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## Abbreviations

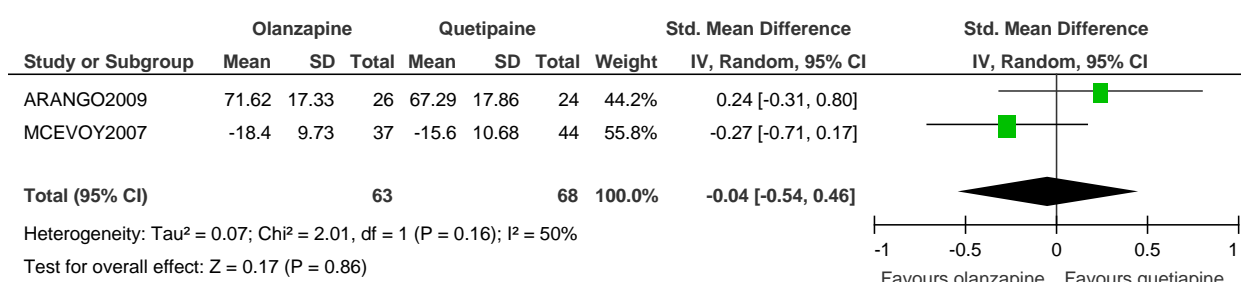
AIMS	Abnormal Involuntary Movement Scale
AP	antipsychotic
BARS	Barnes Akathisia Rating Scale
BMI	body mass index
BP	blood pressure
BPM	beats per minute
BPRS (-C, -P)	Brief Psychiatric Rating Scale (- Children, - Psychotic Subscale)
CDSS	Calgary Depression Scale for Schizophrenia
CGAS	Children's Global Assessment Scale
CGI (-S)	Clinical Global Impression scale (-Severity)
CI	confidence interval
CPRS	Comprehensive Psychopathological Rating Scale
EPS	extrapyramidal symptom
GAF	Global Assessment of Functioning
HAM-D	Hamilton Depression Rating Scale
MADRS	Montgomery-Åsberg Depression Rating Scale
ODT	orally disintegrating tablet
PANSS	Positive and Negative Syndrome Scale
QLS	Quality of Life Scale
QT (c, B)	the interval between Q and T waves in the electrocardiogram (corrected, Bazett's formula)
SANS	Scale for the Assessment of Negative Symptoms
SAPS	Scale for the Assessment of Positive Symptoms
SAS	Simpson-Angus Extrapyramidal Side Effects Scale
SD	standard deviation
SE	standard error
SOT	standard oral tablet
UKU	Udvalg for Kliniske Undersøgelser
YMRS	Young Mania Rating Scale

## APPENDIX 14C (I): INITIAL TREATMENT WITH ANTIPSYCHOTIC MEDICATION FOR FIRST EPISODE PSYCHOSIS

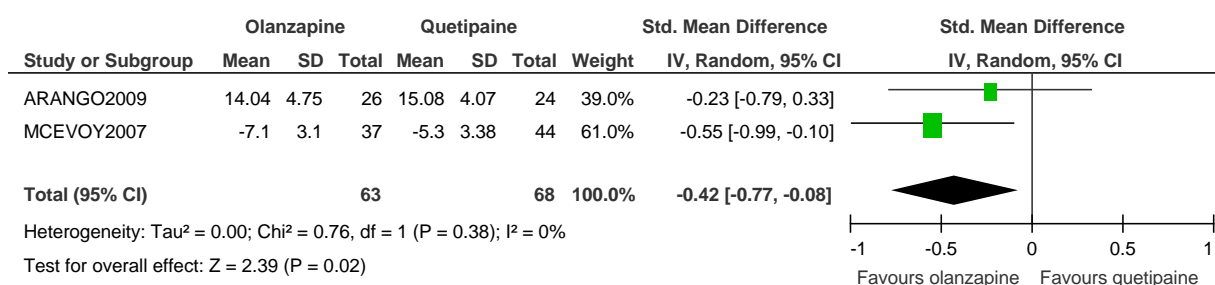
### PHARMACOLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 18 YEARS AND YOUNGER COMBINED WITH THOSE AGED 25 YEARS AND YOUNGER

#### 1. Olanzapine versus quetiapine: post-treatment efficacy outcomes

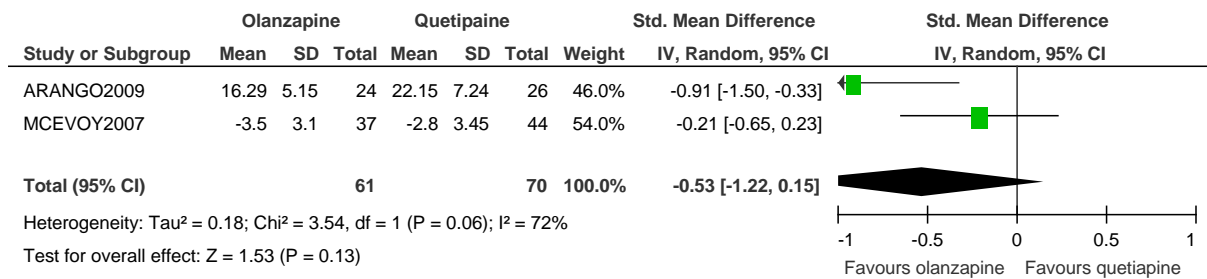
##### 1.1 Mental state: total symptoms (Positive and Negative Syndrome Scale [PANSS]) (mean endpoint: ARANGO2009; mean change: MCEVOY2007)



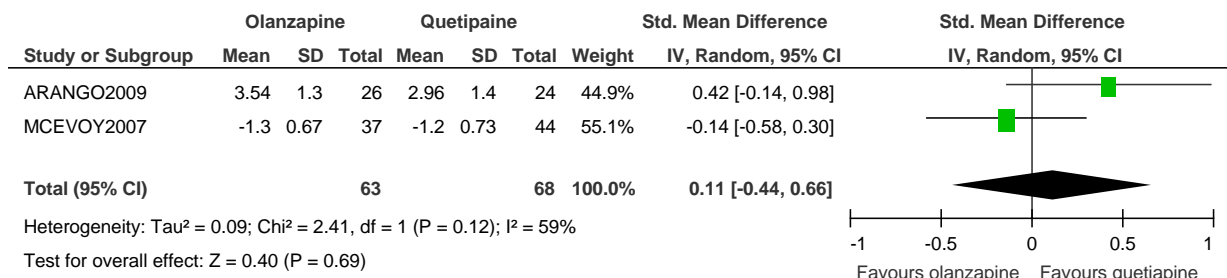
##### 1.2 Mental state: positive symptoms (Scale for the Assessment of Positive Symptoms [SAPS]) (mean endpoint: ARANGO2009; mean change: MCEVOY2007)



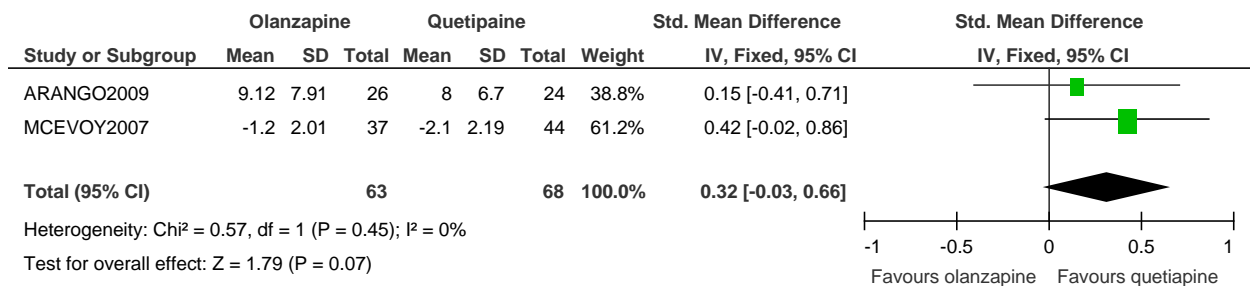
1.3 Mental state: negative symptoms (Scale for the Assessment of Negative Symptoms [SANS]) (mean endpoint: ARANGO2009; mean change: MCEVOY2007)



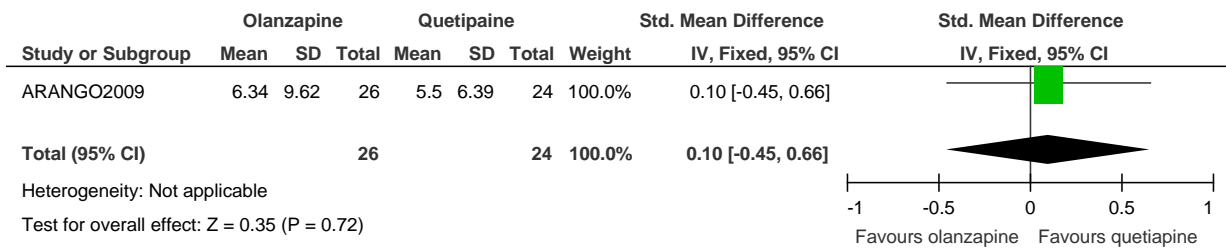
1.4 Global state: severity (Clinical Global Impression - Severity scale [CGI-S]) (mean endpoint: ARANGO2009; mean change: MCEVOY2007)



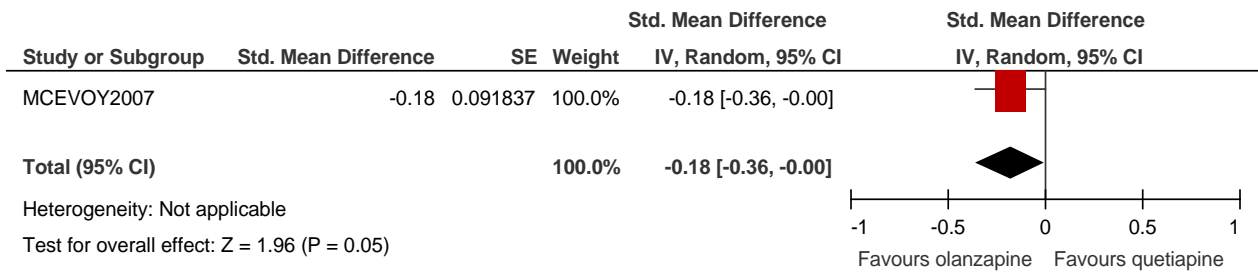
1.5 Mental state: depression (Hamilton Depression Rating Scale [HAM-D], Calgary Depression Scale for Schizophrenia [CDSS]) (mean endpoint: ARANGO2009; mean change: MCEVOY2007)



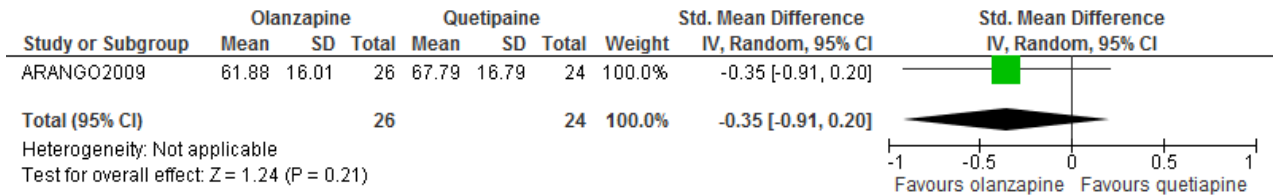
### 1.6 Mental state: mean endpoint mania (Young Mania Rating Scale [YMRS])



### 1.7 Mean change in quality of life (Quality of Life Scale [QLS])

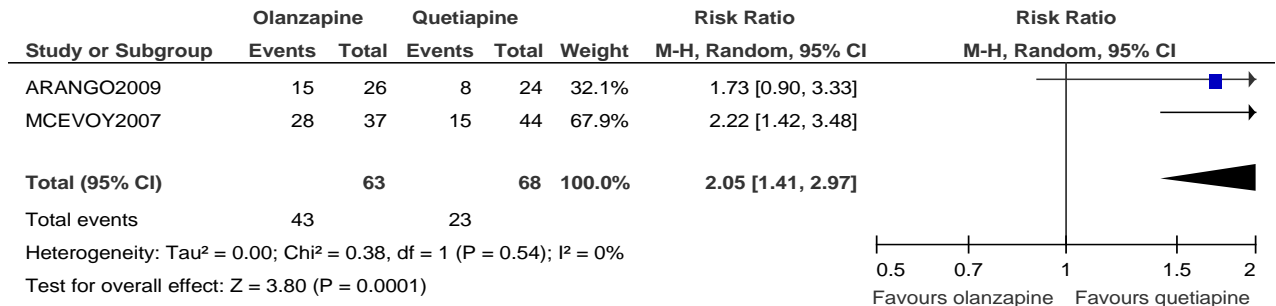


### 1.8 Psychosocial functioning: mean endpoint (Global Assessment of Functioning [GAF])

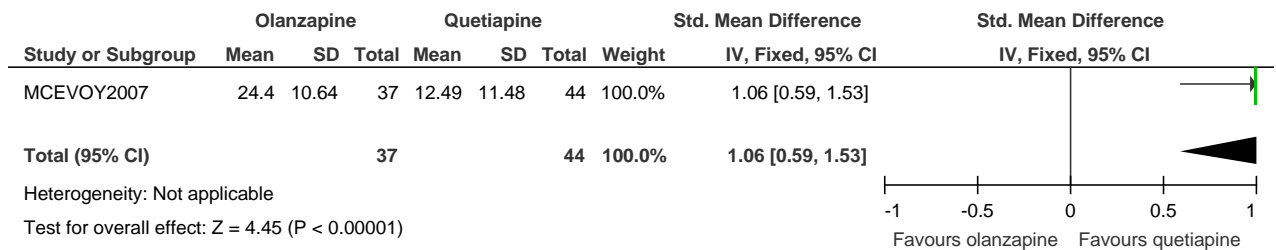


## 2. Olanzapine versus quetiapine: post-treatment side effect outcomes

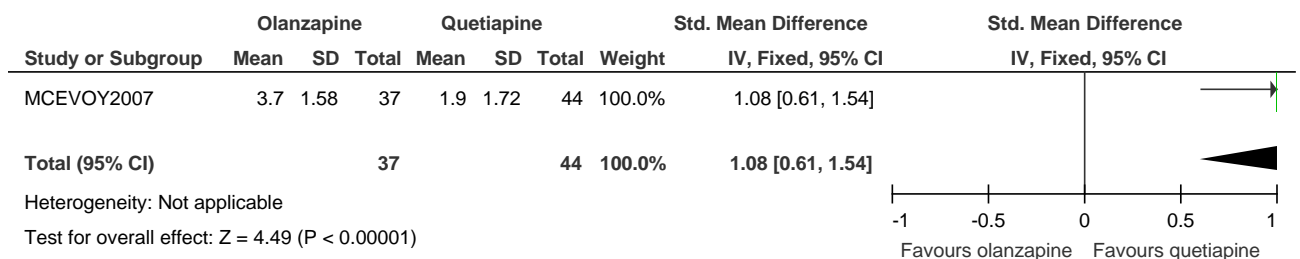
### 2.1 Weight gain (kg, not defined: ARANGO2009; number of participants with weight (lbs) gain of 7% or greater: MCEVOY2007)



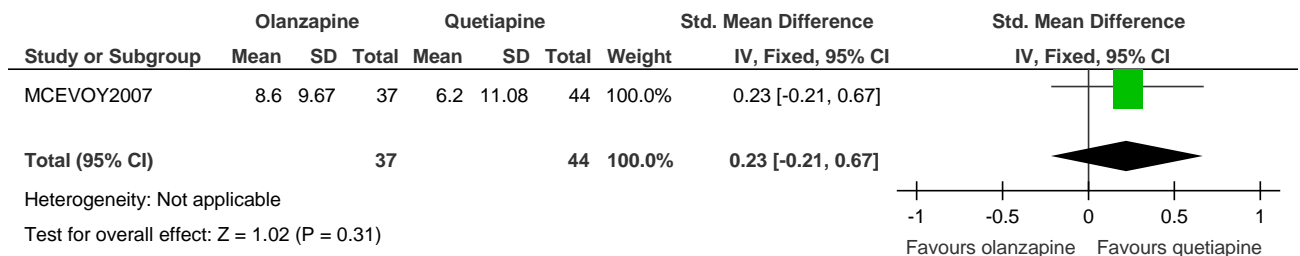
### 2.2 Mean change in weight (lbs)



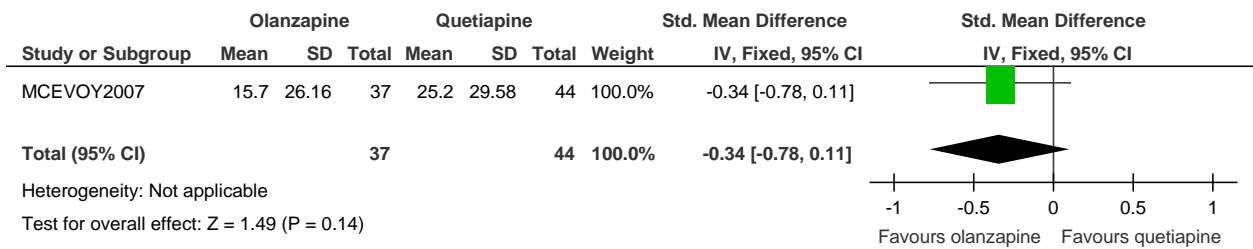
### 2.3 Mean change in BMI (kg/m<sup>2</sup>)



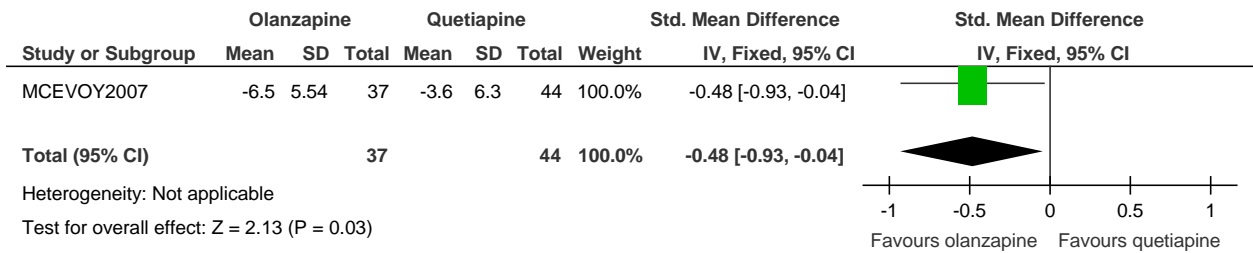
### 2.4 Mean change in fasting serum glucose level (mg/dl)



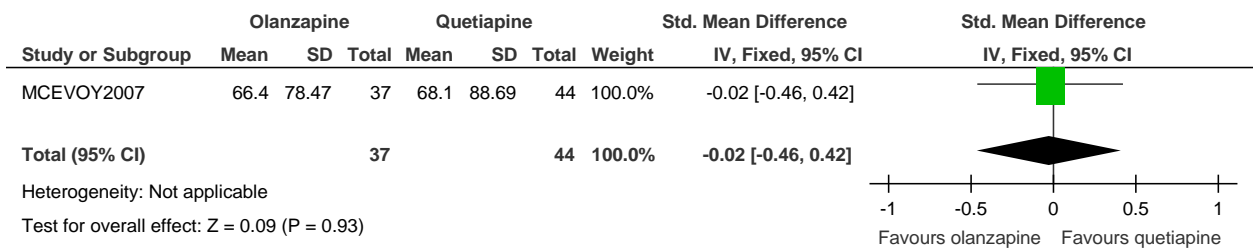
## 2.5 Mean change in fasting total cholesterol (mg/dl)



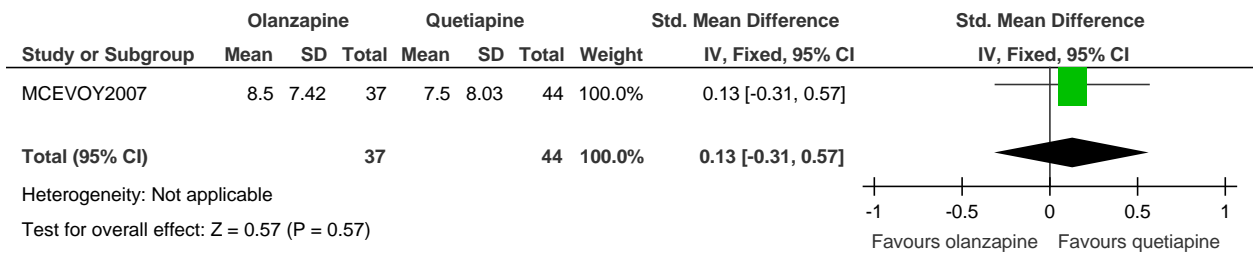
## 2.6 Mean change in fasting high-density lipoprotein cholesterol (mg/dl)



## 2.7 Mean change in fasting triglycerides (mg/dl)

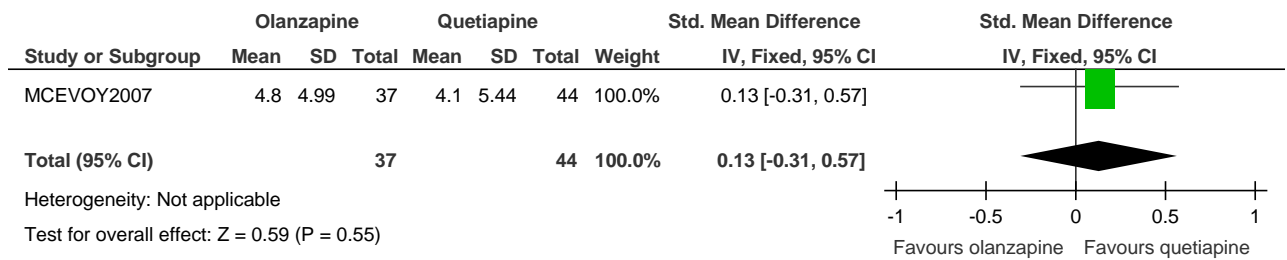


## 2.8 Mean change in systolic BP (mmHg)

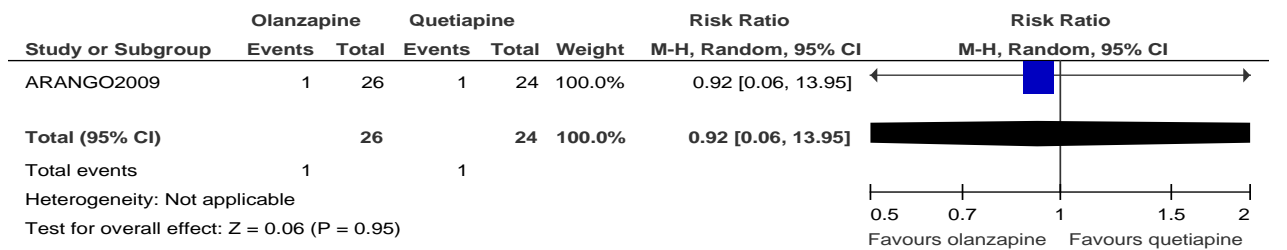




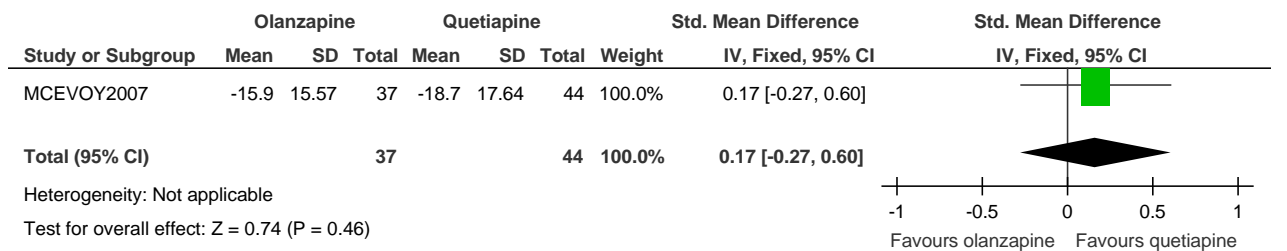
## 2.9 Mean change in diastolic BP (mmHg)



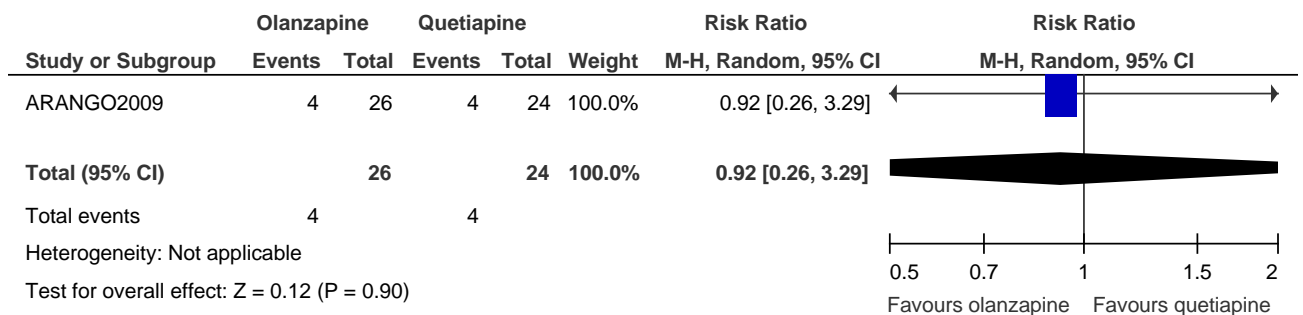
## 2.10 Tachycardia



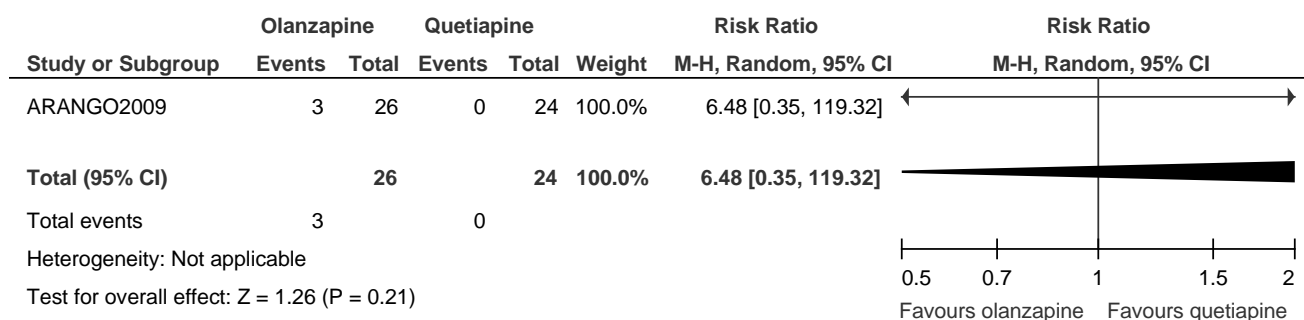
## 2.11 Mean change in prolactin level (mg/dl)



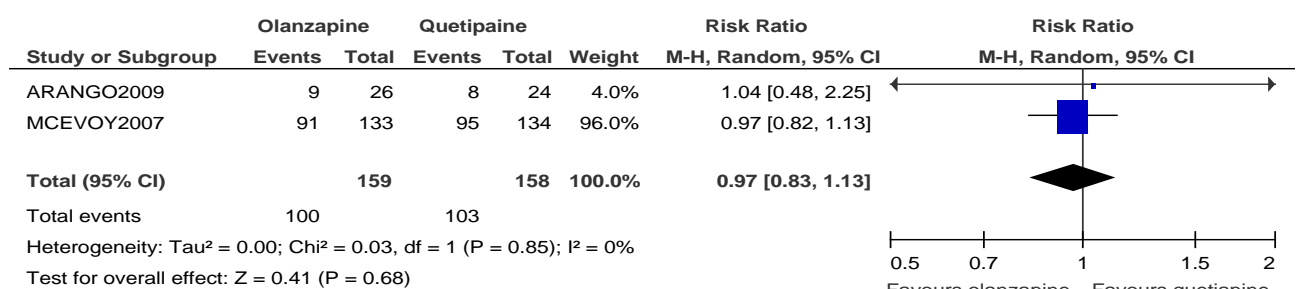
## 2.12 Tremor



## 2.13 Akathisia



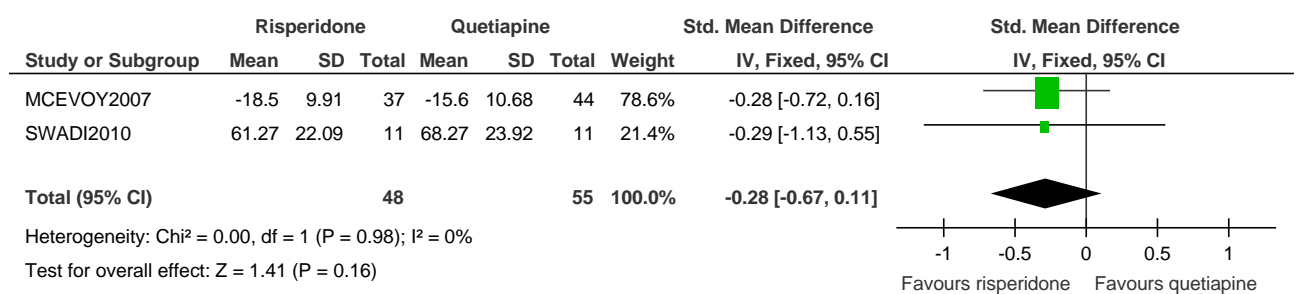
## 2.14 Leaving the study early for any reason



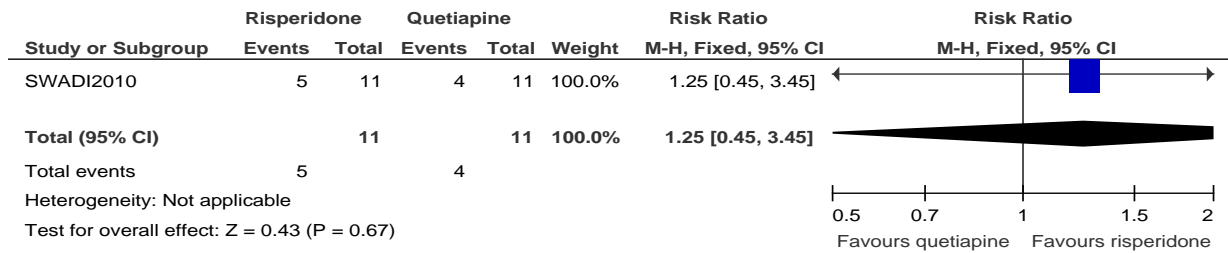
# PHARMACOLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 25 YEARS AND YOUNGER

## 3. Risperidone versus quetiapine: post-treatment efficacy outcomes

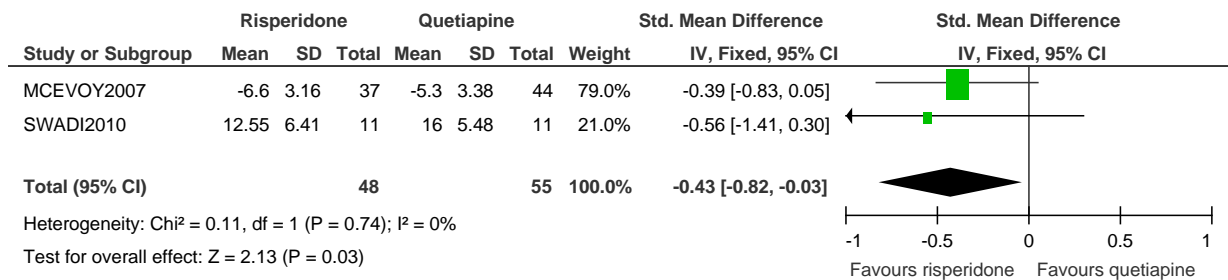
### 3.1 Mental state: mean change in total symptoms (PANSS)



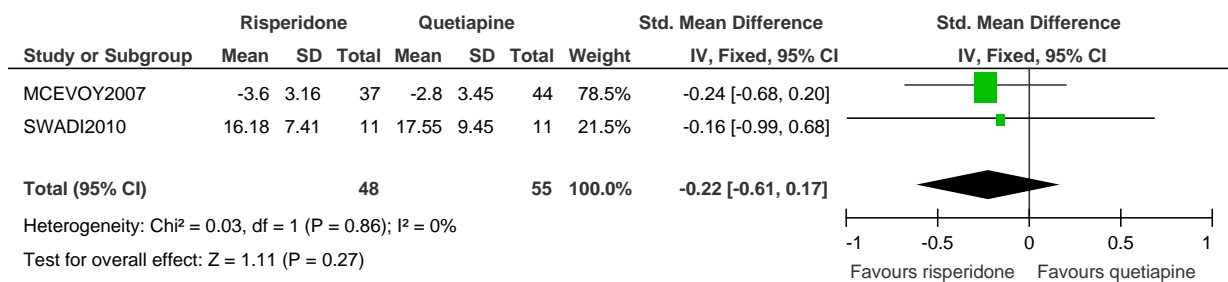
### 3.2 Mental state: response (number of participants with a 30% reduction on the PANSS)



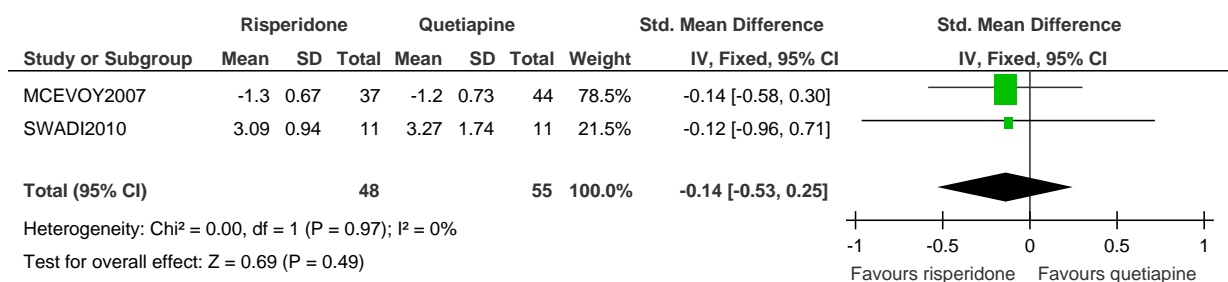
### 3.3 Mental state: mean change in positive symptoms (SAPS)



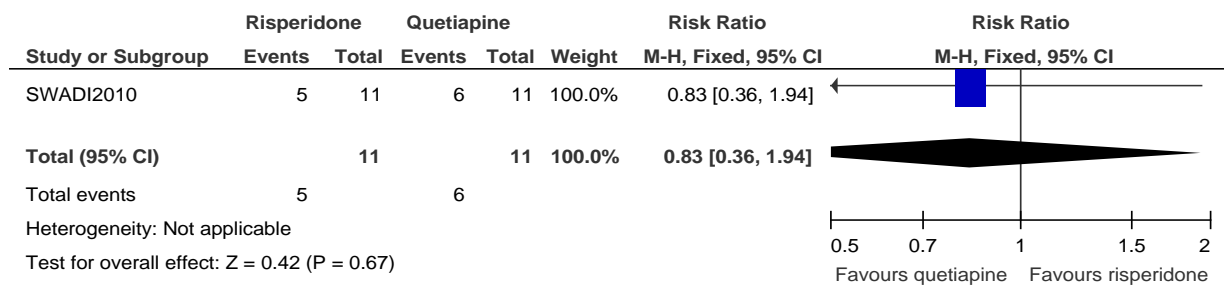
### 3.4 Mental state: mean change in negative symptoms (SANS)



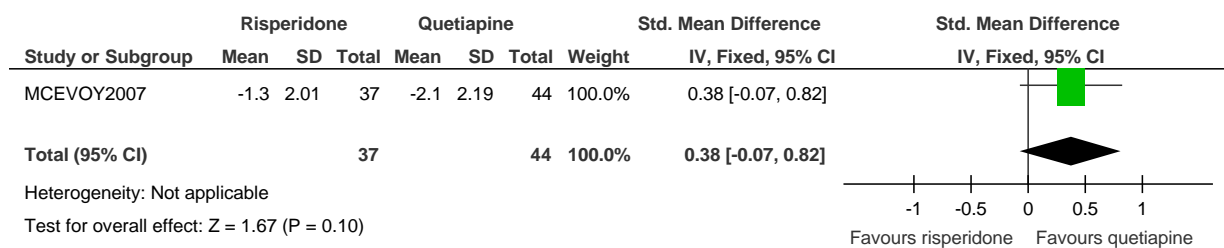
### 3.5 Mean change in global state: severity (CGI-S)



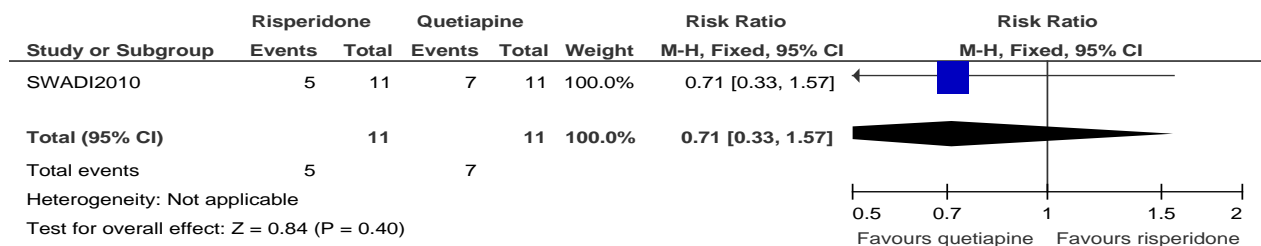
### 3.6 Global state response (number of participants with a 30% reduction CGI-S)



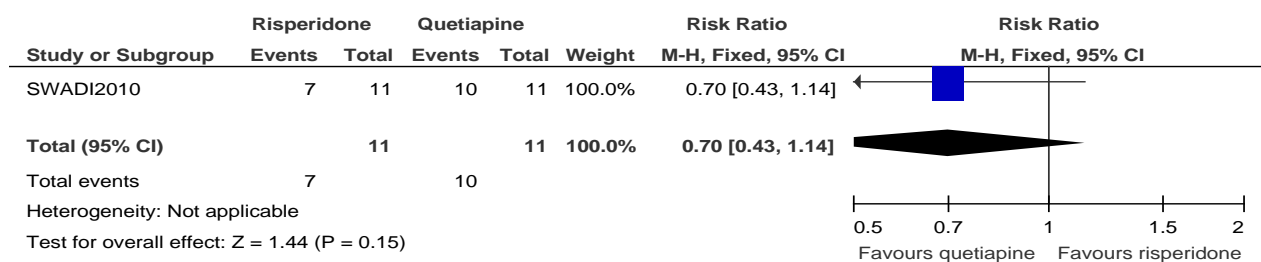
### 3.7 Mental state: mean change in depression (CDSS)



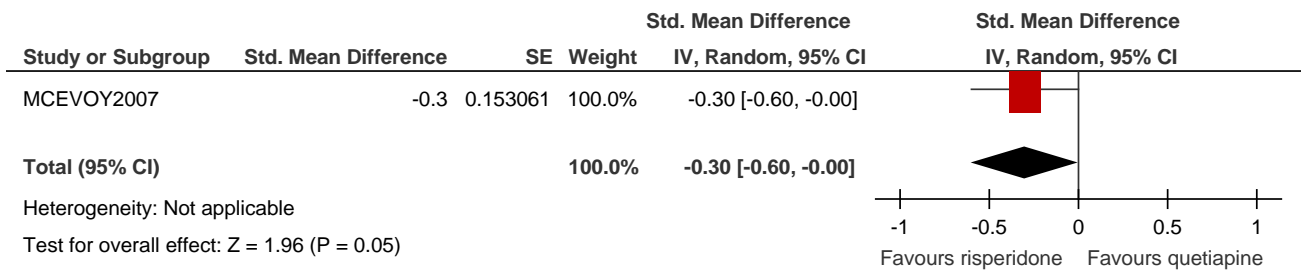
### 3.8 Mental state: depression response (number of participants with a 30% reduction on the HAM-D)



### 3.9 Mental state: mania response (number of participants with a 30% reduction on the YMRS)

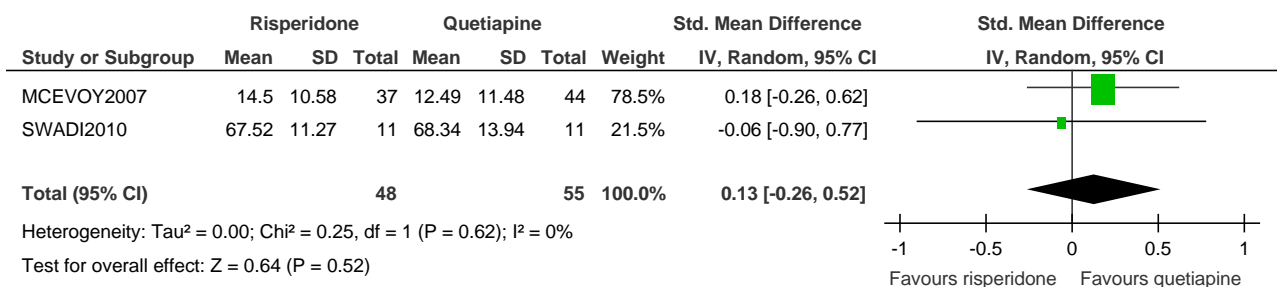


### 3.10 Mean change in quality of life (QLS)

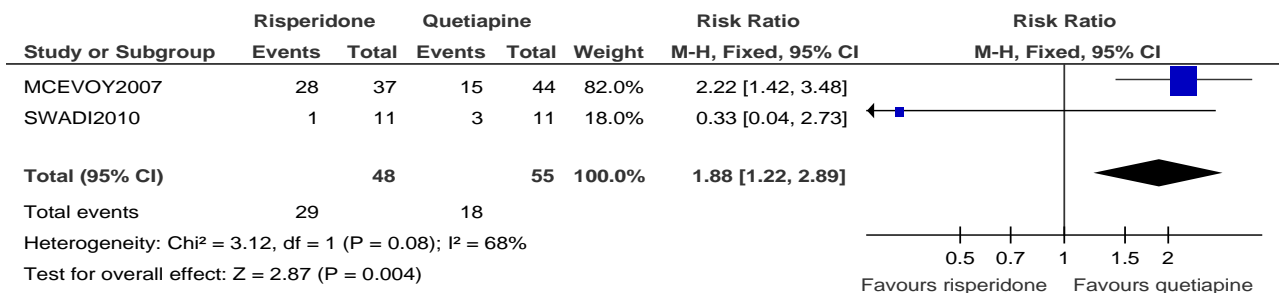


## 4. Risperidone versus quetiapine: post-treatment side effect outcomes

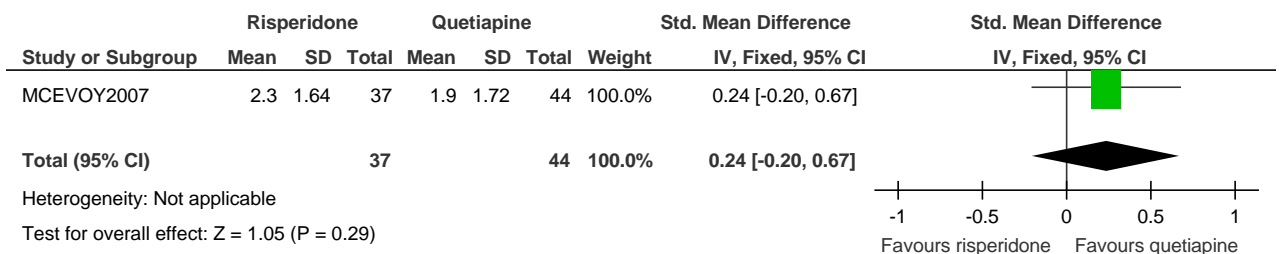
### 4.1 Mean change in weight



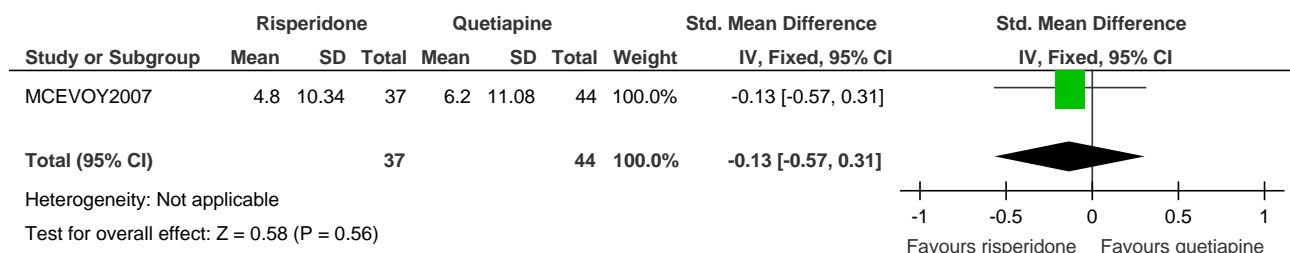
### 4.2 Weight gain (number of participants who gained over 7%)



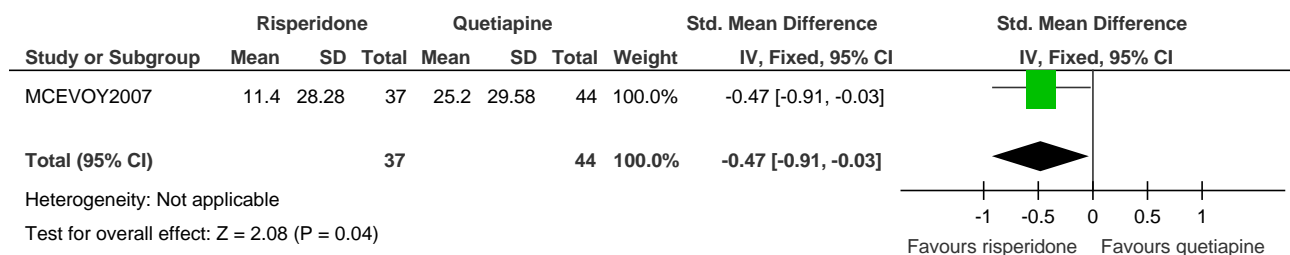
### 4.3 Mean change in BMI (kg/m<sup>2</sup>)



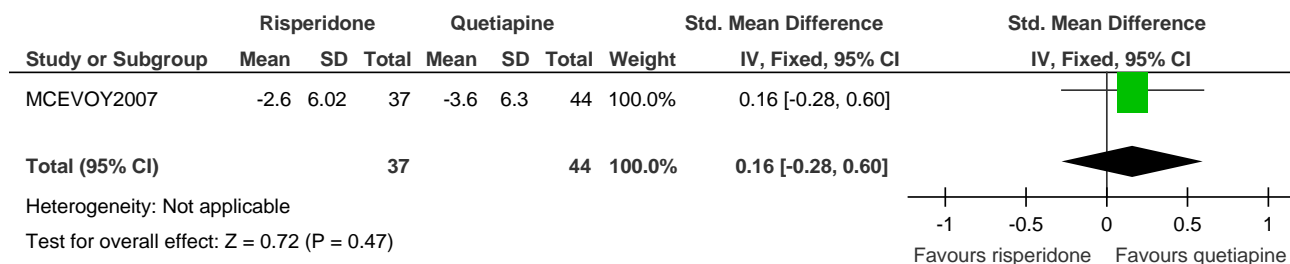
#### 4.4 Mean change in fasting serum glucose level (mg/dl)



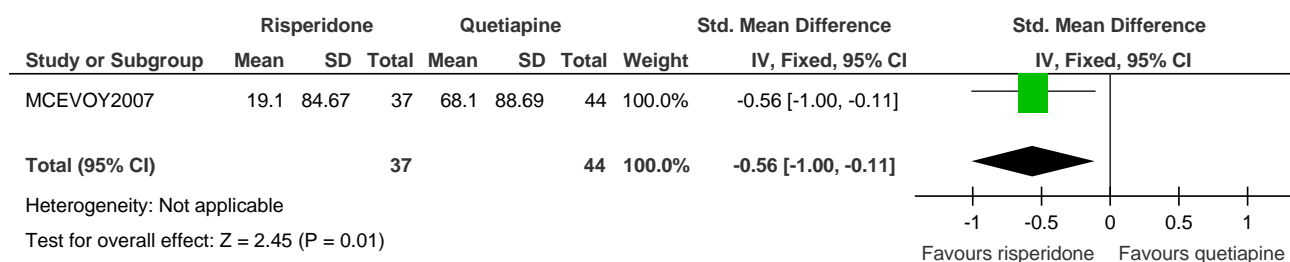
#### 4.5 Mean change in fasting total cholesterol (mg/dl)



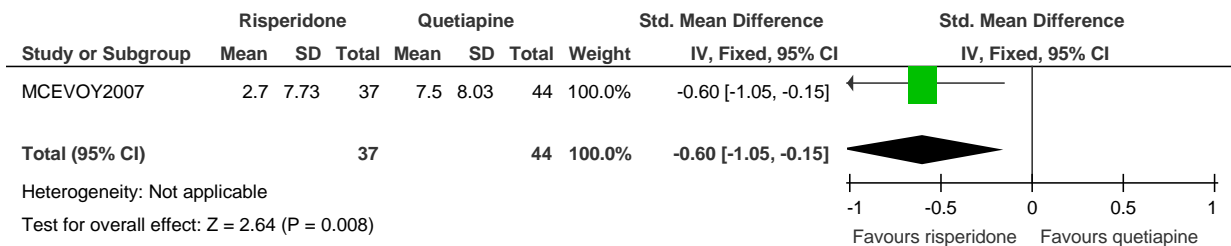
#### 4.6 Mean change in fasting high-density lipoprotein cholesterol (mg/dl)



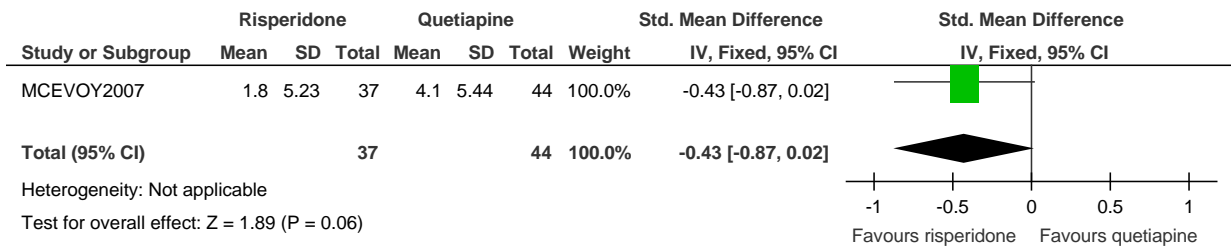
#### 4.7 Mean change in fasting triglycerides (mg/dl)



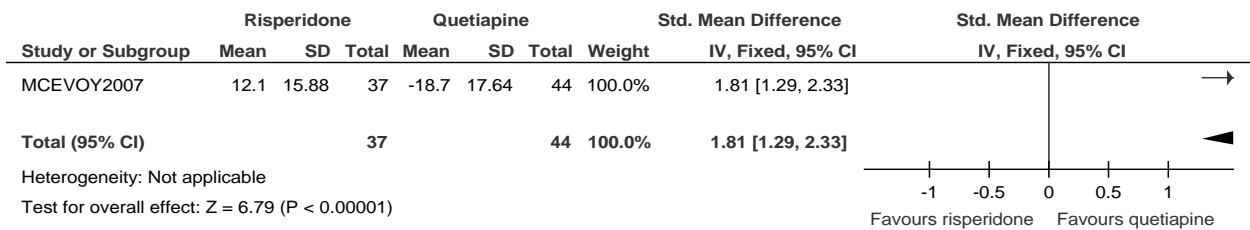
#### 4.8 Mean change in systolic BP (mm Hg)



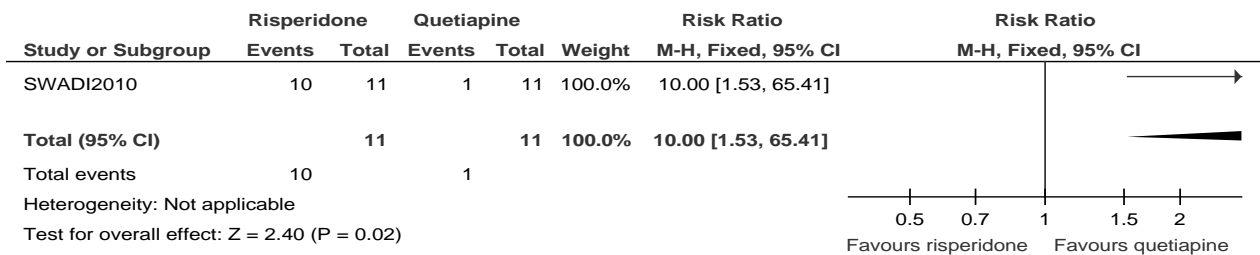
#### 4.9 Mean change in diastolic BP (mm Hg)



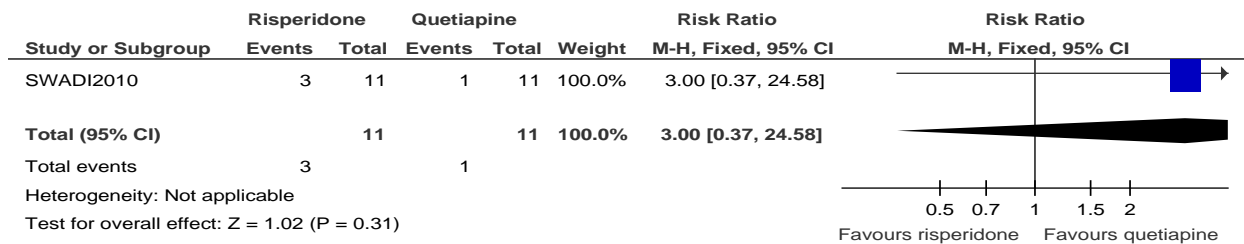
#### 4.10 Mean change in prolactin level (mg/dl)



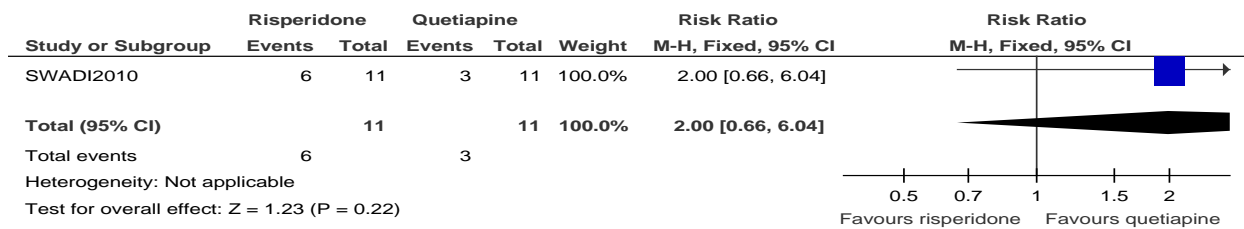
#### 4.11 Elevated prolactin level (mg/dl)



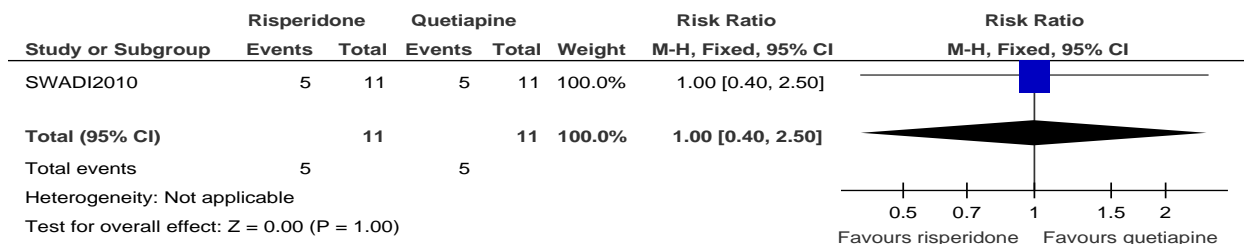
#### 4.12 Extrapyramidal symptoms (EPS) (number of participants with an Abnormal Involuntary Movement Scale [AIMS] score >2)



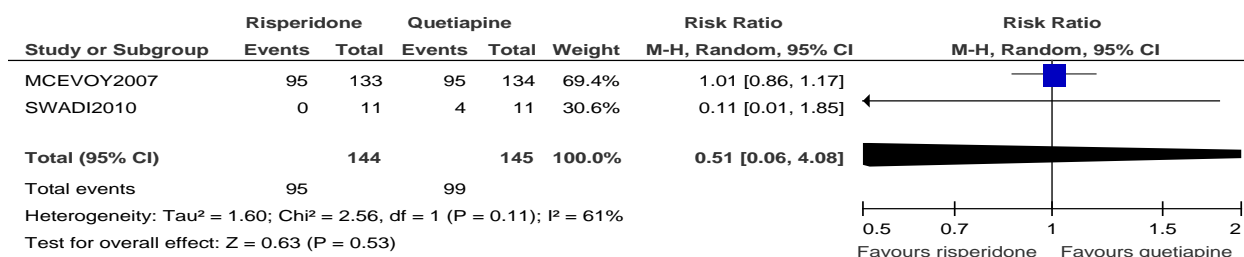
#### 4.13 EPS (number of participants with a Simpson-Angus Extrapyramidal Side Effects Scale [SAS] score >2)



#### 4.14 EPS (number of participants with a Barnes Akathisia Rating Scale [BARS] score >1)



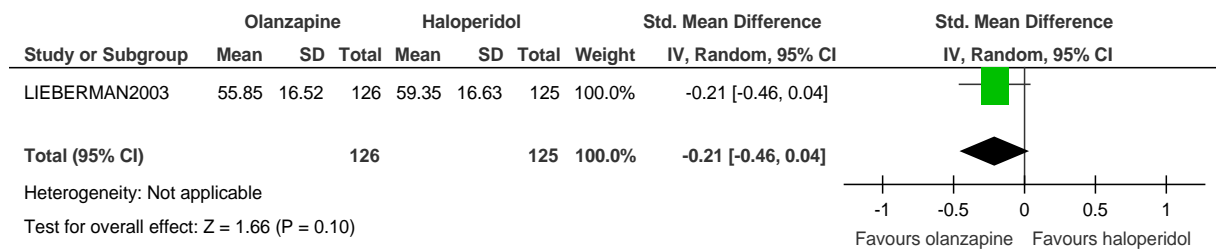
#### 4.15 Leaving the study early for any reason



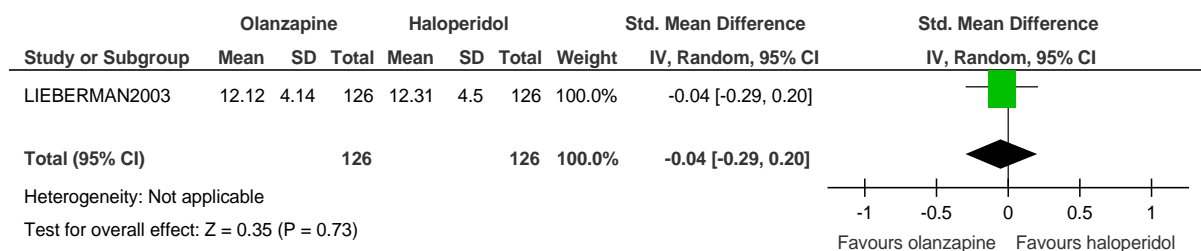


## 5. Olanzapine versus haloperidol: efficacy outcomes at the end of acute treatment (at 12 weeks)

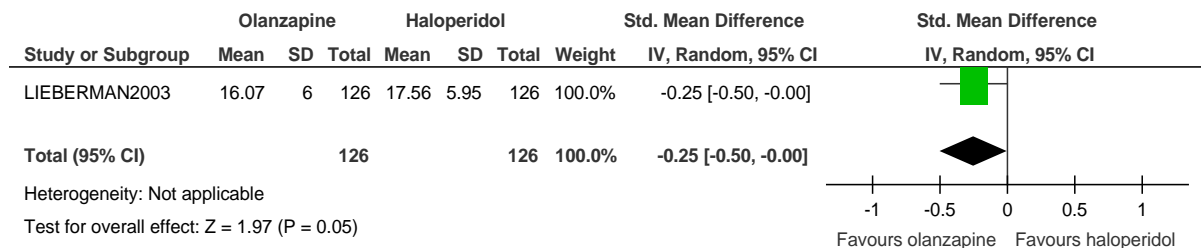
### 5.1 Mental state: mean total symptoms (PANSS) (end of acute phase)



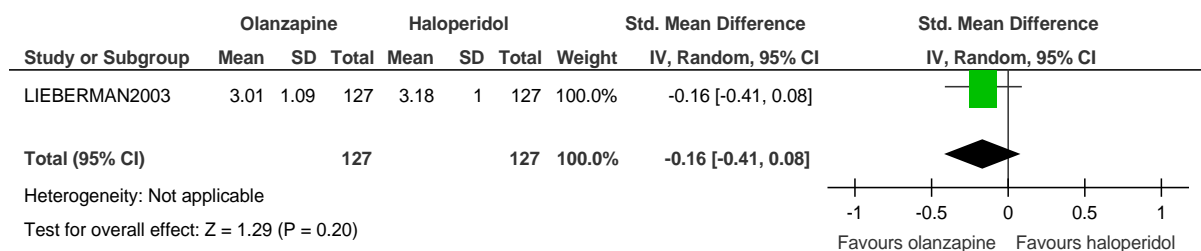
### 5.2 Mental state: mean positive symptoms (SAPS) (end of acute phase)



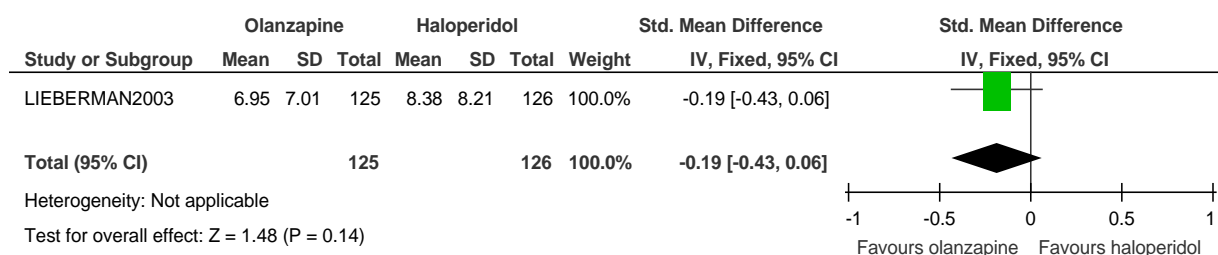
### 5.3 Mental state: mean negative symptoms (SANS) (end of acute phase)



### 5.4 Mental state: mean global state: severity (CGI-S) (end of acute phase)

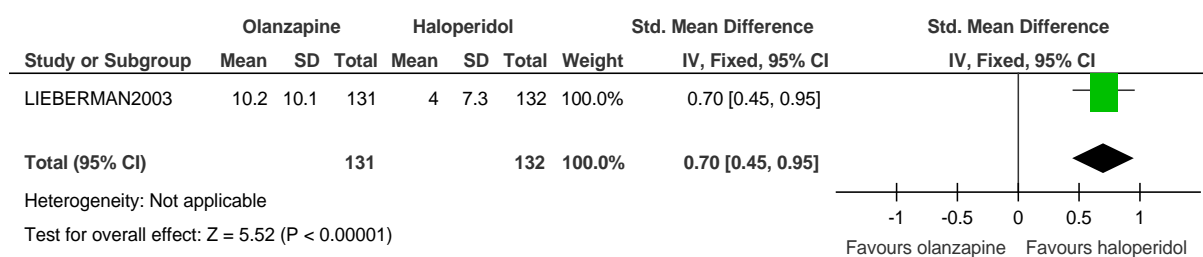


## 5.5 Mental state: mean depression (Montgomery-Åsberg Depression Rating Scale [MADRS]) (end of acute phase)

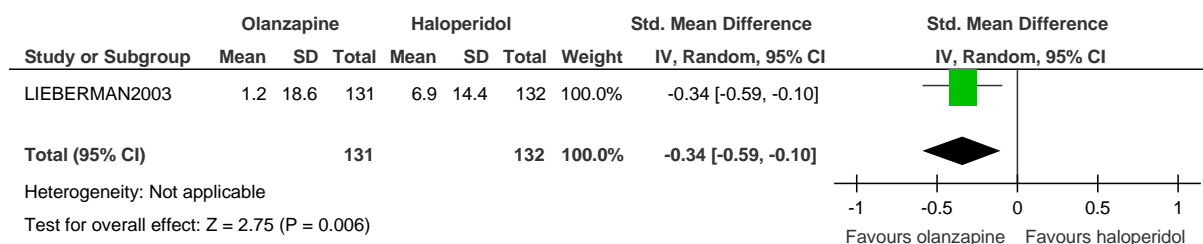


## 6. Olanzapine versus haloperidol: side effect outcomes at the end of acute treatment (at 12 weeks)

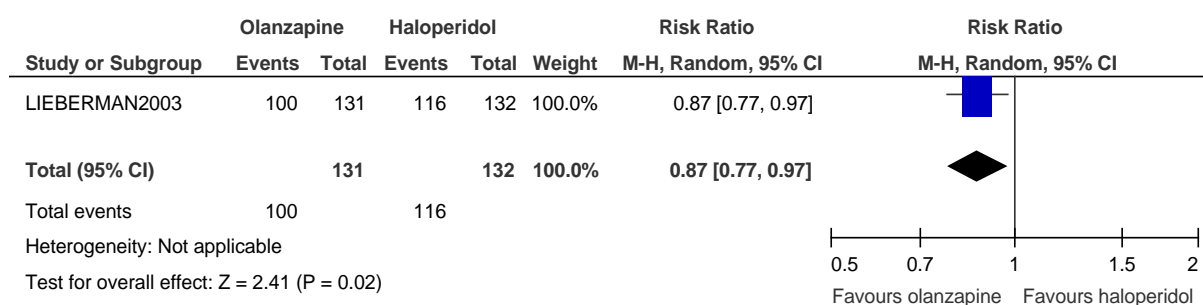
### 6.1 Mean endpoint weight (kg)



### 6.2 Mean endpoint prolactin level (mg/dl)

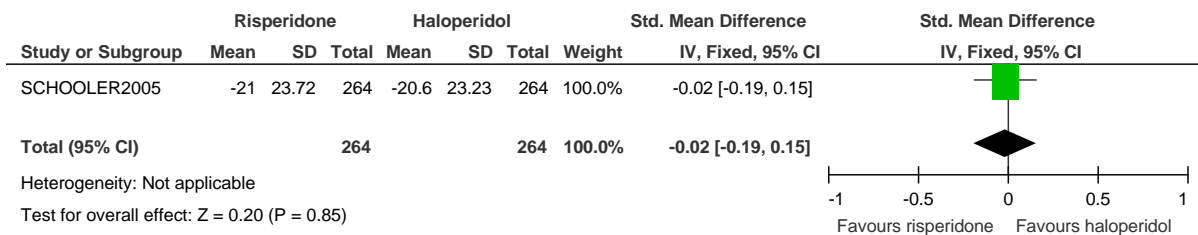


### 6.3 Leaving the study early for any reason

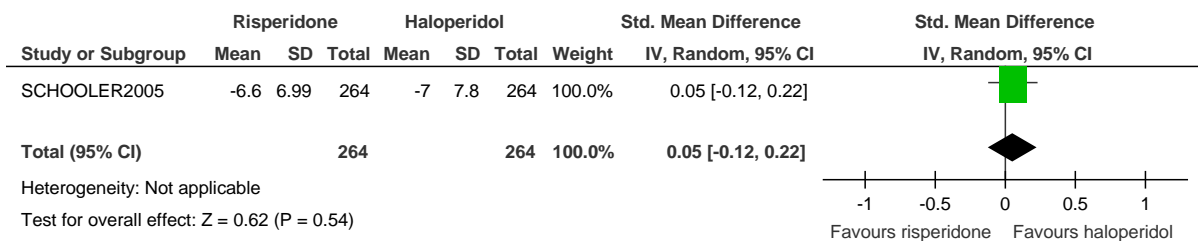


## 7. Haloperidol versus risperidone: efficacy outcomes post-treatment (time point unclear)

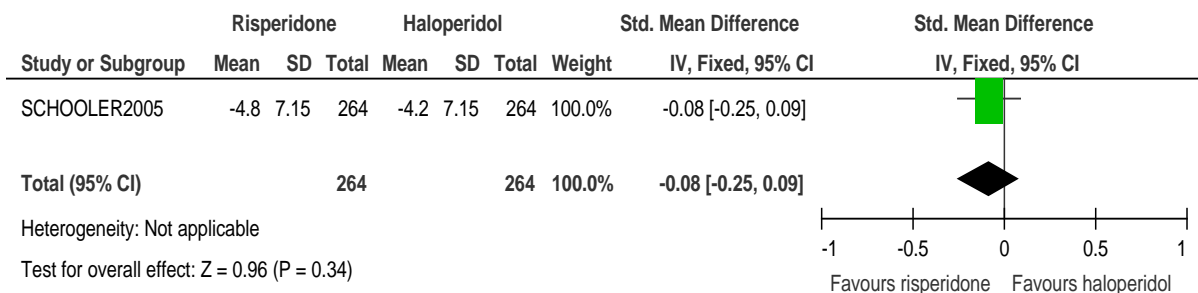
### 7.1 Mental state: mean change in total symptoms (PANSS)



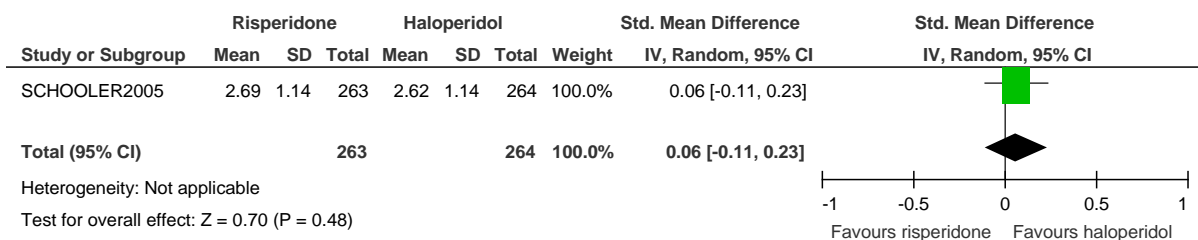
### 7.2 Mental state: mean change in positive symptoms (SAPS)



### 7.3 Mental state: mean change in negative symptoms (SANS)

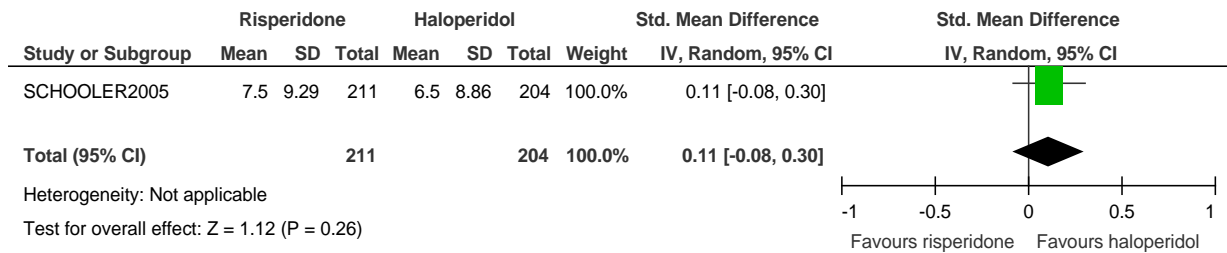


### 7.4 Mean change in global state: severity (CGI-S)

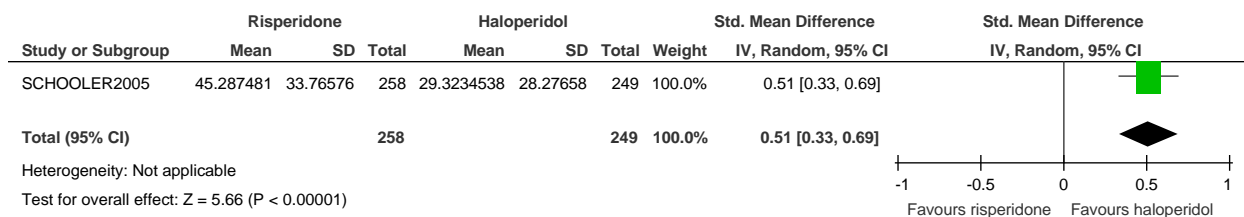


## 8. Haloperidol versus risperidone: side effect outcomes post-treatment (time point unclear)

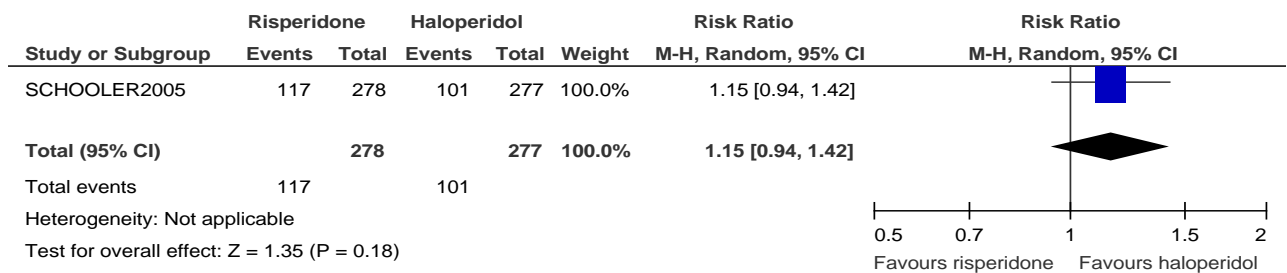
### 8.1 Mean change in weight (lbs)



### 8.2 Mean change in prolactin level (mg/dl)

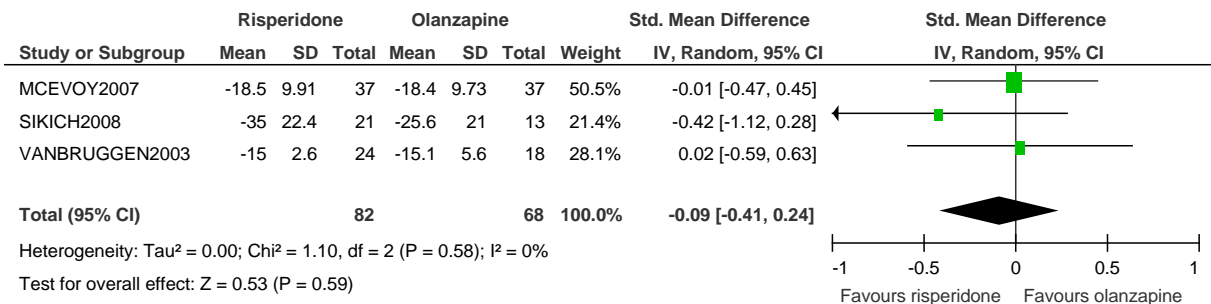


### 8.3 Leaving the study early for any reason

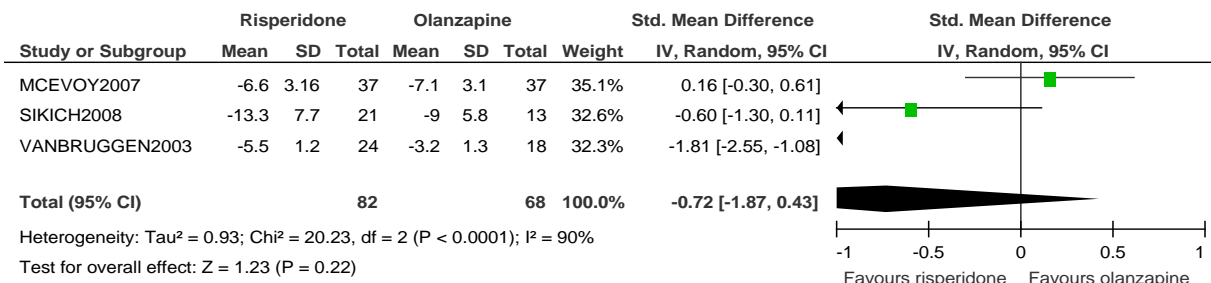


## 9. Risperidone versus olanzapine: post-treatment efficacy outcomes

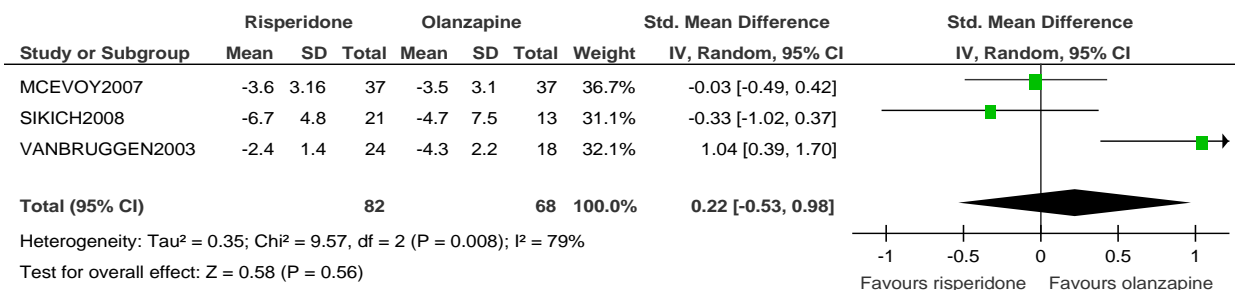
### 9.1 Mental state: mean change in total symptoms (PANSS)



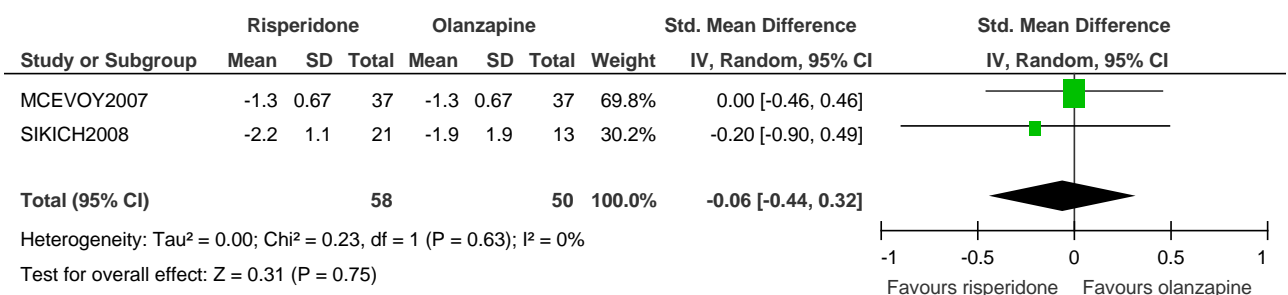
### 9.2 Mental state: mean change in positive symptoms (SAPS, Comprehensive Psychopathological Rating Scale [CPRS] - Positive)



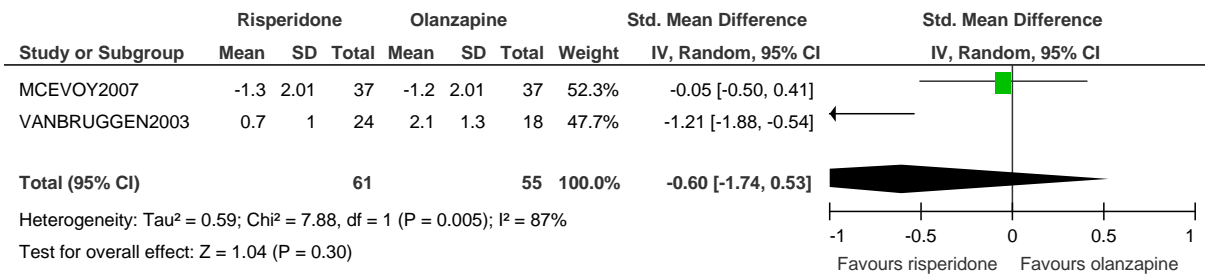
### 9.3 Mental state: mean change in negative symptoms (SANS)



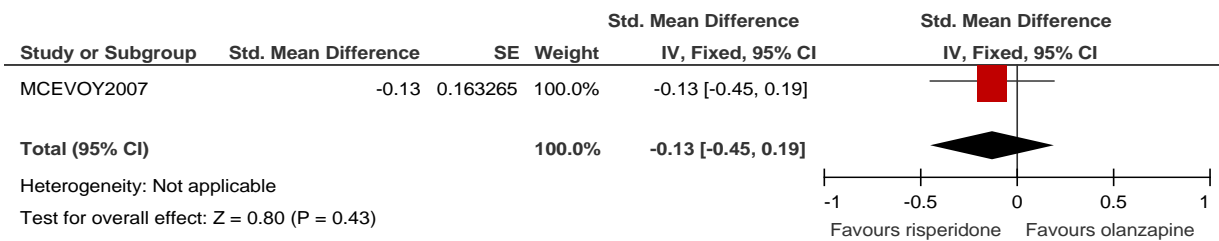
### 9.4 Mean change in global state: severity (CGI-S)



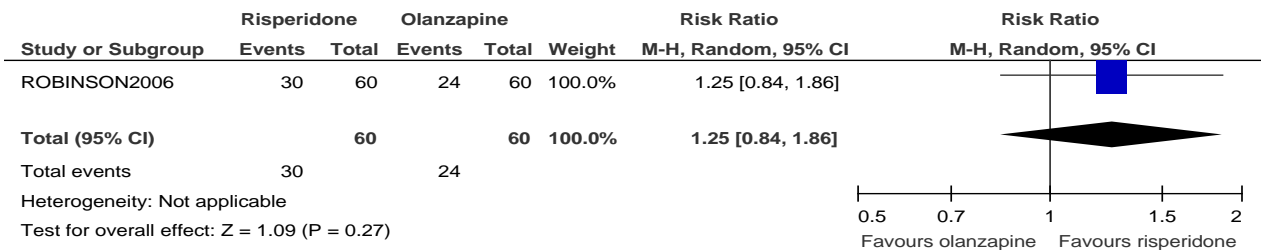
### 9.5 Mental state: mean change in depression (CDSS, PANSS-Depression)



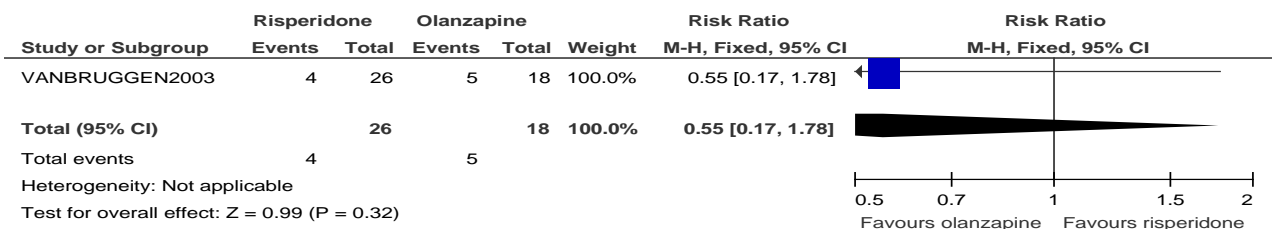
### 9.6 Mean change in quality of life (QLS)



### 9.7 Response (number of participants achieving mild or better on the Schedule for Affective Disorders and Schizophrenia - Change Version with Psychosis and Disorganization Items [SADS-C+PD] Positive Symptom Items plus a CGI rating of much improved or very much improved)

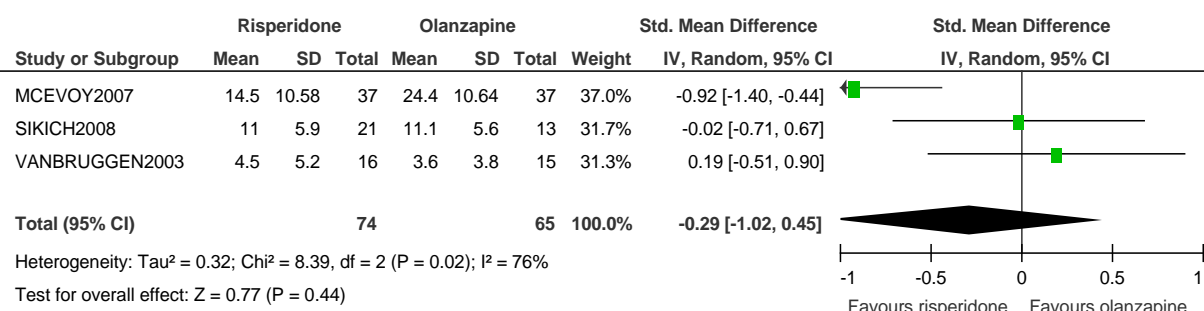


### 9.8 Remission (PANSS)

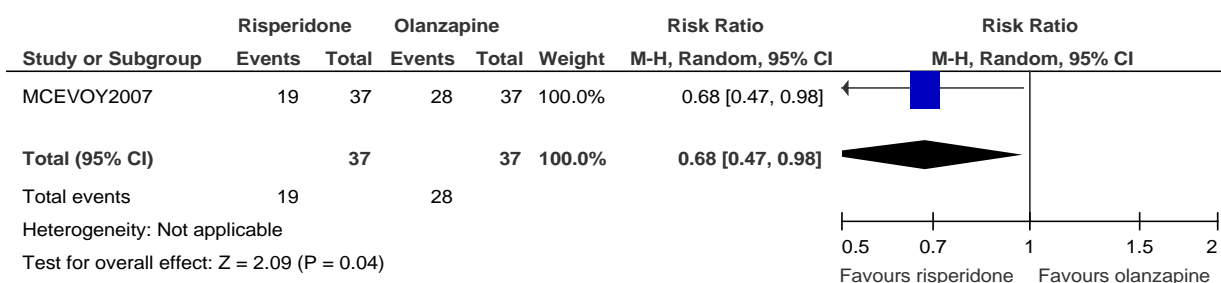


## 10. Risperidone versus olanzapine: post-treatment side effect outcomes

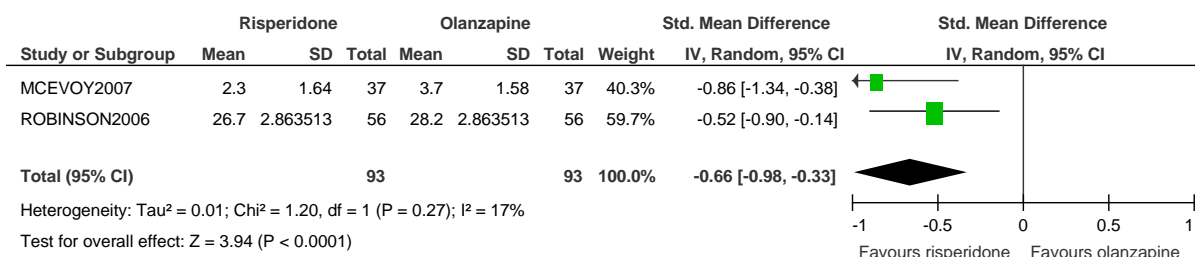
### 10.1 Mean change in weight (kg, lbs)



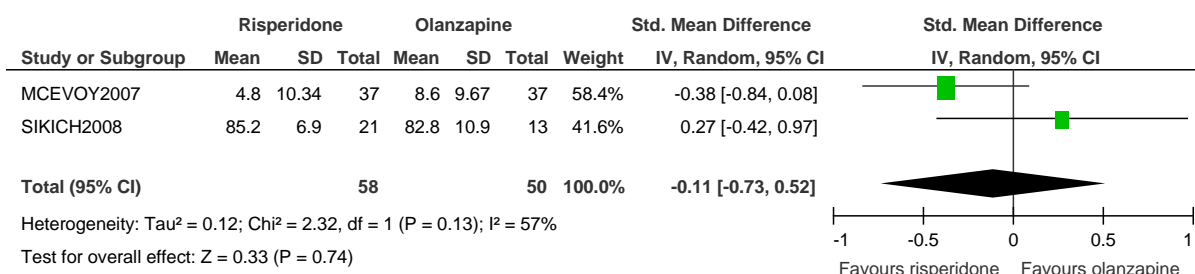
### 10.2 Weight gain (number of participants who gained ≥ 7% )



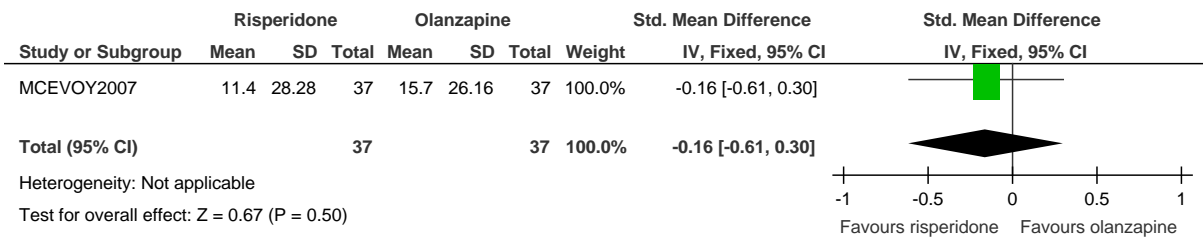
### 10.3 BMI (kg/m<sup>2</sup>) (mean change: MCEVOY2007; mean endpoint: ROBINSON2006)



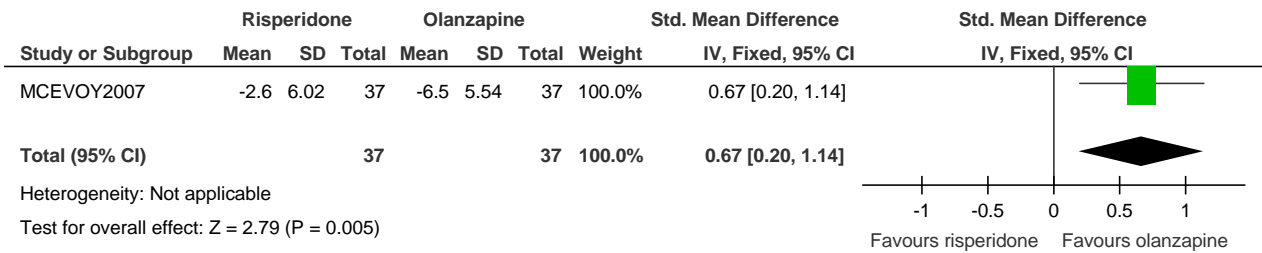
### 10.4 Mean change in fasting serum glucose level (mg/dl)



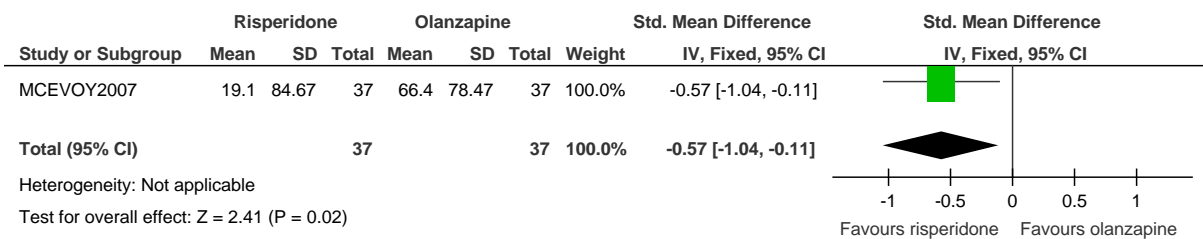
### 10.5 Mean change in fasting total cholesterol (mg/dl)



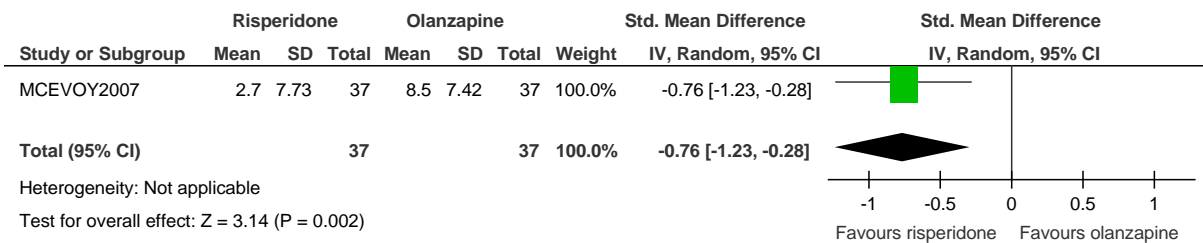
### 10.6 Mean change in fasting high-density lipoprotein cholesterol (mg/dl)



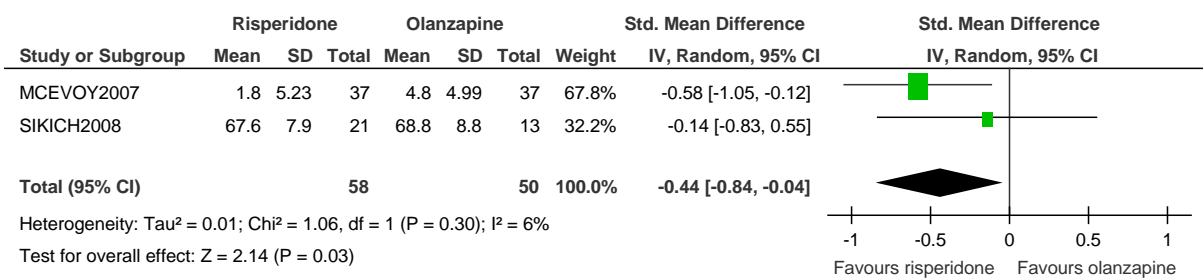
### 10.7 Mean change in fasting triglycerides (mg/dl)



### 10.8 Mean change in systolic BP (mm Hg)

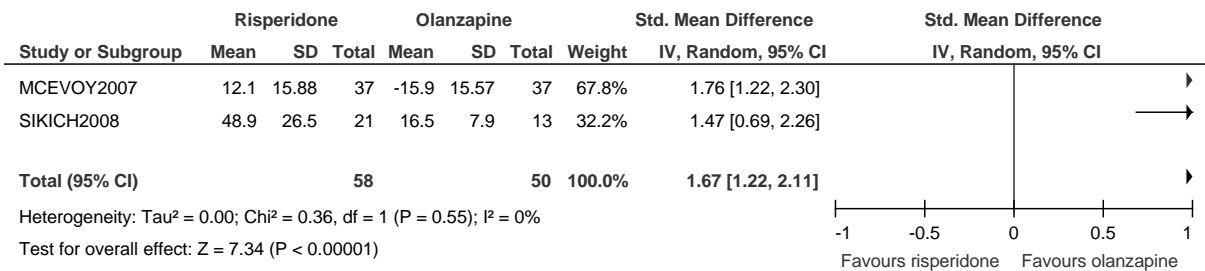


### 10.9 Mean change in diastolic BP (mm Hg)

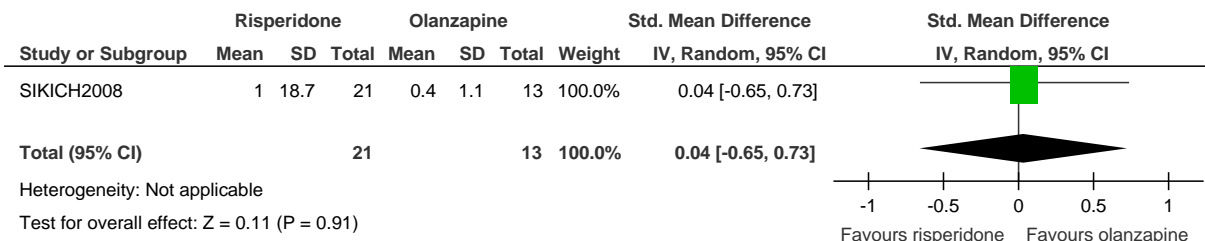




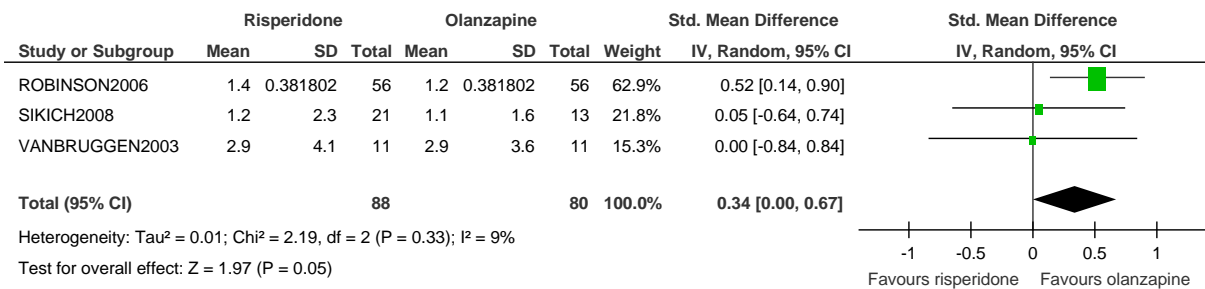
### 10.10 Mean change in prolactin level (mg/ml)



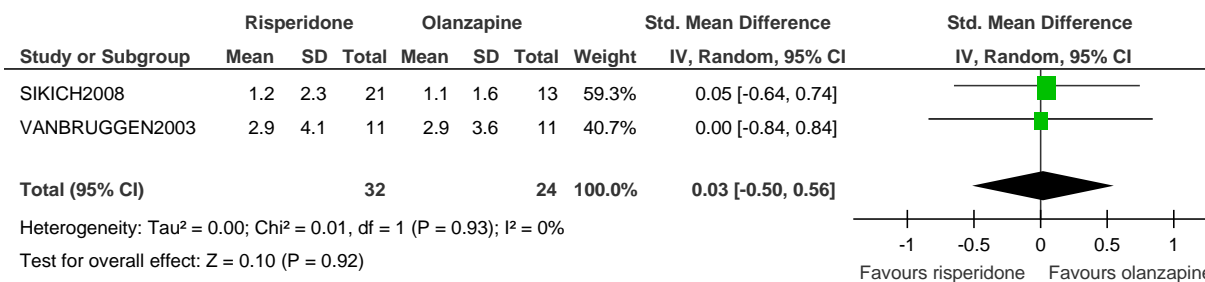
### 10.11 Mean change in EPS (AIMS scores)



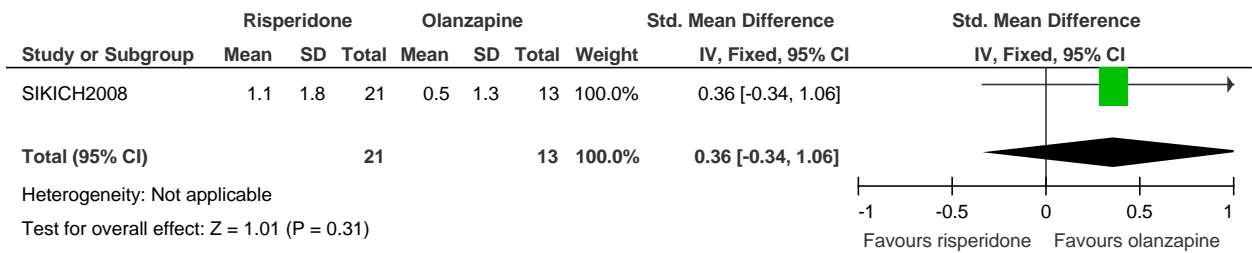
### 10.12 EPS (SAS scores)



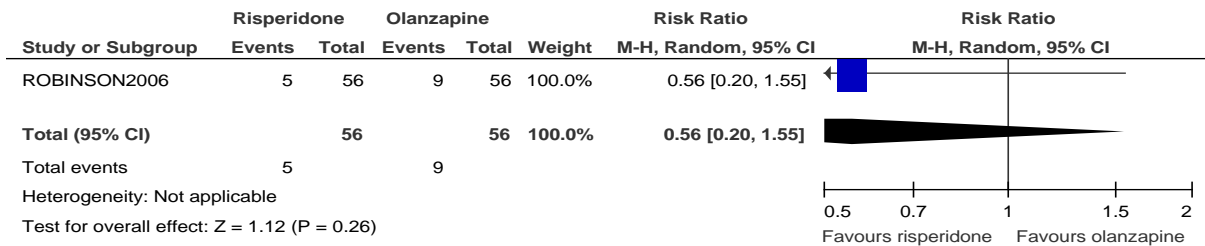
### 10.13 EPS (SAS scores) sensitivity analysis (taking out ROBINSON2006)



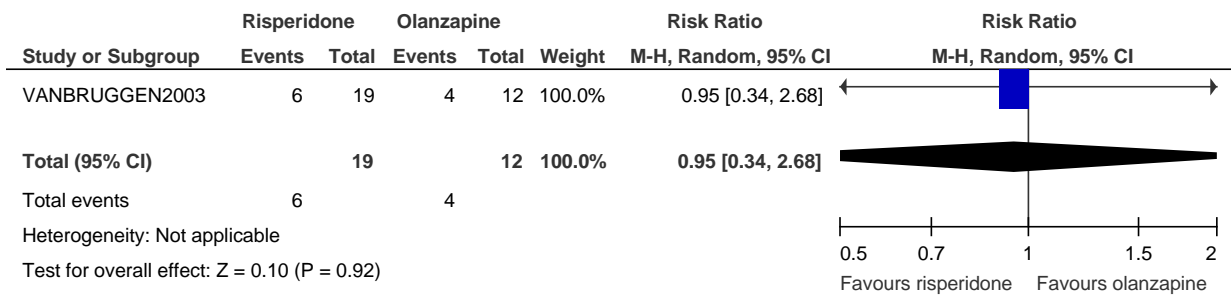
### 10.14 EPS (mean change in BARS scores)



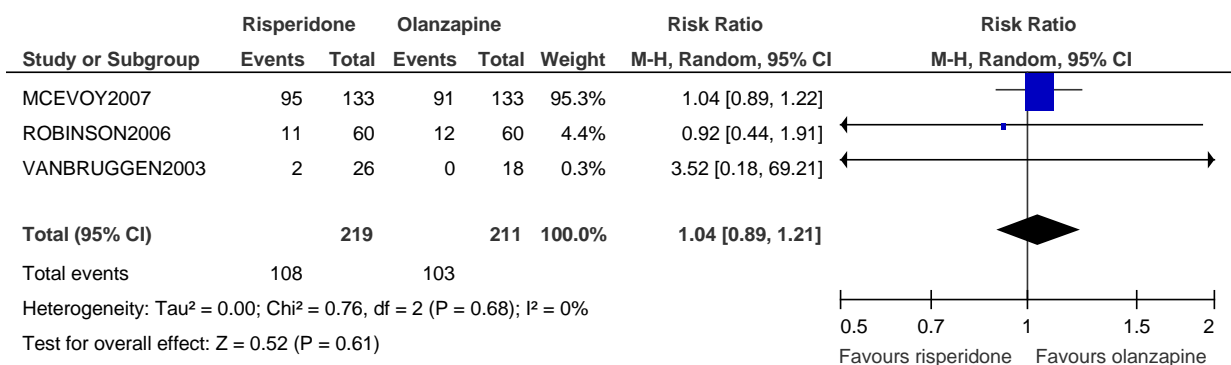
### 10.15 Parkinsonism



### 10.16 Akathisia

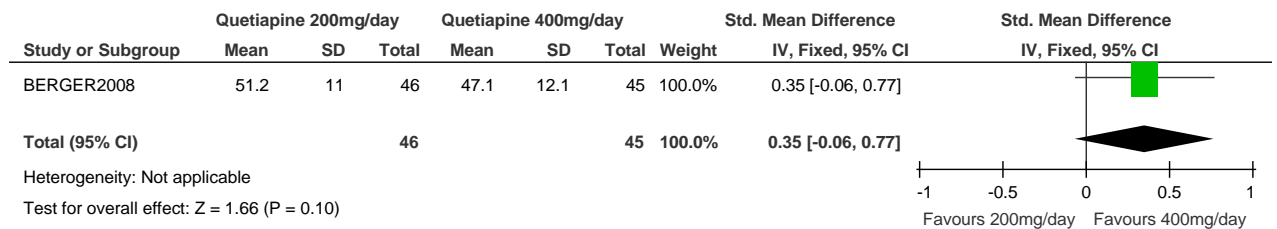


### 10.17 Leaving the study early for any reason

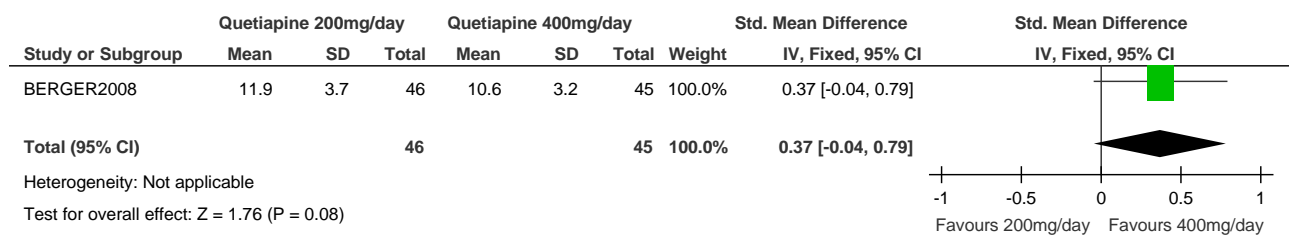


## 11. Quetiapine (200 mg/day) versus quetiapine (400 mg/day): post-treatment efficacy outcomes

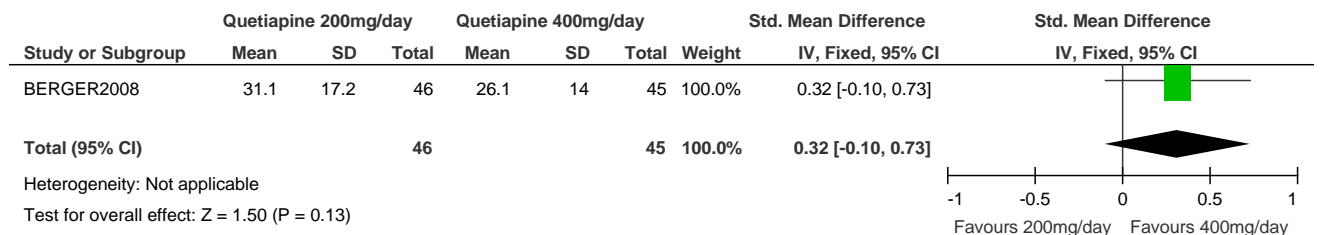
### 11.1 Mental state: mean endpoint total symptoms (PANSS)



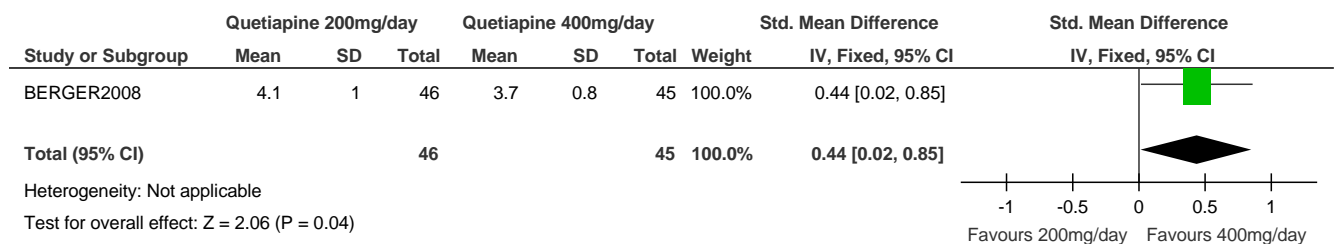
### 11.2 Mental state: mean endpoint positive symptoms (Brief Psychiatric Rating Scale - Psychotic Subscale [BPRS-P])



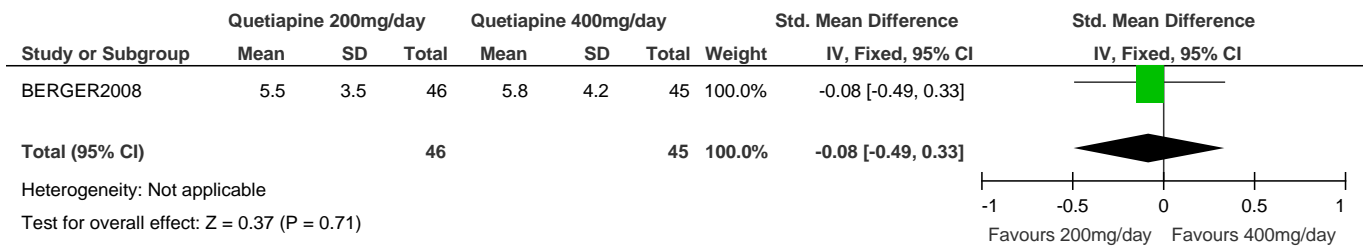
### 11.3 Mental state: mean endpoint negative symptoms (SANS)



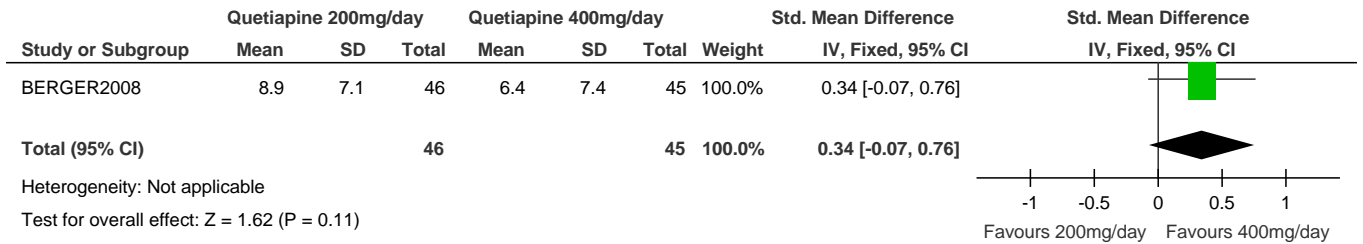
### 11.4 Mean endpoint global state: severity (CGI-S)



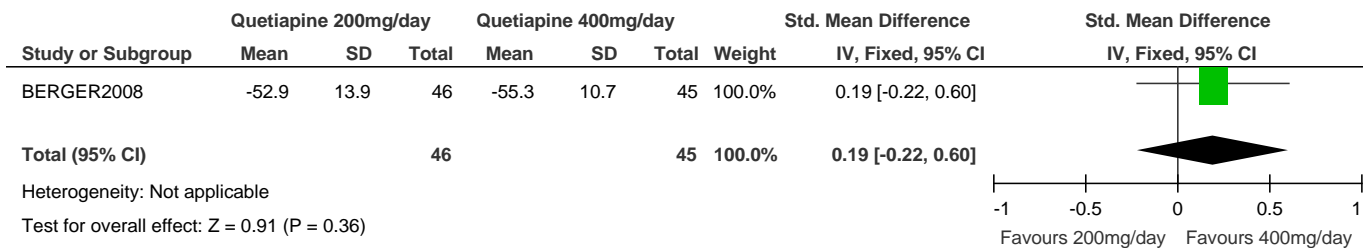
### 11.5 Mental state: mean endpoint depression (CDSS)



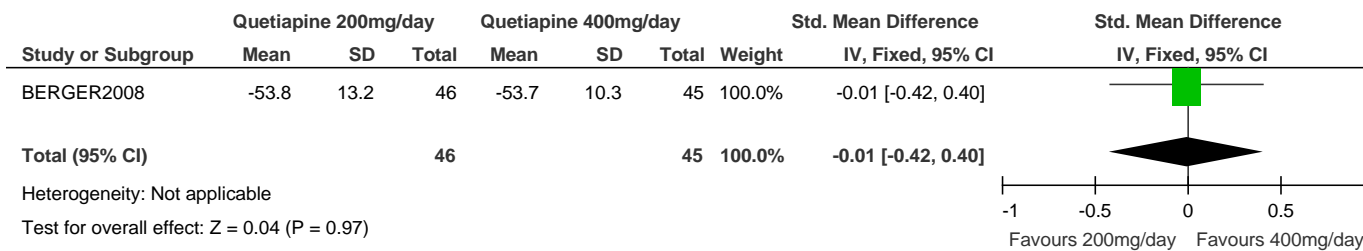
### 11.6 Mental state: mean endpoint mania (YMRS)



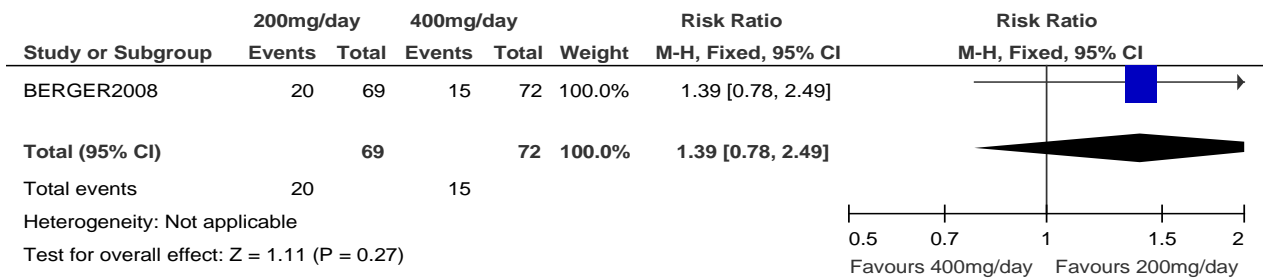
### 11.7 Mean endpoint psychosocial functioning (GAF)



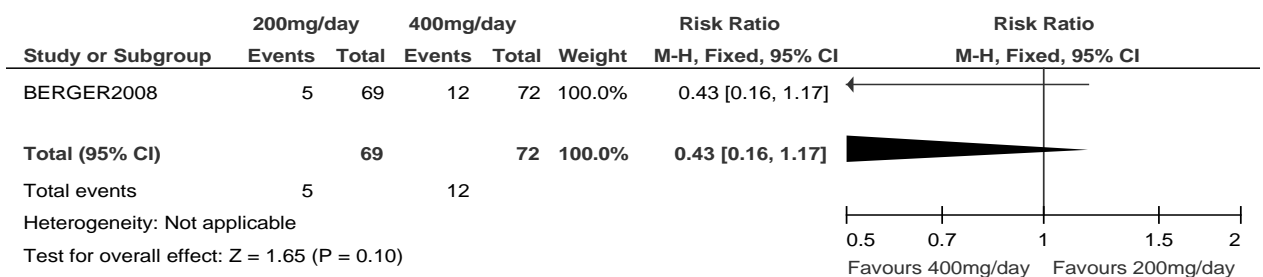
### 11.8 Mean endpoint social functioning (Social and Occupational Functioning Assessment Scale [SOFAS])



## 11.9 Response (BPRS)

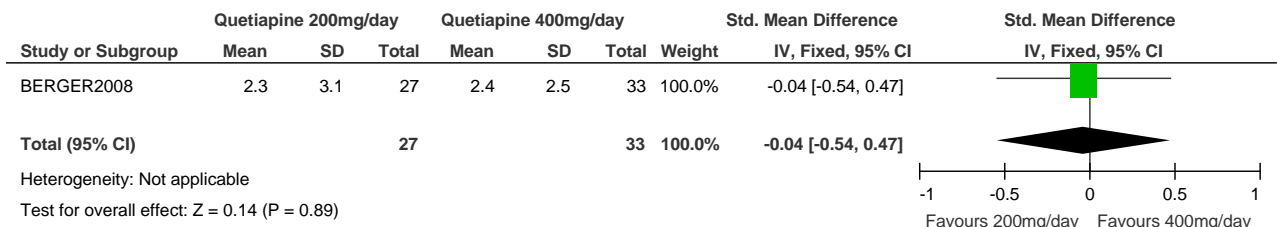


## 11.10 Remission (BPRS)

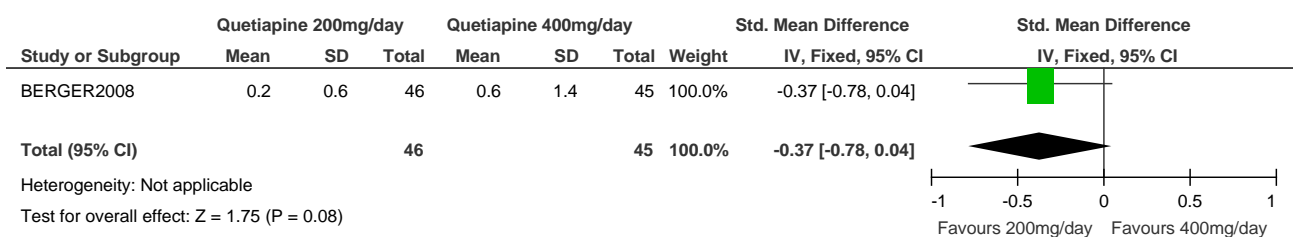


## 12. Quetiapine (200 mg/day) versus quetiapine (400 mg/day): post-treatment side effect outcomes

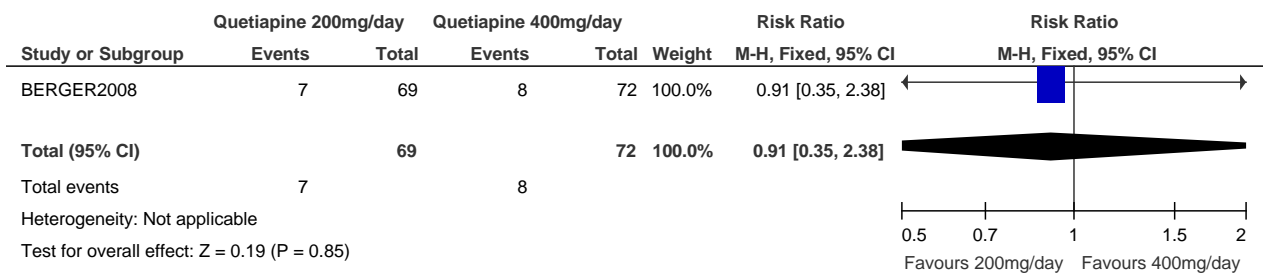
### 12.1 Mean endpoint weight (kg)



### 12.2 EPS (mean endpoint Udvalg for Kliniske Undersøgelser [UKU] scores)



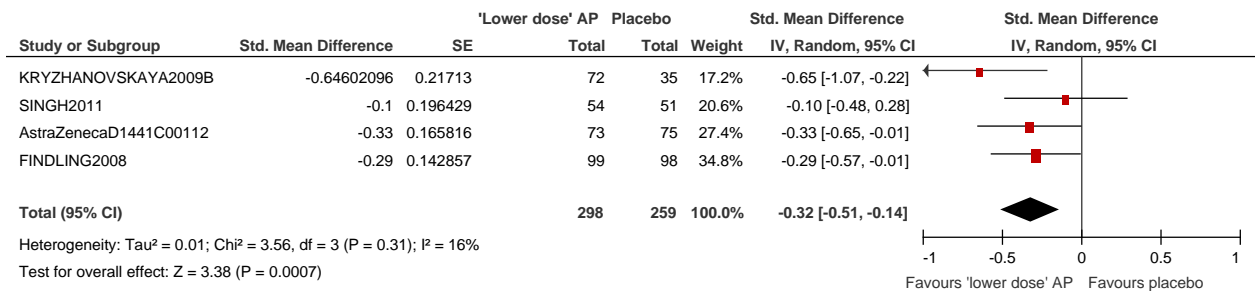
### 12.3 Leaving the study early for any reason



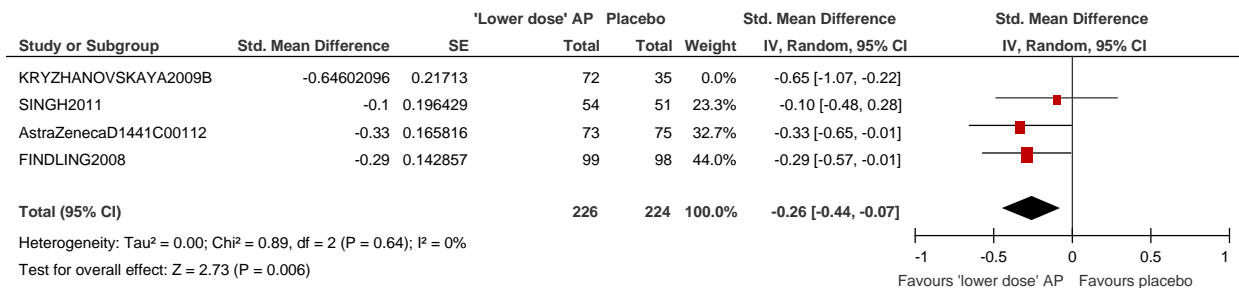
# APPENDIX 14C (II): ANTIPSYCHOTICS IN THE TREATMENT OF SUBSEQUENT ACUTE EPISODES OF PSYCHOSIS AND SCHIZOPHRENIA

## 1. 'Lower dose' antipsychotic versus placebo: post-treatment efficacy outcomes

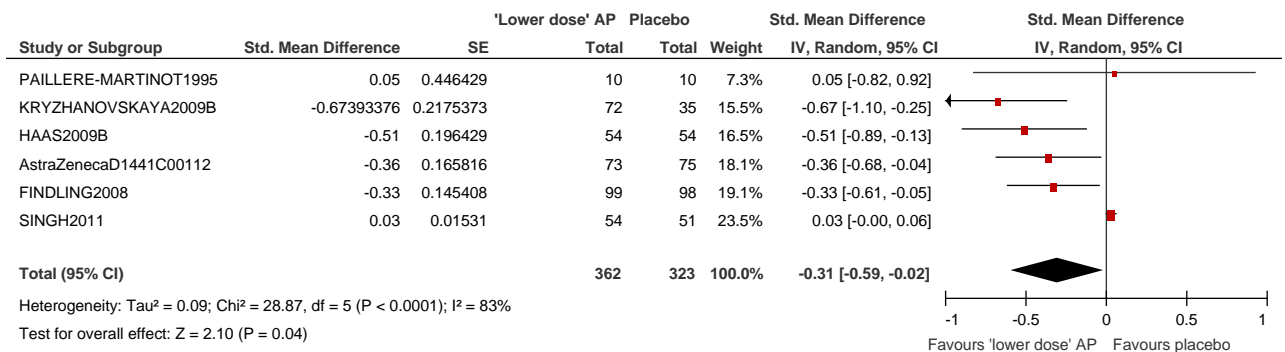
### 1.1 Mental state: total symptoms (PANSS, BPRS)



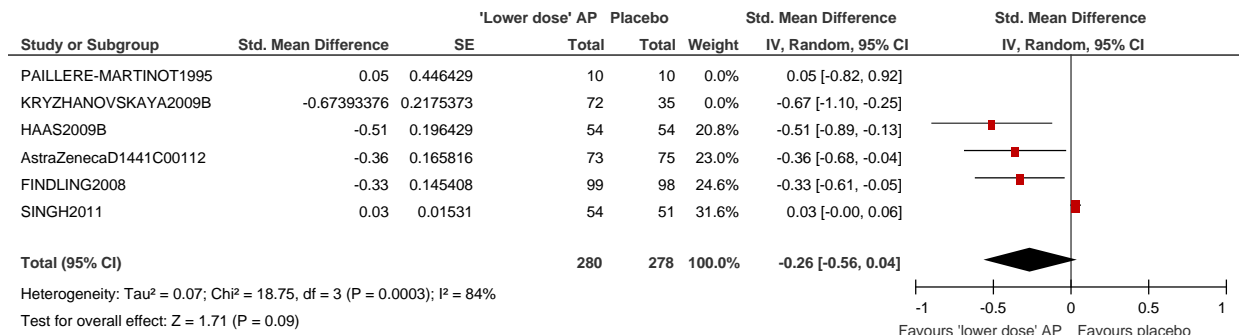
### 1.2 Mental state: mean change in total symptoms (PANSS) sensitivity analysis (taking KRYZHANOVSKAYA2009B out of the analysis)



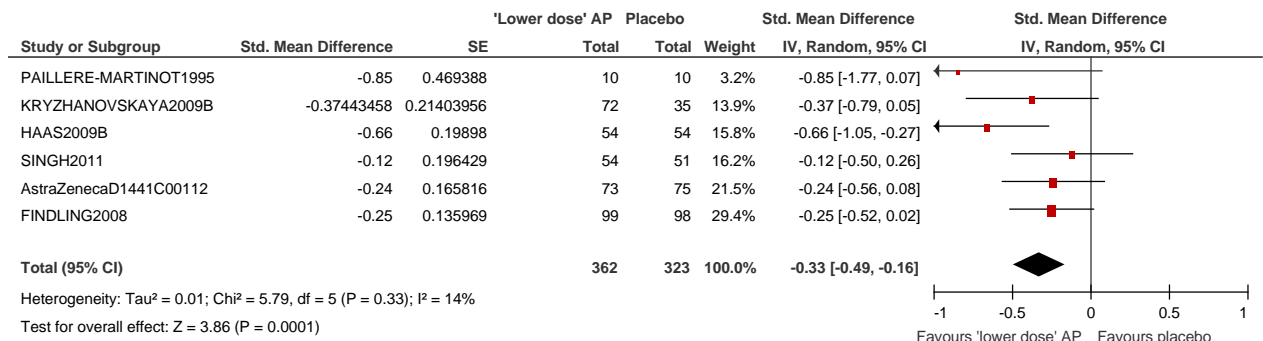
### 1.3 Mental state: positive symptoms (PANSS Positive)



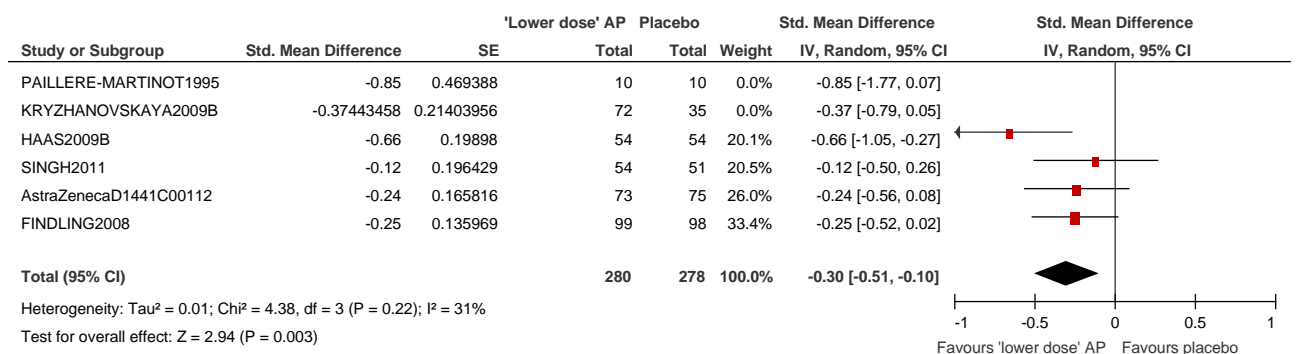
### 1.4 Mental state: mean change in positive symptoms (PANSS Positive) sensitivity analysis (taking out KRYZHANOVSKAYA2009B and PALLIERE-MARTINOT1995)



### 1.5 Mental state: negative symptoms (PANSS Negative)

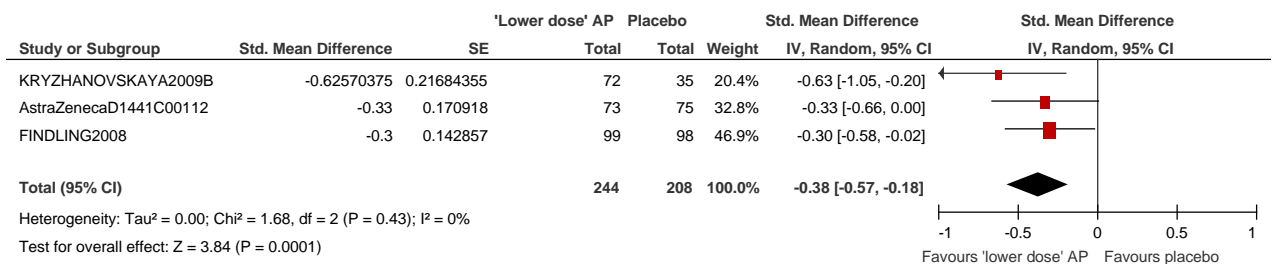


### 1.6 Mental state: mean change in negative symptoms (PANSS Negative) sensitivity analysis (taking out KRYZHANOVSKAYA2009B and PALLIERE-MARTINOT1995)

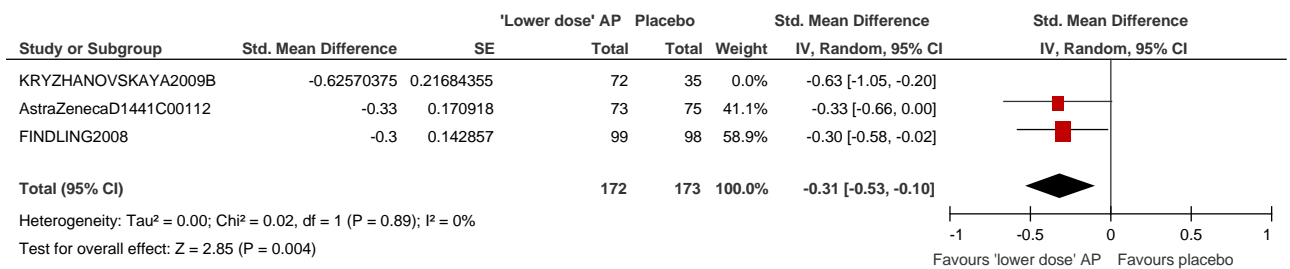




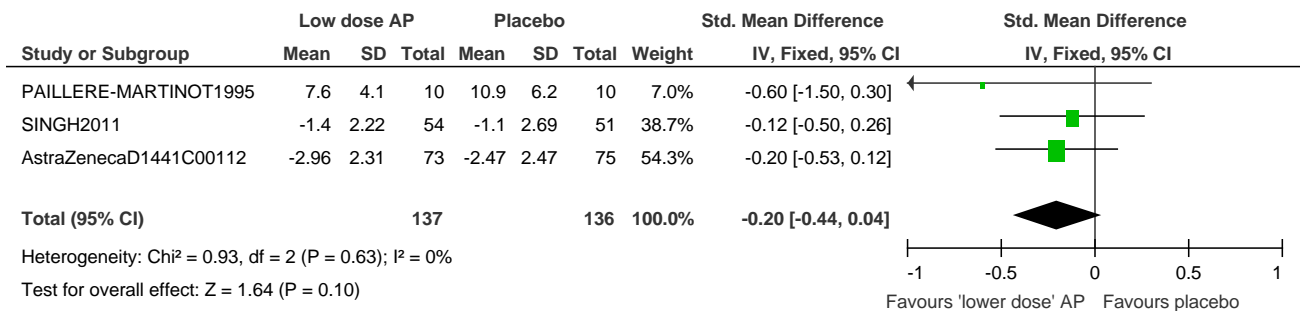
## 1.7 Global state: severity (CGI-S)



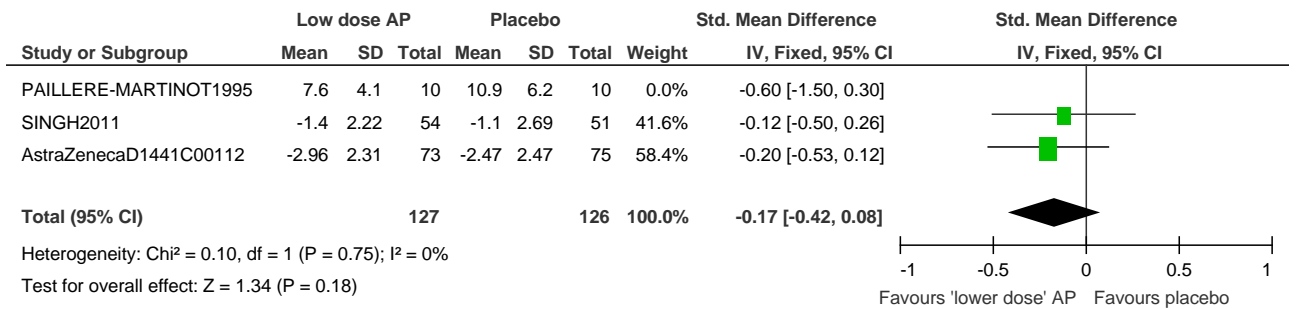
## 1.8 Mean change in global state: severity (CGI-S) sensitivity analysis (taking out KRYZHANOVSKAYA2009B)



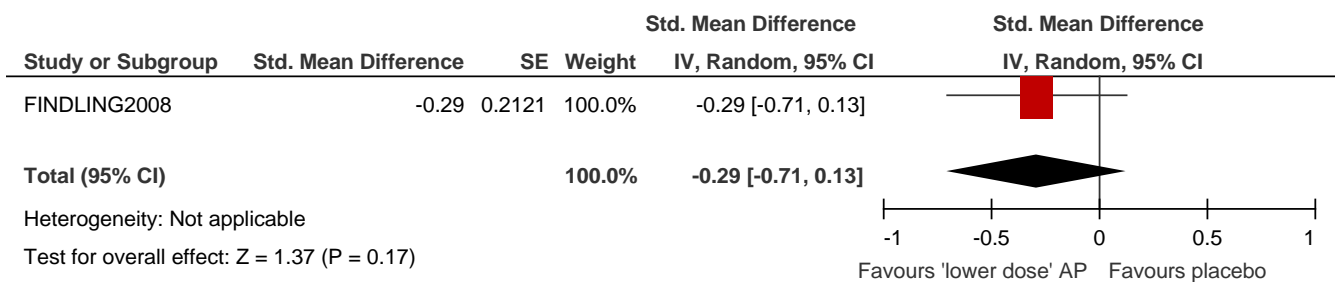
## 1.9 Mental state: depression (PANSS; MADRS)



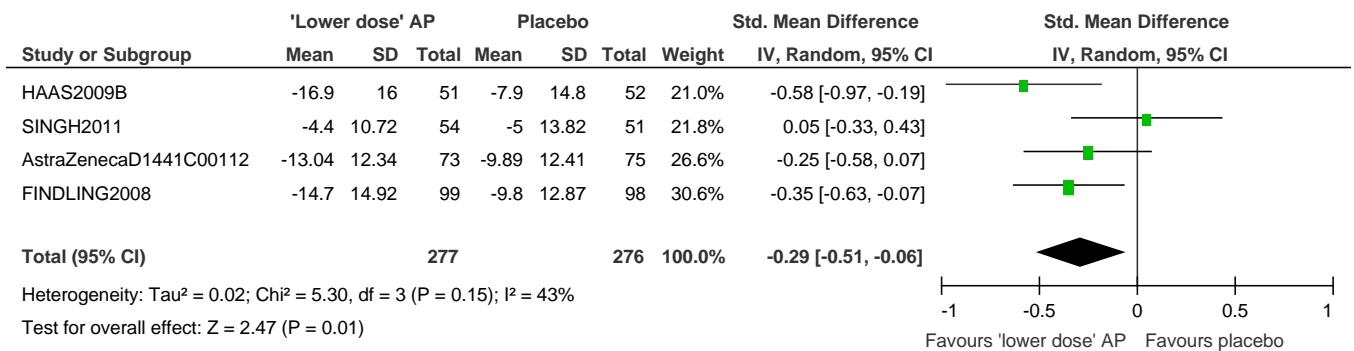
### 1.10 Mean change in depression (PANSS Anxiety and Depression; MADRS) sensitivity analysis (taking out PALLIERE-MARTINOT1995)



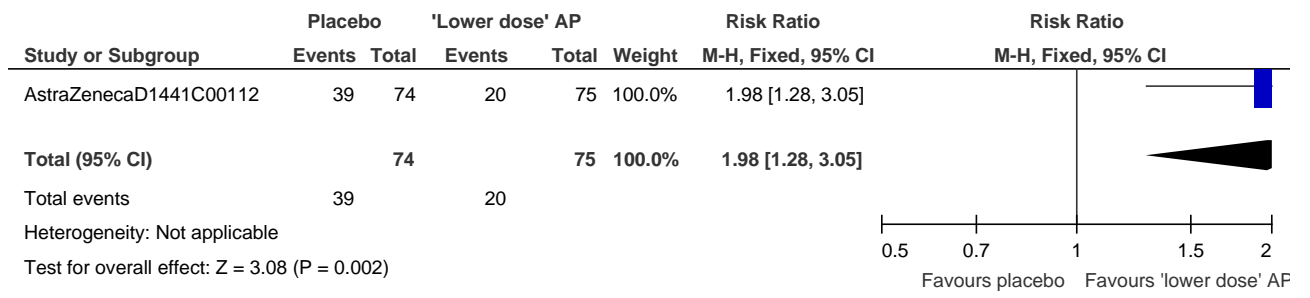
### 1.11 Mean change in quality of life (QLS)



### 1.12 Mean change in psychosocial functioning (Children's Global Assessment Scale [CGAS])

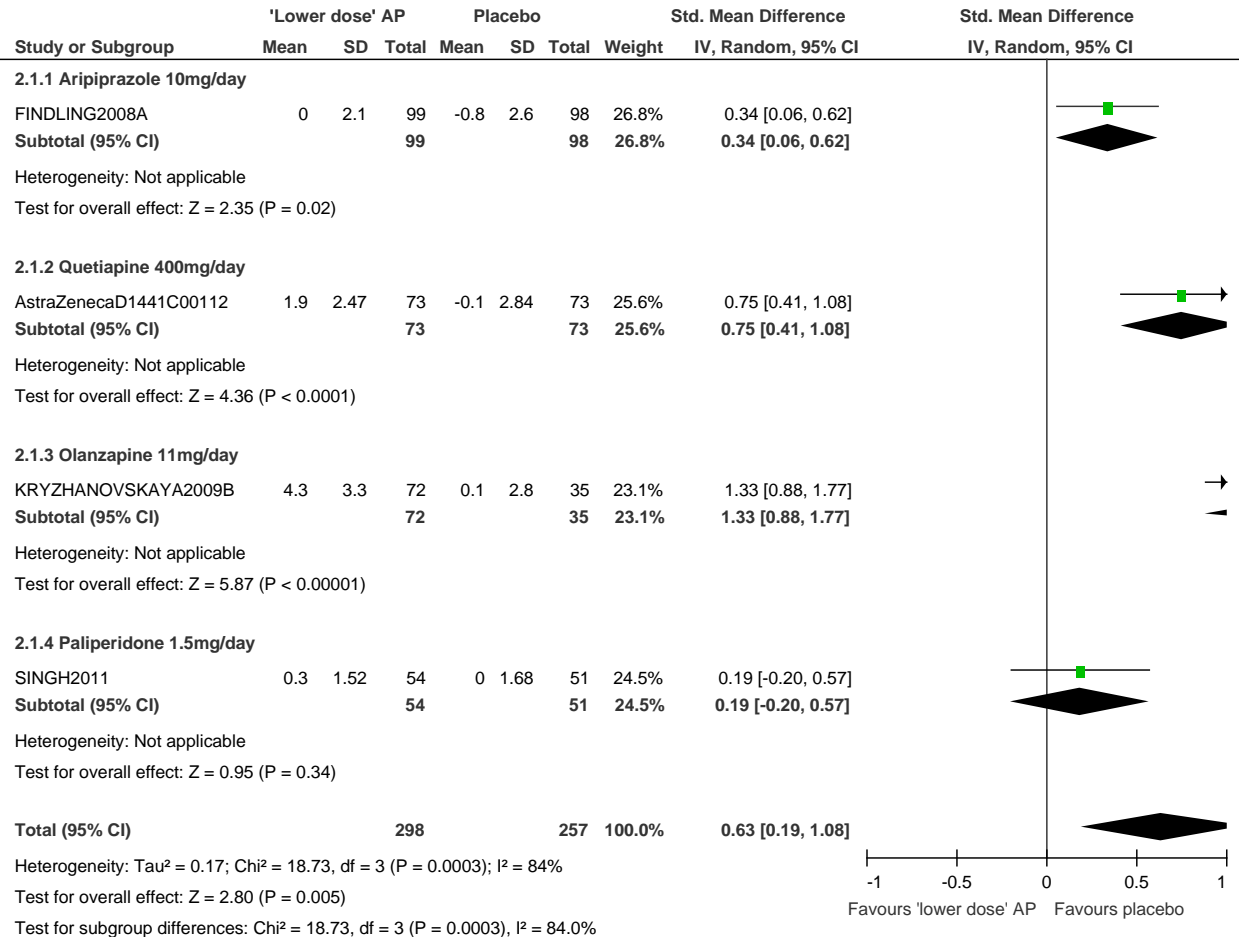


### 1.13 Response (CGI-I)

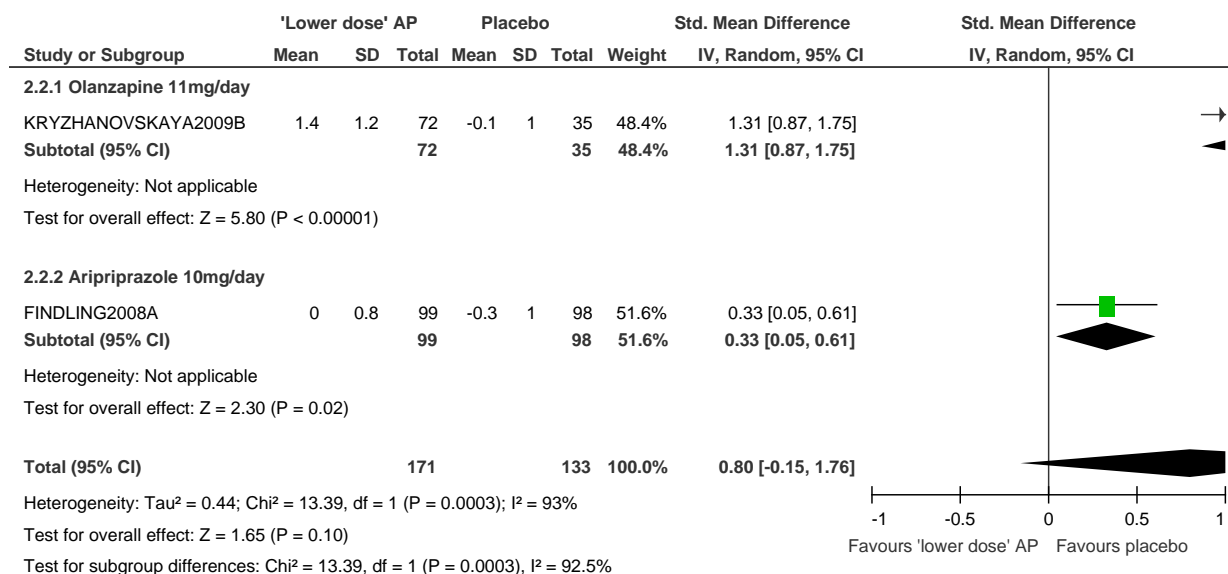


## 2. 'Lower dose' antipsychotic versus placebo: post-treatment side effect outcomes

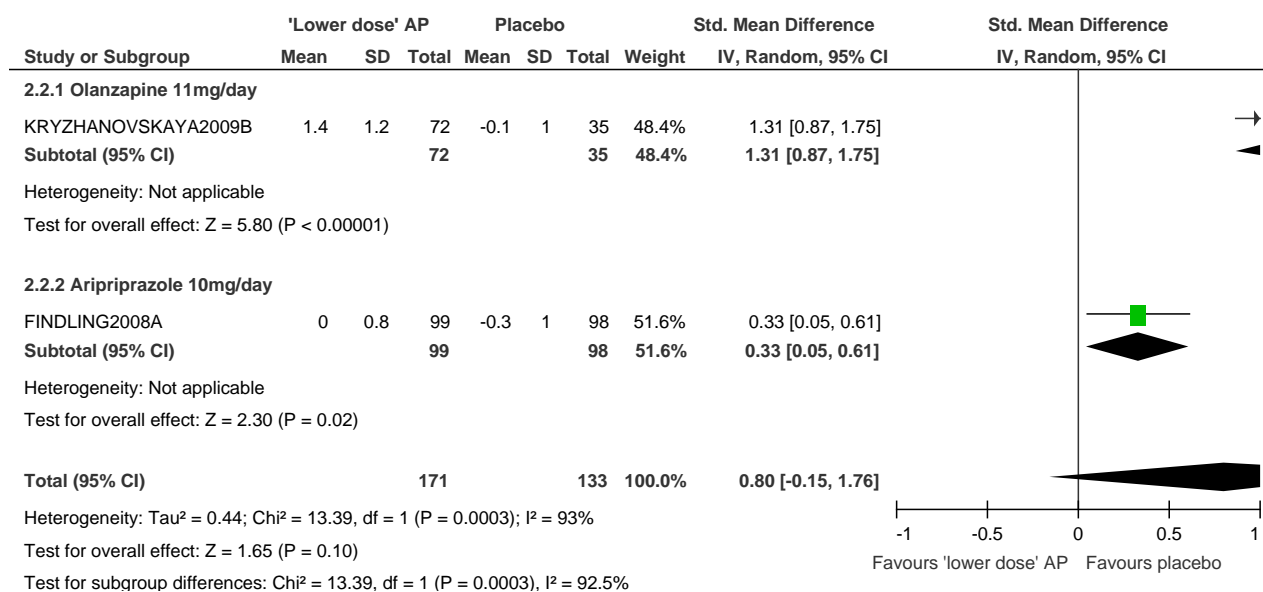
### 2.1 Weight (kg) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A, AstraZenecaD1441C00112, SINGH2011)



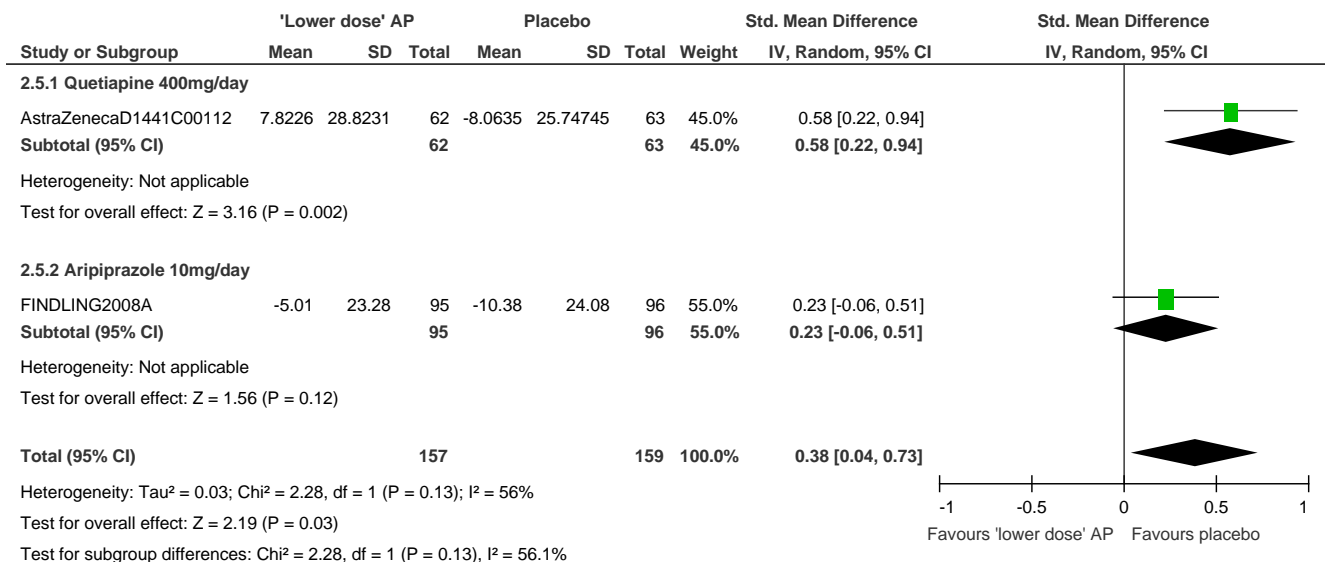
## 2.2 BMI (kg/m<sup>2</sup>) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A)



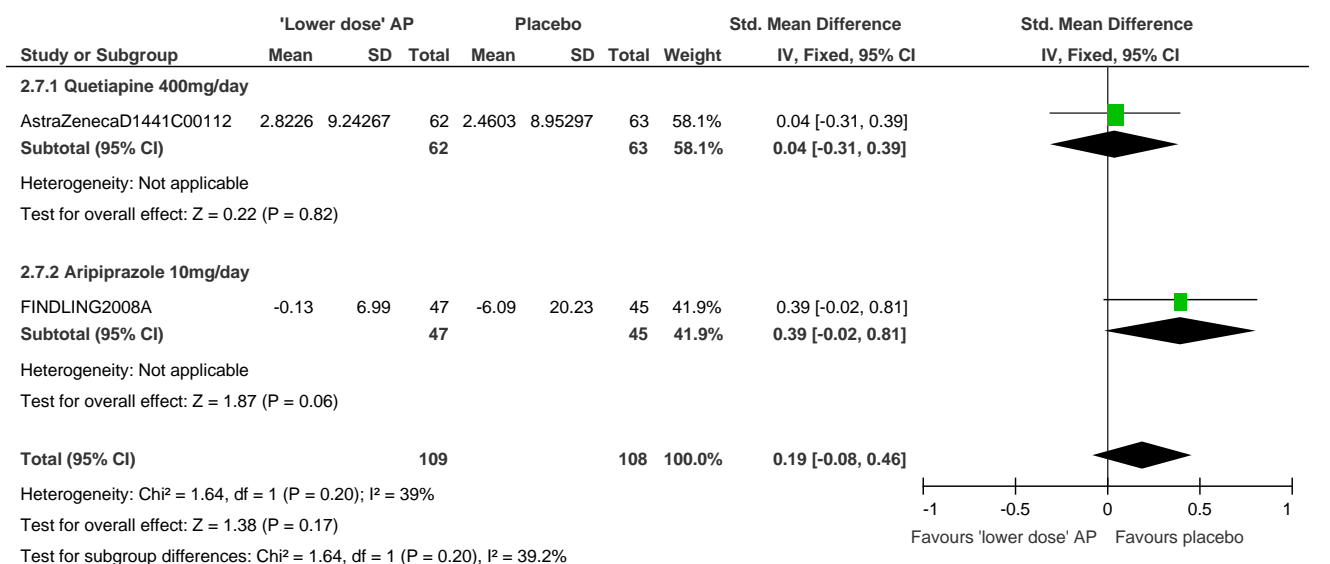
## 2.3 Fasting serum glucose level (mg/dl) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A, AstraZenecaD1441C00112, SINGH2011)



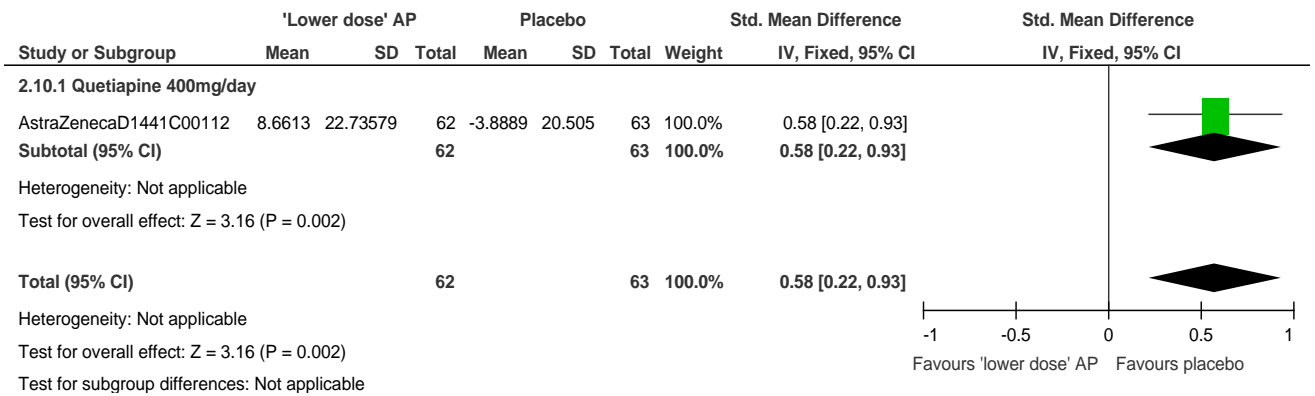
## 2.4 Mean change in fasting total cholesterol (mg/dl)



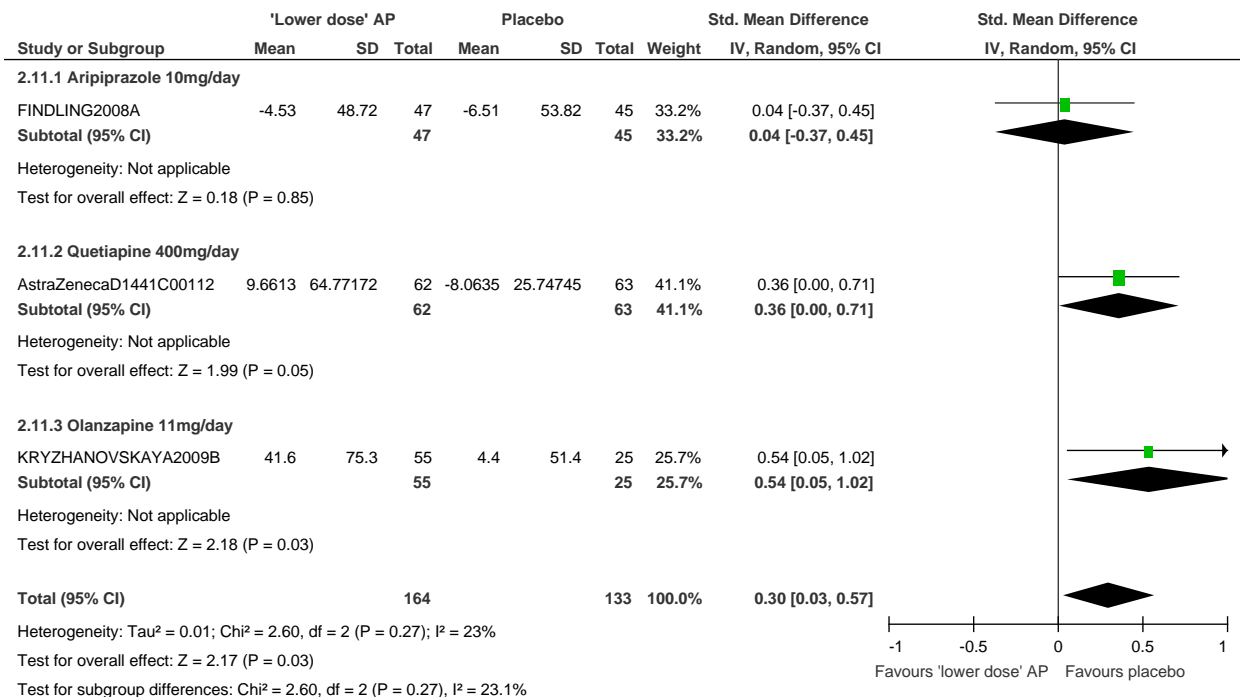
## 2.5 Mean change in fasting high-density lipoprotein cholesterol (mg/dl)



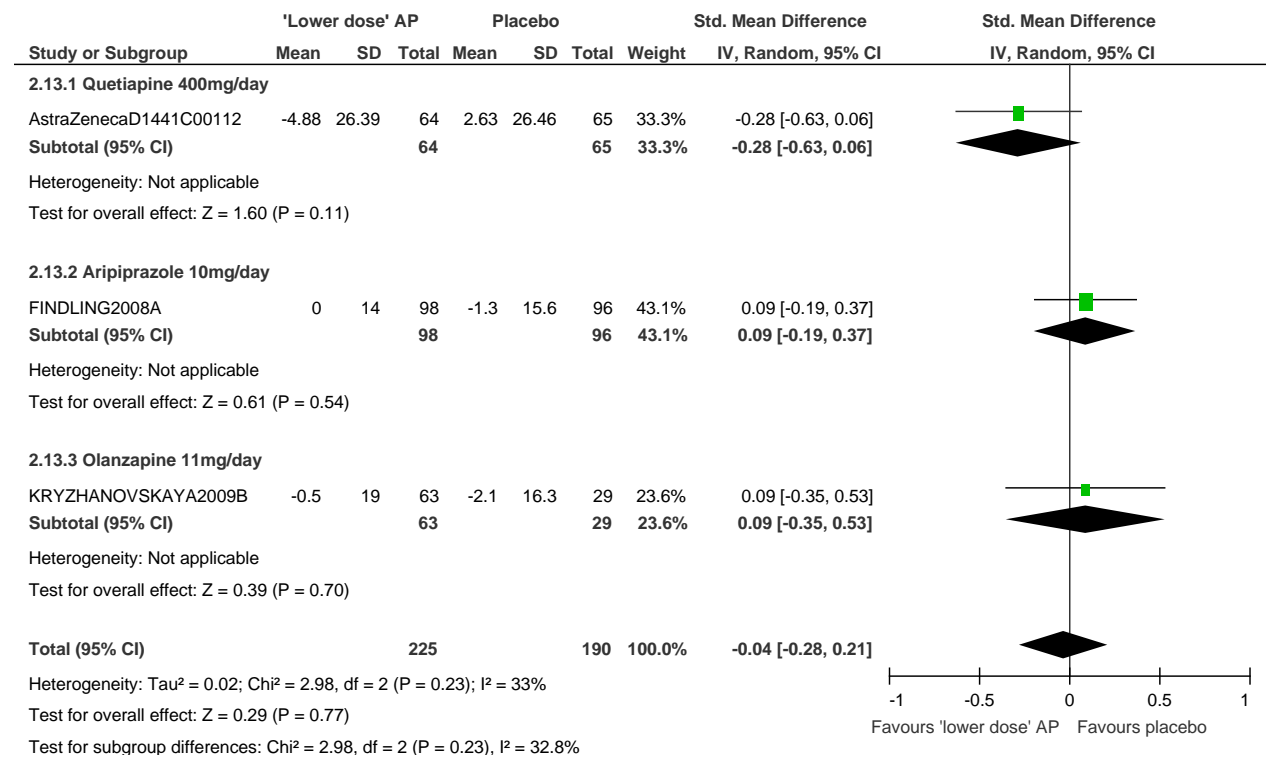
## 2.6 Mean change in fasting low-density lipoprotein cholesterol (mg/dl)



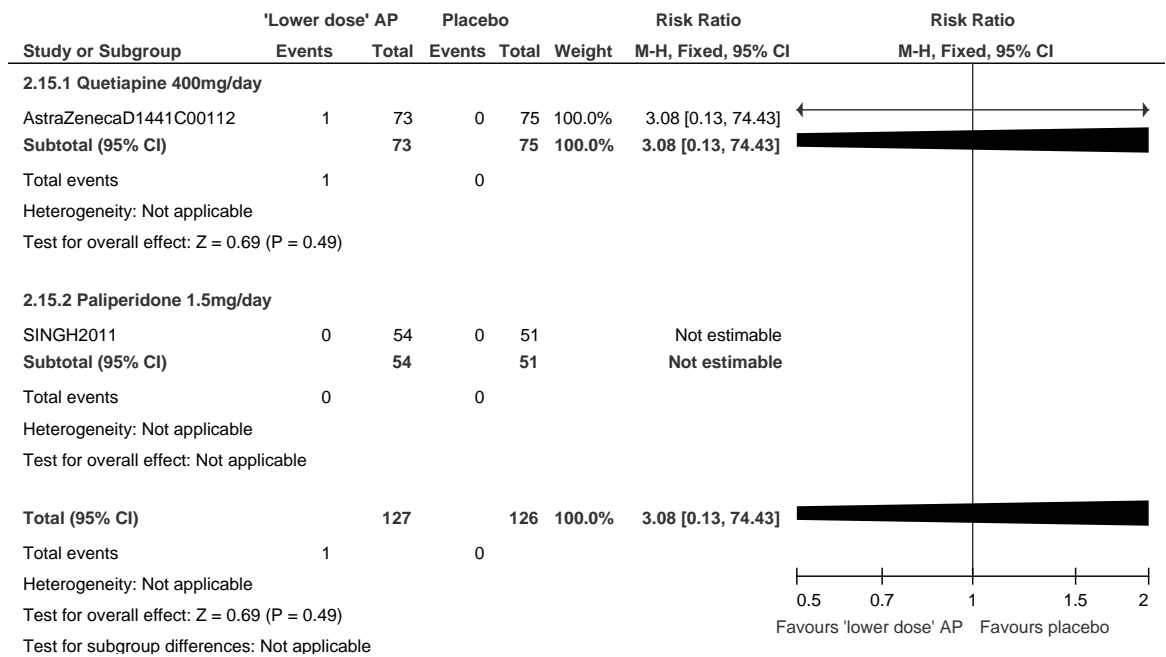
## 2.7 Fasting triglycerides (mg/dl) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A, AstraZenecaD1441C00112)



2.8 QTcB interval (msec) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A, AstraZenecaD1441C00112)

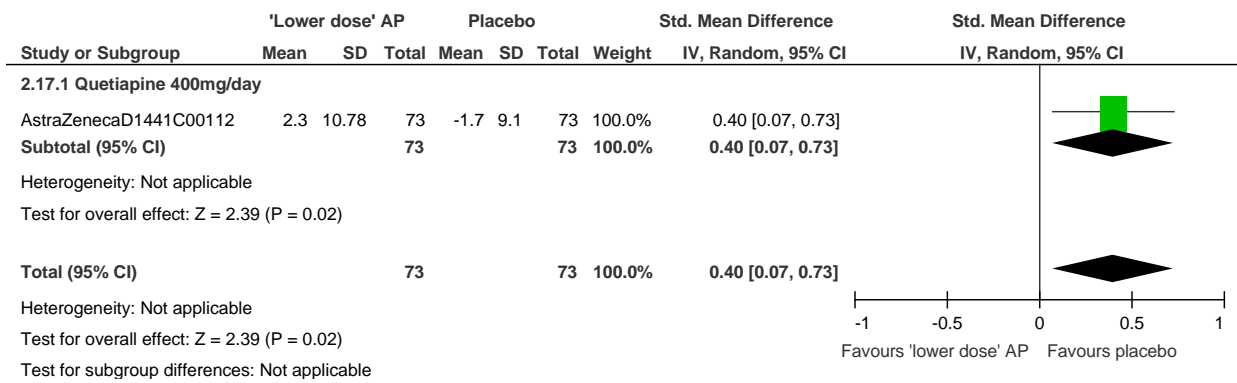


2.9 QTcB interval (msec) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A, AstraZenecaD1441C00112)

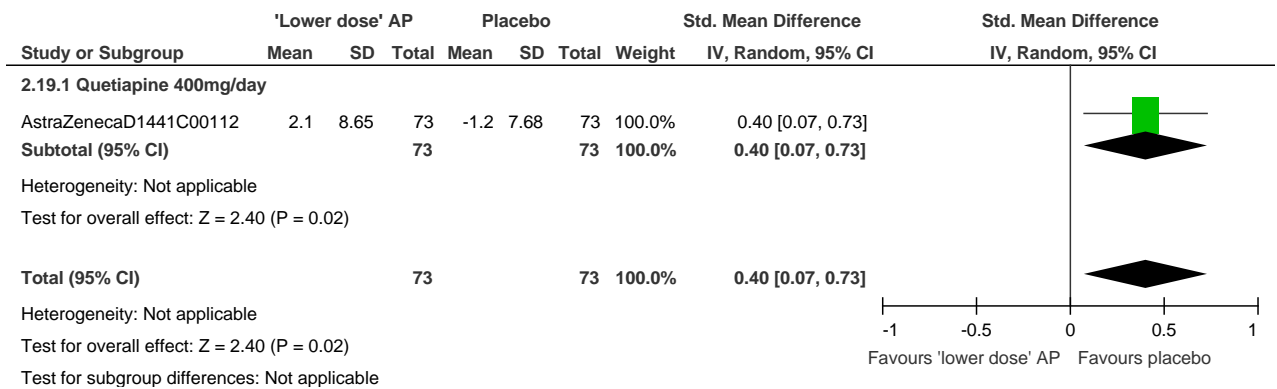




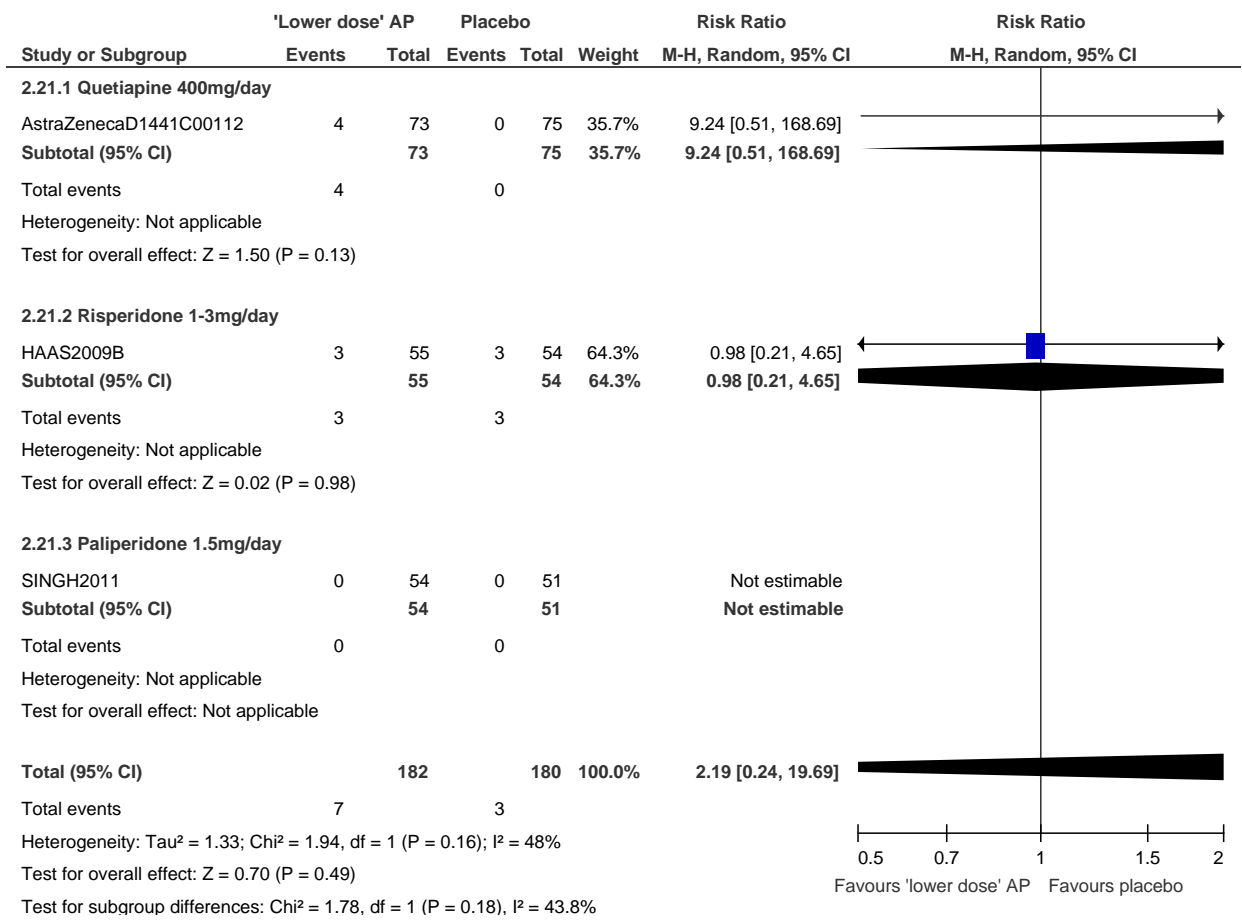
## 2.10 Mean change in systolic BP (mm Hg)



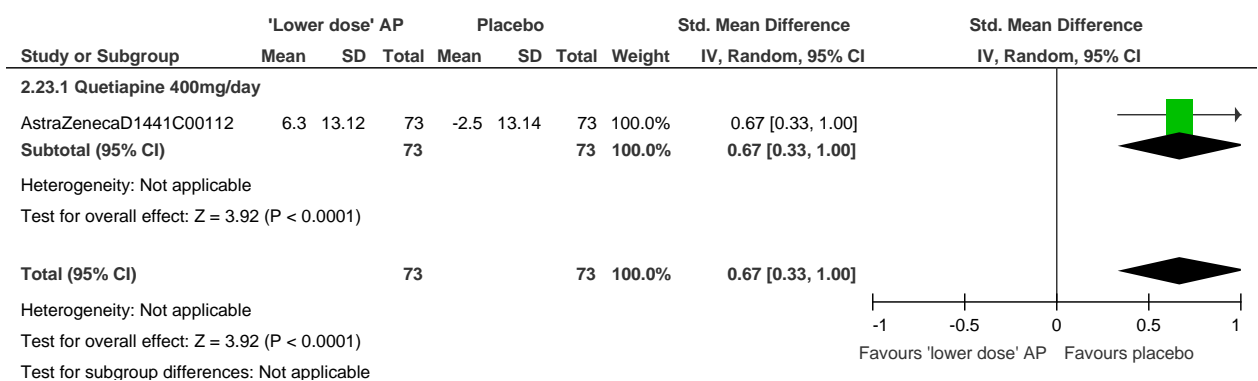
## 2.11 Mean change in diastolic BP (mm Hg)



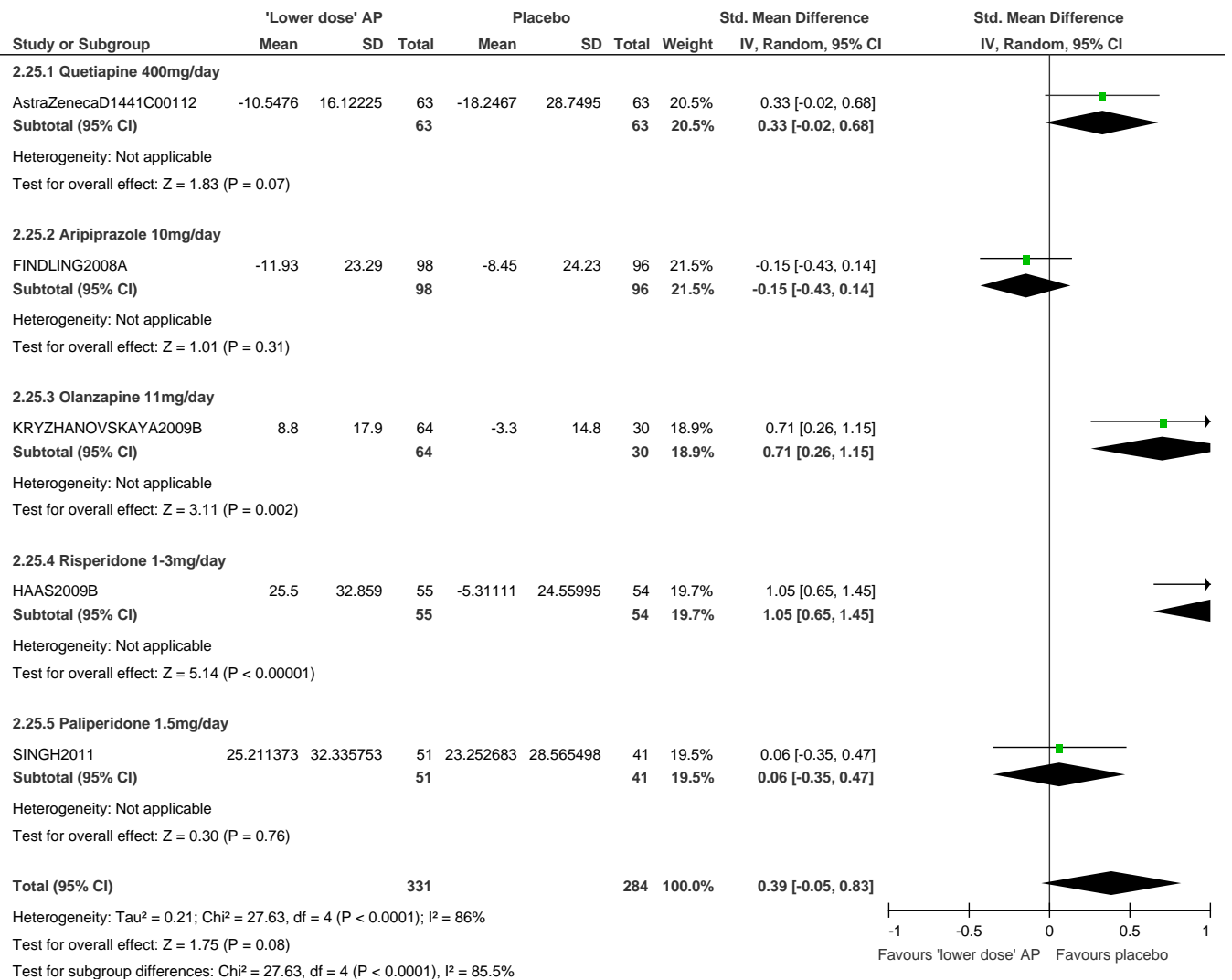
## 2.12 Tachycardia



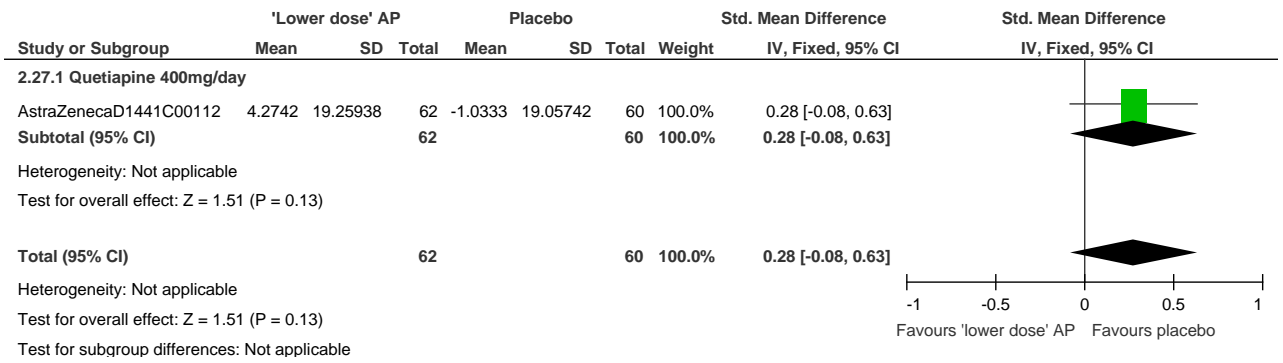
## 2.13 Mean change in standing pulse (BPM)



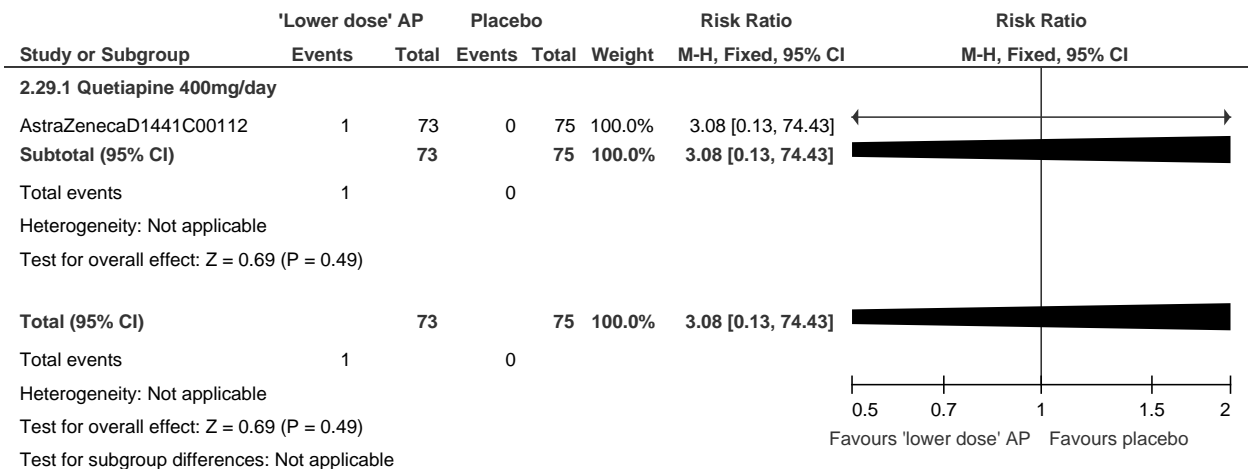
2.14 Prolactin level (mg/dl) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A; AstraZenecaD1441C00112; HAAS2009B; SINGH2011)



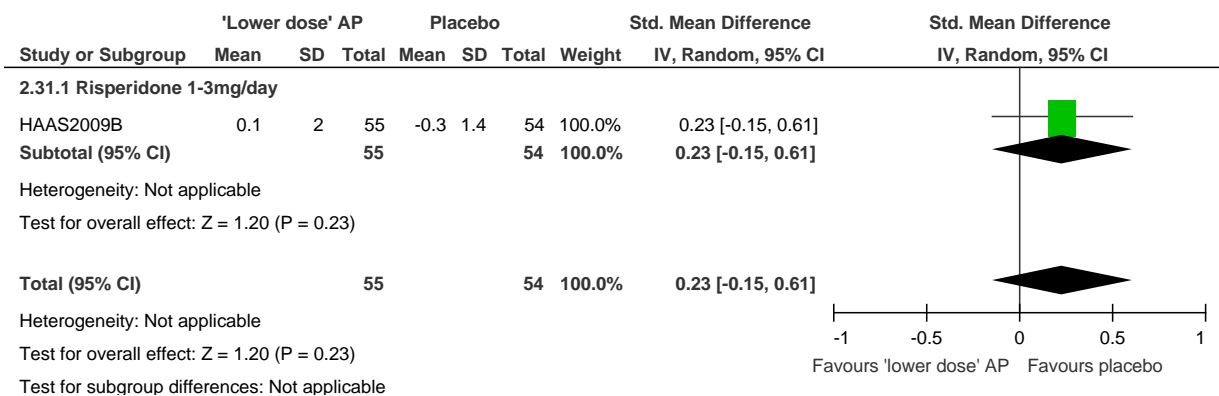
## 2.15 Mean change in insulin level (mg/dl)



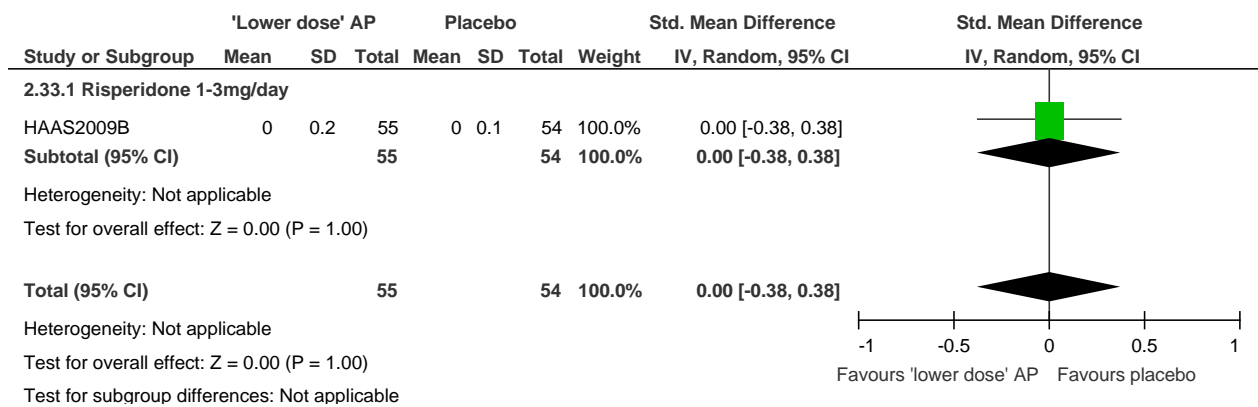
## 2.16 Extrapyrimal disorder



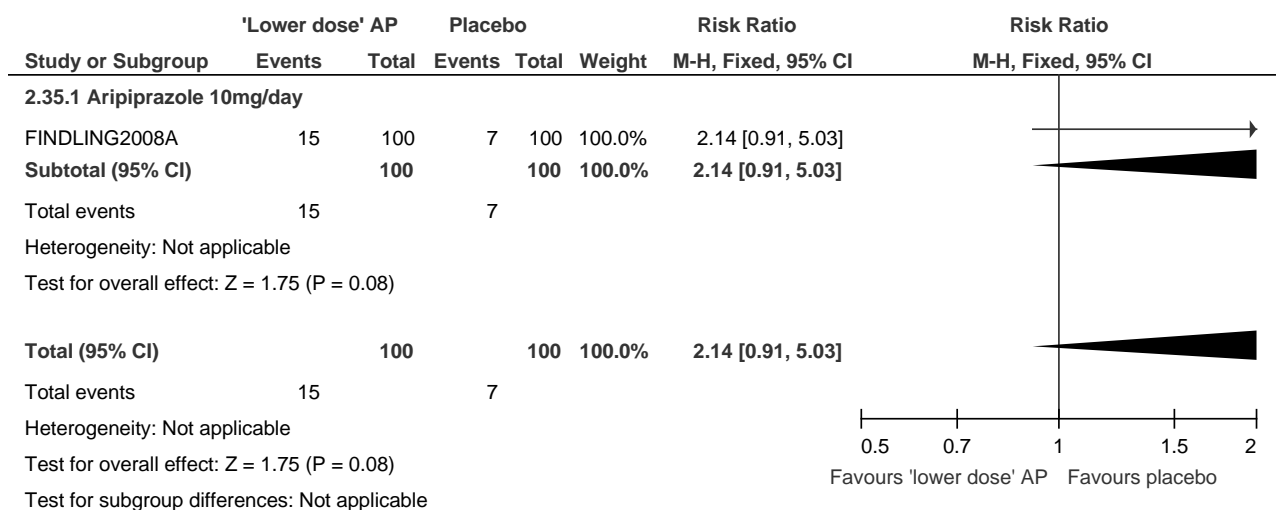
## 2.17 EPS (mean difference in AIMS scores)



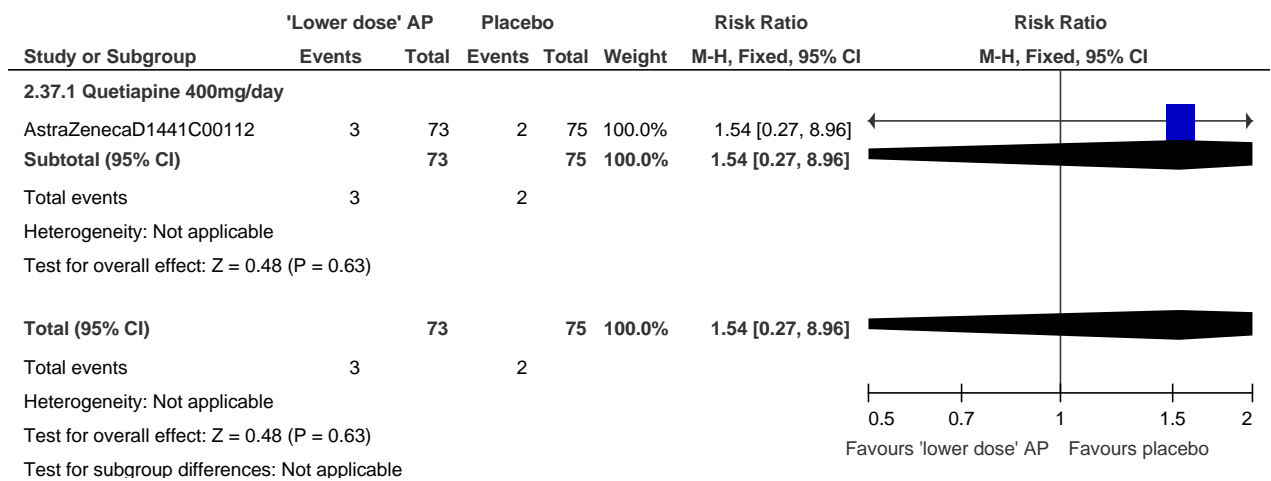
## 2.18 EPS (mean difference in SAS scores)



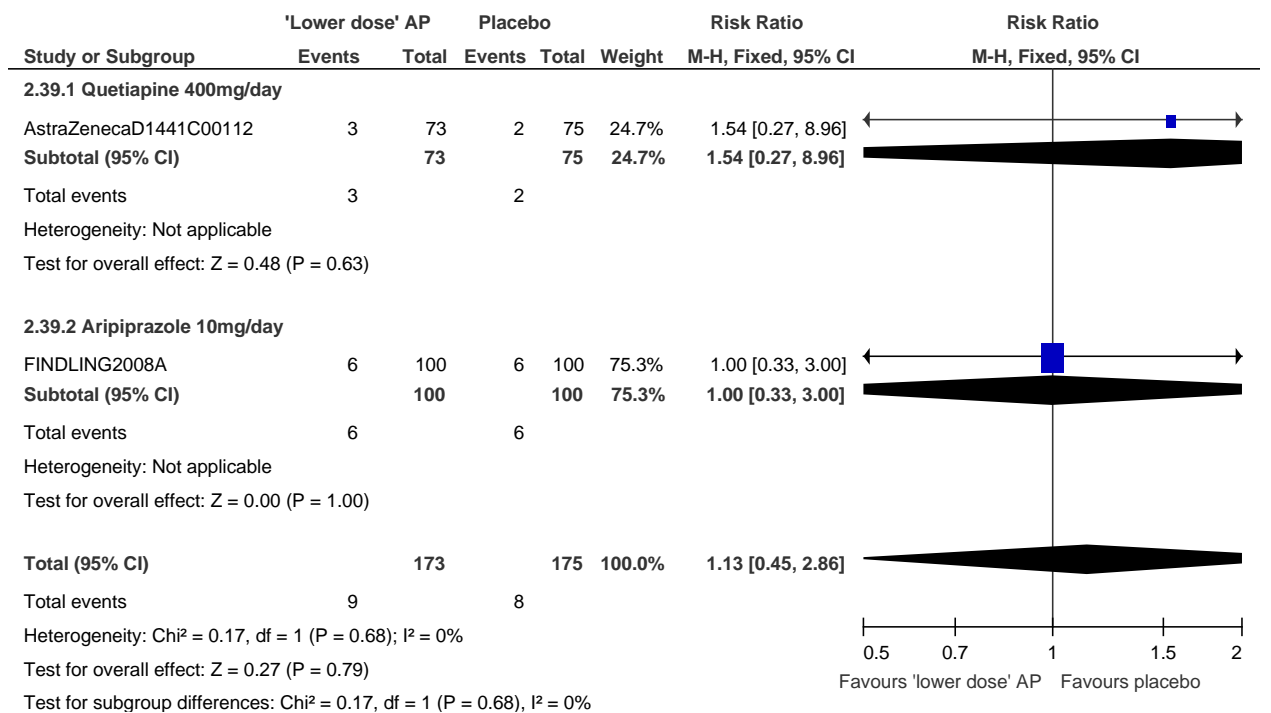
## 2.19 Parkinsonism



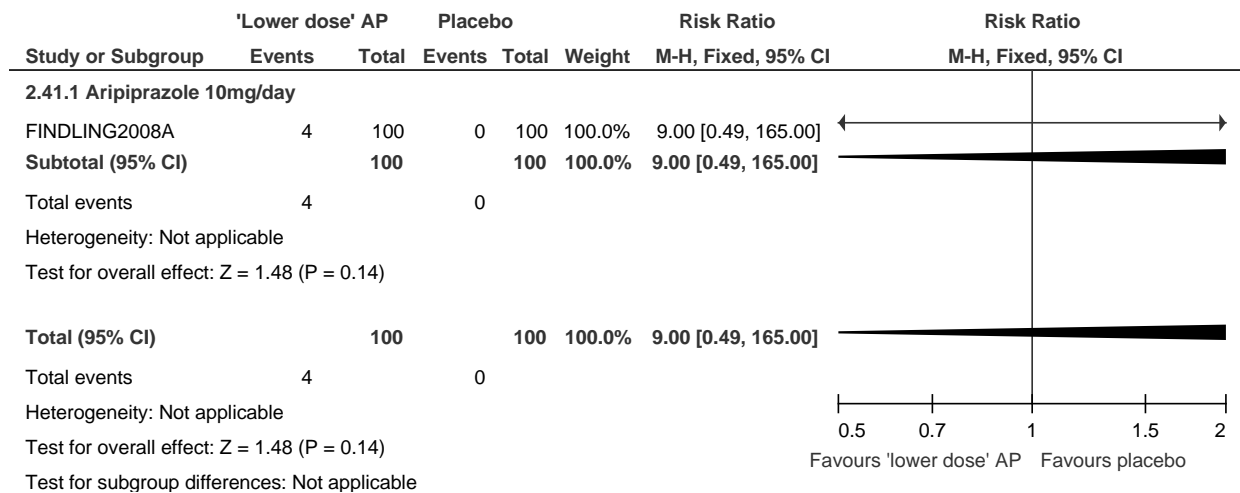
## 2.20 Tremor



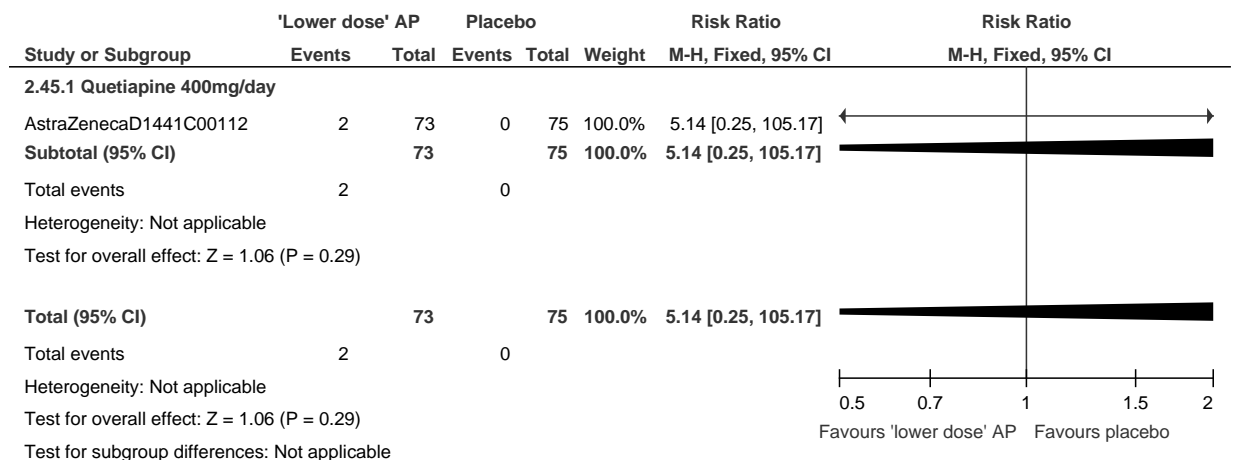
## 2.21 Akathisia



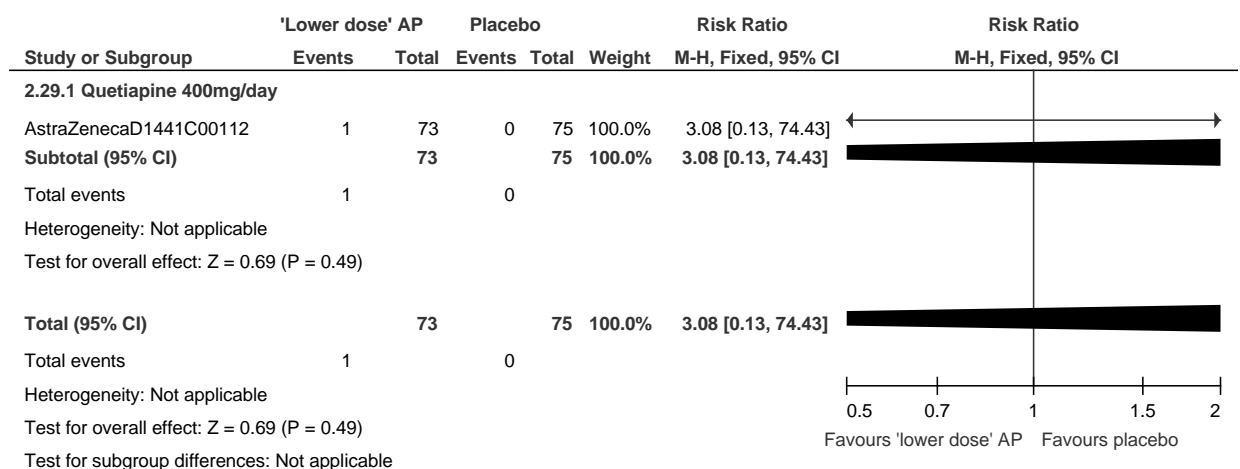
## 2.22 Dystonia



## 2.23 Dyskinesia



## 2.24 Extrapyramidal disorder

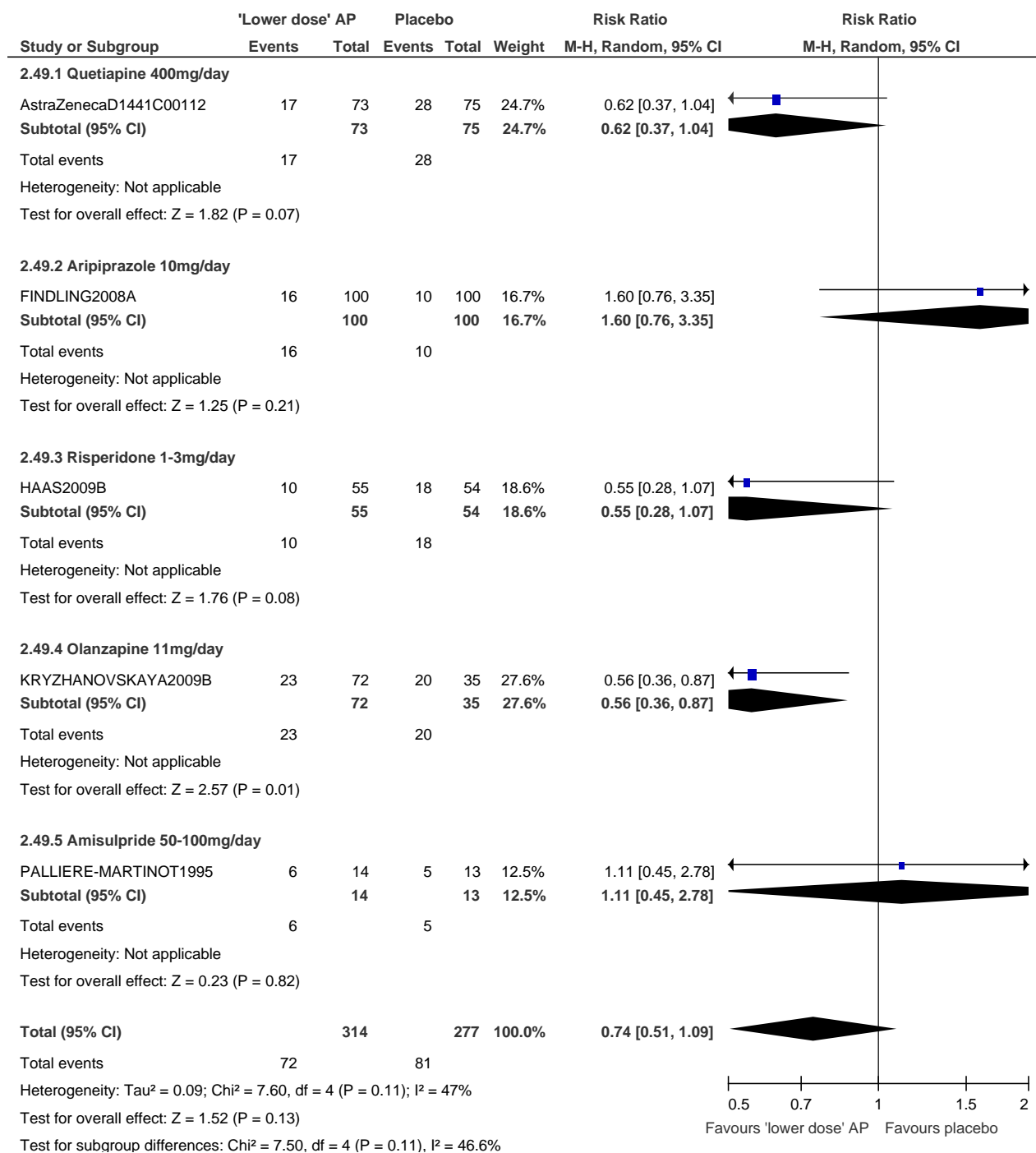


## 2.25 Mortality (including suicide)

Study or Subgroup	'Lower dose' AP		Placebo		Weight	Risk Ratio	Risk Ratio
	Events	Total	Events	Total		M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
<b>2.47.1 Aripiprazole 10mg/day</b>							
FINDLING2008A	0	100	0	100		Not estimable	
<b>Subtotal (95% CI)</b>		<b>100</b>		<b>100</b>		<b>Not estimable</b>	
Total events	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
<b>2.47.2 Risperidone 1-3mg/day</b>							
HAAS2009B	0	55	0	54		Not estimable	
<b>Subtotal (95% CI)</b>		<b>55</b>		<b>54</b>		<b>Not estimable</b>	
Total events	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
<b>Total (95% CI)</b>		<b>155</b>		<b>154</b>		<b>Not estimable</b>	
Total events	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							

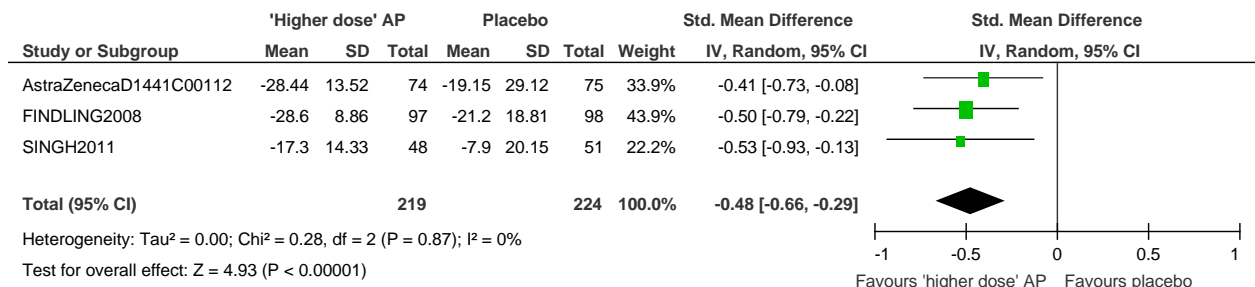


## 2.26 Leaving the study early for any reason

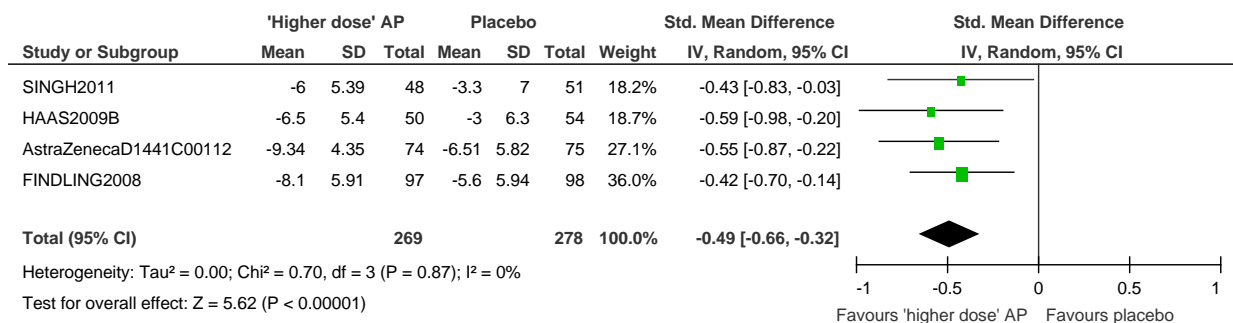


### 3. 'Higher dose' antipsychotic versus placebo: post-treatment efficacy outcomes

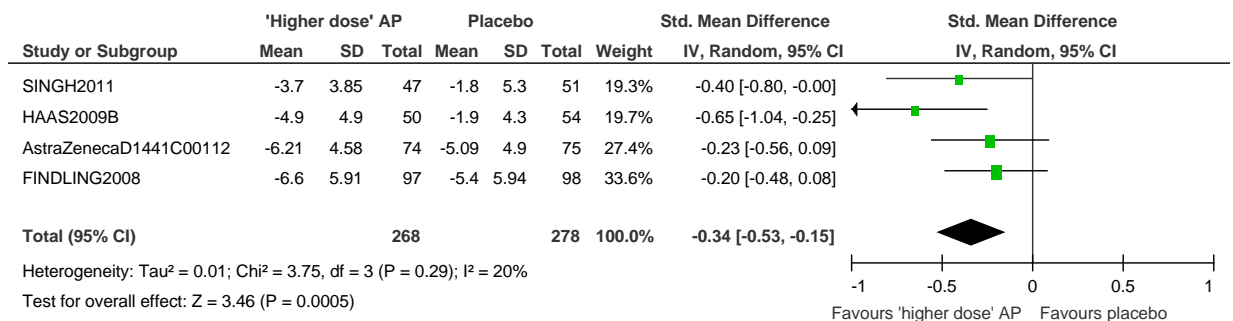
#### 3.1 Mental state: mean change in total symptoms (PANSS)



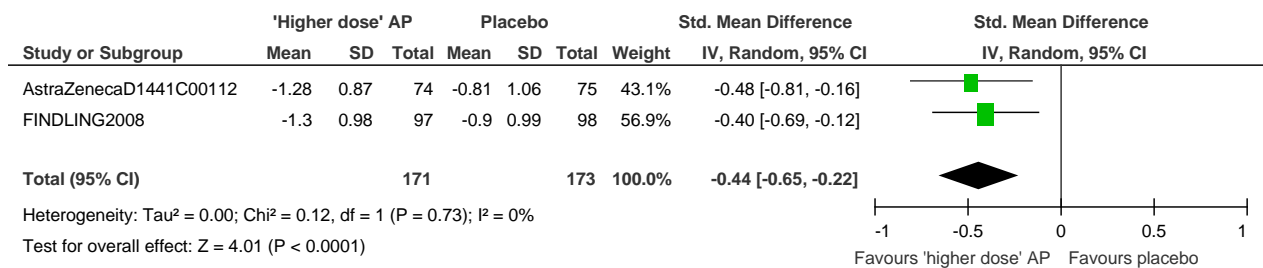
#### 3.2 Mental state: mean change in positive symptoms (SAPS)



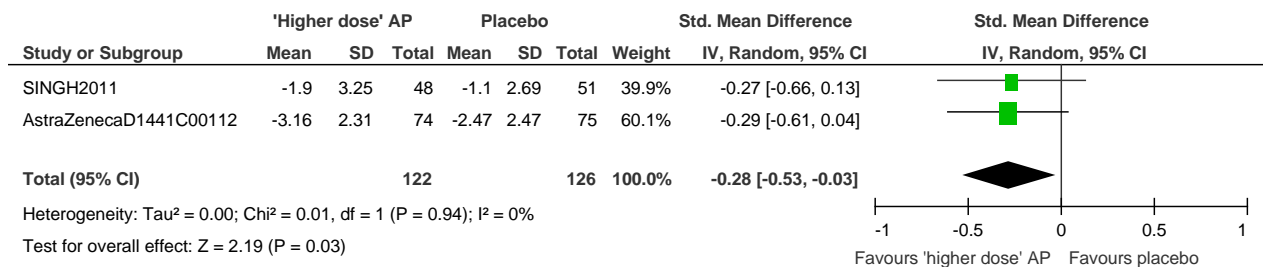
#### 3.3 Mental state: mean change in negative symptoms (SANS)



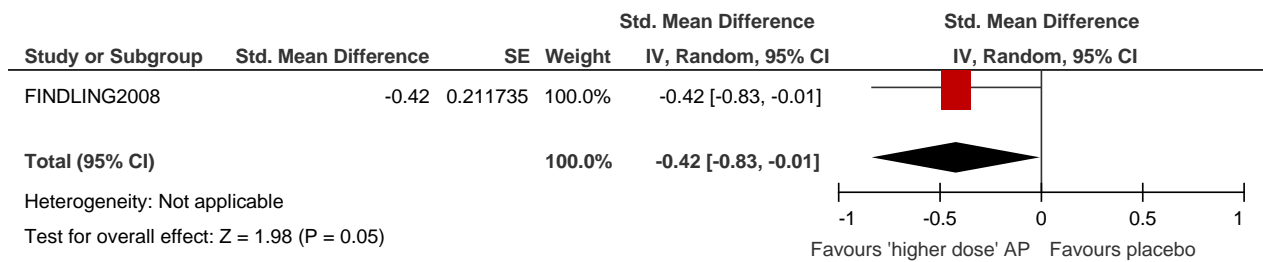
#### 3.4 Mean change in global state: severity (CGI-S)



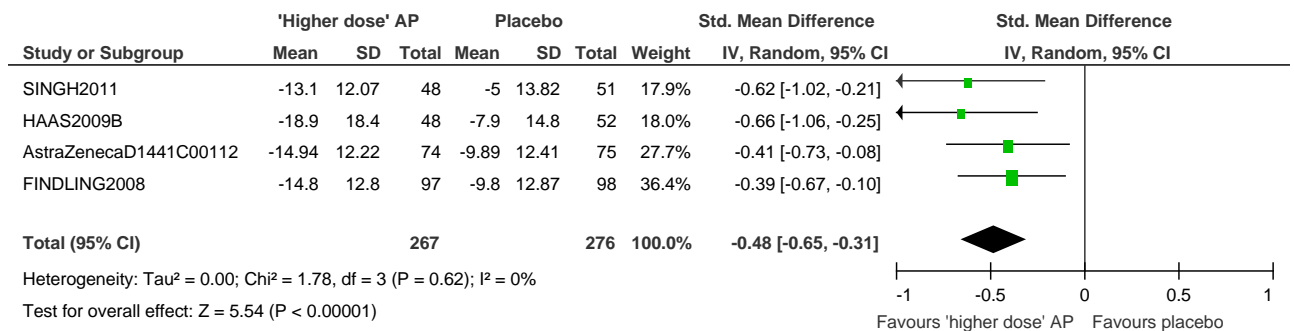
### 3.5 Mean change in depression (PANSS Depression, PANSS Anxiety and Depression)



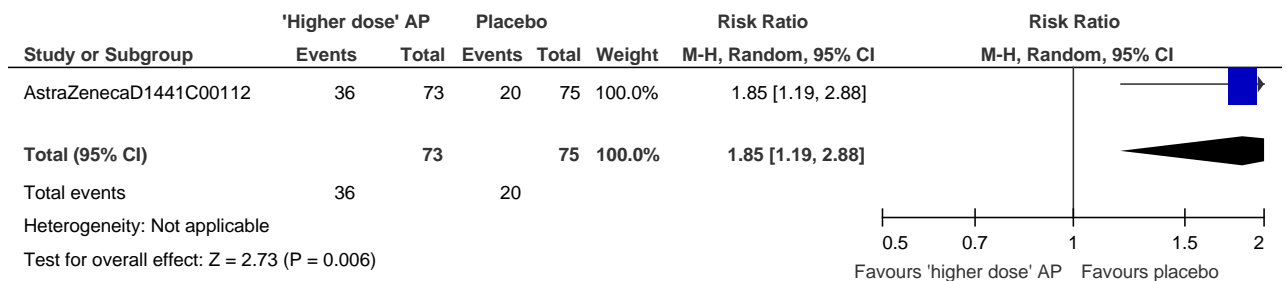
### 3.6 Mean change in quality of life (QLS)



### 3.7 Mean change in psychosocial functioning (CGAS)

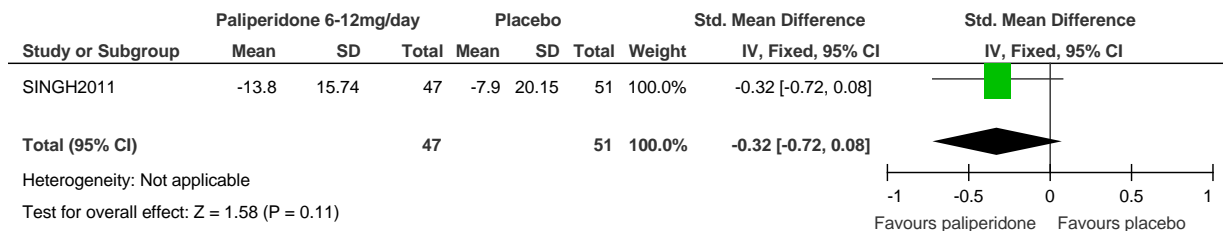


### 3.8 Response (CGI-I)

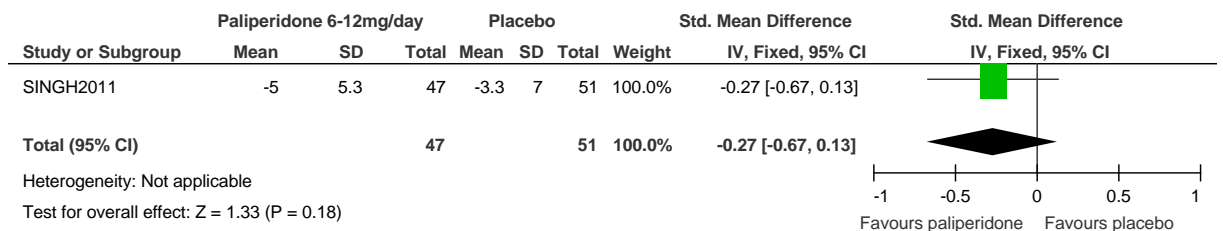


## 4. Additional (high) dose paliperidone versus placebo: post-treatment efficacy outcomes

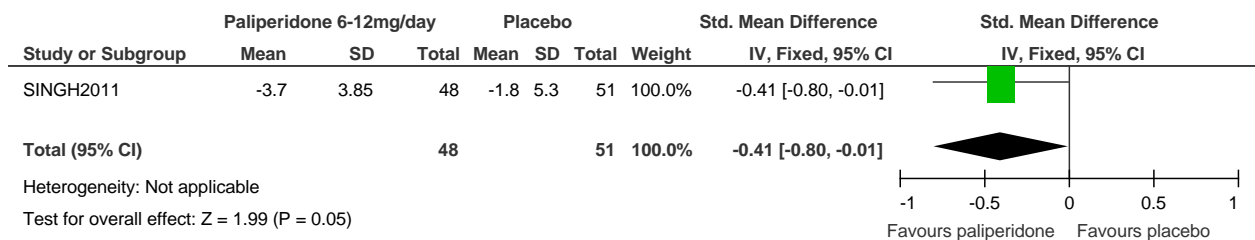
### 4.1 Mental state: mean change in total symptoms (PANSS)



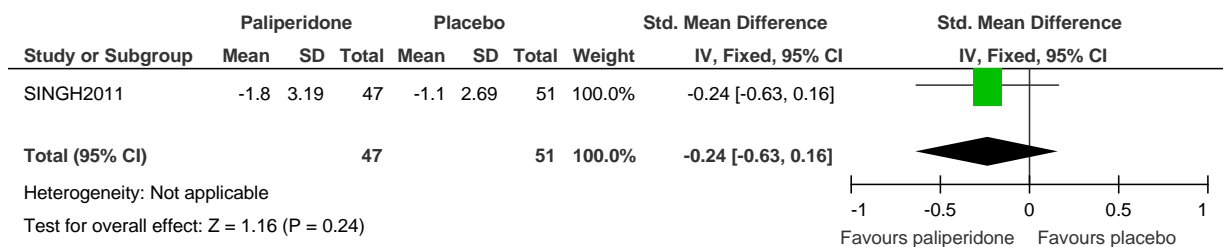
### 4.2 Mental state: mean change in positive symptoms (SAPS)



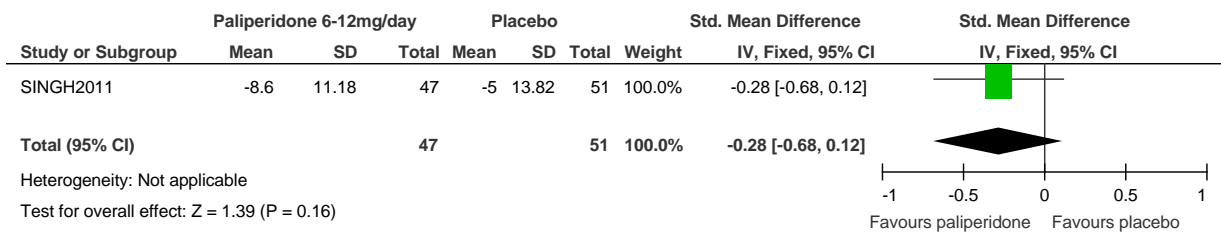
### 4.3 Mental state: mean change in negative symptoms (SANS)



### 4.4 Mental state: mean change in anxiety and depression (PANSS Anxiety and Depression)

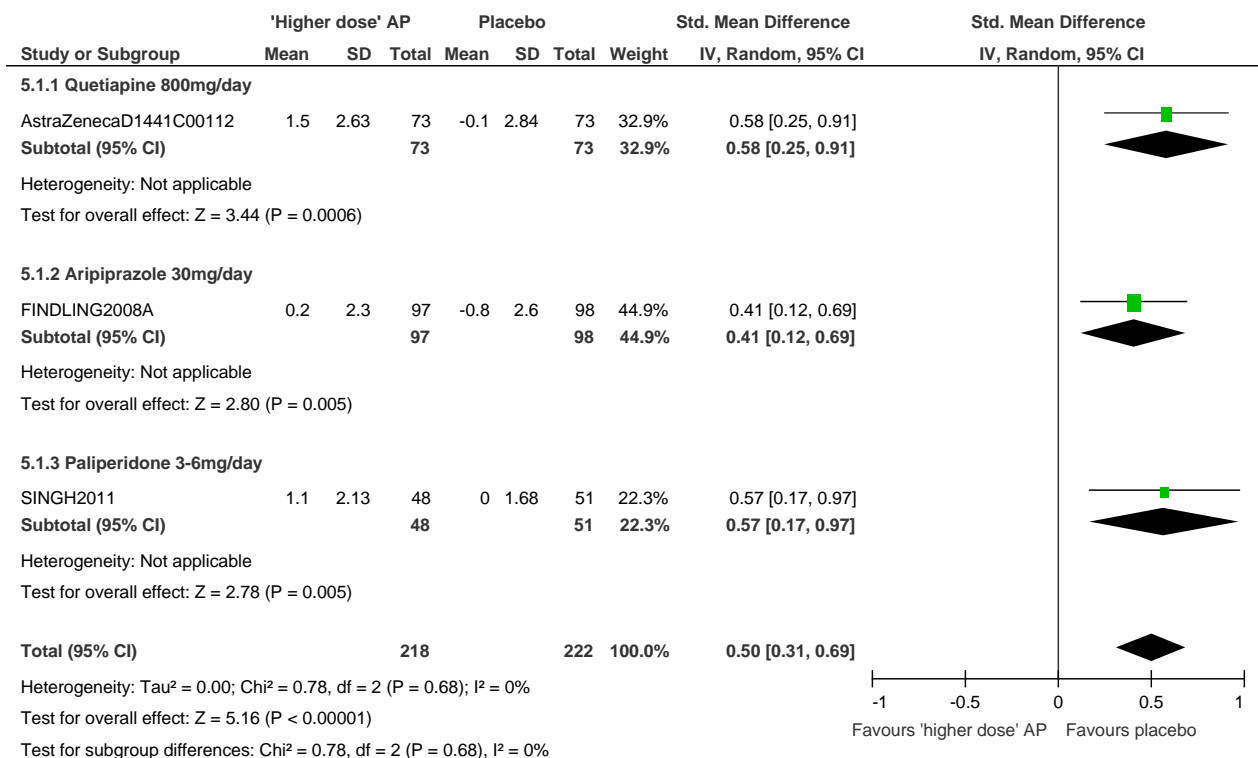


#### 4.5 Mean change in psychosocial functioning (CGAS)

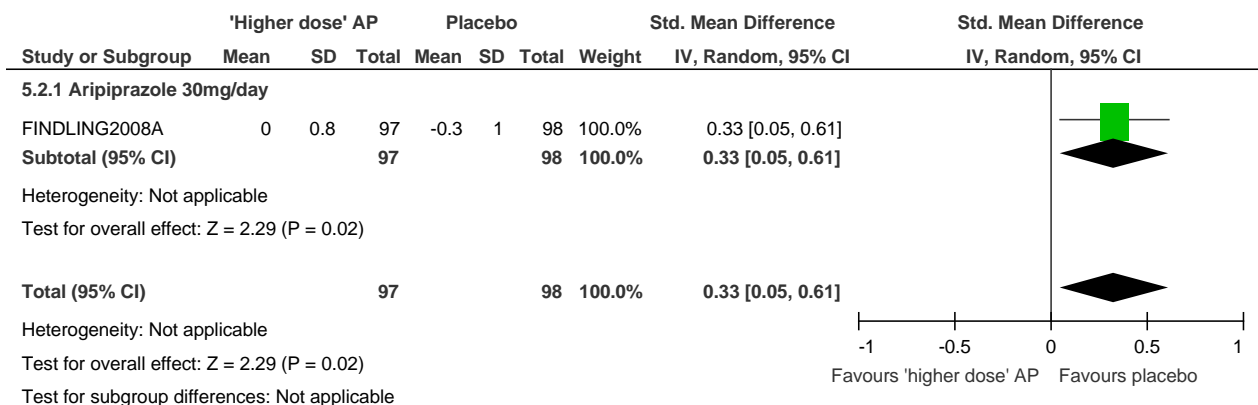


## 5. 'Higher dose' antipsychotic versus placebo: post-treatment side effect outcomes

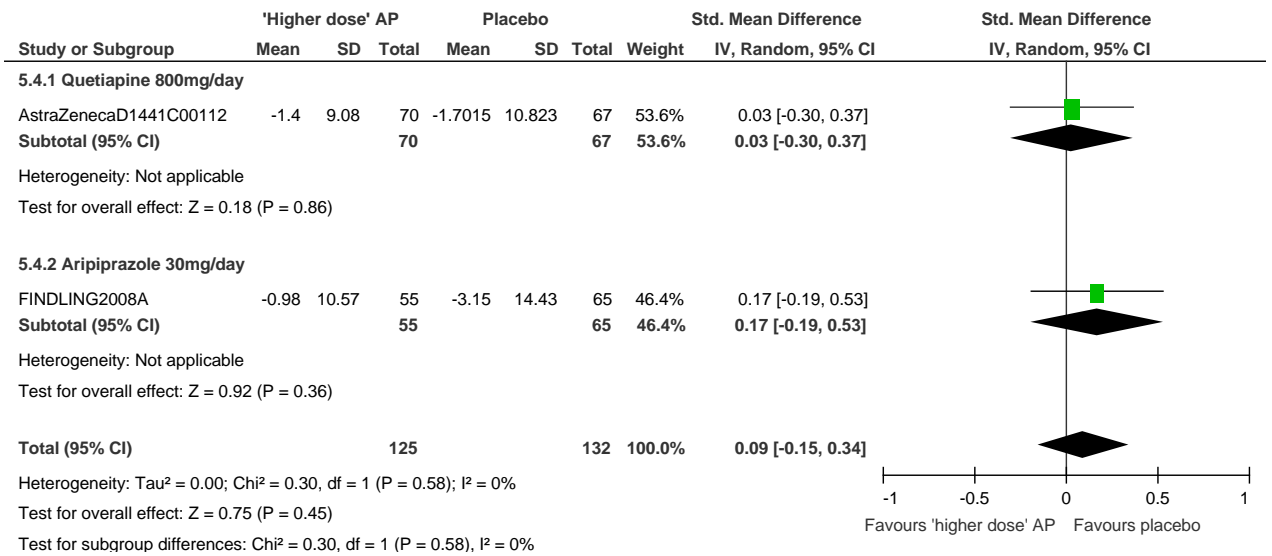
### 5.1 Mean change in weight (kg)



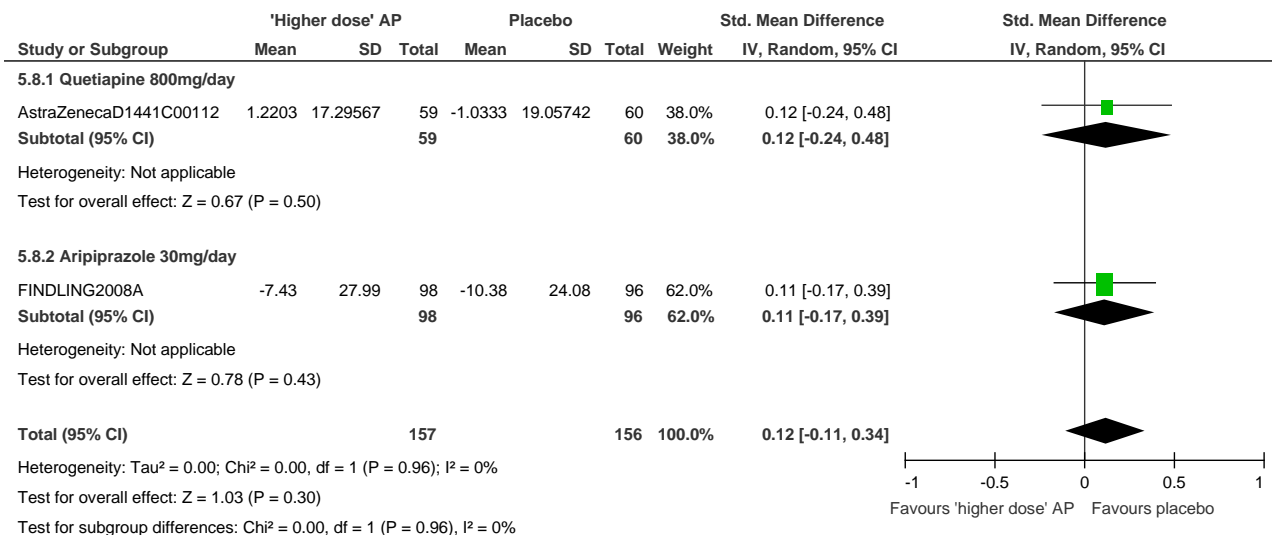
### 5.2 Mean change in BMI (kg/m<sup>2</sup>)



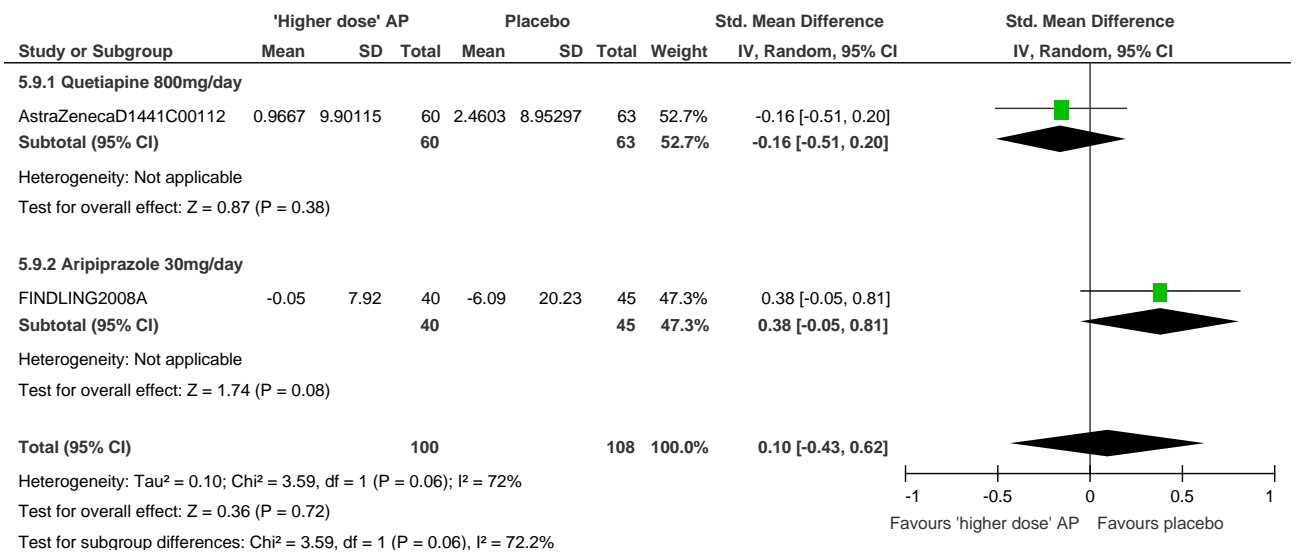
### 5.3 Mean change in fasting serum glucose level (mg/dl)



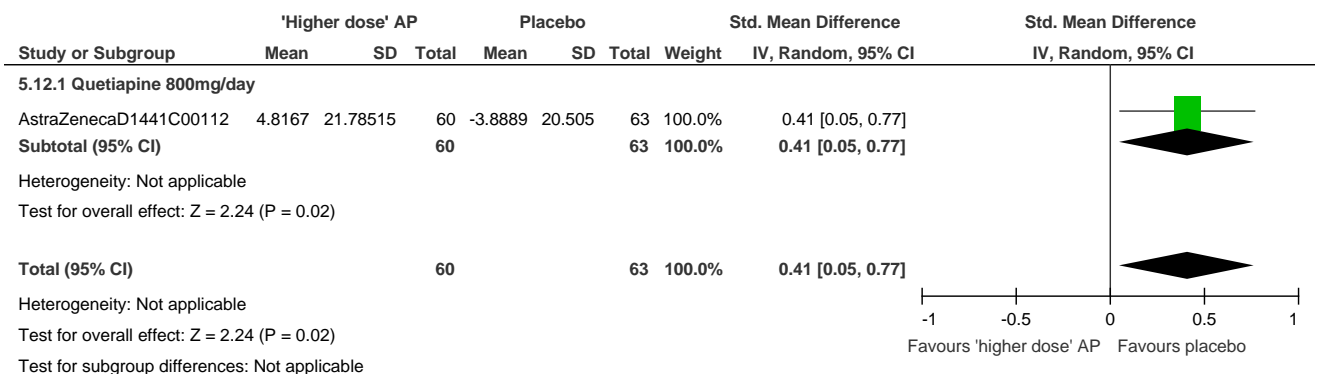
### 5.4 Mean change in fasting total cholesterol (mg/dl)



## 5.5 Mean change in fasting high-density lipoprotein cholesterol (mg/dl)

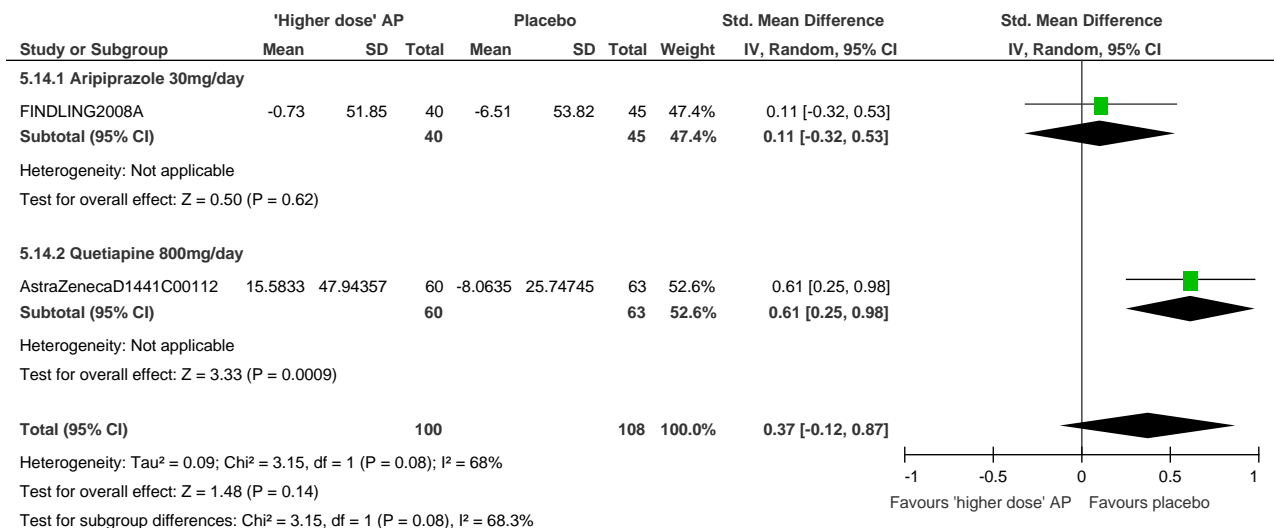


## 5.6 Mean change in fasting low-density lipoprotein cholesterol (mg/dl)

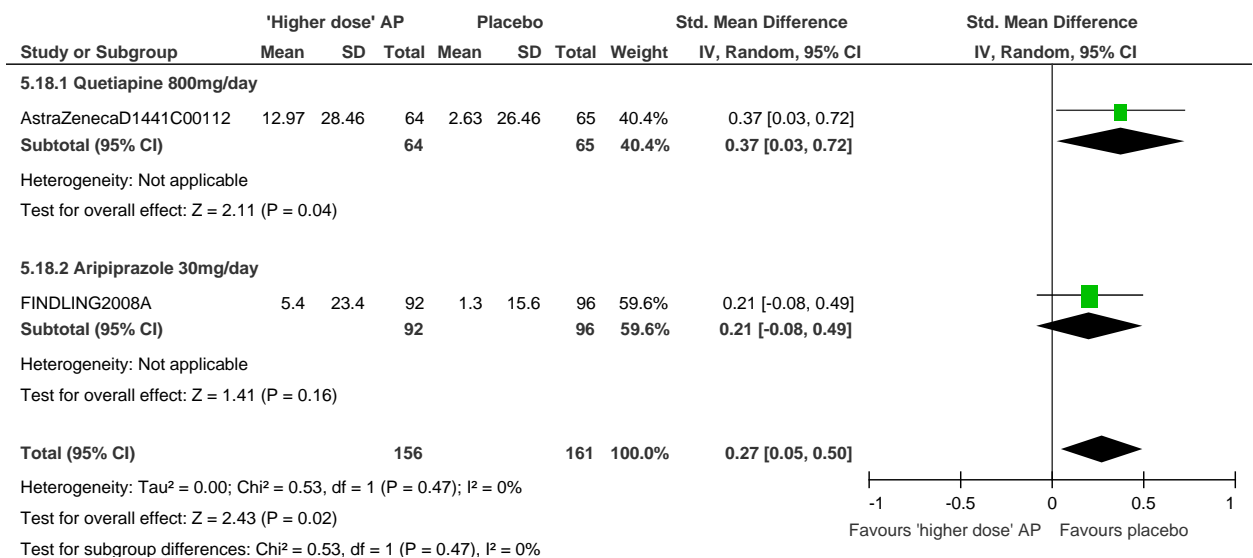




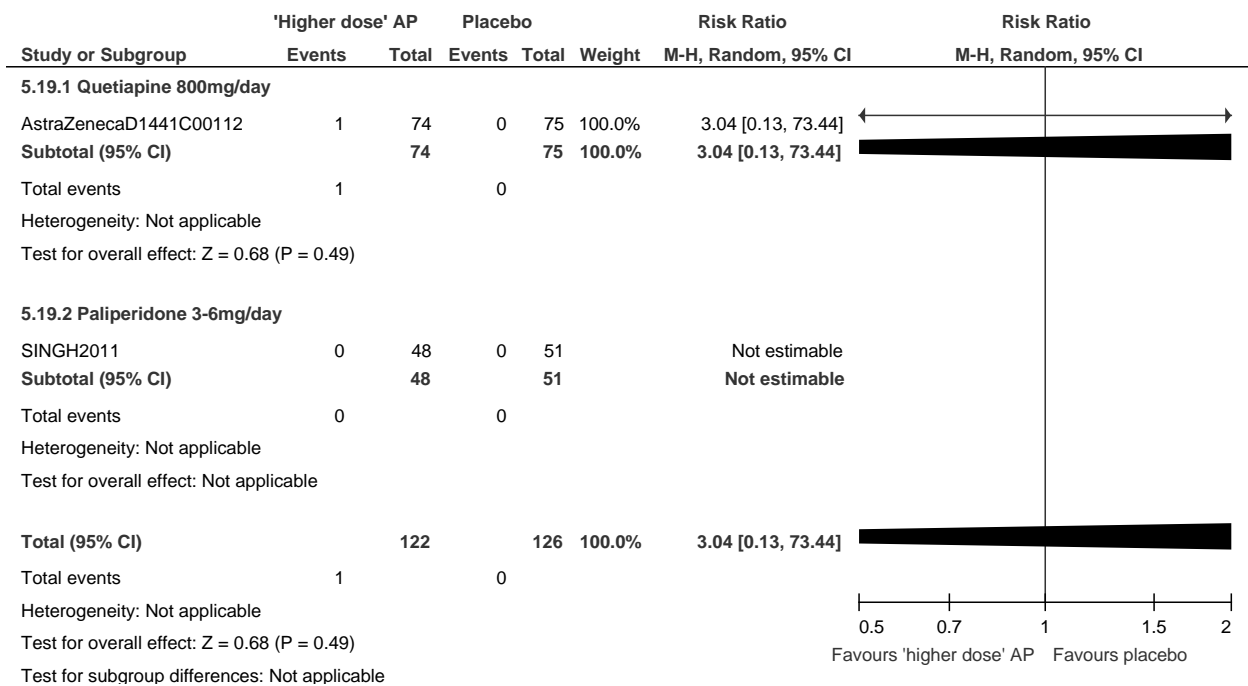
## 5.7 Mean change in fasting triglycerides (mg/dl)



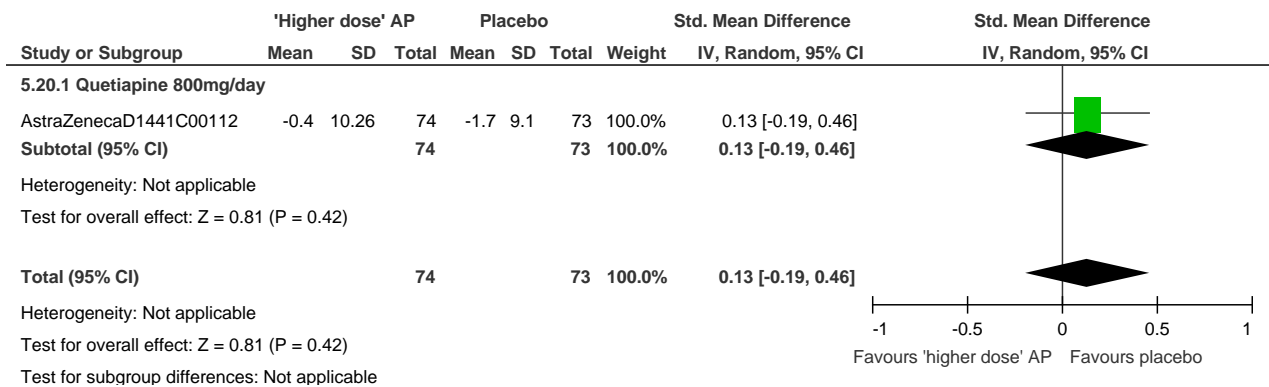
## 5.8 Mean change in QTcB interval (msec)



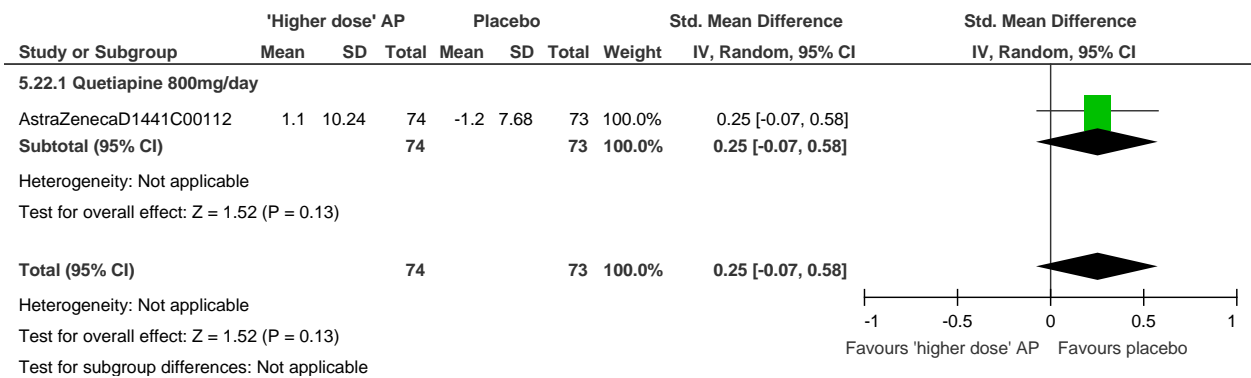
## 5.9 Prolonged QT interval (msec)



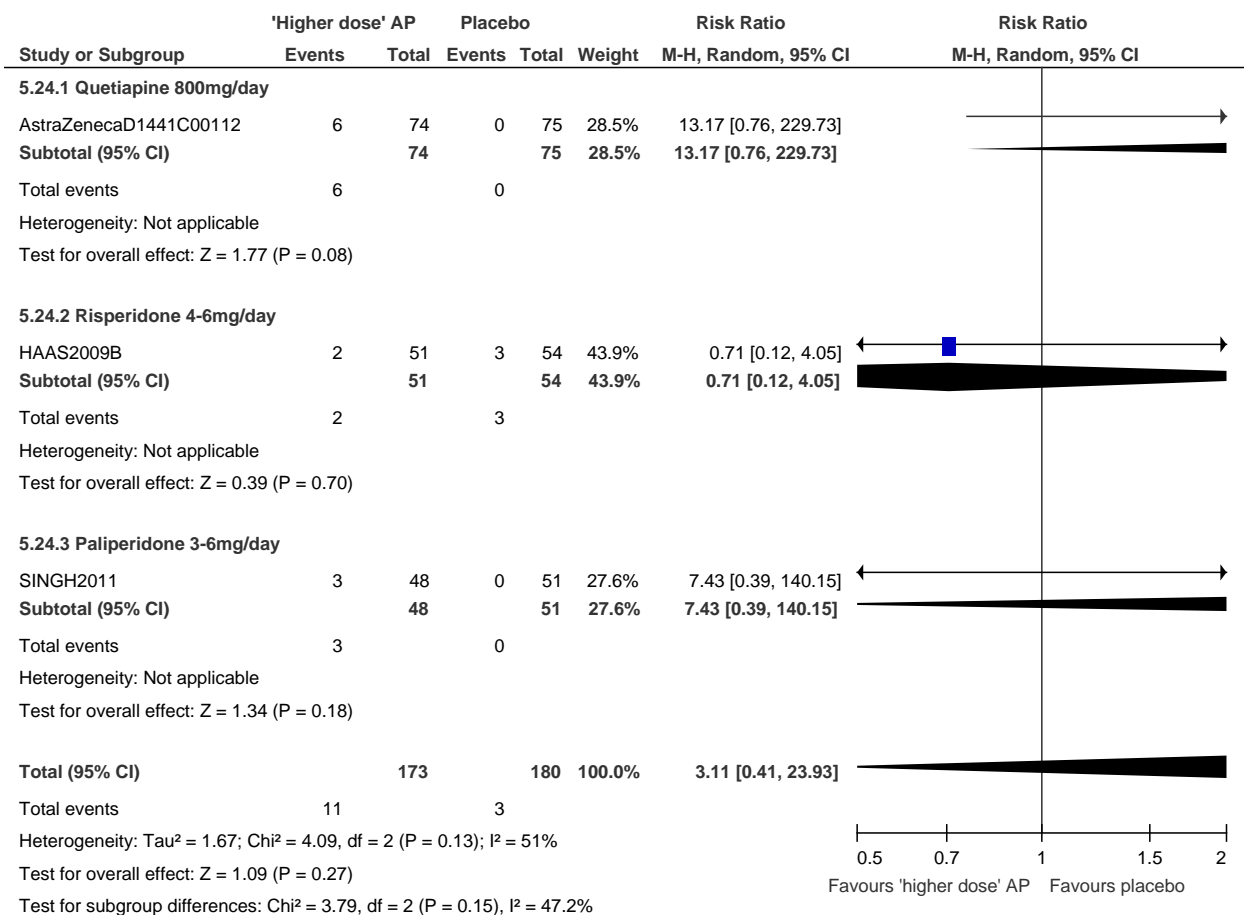
## 5.10 Mean change in systolic BP (mm Hg)



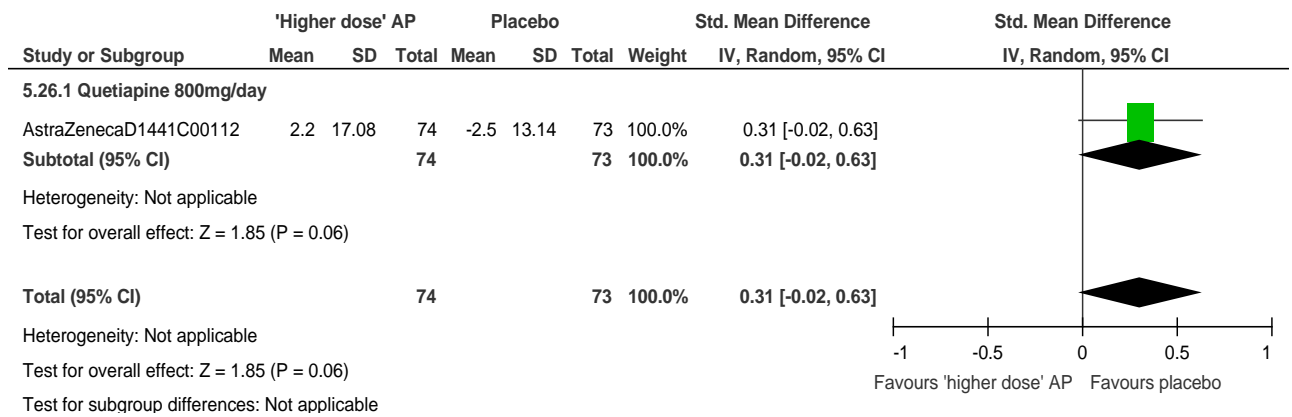
## 5.11 Mean change in diastolic BP (mm Hg)



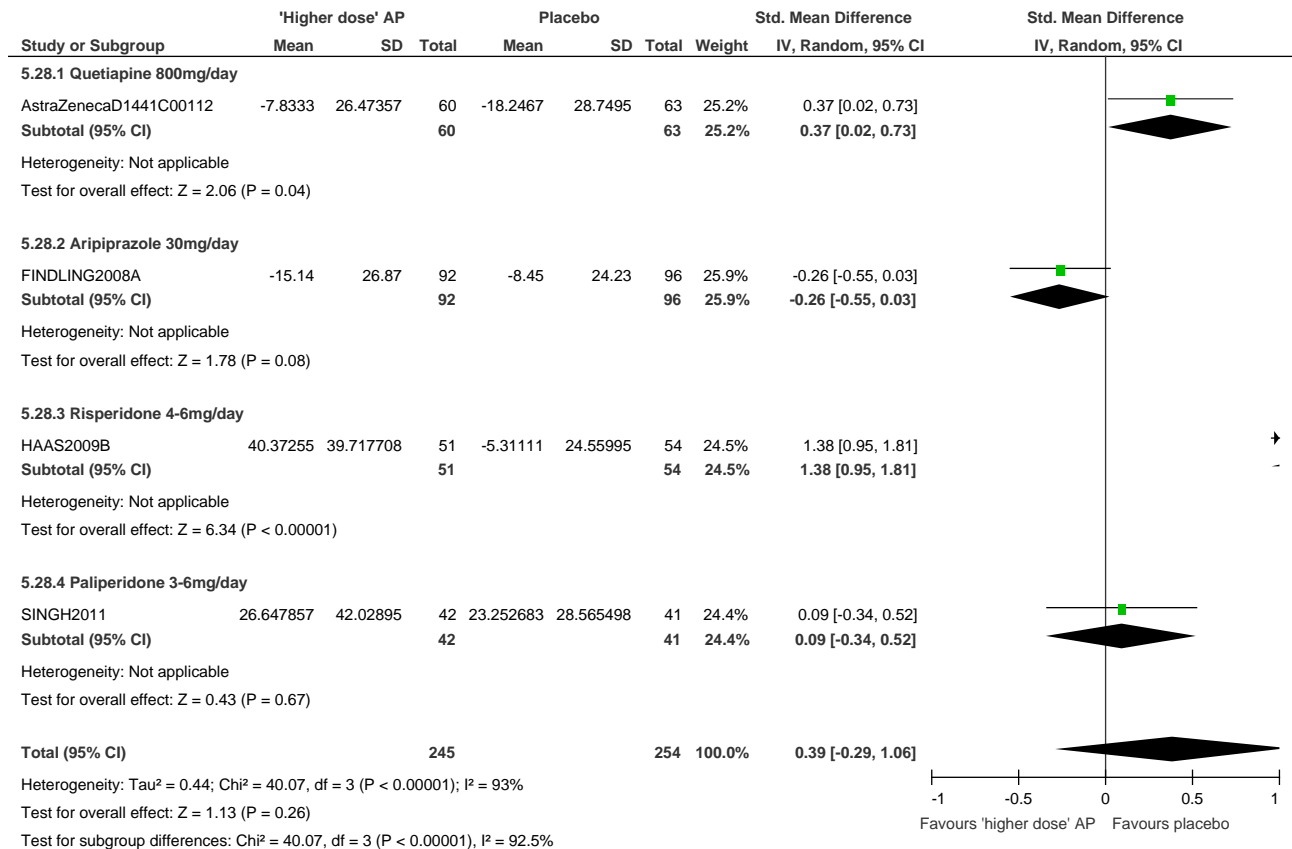
## 5.12 Tachycardia



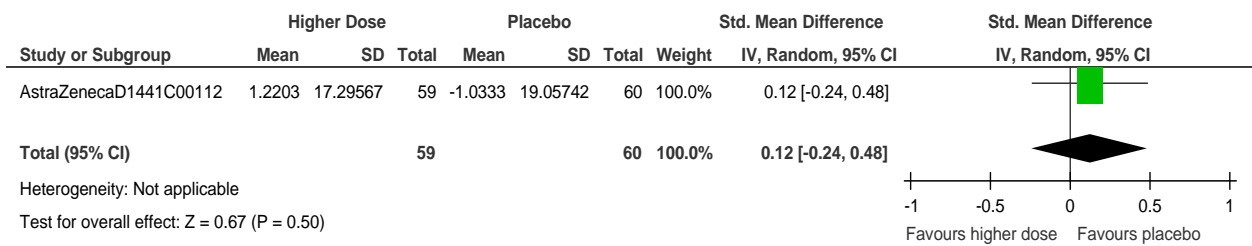
### 5.13 Mean change in standing pulse (BPM)



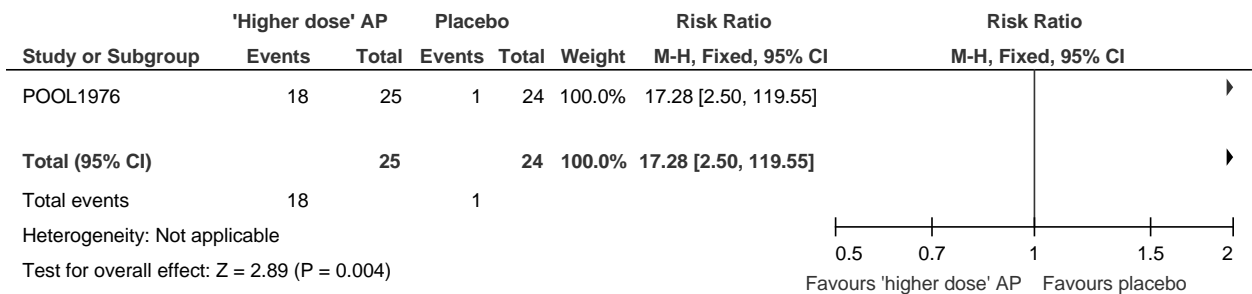
### 5.14 Mean change in prolactin (mg/dl)



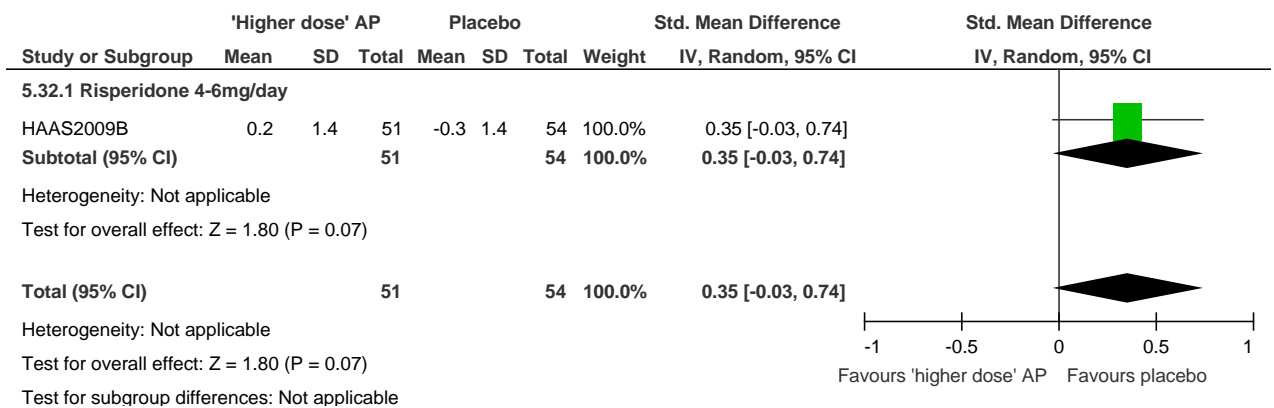
### 5.15 Mean change in insulin level (mg/dl)



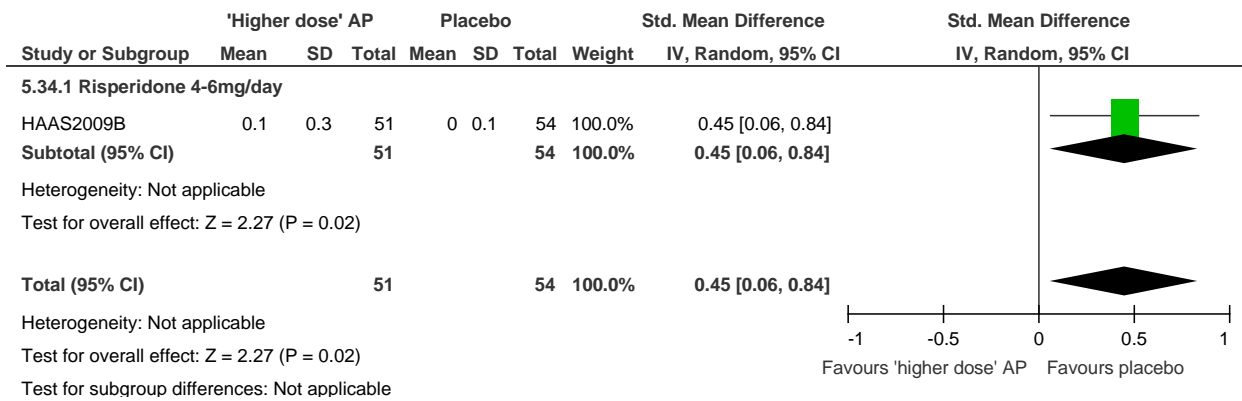
### 5.16 EPS



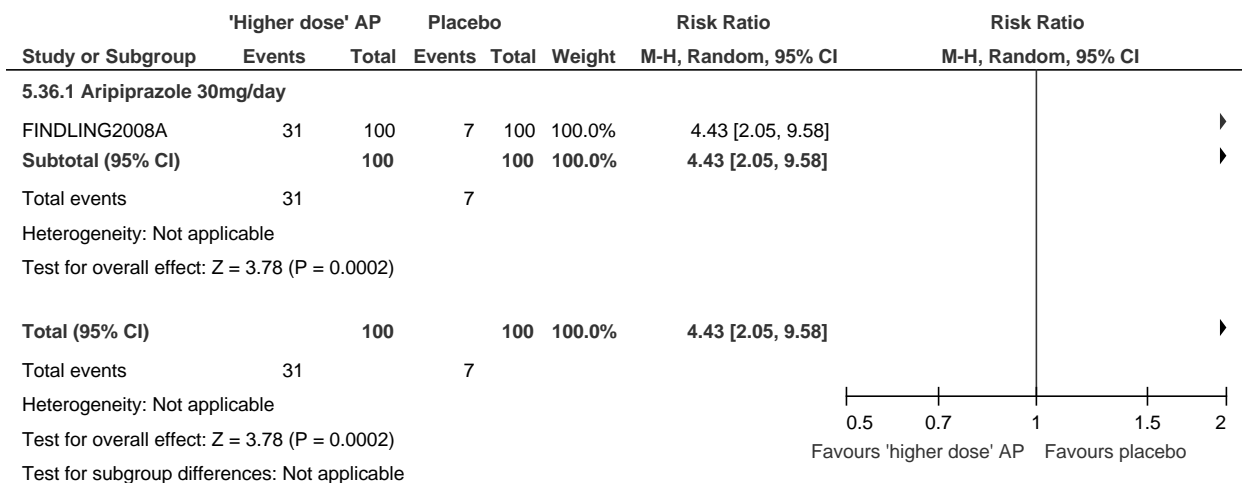
### 5.17 EPS (mean change in AIMS scores)



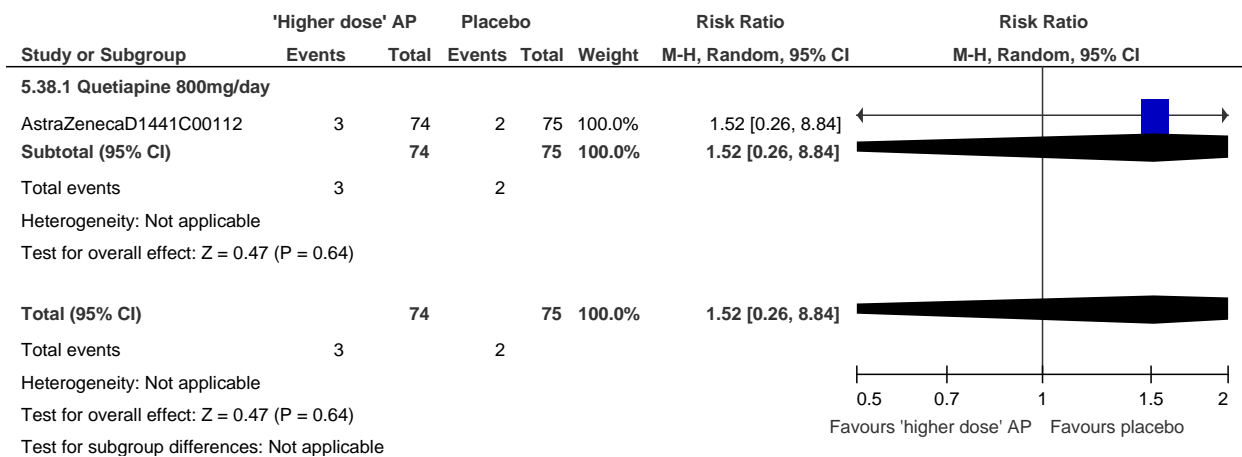
## 5.18 EPS (mean change in SAS scores)



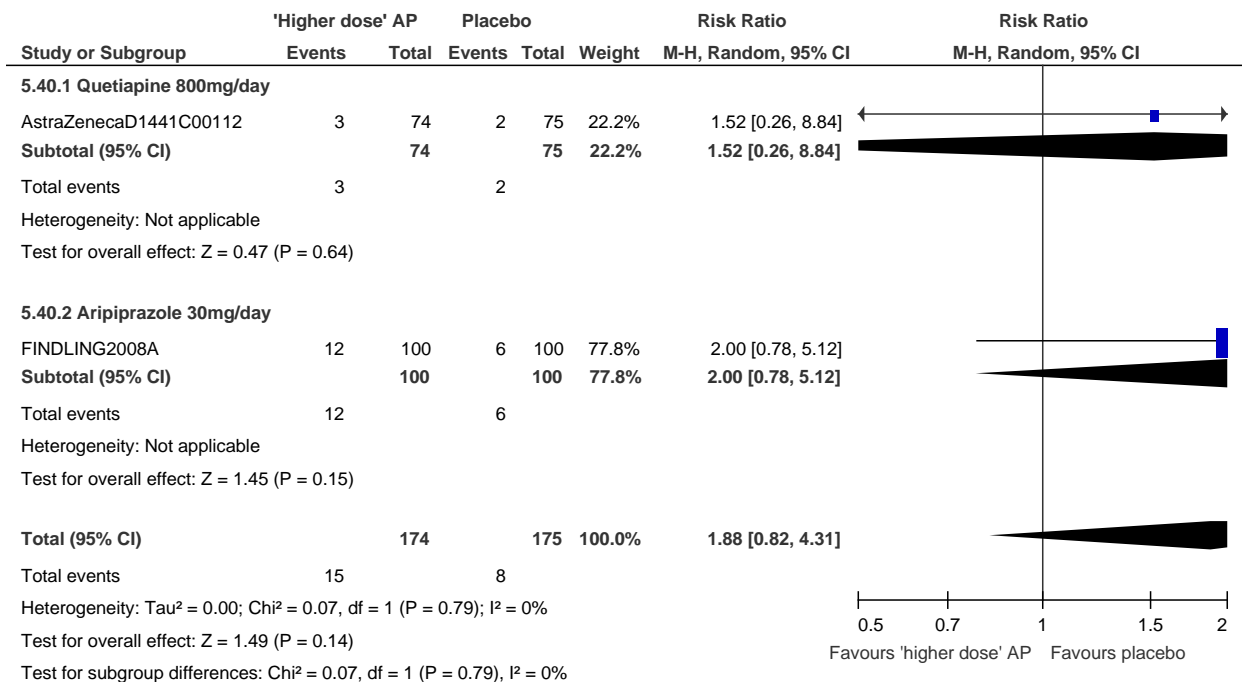
## 5.19 Parkinsonism



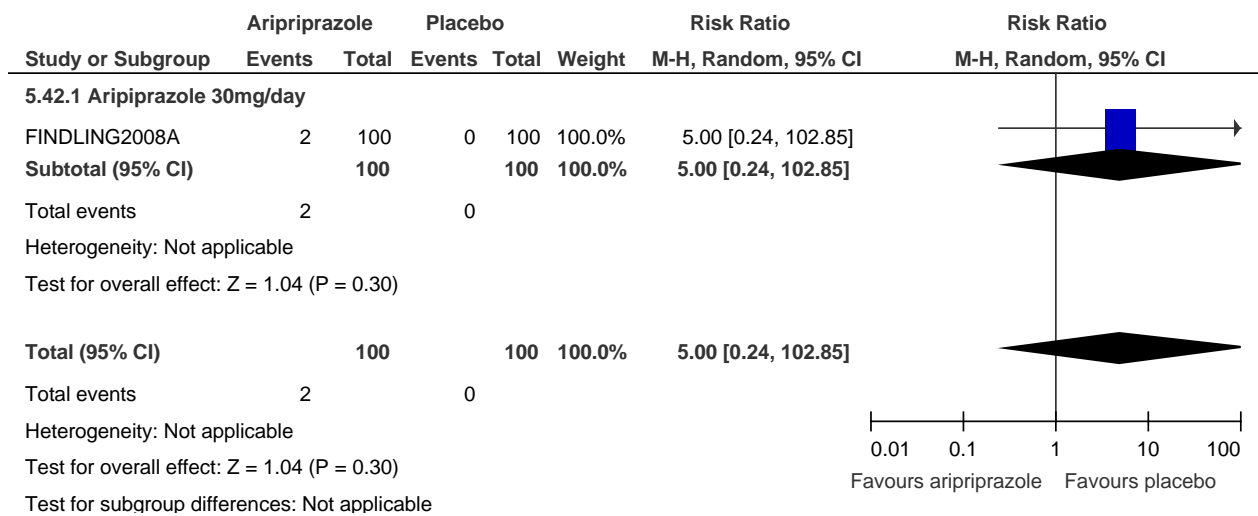
## 5.20 Tremor



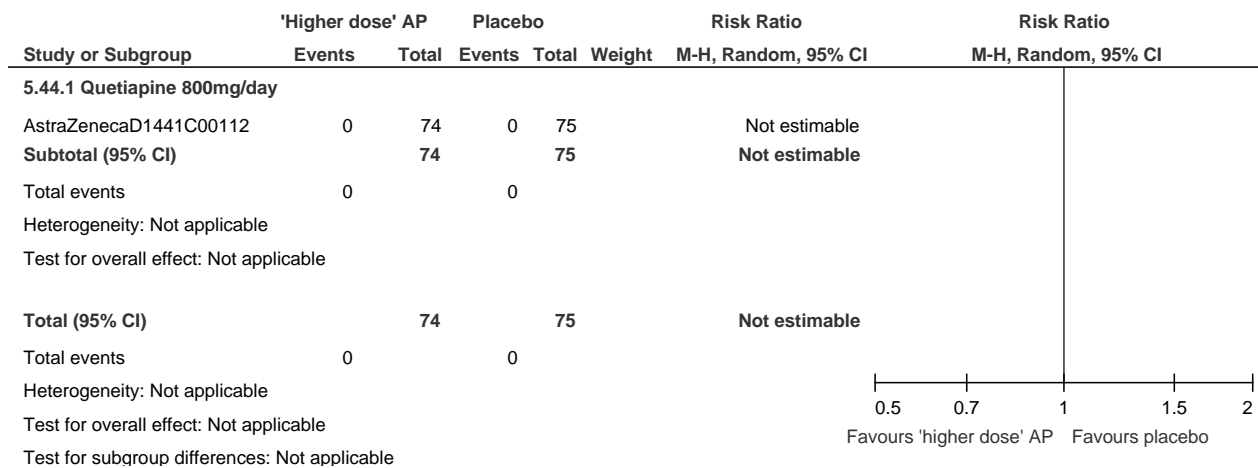
## 5.21 Akathisia



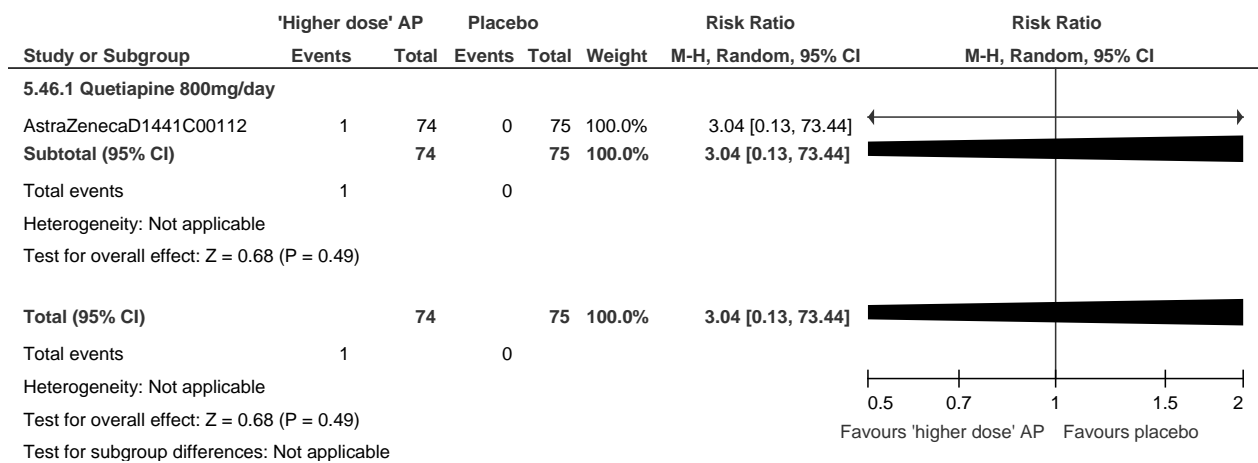
## 5.22 Dystonia



## 5.23 Dyskinesia



## 5.24 Extrapyramidal disorder



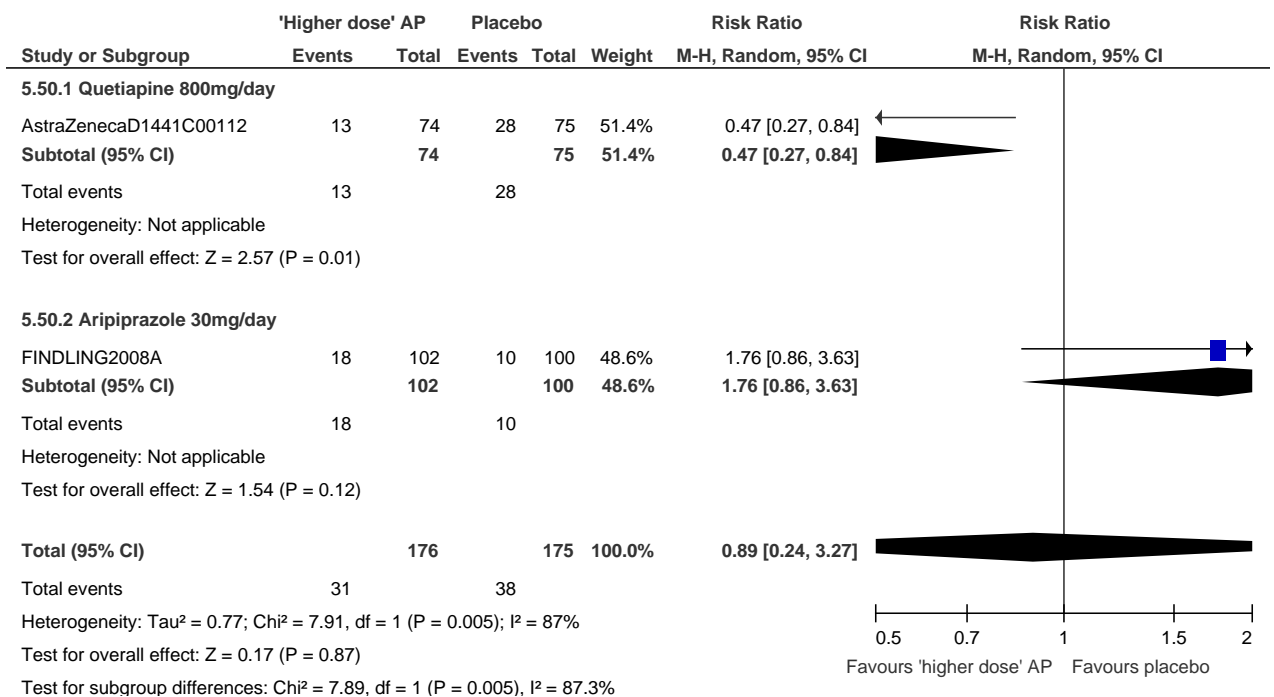


## 5.25 Mortality (including suicide)

Study or Subgroup	'Higher dose' AP		Placebo		Weight	Risk Ratio	Risk Ratio
	Events	Total	Events	Total		M-H, Random, 95% CI	M-H, Random, 95% CI
<b>5.48.1 Aripiprazole 30mg/day</b>							
FINDLING2008A	0	100	0	100		Not estimable	
<b>Subtotal (95% CI)</b>		<b>100</b>		<b>100</b>		<b>Not estimable</b>	
Total events	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
<b>5.48.2 Risperidone 4-6mg/day</b>							
HAAS2009B	0	51	0	54		Not estimable	
<b>Subtotal (95% CI)</b>		<b>51</b>		<b>54</b>		<b>Not estimable</b>	
Total events	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
<b>Total (95% CI)</b>		<b>151</b>		<b>154</b>		<b>Not estimable</b>	
Total events	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							

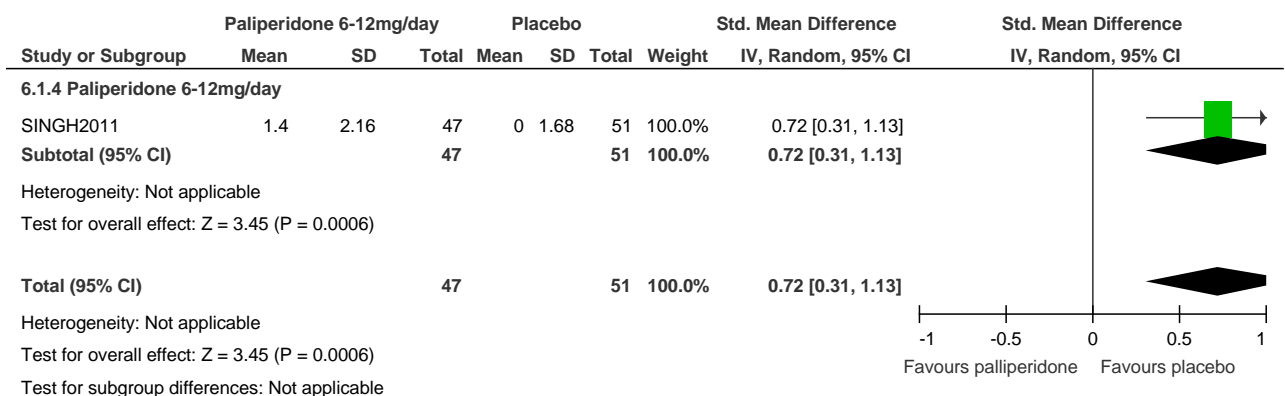
0.5    0.7    1    1.5    2  
 Favours 'higher dose' AP    Favours placebo

## 5.26 Leaving the study early for any reason

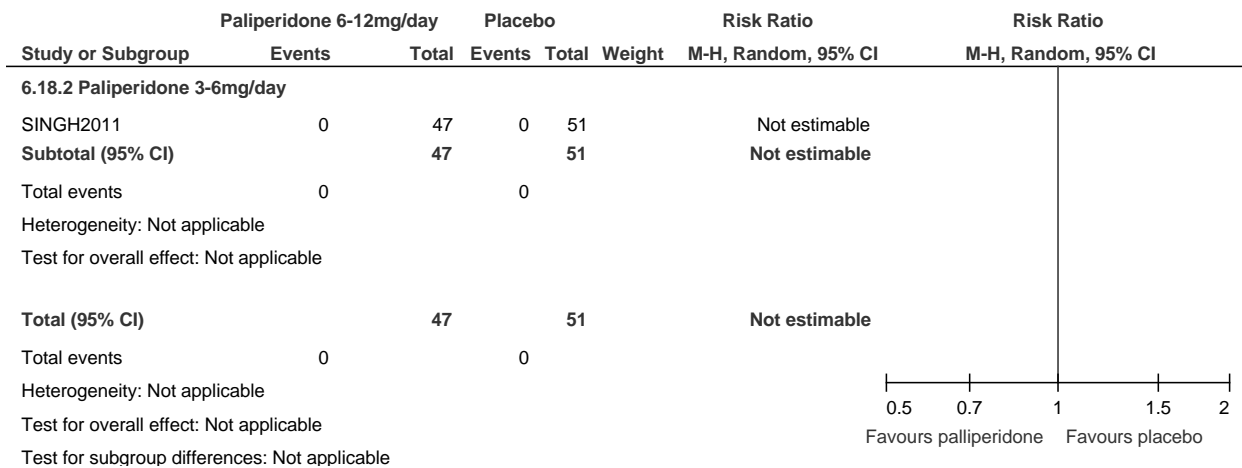


## 6. Additional (high) dose paliperidone versus placebo: post-treatment side effect outcomes

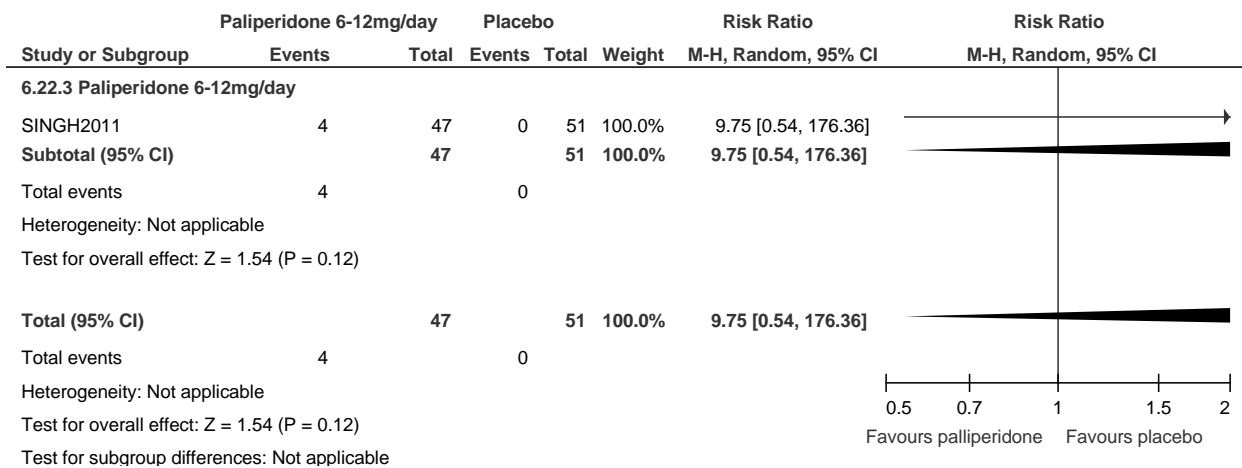
### 6.1 Mean change in weight (kg)



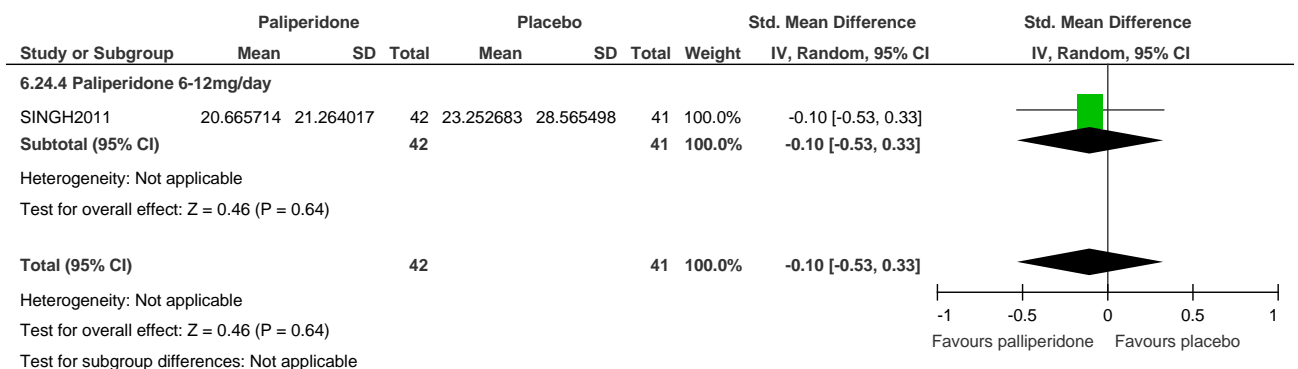
## 6.2 Prolonged QT interval



## 6.3 Tachycardia

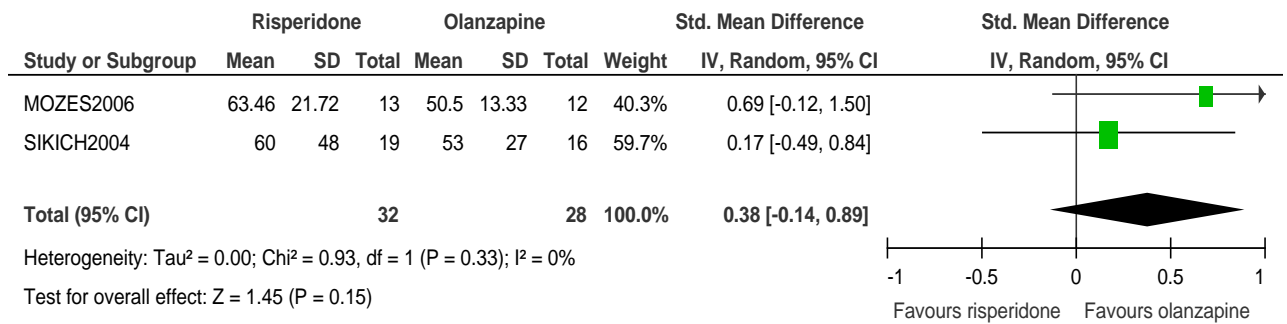


## 6.4 Prolactin (mg/dl)

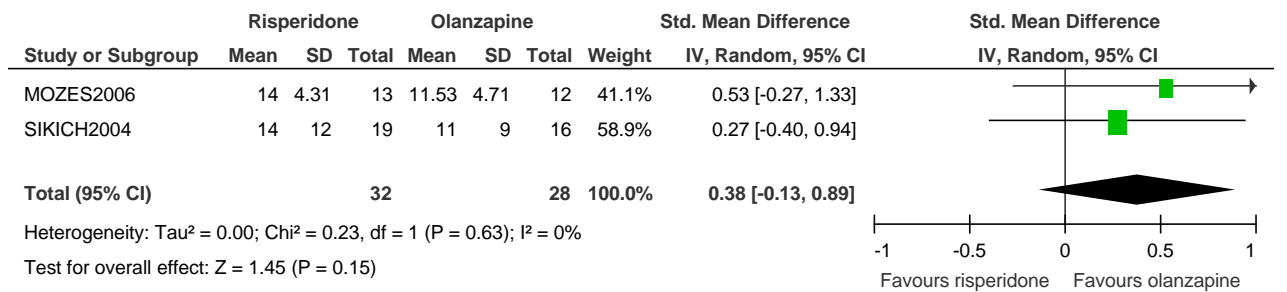


## 7. Risperidone versus olanzapine: post-treatment efficacy outcomes

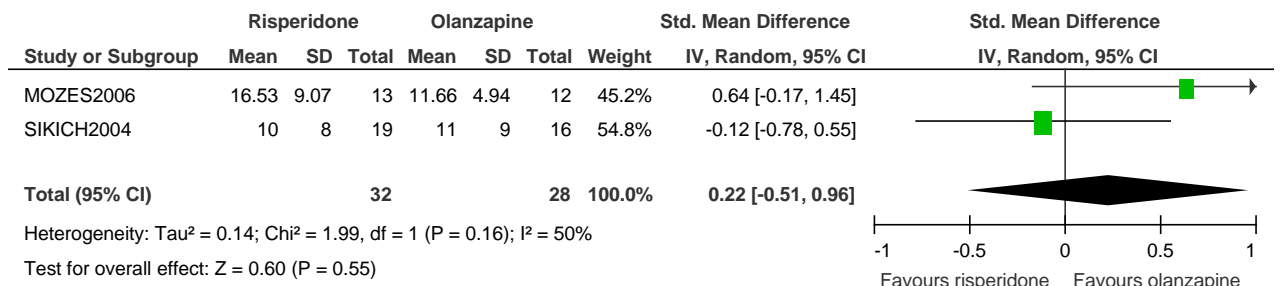
### 7.1 Mental state: mean endpoint total symptoms (PANSS, BPRS-C)



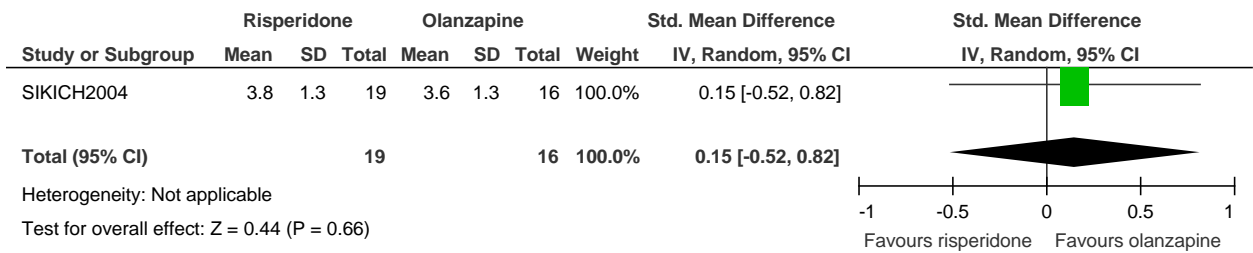
### 7.2 Mental state: mean endpoint positive symptoms (PANSS Positive, CPRS Positive)



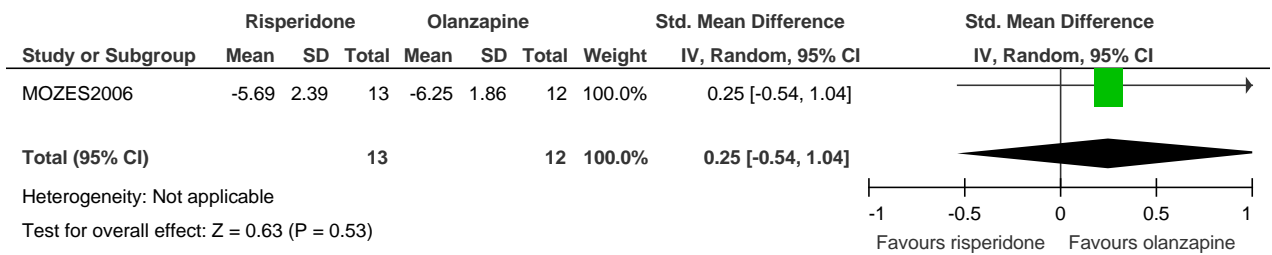
### 7.3 Mental state: mean endpoint negative symptoms (PANSS Negative, CPRS Negative)



## 7.4 Mean endpoint global state: severity (CGI-S)

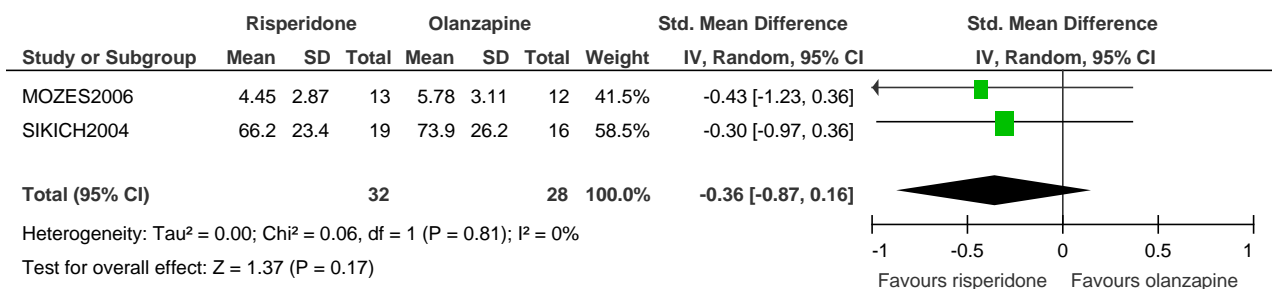


## 7.5 Mean endpoint psychosocial functioning (CGAS)

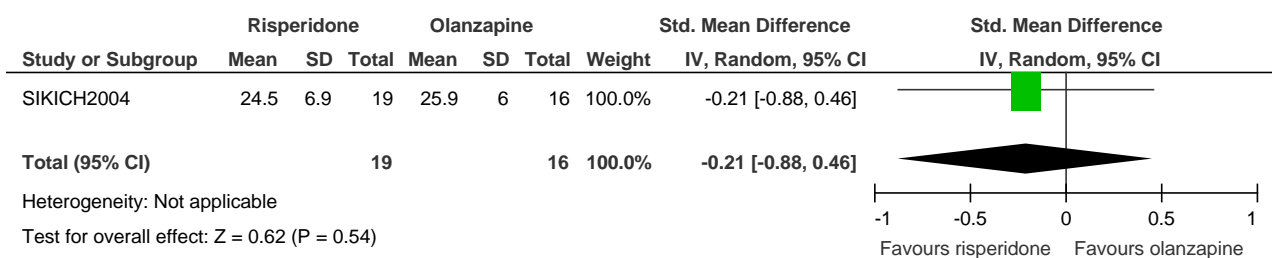


## 8. Risperidone versus olanzapine: post-treatment side effect outcomes

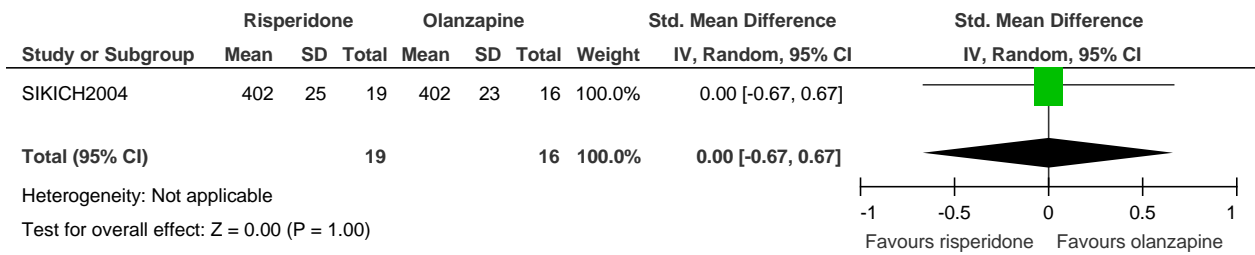
### 8.1 Weight (kg)



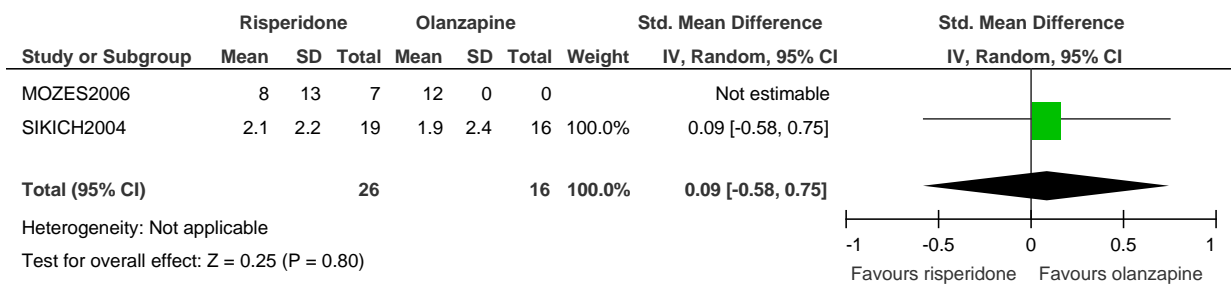
### 8.2 Mean endpoint BMI (kg/m<sup>2</sup>)



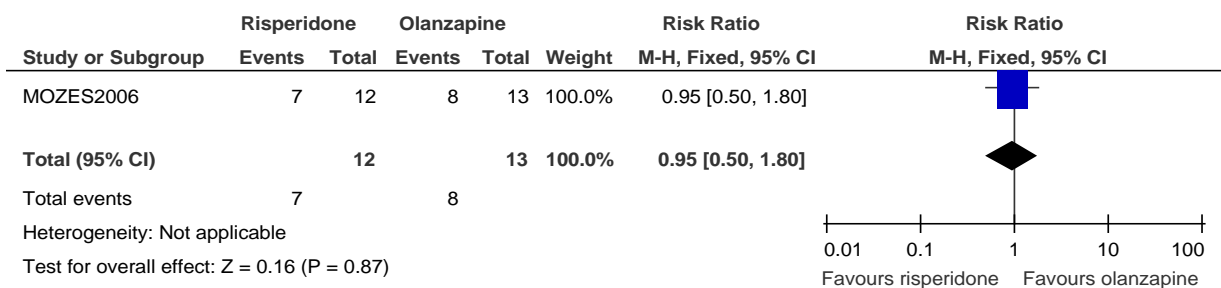
### 8.3 Mean endpoint QT interval (msec)



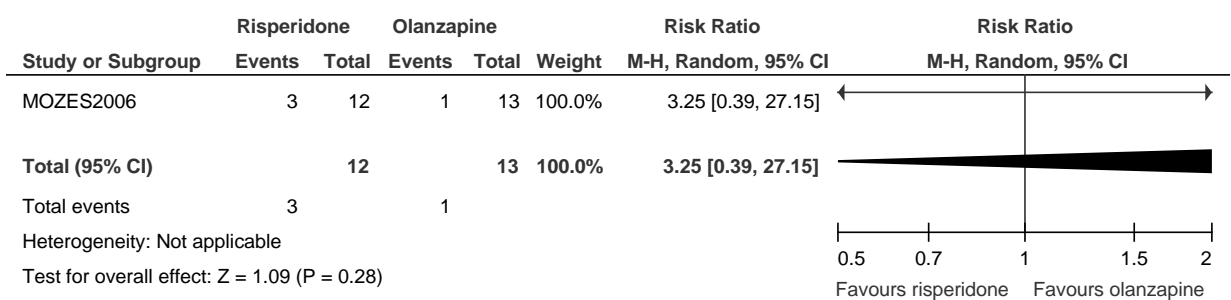
### 8.4 Mean endpoint EPS (SAS scores)



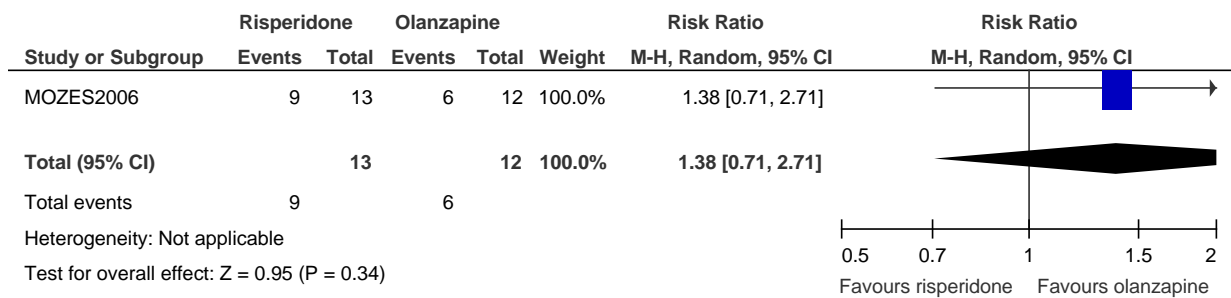
### 8.5 EPS (number of participants who developed EPS measured using SAS)



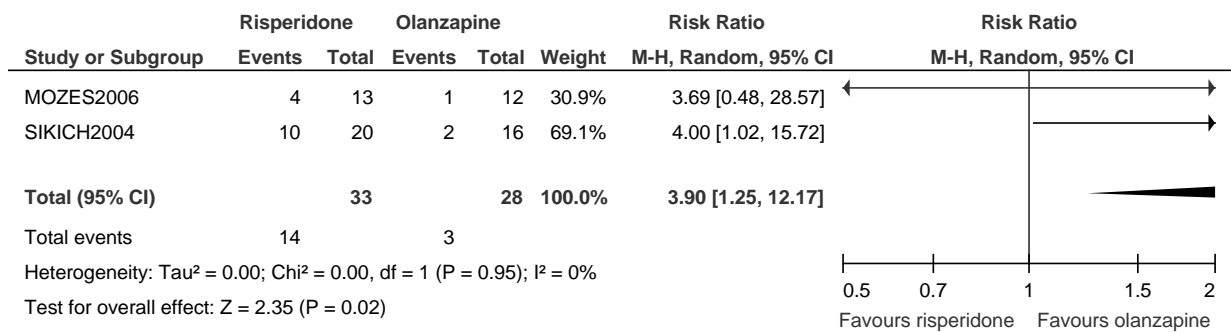
### 8.6 Mean endpoint EPS (BARS scores)



## 8.7 Tremor

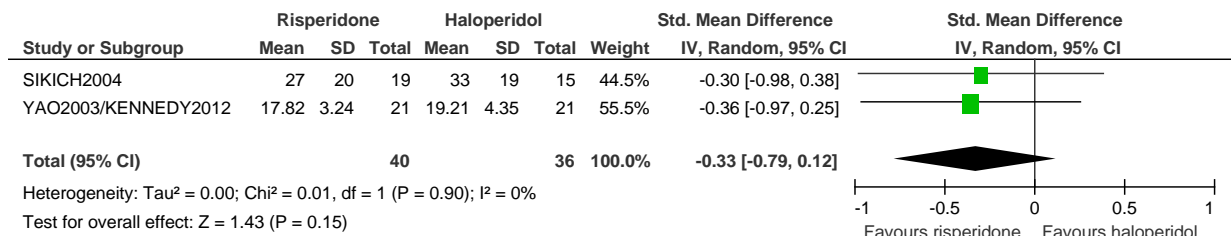


## 8.8 Leaving the study early for any reason

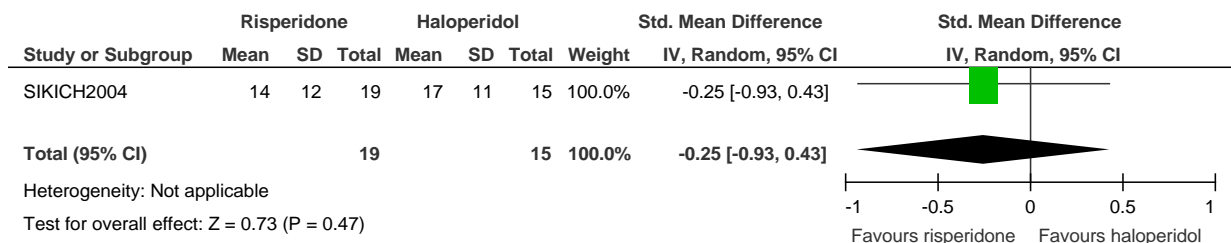


## 9. Risperidone versus haloperidol: post-treatment efficacy outcomes

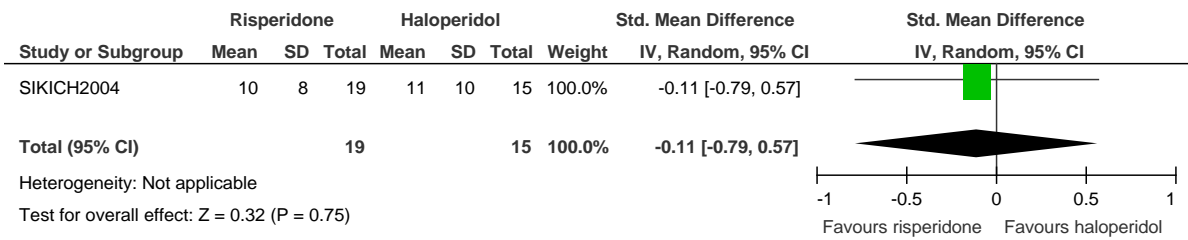
### 9.1 Mental state: mean endpoint total symptoms (BPRS)



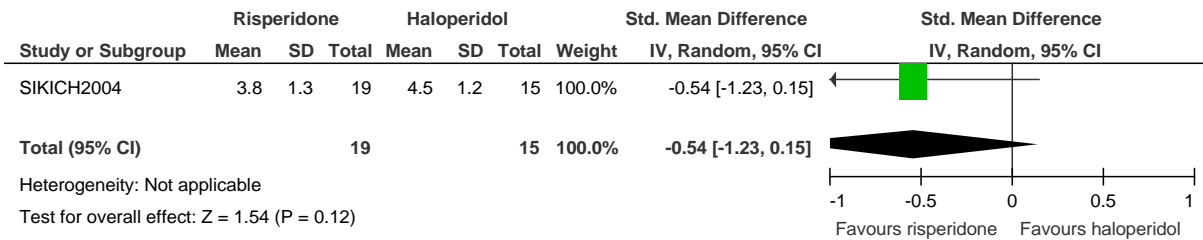
### 9.2 Mental state: mean endpoint positive symptoms (CPRS-Positive)



### 9.3 Mental state: mean endpoint negative symptoms (CPRS-Negative)

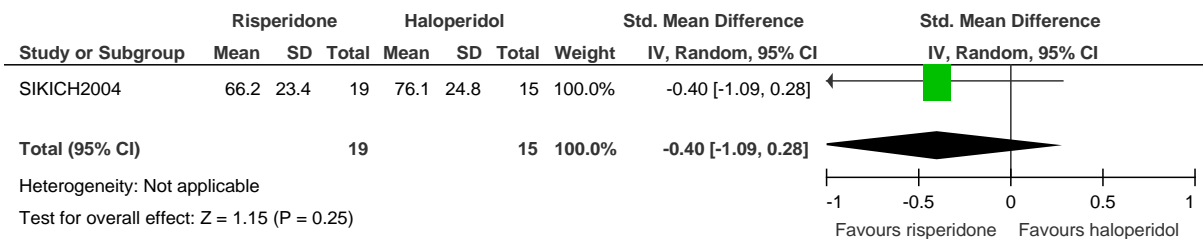


### 9.4 Mean endpoint global state: severity (CGI-S)

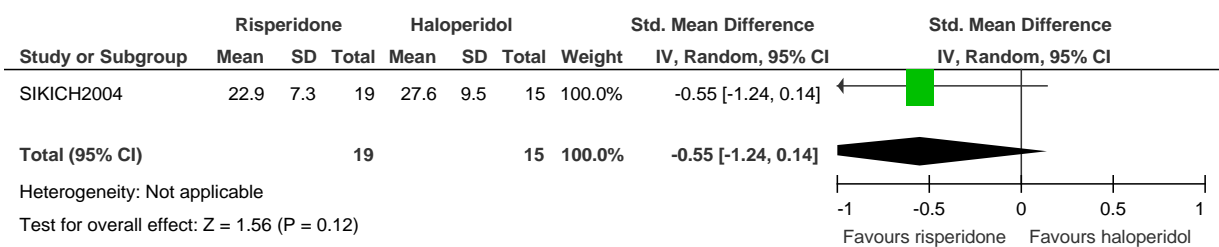


## 10. Risperidone versus haloperidol: post-treatment side effect outcomes

### 10.1 Mean endpoint weight (kg)

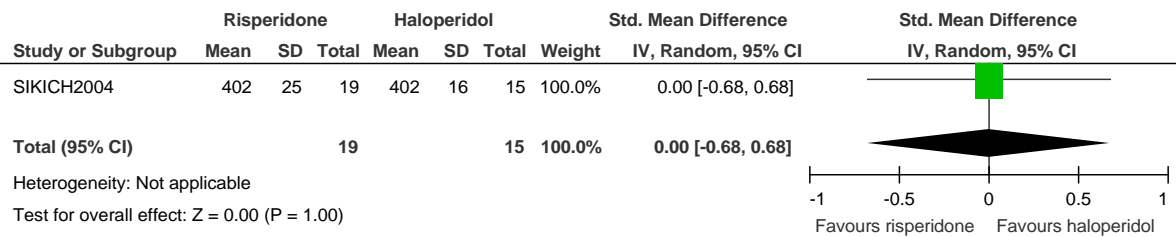


### 10.2 Mean endpoint BMI (kg/m<sup>2</sup>)

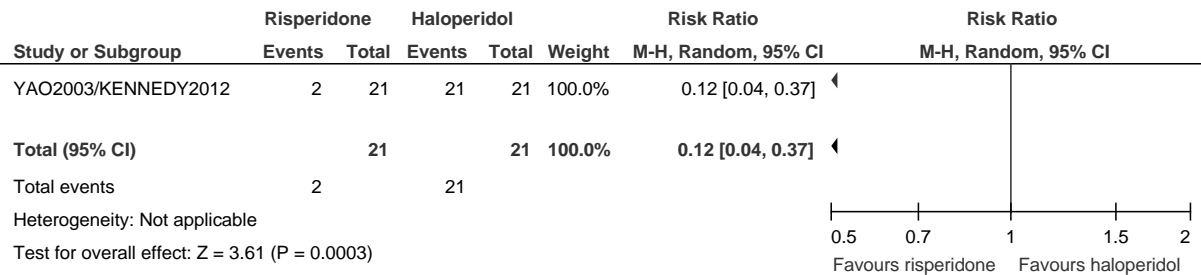




### 10.3 Mean endpoint QT interval (msec)



### 10.4 EPS

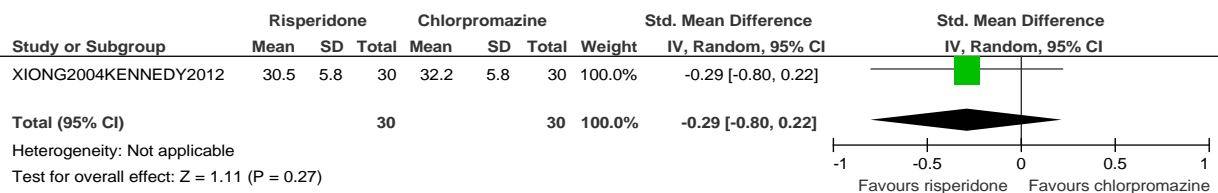


### 10.5 Leaving the study early for any reason



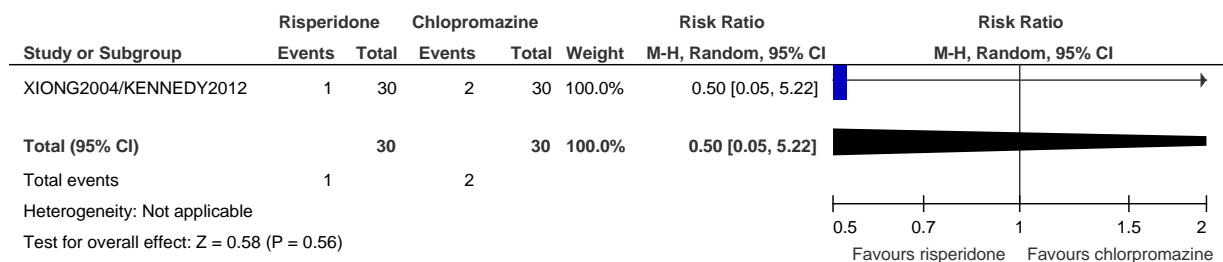
## 11. Chlorpromazine versus risperidone: post-treatment efficacy outcomes

### 11.1 Mental state: total symptoms (BPRS)



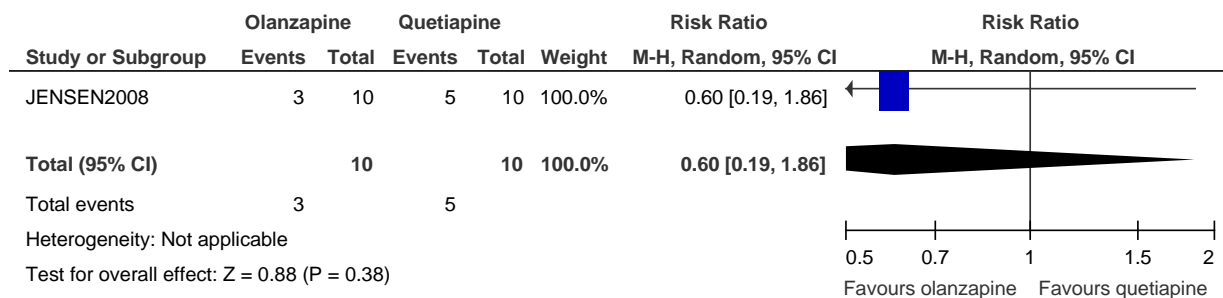
## 12. Chlorpromazine versus risperidone: post-treatment side effect outcomes

### 12.1 Tremor



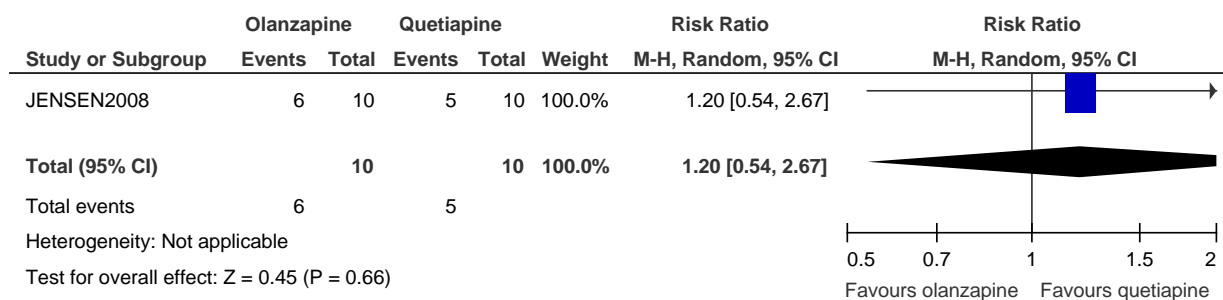
## 13. Olanzapine versus quetiapine: post-treatment efficacy outcomes

### 13.1 Response (40% reduction in PANSS total and subscale scores)

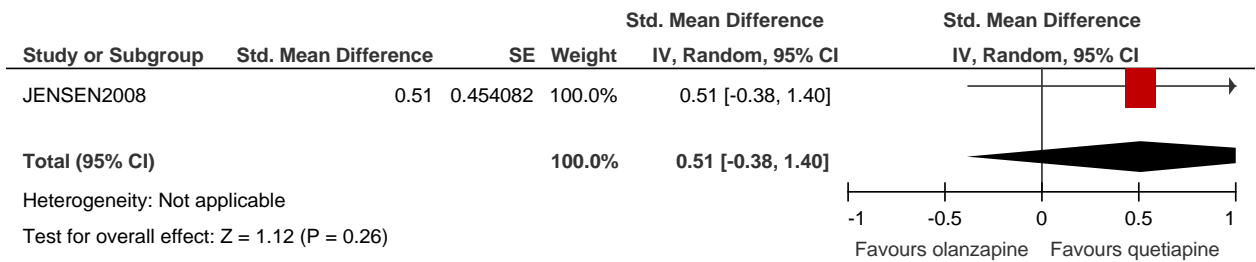


## 14. Olanzapine versus quetiapine: post-treatment side effect outcomes

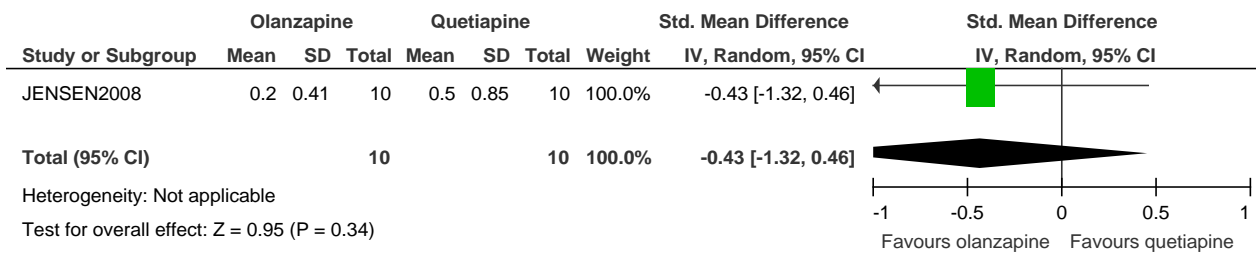
### 14.1 Weight gain (number of participants with kg gain of >7% from baseline)



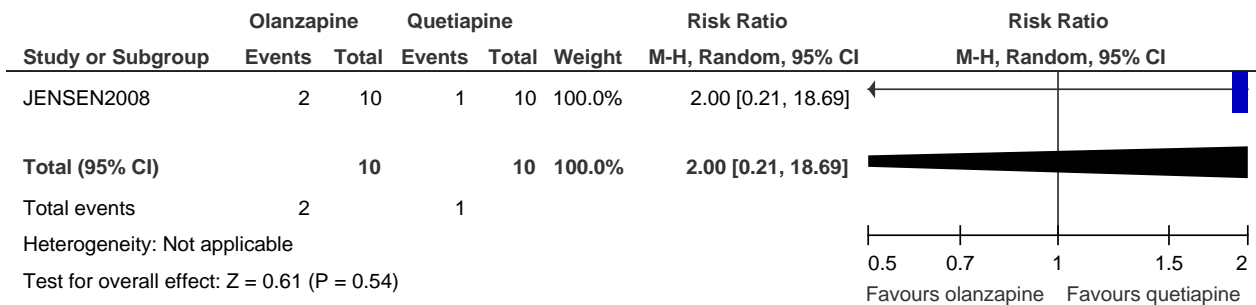
## 14.2 Mean endpoint BMI (kg/m<sup>2</sup>)



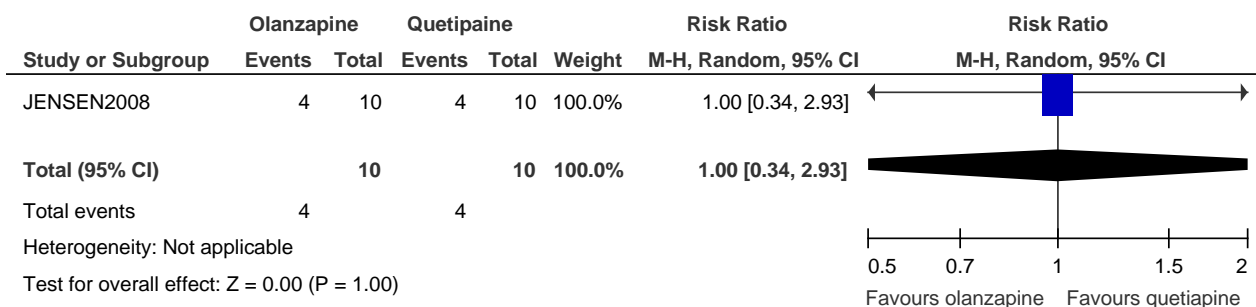
## 14.3 Mean endpoint EPS (SAS scores)



## 14.4 Akathisia

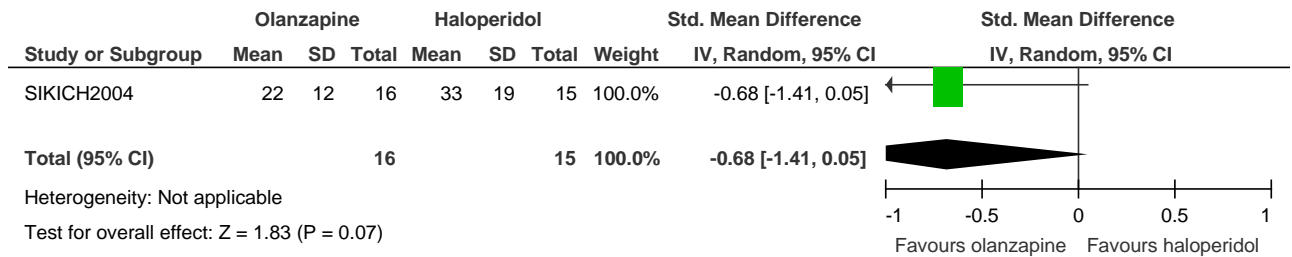


## 14.5 Leaving the study early for any reason

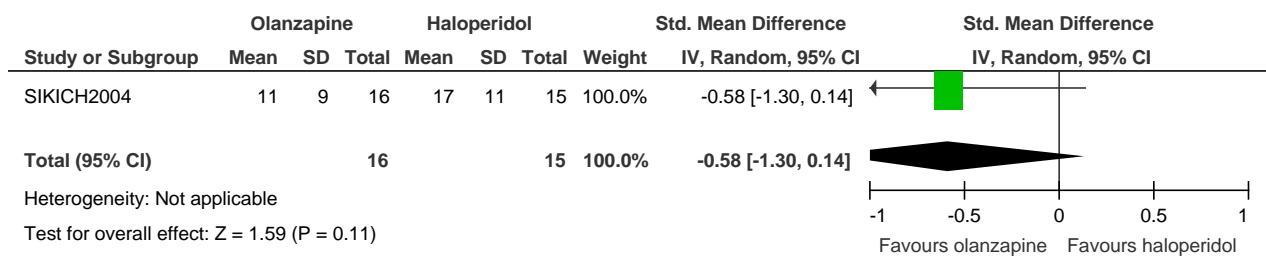


## 15. Olanzapine versus haloperidol: post-treatment efficacy outcomes

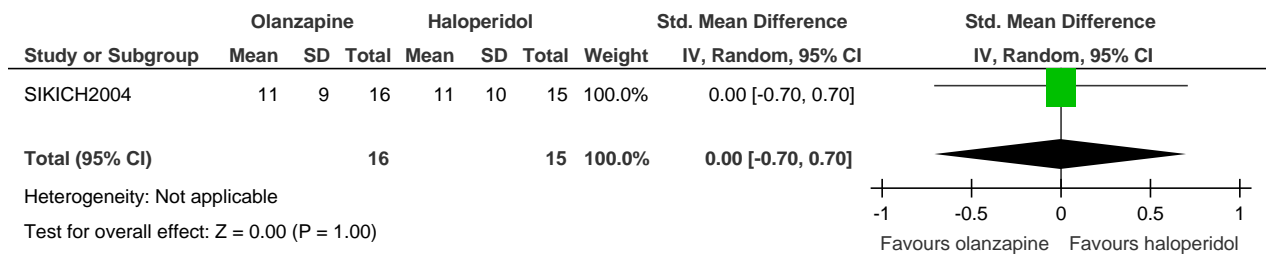
### 15.1 Mental state: mean endpoint total symptoms (BPRS-C)



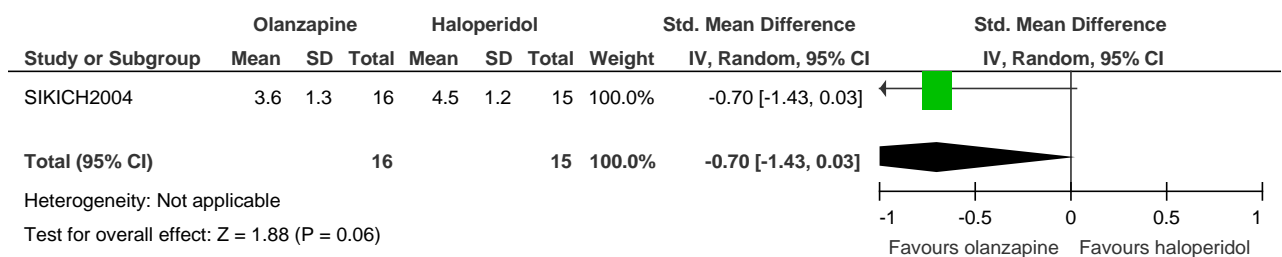
### 15.2 Mental state: mean endpoint in positive symptoms (CPRS Positive)



### 15.3 Mental state: mean endpoint negative symptoms (CPRS Negative)

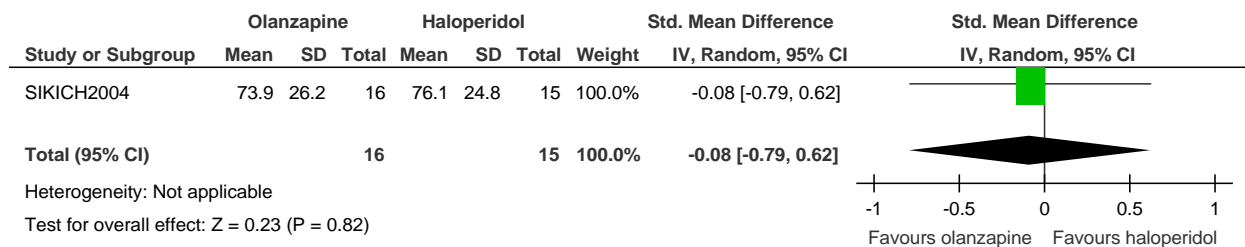


### 15.4 Mean endpoint in global state: severity (CGI-S)

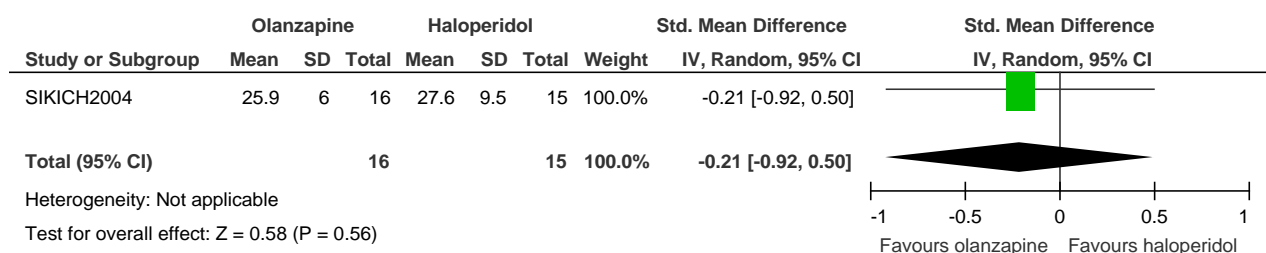


## 16. Olanzapine versus haloperidol: post-treatment side effect outcomes

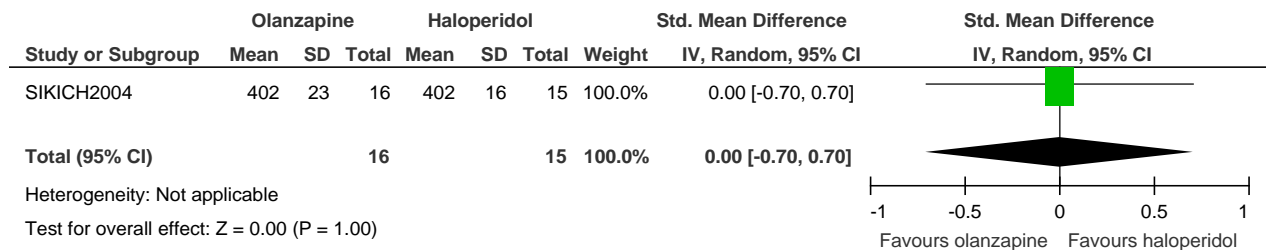
### 16.1 Mean endpoint in weight (kg)



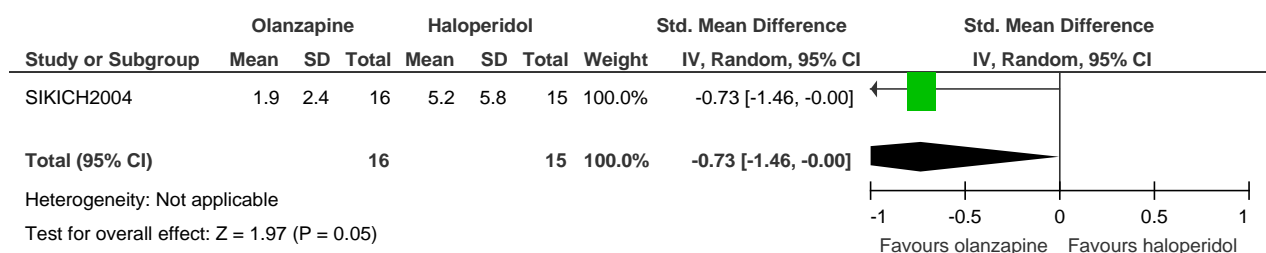
### 16.2 Mean endpoint BMI (kg/m<sup>2</sup>)



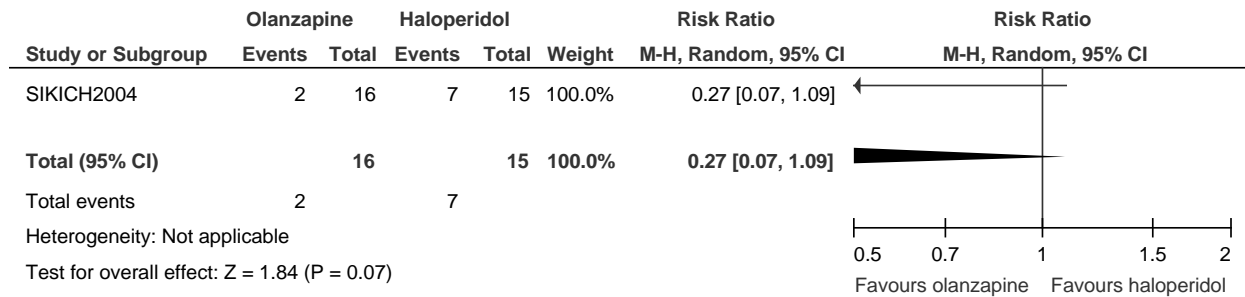
### 16.3 Mean endpoint QT interval (msec)



### 16.4 Mean endpoint EPS (SAS scores)

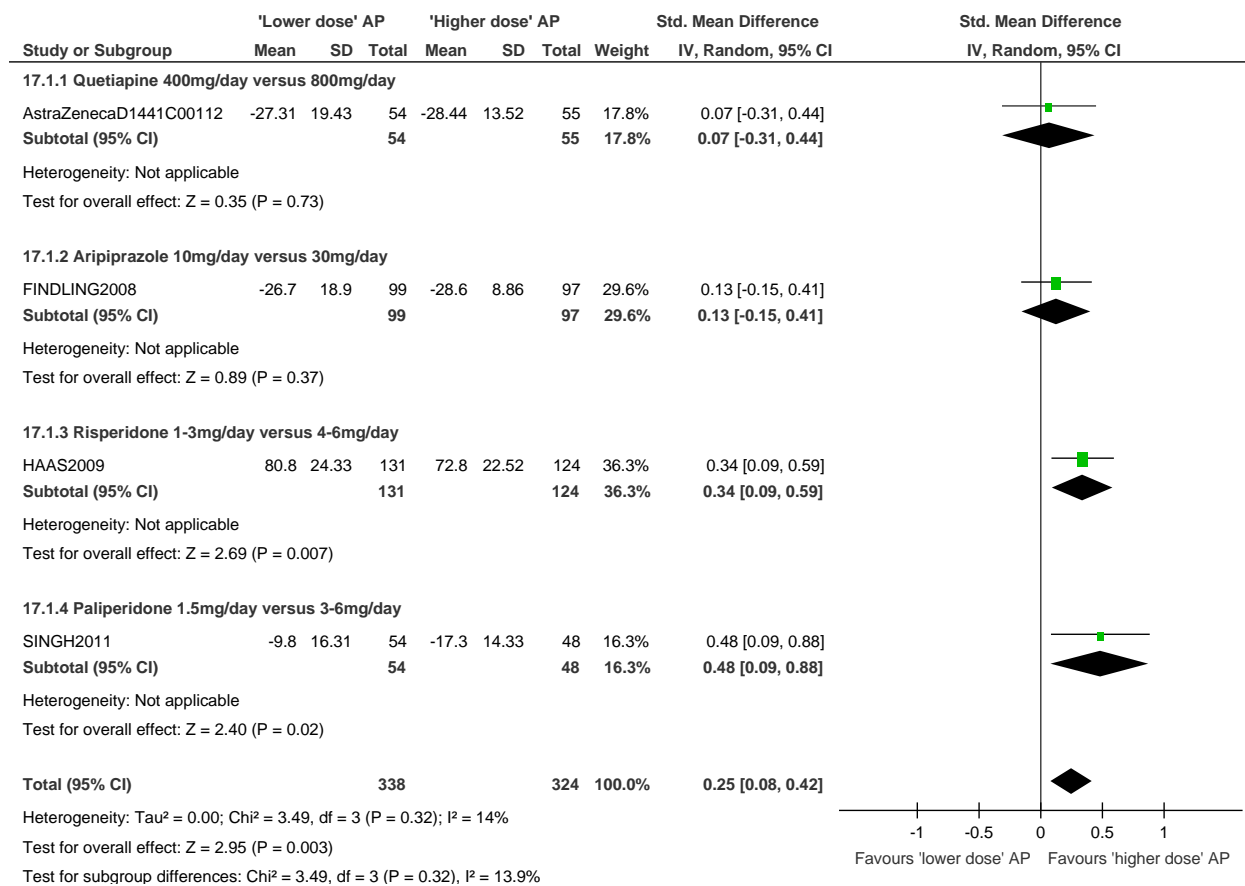


## 16.5 Leaving the study early for any reason

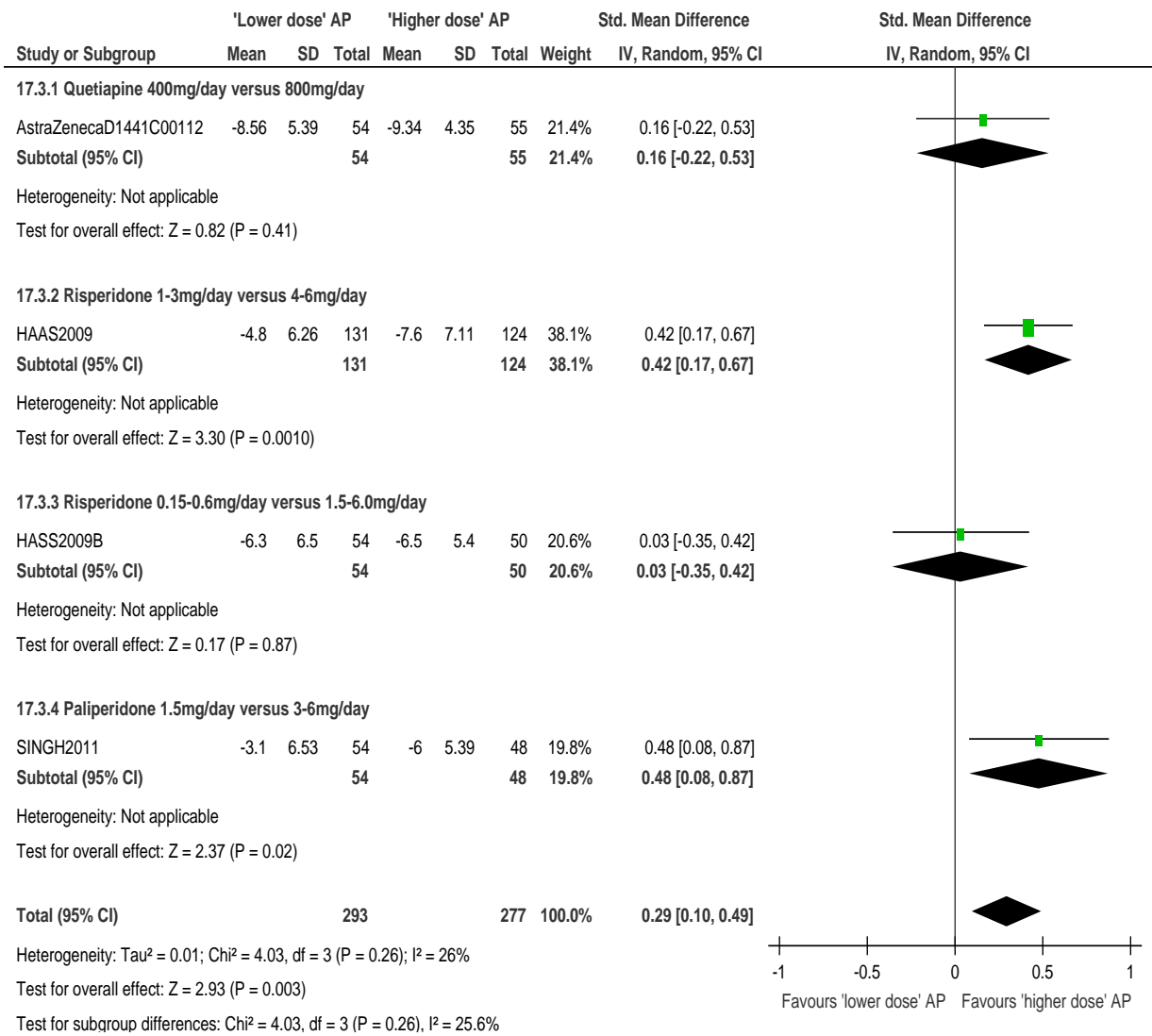


## 17. 'Lower dose' antipsychotic medication versus 'higher dose' antipsychotic medication: post-treatment efficacy outcomes

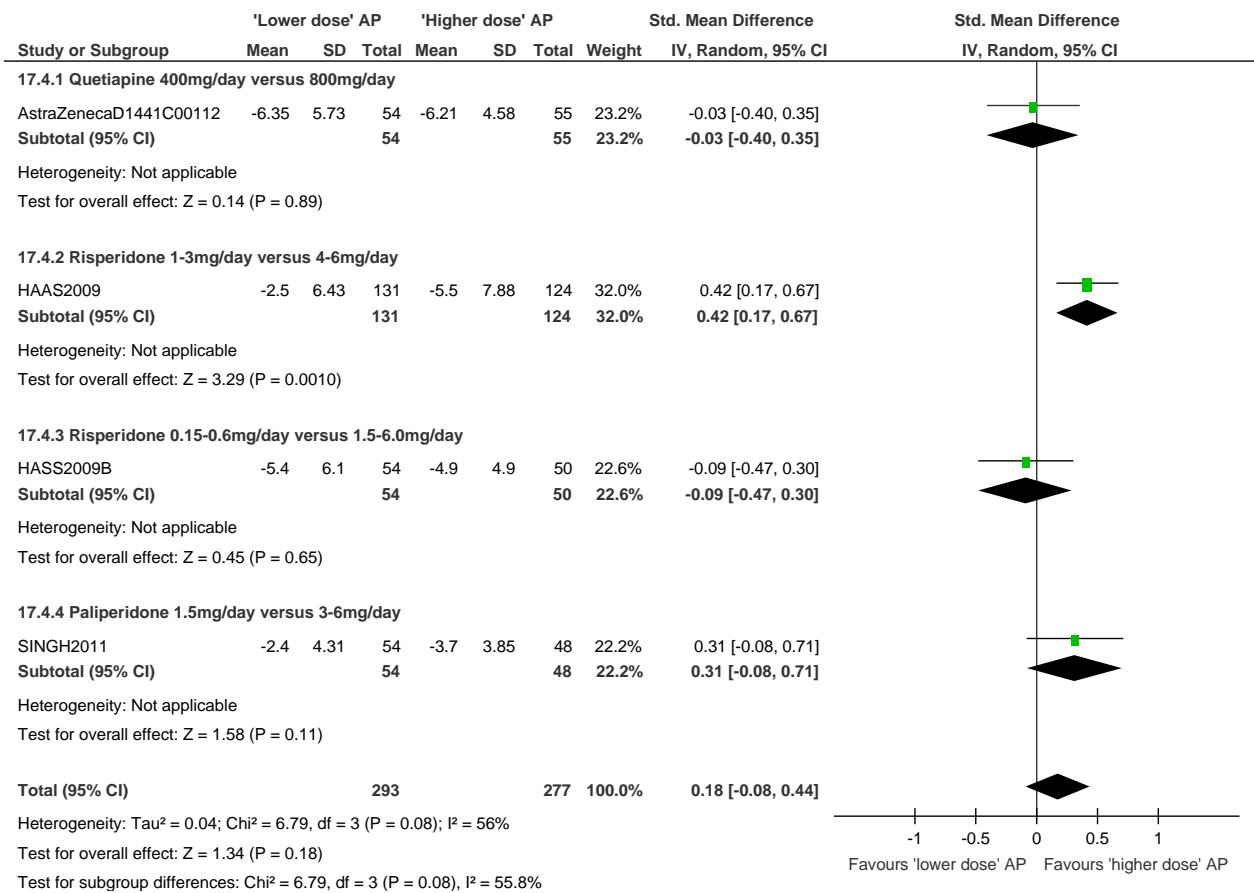
### 17.1 Mental state: mean change in total symptoms (PANSS)



## 17.2 Mental state: mean change in positive symptoms (PANSS positive)

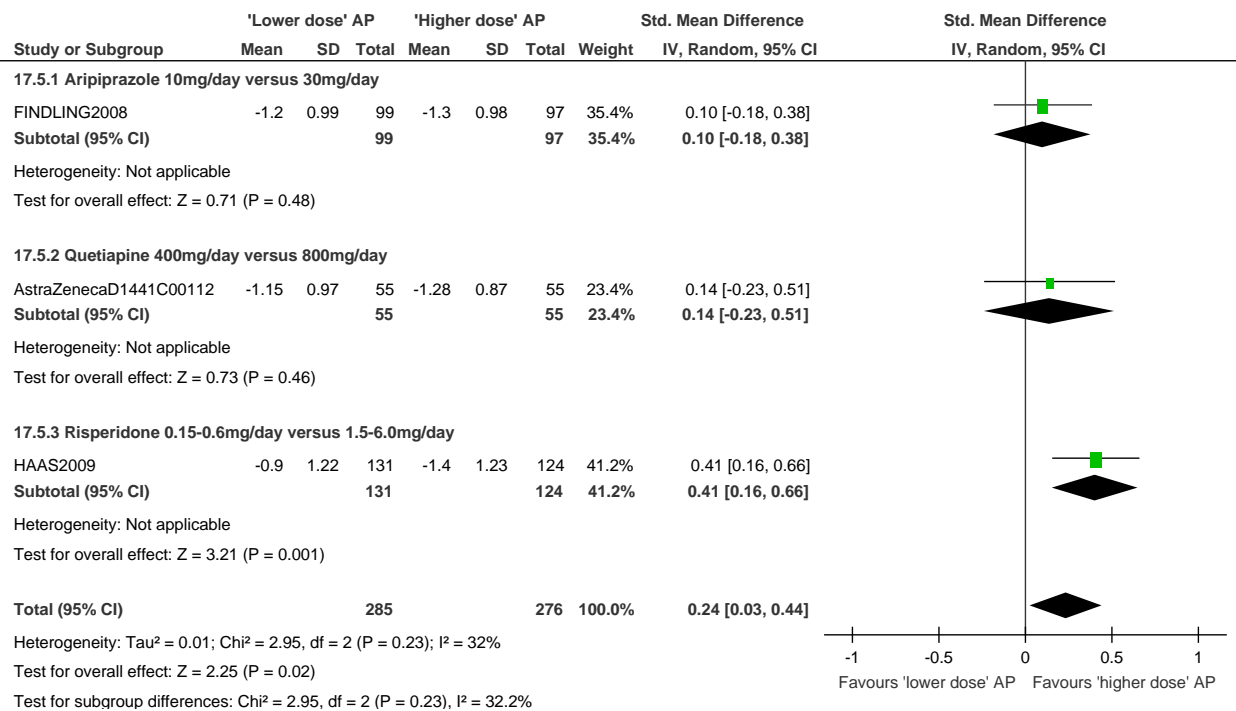


### 17.3 Mental state: mean change in negative symptoms (PANSS Negative)

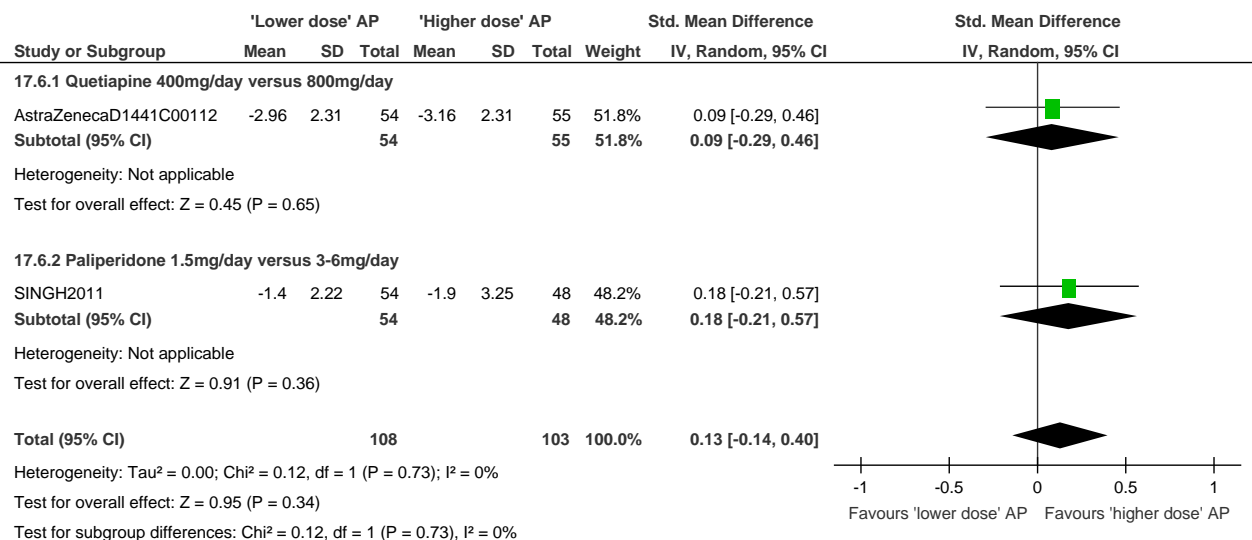




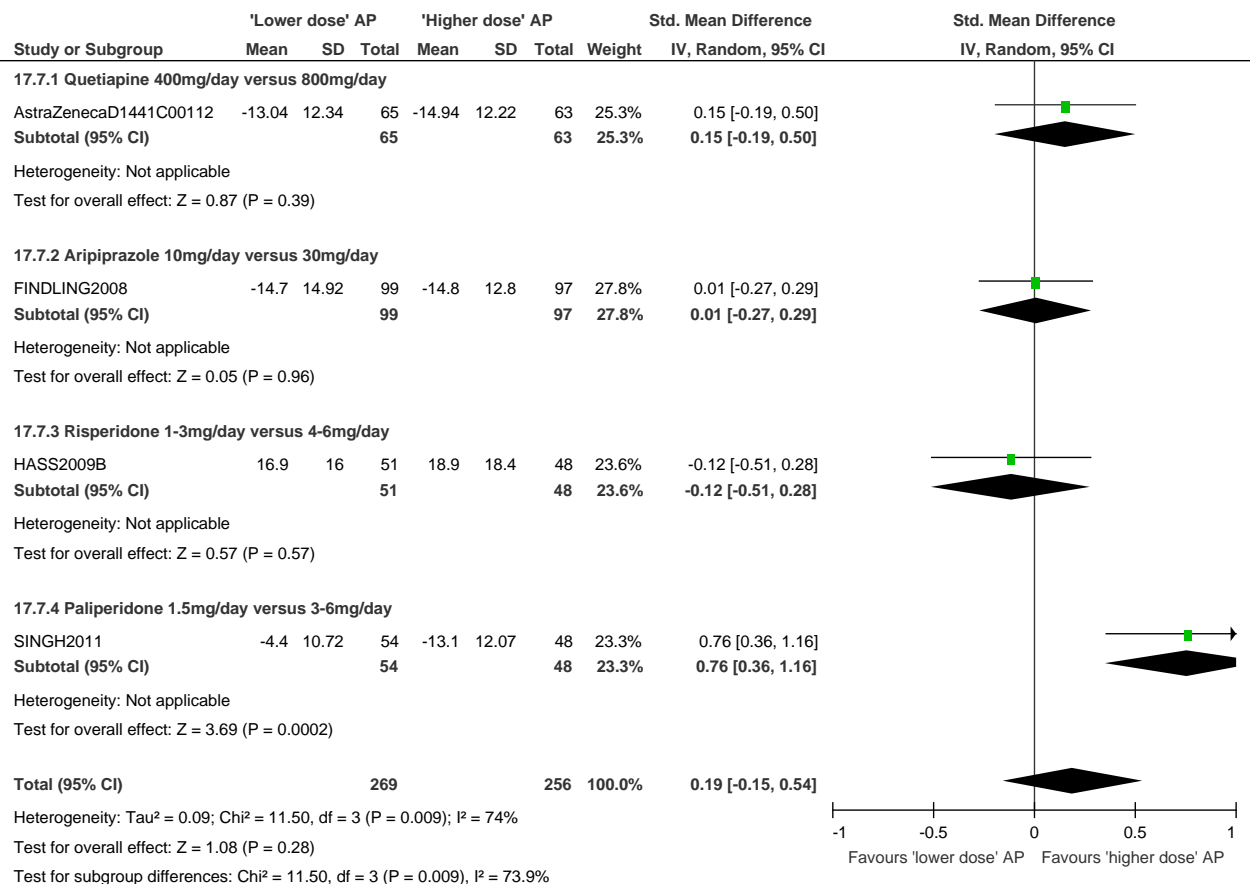
## 17.4 Global state (CGI-S)



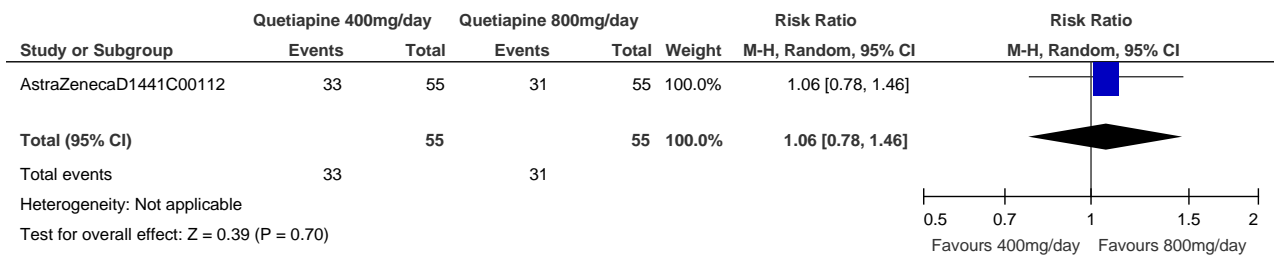
## 17.5 Depression (PANSS Depression; Anxiety and Depression)



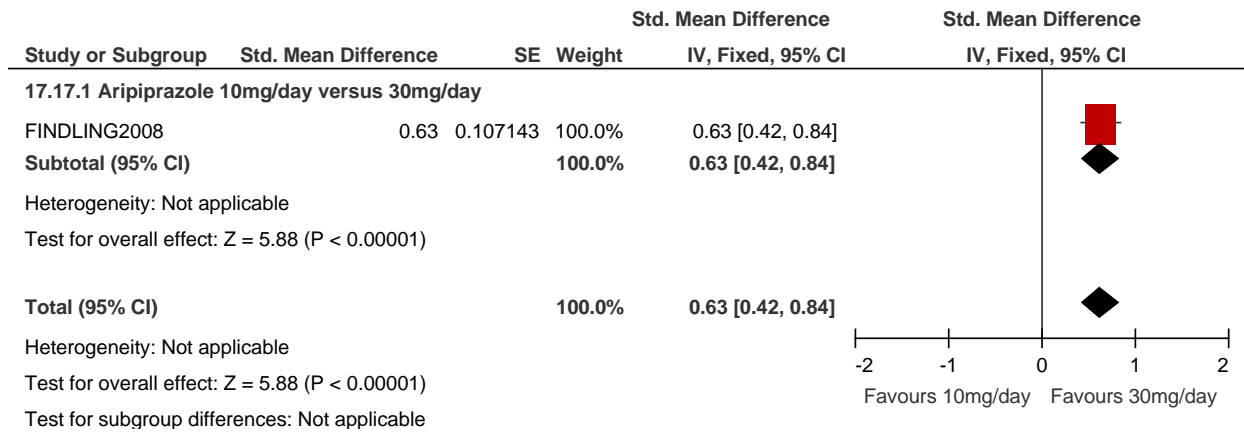
## 17.6 Psychosocial functioning (CGAS)



## 17.7 Response (CGI-I)

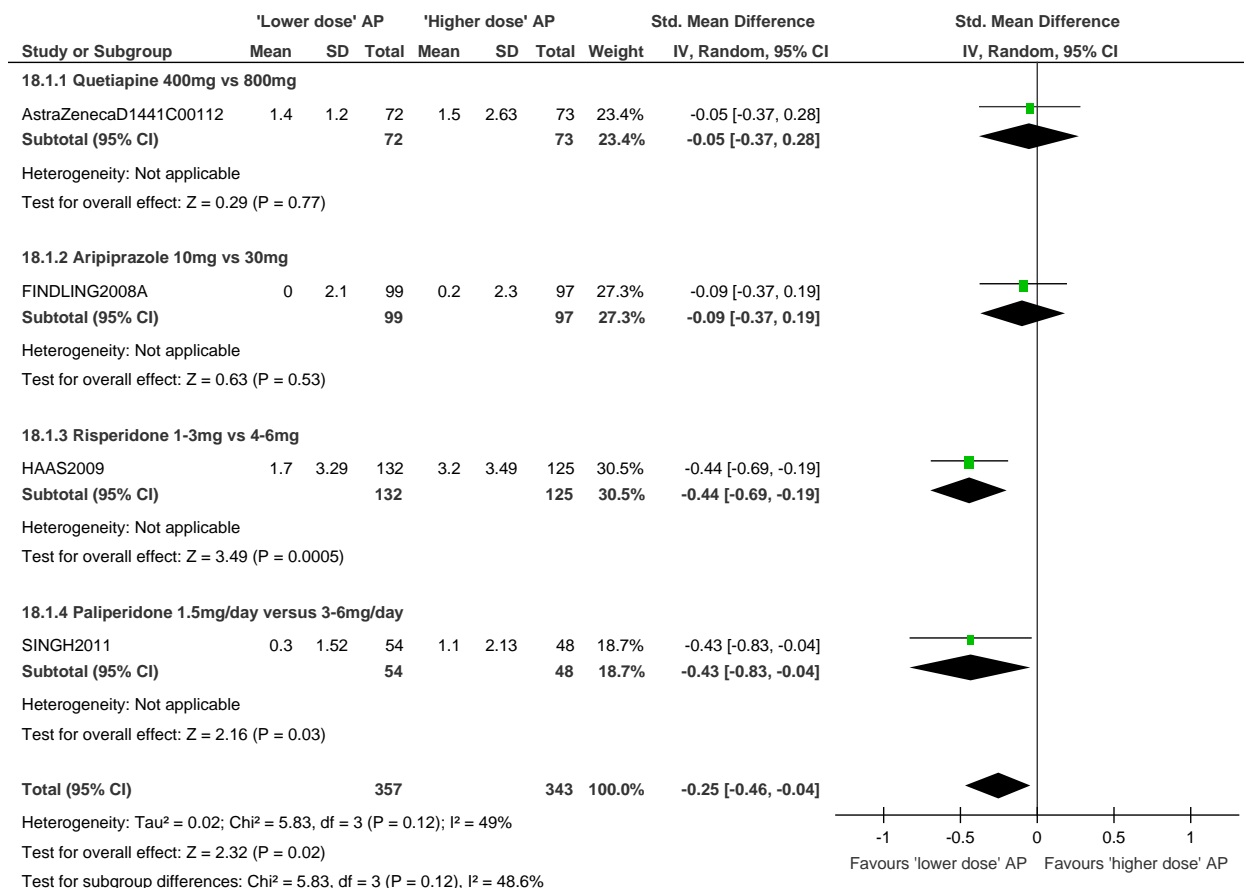


## 17.8 Quality of life (calculated using total and overall scores from the Paediatric Quality of Life Enjoyment and Satisfaction Questionnaire)

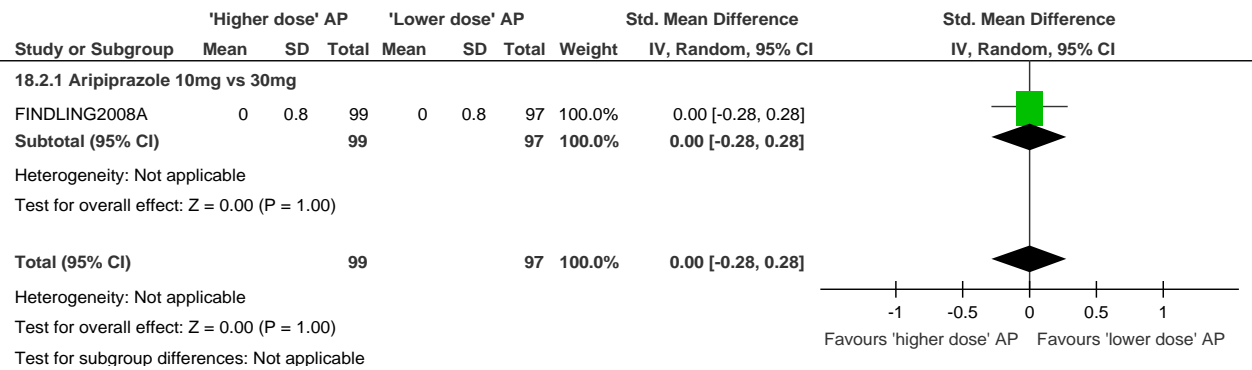


## 18. 'Lower dose' antipsychotic medication versus 'higher dose' antipsychotic medication: post-treatment side effect outcomes

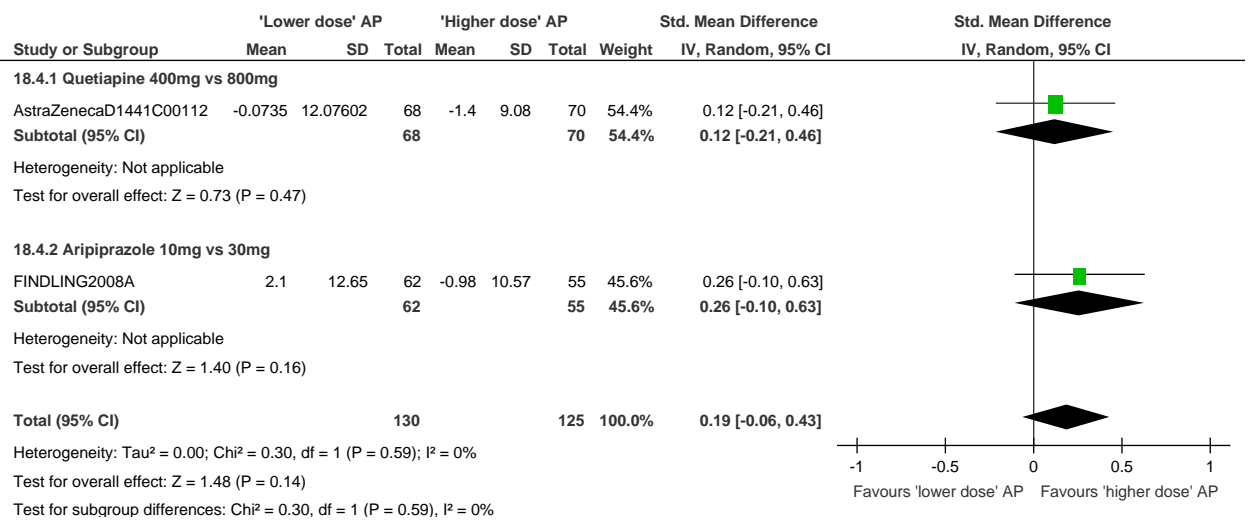
### 18.1 Mean change in weight (kg)



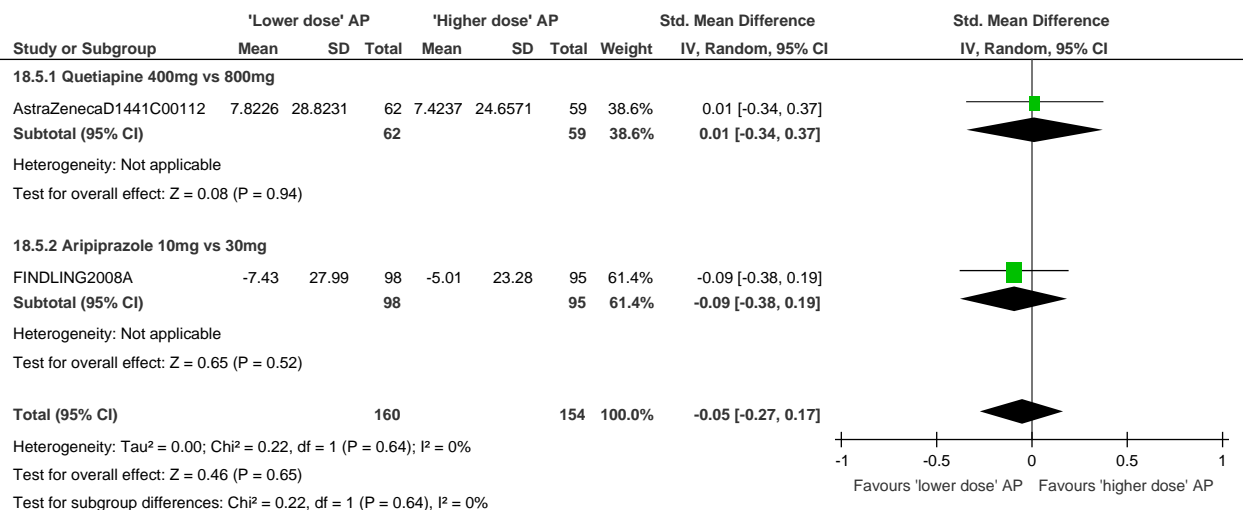
## 18.2 Mean change in BMI (kg/m<sup>2</sup>)



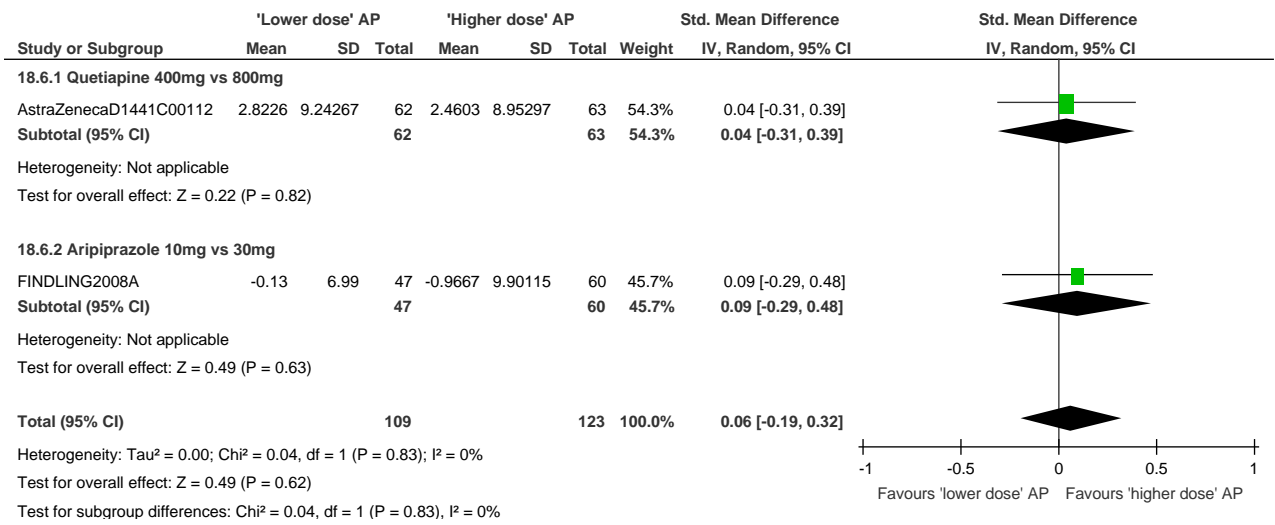
## 18.3 Mean change in fasting serum glucose level (mg/dl)



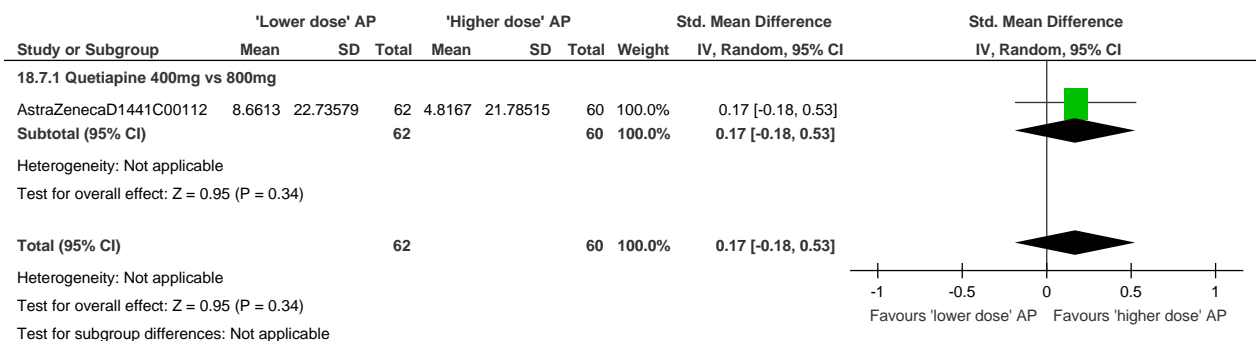
## 18.4 Mean change in fasting total cholesterol (mg/dl)



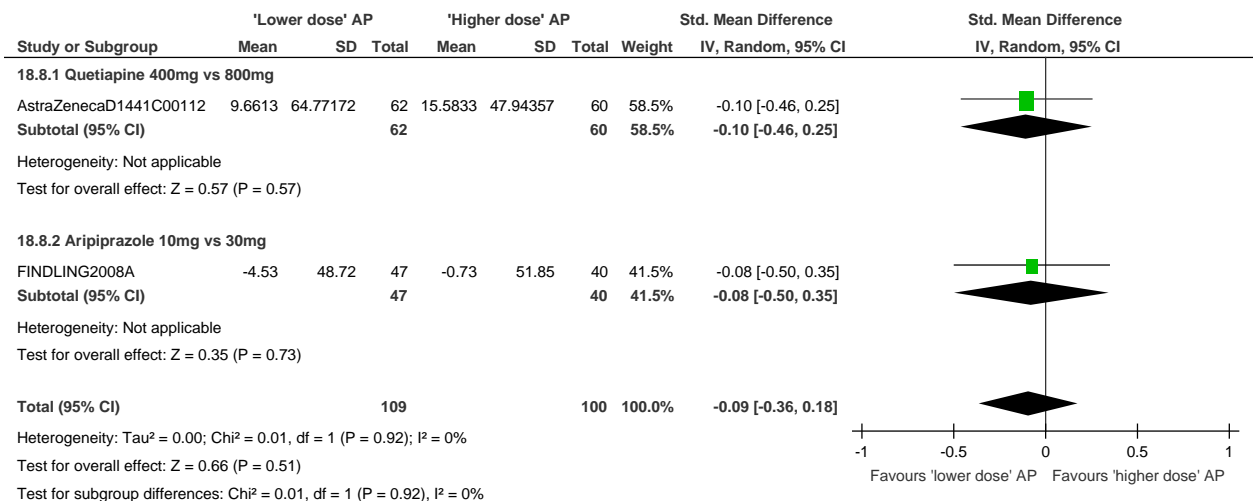
## 18.5 Mean change in fasting high-density lipoprotein cholesterol level (mg/dl)



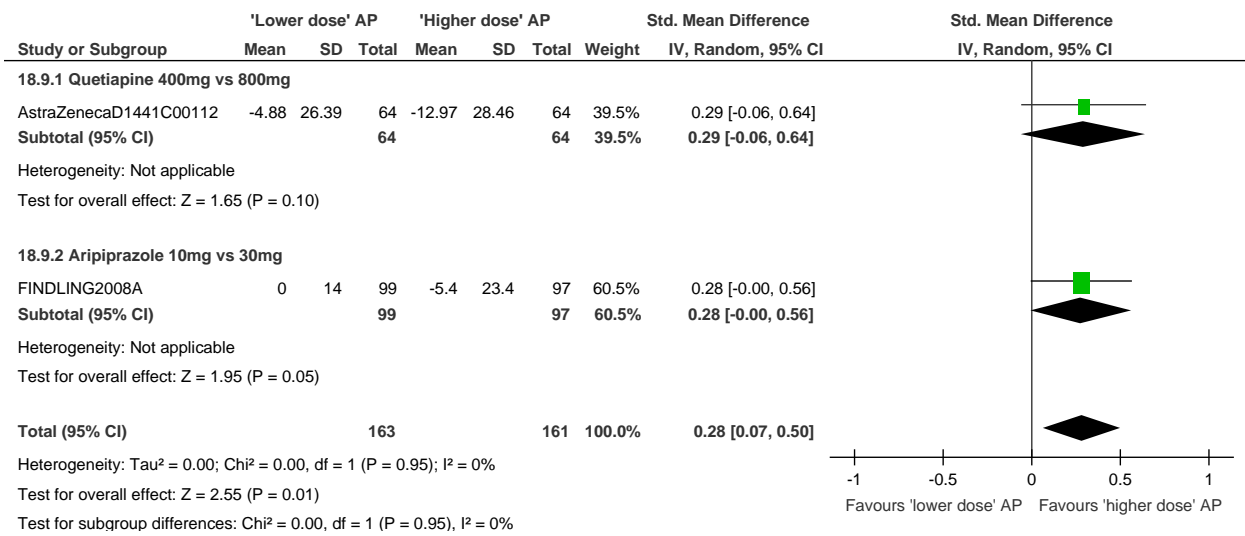
## 18.6 Mean change in low-density lipoprotein cholesterol level (mg/dl)



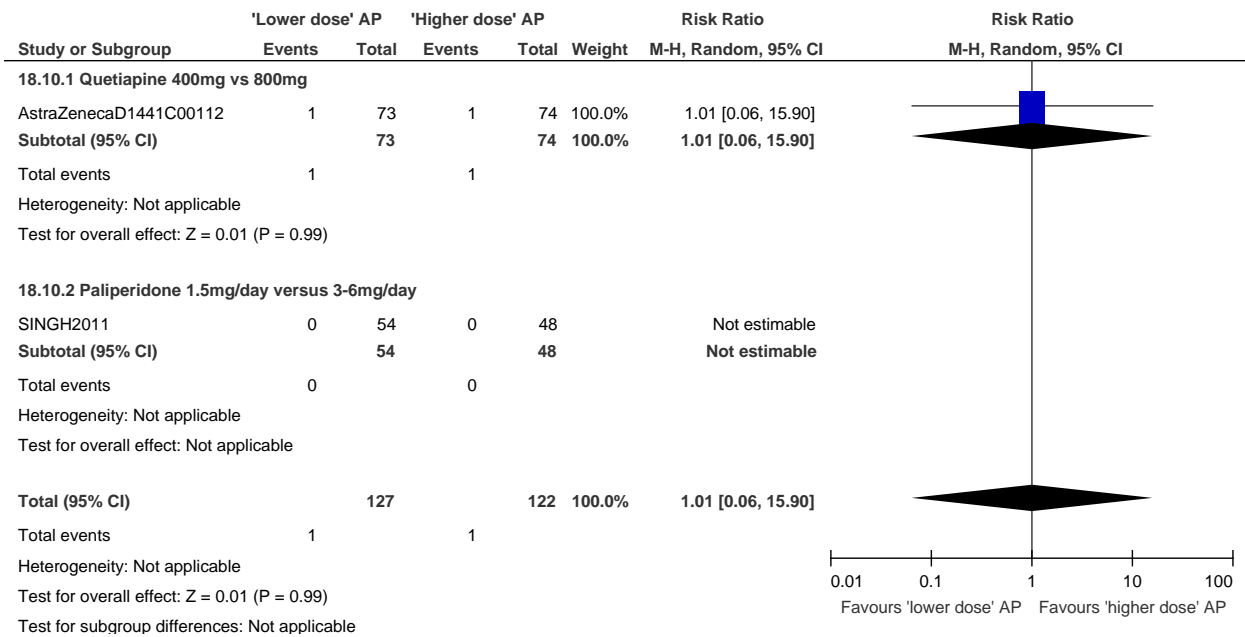
## 18.7 Mean change in fasting triglycerides (mg/dl)



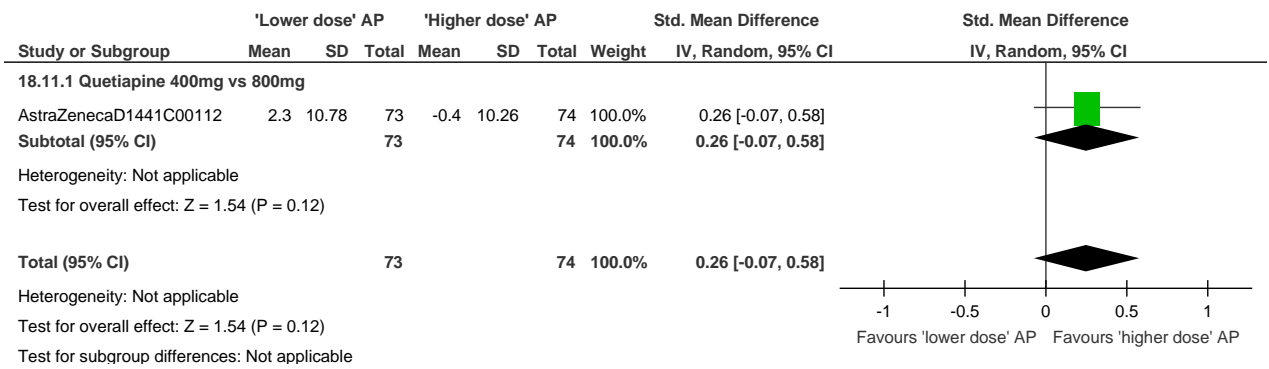
## 18.8 Mean change in QT interval (msec)



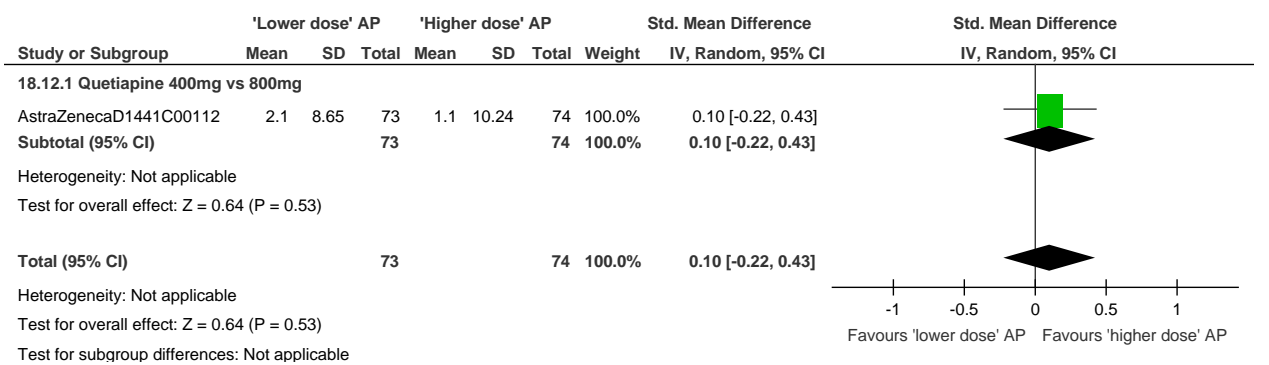
## 18.9 Mean change in prolonged QT interval (msec)



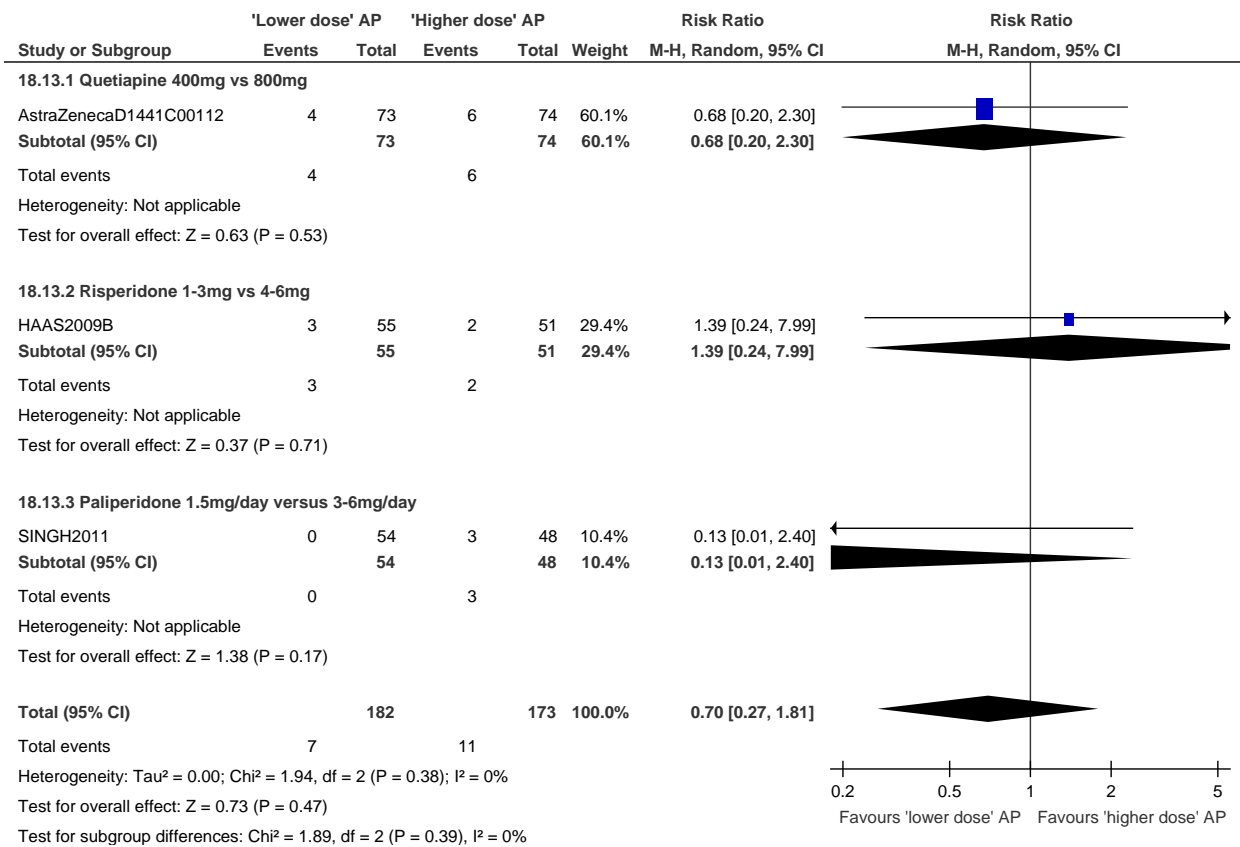
## 18.10 Mean change in systolic BP (mm Hg)



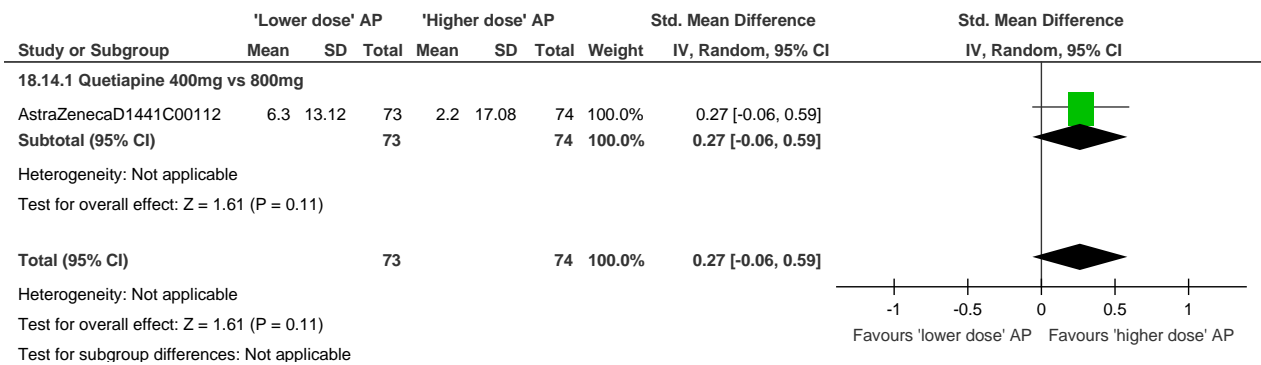
## 18.11 Mean change in diastolic BP (mm Hg)



## 18.12 Tachycardia

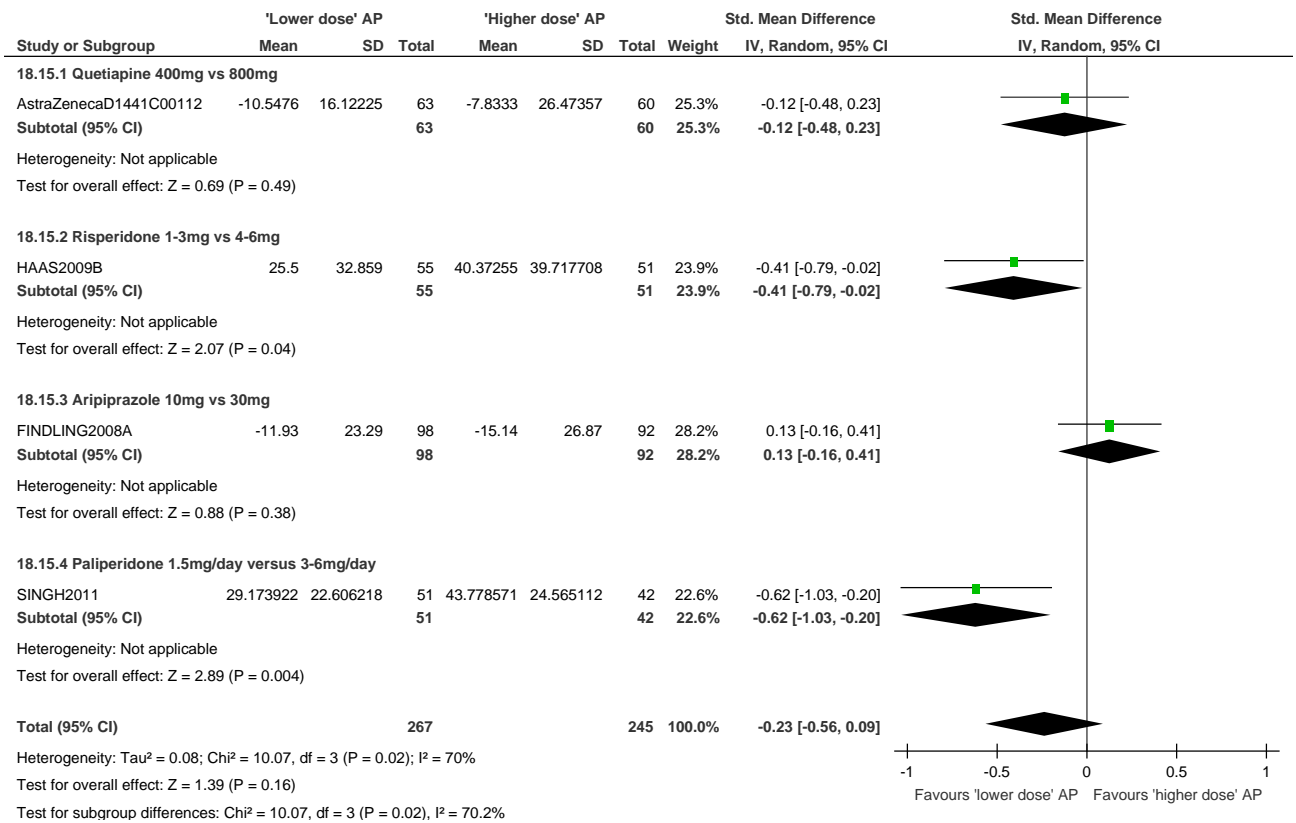


## 18.13 Mean change in standing pulse (BPM)

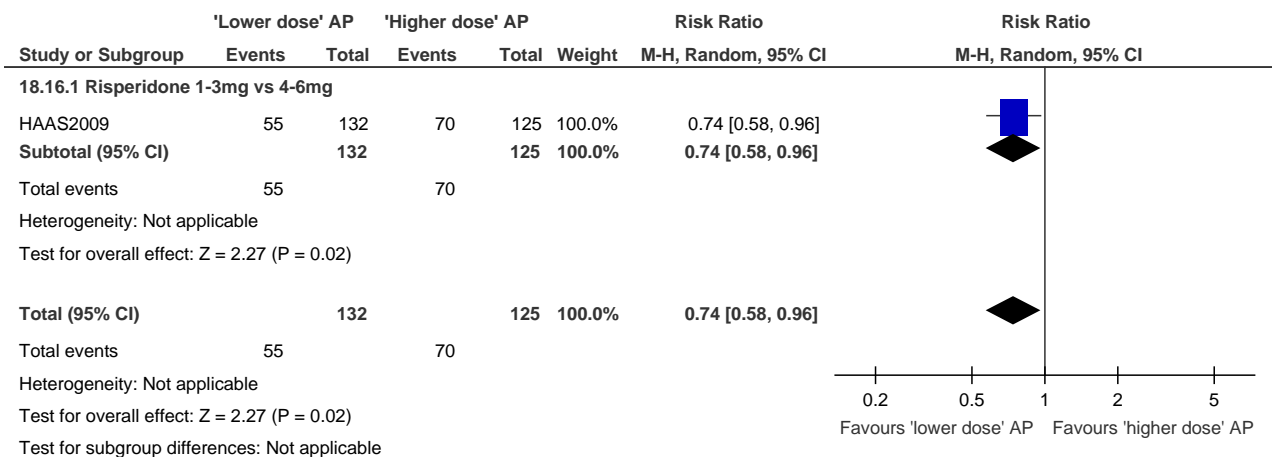




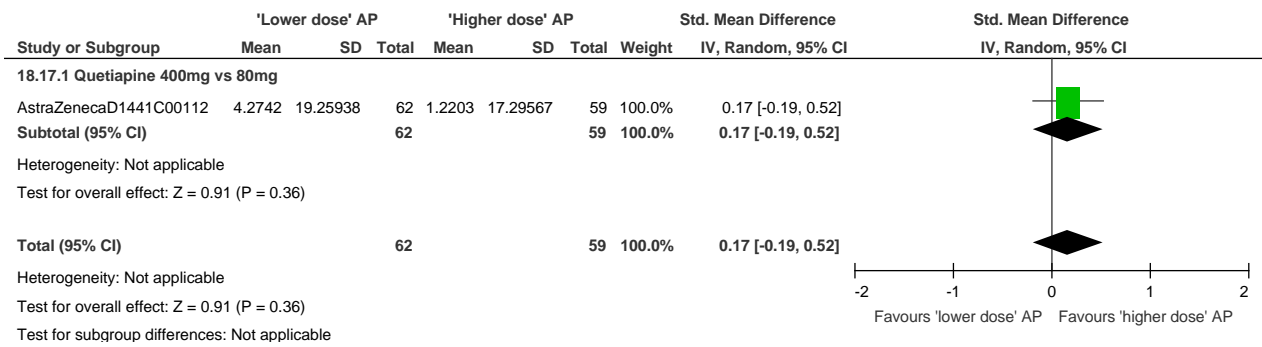
## 18.14 Mean change in prolactin level (mg/dl)



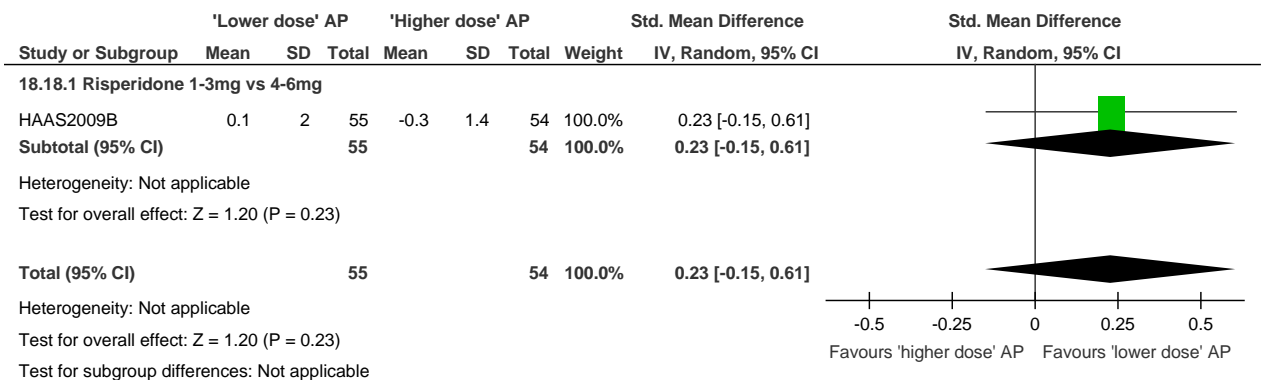
## 18.15 Elevated prolactin level (mg/dl)



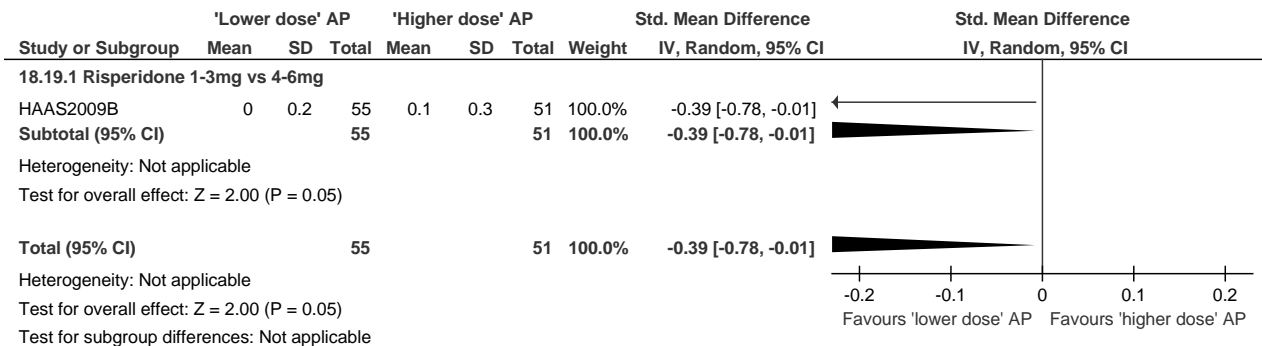
### 18.16 Mean change in insulin level (mg/dl)



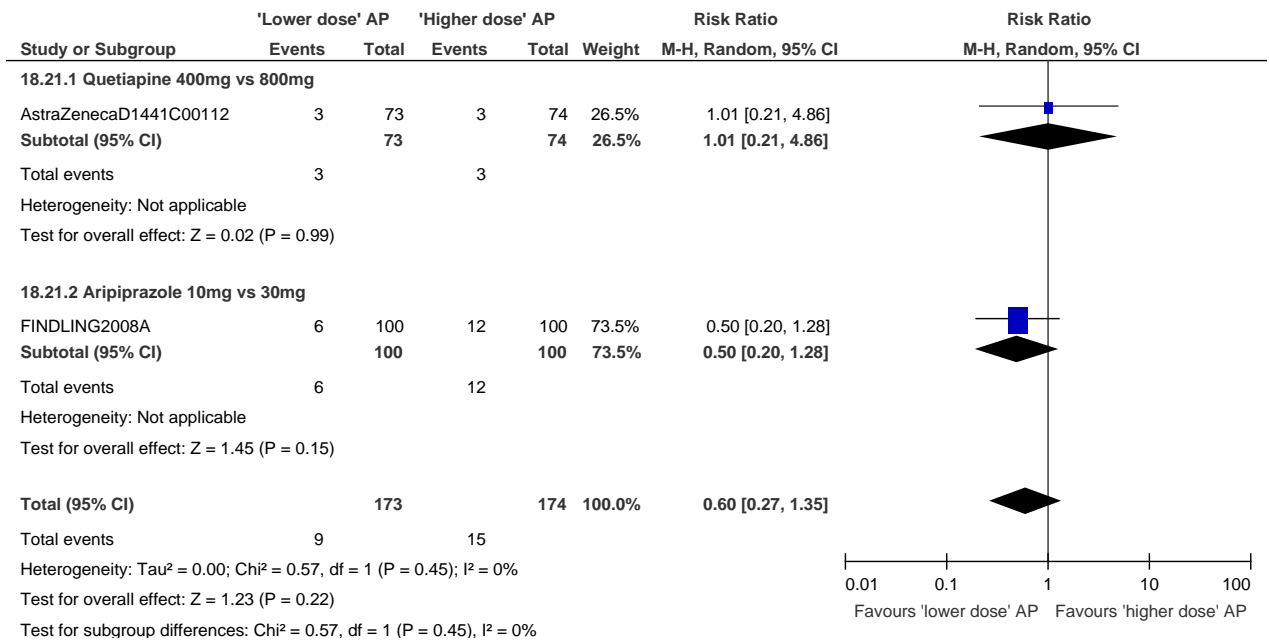
### 18.17 Mean change in EPS (AIMS scores)



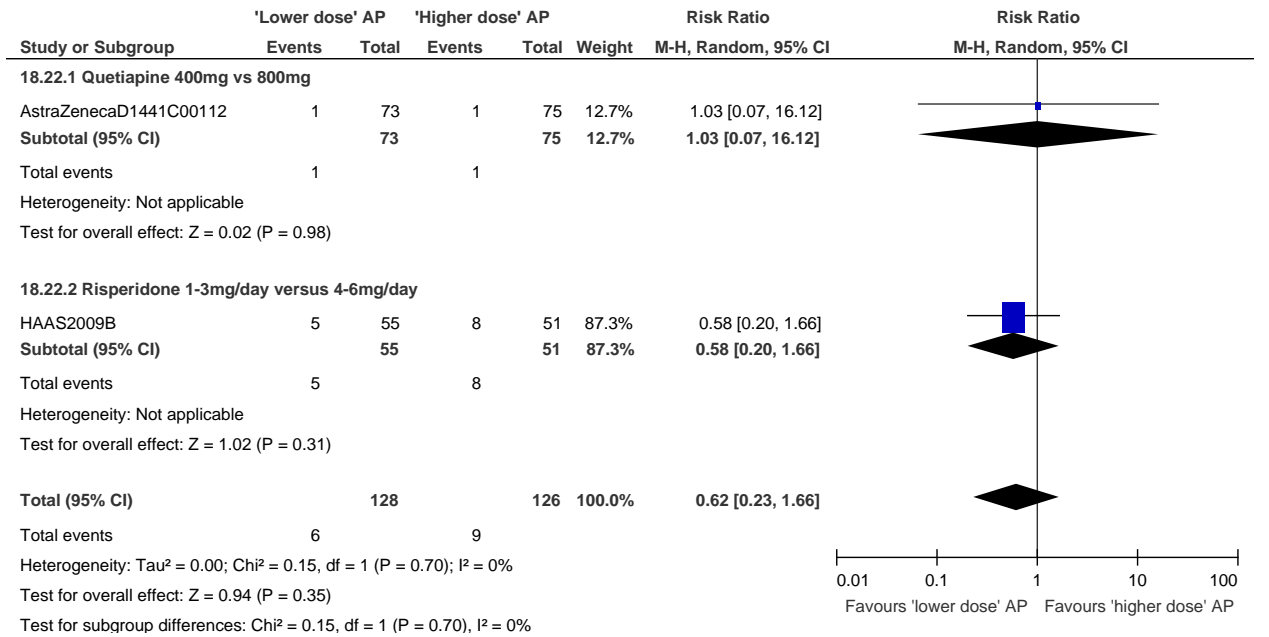
### 18.18 Mean change in EPS (SAS scores)



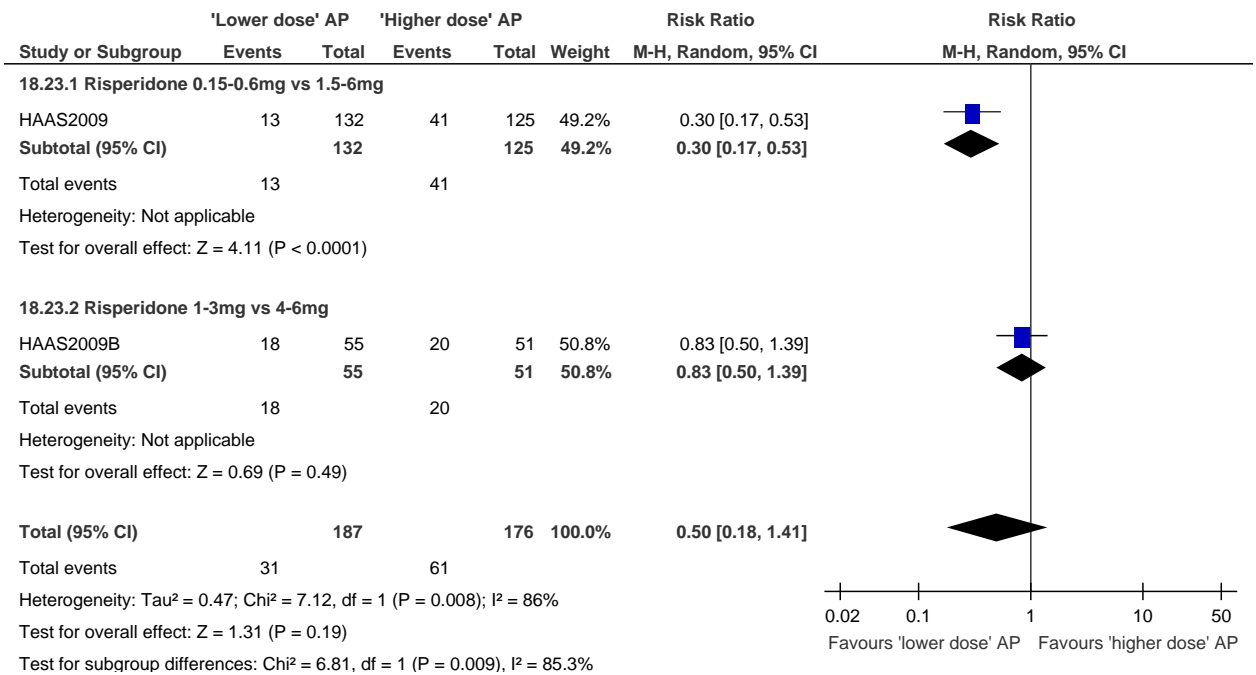
## 18.19 Akathisia



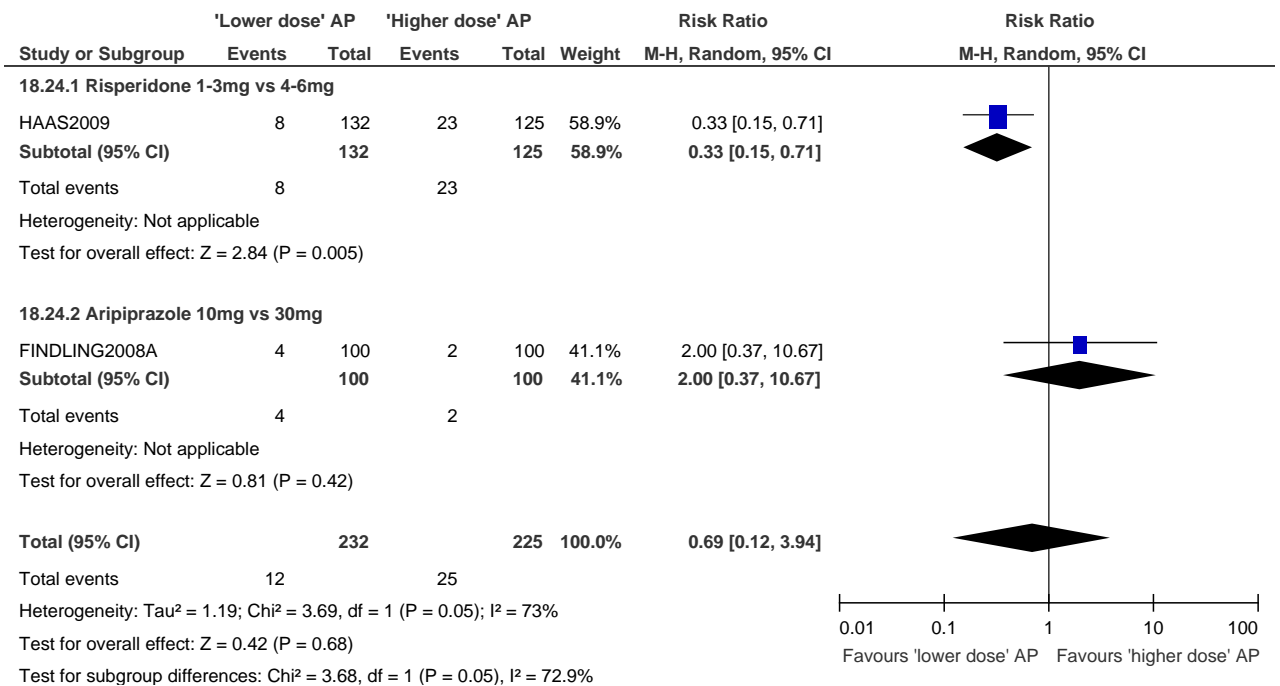
## 18.20 Extrapyramidal disorder



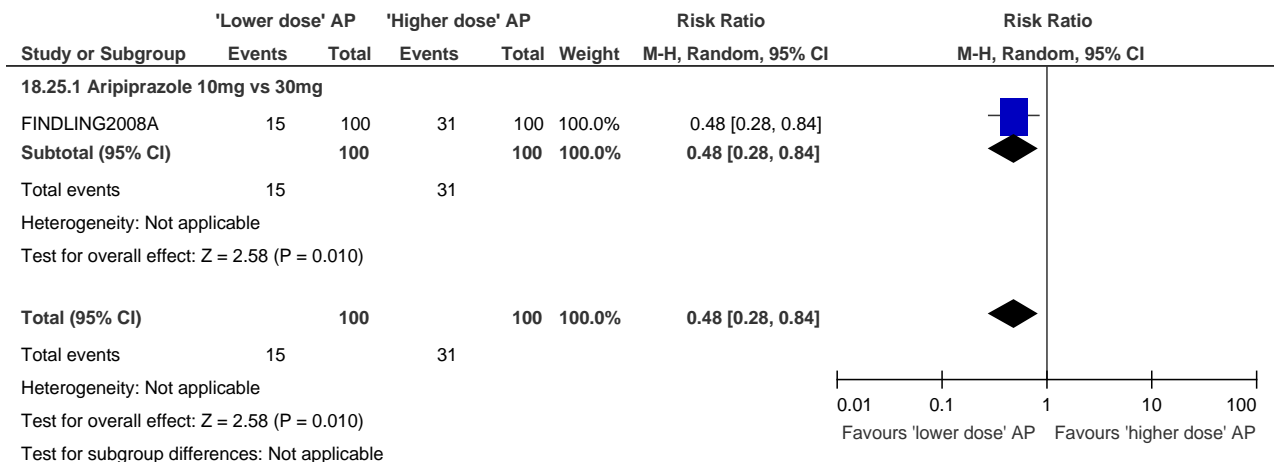
## 18.21 EPS



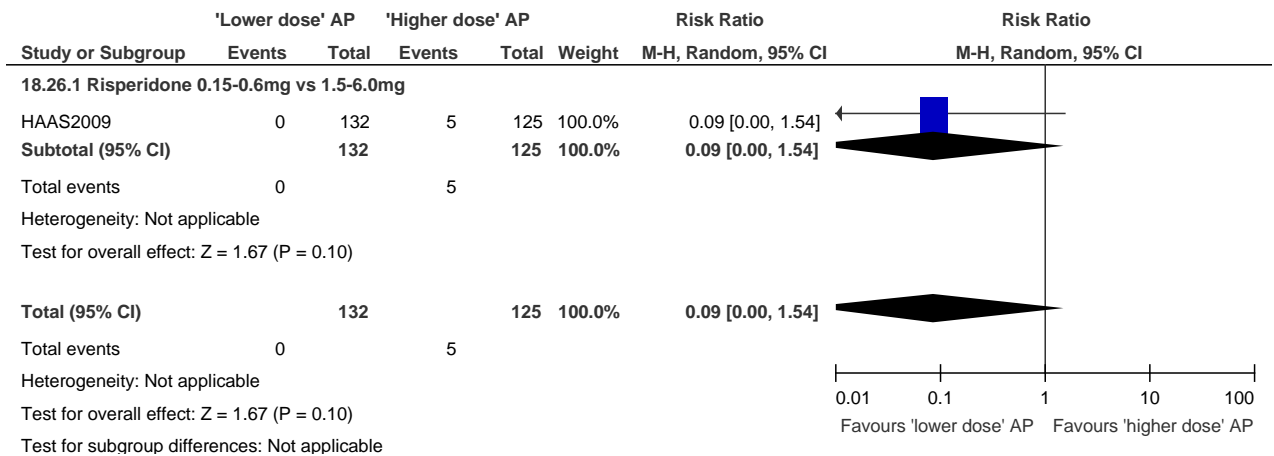
## 18.22 Dystonia



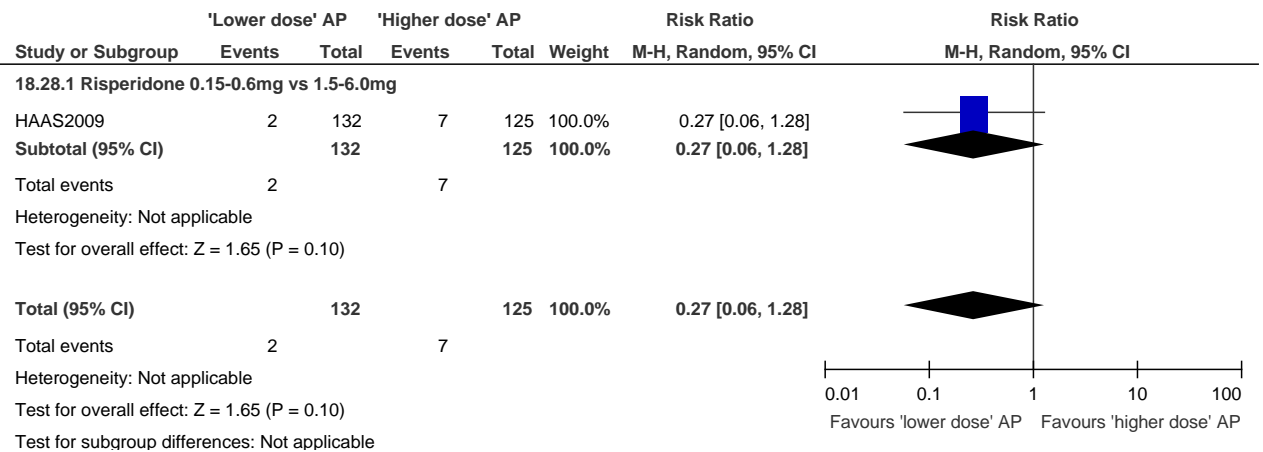
## 18.23 Parkinsonism



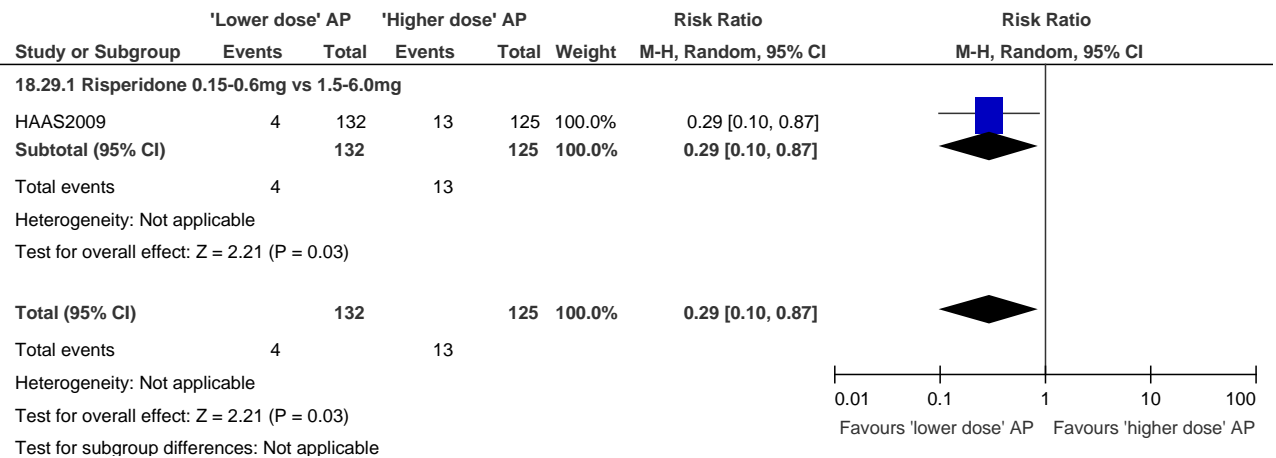
## 18.24 Parkinsonism symptoms



## 18.25 Dyskinesia



## 18.26 Tremor

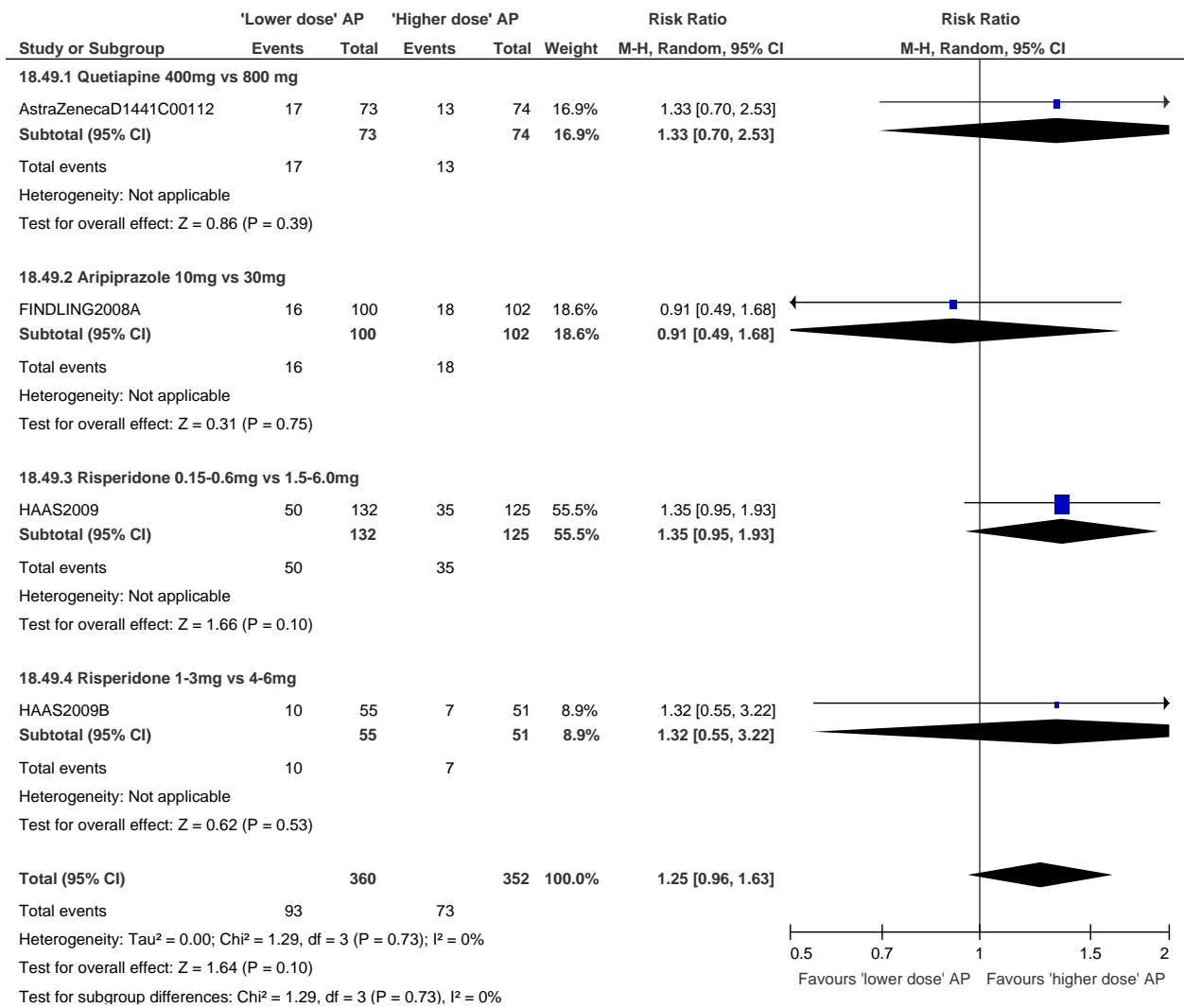


## 18.27 Mortality (including suicide)

Study or Subgroup	'Lower dose' AP		'Higher dose' AP		Weight	Risk Ratio	Risk Ratio
	Events	Total	Events	Total		M-H, Random, 95% CI	M-H, Random, 95% CI
<b>18.30.1 Risperidone 1-3mg vs 4-6mg</b>							
HAAS2009B	0	55	0	51		Not estimable	
<b>Subtotal (95% CI)</b>		<b>55</b>		<b>51</b>		<b>Not estimable</b>	
Total events	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
<b>18.30.2 Aripiprazole 10mg vs 30mg</b>							
FINDLING2008A	0	100	0	100		Not estimable	
<b>Subtotal (95% CI)</b>		<b>100</b>		<b>100</b>		<b>Not estimable</b>	
Total events	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
<b>Total (95% CI)</b>		<b>155</b>		<b>151</b>		<b>Not estimable</b>	
Total events	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							

0.01 0.1 1 10 100  
Favours 'Lower dose' AP Favours 'Higher dose' AP

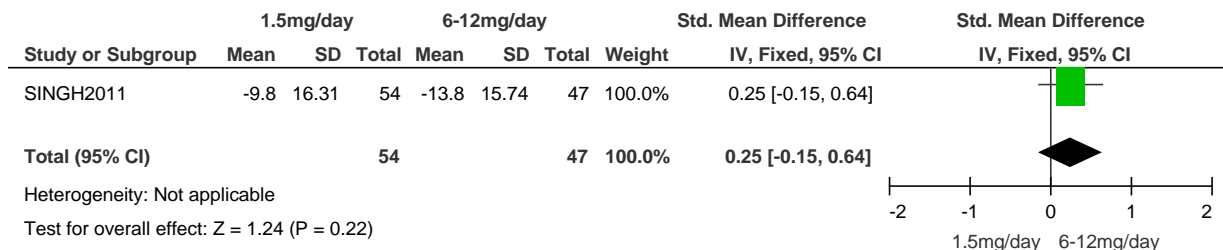
## 18.28 Leaving the study early for any reason



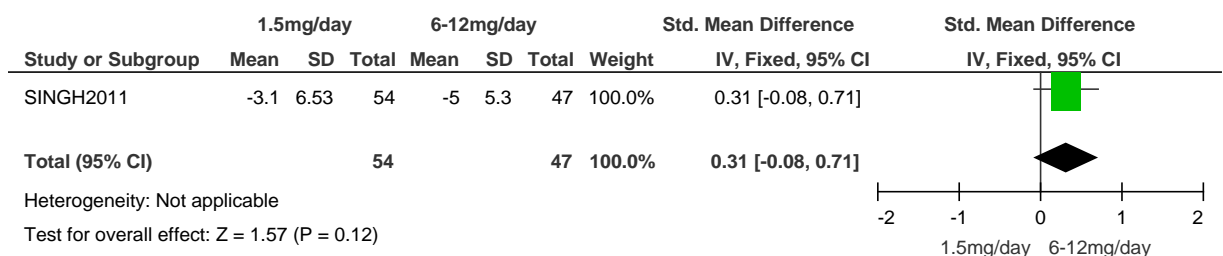


## 19. 'Lower dose' paliperidone (1.5mg/day) versus additional (high dose) paliperidone (6 to 12mg/day): post-treatment efficacy outcomes

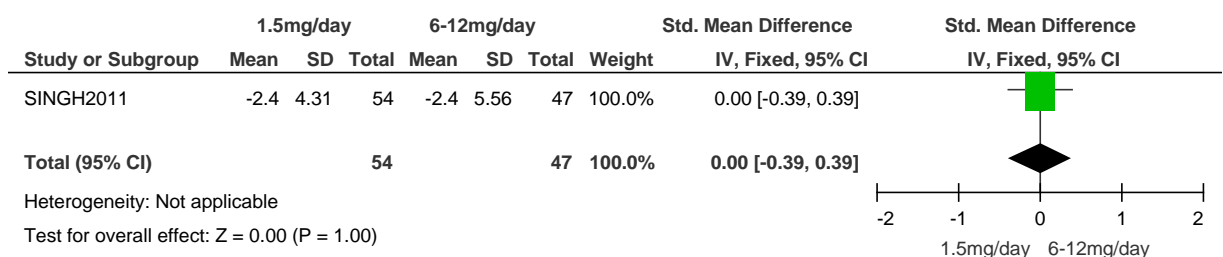
### 19.1 Mental state: mean change in total symptoms (PANSS)



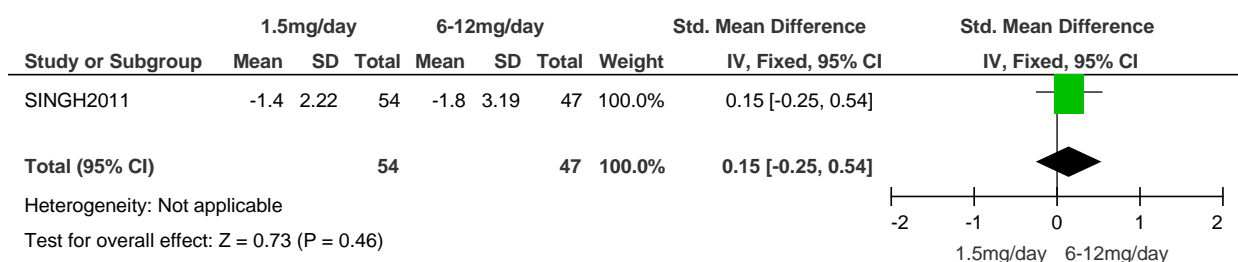
### 19.2 Mental state: mean change in positive symptoms (PANSS Positive)



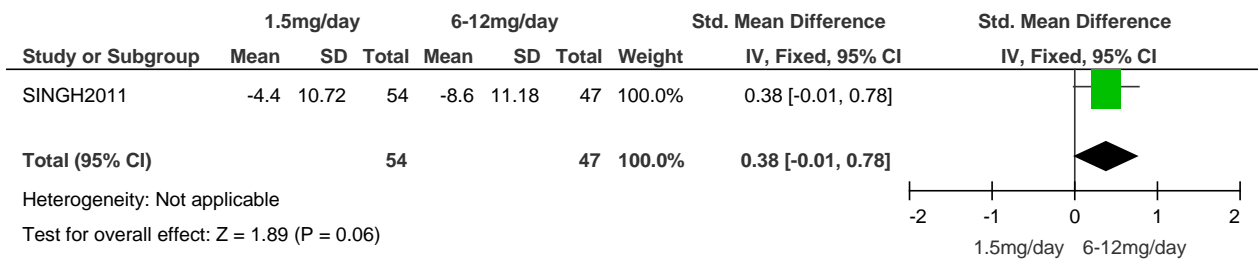
### 19.3 Mental state: mean change in negative symptoms (PANSS Negative)



### 19.4 Mean change in depression (PANSS Anxiety and Depression)

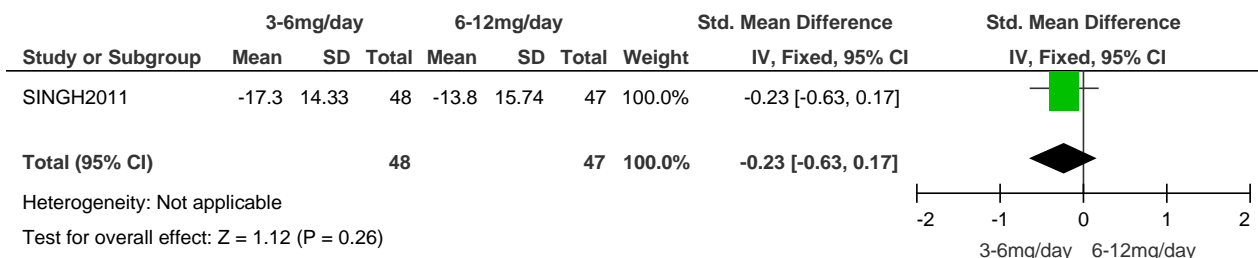


## 19.5 Mean change in psychosocial functioning (CGAS)

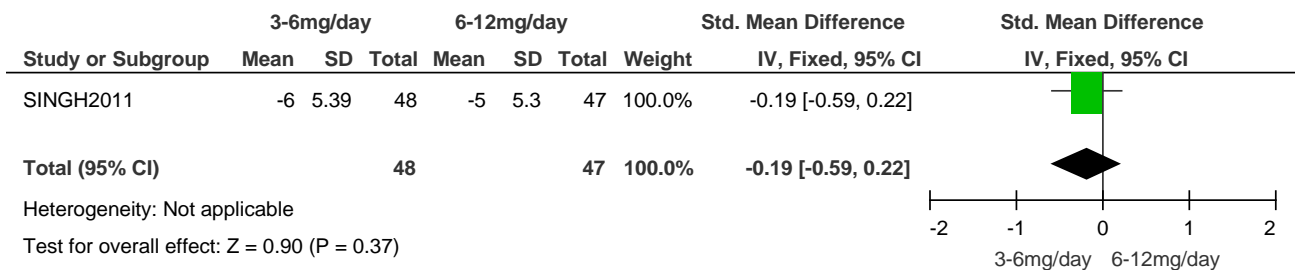


## 20. 'Higher dose' paliperidone (3 to 6mg/day) versus additional (high dose) paliperidone (6 to 12mg/day): post-treatment efficacy outcomes

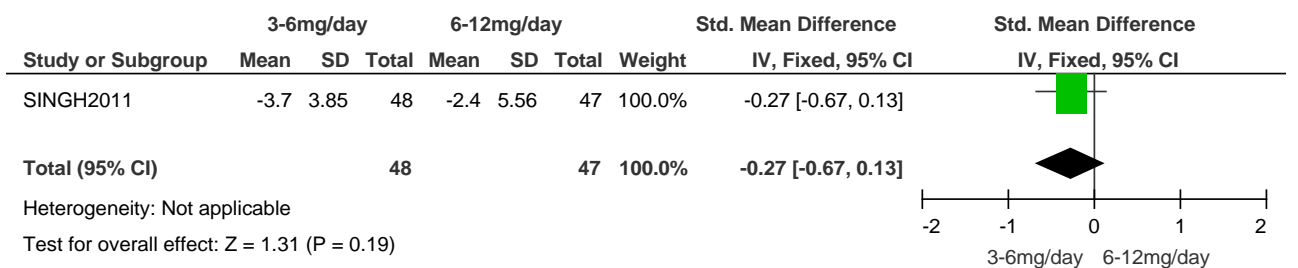
### 20.1 Mental state: mean change in total symptoms (PANSS)



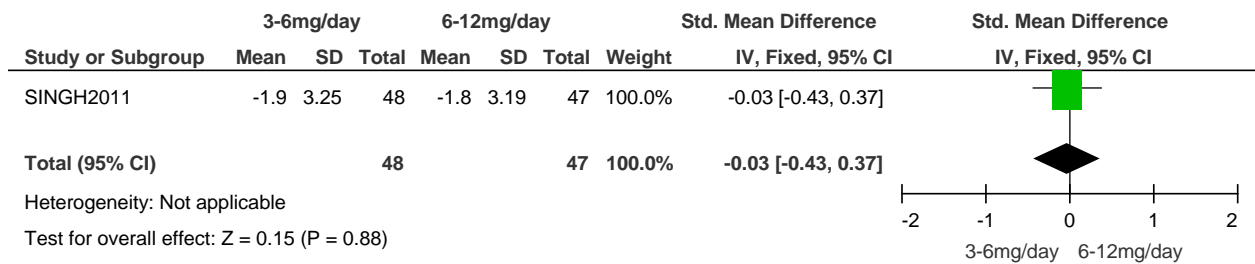
### 20.2 Mental state: mean change in positive symptoms (PANSS positive)



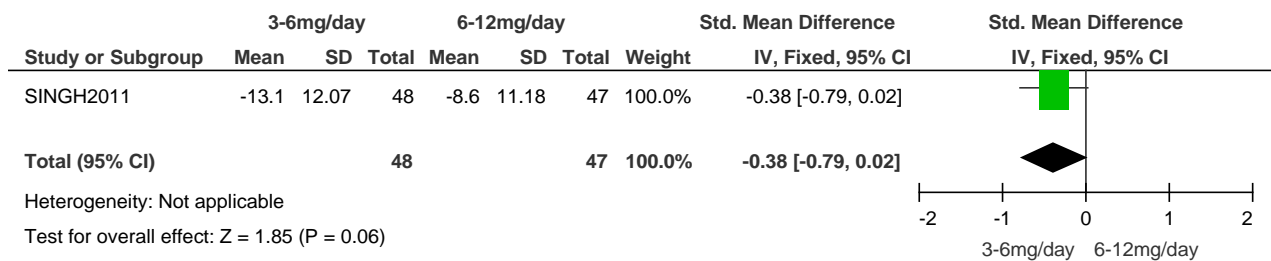
### 20.3 Mental state: mean change in negative symptoms (PANSS negative)



## 20.4 Mean change in depression (PANSS Anxiety and Depression)

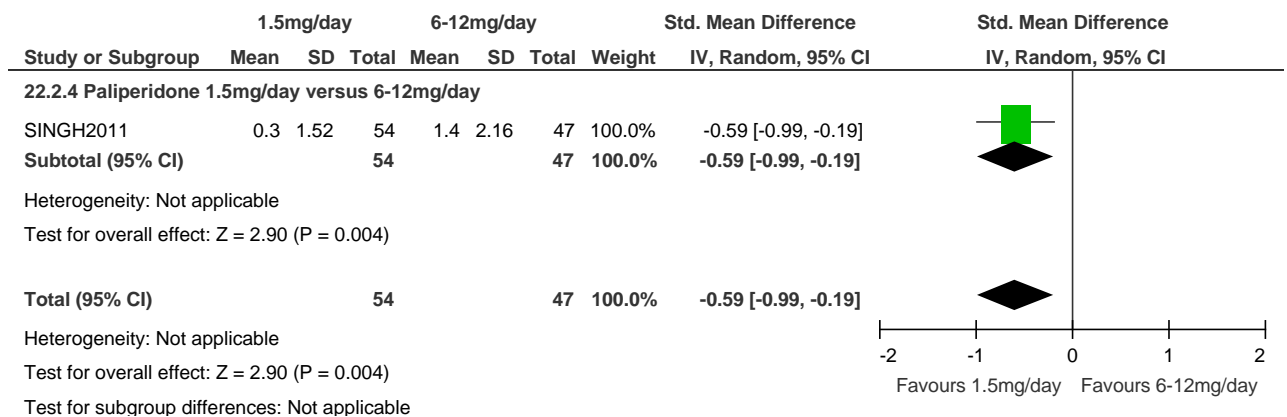


## 20.5 Mean change in psychosocial functioning (CGAS)

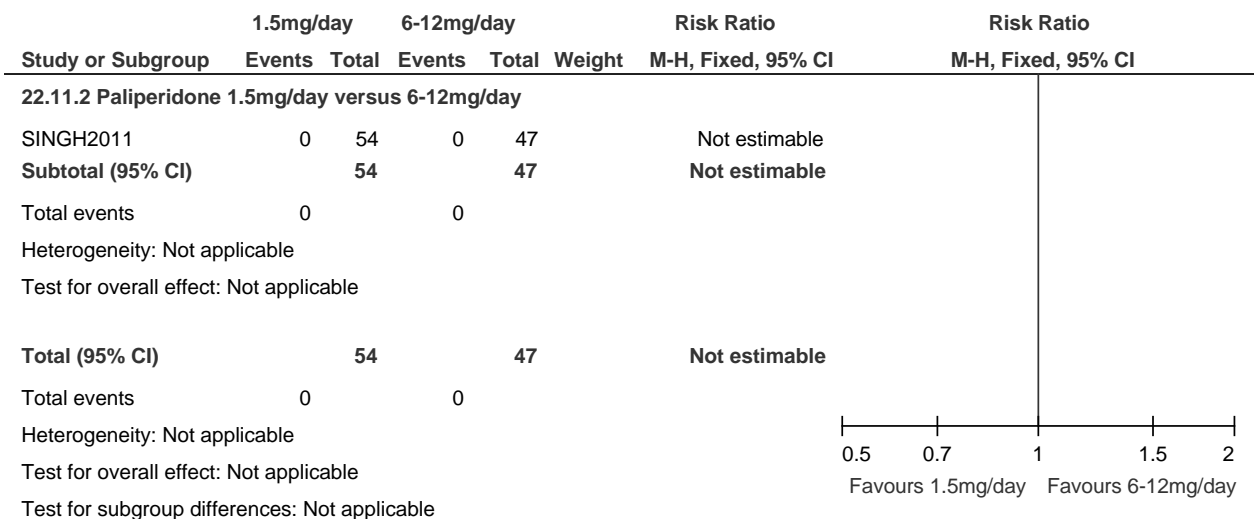


## 21. 'Lower dose' paliperidone (1.5mg/day) versus additional (high dose) paliperidone (6 to 12mg/day): post-treatment side effect outcomes

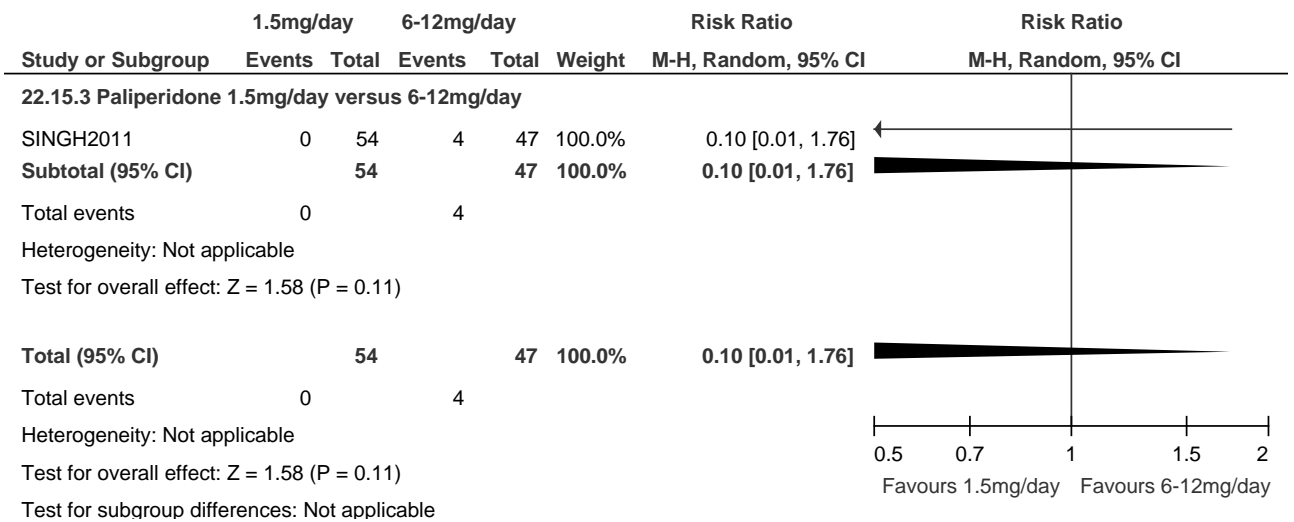
### 21.1 Mean change in weight (kg)



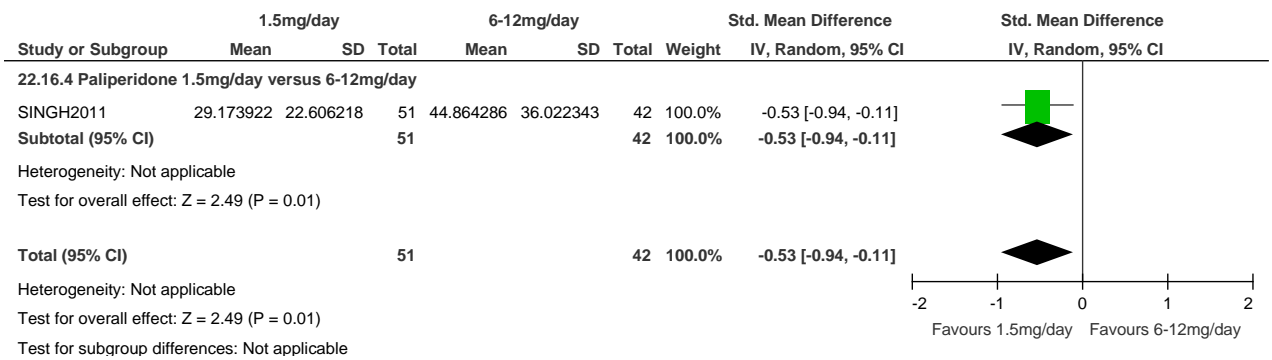
## 21.2 Prolonged QT interval (msec)



## 21.3 Tachycardia

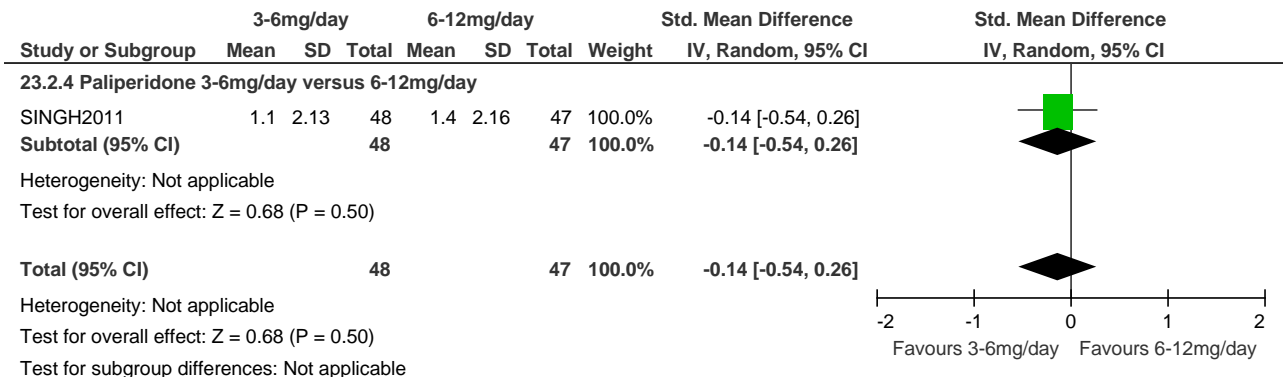


## 21.4 Mean change in prolactin level (mg/dl)

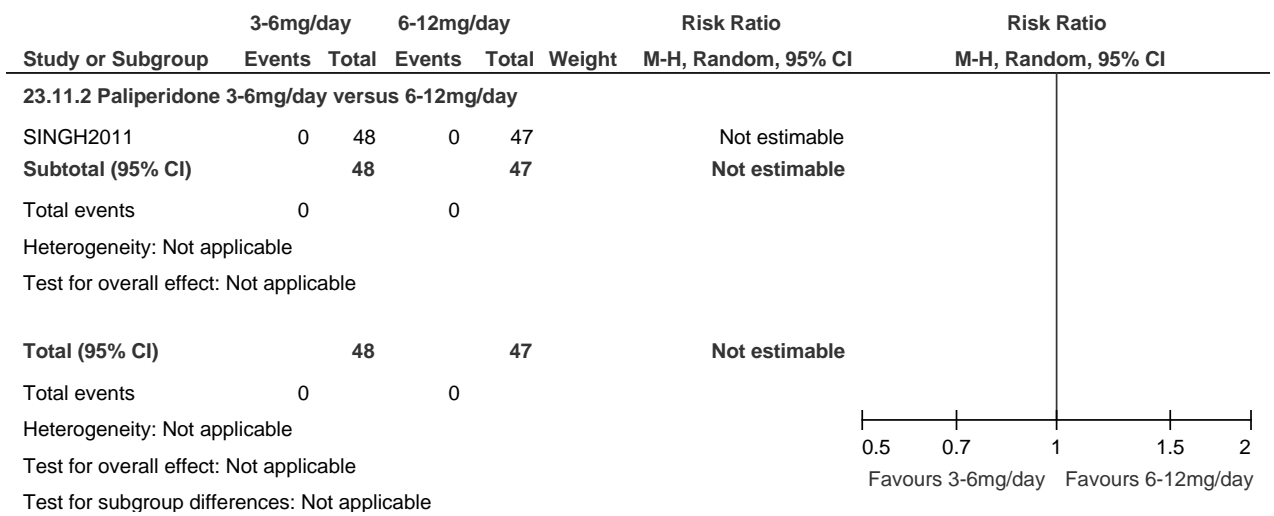


## 22. 'Higher dose' paliperidone (3 to 6mg/day) versus additional (high dose) paliperidone (6 to 12mg/day): post-treatment side effect outcomes

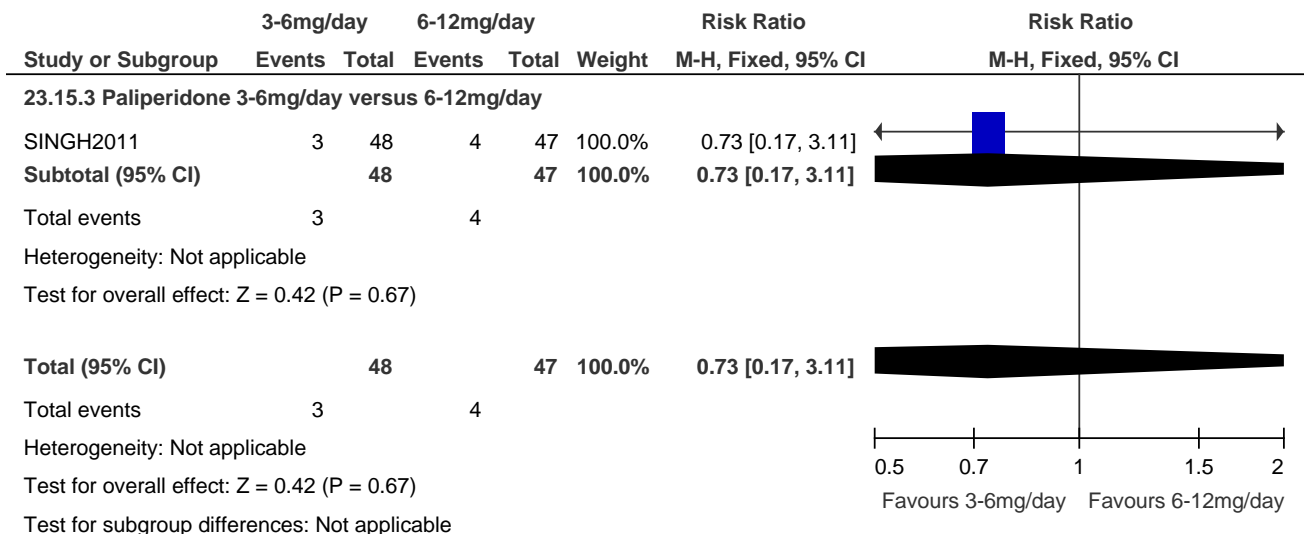
### 22.1 Mean change in weight (kg)



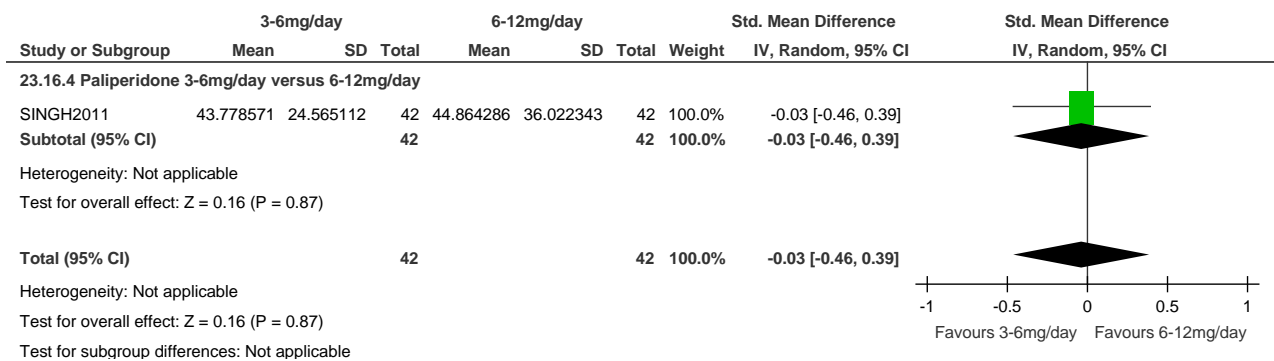
## 22.2 Prolonged QT interval (msec)



## 22.3 Tachycardia



## 22.4 Mean change in prolactin level (mg/dl)

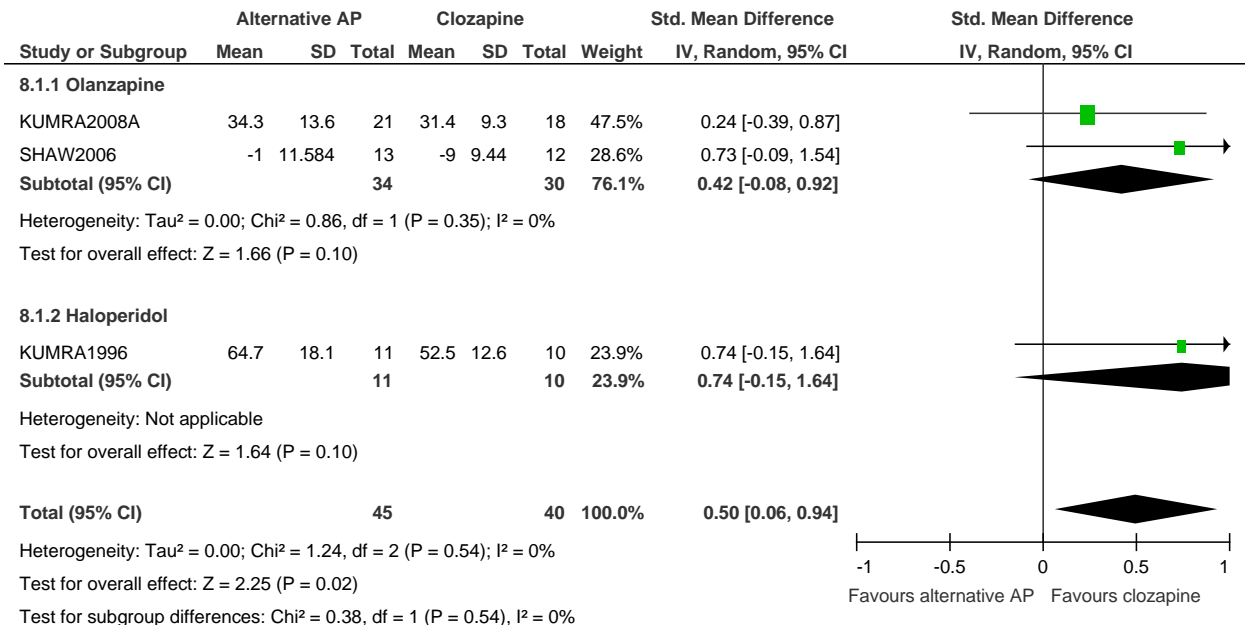


# APPENDIX 14C (III): TREATMENT RESISTANT PSYCHOSIS AND SCHIZOPHRENIA

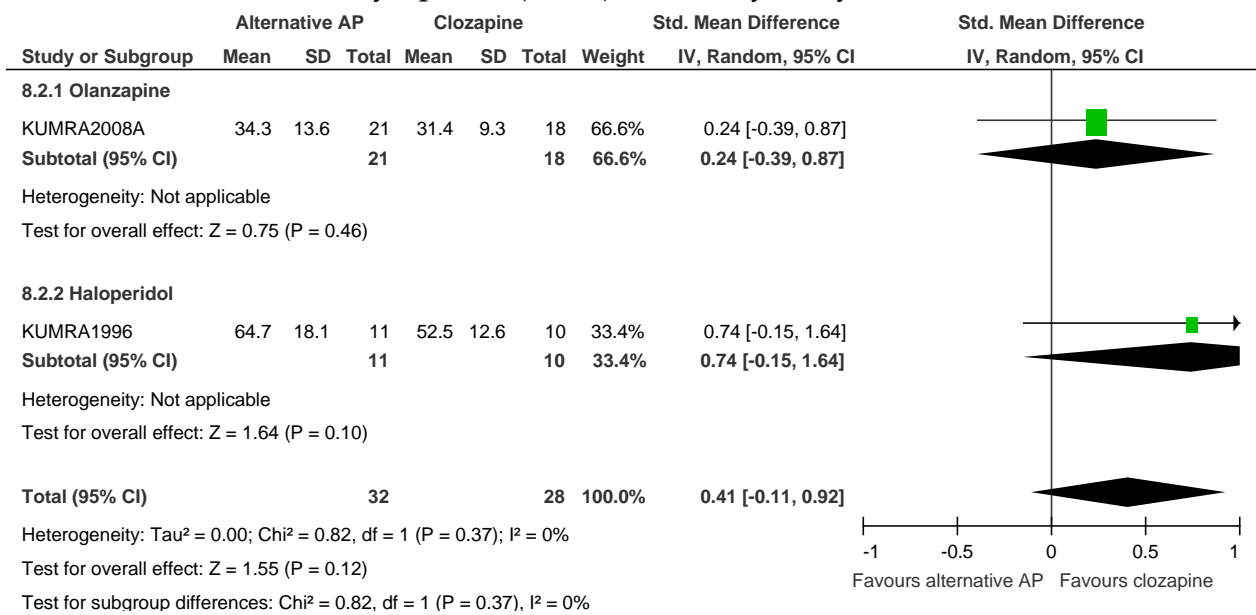
## PHARMACOLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 18 YEARS AND YOUNGER

### 1. Clozapine versus another antipsychotic: post-treatment efficacy outcomes

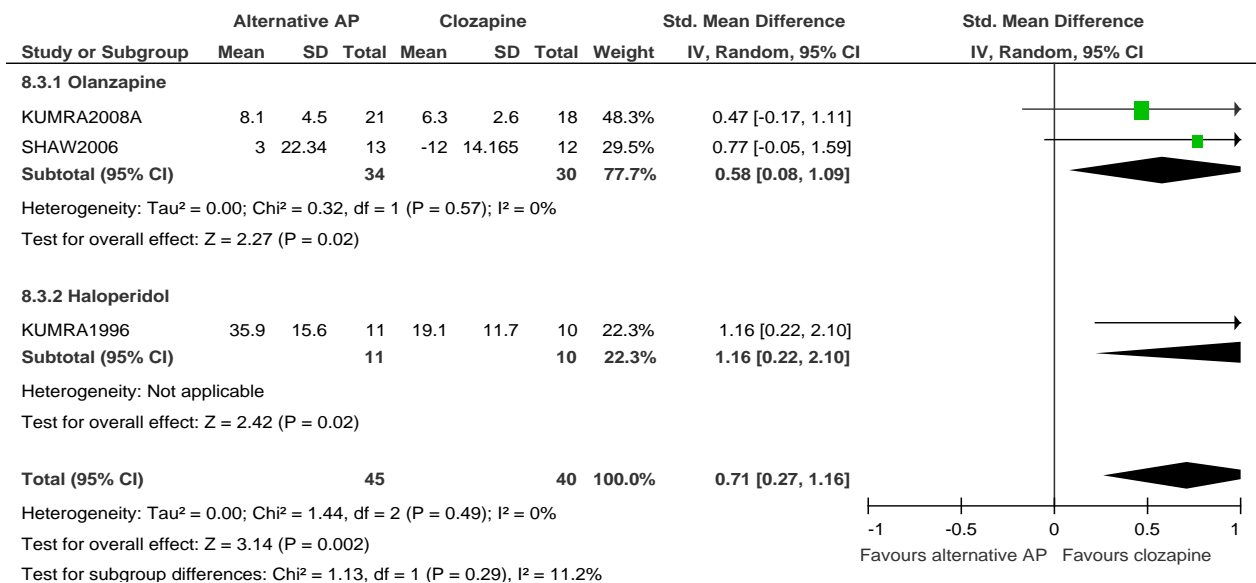
#### 1.1 Mental state: total symptoms (BPRS)



## 1.2 Mental state: total symptoms (BPRS) sensitivity analysis

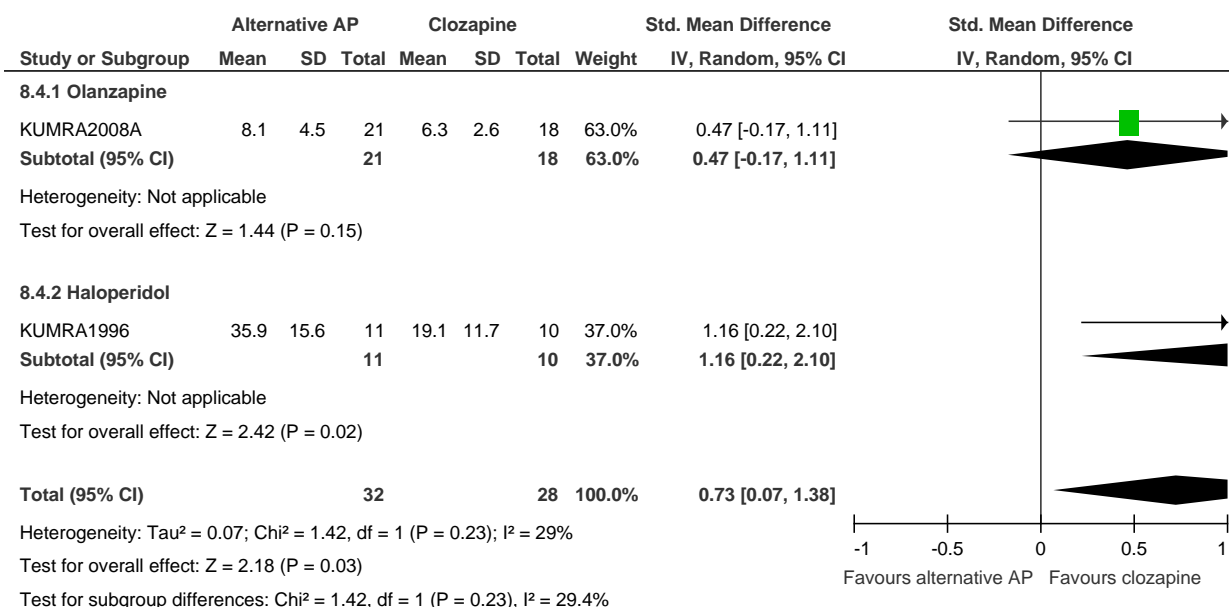


## 1.3 Mental state: positive symptoms (SAPS, BPRS Positive)

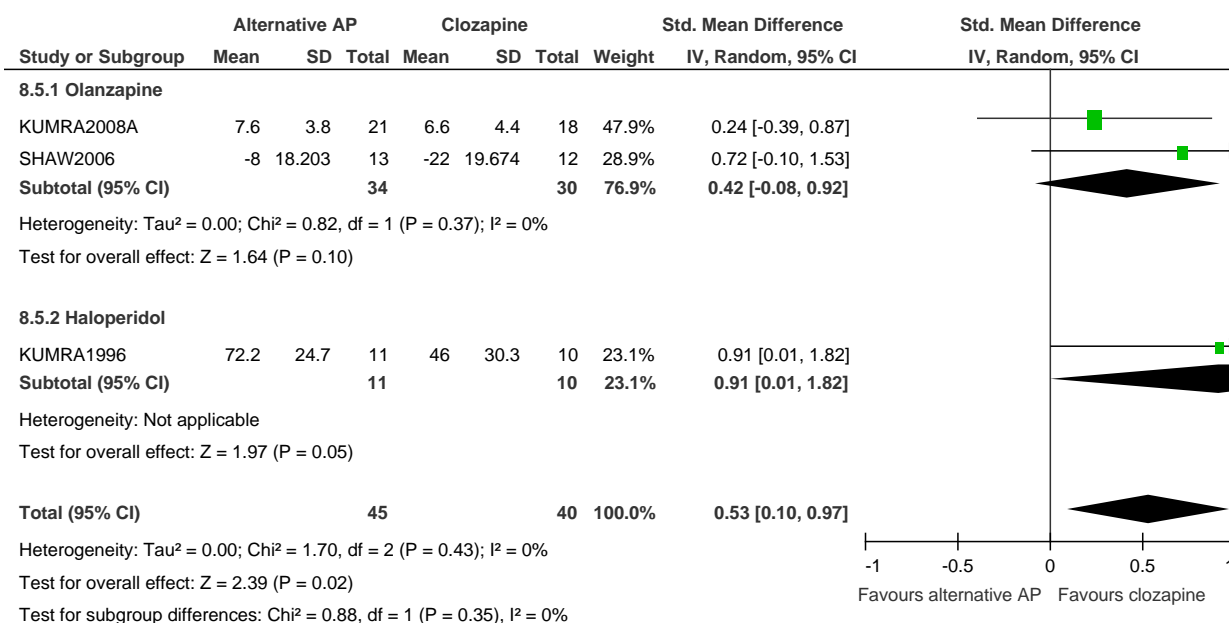




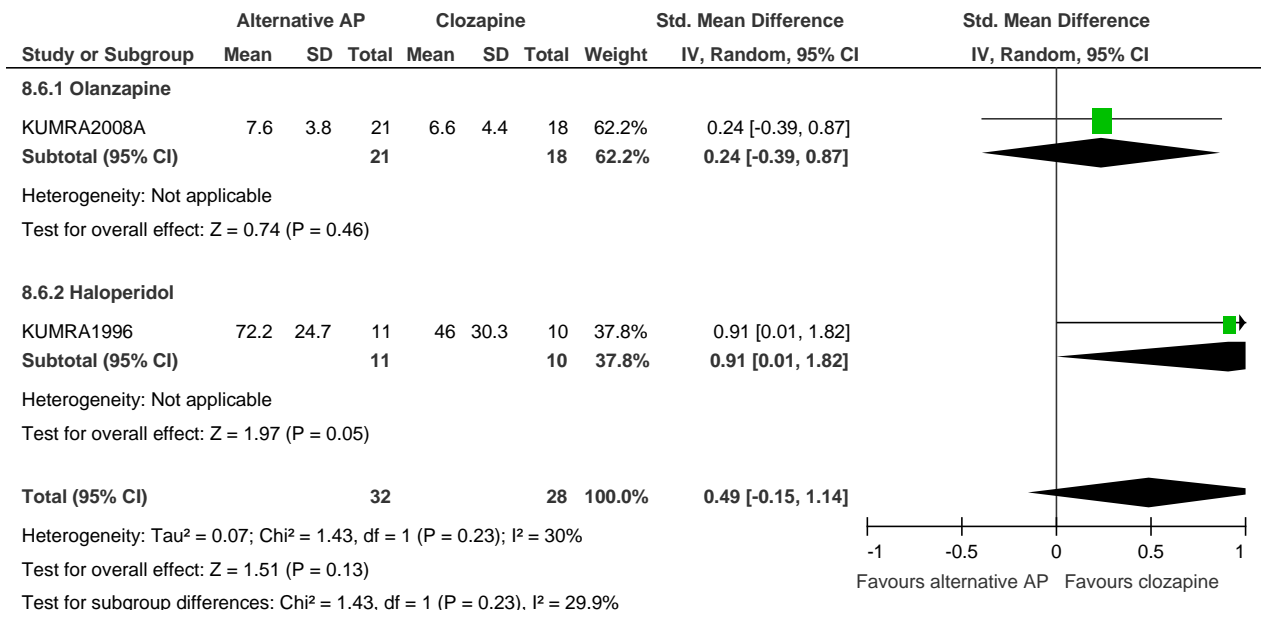
## 1.4 Mental state: positive symptoms (SAPS, BPRS Positive) sensitivity analyses



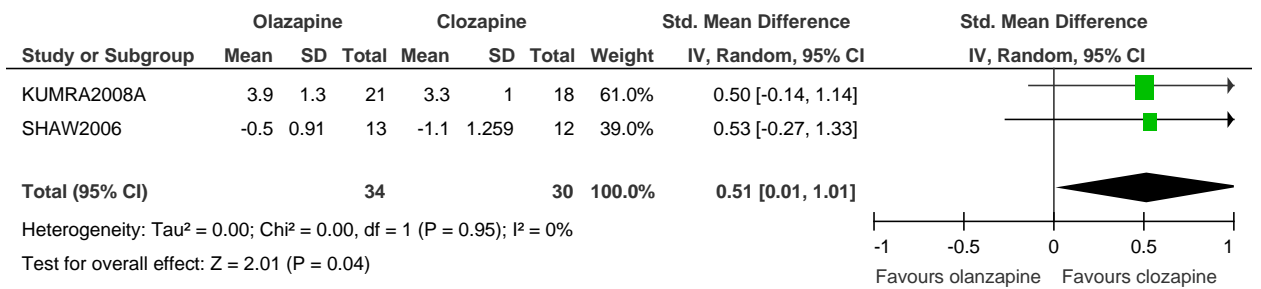
## 1.5 Mental state: negative symptoms (SANS)



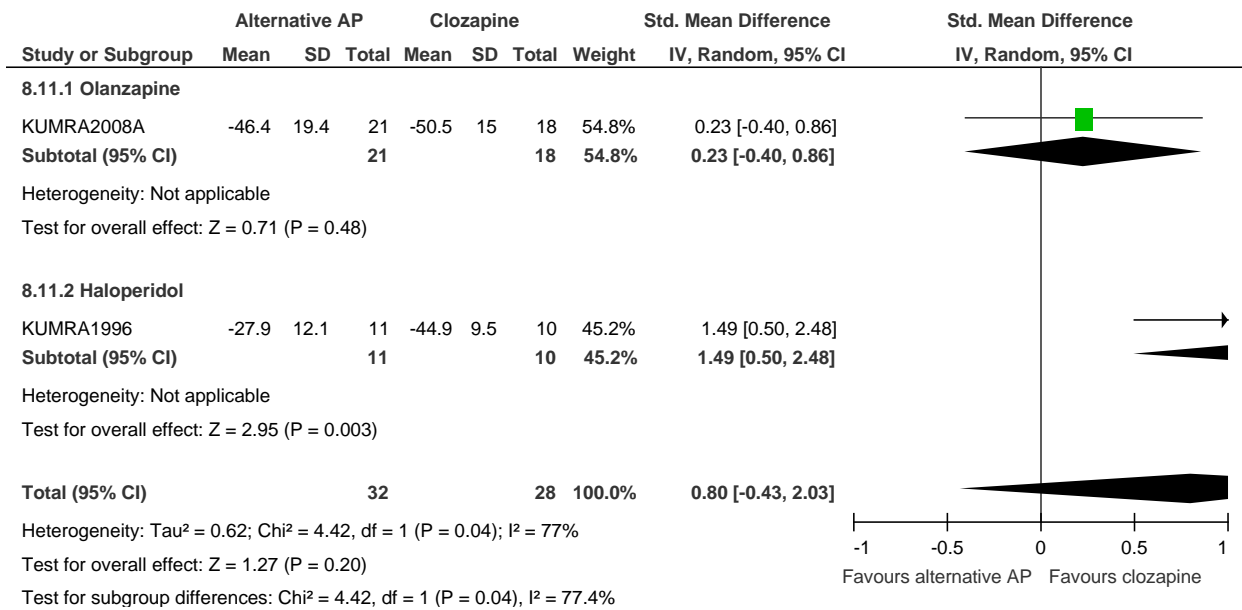
## 1.6 Mental state: negative symptoms (SANS) sensitivity analyses



## 1.7 Global state: severity (CGI-S)

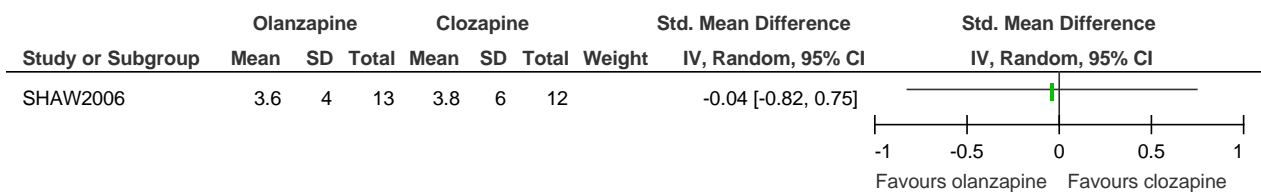


## 1.8 Functioning: psychosocial (CGAS)

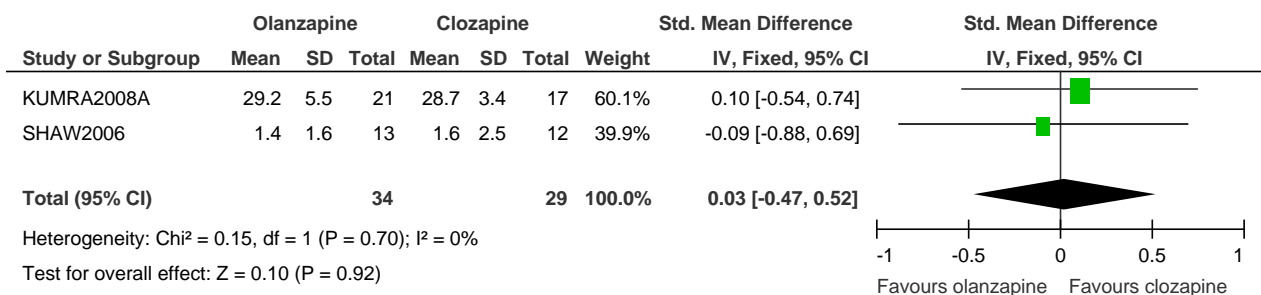


## 2. Clozapine versus another antipsychotic: post-treatment side effect outcomes

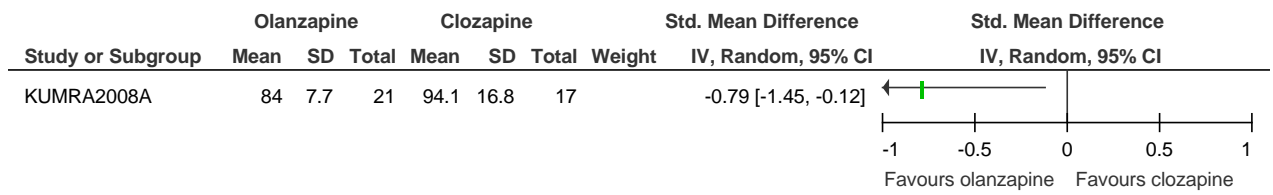
### 2.1 Weight (lbs)



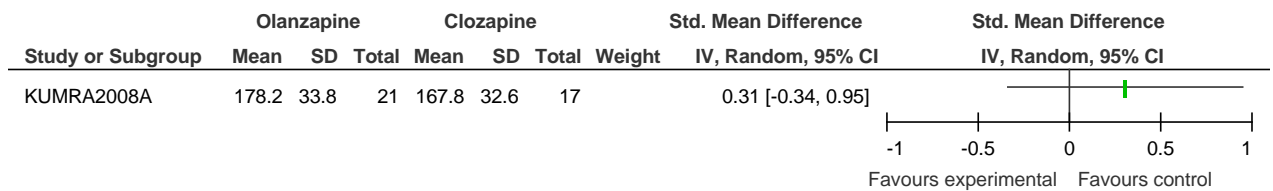
### 2.2 BMI (kg/m<sup>2</sup>)



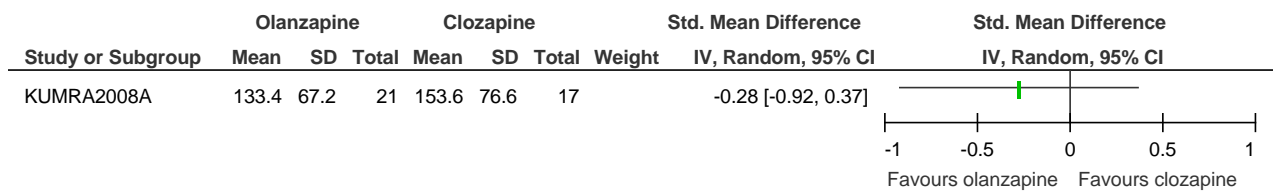
### 2.3 Fasting serum glucose level mg/dl



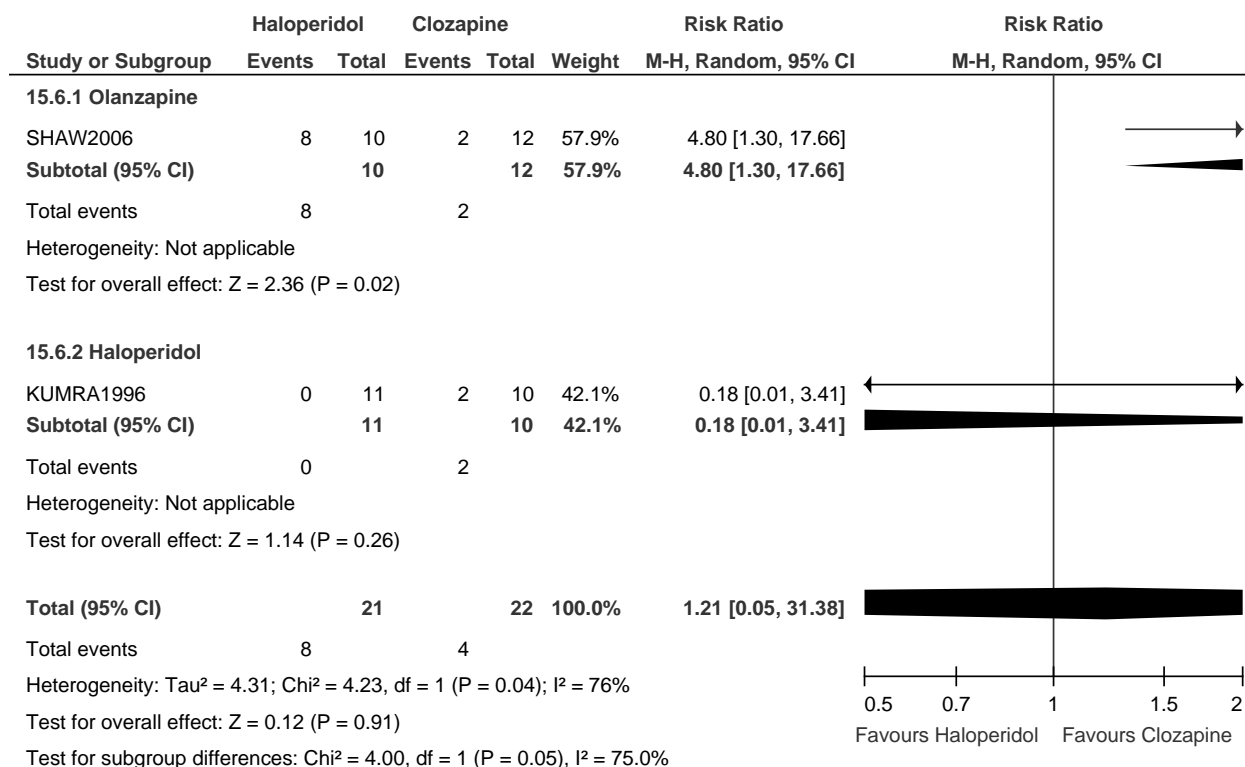
### 2.4 Fasting total cholesterol mg/dl



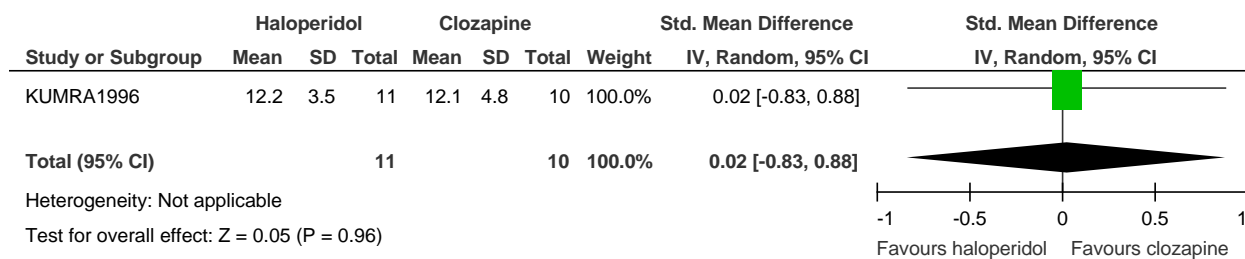
### 2.5 Fasting triglycerides mg/dl



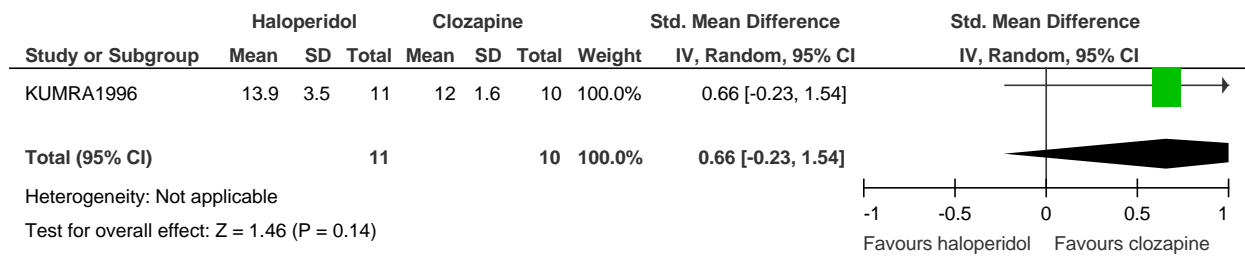
## 2.6 Tachycardia (number of participants)



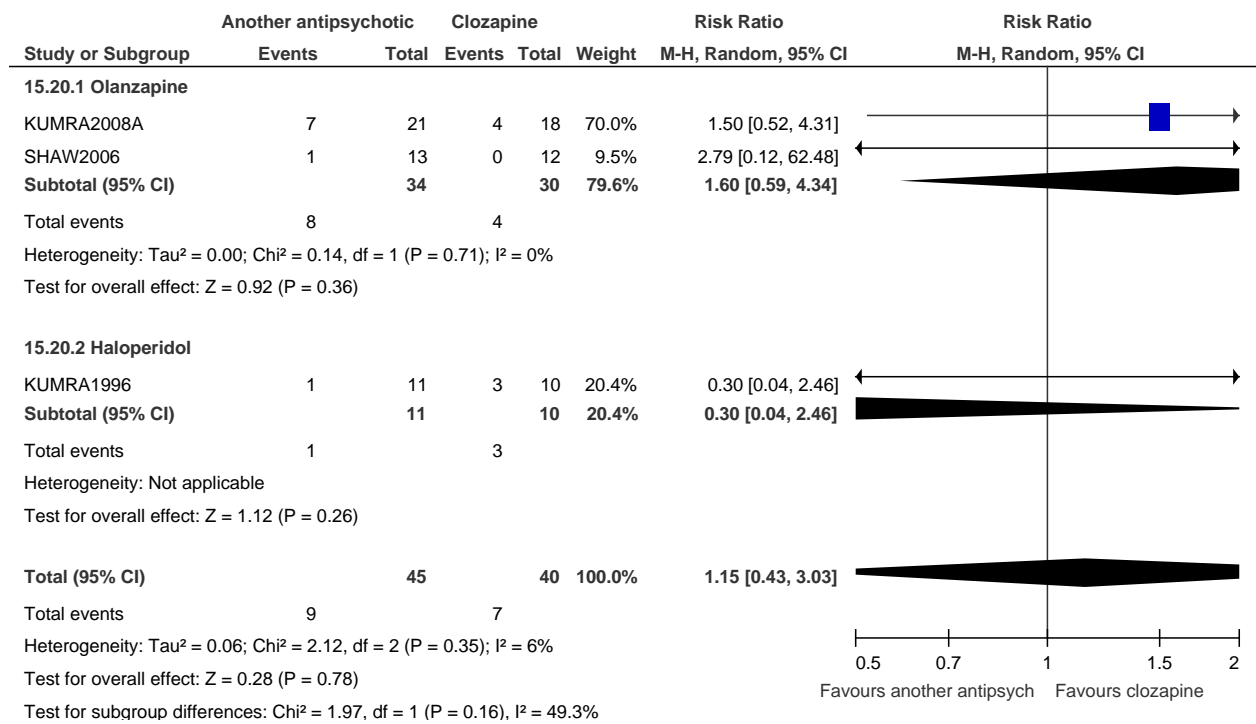
## 2.7 EPS (AIMS)



## 2.8 EPS (SAS)



## 2.9 Leaving the study early for any reason

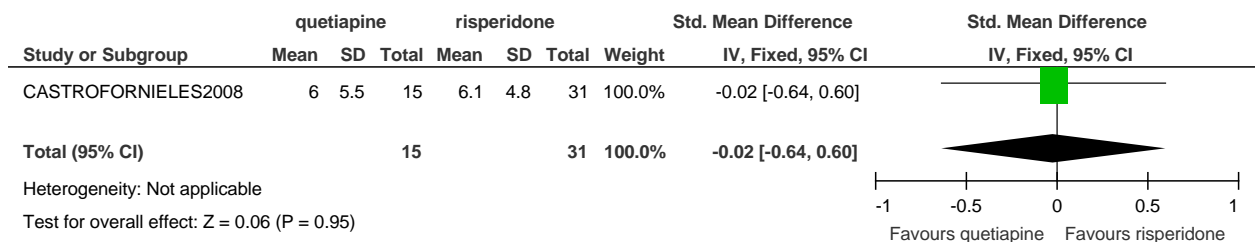


## APPENDIX 14C (IV): OBSERVATIONAL STUDIES - SIDE EFFECTS

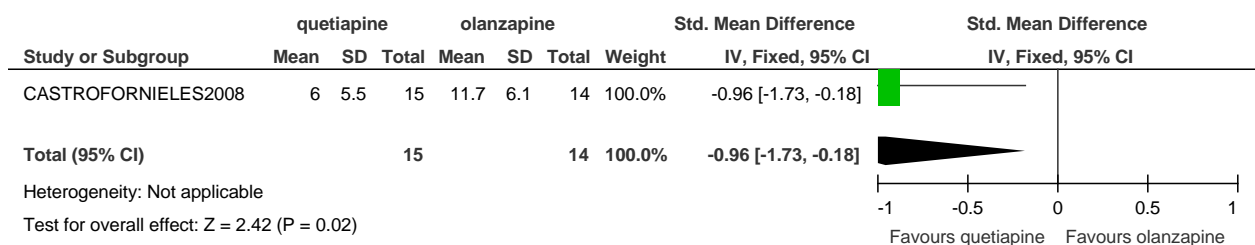
### PHARMACOLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 18 YEARS AND YOUNGER

#### 1. Weight change (kg)

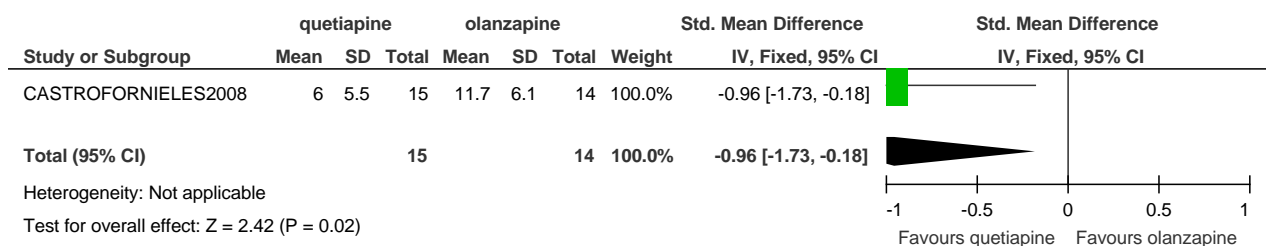
##### 1.1 Quetiapine versus risperidone: post-treatment



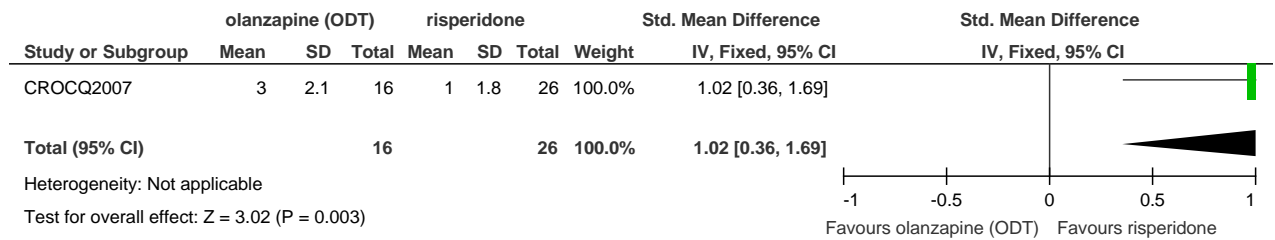
##### 1.2 Quetiapine versus olanzapine: post-treatment



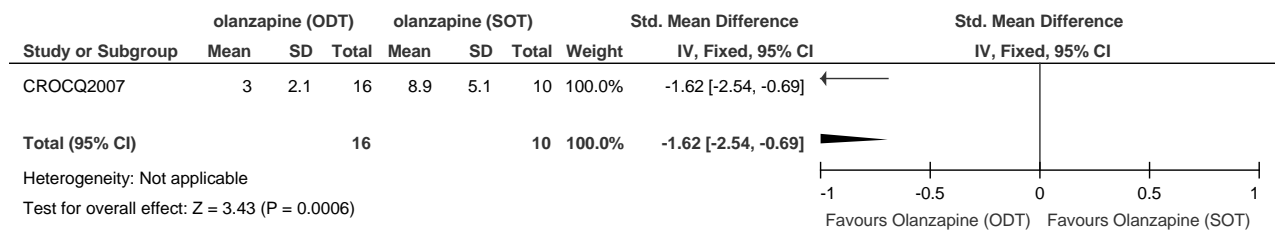
##### 1.3 Olanzapine (standard oral tablet [SOT]) versus risperidone: post-treatment



## 1.4 Olanzapine (orally disintegrating tablet [ODT]) versus risperidone: post-treatment

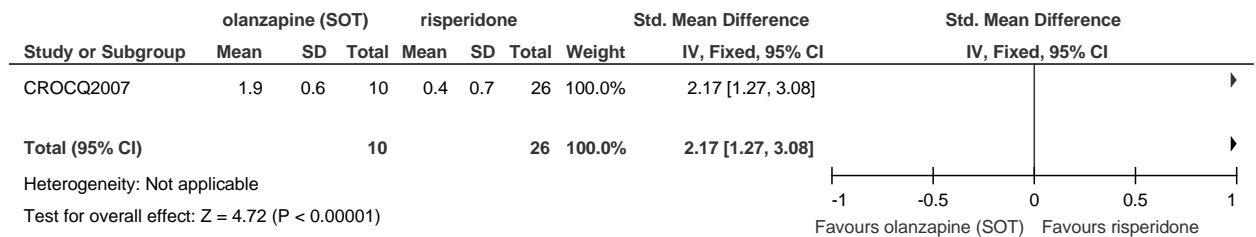


## 1.5 Olanzapine (SOT) versus olanzapine (ODT): post-treatment

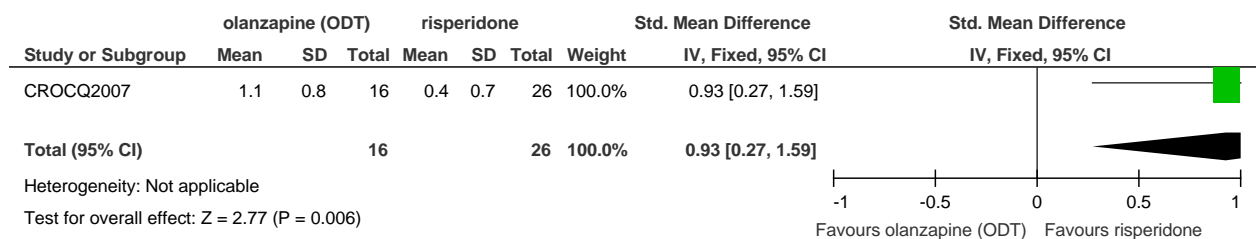


## 2. BMI change

### 2.1 Olanzapine (SOT) versus risperidone: post-treatment

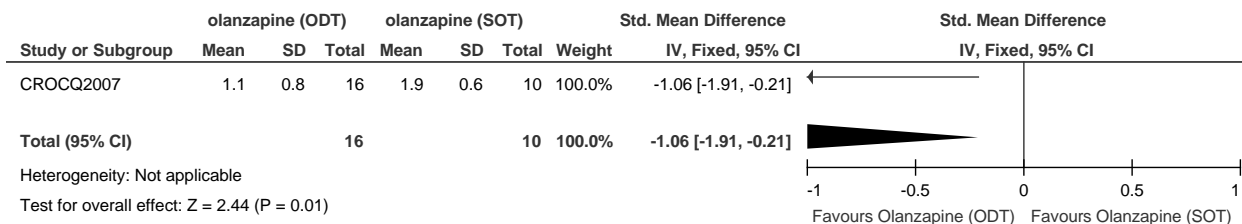


### 2.2 Olanzapine (ODT) versus risperidone: post-treatment



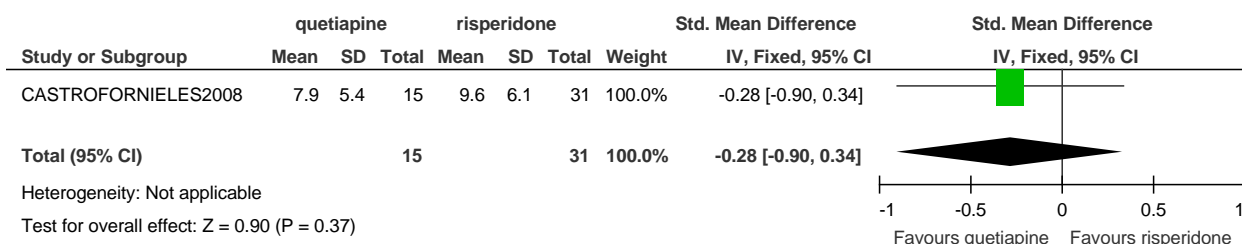


### 2.3 Olanzapine (SOT) versus olanzapine (ODT): post-treatment

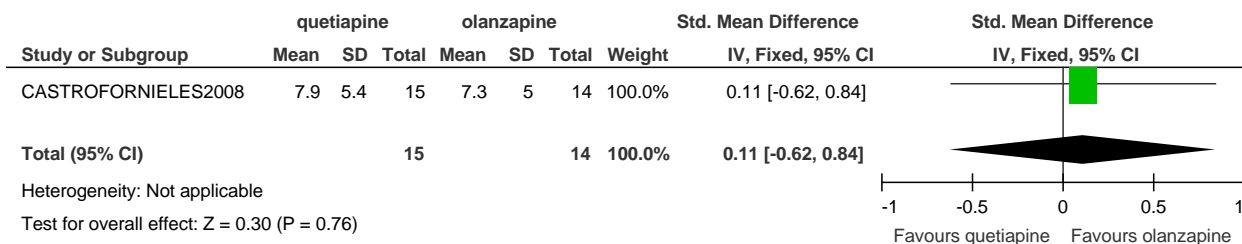


## 3. Neurological: UKU

### 3.1 Quetiapine versus risperidone: post-treatment



### 3.2 Quetiapine versus olanzapine: post-treatment



### 3.3 Olanzapine (SOT) versus risperidone: post-treatment

