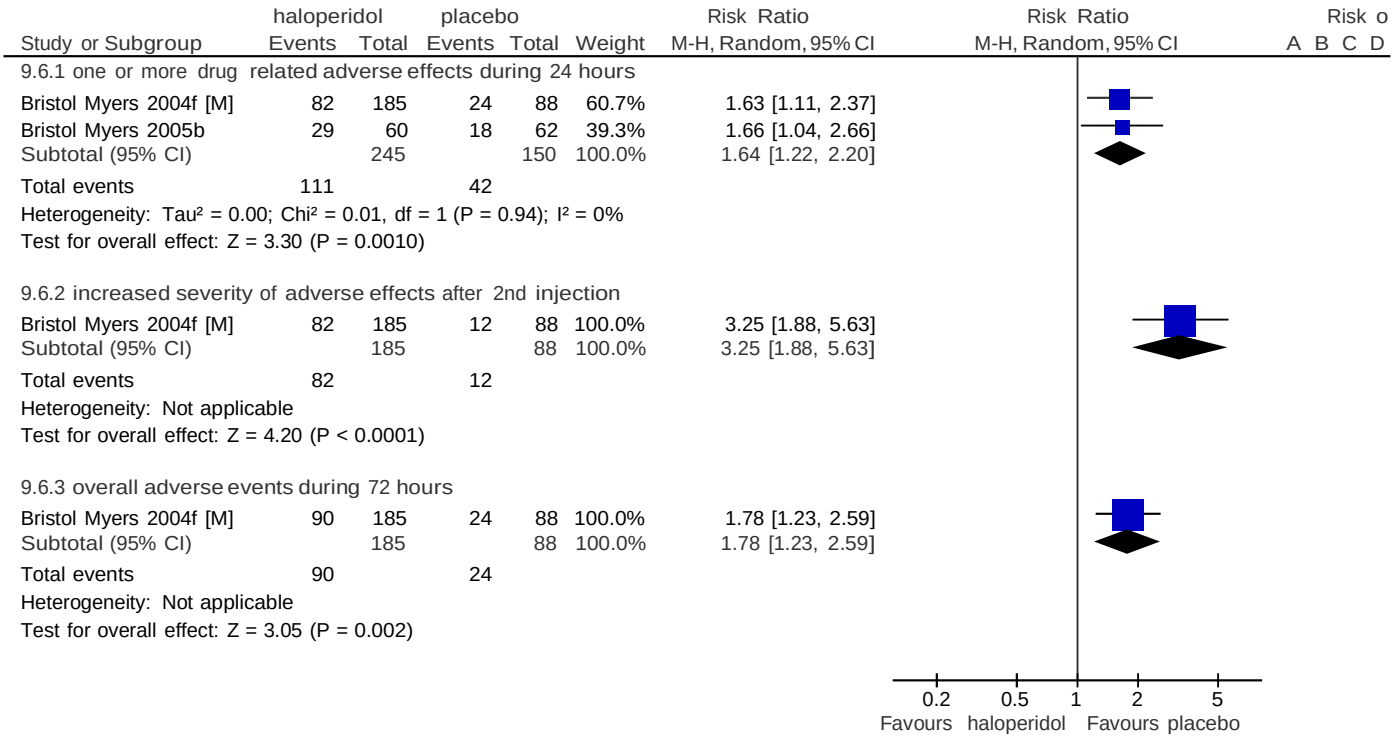


Test for subgroup differences: Chi² = 0.44, df = 1 (P = 0.51), I² = 0%

Risk of bias legend

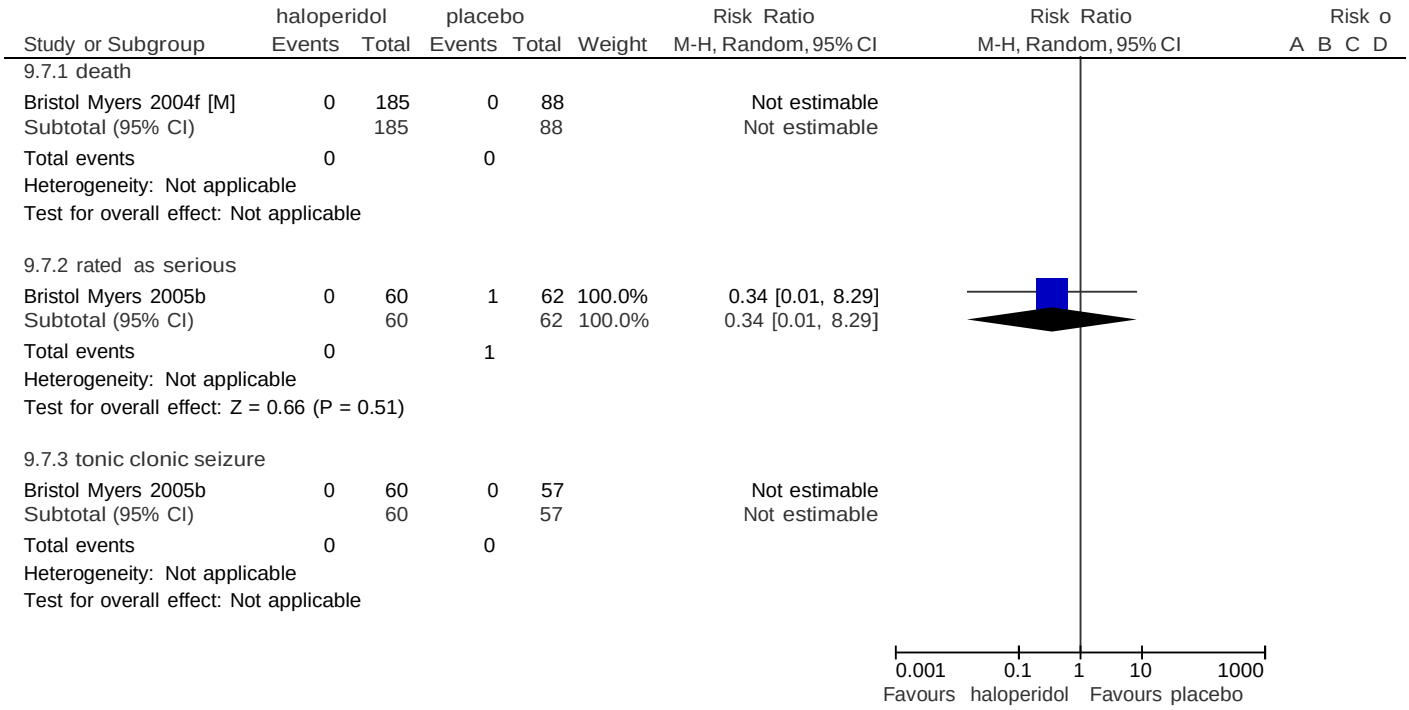
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other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

9.6 ADVERSE EFFECTS: 1. GENERAL



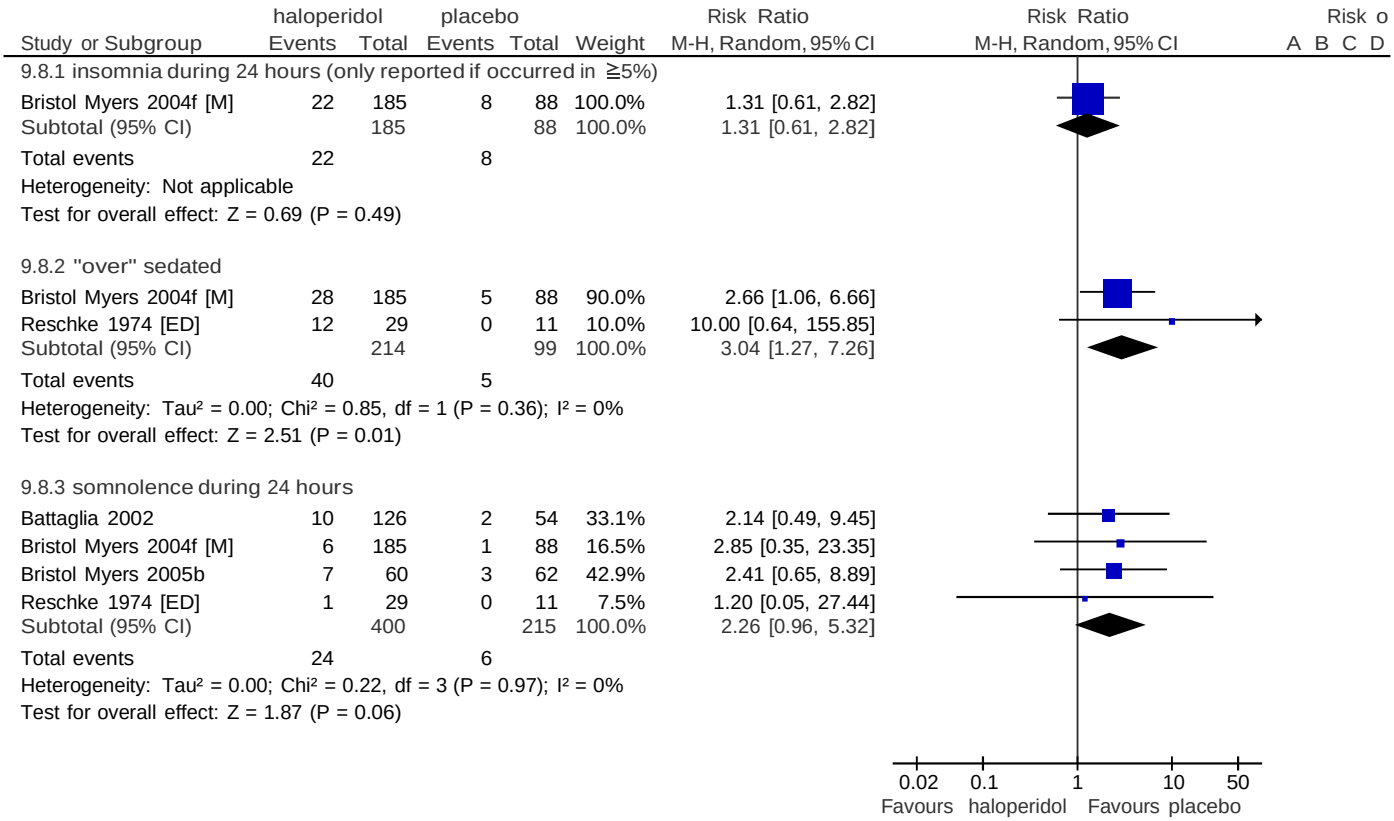
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

9.7 ADVERSE EFFECTS: 2. GENERAL – SERIOUS



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

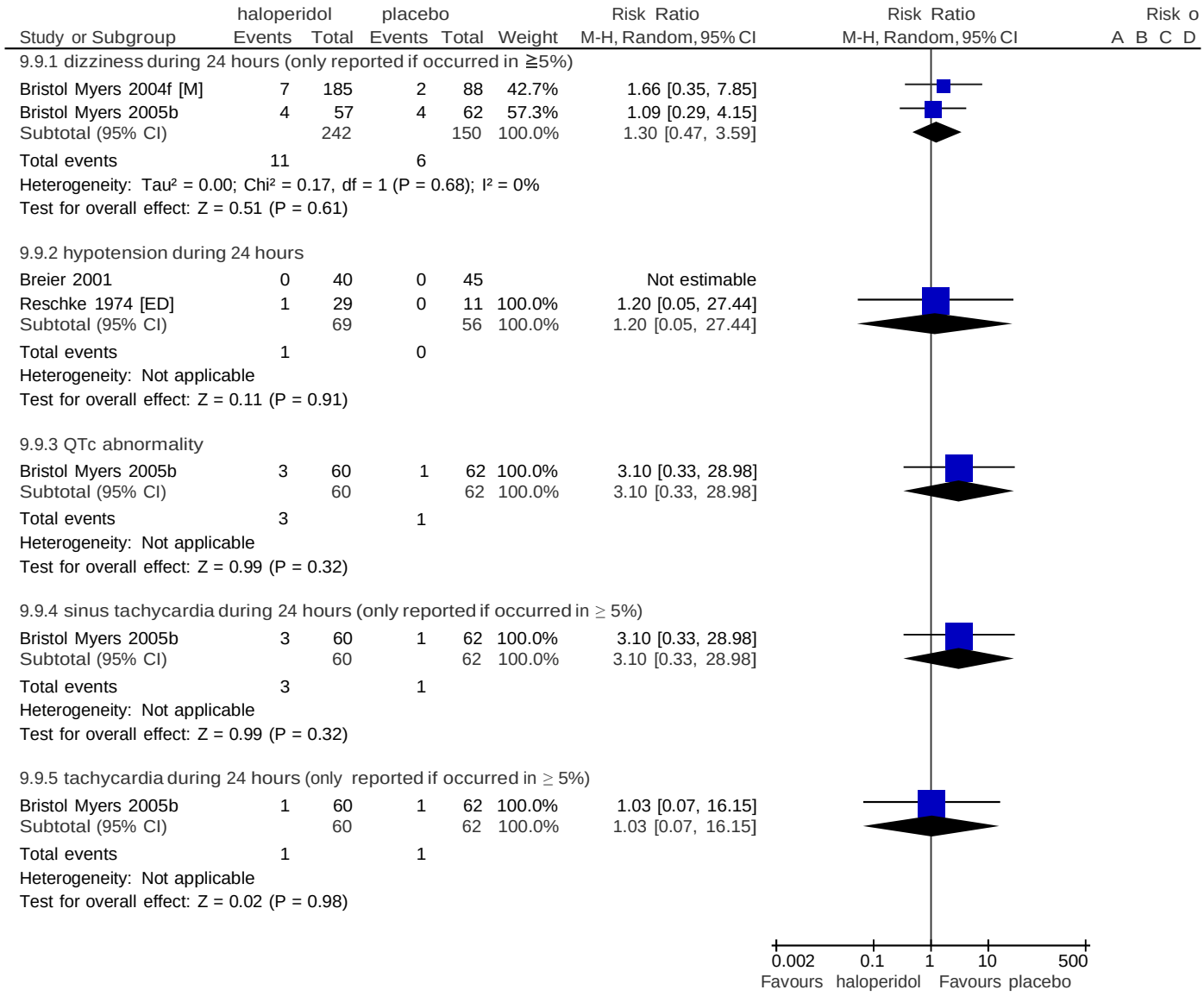
9.8 ADVERSE EFFECTS: 3. SPECIFIC – AROUSAL LEVEL



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

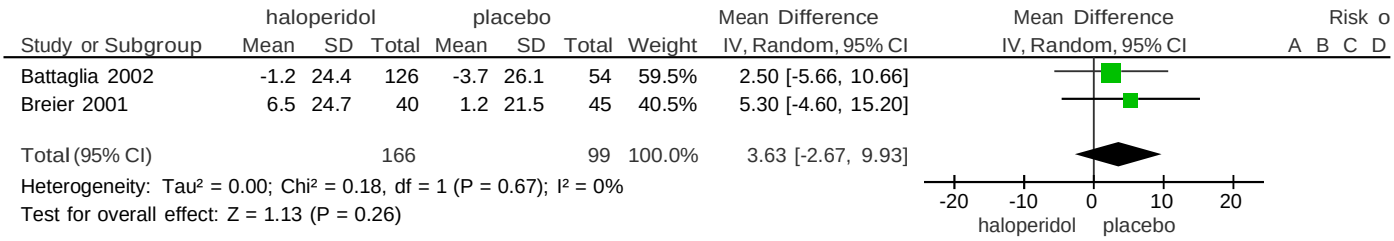
9.9 ADVERSE EFFECTS: 4A. SPECIFIC – CARDIAC: I. MISCELLANEOUS OUTCOMES



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

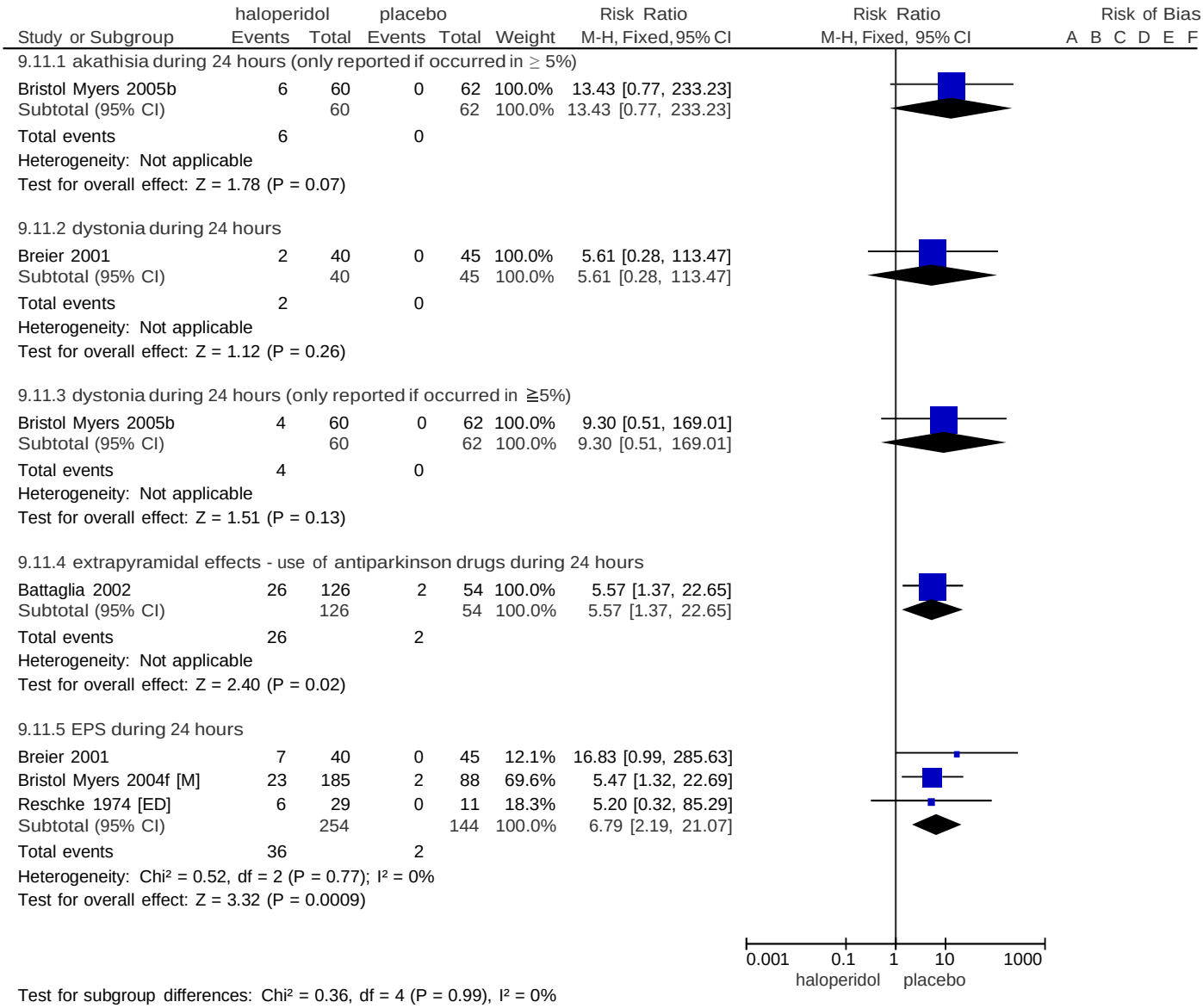
9.10 ADVERSE EFFECTS: 4B. SPECIFIC – CARDIAC: II. QTC INTERVAL (AVERAGE CHANGE AT 24 HOURS)



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

9.11 ADVERSE EFFECTS: 5A. SPECIFIC – MOVEMENT DISORDERS

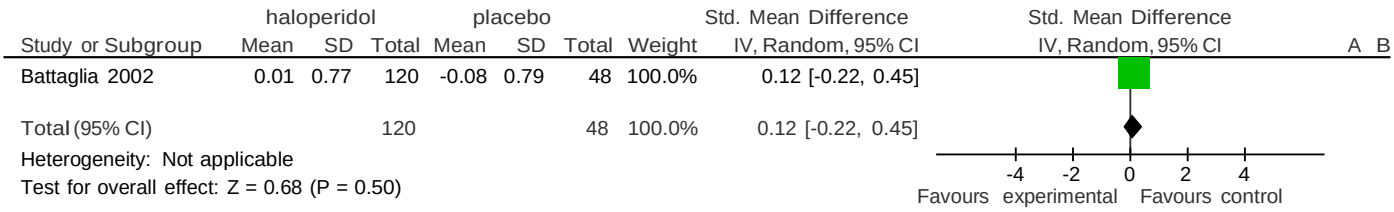


Test for subgroup differences: Chi² = 0.36, df = 4 (P = 0.99), I² = 0%

Risk of bias legend

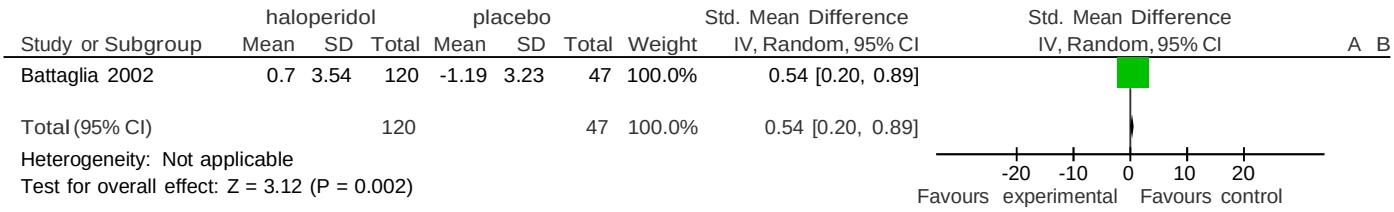
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other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

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



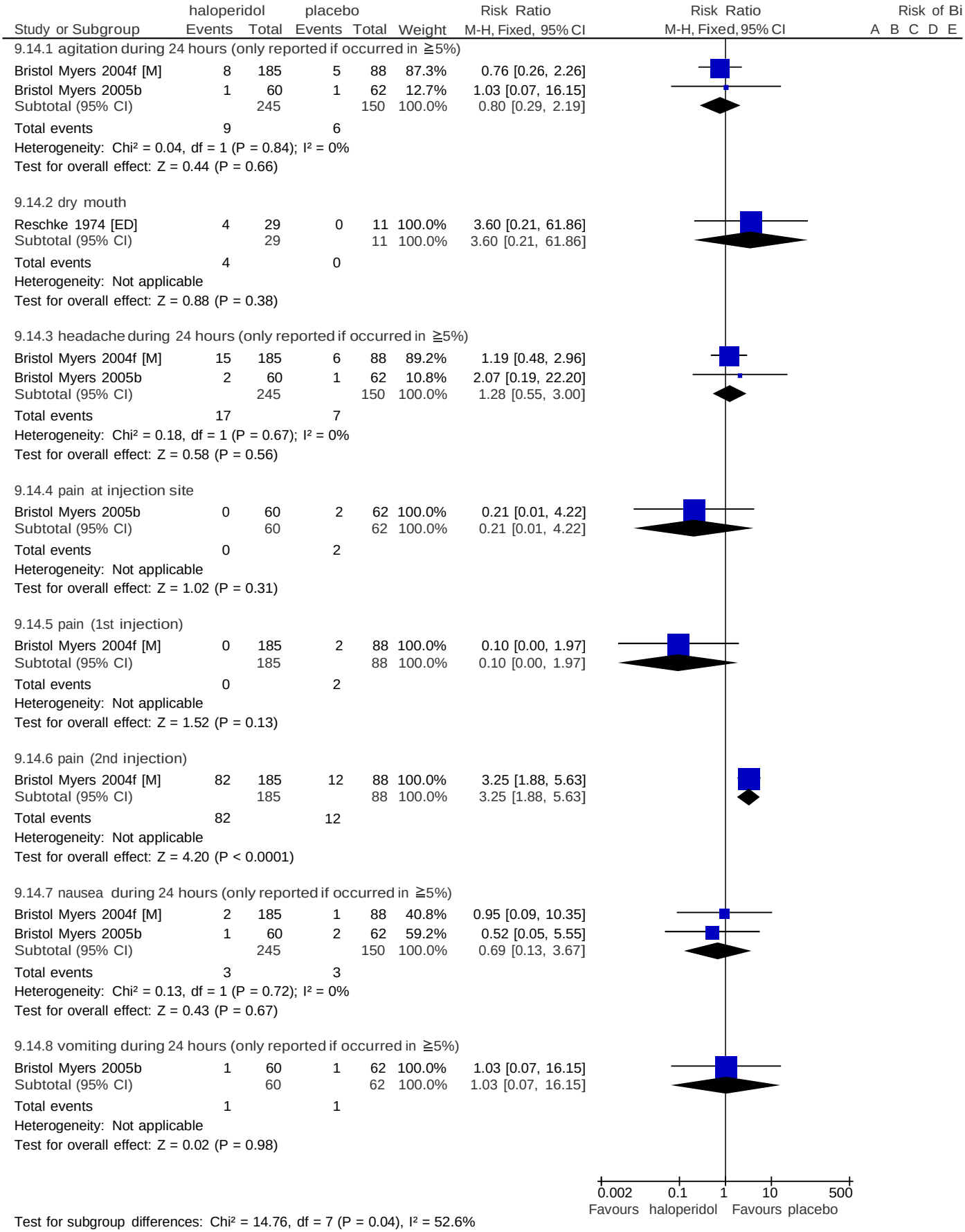
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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



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

9.14 ADVERSE EFFECTS: 6. SPECIFIC – MISCELLANEOUS



Test for subgroup differences: Chi² = 14.76, df = 7 (P = 0.04), I² = 52.6%

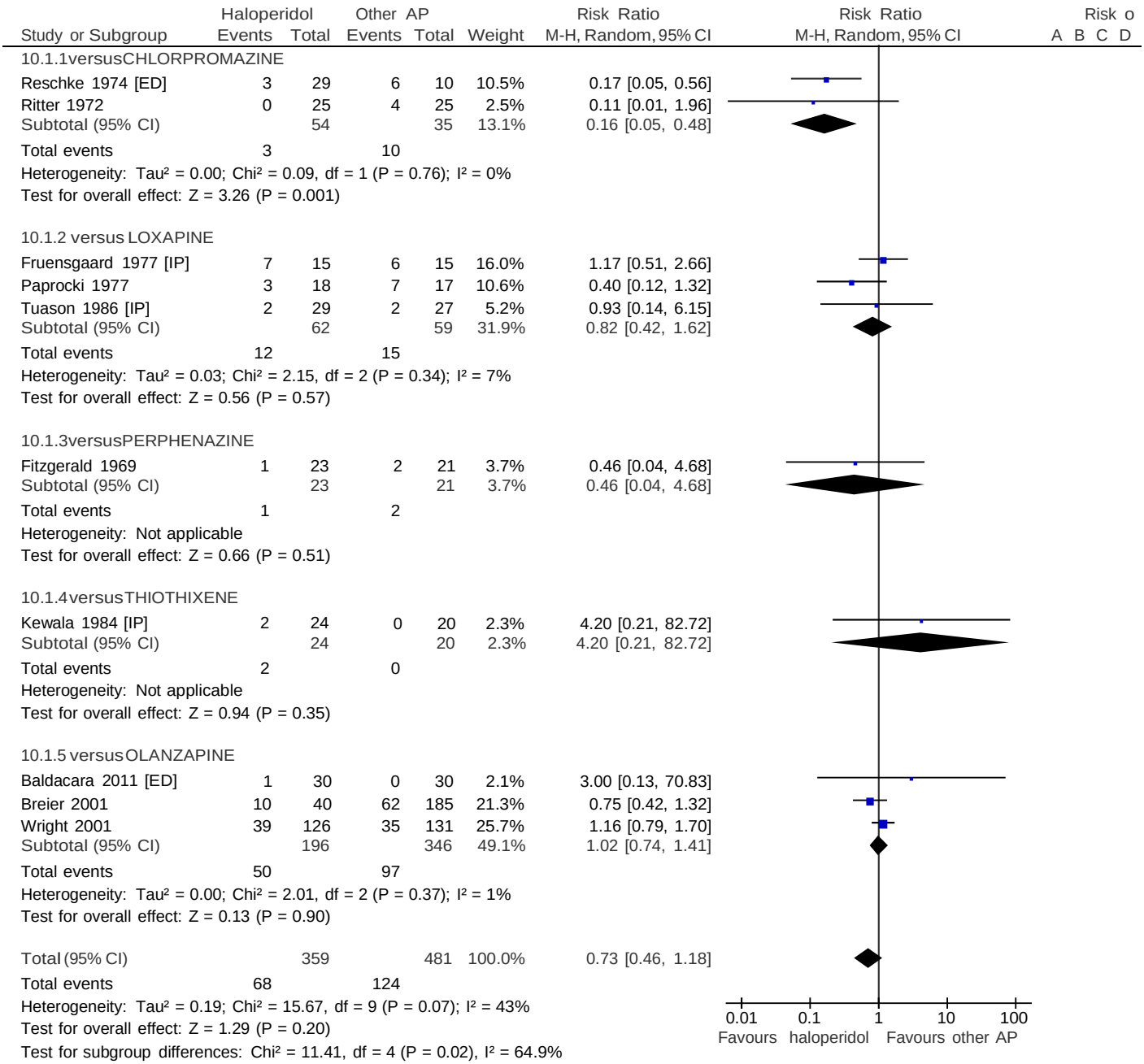
Risk of bias legend

(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

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

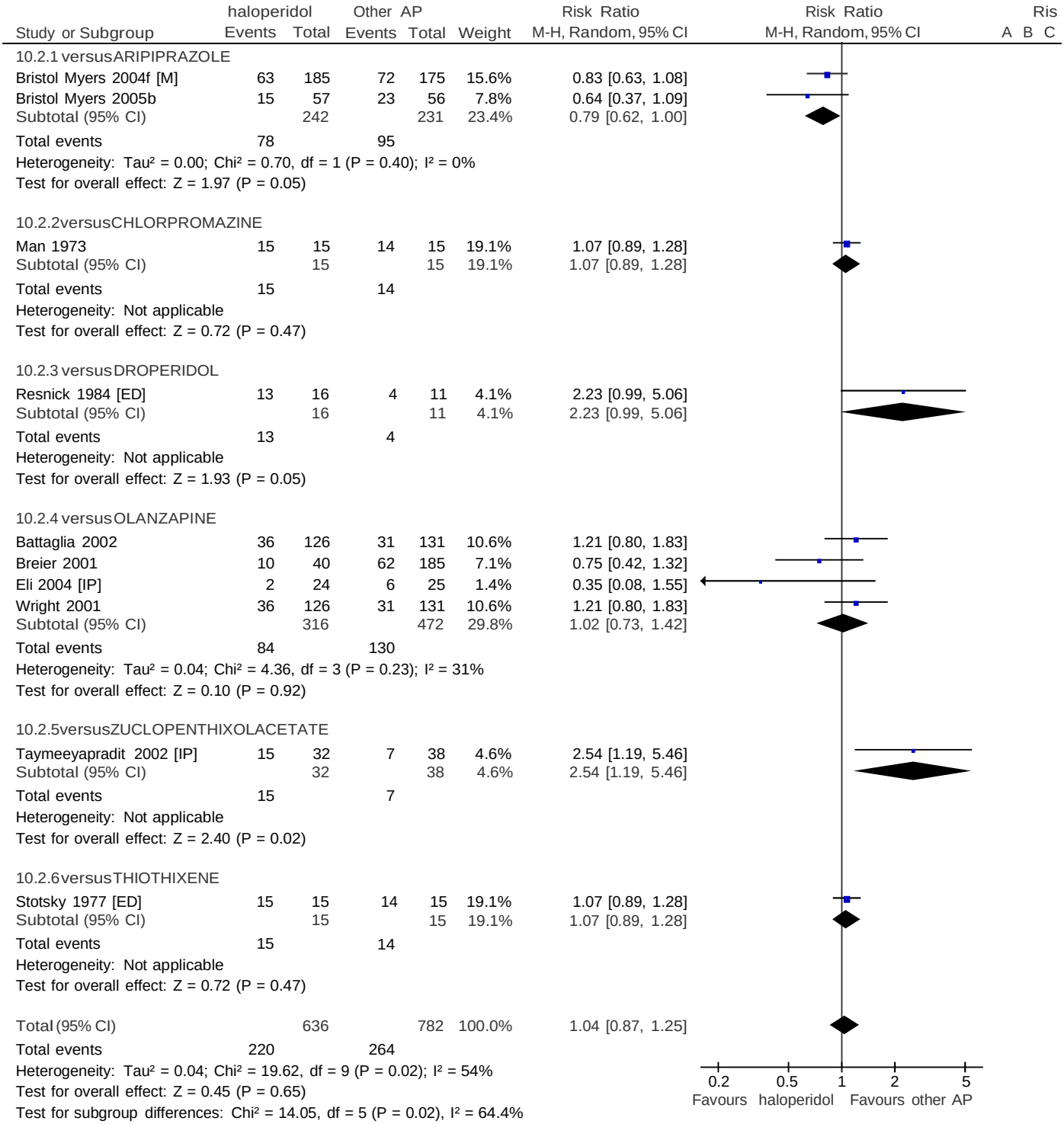
10.1 GLOBAL IMPRESSION: 1. NOT IMPROVED



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

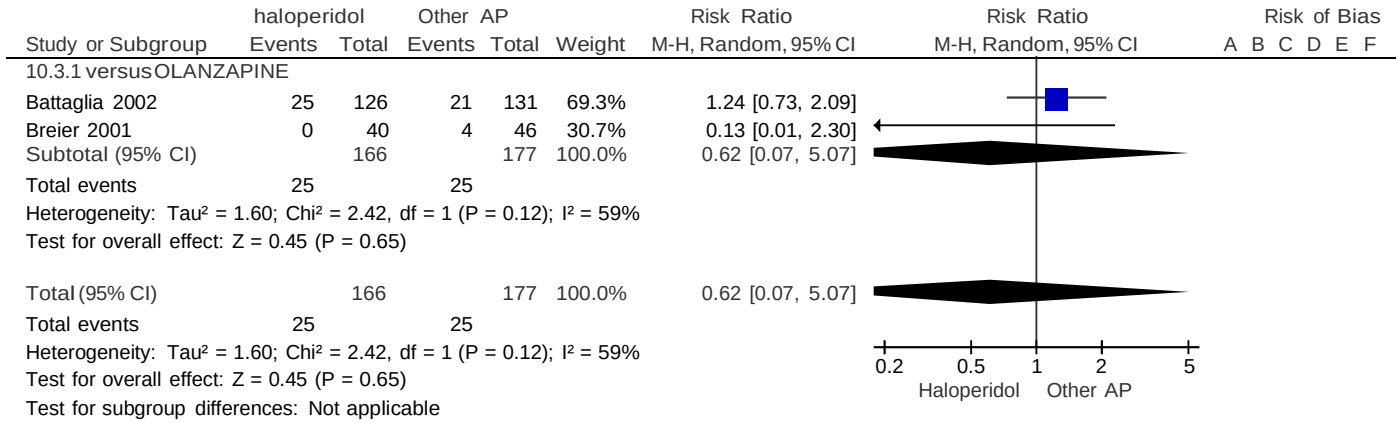
10.2 GLOBAL IMPRESSION: 2. REPEATED NEED FOR RAPID TRANQUILLISATION: NEEDING ADDITIONAL INJECTION



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

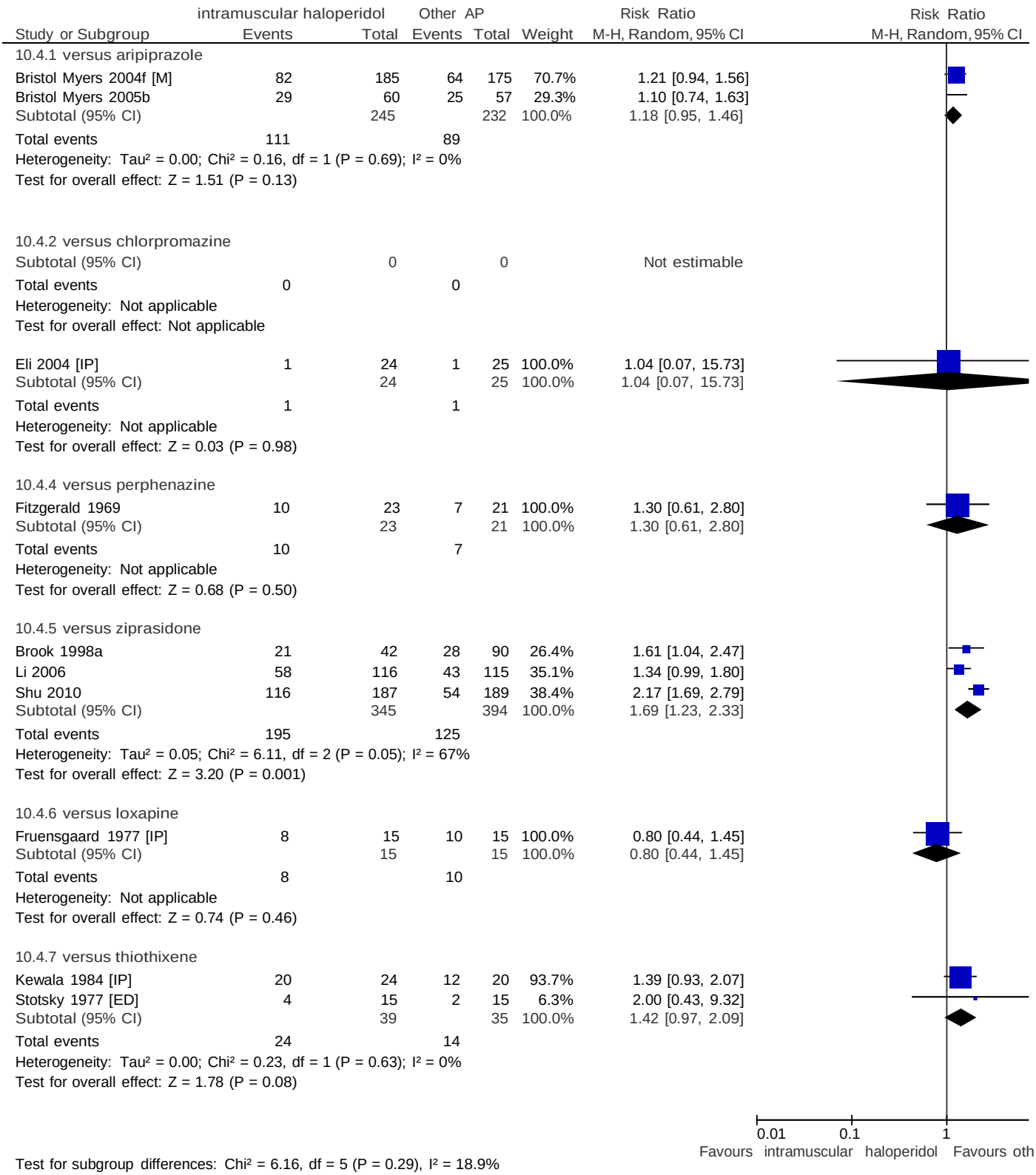
10.3 GLOBAL IMPRESSION: 3. NEED FOR ADDITIONAL BENZODIAZEPINE



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

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

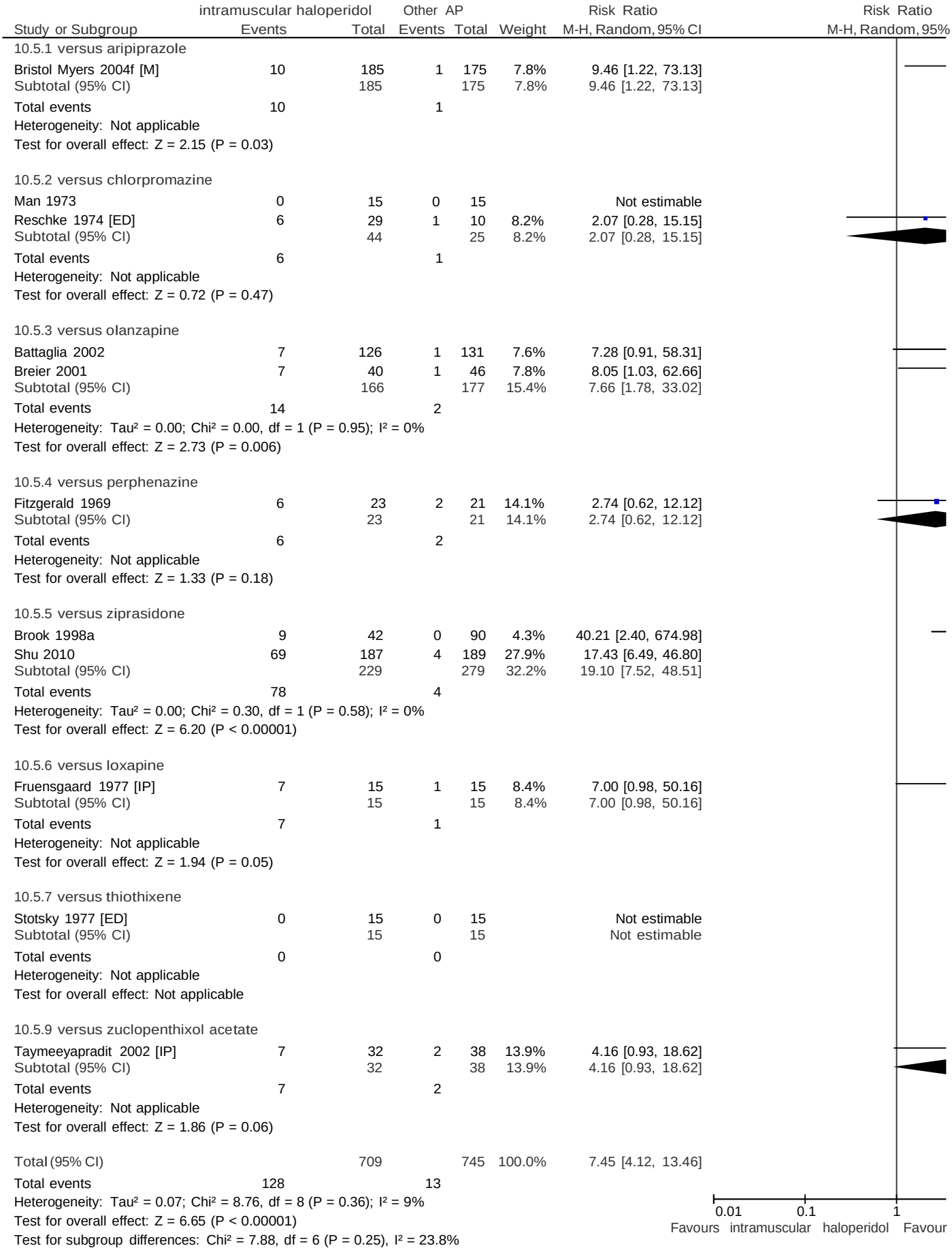


Test for subgroup differences: Chi² = 6.16, df = 5 (P = 0.29), I² = 18.9%

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

10.5 ADVERSE EFFECTS: EXTRAPYRAMIDAL SYMPTOMS



Risk of bias legend

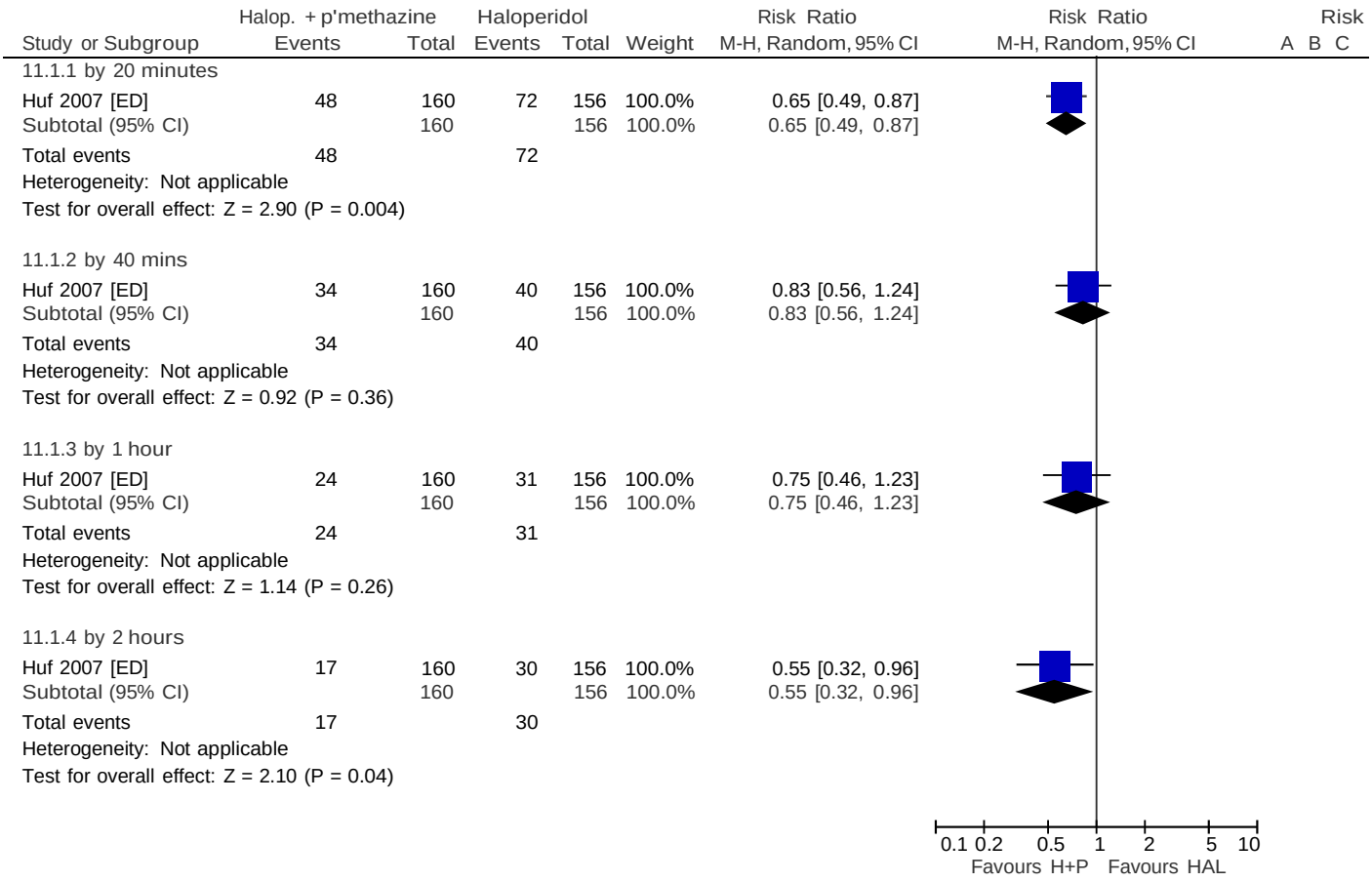
(A) Random sequence generation (selection bias)

(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

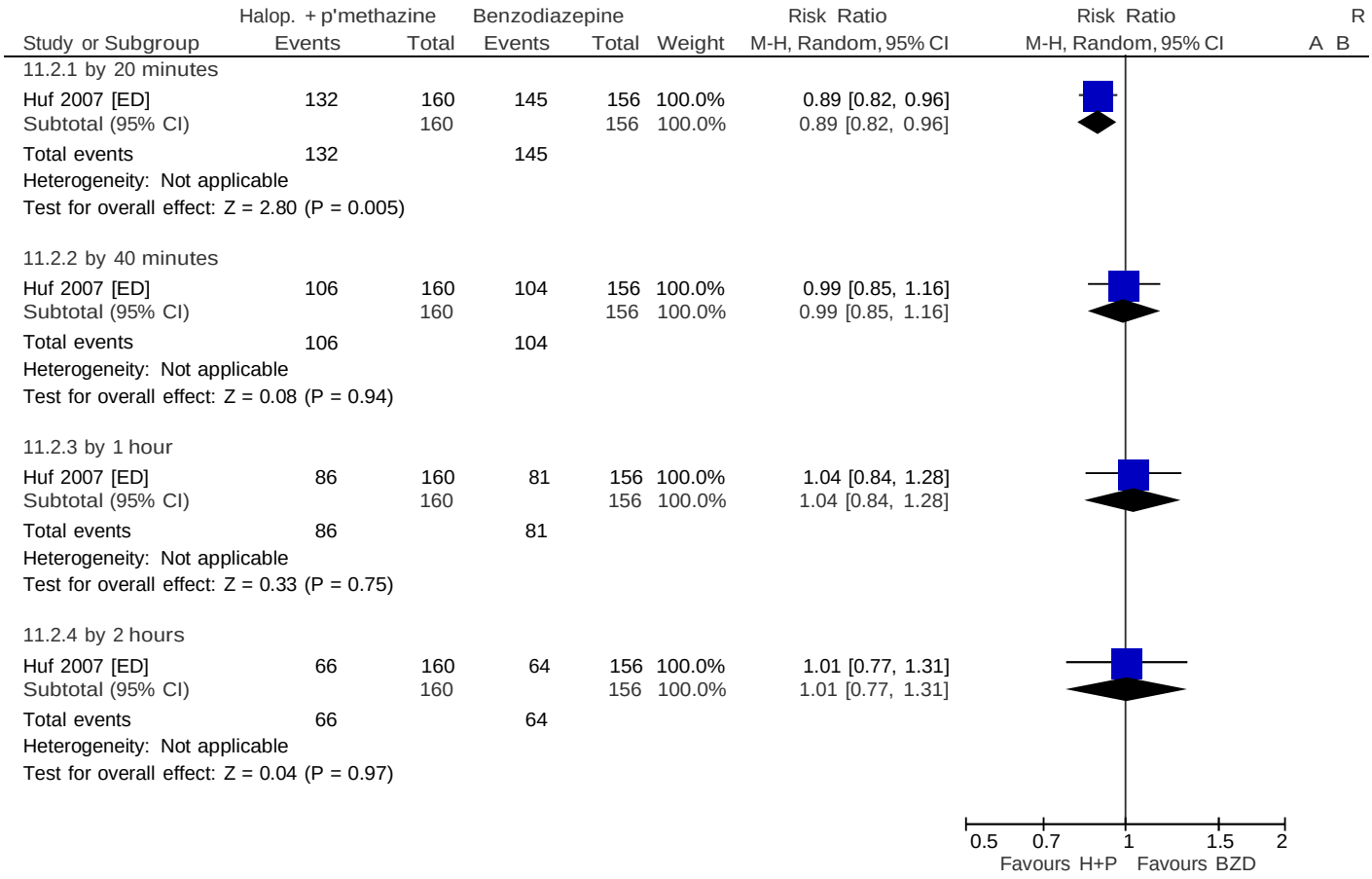
11 INTRAMUSCULAR HALOPERIDOL PLUS ANTIHISTAMINE VERSUS HALOPERIDOL [ADAPTED FROM HUF 2011]

11.1 GLOBAL IMPRESSION: 1. NOT TRANQUIL OR ASLEEP



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

11.2 GLOBAL IMPRESSION: 2. NOT ASLEEP

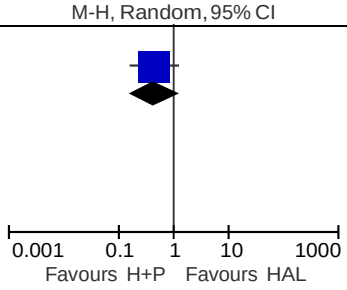


Risk of bias legend

(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

11.3 GLOBAL IMPRESSION: 3. ADDITIONAL TRANQUILLISING DRUGS

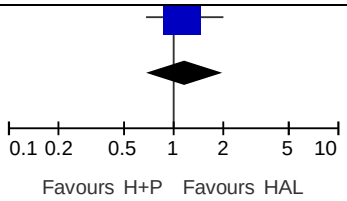
Study or Subgroup	Halop. + p'methazine Events	Total	Haloperidol Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
11.3.1 by 2 hours						
Huf 2007 [ED]	5	157	11	154	100.0%	0.45 [0.16, 1.25]
Subtotal (95% CI)		157		154	100.0%	0.45 [0.16, 1.25]
Total events	5		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.53 (P = 0.13)						



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

Study or Subgroup	Halop. + p'methazine Events	Total	Haloperidol Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Huf 2007 [ED]	25	154	20	144	100.0%	1.17 [0.68, 2.01]
Total (95% CI)		154		144	100.0%	1.17 [0.68, 2.01]
Total events	25		20			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.56 (P = 0.57)						



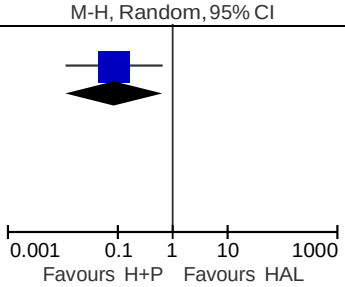
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

11.5 ADVERSE EFFECTS: 1. ANY SERIOUS ADVERSE EFFECT

Study or Subgroup	Halop. + p'methazine Events	Total	Haloperidol Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk A B C
11.5.1 by 24 hours								
Huf 2007 [ED]	1	153	11	145	100.0%	0.09 [0.01, 0.66]		
Subtotal (95% CI)		153		145	100.0%	0.09 [0.01, 0.66]		
Total events	1		11					

Heterogeneity: Not applicable

Test for overall effect: Z = 2.36 (P = 0.02)



Test for subgroup differences: Not applicable

Risk of bias legend

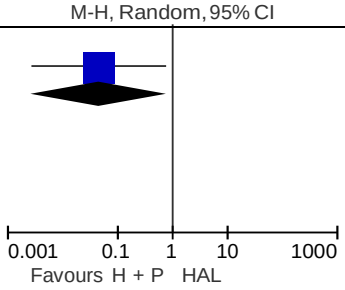
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other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

11.6 ADVERSE EFFECTS: 2. ACUTE DYSTONIA

Study or Subgroup	Halop. + p'methazine Events	Total	Haloperidol Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk A B C
11.6.1 by 24 hours								
Huf 2007 [ED]	0	153	10	145	100.0%	0.05 [0.00, 0.76]		
Subtotal (95% CI)		153		145	100.0%	0.05 [0.00, 0.76]		
Total events	0		10					

Heterogeneity: Not applicable

Test for overall effect: Z = 2.15 (P = 0.03)



Test for subgroup differences: Not applicable

Risk of bias legend

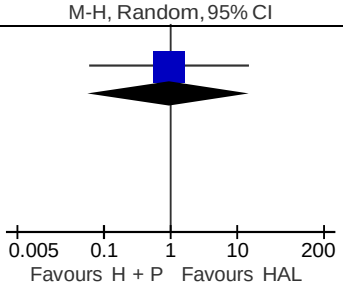
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other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

11.7 ADVERSE EFFECTS: 3. SEIZURE

Study or Subgroup	Halop. + p'methazine Events	Total	Haloperidol Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk A B C
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 applicable

Test for overall effect: Z = 0.04 (P = 0.97)



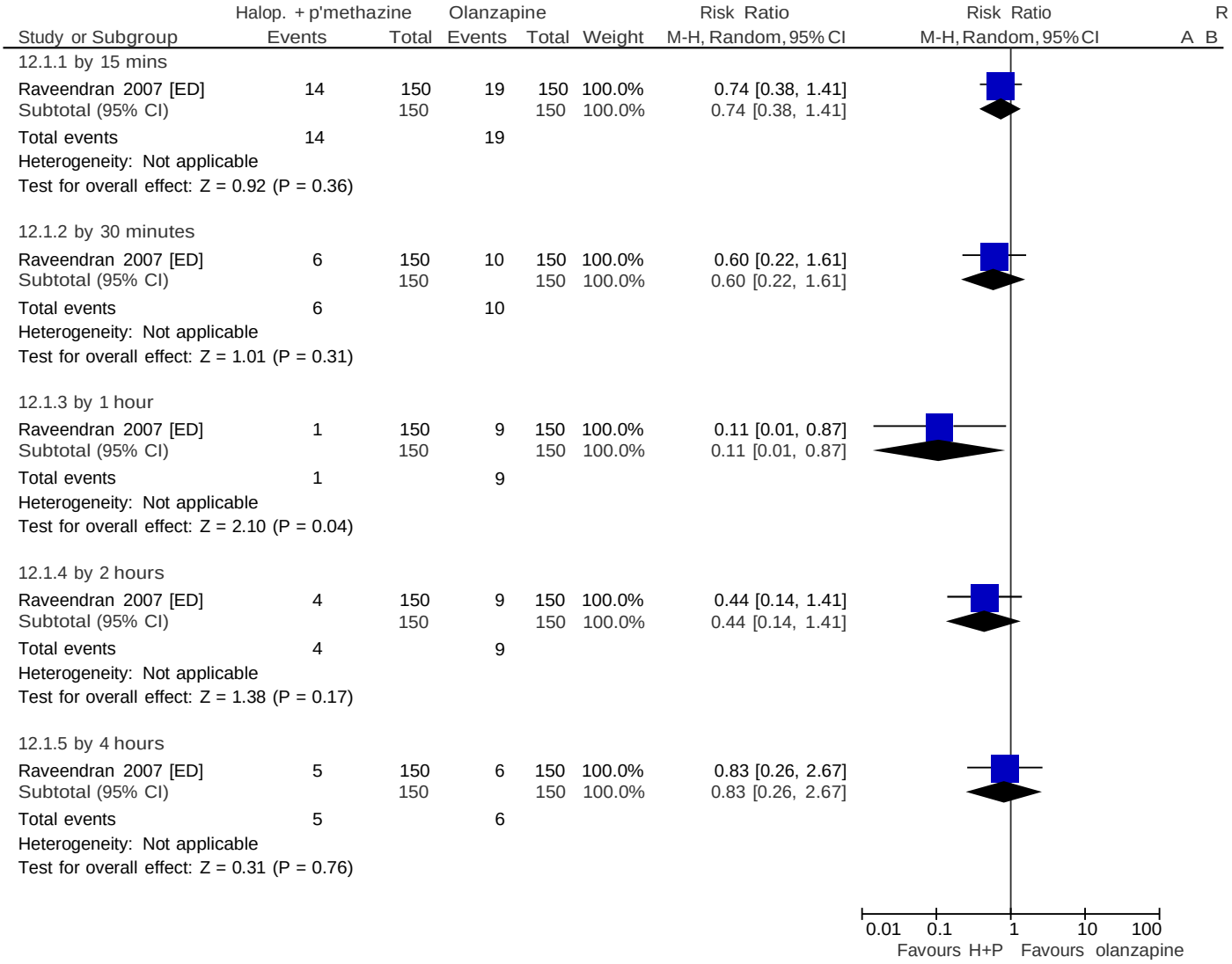
Test for subgroup differences: Not applicable

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

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

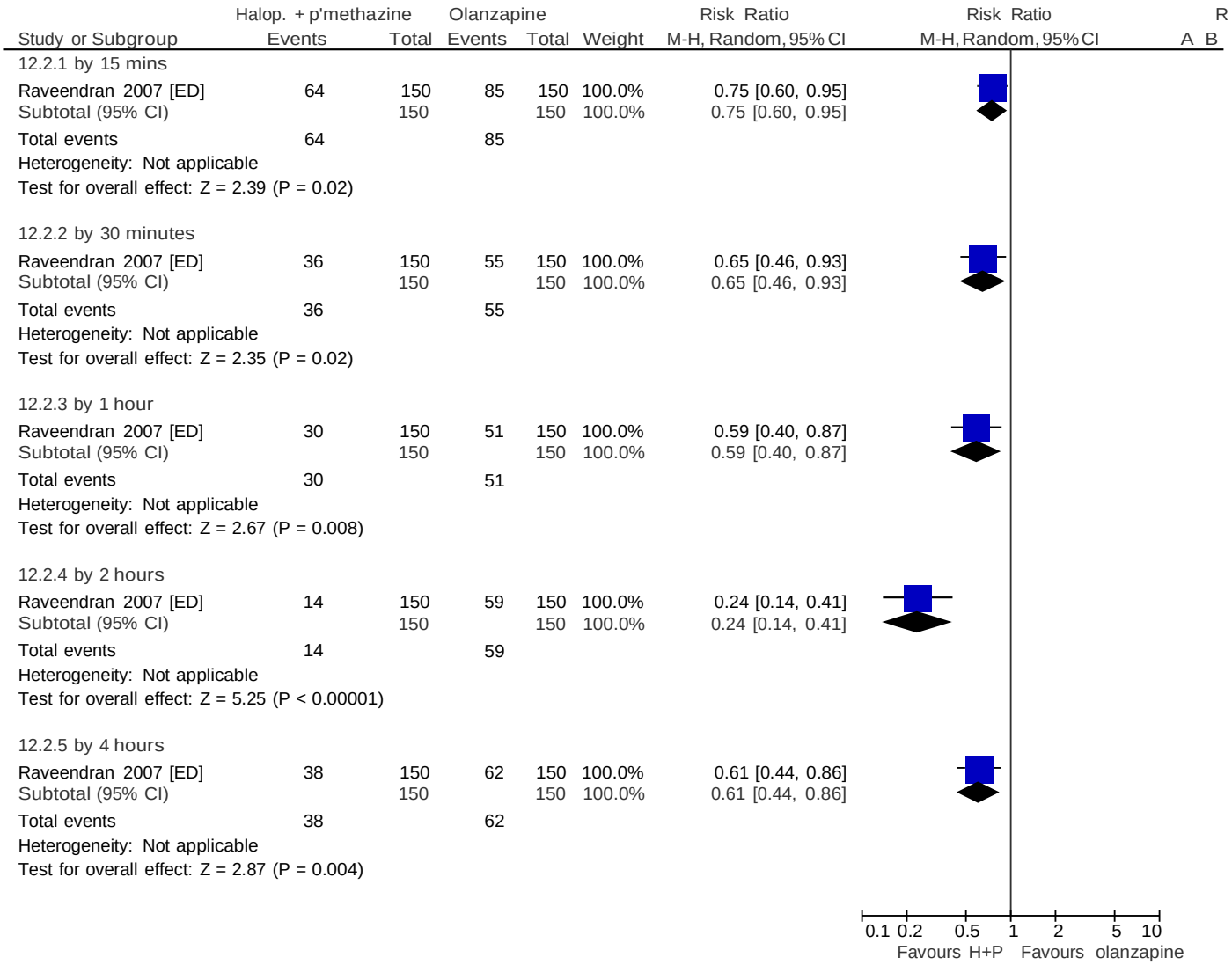
12.1 GLOBAL IMPRESSION: 1. NOT TRANQUIL OR ASLEEP



Risk of bias legend

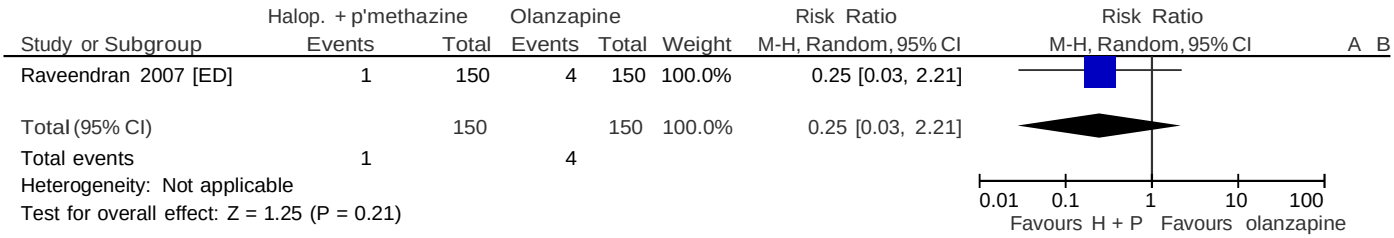
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other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

12.2 GLOBAL IMPRESSION: 2. NOT ASLEEP



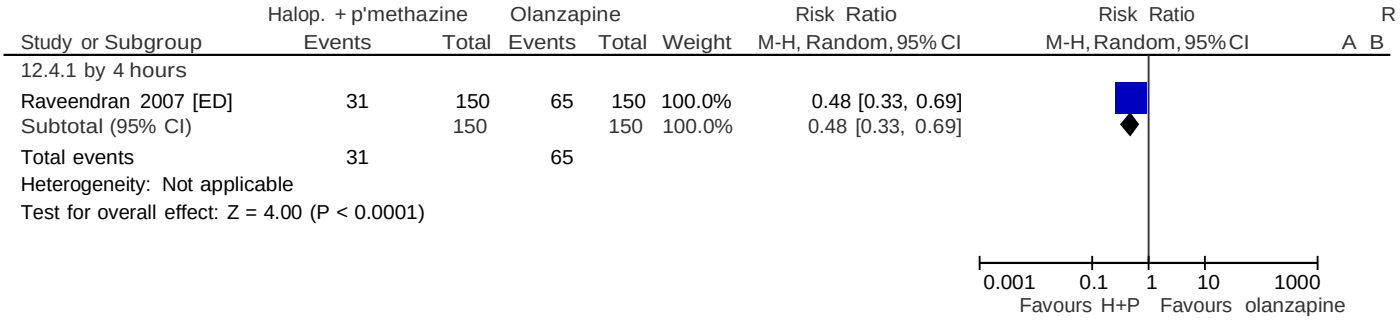
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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



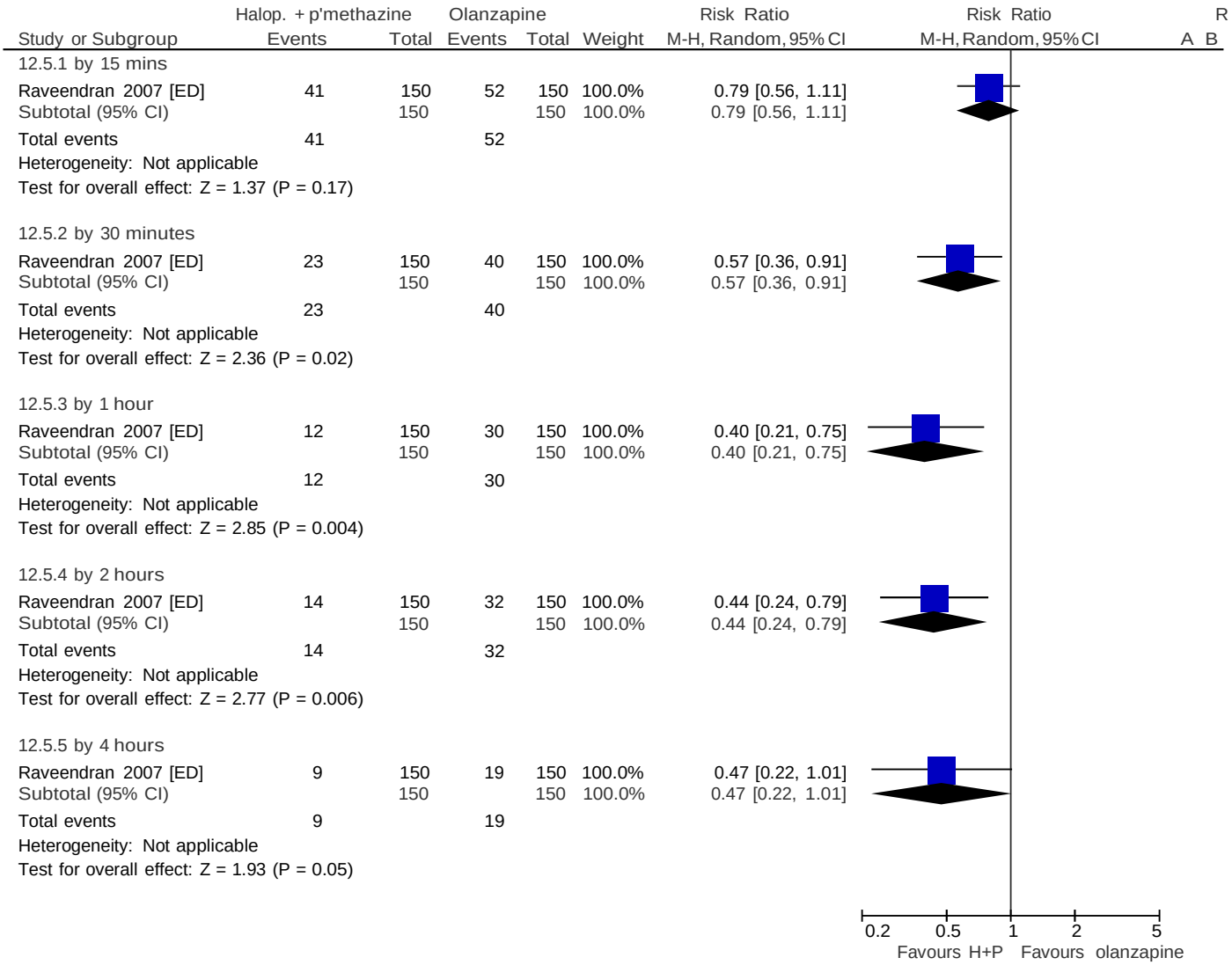
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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



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

12.5 GLOBAL IMPRESSION: 5. NOT CLINICALLY IMPROVED



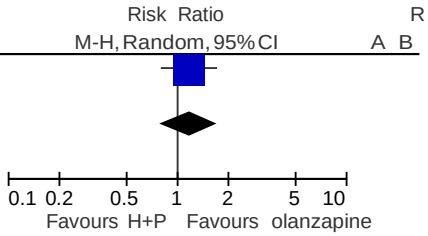
Risk of bias legend

(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

12.6 GLOBAL IMPRESSION: 6.FURTHER OBSERVATION AFTER 4 HOURS

Study or Subgroup	Halop. + p'methazine Events	Total	Olanzapine Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
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		36			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.79 (P = 0.43)



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

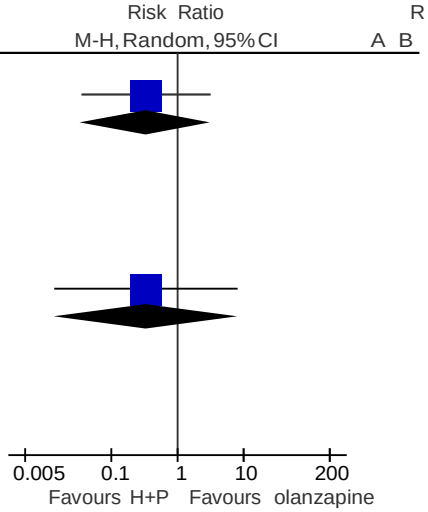
12.7 ADVERSE EFFECTS: 1. SERIOUS ADVERSE EFFECT

Study or Subgroup	Halop. + p'methazine Events	Total	Olanzapine Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
12.7.1 by 4 hours						
Raveendran 2007 [ED]	1	150	3	150	100.0%	0.33 [0.04, 3.17]
Subtotal (95% CI)		150		150	100.0%	0.33 [0.04, 3.17]
Total events	1		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.96 (P = 0.34)

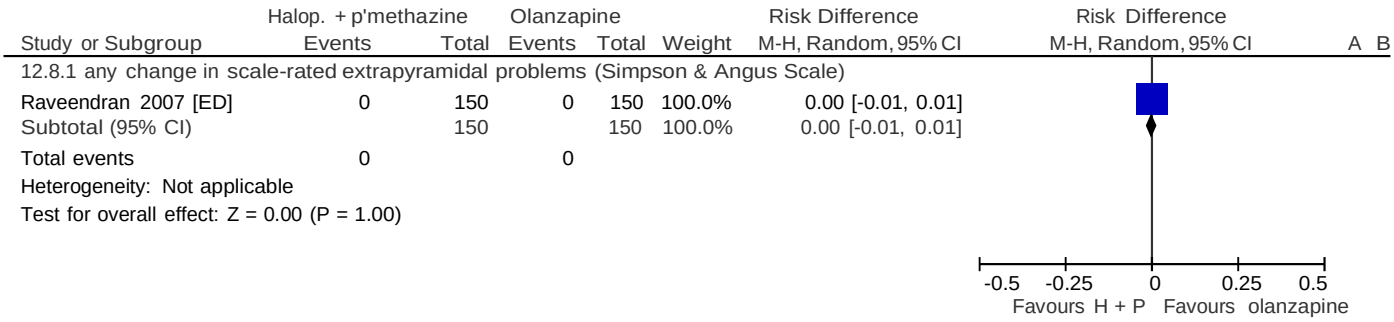
12.7.2 at 2 weeks						
Raveendran 2007 [ED]	0	150	1	150	100.0%	0.33 [0.01, 8.12]
Subtotal (95% CI)		150		150	100.0%	0.33 [0.01, 8.12]
Total events	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.67 (P = 0.50)



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

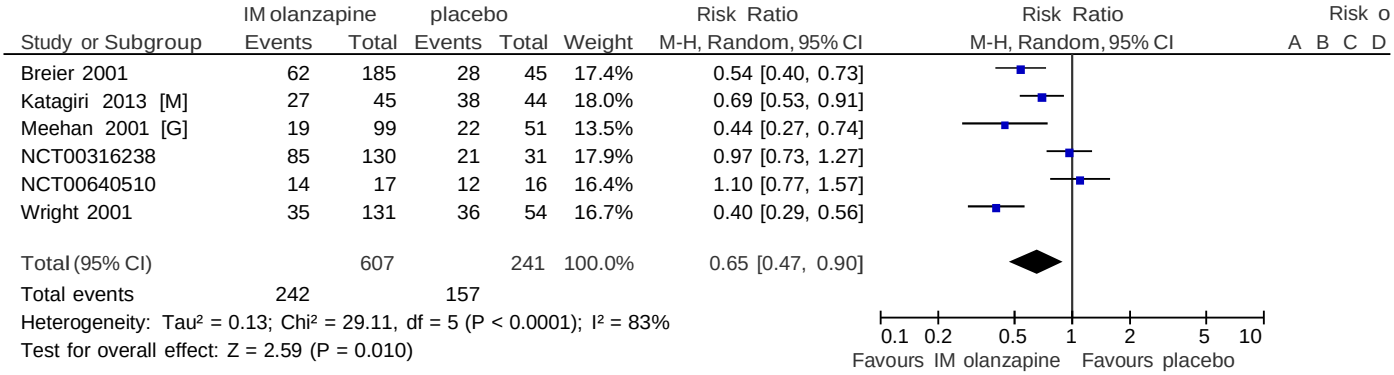
12.8 ADVERSE EFFECTS: 2. EXTRAPYRAMIDAL PROBLEMS – 0-4 HOURS



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

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

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

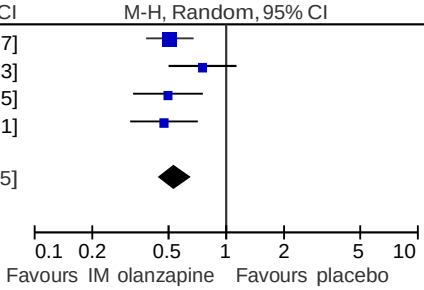


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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

Study or Subgroup	IM olanzapine Events	Total	placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Breier 2001	62	185	33	50	39.4%	0.51 [0.38, 0.67]
Katagiri 2013 [M]	20	45	26	44	20.4%	0.75 [0.50, 1.13]
Meehan 2001 [G]	26	99	27	51	19.5%	0.50 [0.33, 0.75]
Wright 2001	31	131	27	54	20.6%	0.47 [0.32, 0.71]
Total (95% CI)		460		199	100.0%	0.54 [0.45, 0.65]
Total events	139		113			

Heterogeneity: Tau² = 0.00; Chi² = 3.26, df = 3 (P = 0.35); I² = 8%
Test for overall effect: Z = 6.31 (P < 0.00001)

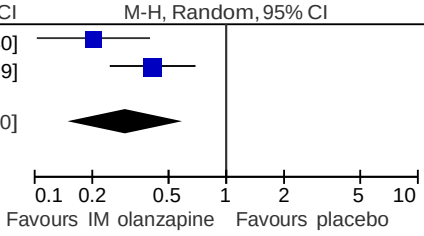


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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

Study or Subgroup	IM olanzapine Events	Total	placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Breier 2001	12	185	16	50	44.9%	0.20 [0.10, 0.40]
Wright 2001	21	131	21	54	55.1%	0.41 [0.25, 0.69]
Total (95% CI)		316		104	100.0%	0.30 [0.15, 0.60]
Total events	33		37			

Heterogeneity: Tau² = 0.16; Chi² = 2.66, df = 1 (P = 0.10); I² = 62%
Test for overall effect: Z = 3.41 (P = 0.0006)

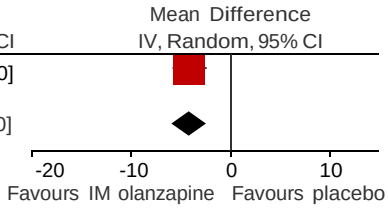


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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

Study or Subgroup	Mean Difference	SE	IM olanzapine Total	placebo Total	Weight	Mean Difference IV, Random, 95% CI
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 applicable
Test for overall effect: Z = 4.86 (P < 0.00001)

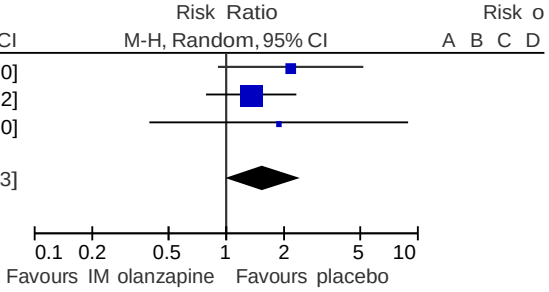


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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

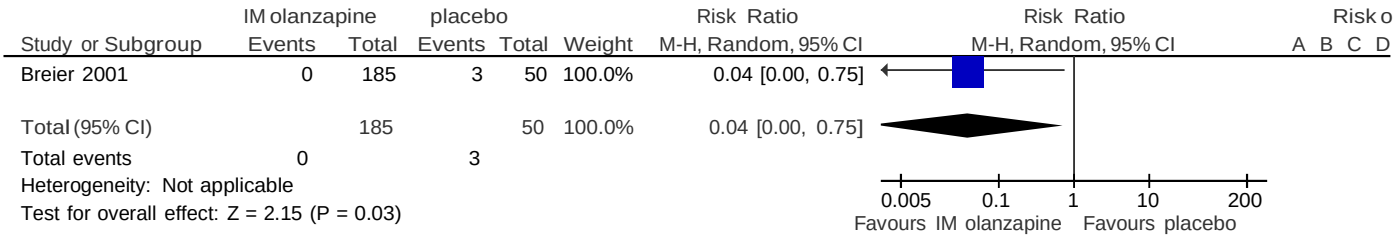
Study or Subgroup	IM olanzapine Events	Total	placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Katagiri 2013 [M]	13	45	6	45	25.5%	2.17 [0.90, 5.20]
Meehan 2001 [G]	34	99	13	51	66.4%	1.35 [0.78, 2.32]
NCT00640510	4	17	2	16	8.1%	1.88 [0.40, 8.90]
Total (95% CI)		161		112	100.0%	1.56 [1.00, 2.43]
Total events	51		21			

Heterogeneity: Tau² = 0.00; Chi² = 0.88, df = 2 (P = 0.64); I² = 0%
Test for overall effect: Z = 1.98 (P = 0.05)



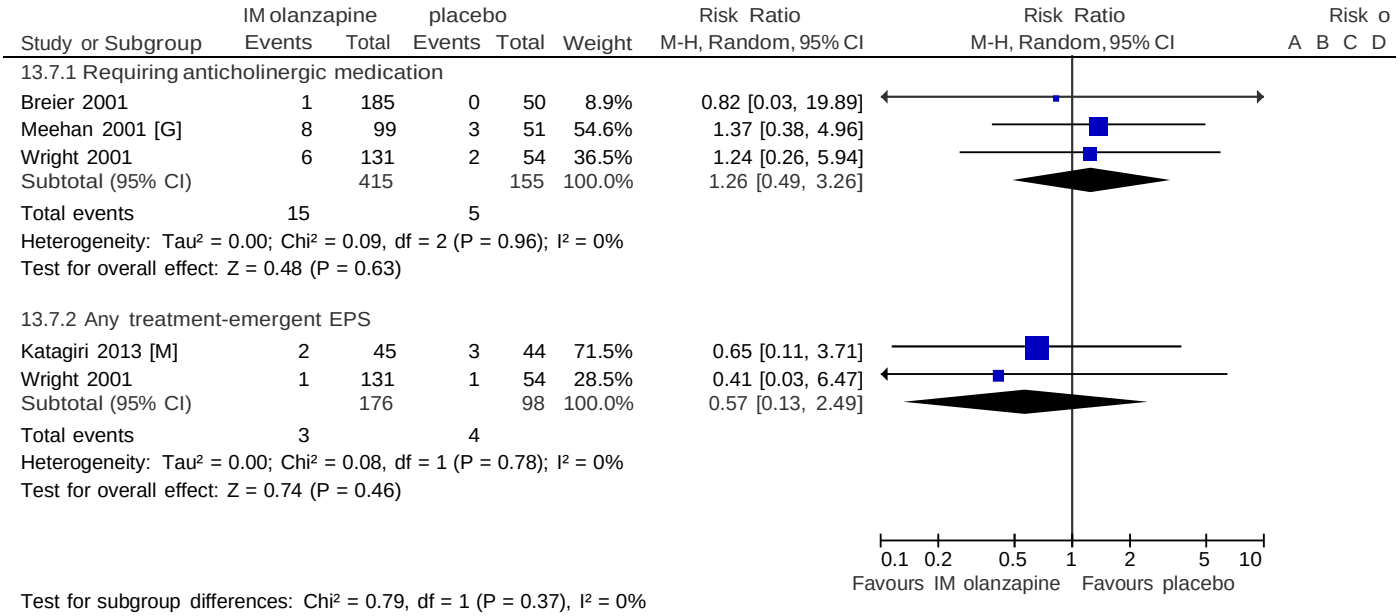
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

13.6 ADVERSE EFFECTS: 2. ANXIETY – 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

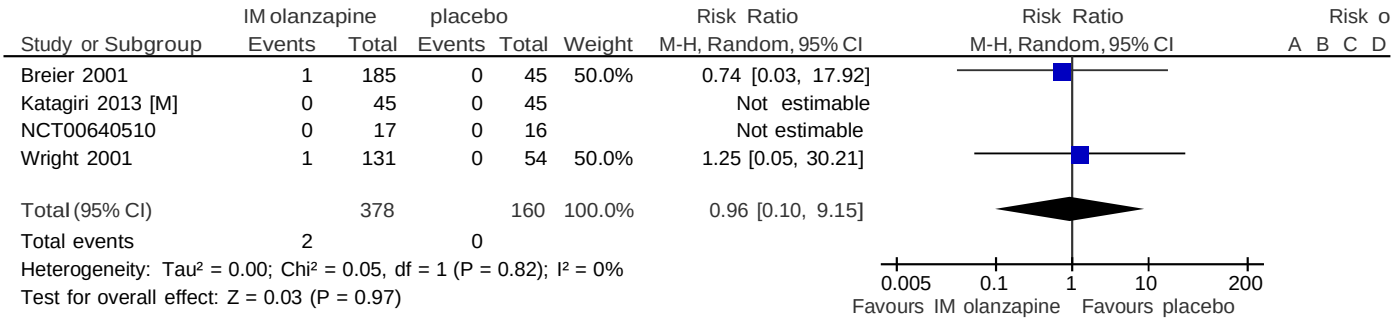
13.7 ADVERSE EFFECTS: 3. EXTRAPYRAMIDAL SYMPTOMS – BY 24 HOURS



Test for subgroup differences: Chi² = 0.79, df = 1 (P = 0.37), I² = 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

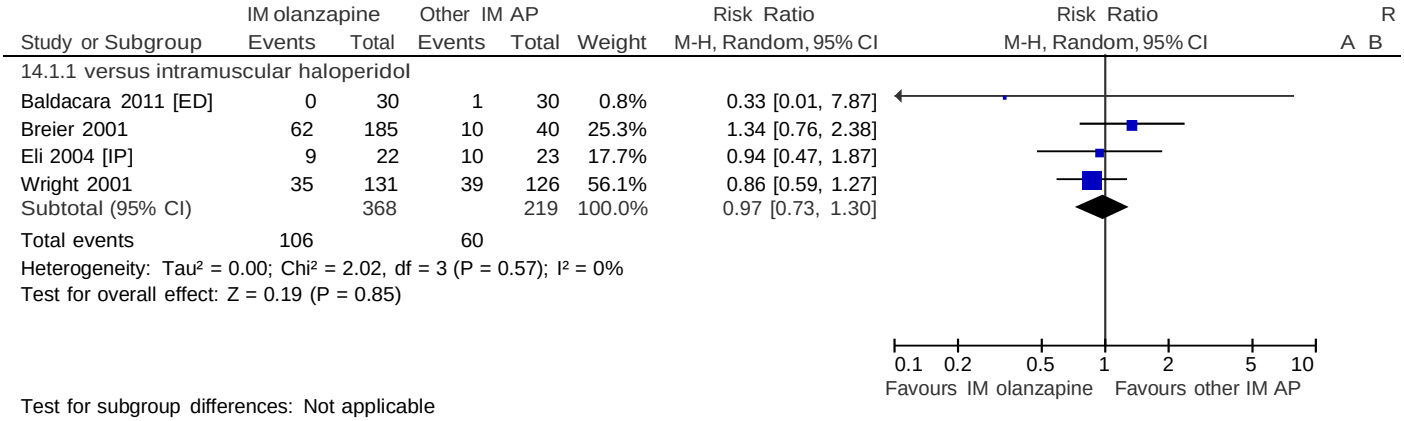
13.8 ADVERSE EFFECTS: 4. SERIOUS ADVERSE EVENT – BY 24 HOURS



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

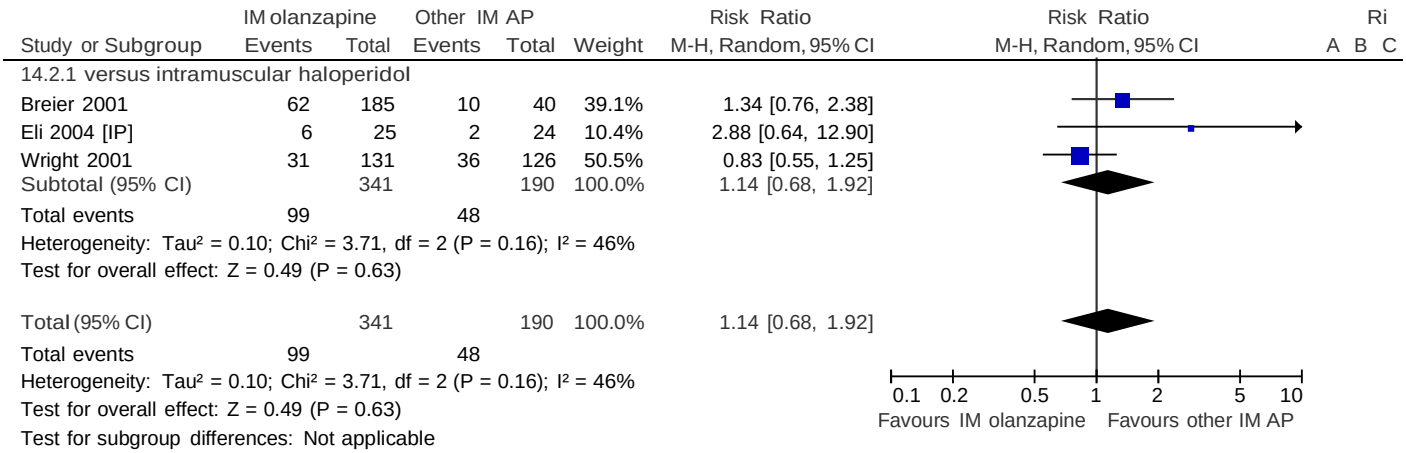
14.1 GLOBAL IMPRESSION: 1. NOT IMPROVED



Test for subgroup differences: Not applicable

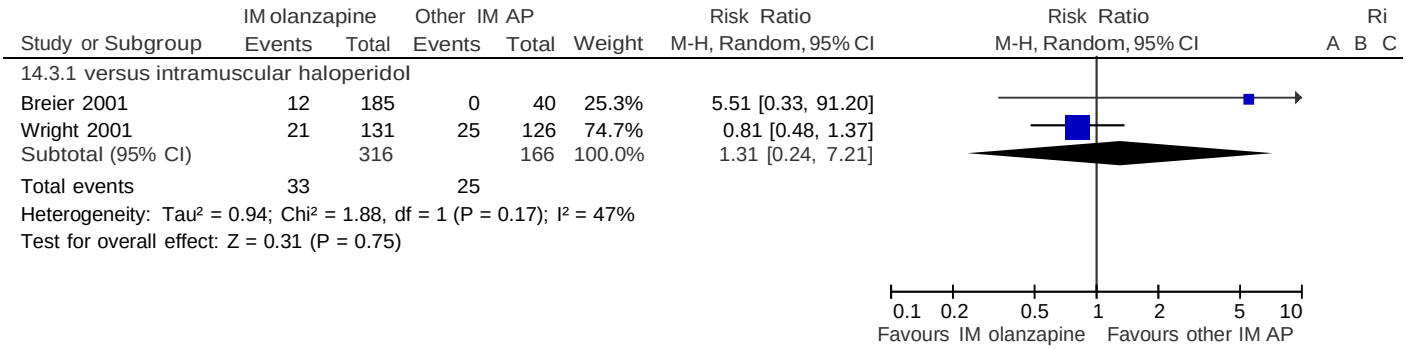
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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



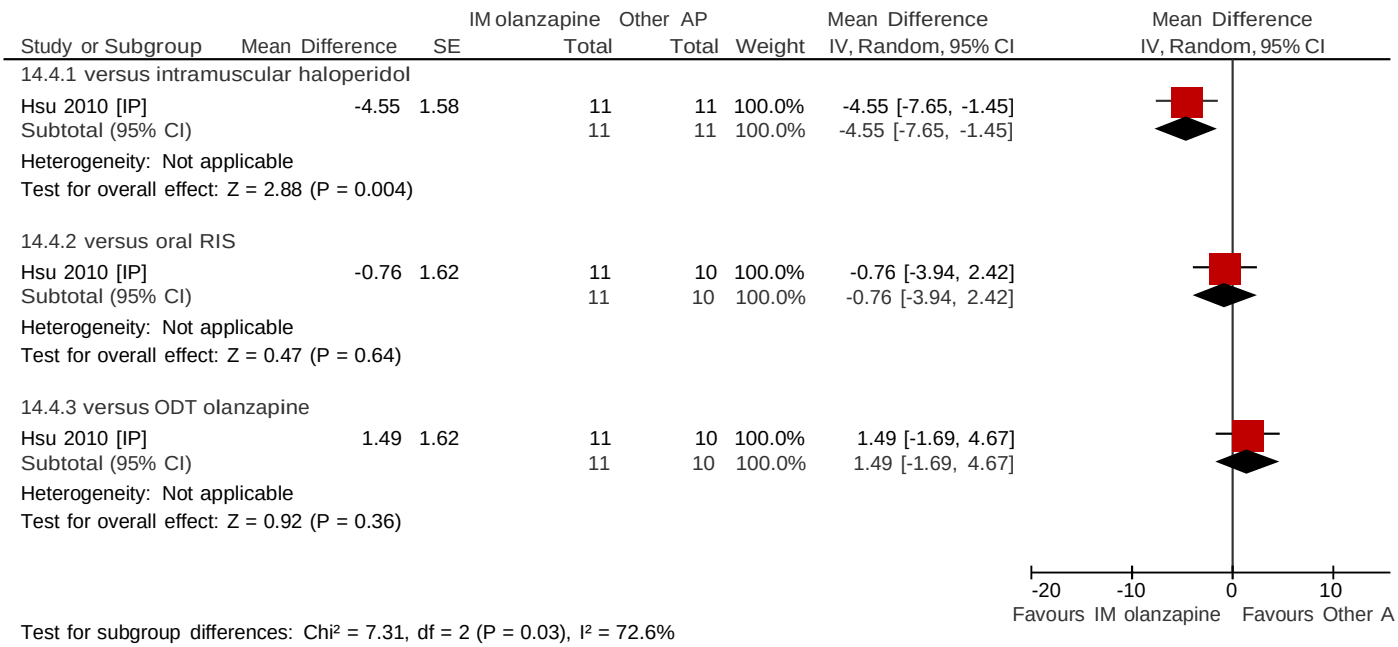
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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



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

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

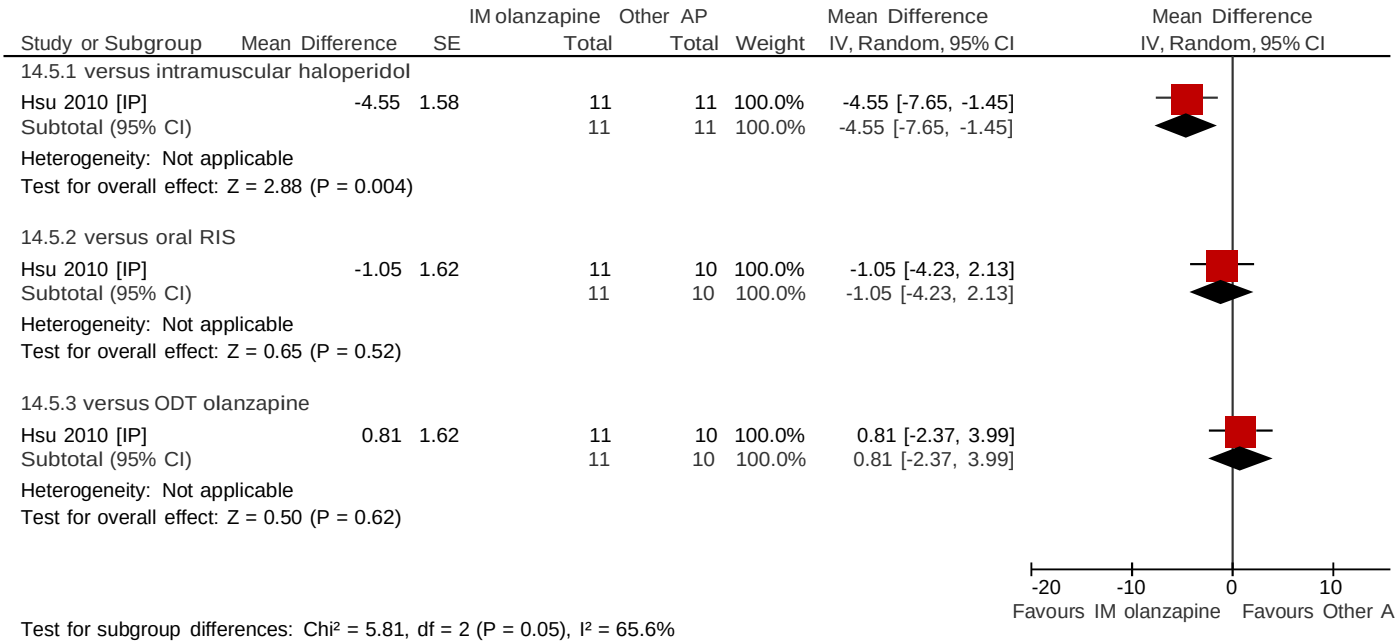


Test for subgroup differences: Chi² = 7.31, df = 2 (P = 0.03), I² = 72.6%

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

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

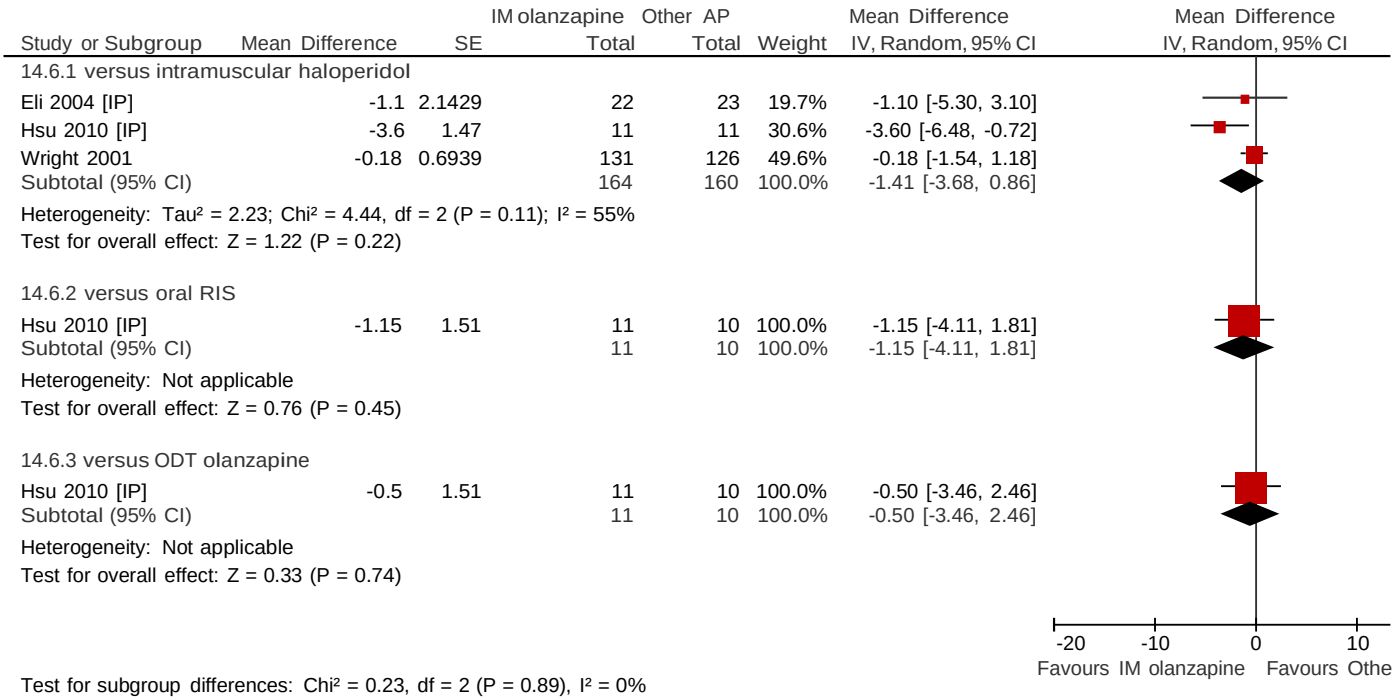


Test for subgroup differences: Chi² = 5.81, df = 2 (P = 0.05), I² = 65.6%

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

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

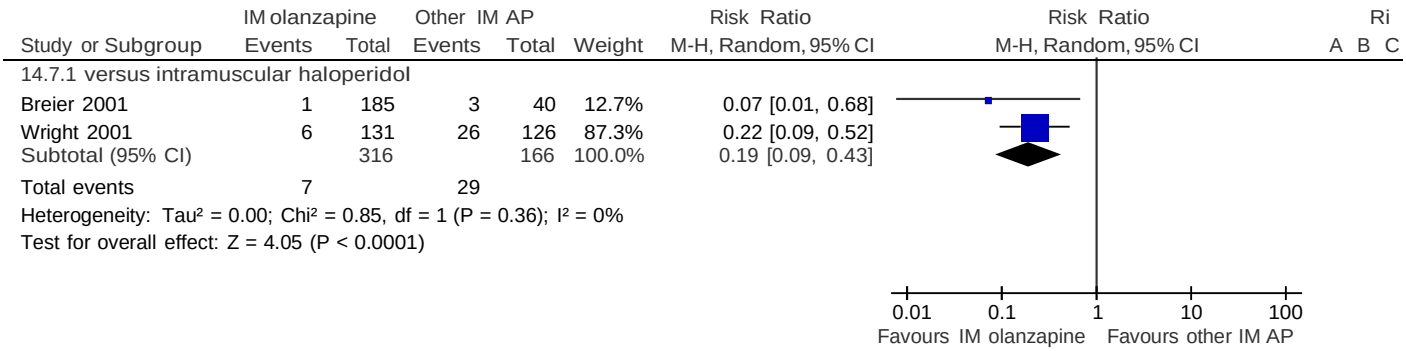


Test for subgroup differences: Chi² = 0.23, df = 2 (P = 0.89), I² = 0%

Risk of bias legend

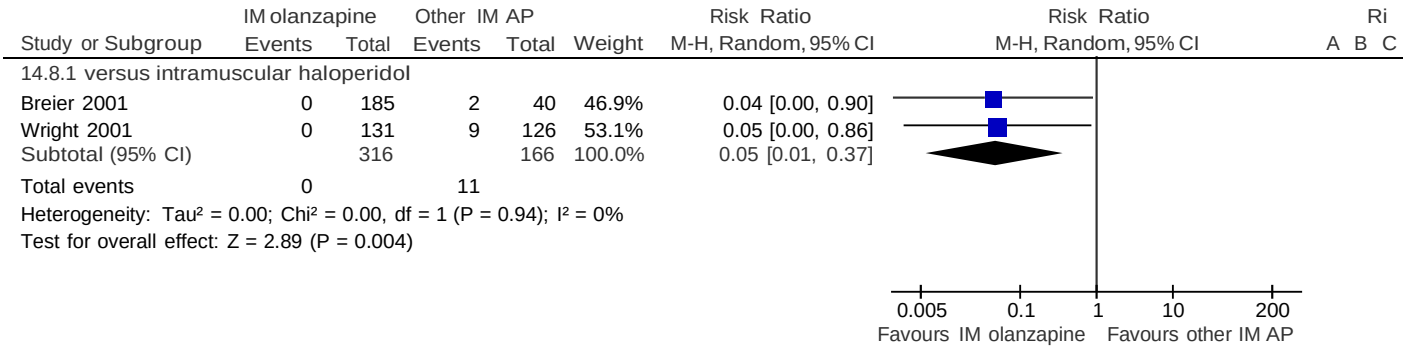
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other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

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



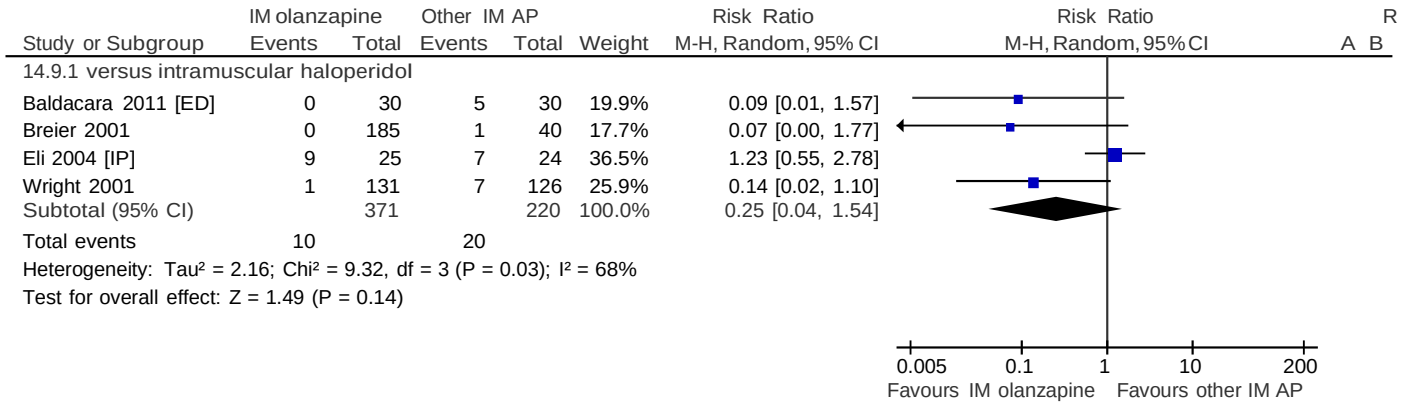
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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



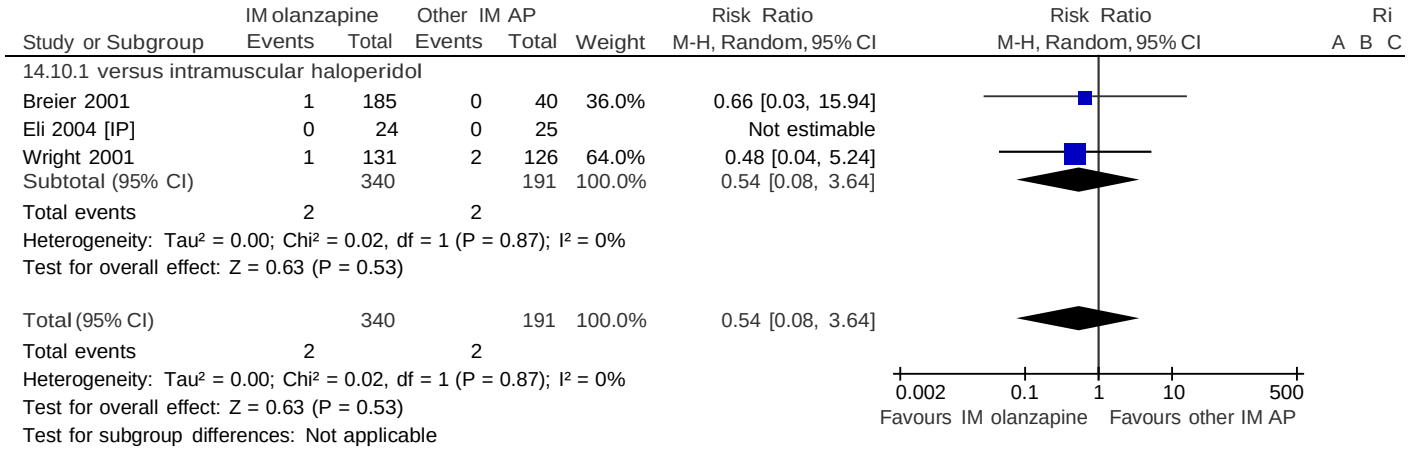
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

14.9 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

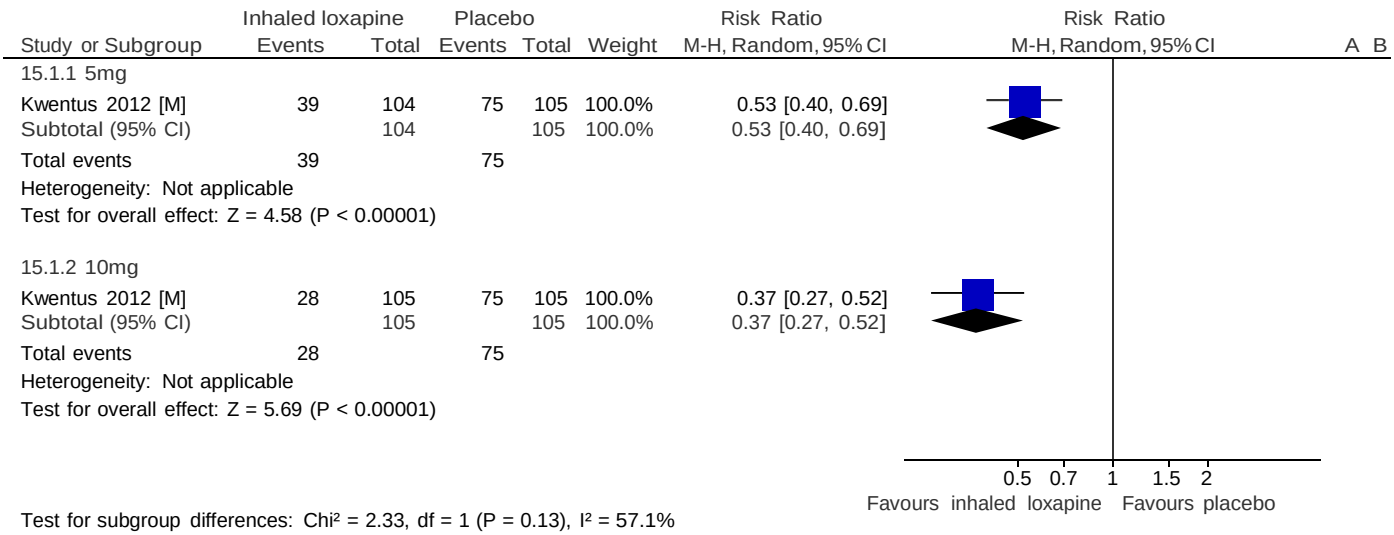
14.10 ADVERSE EFFECTS: 2. SERIOUS ADVERSE EVENT



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 INHALED LOXAPINE VERSUS PLACEBO [NCCMH]

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

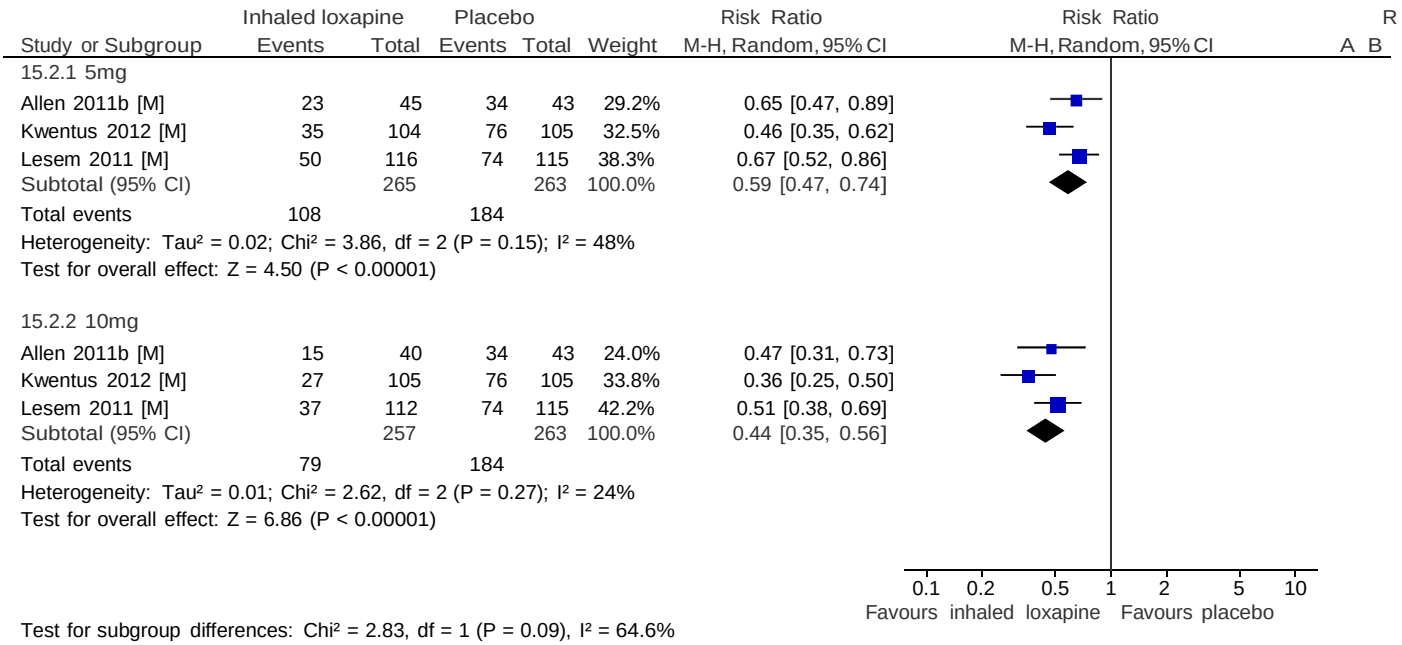


Test for subgroup differences: Chi² = 2.33, df = 1 (P = 0.13), I² = 57.1%

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

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

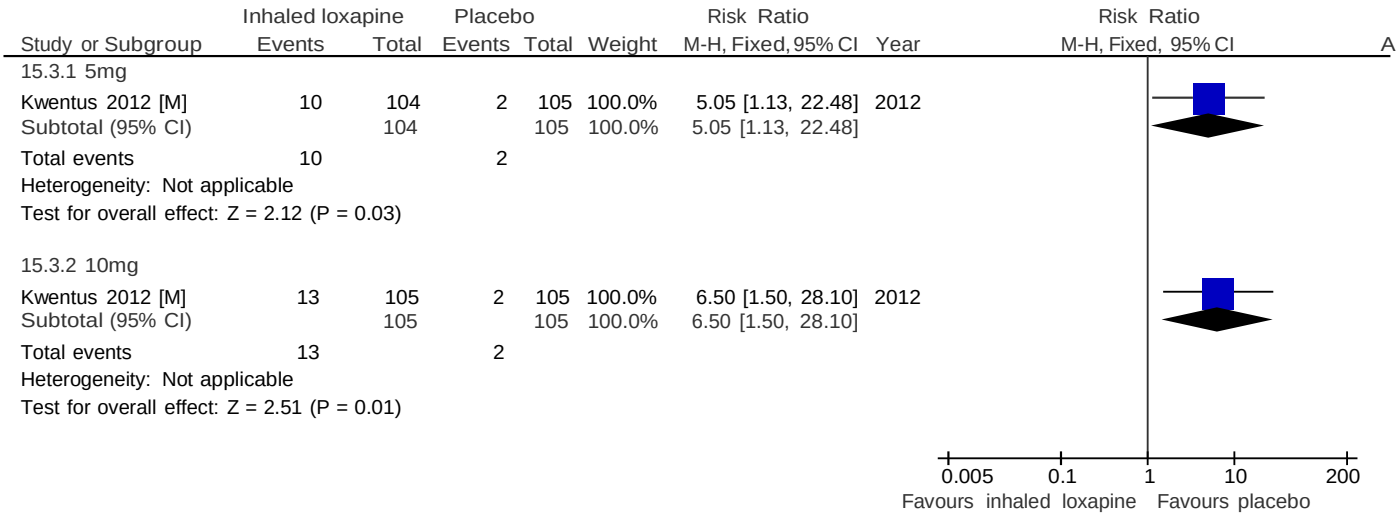


Test for subgroup differences: Chi² = 2.83, df = 1 (P = 0.09), I² = 64.6%

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)

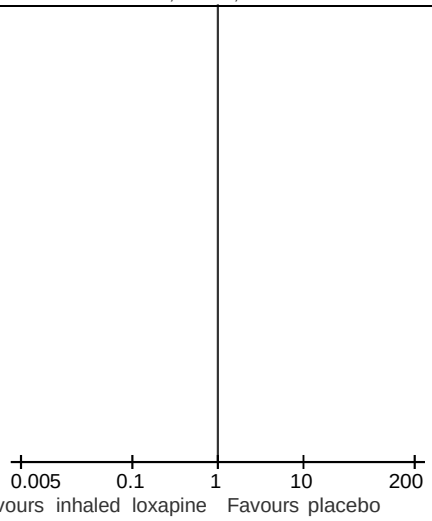


Risk of bias legend

(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

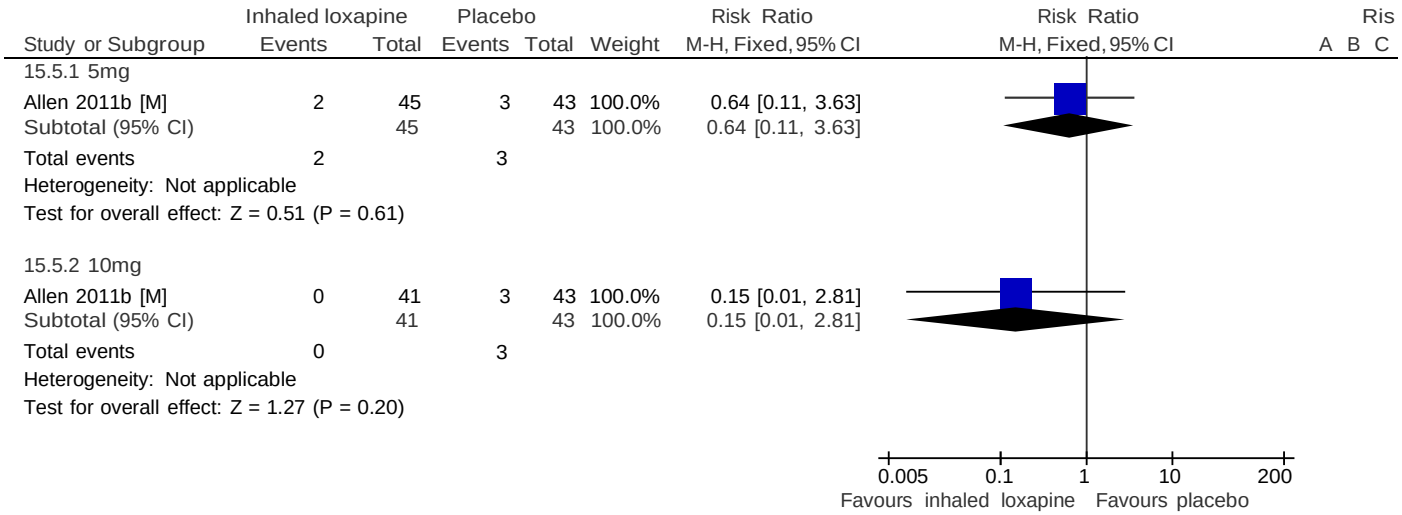
15.4 GLOBAL IMPRESSION: 4. UNAROUSABLE (ACES)

Study or Subgroup	Inhaled loxapine Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI	Ris A B C
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 applicable								
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 applicable								
Test for overall effect: 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

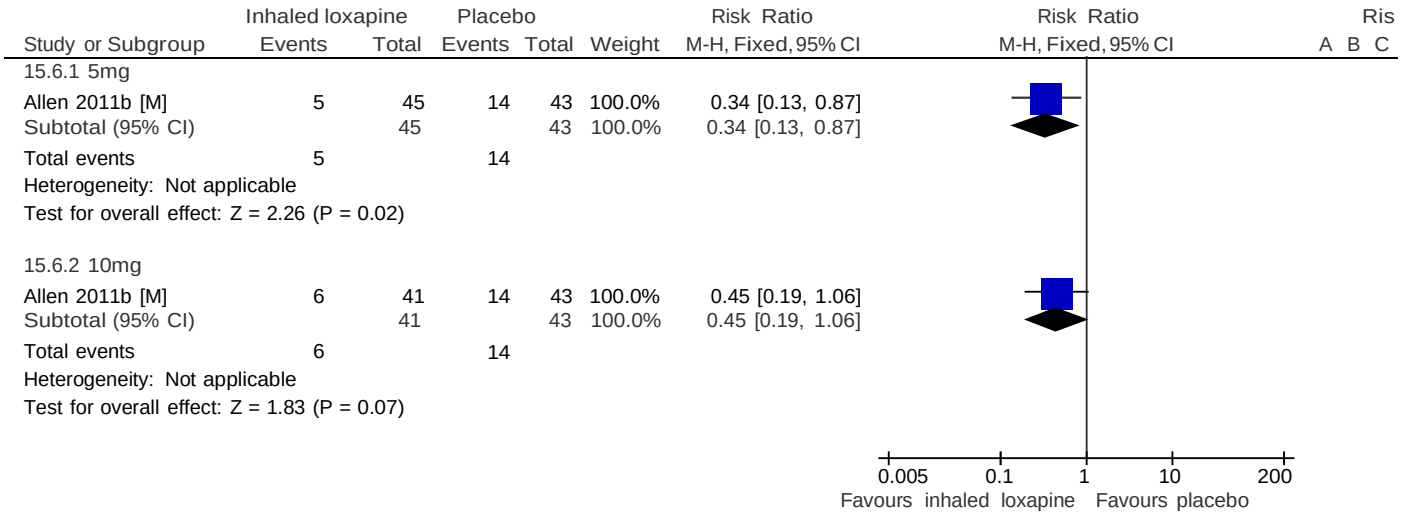
15.5 GLOBAL IMPRESSION: 5. NEED FOR RESCUE MEDICATION AT 4 HOURS



Risk of bias legend

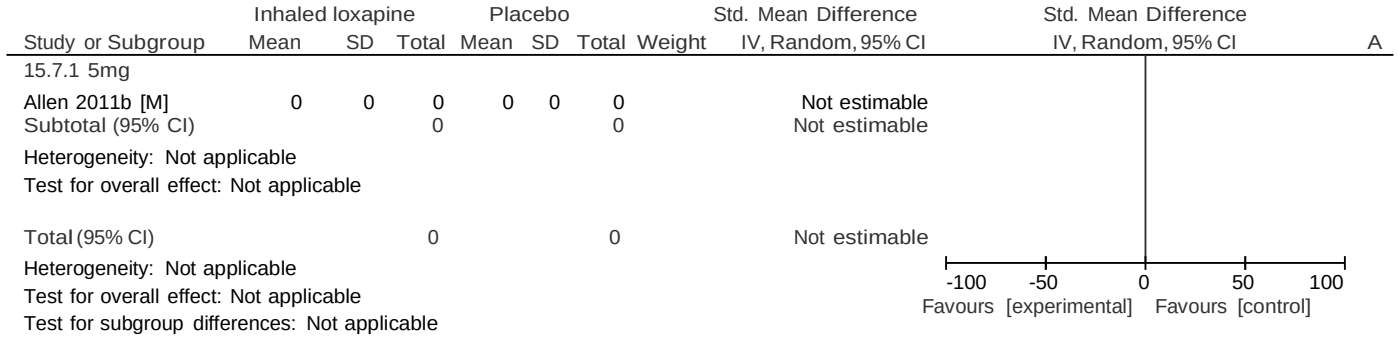
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other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

15.6 GLOBAL IMPRESSION: 5. NEED FOR RESCUE MEDICATION AT 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

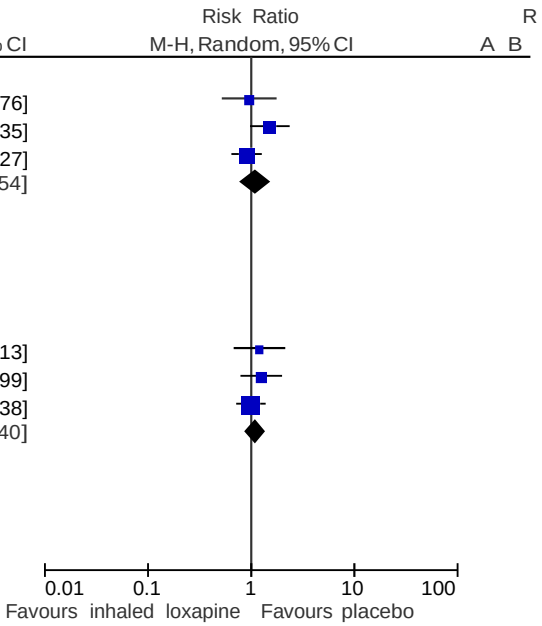
15.7 BEHAVIOUR: 1A. AVERAGE CHANGE SCORE (PANSS-EC) – MEDIUM TERM (2 HOURS)



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

15.8 ADVERSE EFFECTS: 1. AT LEAST ONE ADVERSE EFFECT

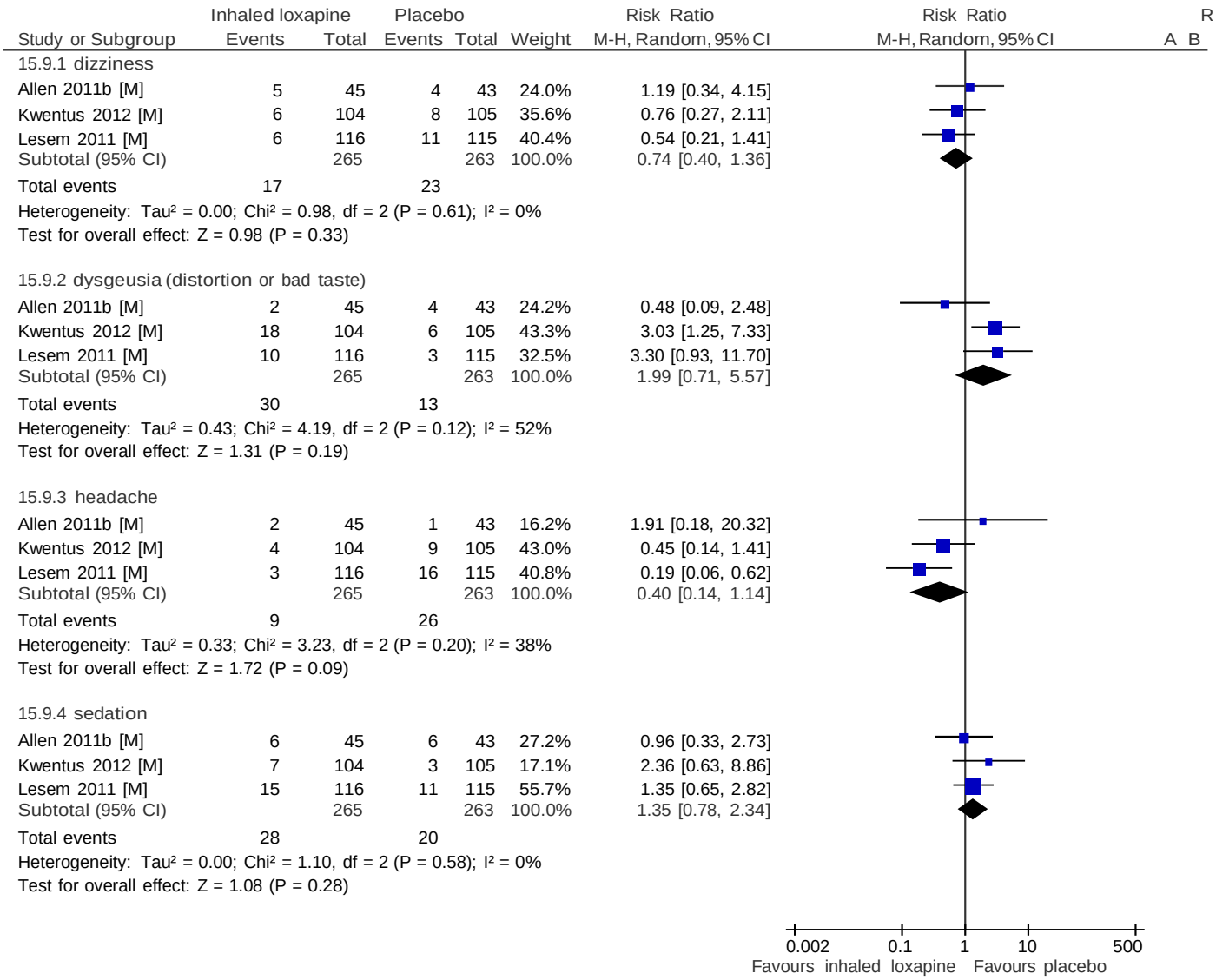
Study or Subgroup	Inhaled loxapine Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
15.8.1 5mg Allen						
2011b [M]	14	45	14	43	22.4%	0.96 [0.52, 1.76]
Kwentus 2012 [M]	36	104	24	105	34.0%	1.51 [0.98, 2.35]
Lesem 2011 [M]	40	116	44	115	43.6%	0.90 [0.64, 1.27]
Subtotal (95% CI)		265		263	100.0%	1.09 [0.77, 1.54]
Total events	90		82			
Heterogeneity: Tau² = 0.04; Chi² = 3.51, df = 2 (P = 0.17); I² = 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]	43	113	44	115	54.4%	0.99 [0.71, 1.38]
Subtotal (95% CI)		259		263	100.0%	1.10 [0.86, 1.40]
Total events	89		82			
Heterogeneity: Tau² = 0.00; Chi² = 0.74, df = 2 (P = 0.69); I² = 0%						
Test for overall effect: Z = 0.73 (P = 0.46)						



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

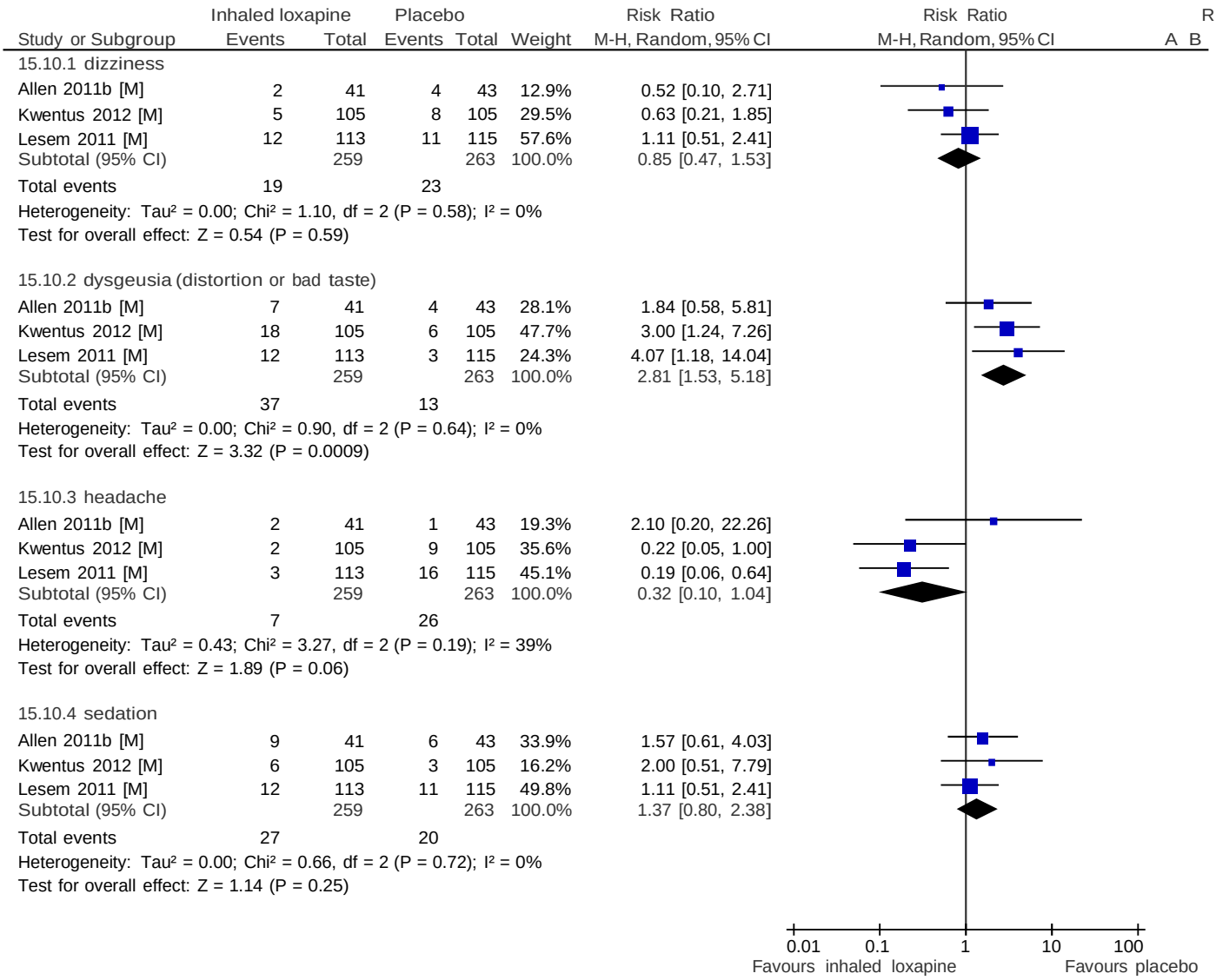
15.9 ADVERSE EFFECTS: 2. TREATMENT-EMERGENT ADVERSE EFFECTS IN ≥ 5% OF PATIENTS – 5 MG VERSUS PLACEBO



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

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

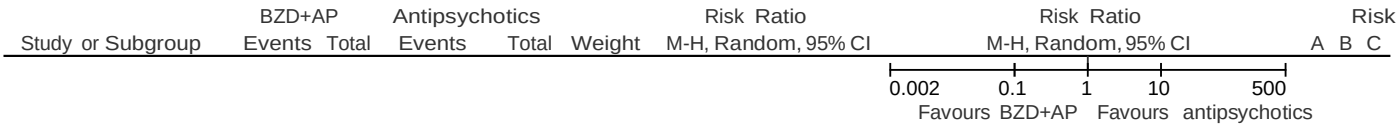


Risk of bias legend

(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

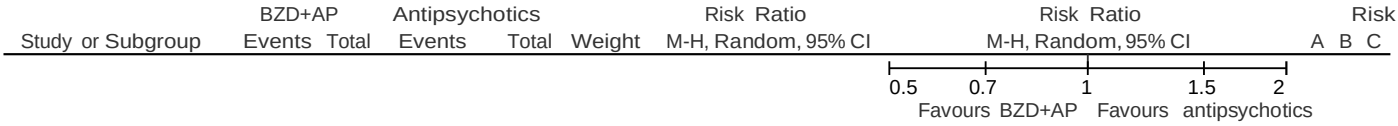
16 INTRAVENEOUS BENZODIAZEPINE VERSUS INTRAVENEOUS HALOPERIDOL (FOR ACUTE BEHAVIOUR DUE TO PSYCHOSIS)

16.1 GLOBAL IMPRESSION: 1. NO IMPROVEMENT



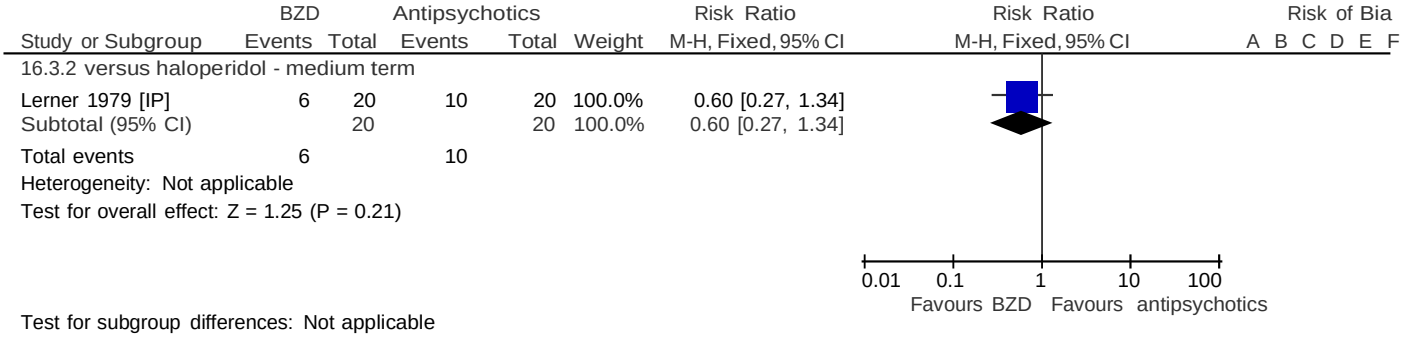
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

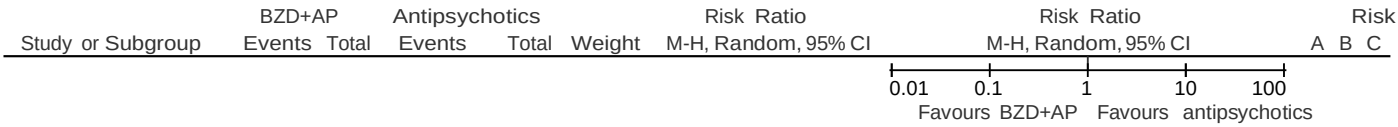
16.3 GLOBAL IMPRESSION: 3. SEDATION



Test for subgroup differences: Not applicable

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

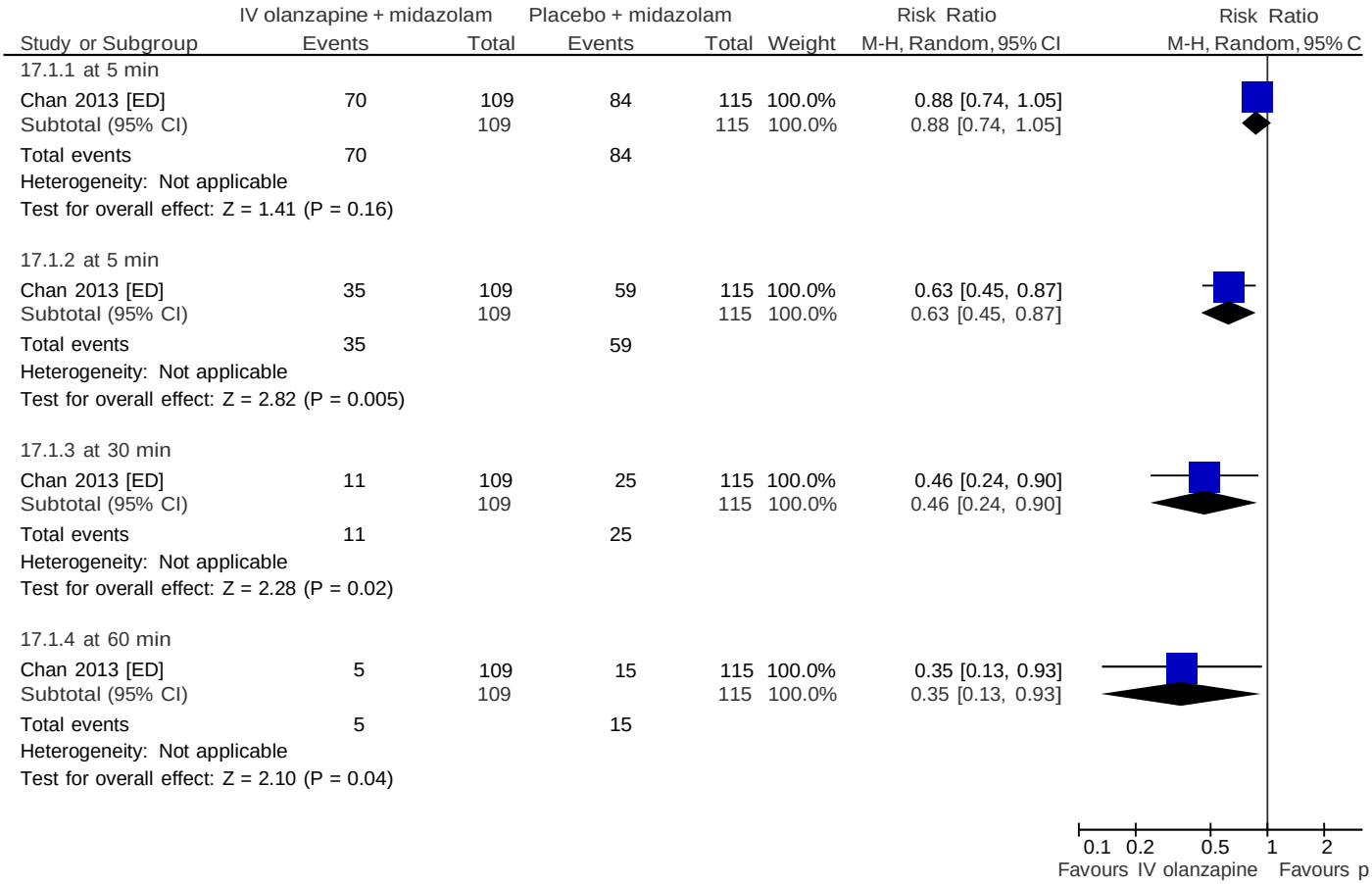
16.4 ADVERSE EFFECTS



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 INTRAVENEOUS OLANZAPINE PLUS MIDAZOLAM VERSUS PLACEBO PLUS MIDAZOLAM [NCCMH]

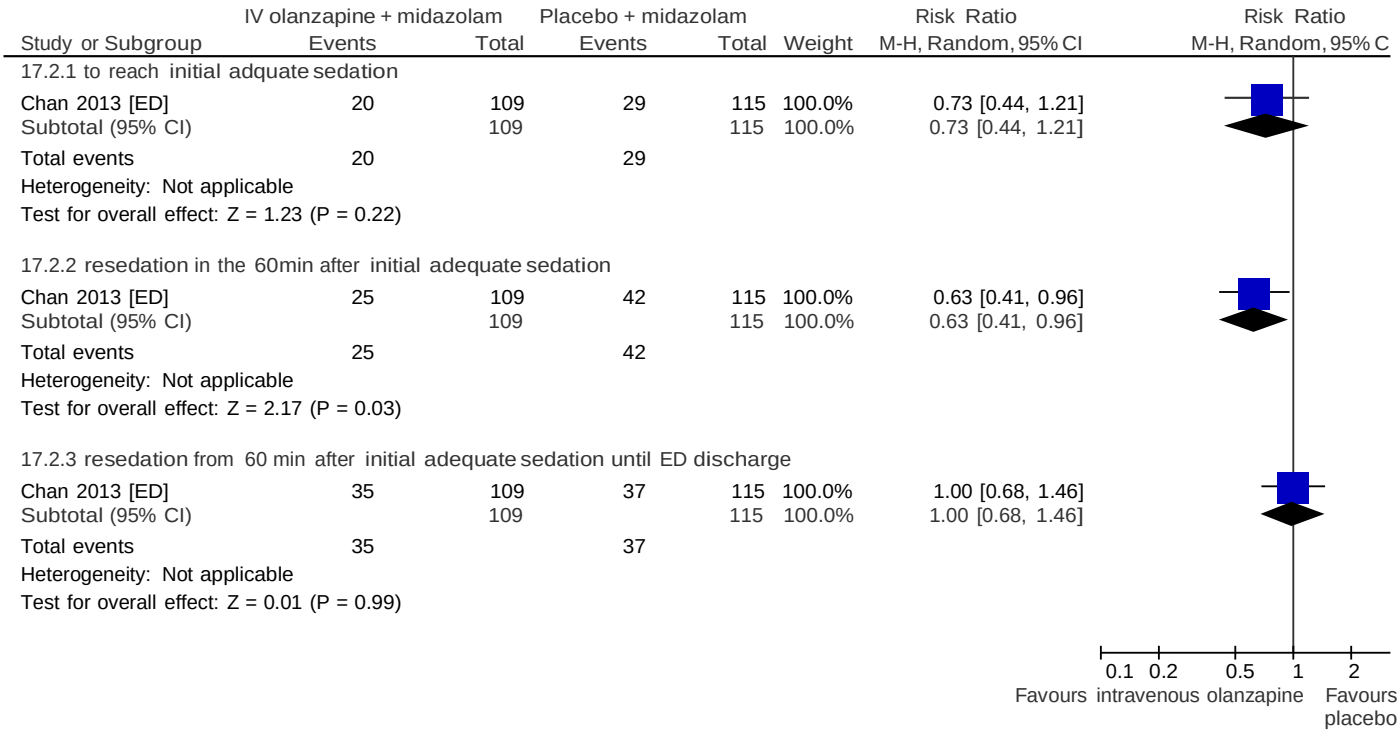
17.1 GLOBAL IMPRESSION: 1. NOT ADEQUATELY SEDATED



Risk of bias legend

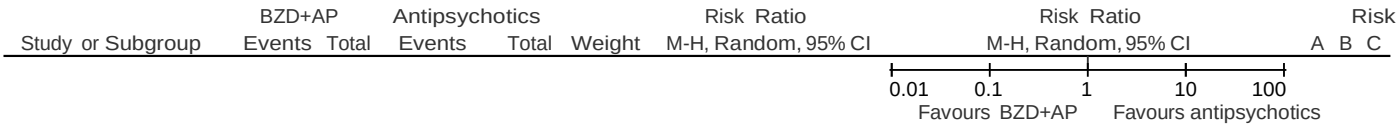
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other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

17.2 GLOBAL IMPRESSION: 2. REQUIRING ADDITIONAL INTRAMUSCULAR INJECTION



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



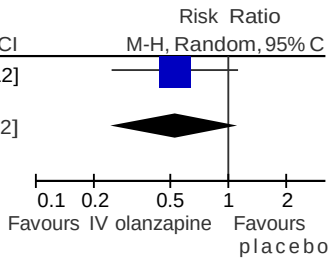
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

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

Study or Subgroup	IV olanzapine + midazolam Events	Total	Placebo + midazolam Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
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 applicable

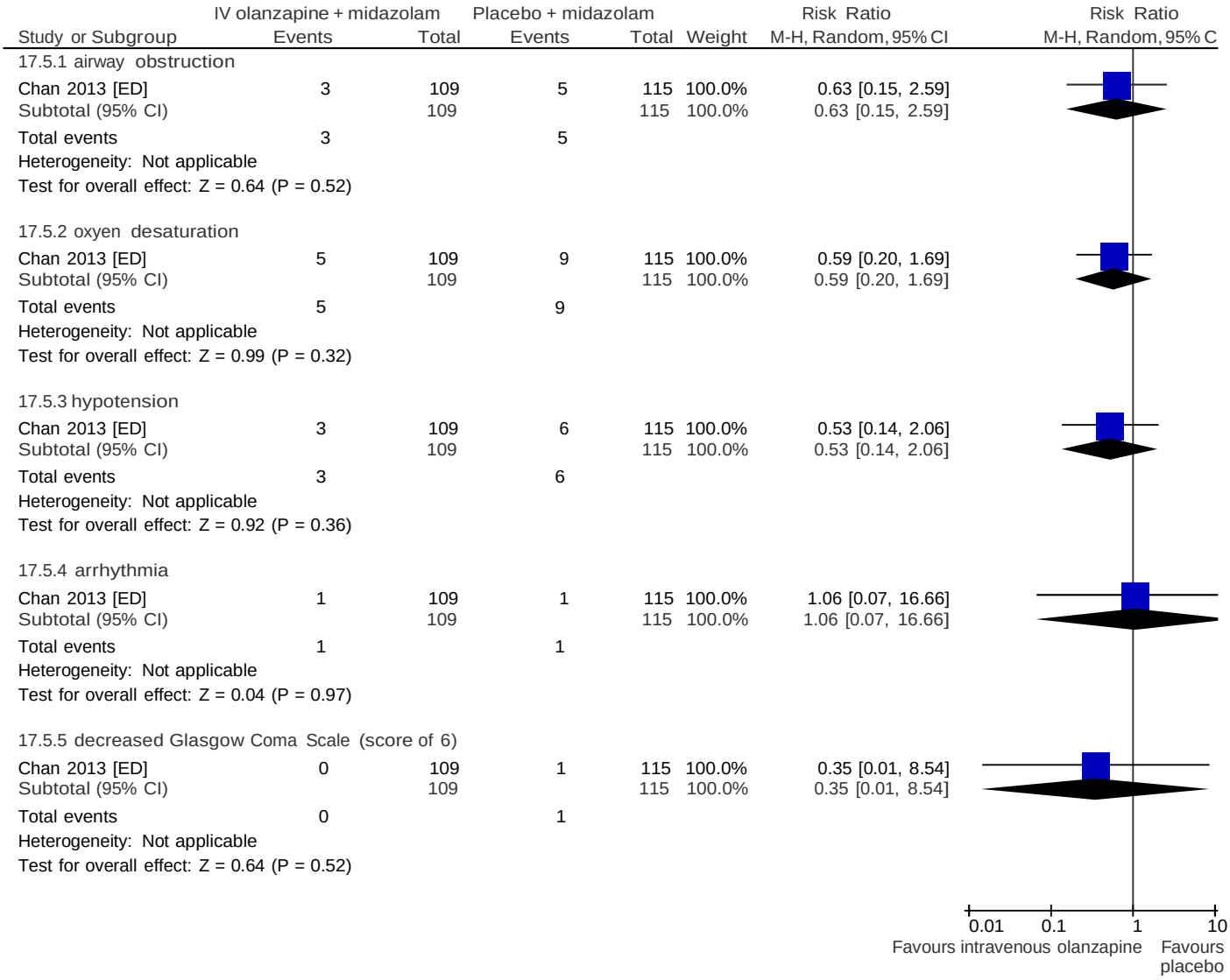
Test for overall effect: Z = 1.66 (P = 0.10)



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

17.5 ADVERSE EFFECTS: 2. OTHER – 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