

**APPENDIX 14C: CLINICAL EVIDENCE FOREST PLOTS:
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Abbreviations

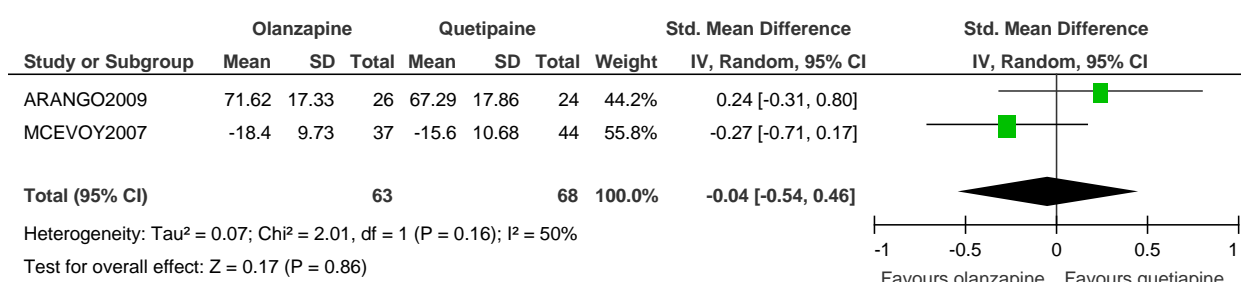
AIMS	Abnormal Involuntary Movement Scale
AP	antipsychotic
BARS	Barnes Akathisia Rating Scale
BMI	body mass index
BP	blood pressure
BPM	beats per minute
BPRS (-C, -P)	Brief Psychiatric Rating Scale (- Children, - Psychotic Subscale)
CDSS	Calgary Depression Scale for Schizophrenia
CGAS	Children's Global 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

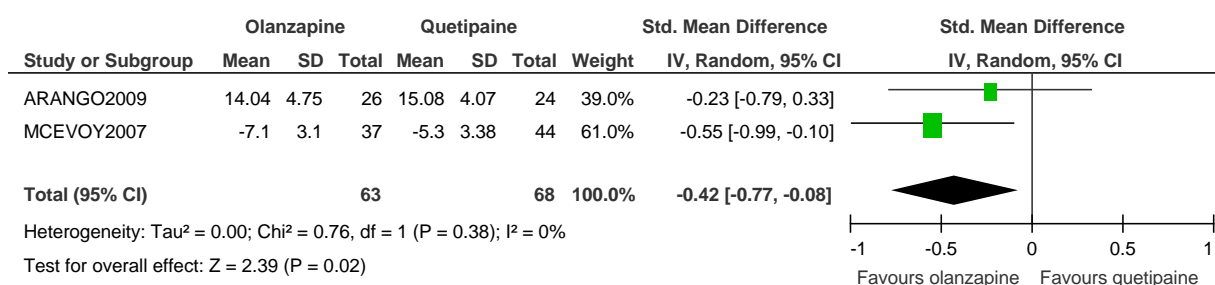
PHARMACOLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 18 YEARS AND YOUNGER COMBINED WITH THOSE AGED 25 YEARS AND YOUNGER

1. Olanzapine versus quetiapine: post-treatment efficacy outcomes

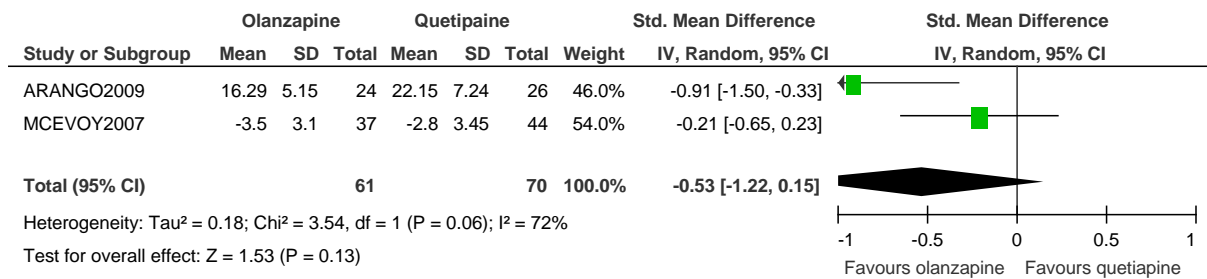
1.1 Mental state: total symptoms (Positive and Negative Syndrome Scale [PANSS]) (mean endpoint: ARANGO2009; mean change: MCEVOY2007)



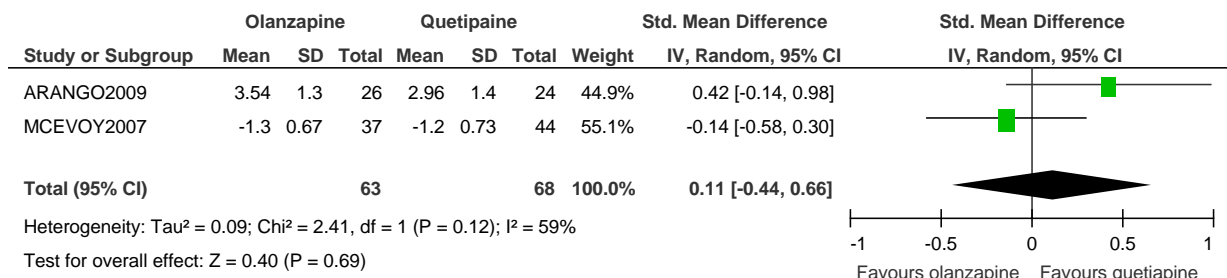
1.2 Mental state: positive symptoms (Scale for the Assessment of Positive Symptoms [SAPS]) (mean endpoint: ARANGO2009; mean change: MCEVOY2007)



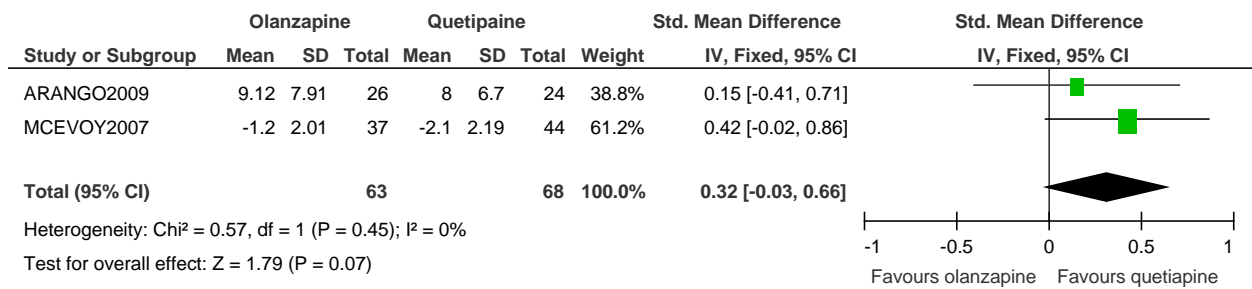
1.3 Mental state: negative symptoms (Scale for the Assessment of Negative Symptoms [SANS]) (mean endpoint: ARANGO2009; mean change: MCEVOY2007)



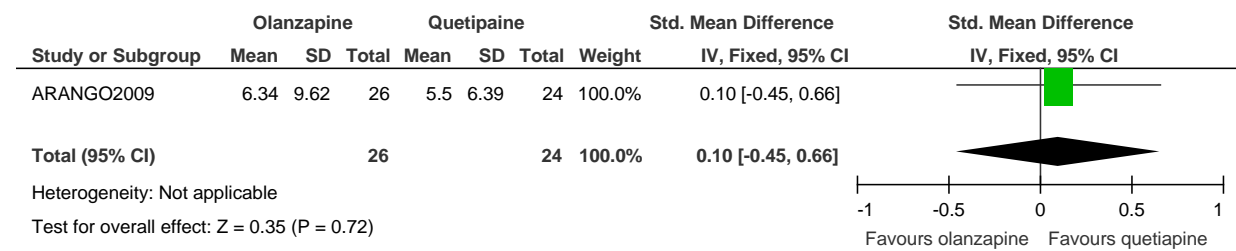
1.4 Global state: severity (Clinical Global Impression - Severity scale [CGI-S]) (mean endpoint: ARANGO2009; mean change: MCEVOY2007)



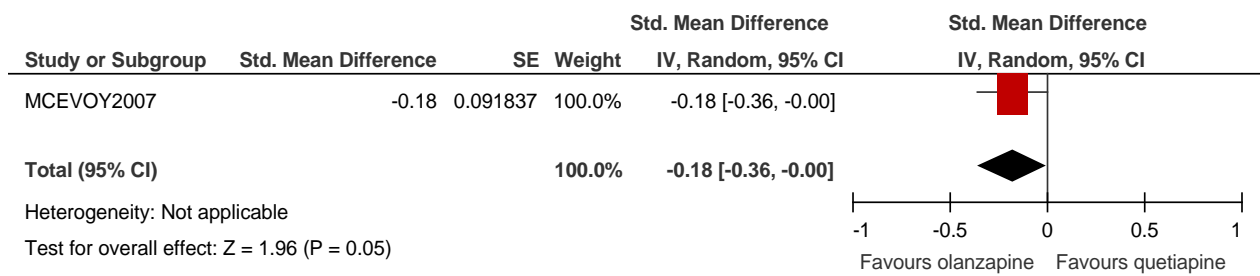
1.5 Mental state: depression (Hamilton Depression Rating Scale [HAM-D], Calgary Depression Scale for Schizophrenia [CDSS]) (mean endpoint: ARANGO2009; mean change: MCEVOY2007)



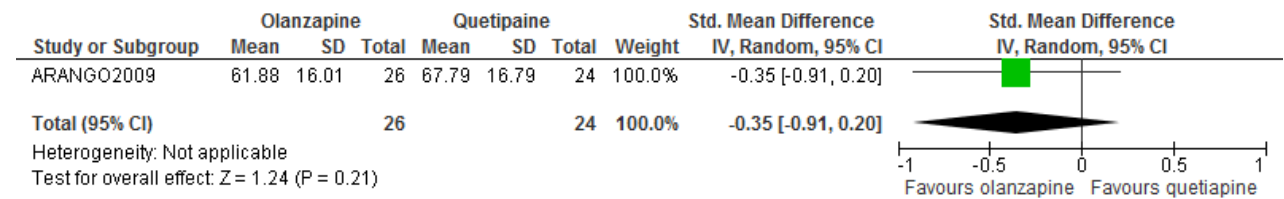
1.6 Mental state: mean endpoint mania (Young Mania Rating Scale [YMRS])



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

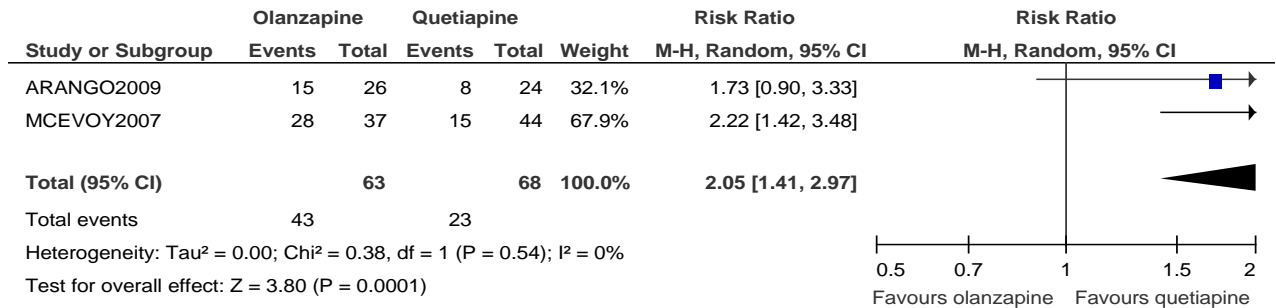


1.8 Psychosocial functioning: mean endpoint (Global Assessment of Functioning [GAF])

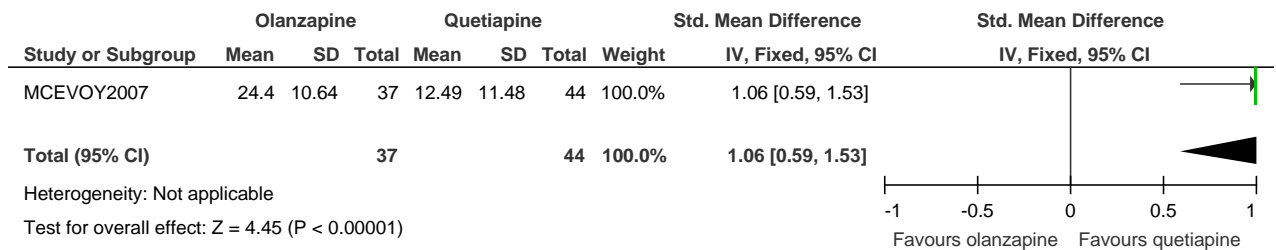


2. Olanzapine versus quetiapine: post-treatment side effect outcomes

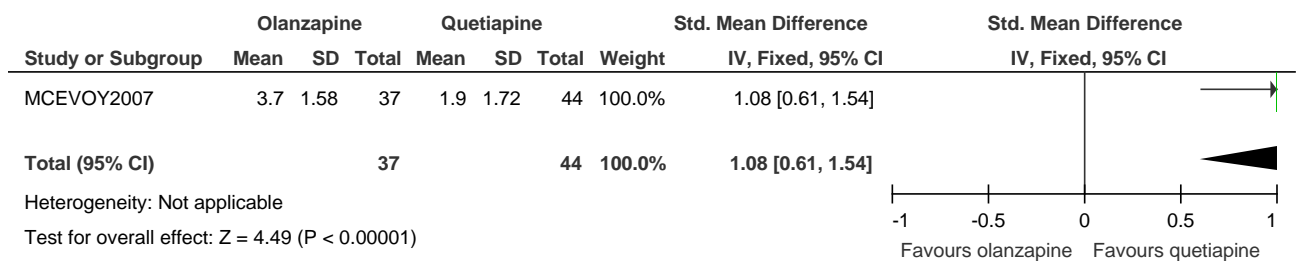
2.1 Weight gain (kg, not defined: ARANGO2009; number of participants with weight (lbs) gain of 7% or greater: MCEVOY2007)



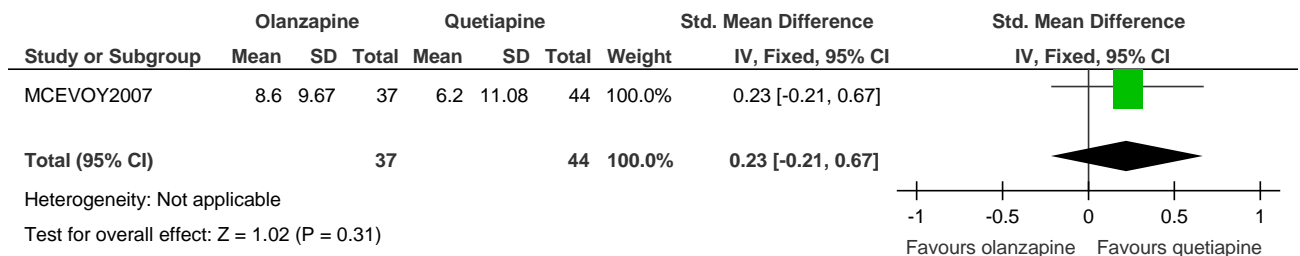
2.2 Mean change in weight (lbs)



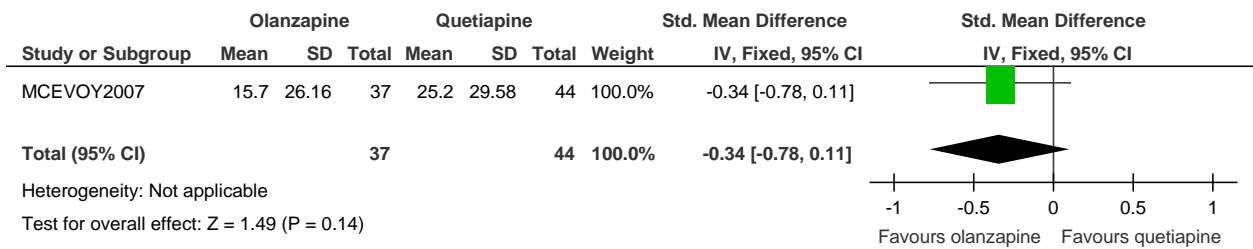
2.3 Mean change in BMI (kg/m²)



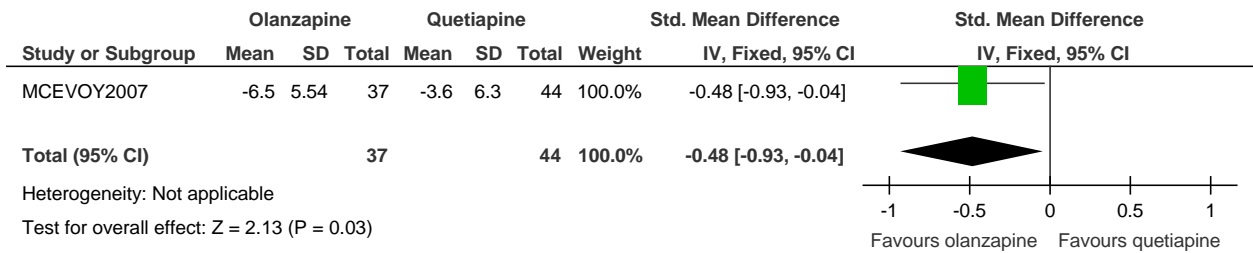
2.4 Mean change in fasting serum glucose level (mg/dl)



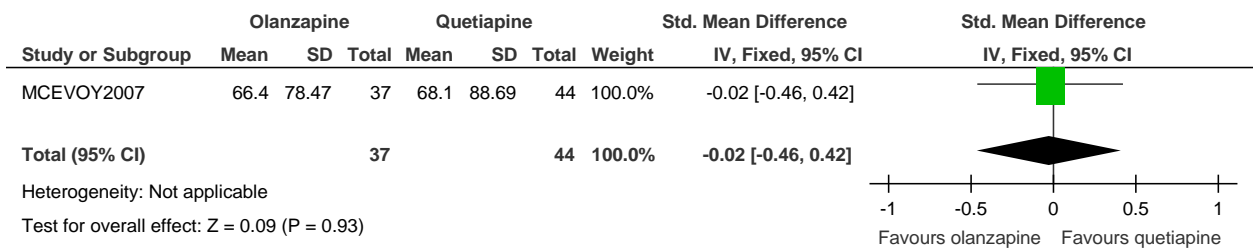
2.5 Mean change in fasting total cholesterol (mg/dl)



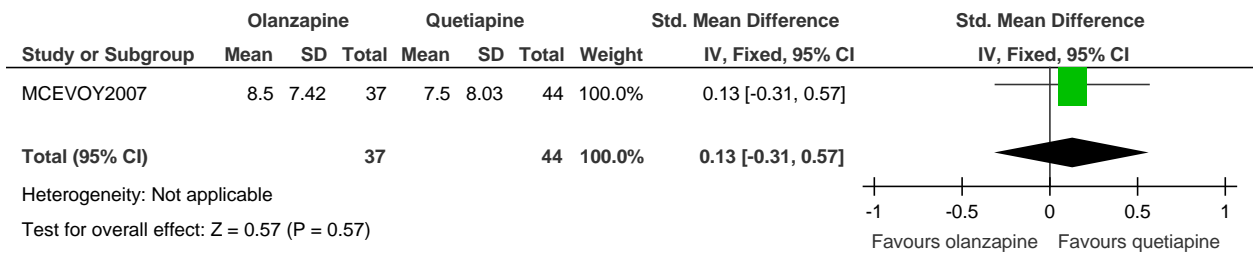
2.6 Mean change in fasting high-density lipoprotein cholesterol (mg/dl)



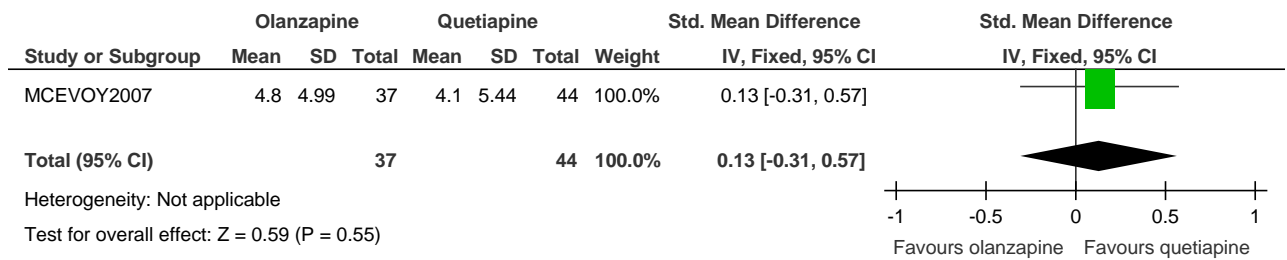
2.7 Mean change in fasting triglycerides (mg/dl)



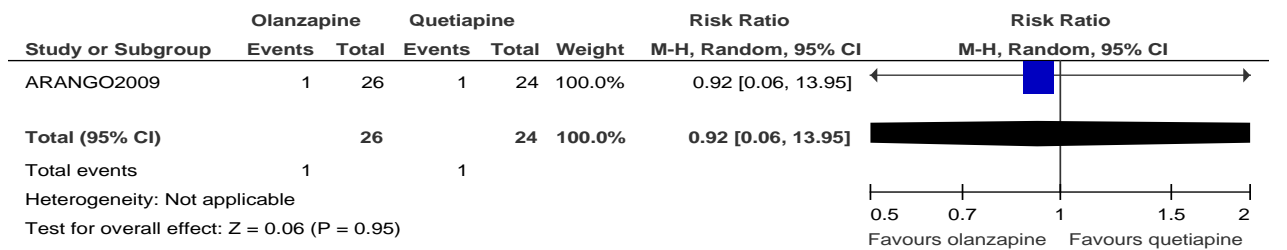
2.8 Mean change in systolic BP (mmHg)



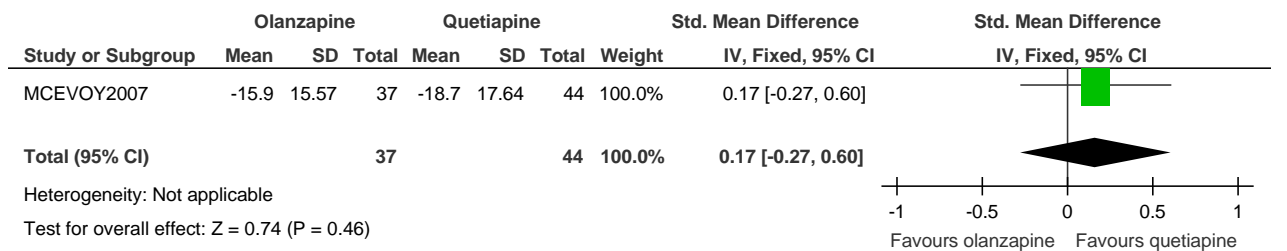
2.9 Mean change in diastolic BP (mmHg)



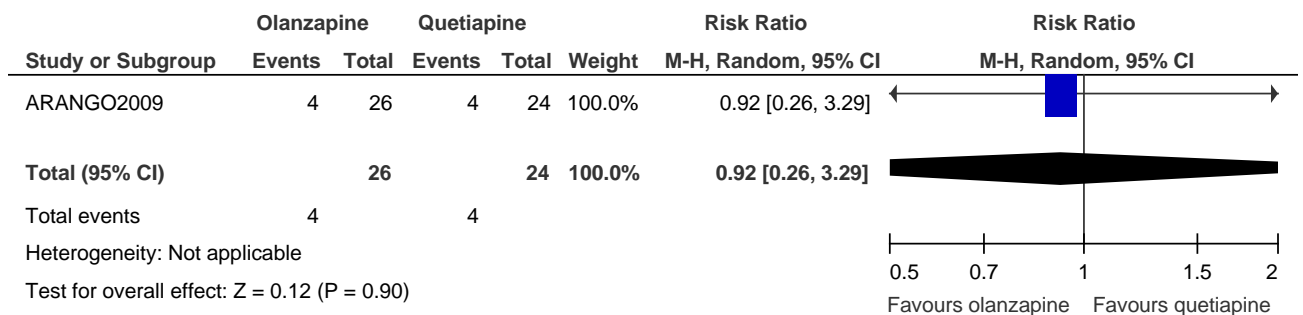
2.10 Tachycardia



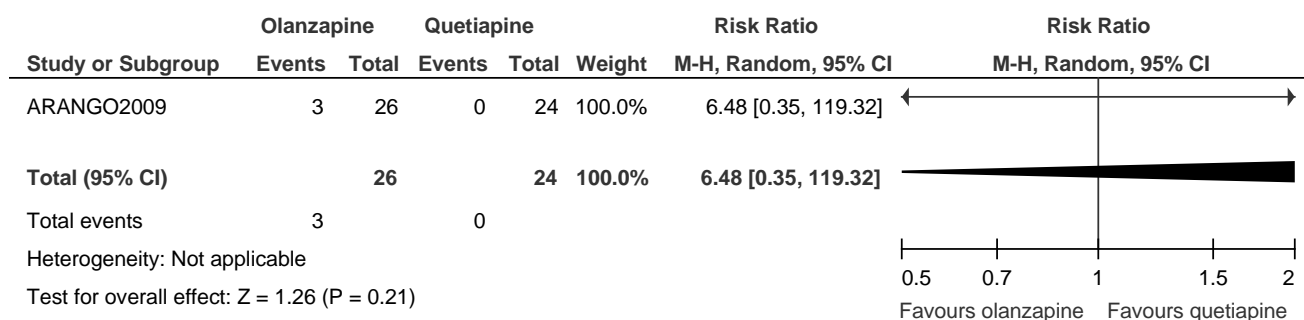
2.11 Mean change in prolactin level (mg/dl)



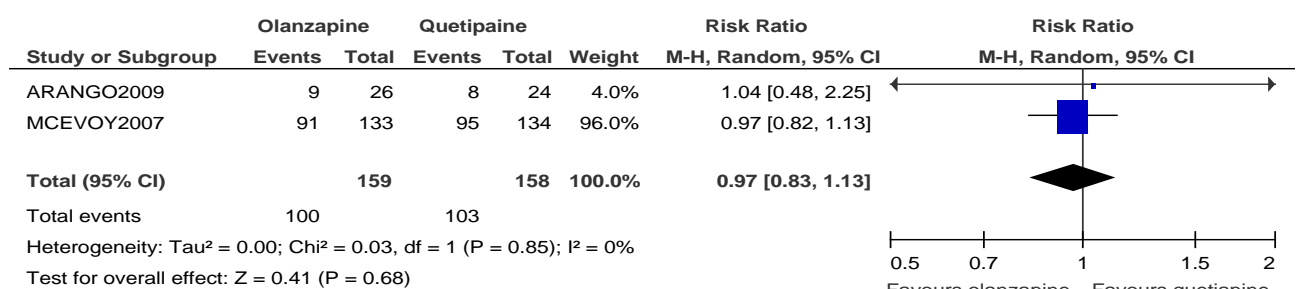
2.12 Tremor



2.13 Akathisia



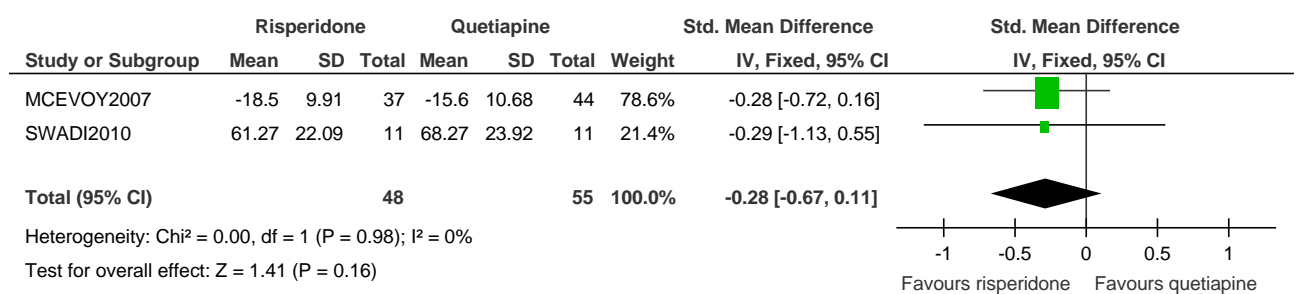
2.14 Leaving the study early for any reason



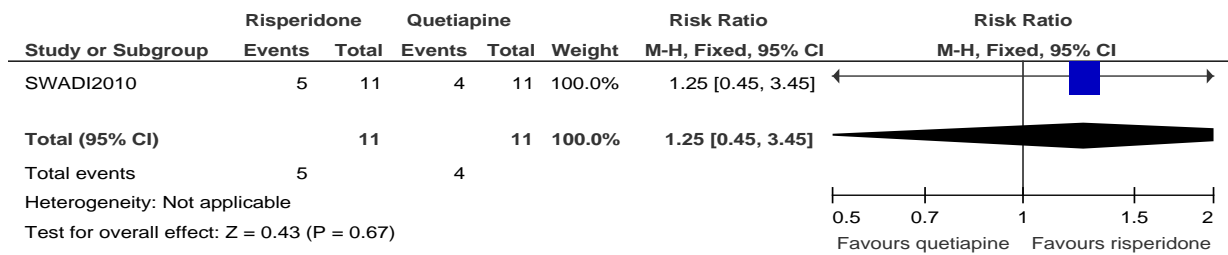
PHARMACOLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 25 YEARS AND YOUNGER

3. Risperidone versus quetiapine: post-treatment efficacy outcomes

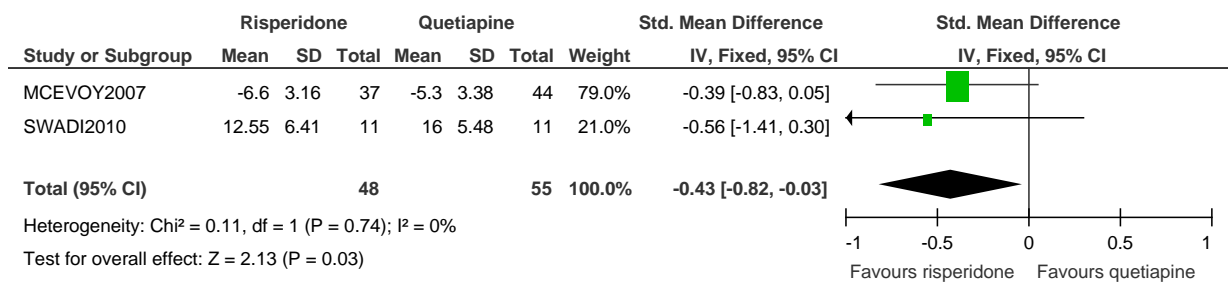
3.1 Mental state: mean change in total symptoms (PANSS)



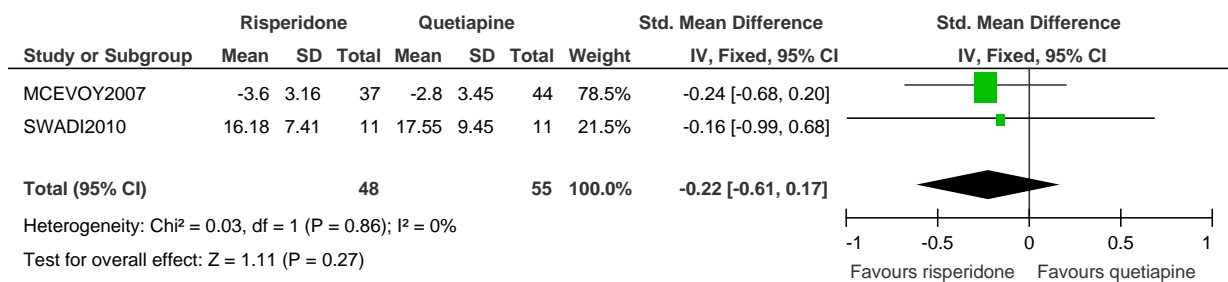
3.2 Mental state: response (number of participants with a 30% reduction on the PANSS)



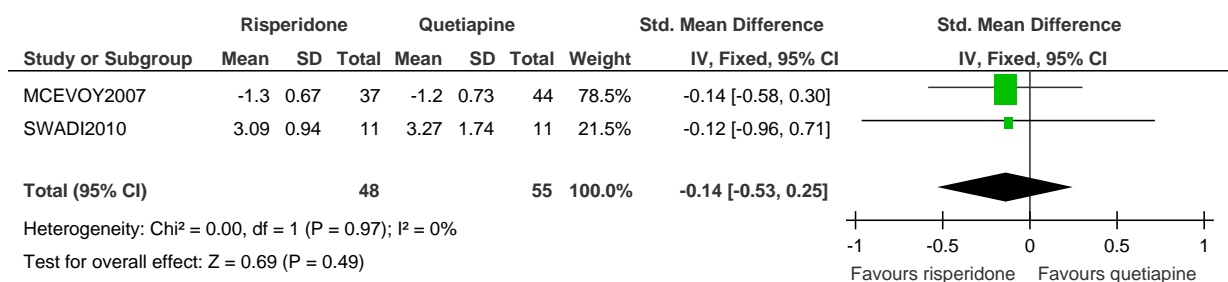
3.3 Mental state: mean change in positive symptoms (SAPS)



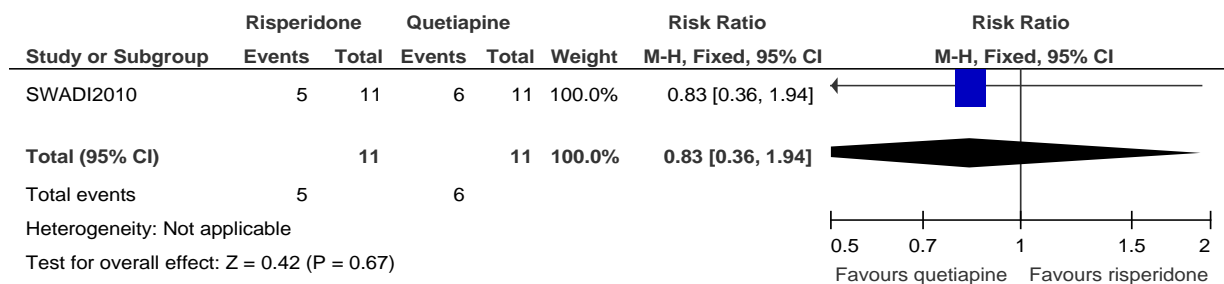
3.4 Mental state: mean change in negative symptoms (SANS)



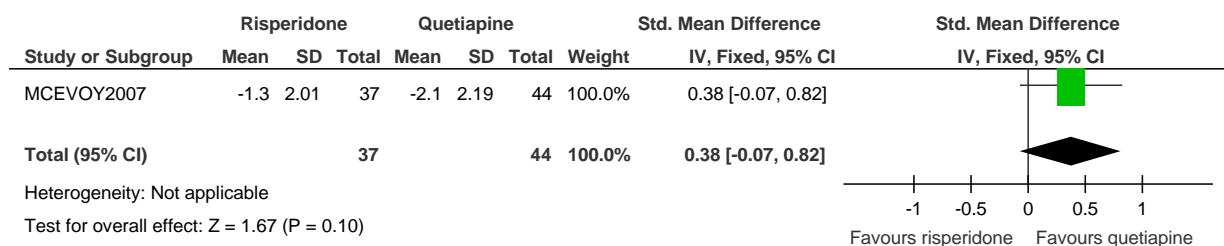
3.5 Mean change in global state: severity (CGI-S)



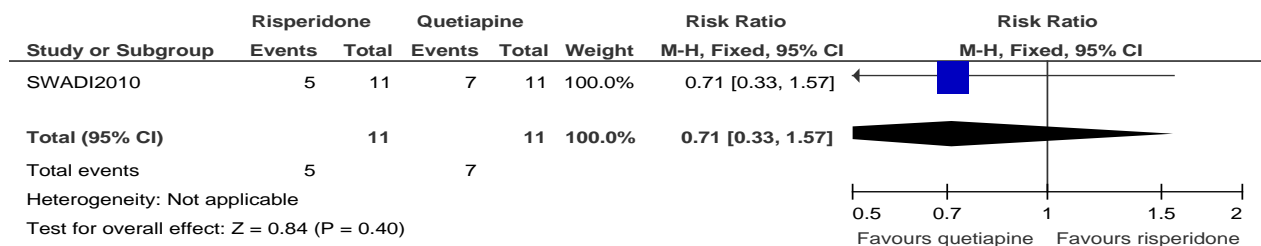
3.6 Global state response (number of participants with a 30% reduction CGI-S)



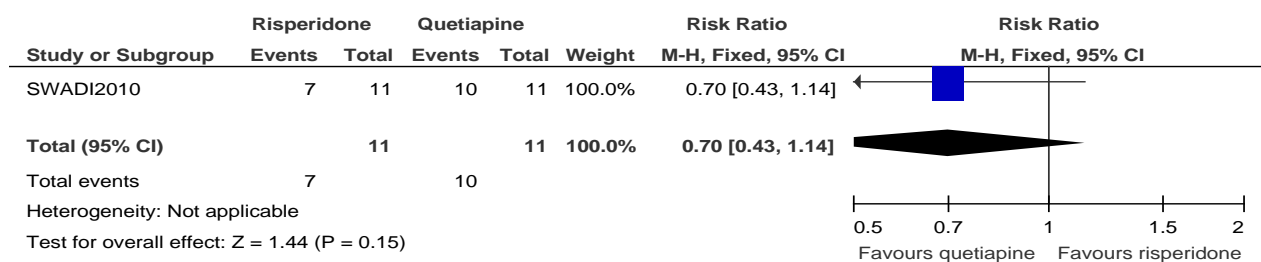
3.7 Mental state: mean change in depression (CDSS)



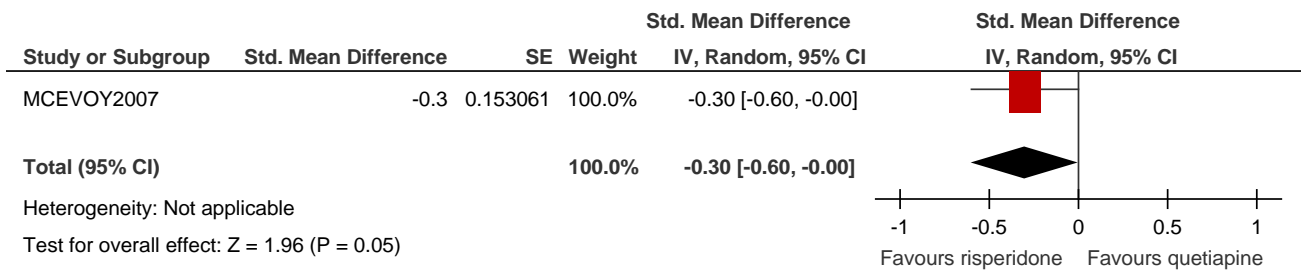
3.8 Mental state: depression response (number of participants with a 30% reduction on the HAM-D)



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

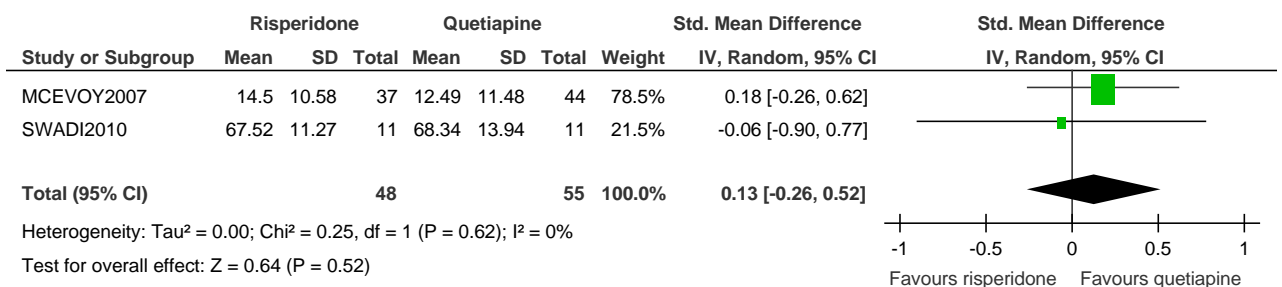


3.10 Mean change in quality of life (QLS)

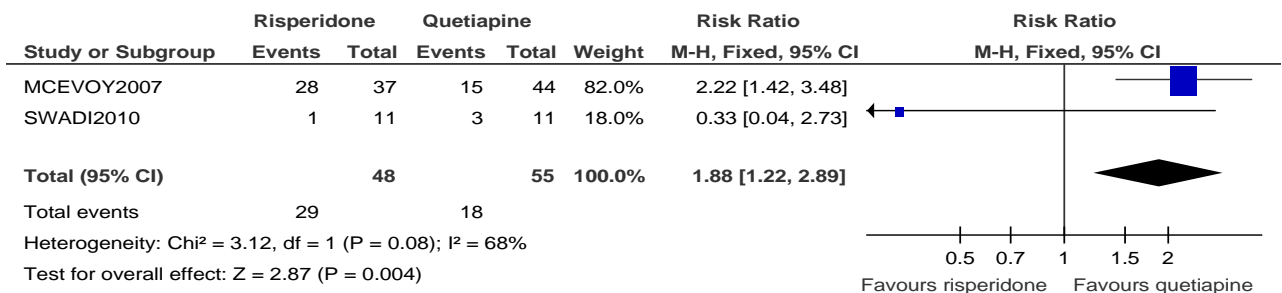


4. Risperidone versus quetiapine: post-treatment side effect outcomes

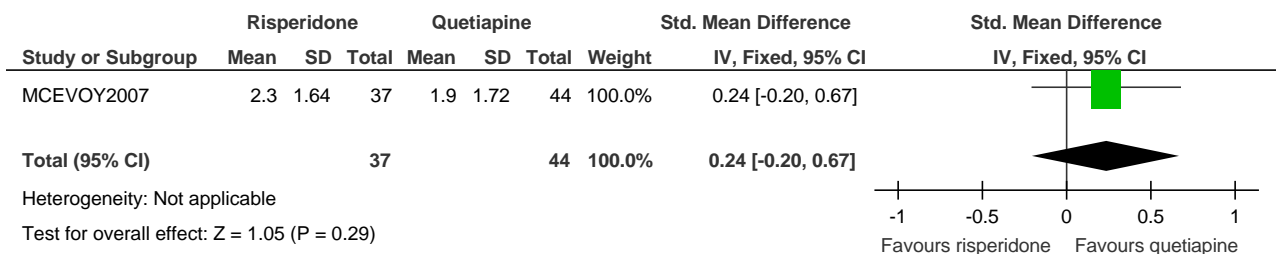
4.1 Mean change in weight



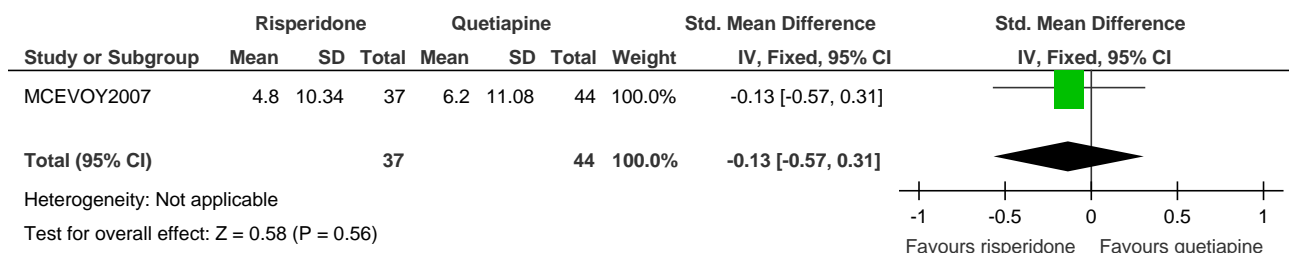
4.2 Weight gain (number of participants who gained over 7%)



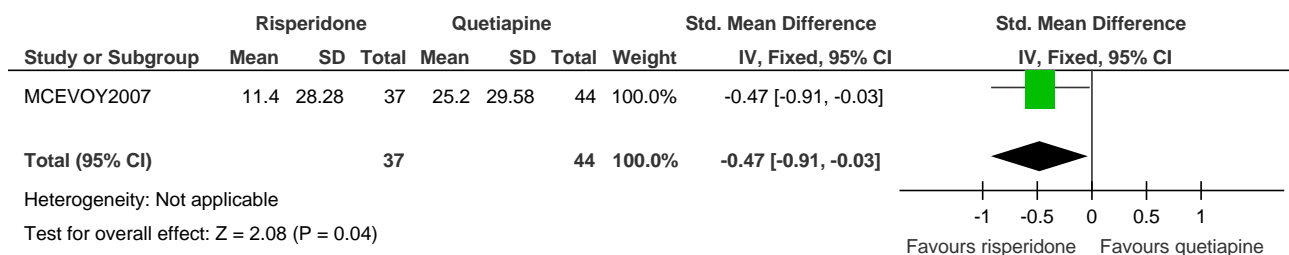
4.3 Mean change in BMI (kg/m²)



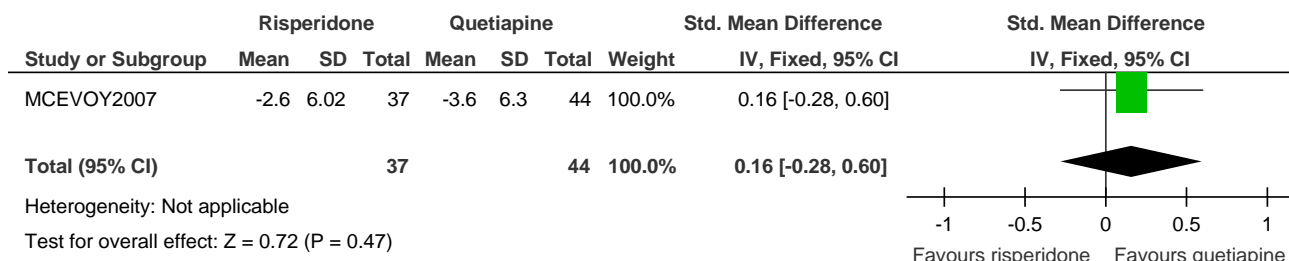
4.4 Mean change in fasting serum glucose level (mg/dl)



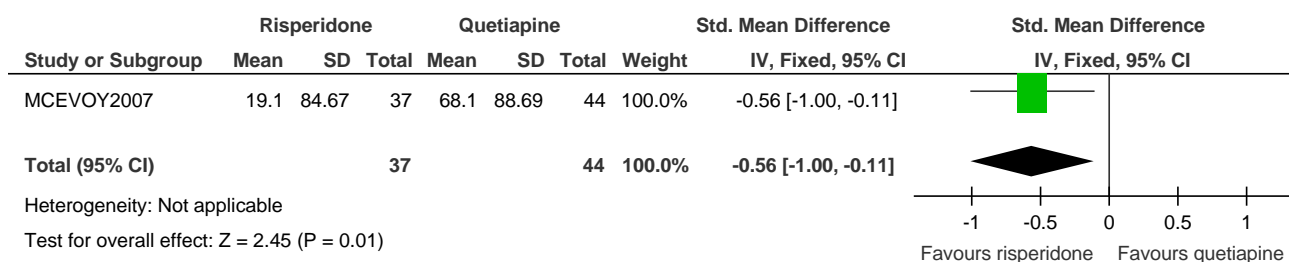
4.5 Mean change in fasting total cholesterol (mg/dl)



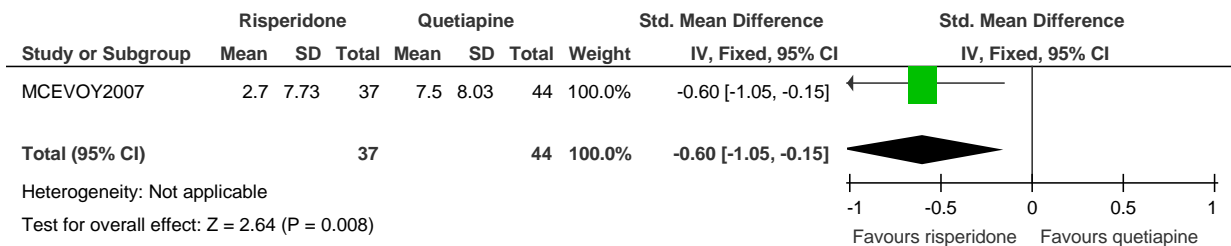
4.6 Mean change in fasting high-density lipoprotein cholesterol (mg/dl)



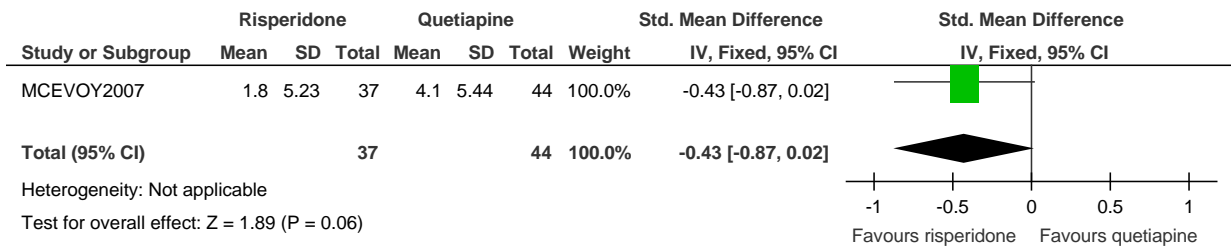
4.7 Mean change in fasting triglycerides (mg/dl)



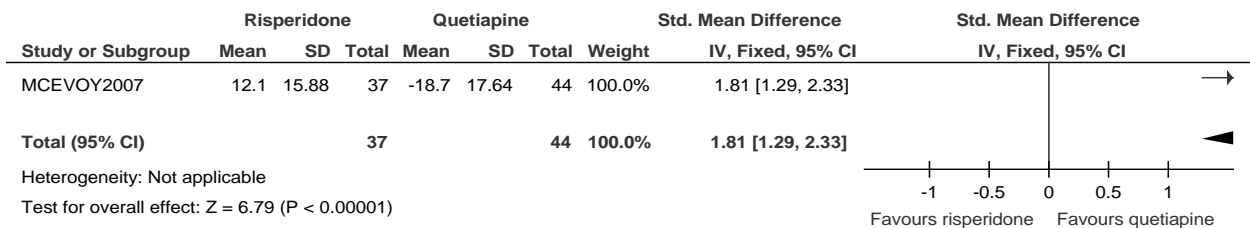
4.8 Mean change in systolic BP (mm Hg)



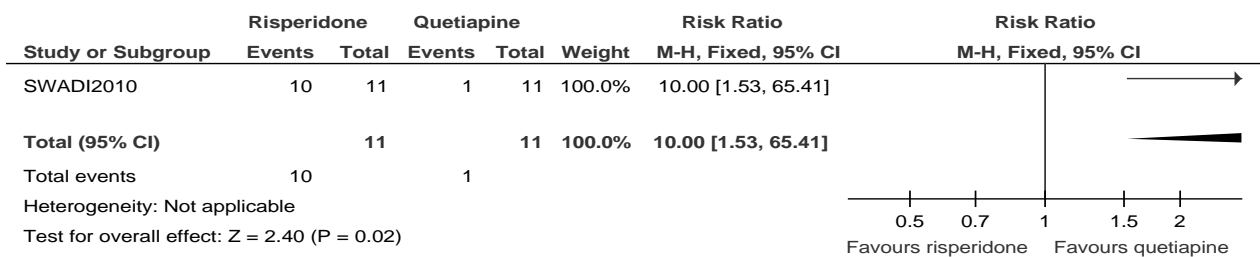
4.9 Mean change in diastolic BP (mm Hg)



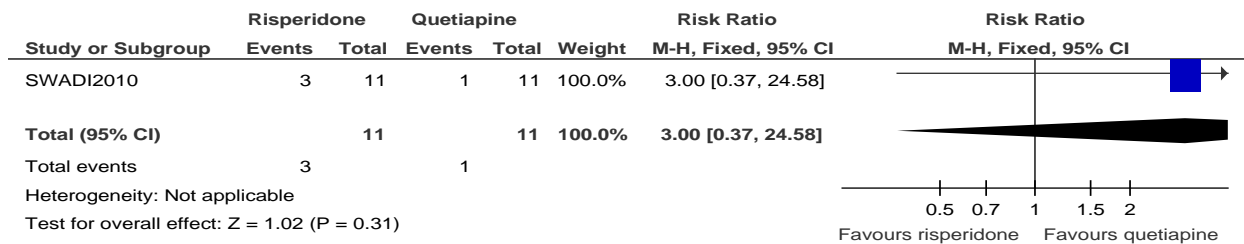
4.10 Mean change in prolactin level (mg/dl)



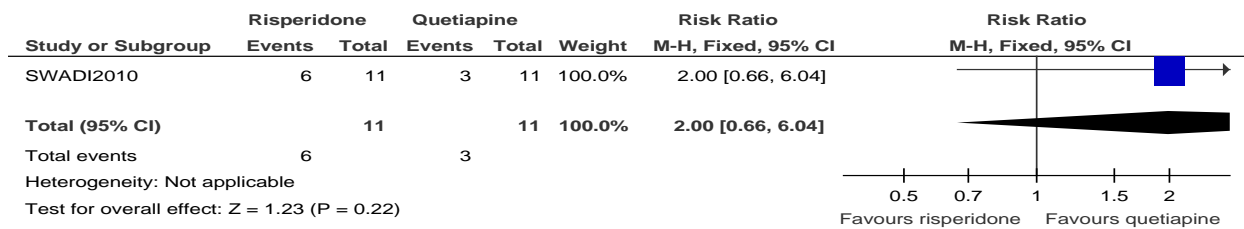
4.11 Elevated prolactin level (mg/dl)



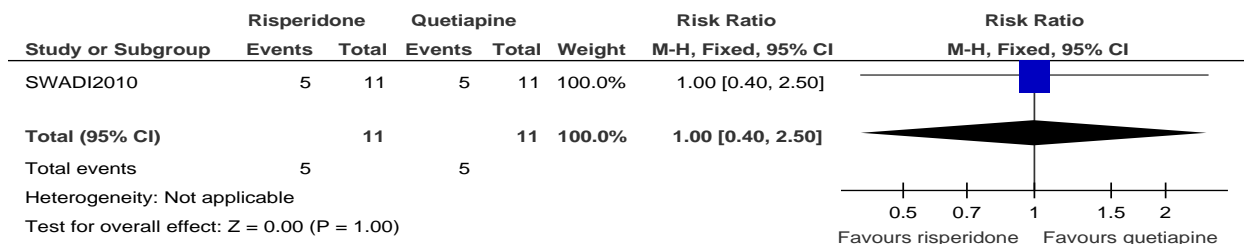
4.12 Extrapyramidal symptoms (EPS) (number of participants with an Abnormal Involuntary Movement Scale [AIMS] score >2)



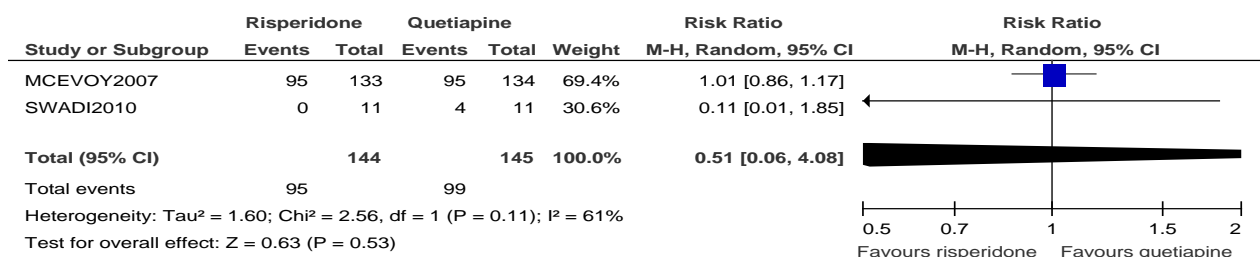
4.13 EPS (number of participants with a Simpson-Angus Extrapyramidal Side Effects Scale [SAS] score >2)



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

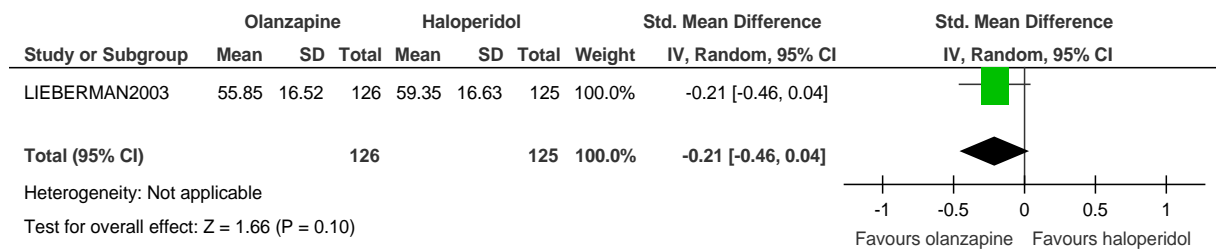


4.15 Leaving the study early for any reason

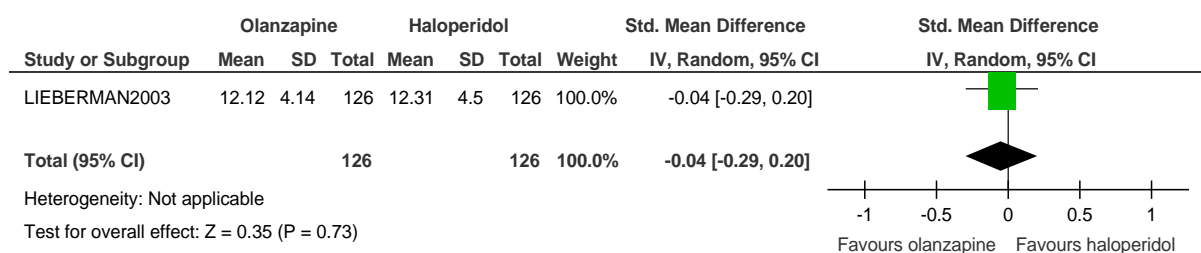


5. Olanzapine versus haloperidol: efficacy outcomes at the end of acute treatment (at 12 weeks)

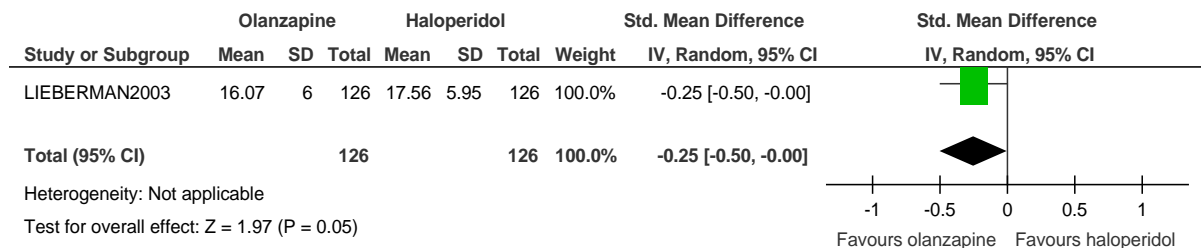
5.1 Mental state: mean total symptoms (PANSS) (end of acute phase)



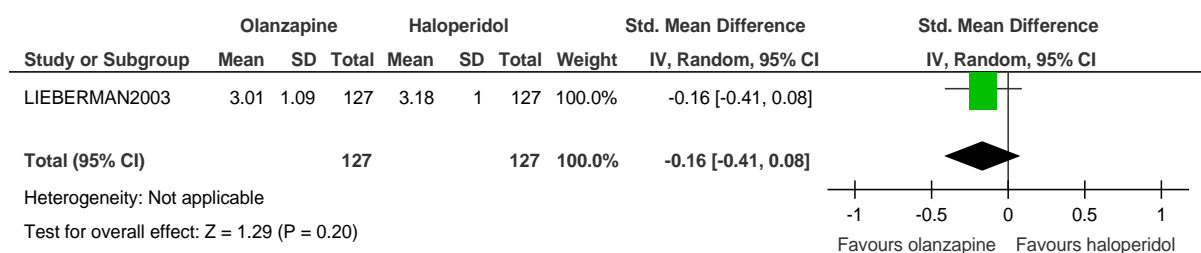
5.2 Mental state: mean positive symptoms (SAPS) (end of acute phase)



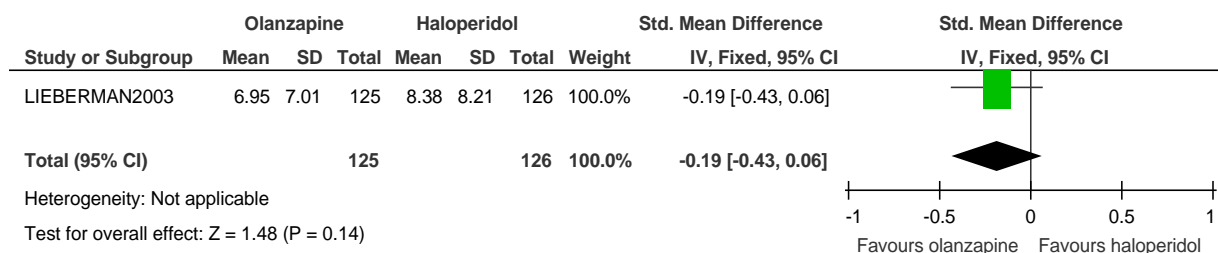
5.3 Mental state: mean negative symptoms (SANS) (end of acute phase)



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

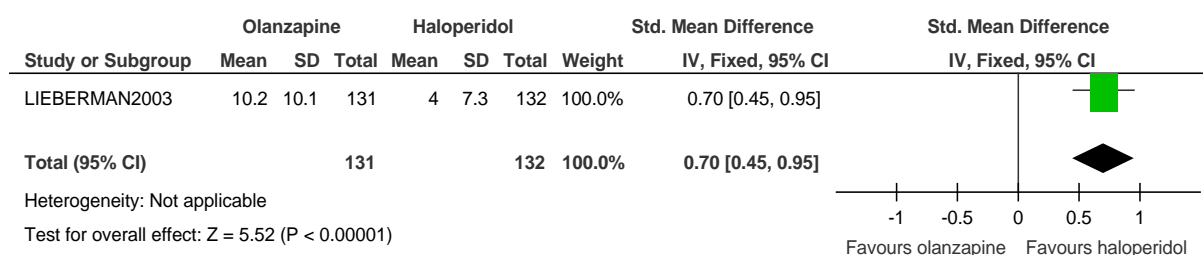


5.5 Mental state: mean depression (Montgomery-Åsberg Depression Rating Scale [MADRS]) (end of acute phase)

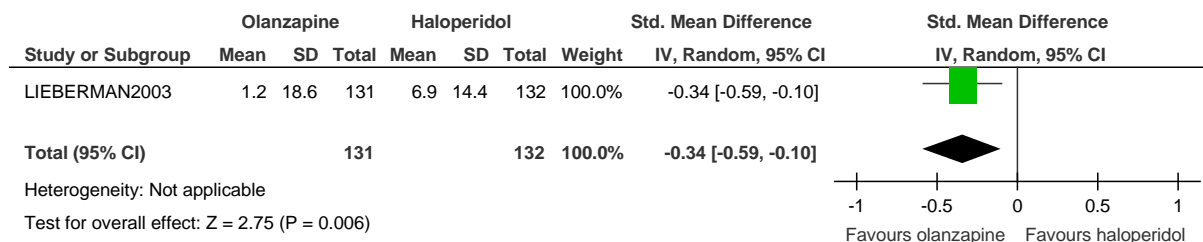


6. Olanzapine versus haloperidol: side effect outcomes at the end of acute treatment (at 12 weeks)

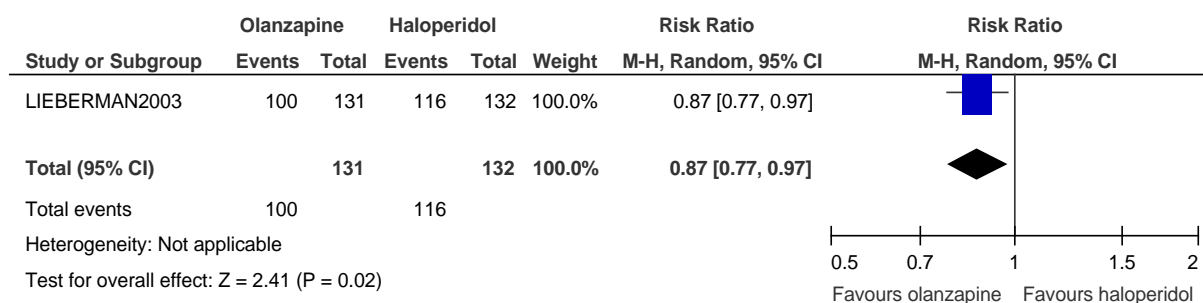
6.1 Mean endpoint weight (kg)



6.2 Mean endpoint prolactin level (mg/dl)

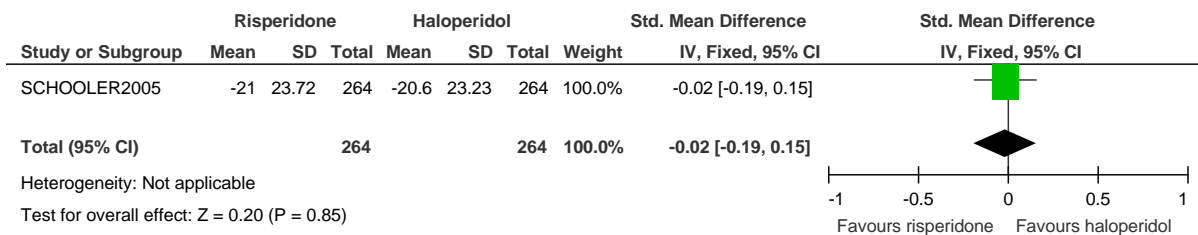


6.3 Leaving the study early for any reason

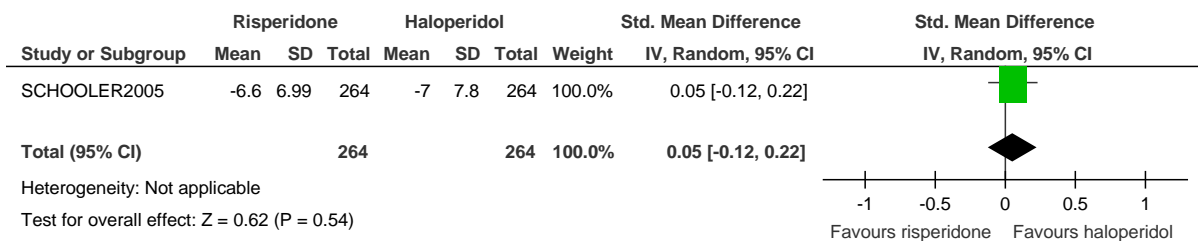


7. Haloperidol versus risperidone: efficacy outcomes post-treatment (time point unclear)

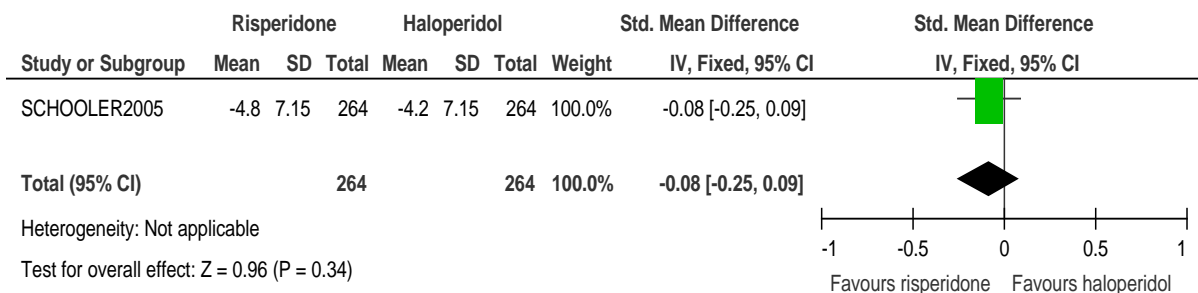
7.1 Mental state: mean change in total symptoms (PANSS)



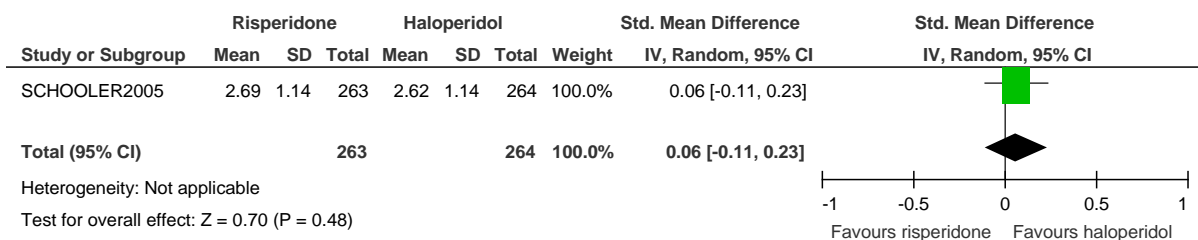
7.2 Mental state: mean change in positive symptoms (SAPS)



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

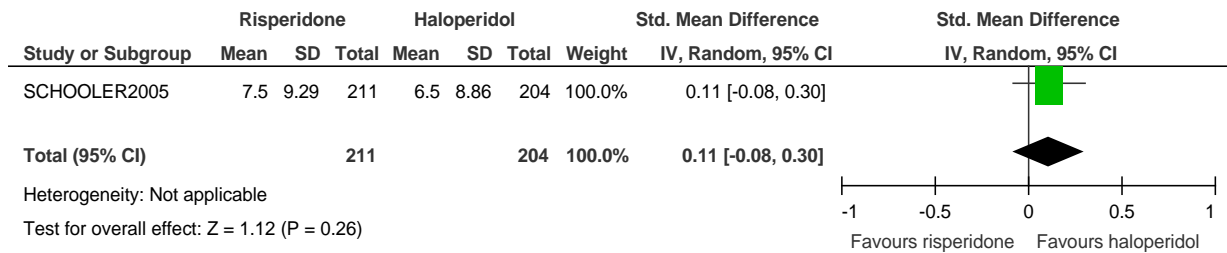


7.4 Mean change in global state: severity (CGI-S)

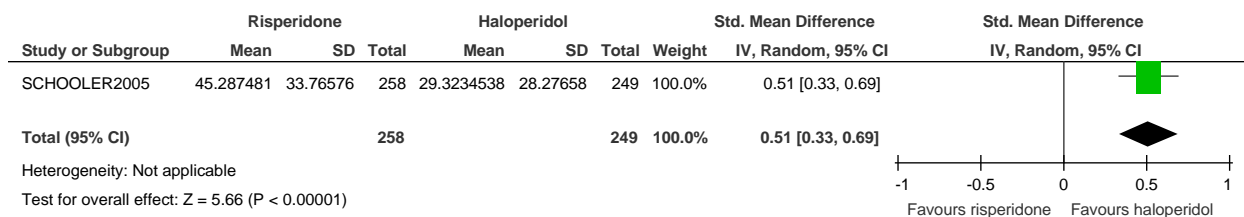


8. Haloperidol versus risperidone: side effect outcomes post-treatment (time point unclear)

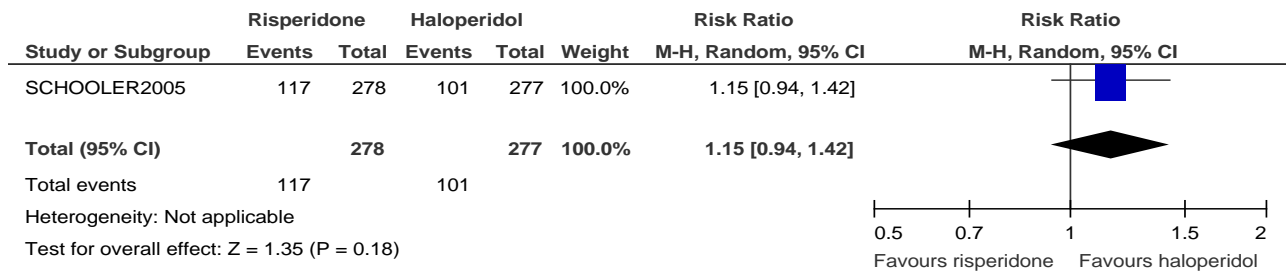
8.1 Mean change in weight (lbs)



8.2 Mean change in prolactin level (mg/dl)

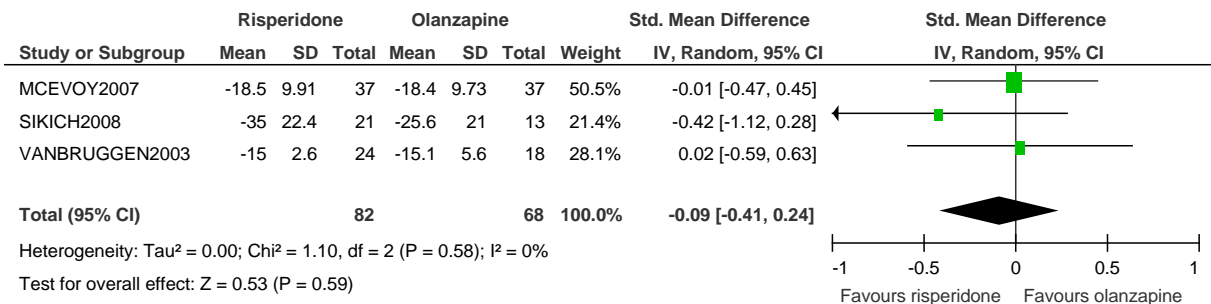


8.3 Leaving the study early for any reason

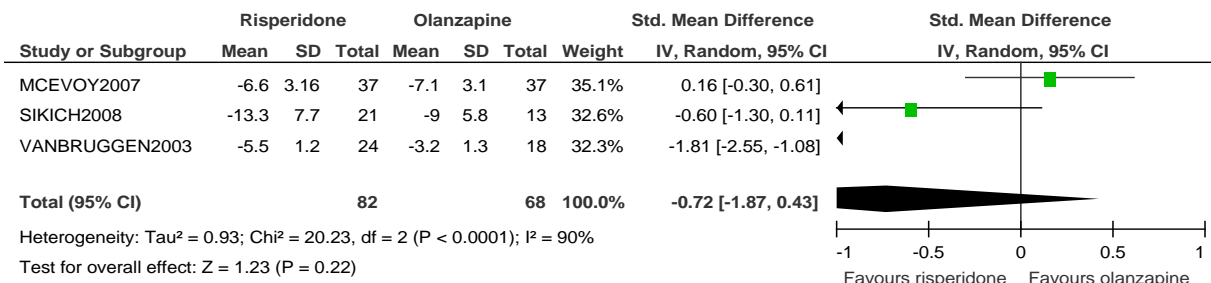


9. Risperidone versus olanzapine: post-treatment efficacy outcomes

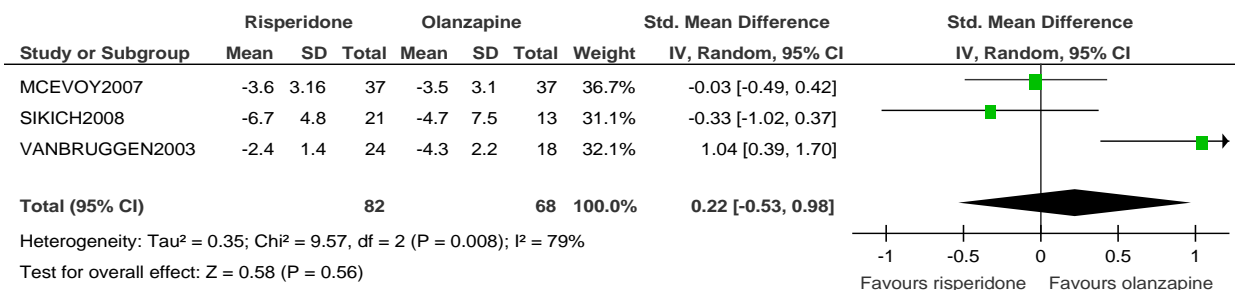
9.1 Mental state: mean change in total symptoms (PANSS)



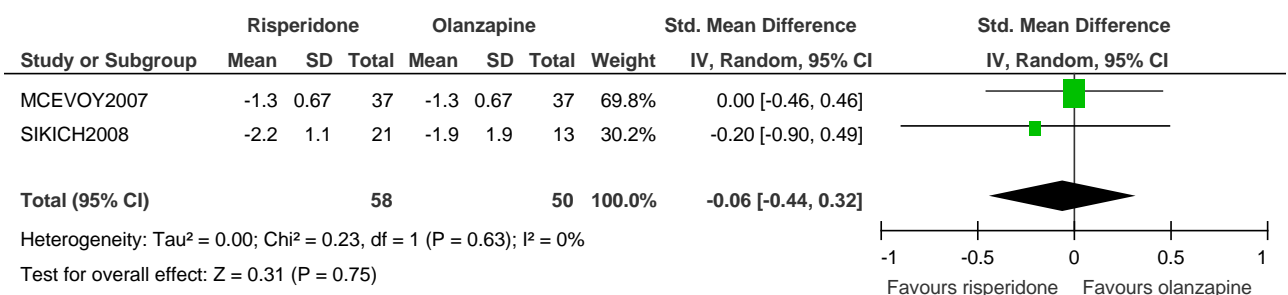
9.2 Mental state: mean change in positive symptoms (SAPS, Comprehensive Psychopathological Rating Scale [CPRS] - Positive)



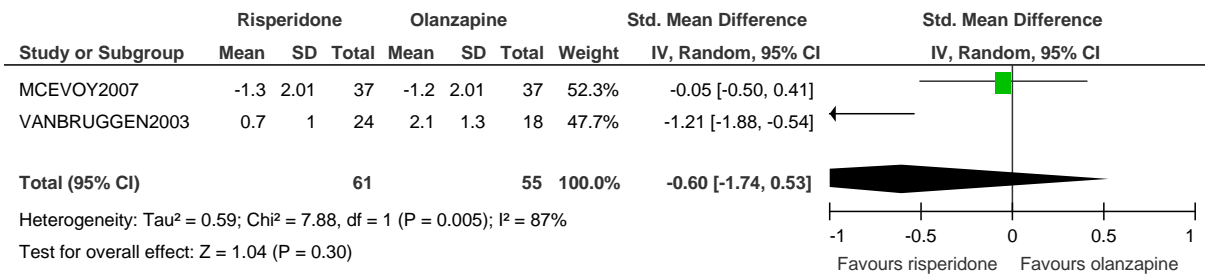
9.3 Mental state: mean change in negative symptoms (SANS)



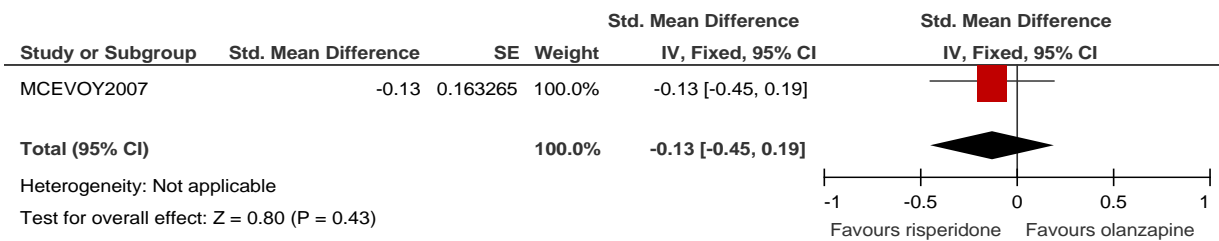
9.4 Mean change in global state: severity (CGI-S)



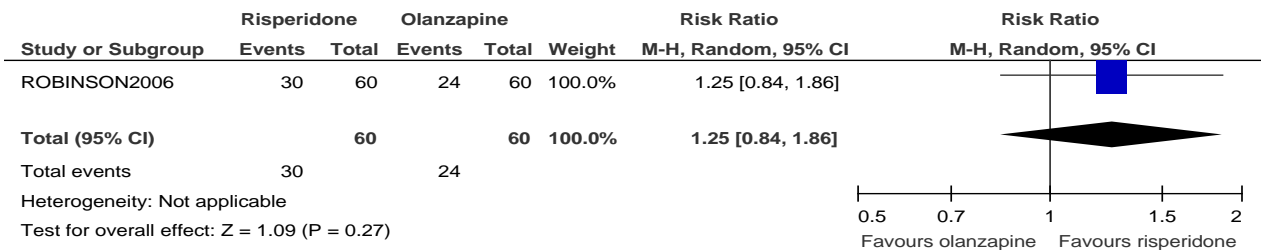
9.5 Mental state: mean change in depression (CDSS, PANSS-Depression)



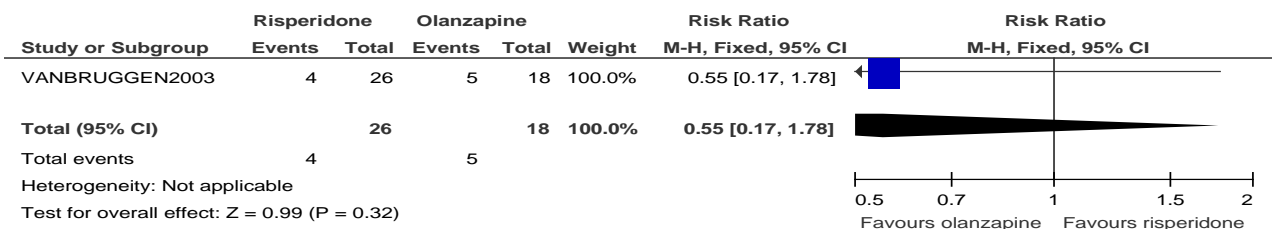
9.6 Mean change in quality of life (QLS)



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)

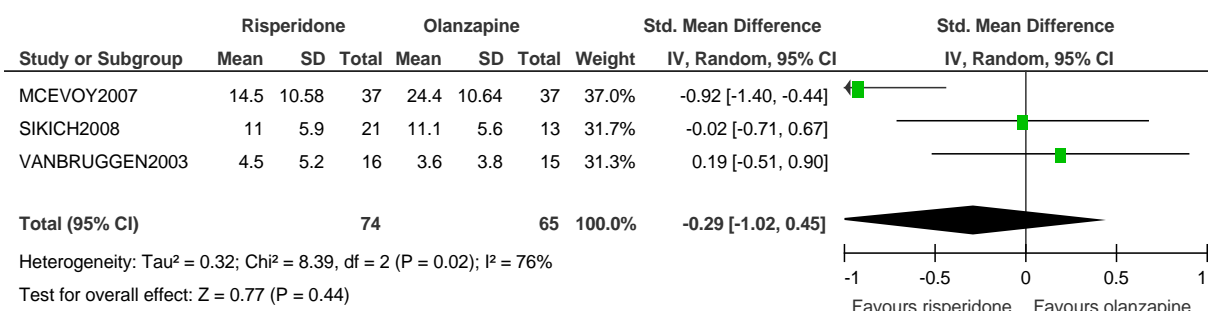


9.8 Remission (PANSS)

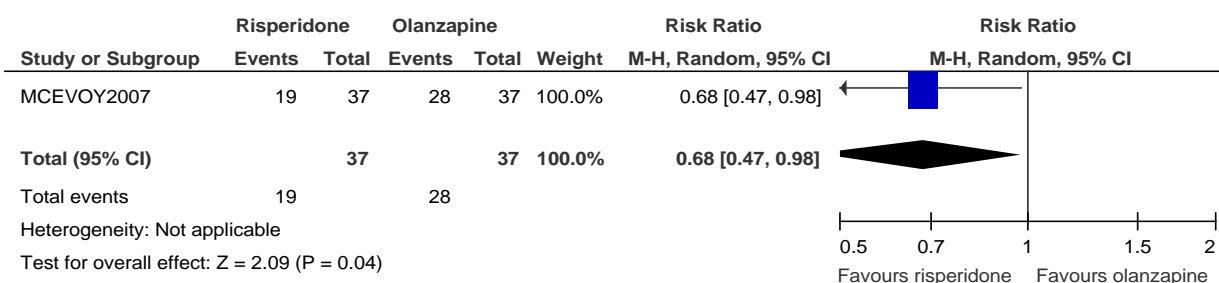


10. Risperidone versus olanzapine: post-treatment side effect outcomes

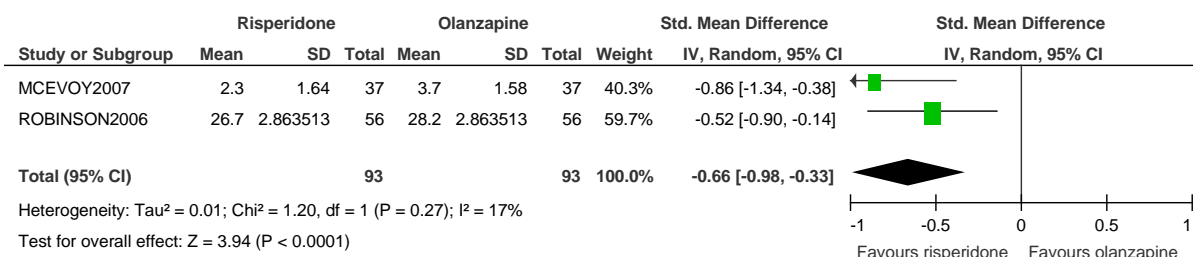
10.1 Mean change in weight (kg, lbs)



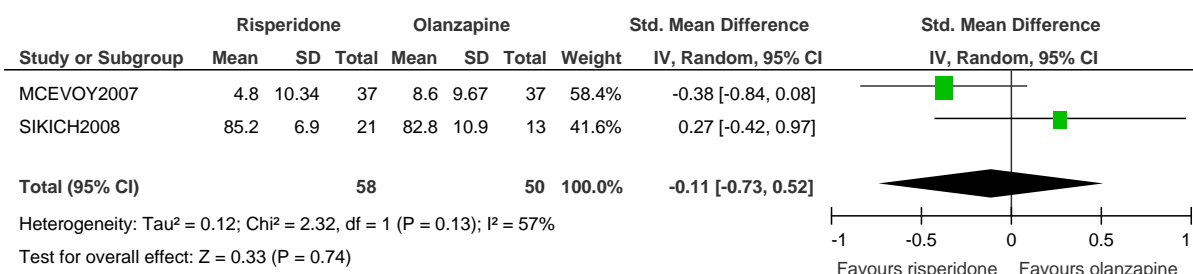
10.2 Weight gain (number of participants who gained ≥ 7%)



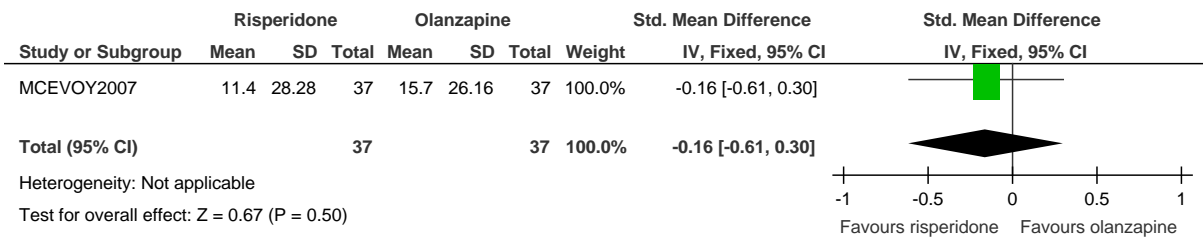
10.3 BMI (kg/m²) (mean change: MCEVOY2007; mean endpoint: ROBINSON2006)



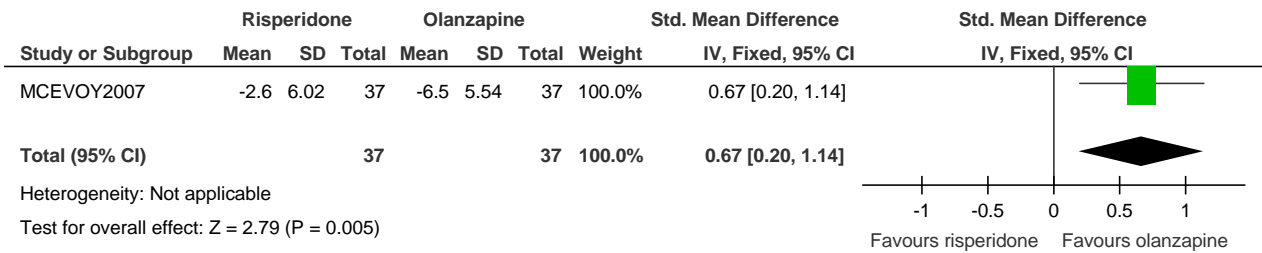
10.4 Mean change in fasting serum glucose level (mg/dl)



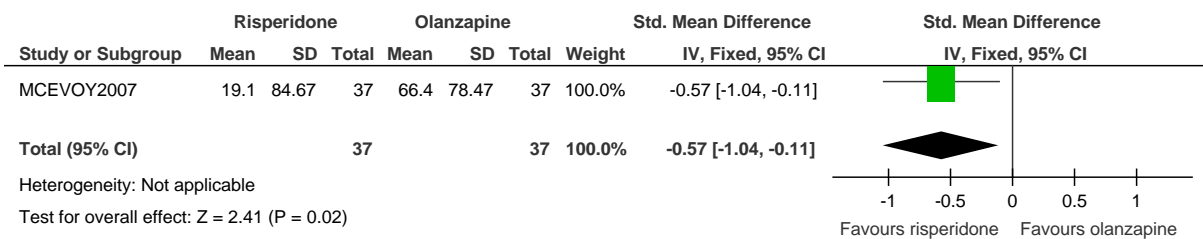
10.5 Mean change in fasting total cholesterol (mg/dl)



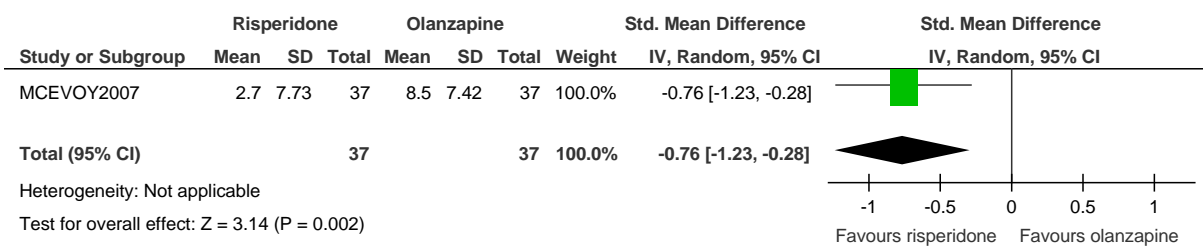
10.6 Mean change in fasting high-density lipoprotein cholesterol (mg/dl)



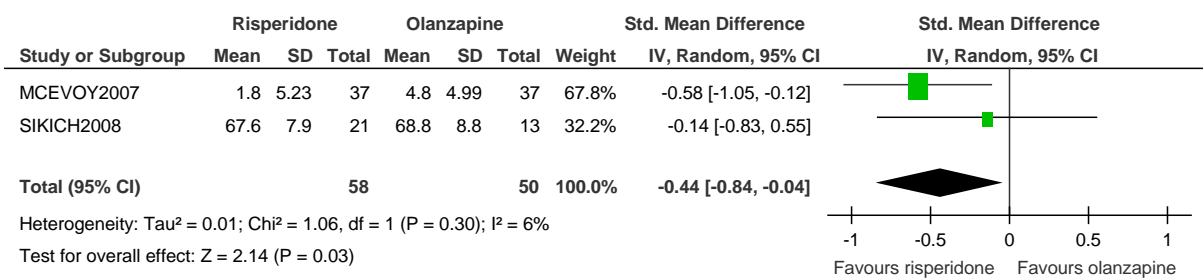
10.7 Mean change in fasting triglycerides (mg/dl)



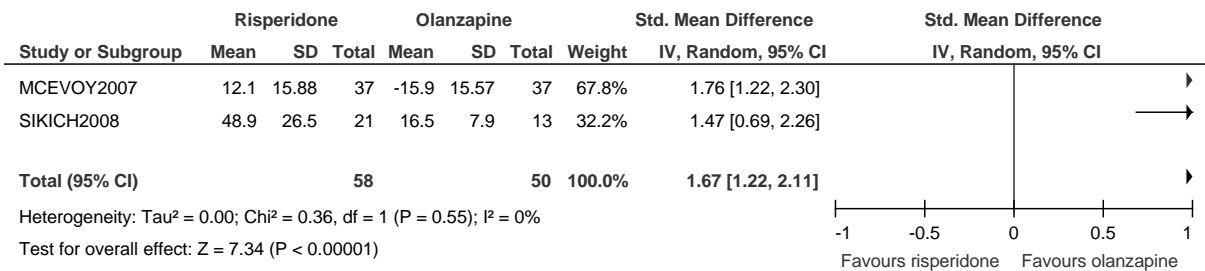
10.8 Mean change in systolic BP (mm Hg)



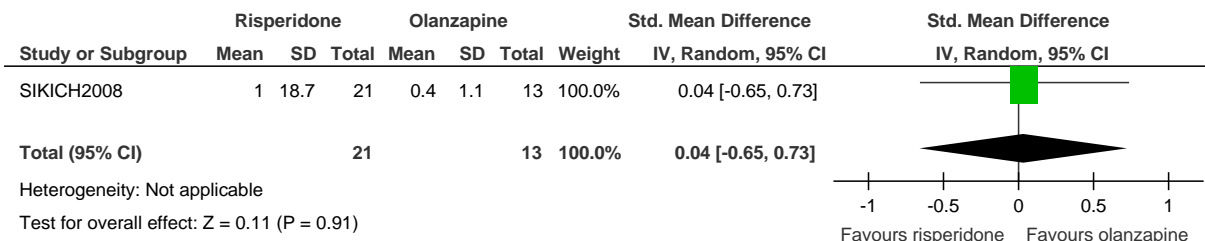
10.9 Mean change in diastolic BP (mm Hg)



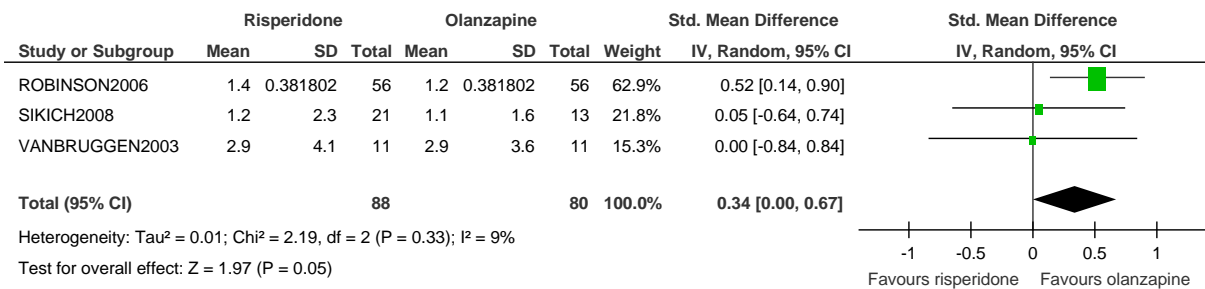
10.10 Mean change in prolactin level (mg/ml)



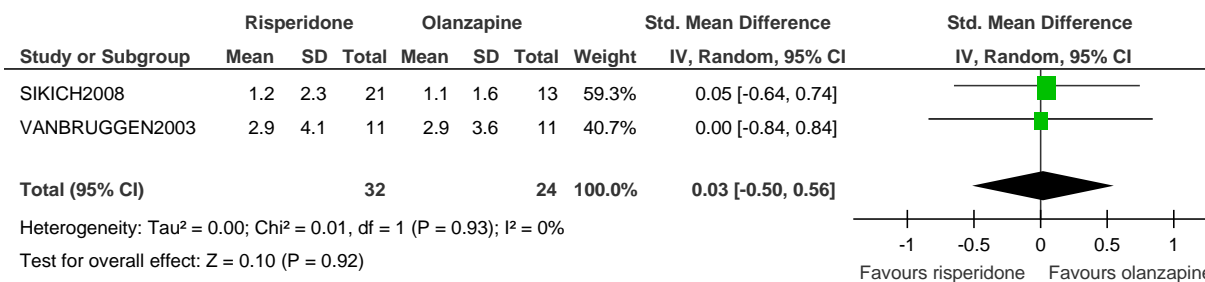
10.11 Mean change in EPS (AIMS scores)



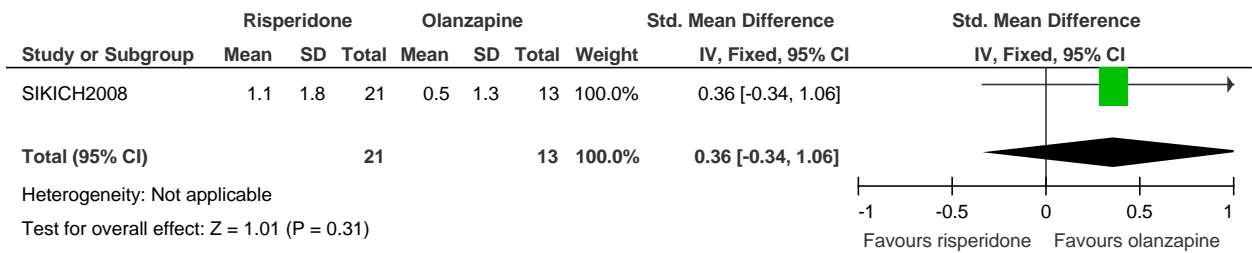
10.12 EPS (SAS scores)



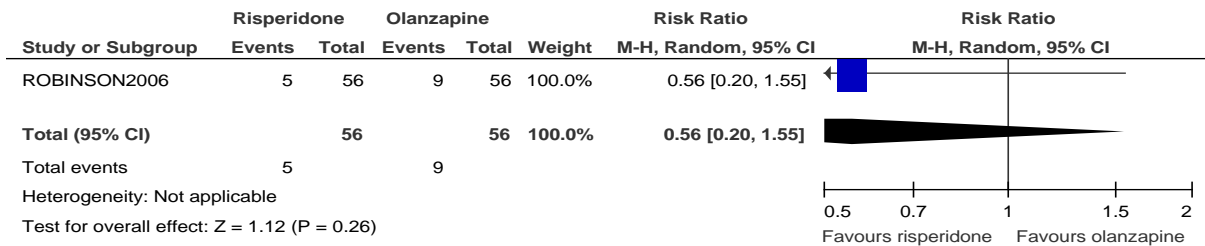
10.13 EPS (SAS scores) sensitivity analysis (taking out ROBINSON2006)



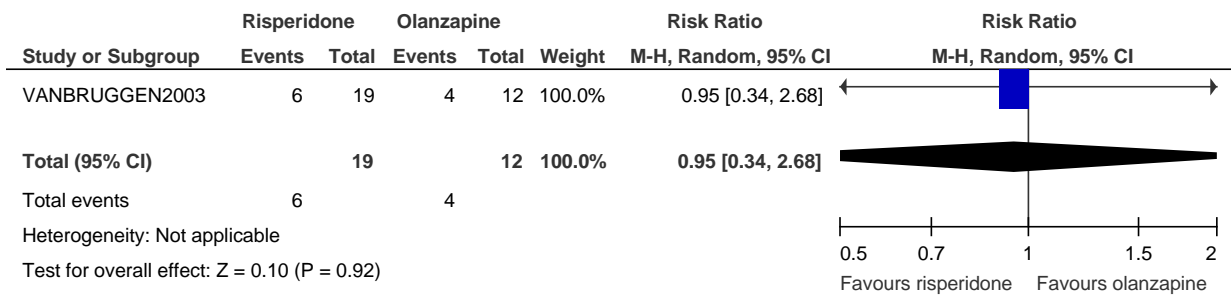
10.14 EPS (mean change in BARS scores)



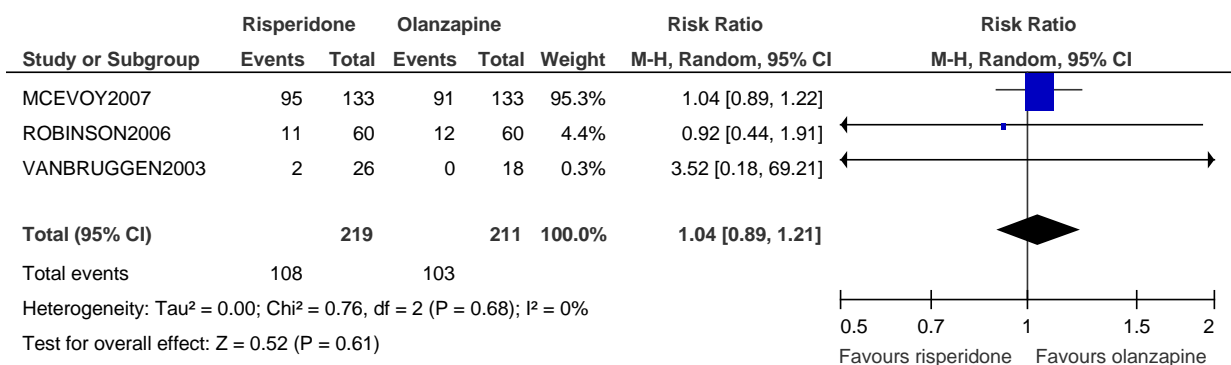
10.15 Parkinsonism



10.16 Akathisia

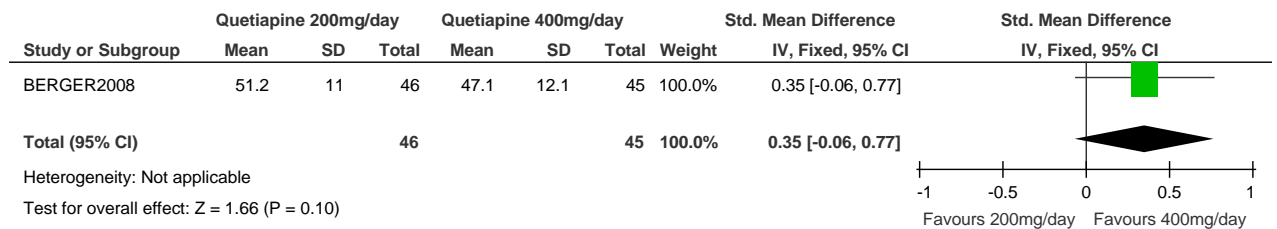


10.17 Leaving the study early for any reason

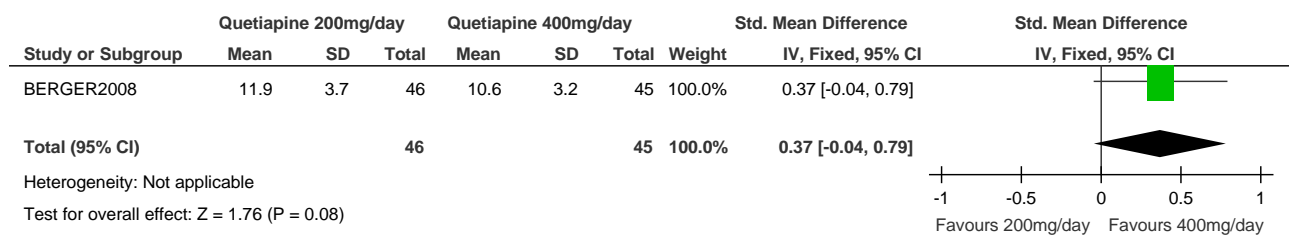


11. Quetiapine (200 mg/day) versus quetiapine (400 mg/day): post-treatment efficacy outcomes

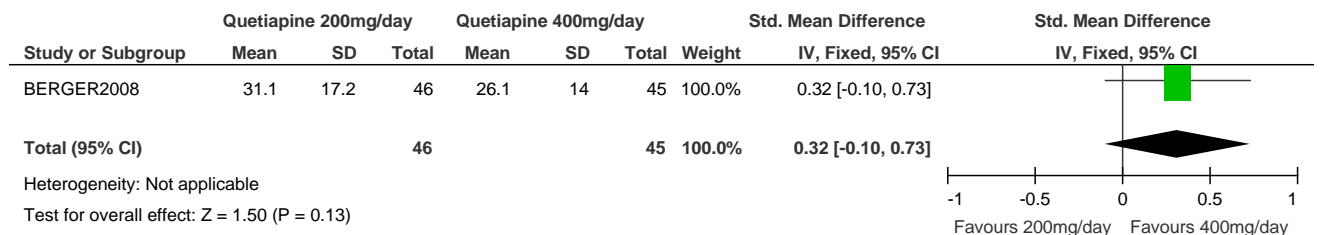
11.1 Mental state: mean endpoint total symptoms (PANSS)



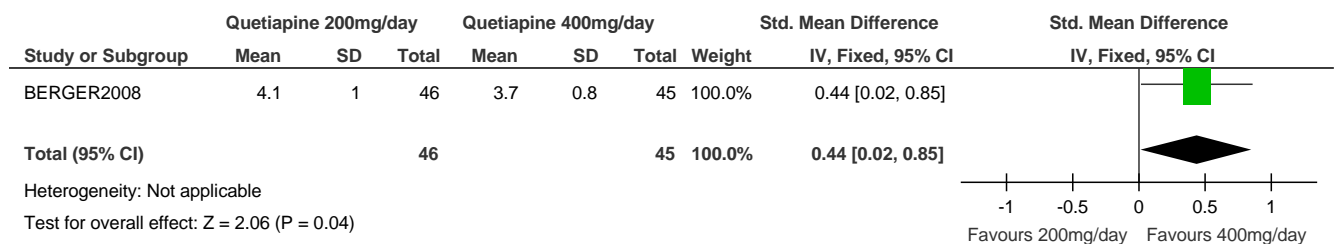
11.2 Mental state: mean endpoint positive symptoms (Brief Psychiatric Rating Scale - Psychotic Subscale [BPRS-P])



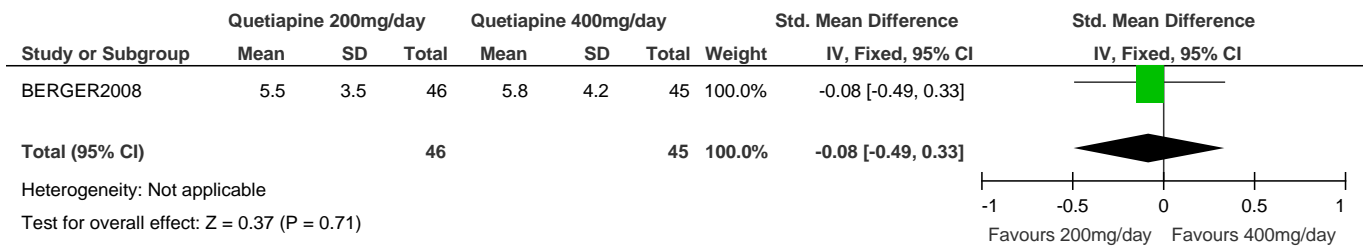
11.3 Mental state: mean endpoint negative symptoms (SANS)



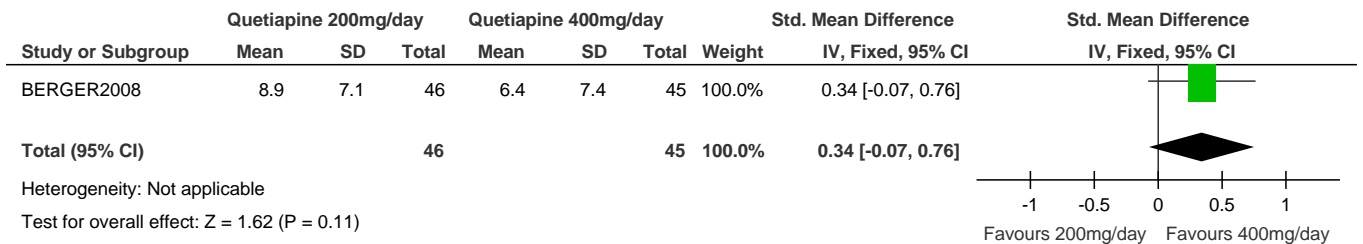
11.4 Mean endpoint global state: severity (CGI-S)



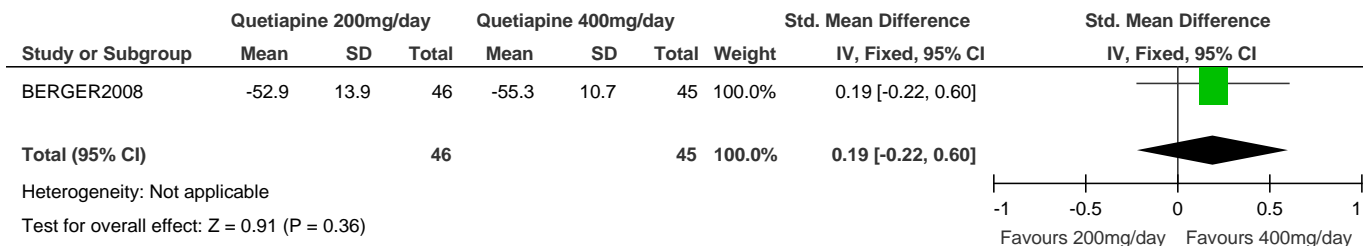
11.5 Mental state: mean endpoint depression (CDSS)



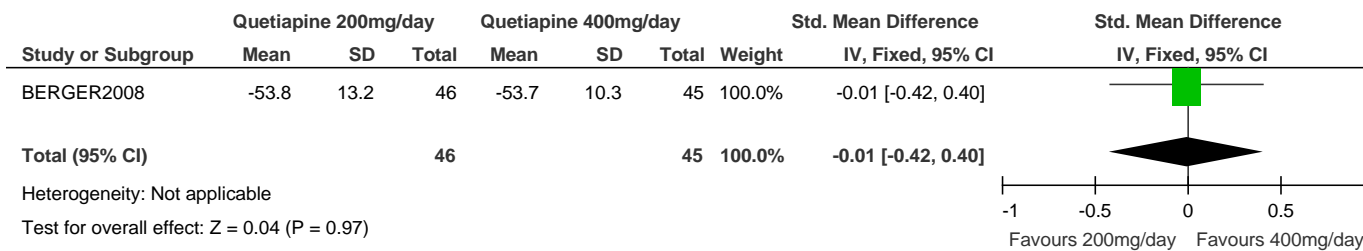
11.6 Mental state: mean endpoint mania (YMRS)



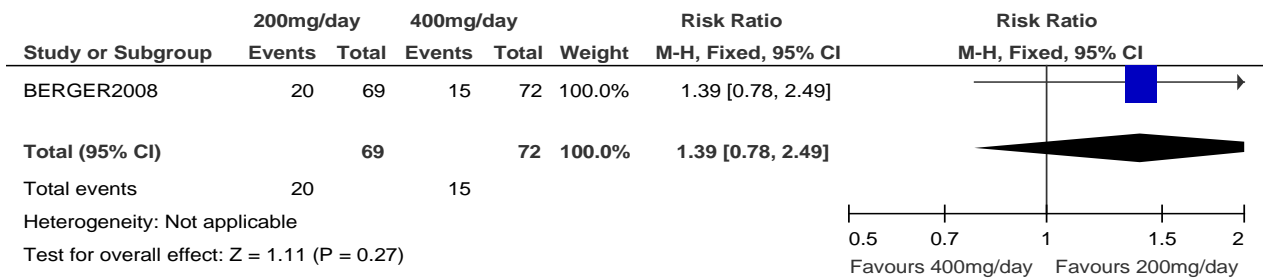
11.7 Mean endpoint psychosocial functioning (GAF)



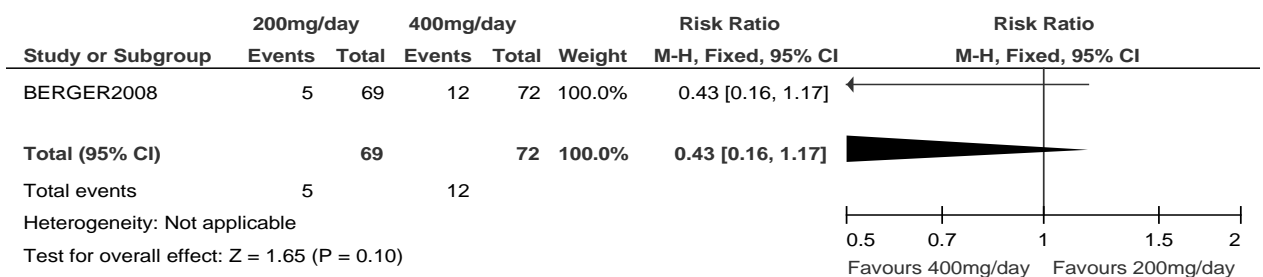
11.8 Mean endpoint social functioning (Social and Occupational Functioning Assessment Scale [SOFAS])



11.9 Response (BPRS)

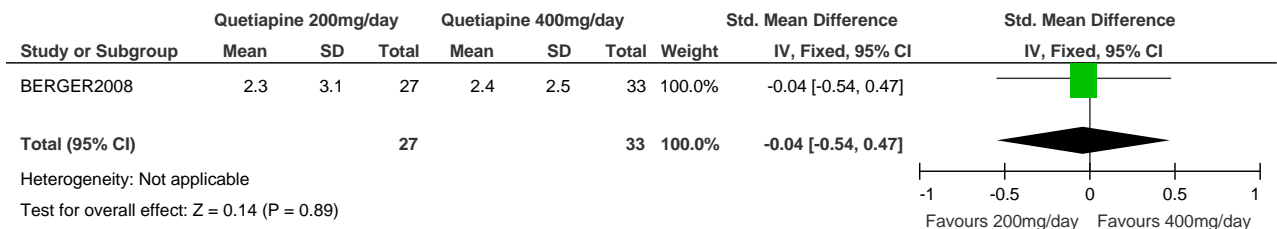


11.10 Remission (BPRS)

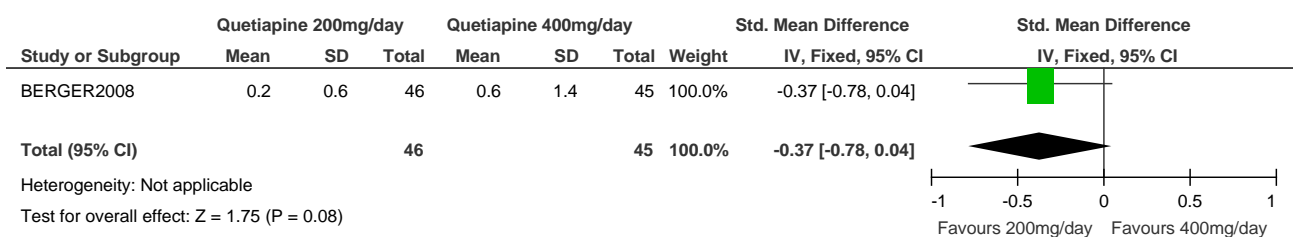


12. Quetiapine (200 mg/day) versus quetiapine (400 mg/day): post-treatment side effect outcomes

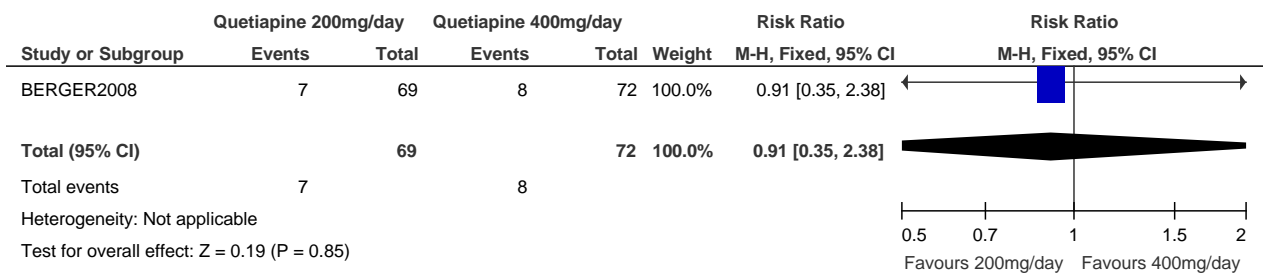
12.1 Mean endpoint weight (kg)



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



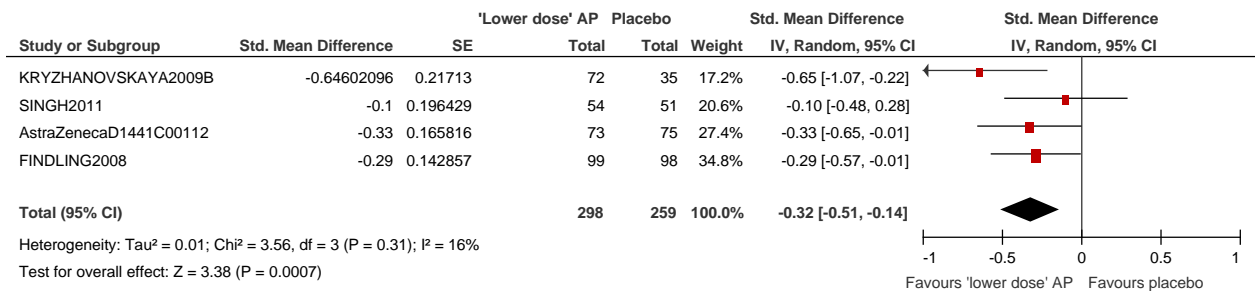
12.3 Leaving the study early for any reason



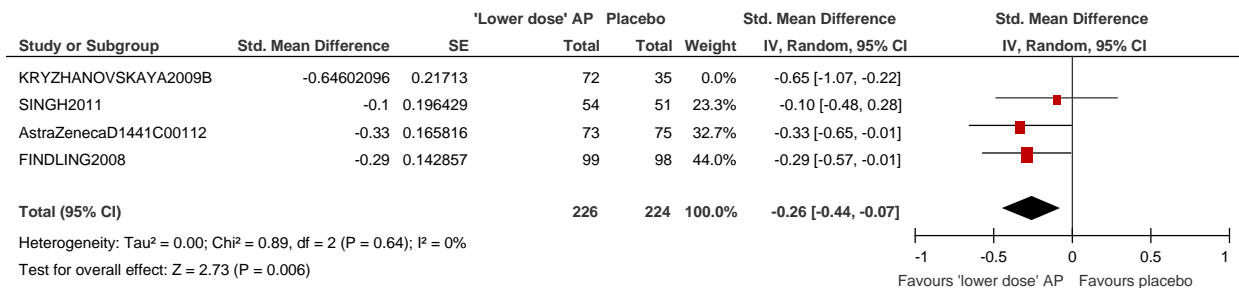
APPENDIX 14C (II): ANTIPSYCHOTICS IN THE TREATMENT OF SUBSEQUENT ACUTE EPISODES OF PSYCHOSIS AND SCHIZOPHRENIA

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

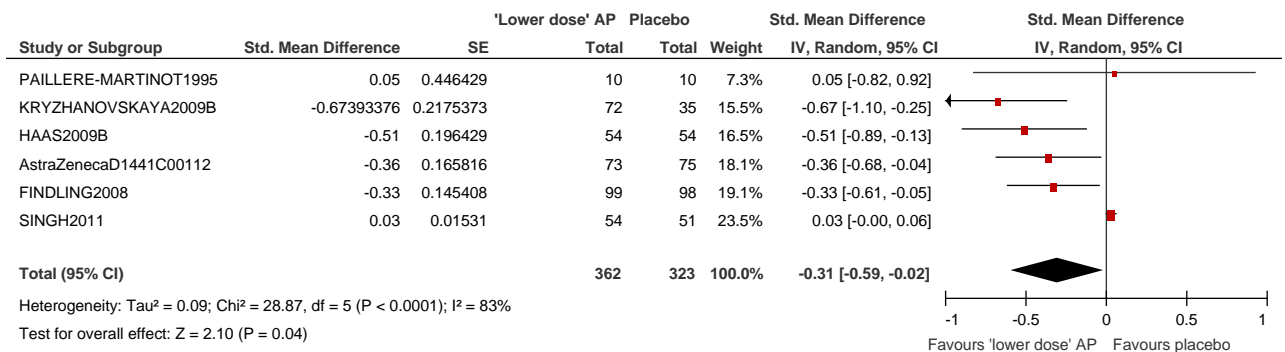
1.1 Mental state: total symptoms (PANSS, BPRS)



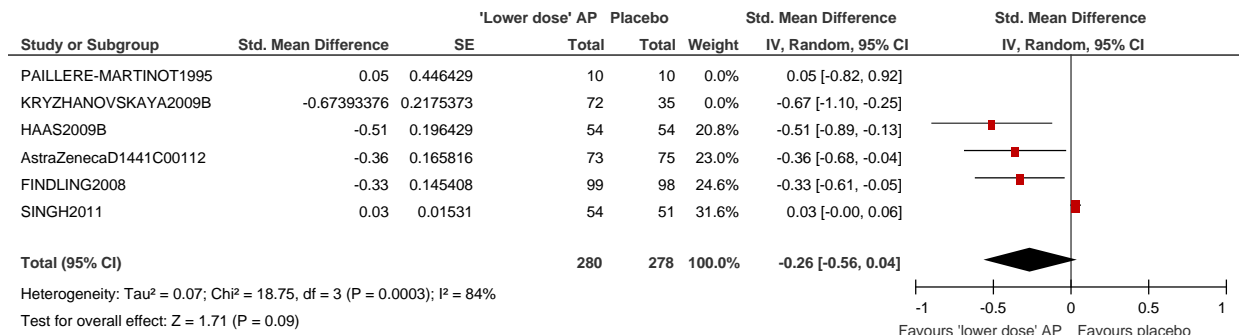
1.2 Mental state: mean change in total symptoms (PANSS) sensitivity analysis (taking KRYZHANOVSKAYA2009B out of the analysis)



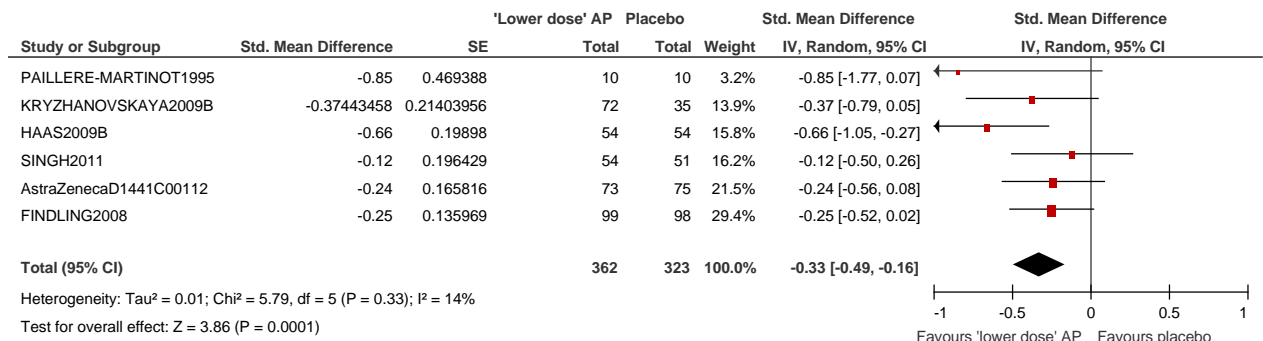
1.3 Mental state: positive symptoms (PANSS Positive)



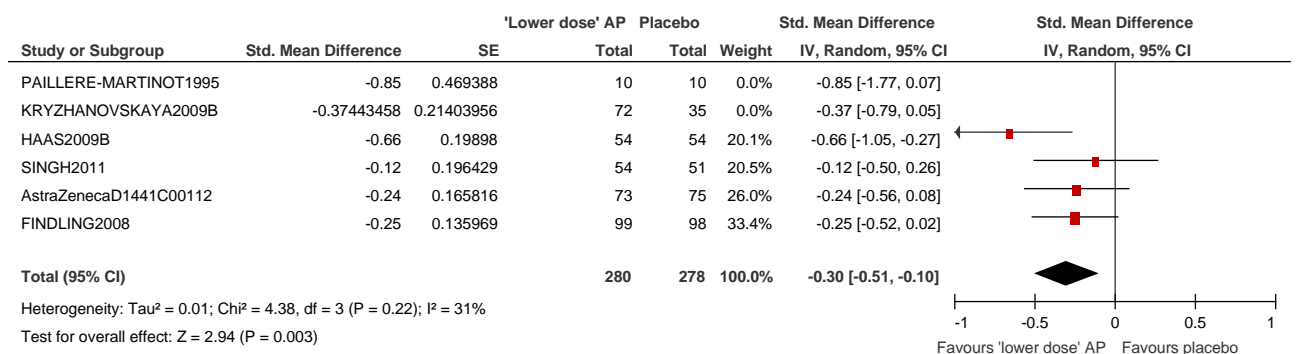
1.4 Mental state: mean change in positive symptoms (PANSS Positive) sensitivity analysis (taking out KRYZHANOVSKAYA2009B and PALLIERE-MARTINOT1995)



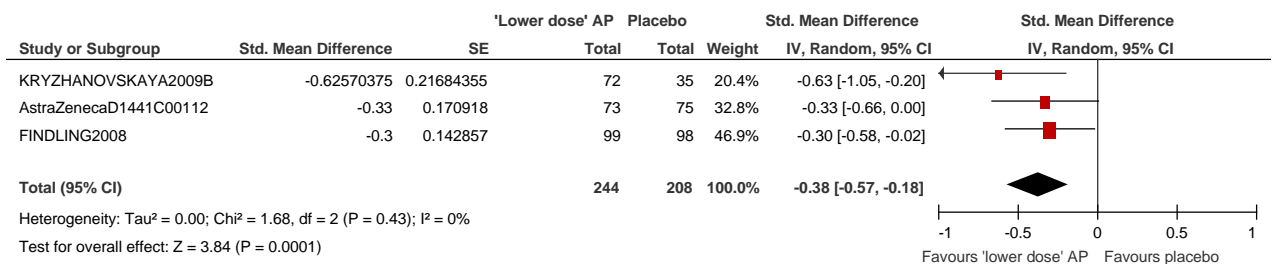
1.5 Mental state: negative symptoms (PANSS Negative)



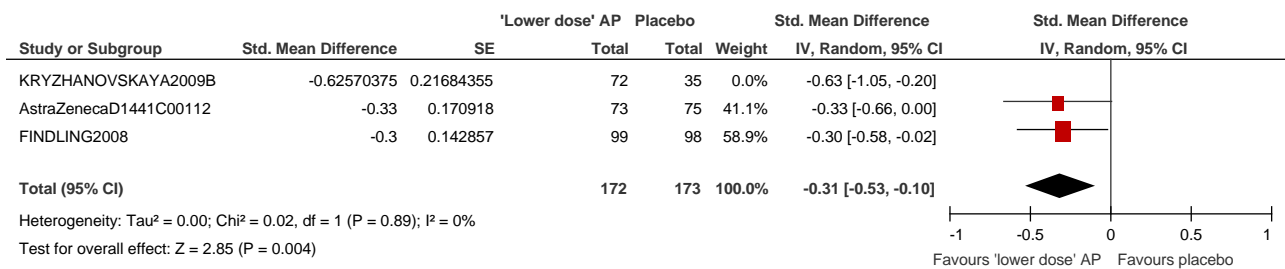
1.6 Mental state: mean change in negative symptoms (PANSS Negative) sensitivity analysis (taking out KRYZHANOVSKAYA2009B and PALLIERE-MARTINOT1995)



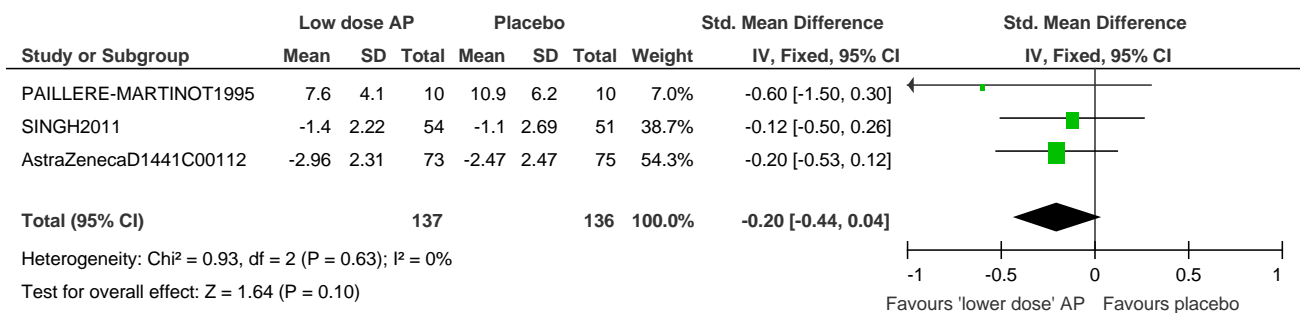
1.7 Global state: severity (CGI-S)



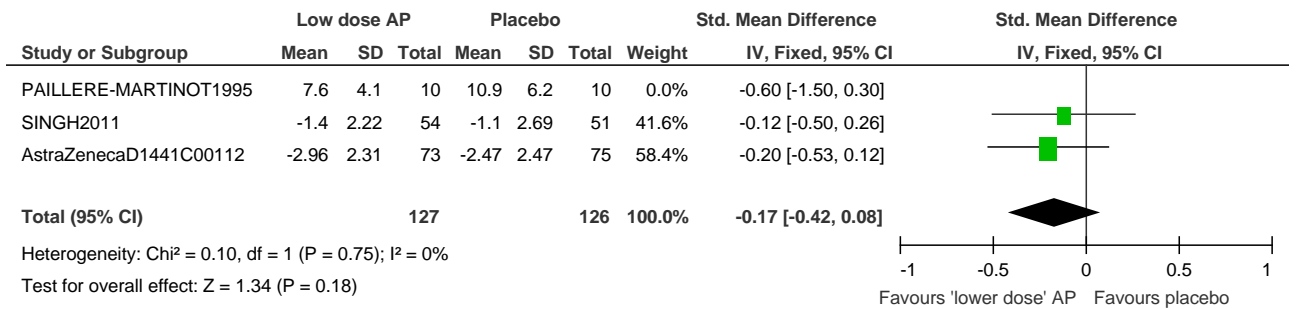
1.8 Mean change in global state: severity (CGI-S) sensitivity analysis (taking out KRYZHANOVSKAYA2009B)



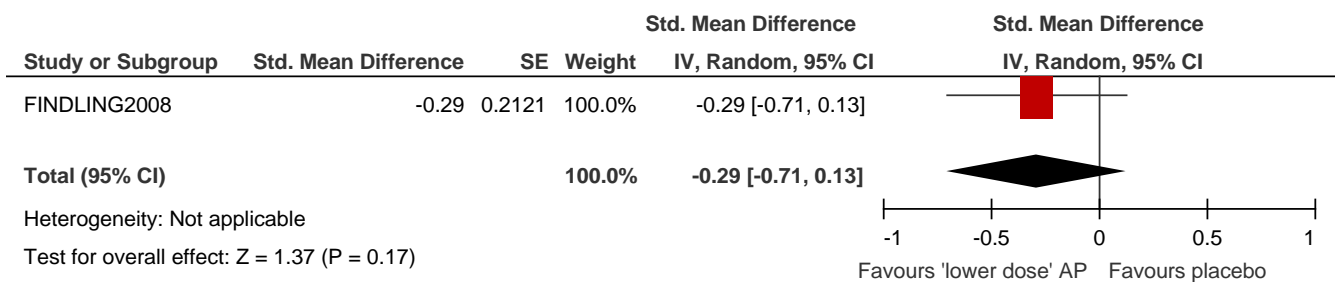
1.9 Mental state: depression (PANSS; MADRS)



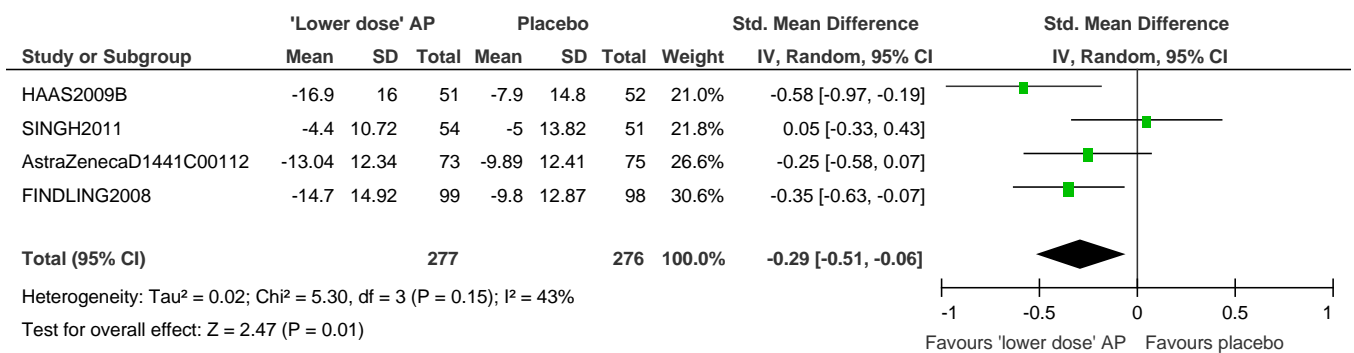
1.10 Mean change in depression (PANSS Anxiety and Depression; MADRS) sensitivity analysis (taking out PALLIERE-MARTINOT1995)



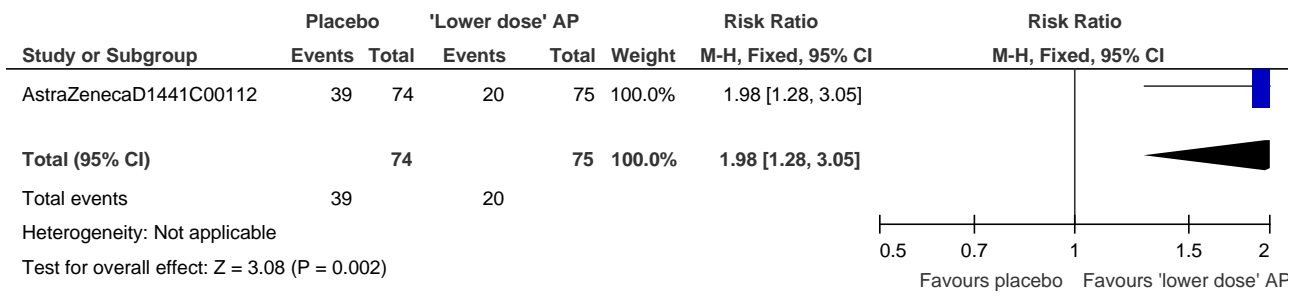
1.11 Mean change in quality of life (QLS)



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

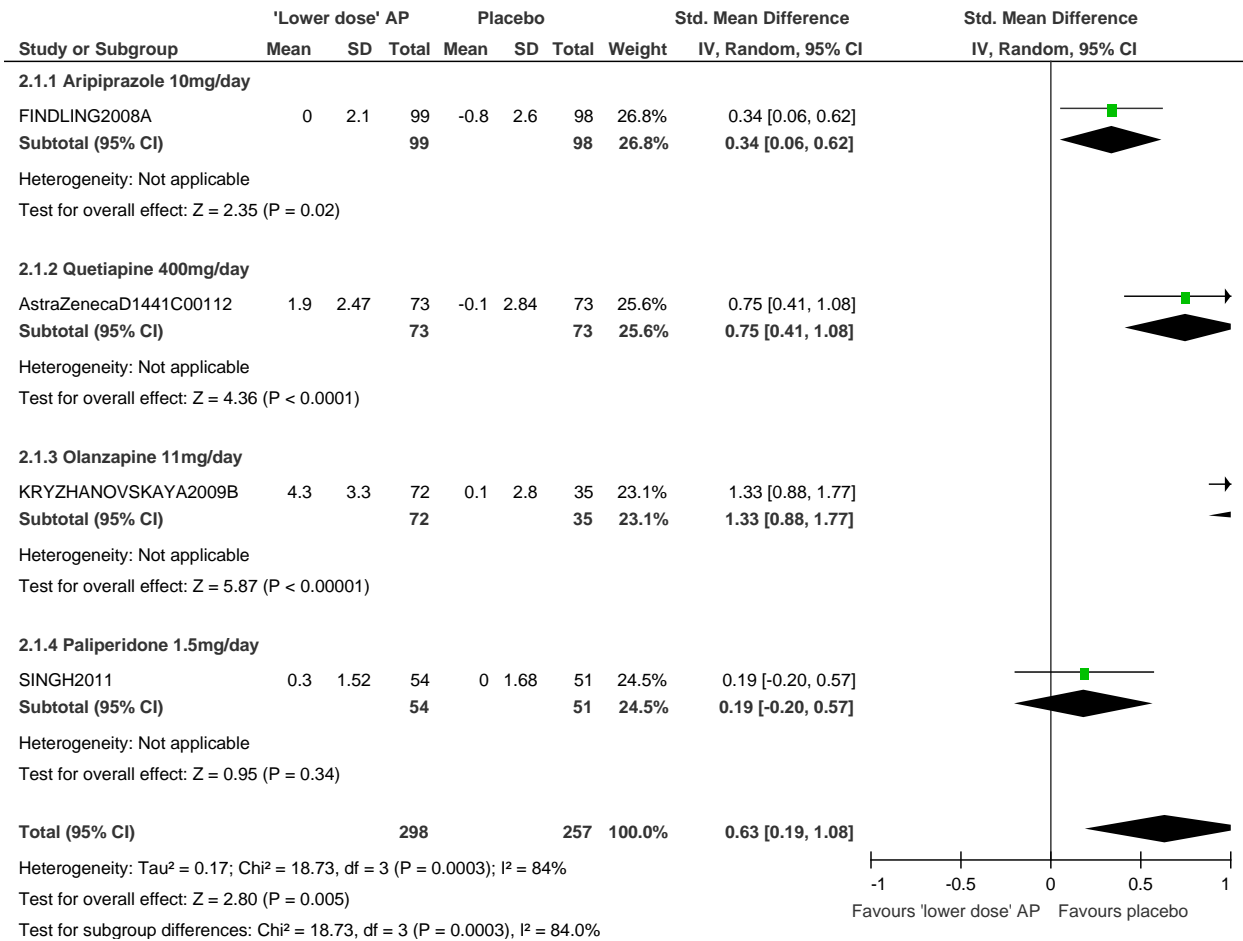


1.13 Response (CGI-I)

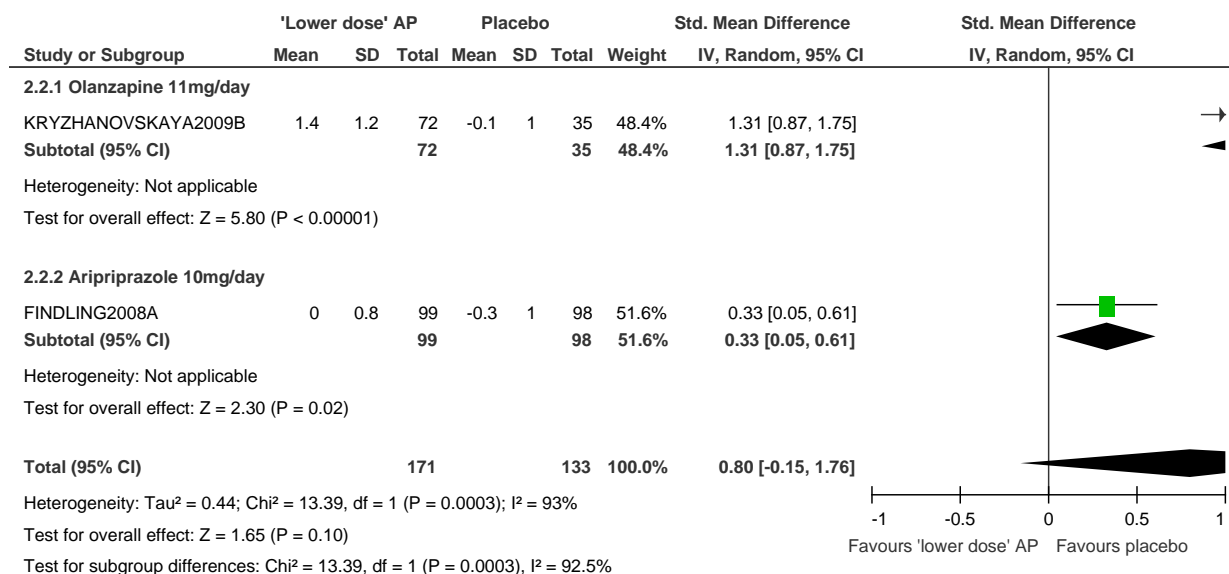


2. 'Lower dose' antipsychotic versus placebo: post-treatment side effect outcomes

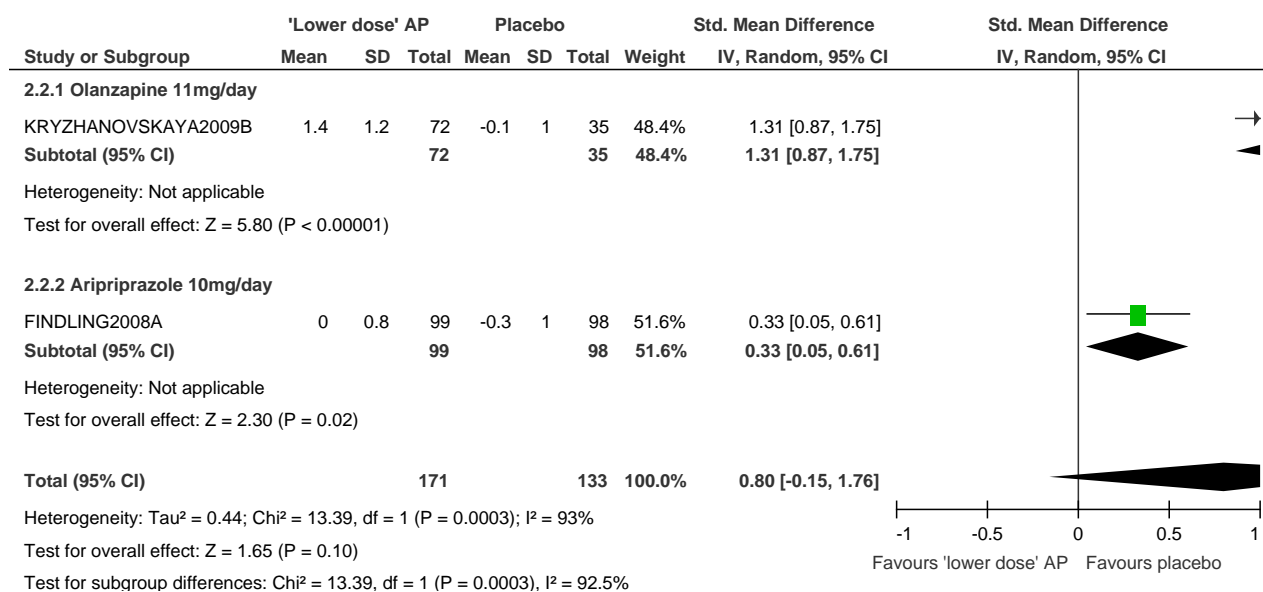
2.1 Weight (kg) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A, AstraZenecaD1441C00112, SINGH2011)



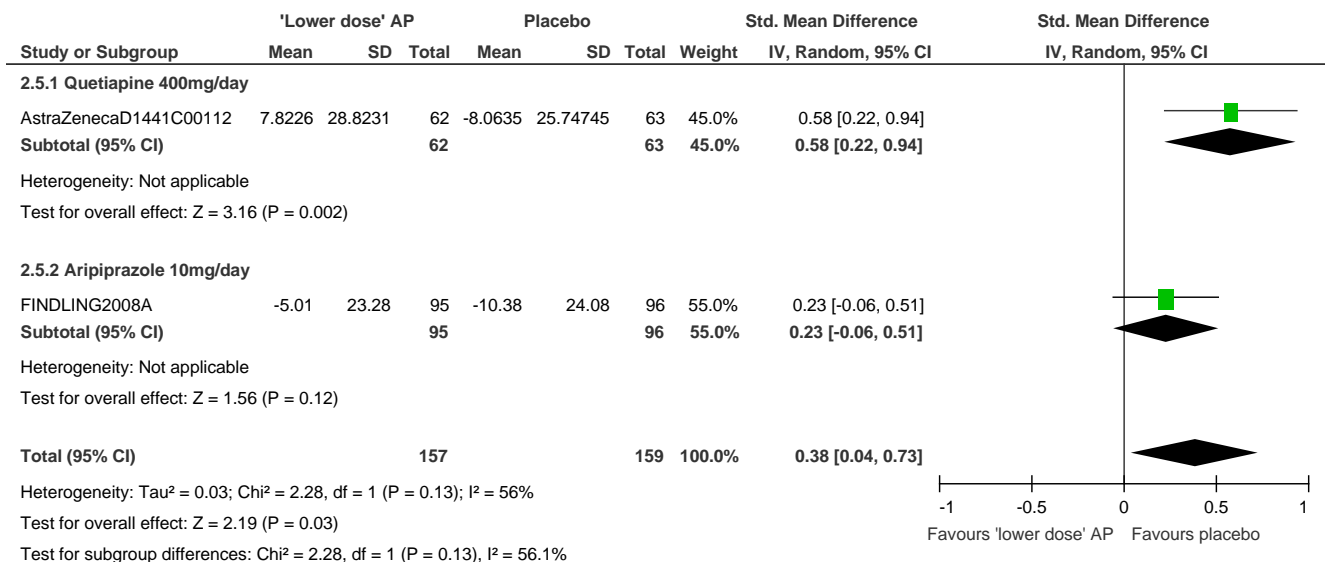
2.2 BMI (kg/m²) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A)



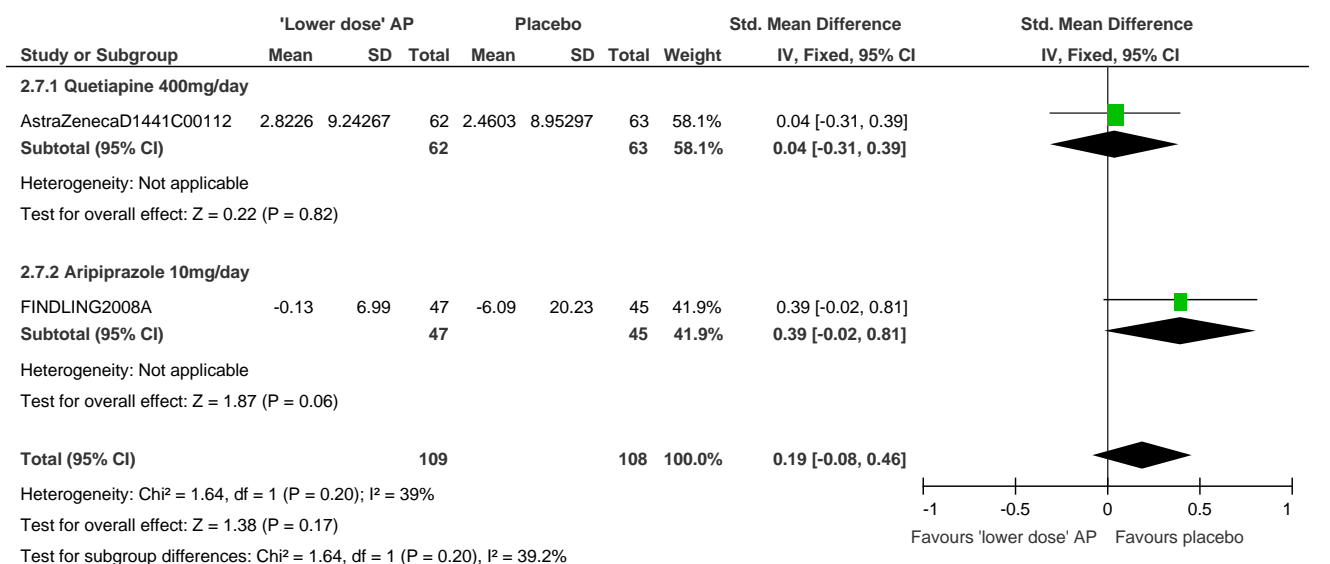
2.3 Fasting serum glucose level (mg/dl) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A, AstraZenecaD1441C00112, SINGH2011)



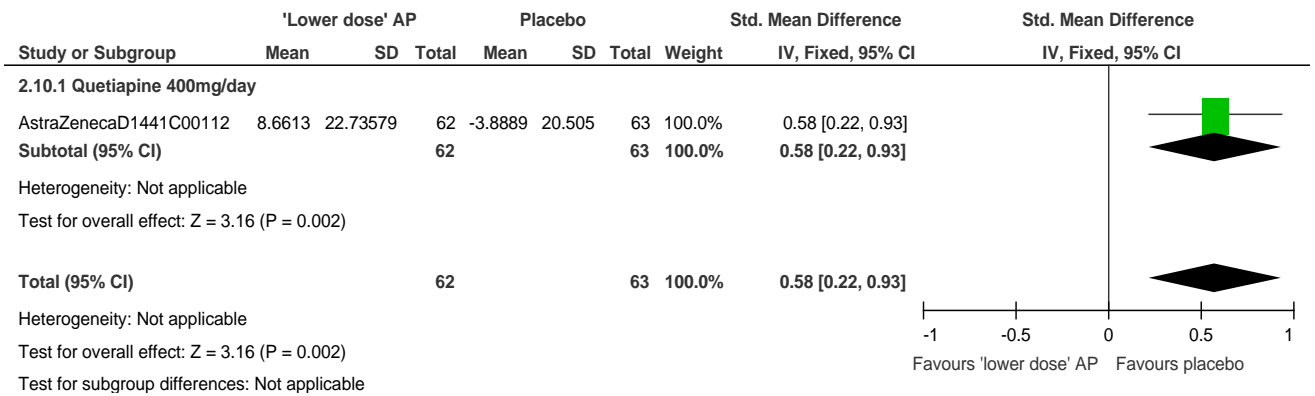
2.4 Mean change in fasting total cholesterol (mg/dl)



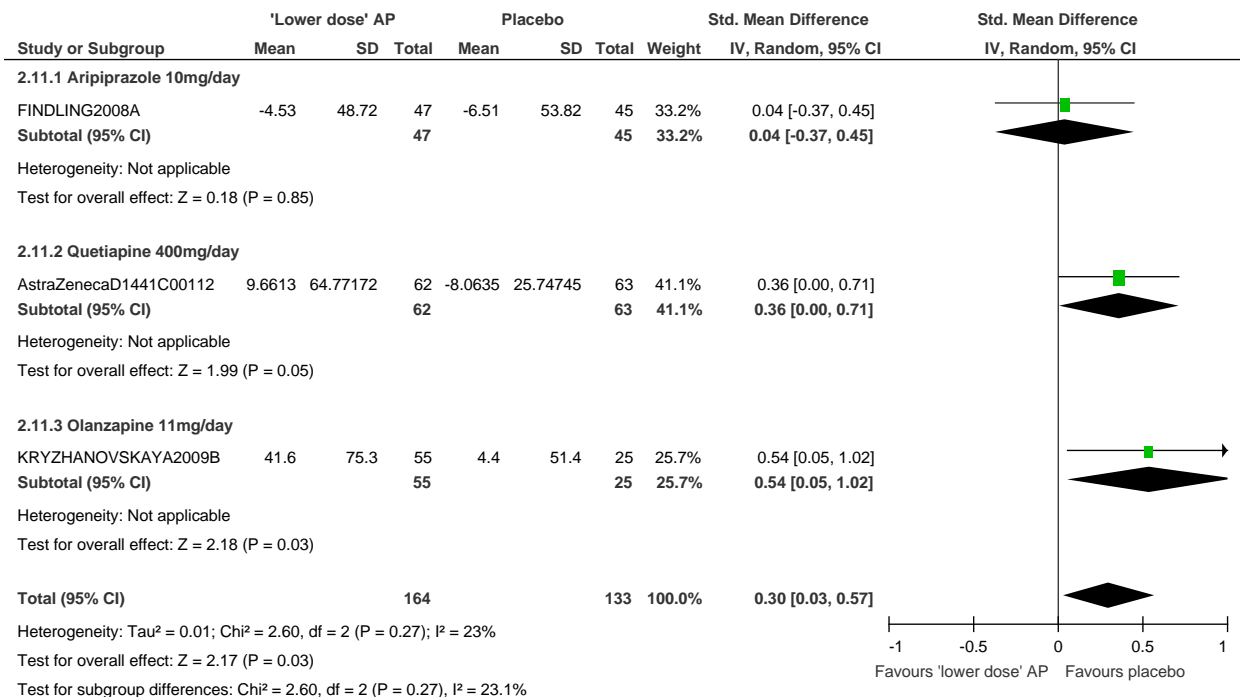
2.5 Mean change in fasting high-density lipoprotein cholesterol (mg/dl)



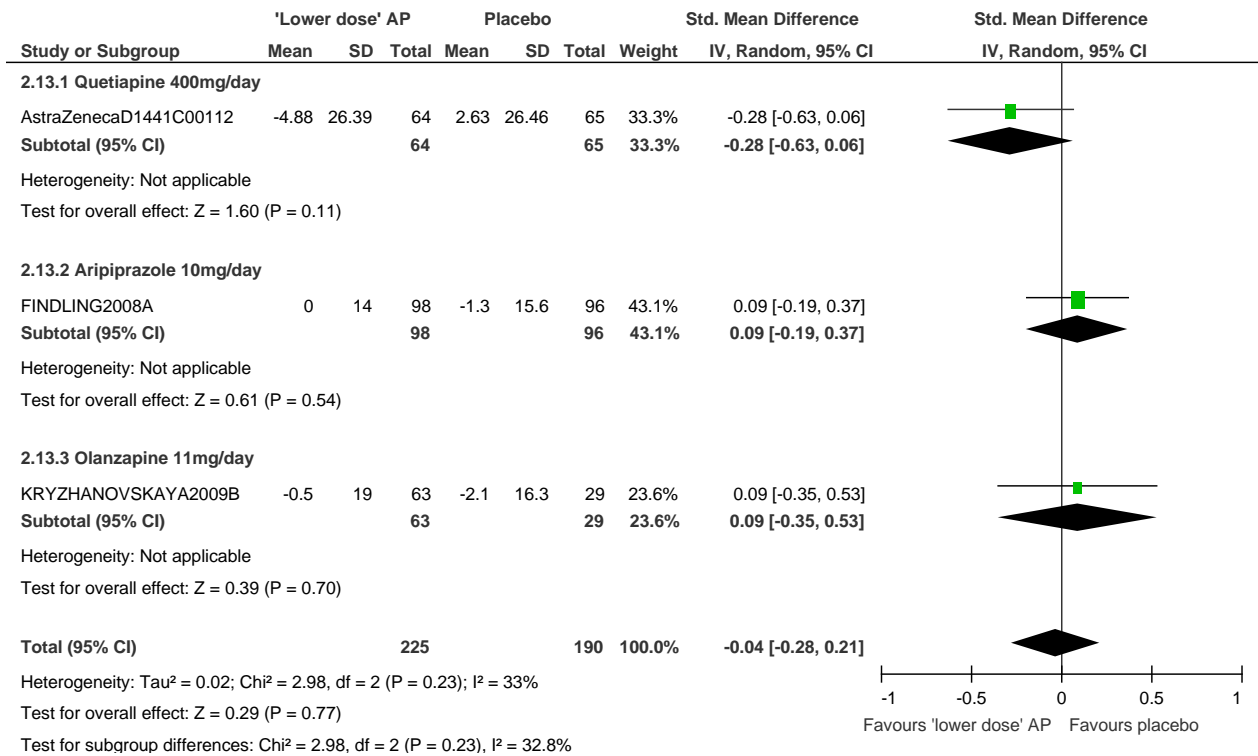
2.6 Mean change in fasting low-density lipoprotein cholesterol (mg/dl)



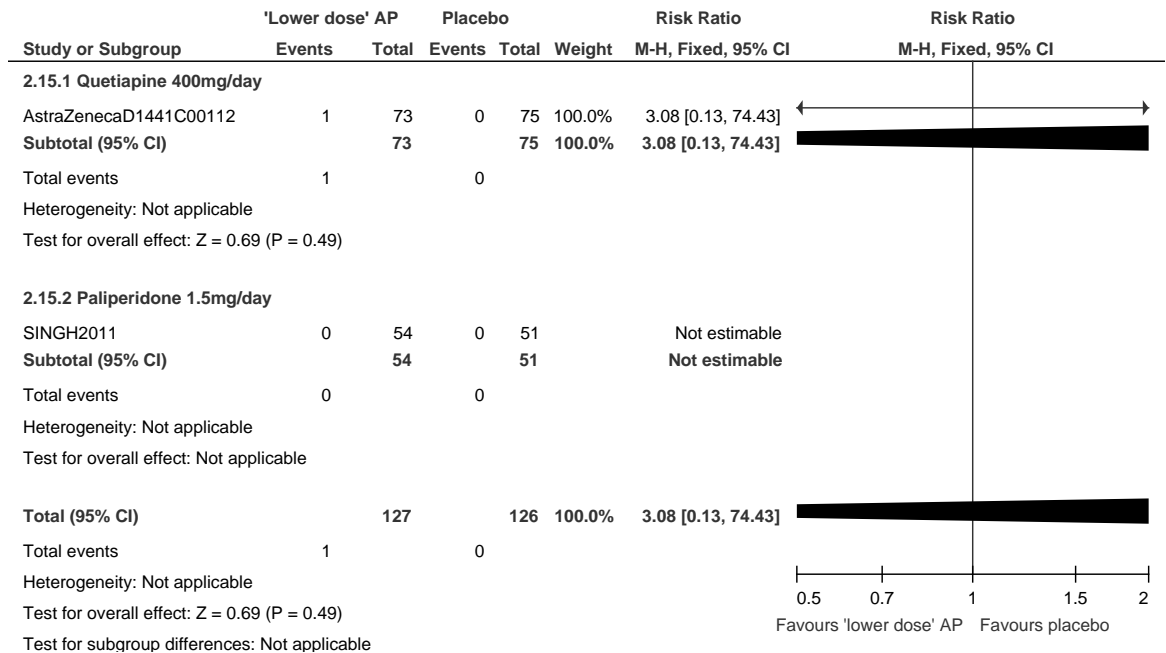
2.7 Fasting triglycerides (mg/dl) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A, AstraZenecaD1441C00112)



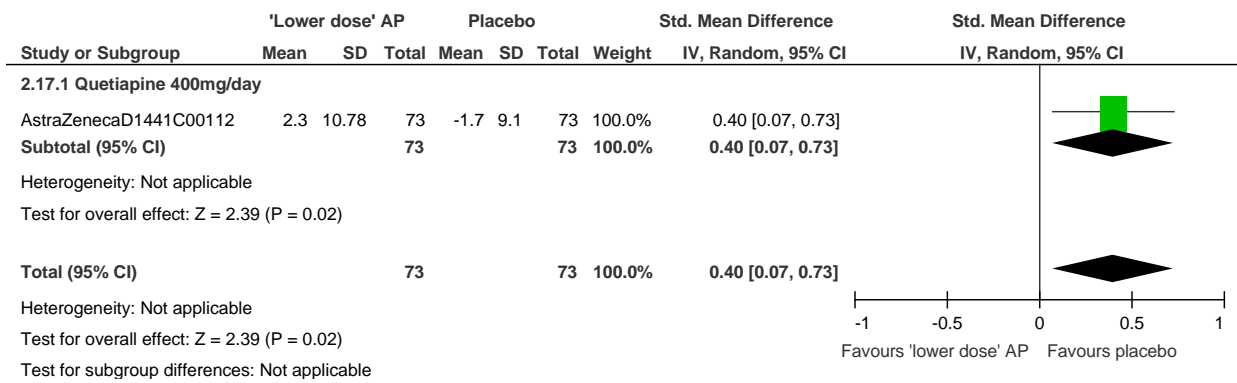
2.8 QTcB interval (msec) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A, AstraZenecaD1441C00112)



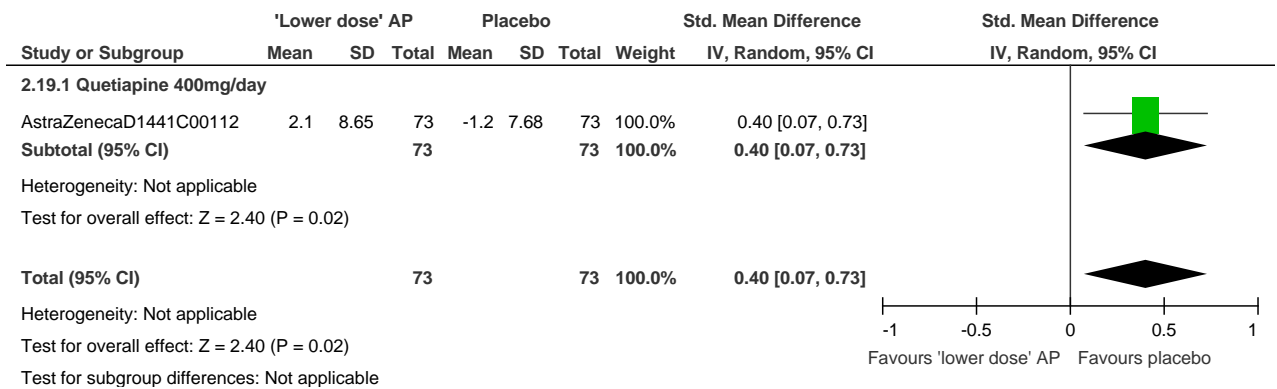
2.9 QTcB interval (msec) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A, AstraZenecaD1441C00112)



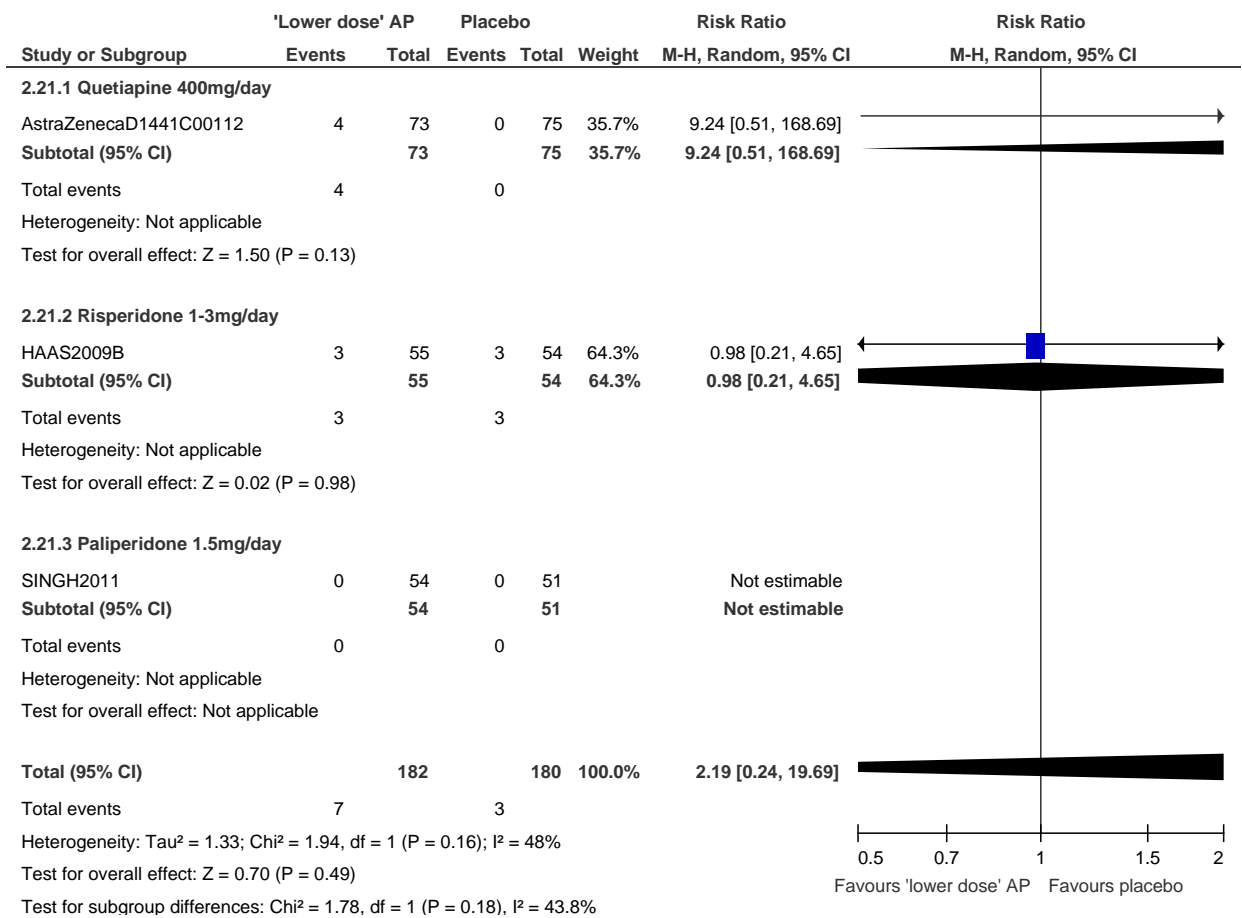
2.10 Mean change in systolic BP (mm Hg)



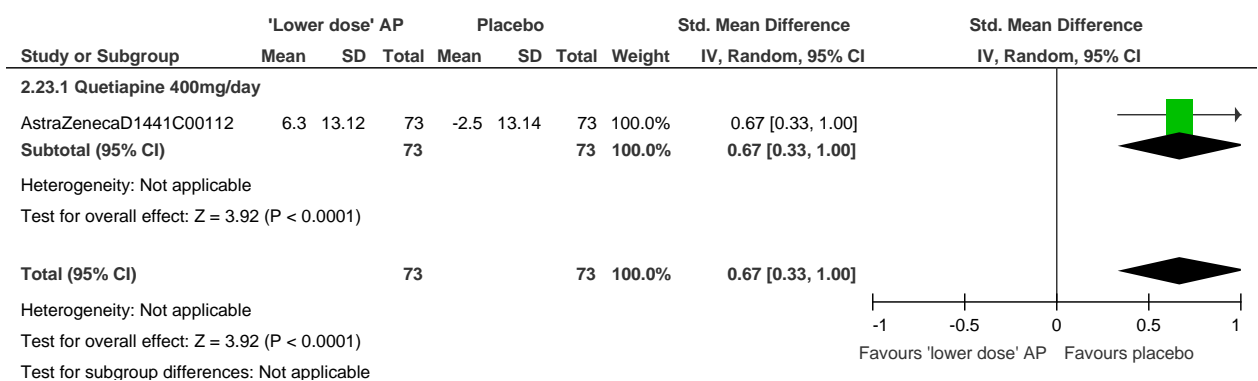
2.11 Mean change in diastolic BP (mm Hg)



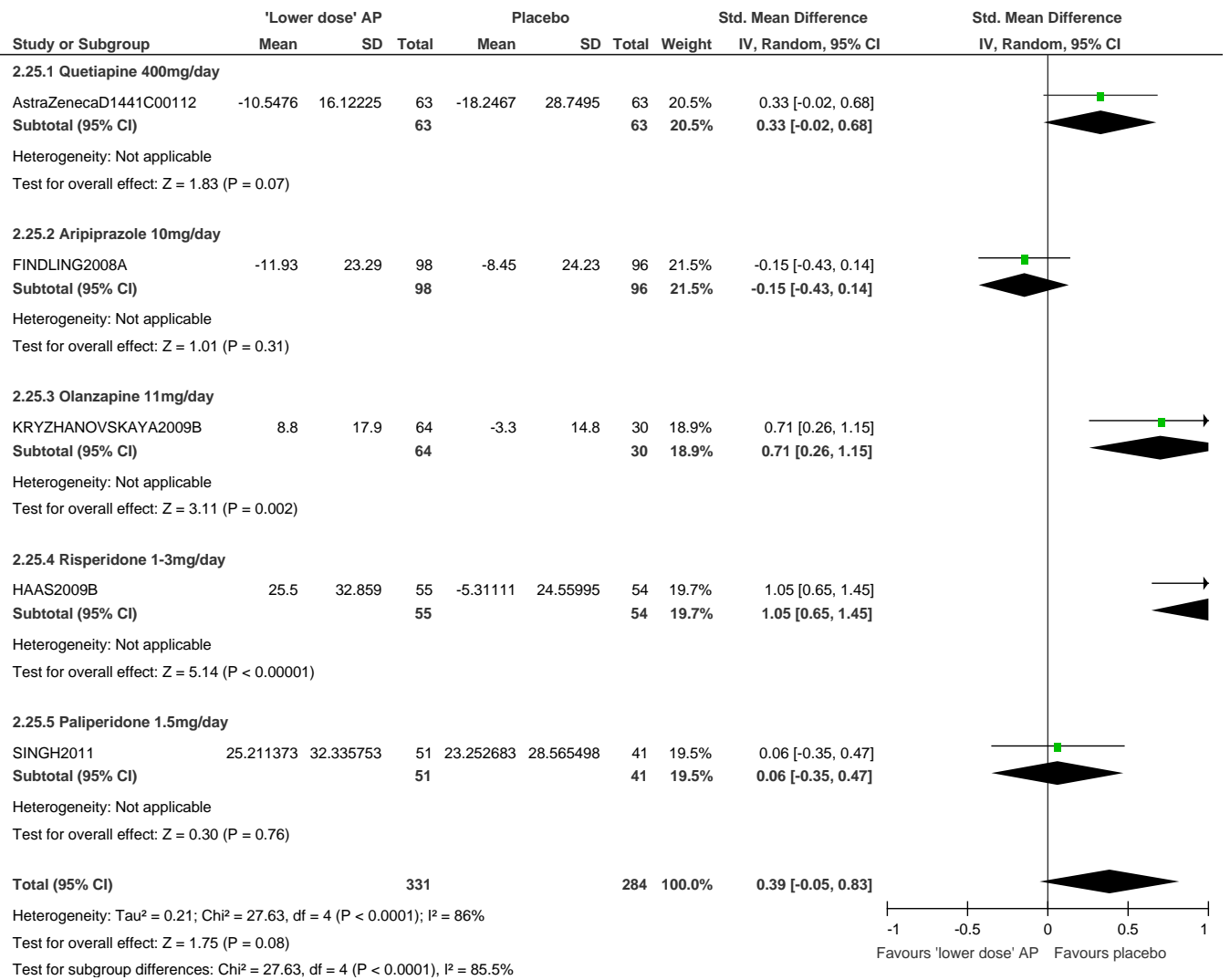
2.12 Tachycardia



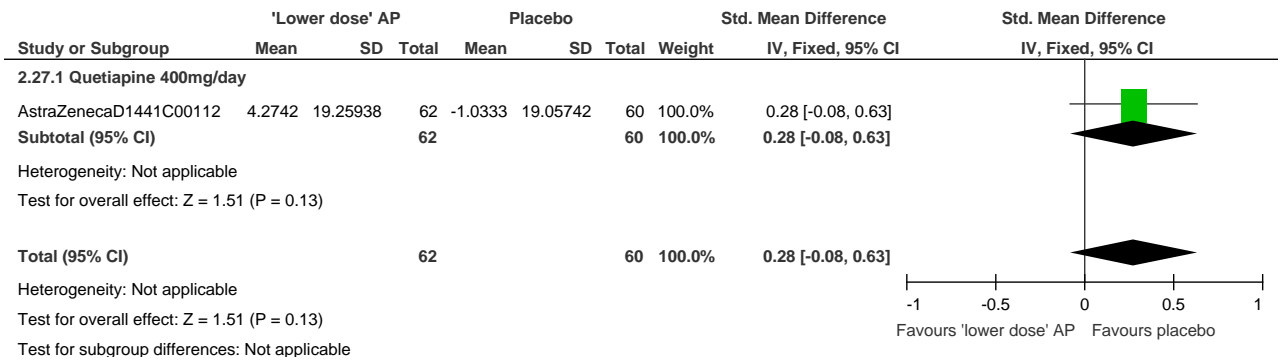
2.13 Mean change in standing pulse (BPM)



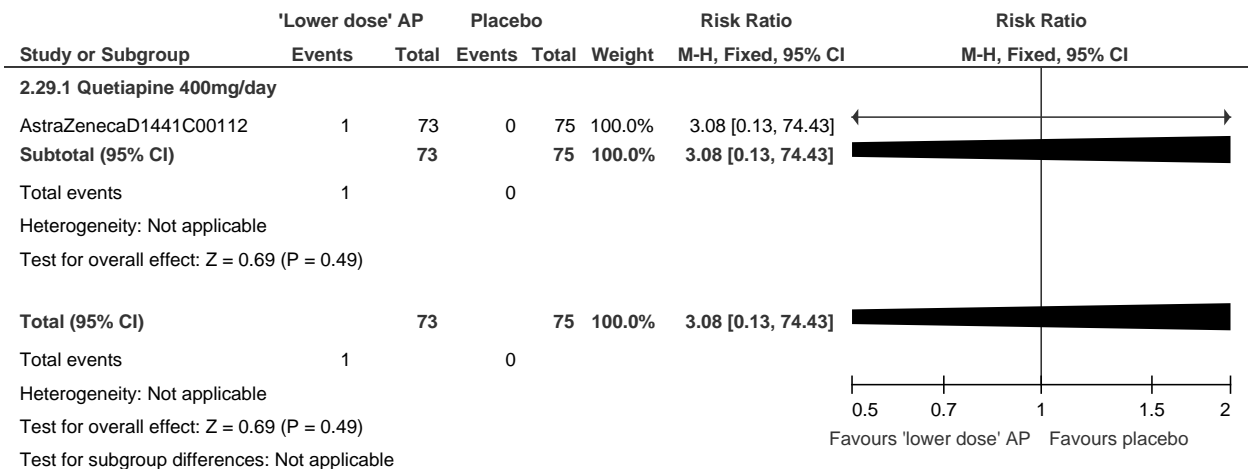
2.14 Prolactin level (mg/dl) (mean endpoint: KRYZHANOVSKAYA2009B; mean change: FINDLING2008A; AstraZenecaD1441C00112; HAAS2009B; SINGH2011)



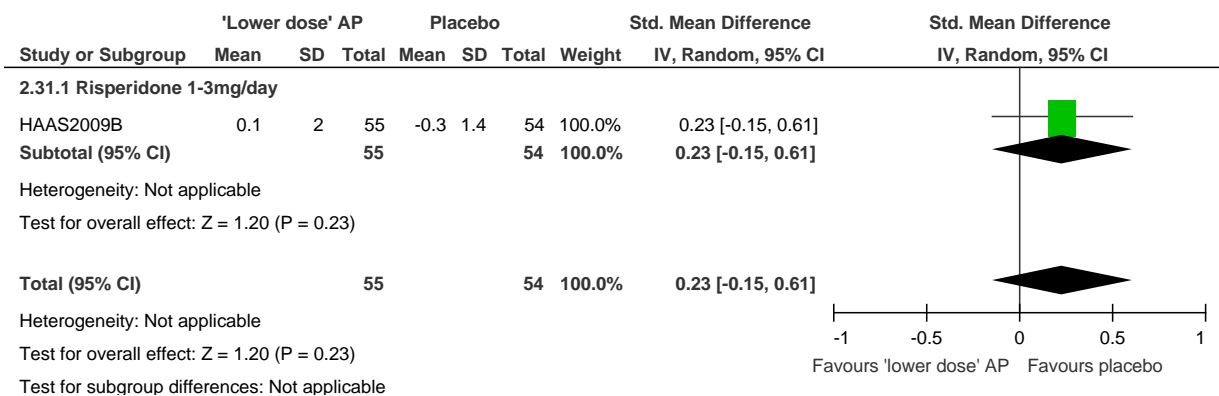
2.15 Mean change in insulin level (mg/dl)



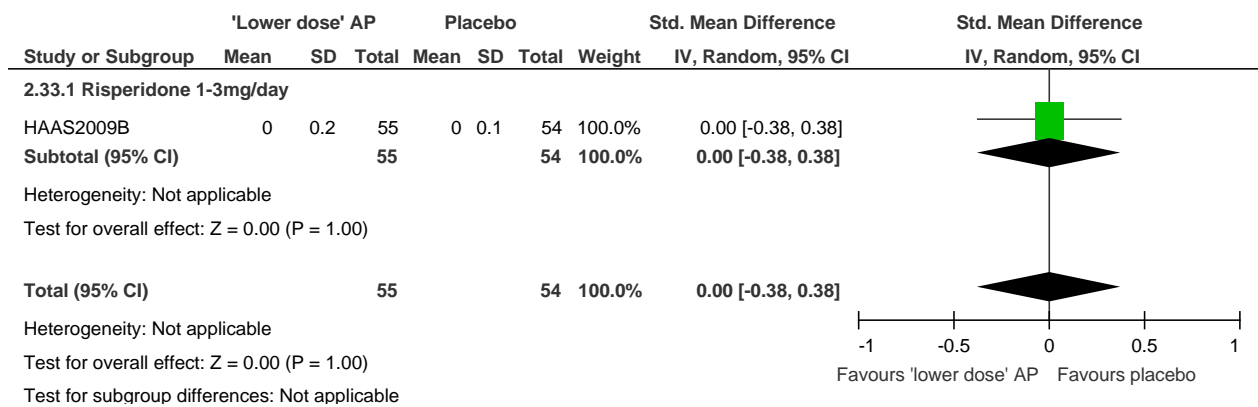
2.16 Extrapyrimal disorder



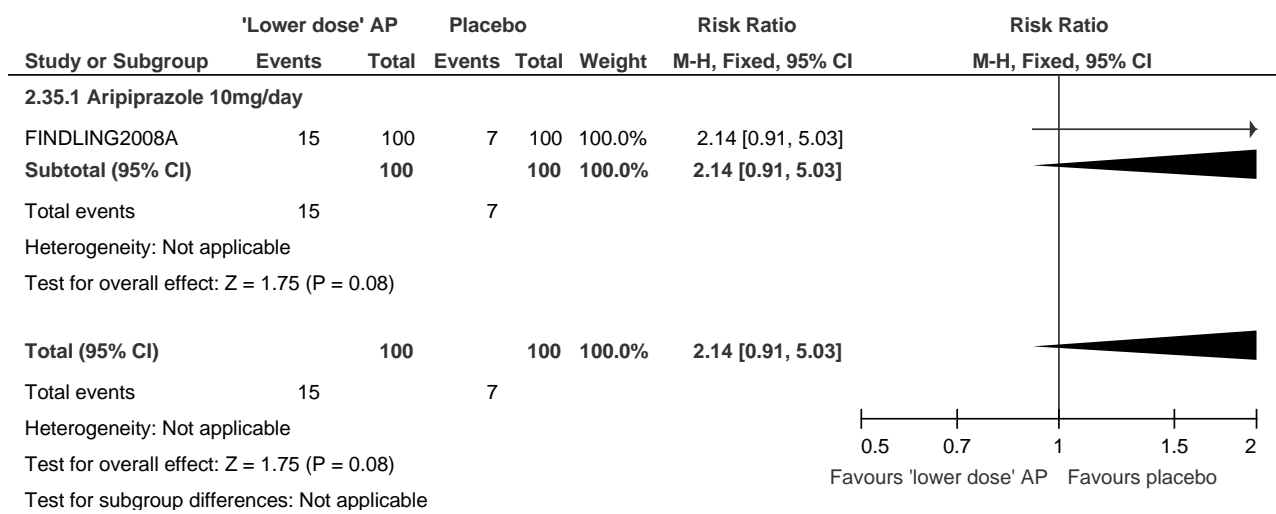
2.17 EPS (mean difference in AIMS scores)



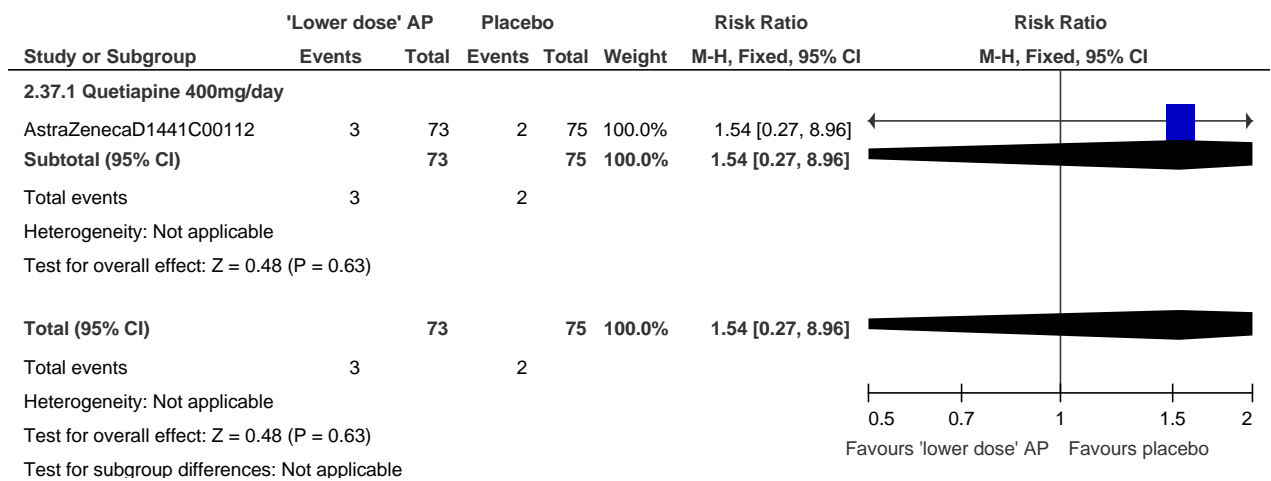
2.18 EPS (mean difference in SAS scores)



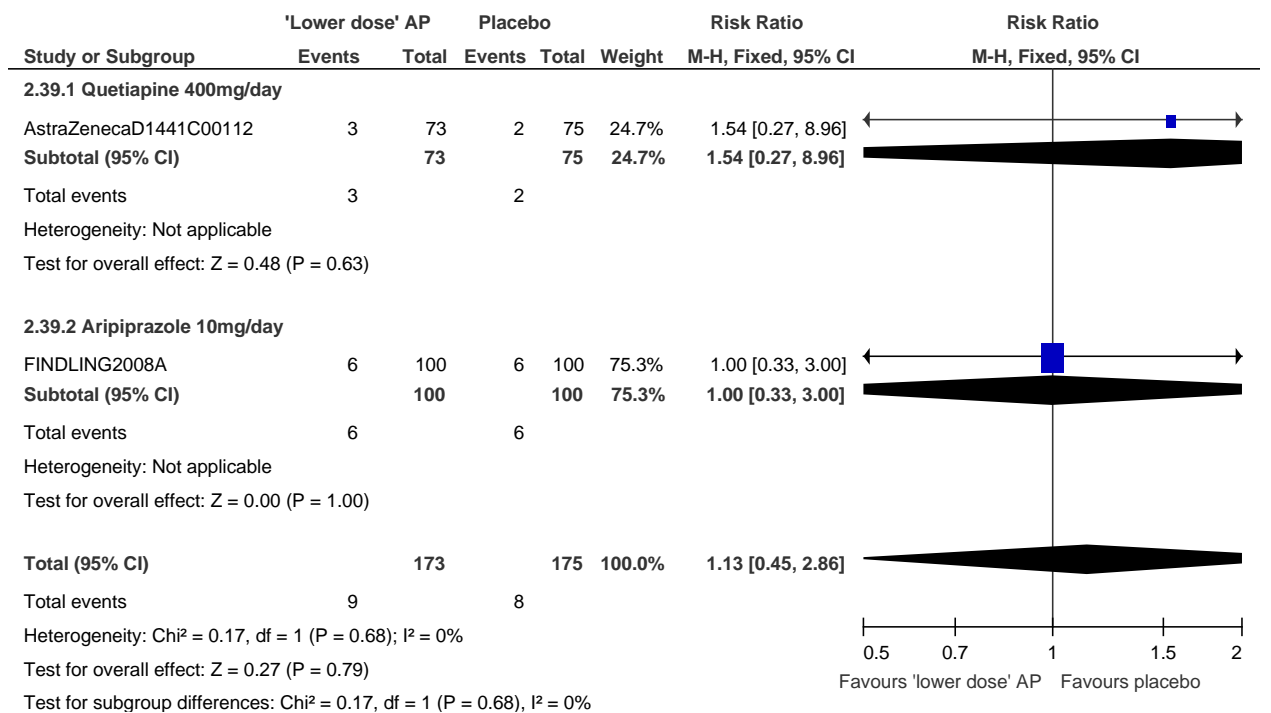
2.19 Parkinsonism



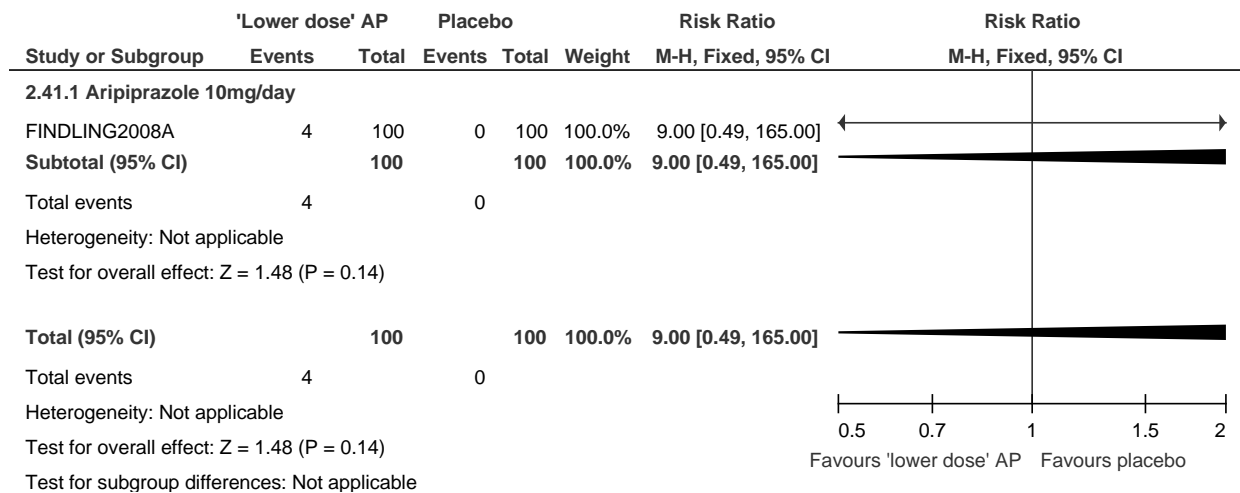
2.20 Tremor



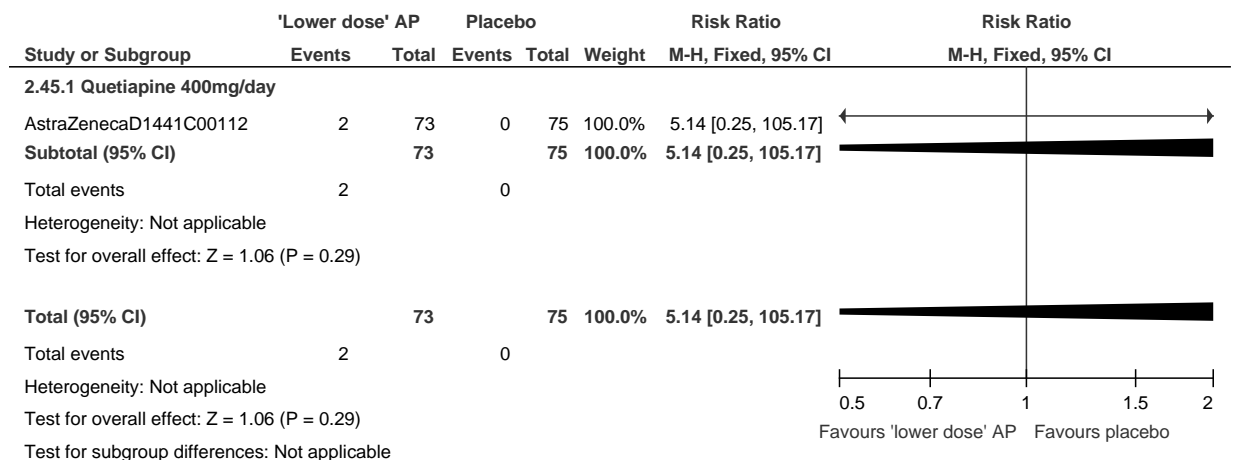
2.21 Akathisia



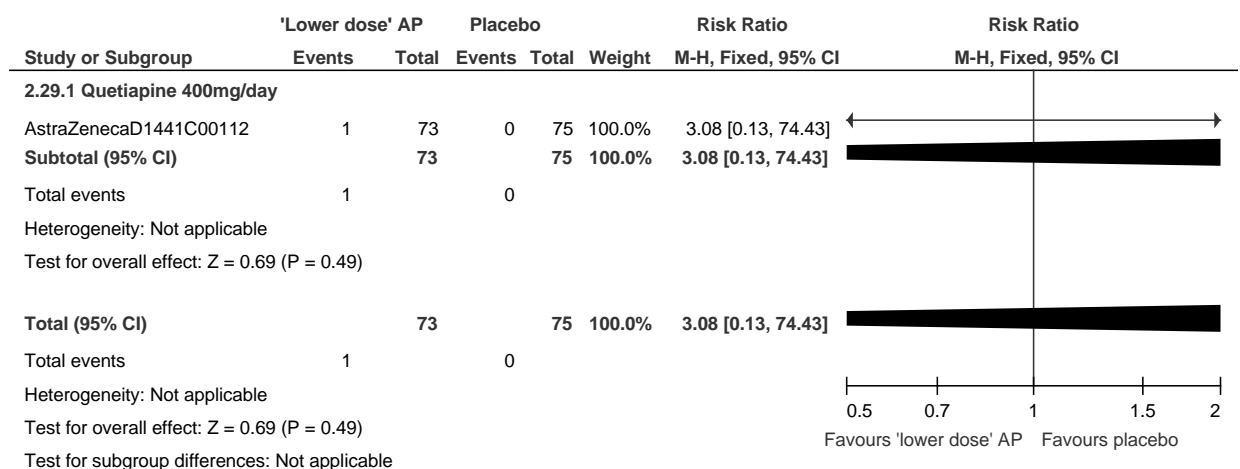
2.22 Dystonia



2.23 Dyskinesia



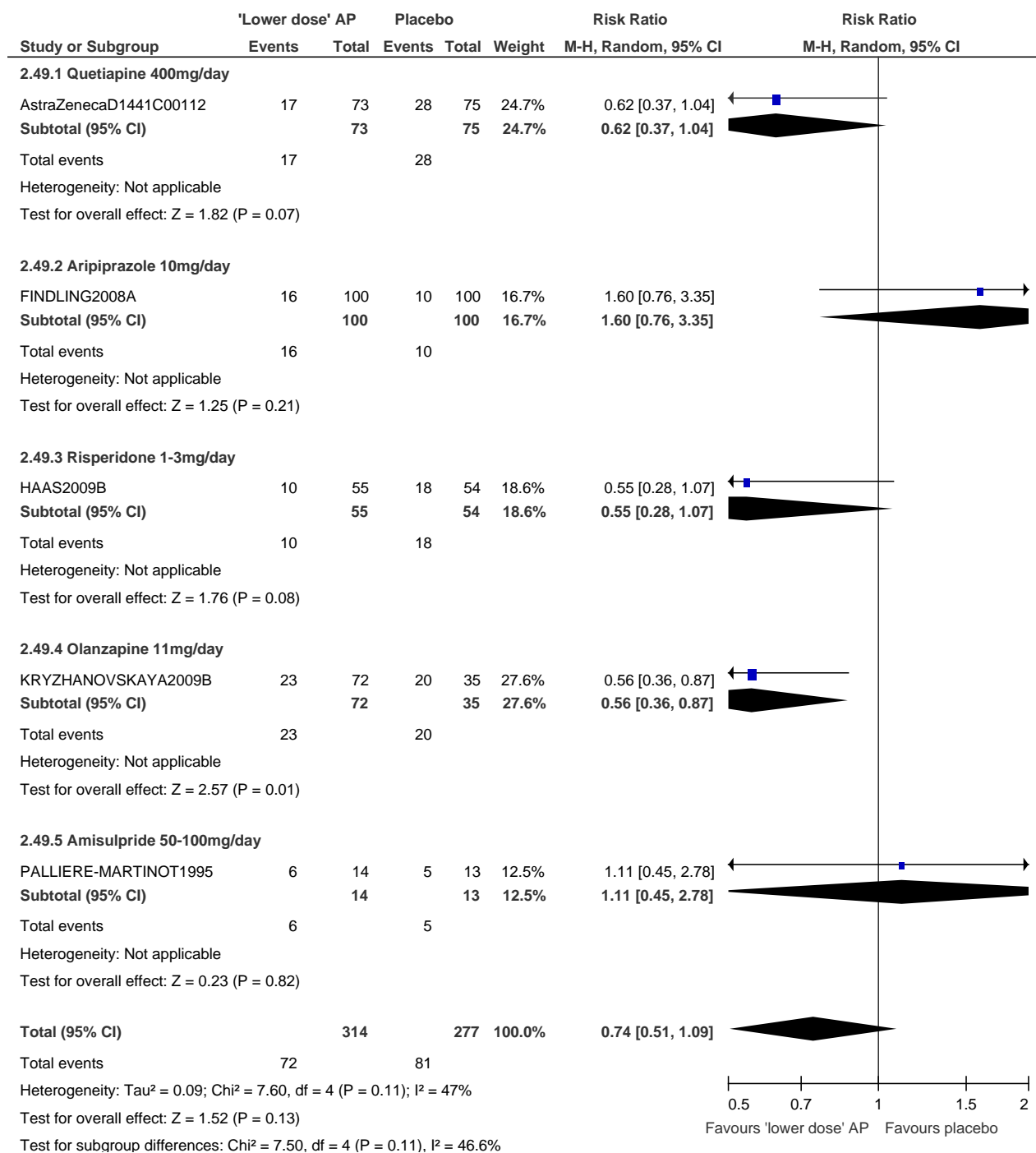
2.24 Extrapyramidal disorder



2.25 Mortality (including suicide)

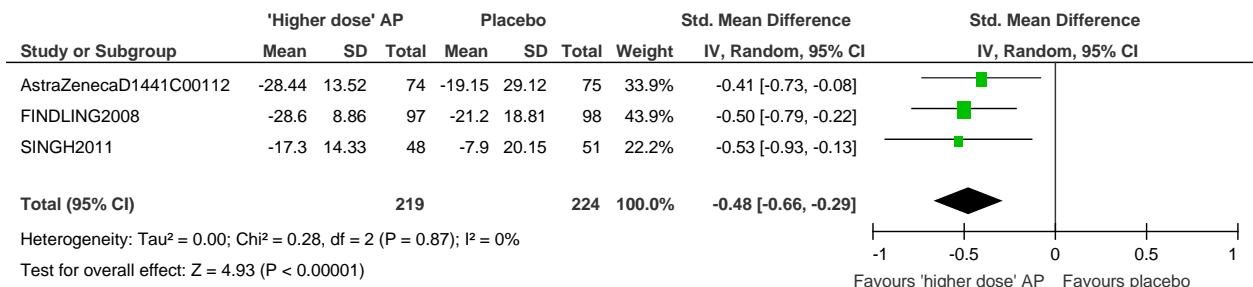
Study or Subgroup	'Lower dose' AP		Placebo		Weight	Risk Ratio	Risk Ratio
	Events	Total	Events	Total		M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
2.47.1 Aripiprazole 10mg/day							
FINDLING2008A	0	100	0	100		Not estimable	
Subtotal (95% CI)		100		100		Not estimable	
Total events	0		0				
Heterogeneity: Not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

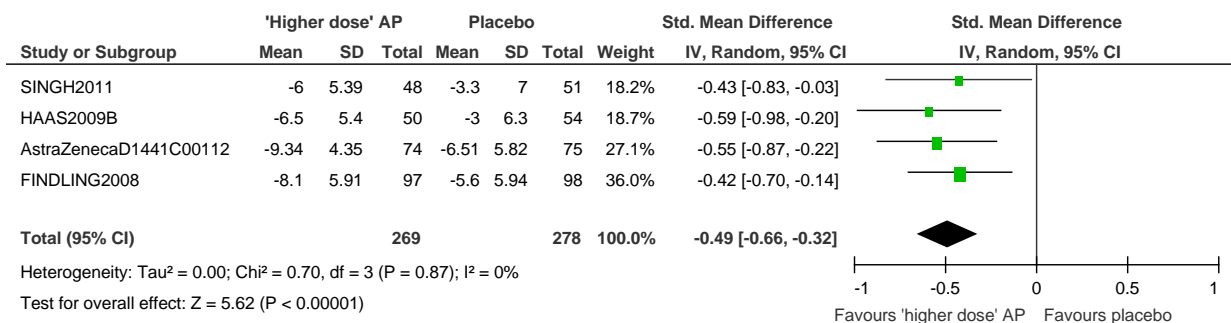


3. 'Higher dose' antipsychotic versus placebo: post-treatment efficacy outcomes

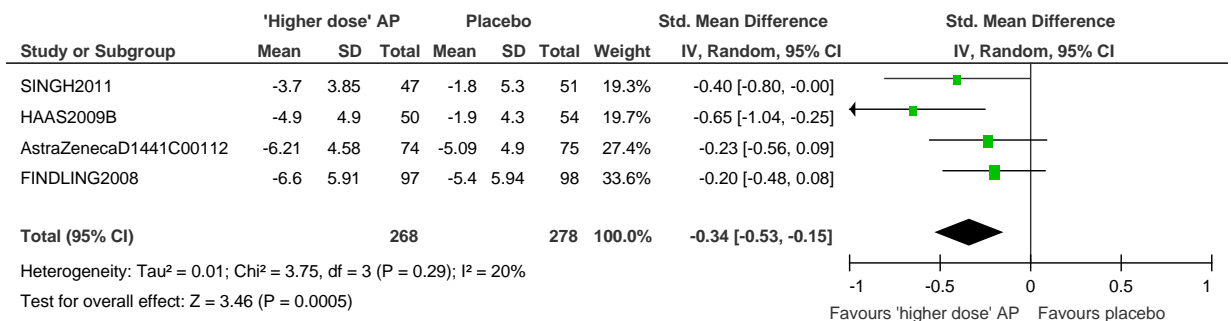
3.1 Mental state: mean change in total symptoms (PANSS)



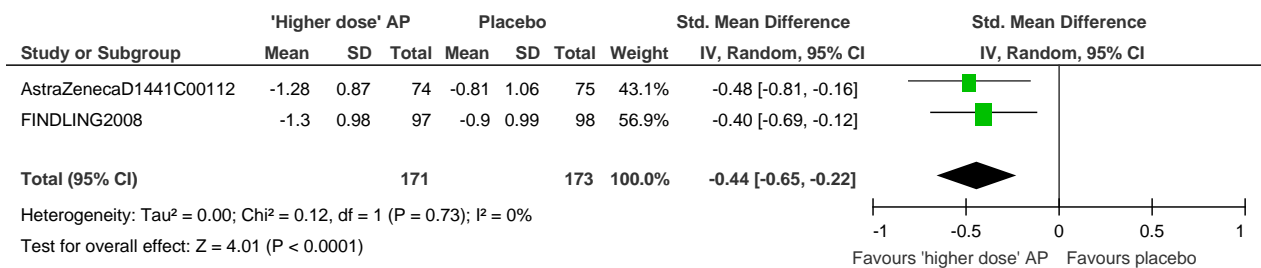
3.2 Mental state: mean change in positive symptoms (SAPS)



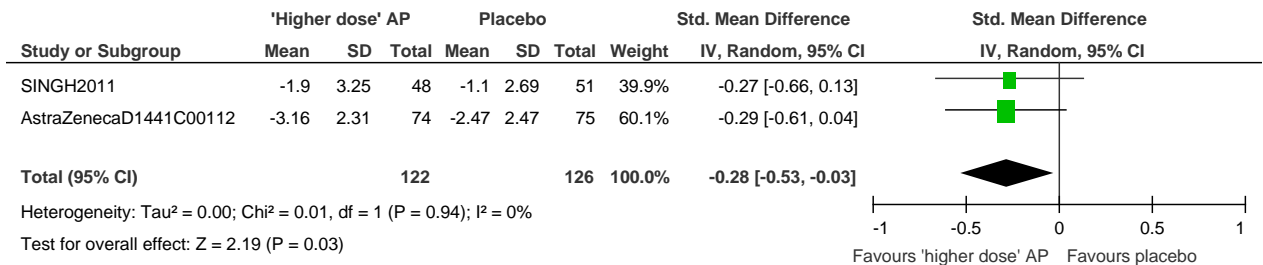
3.3 Mental state: mean change in negative symptoms (SANS)



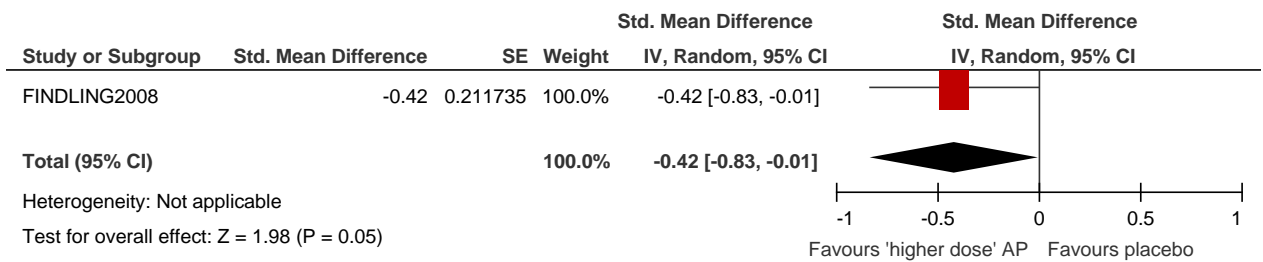
3.4 Mean change in global state: severity (CGI-S)



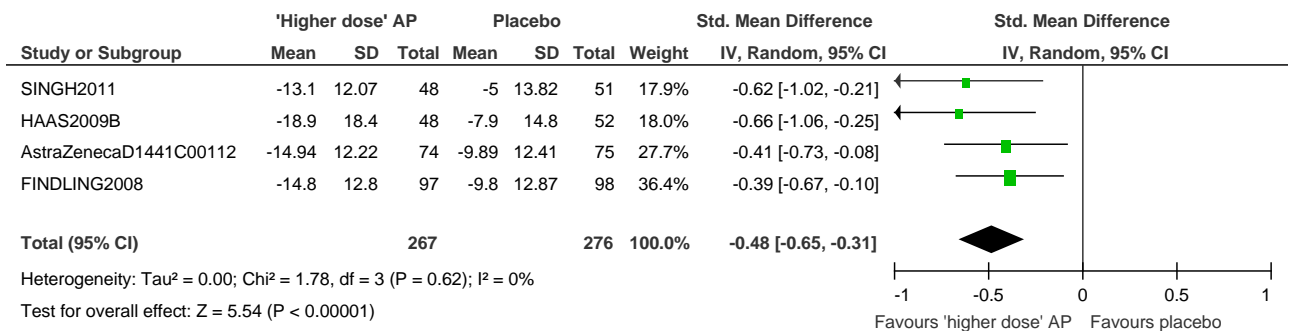
3.5 Mean change in depression (PANSS Depression, PANSS Anxiety and Depression)



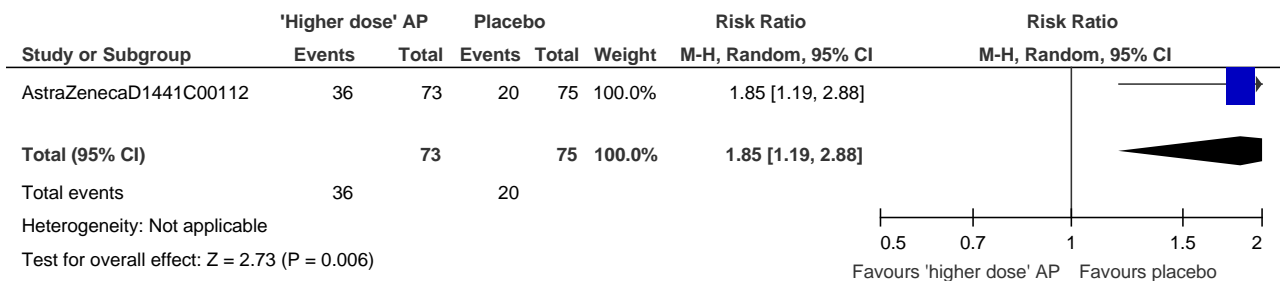
3.6 Mean change in quality of life (QLS)



3.7 Mean change in psychosocial functioning (CGAS)

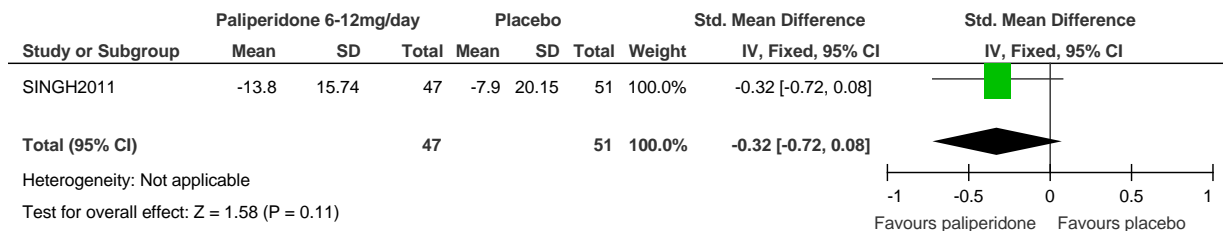


3.8 Response (CGI-I)

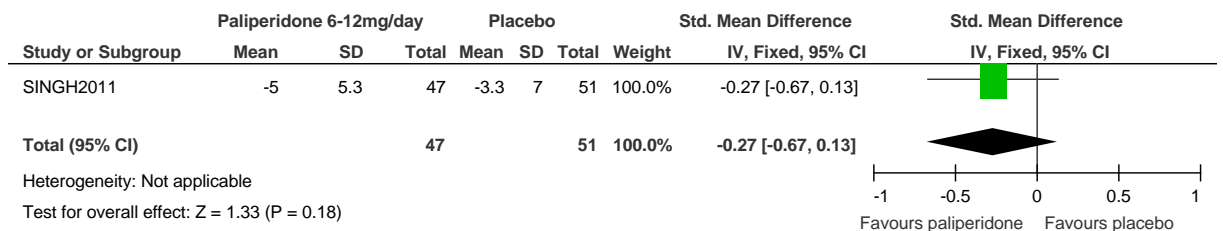


4. Additional (high) dose paliperidone versus placebo: post-treatment efficacy outcomes

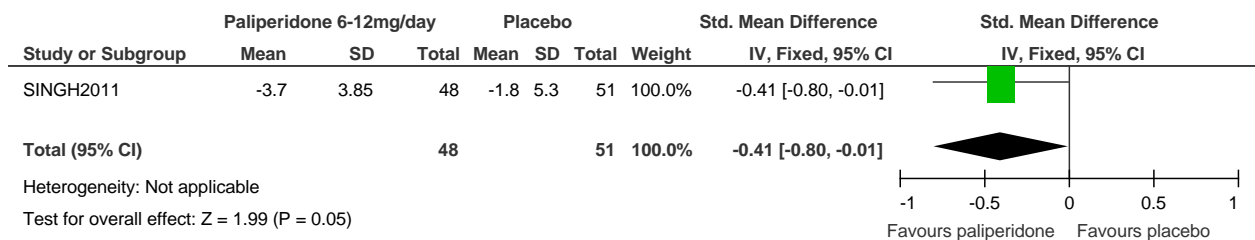
4.1 Mental state: mean change in total symptoms (PANSS)



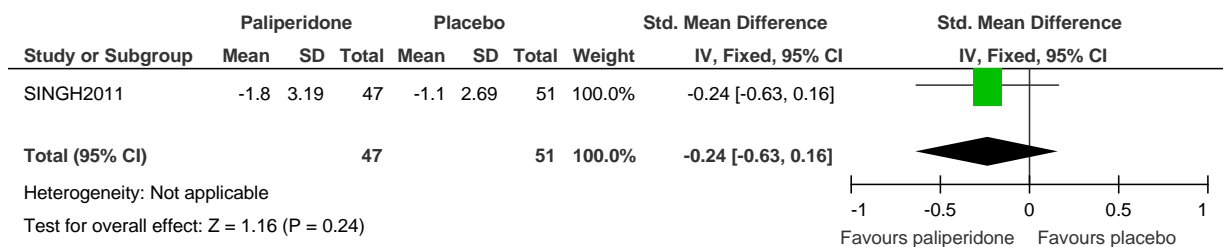
4.2 Mental state: mean change in positive symptoms (SAPS)



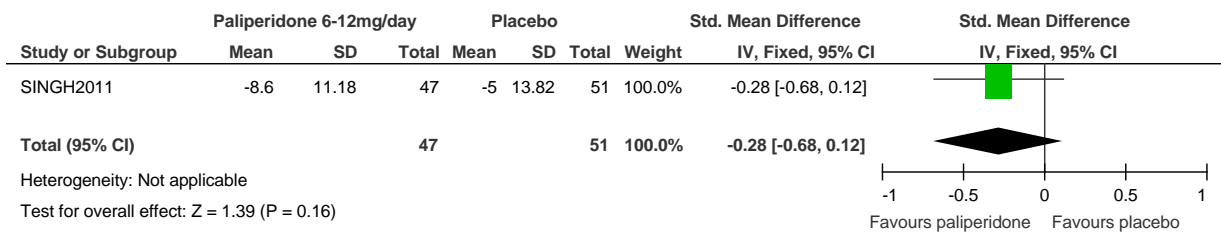
4.3 Mental state: mean change in negative symptoms (SANS)



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

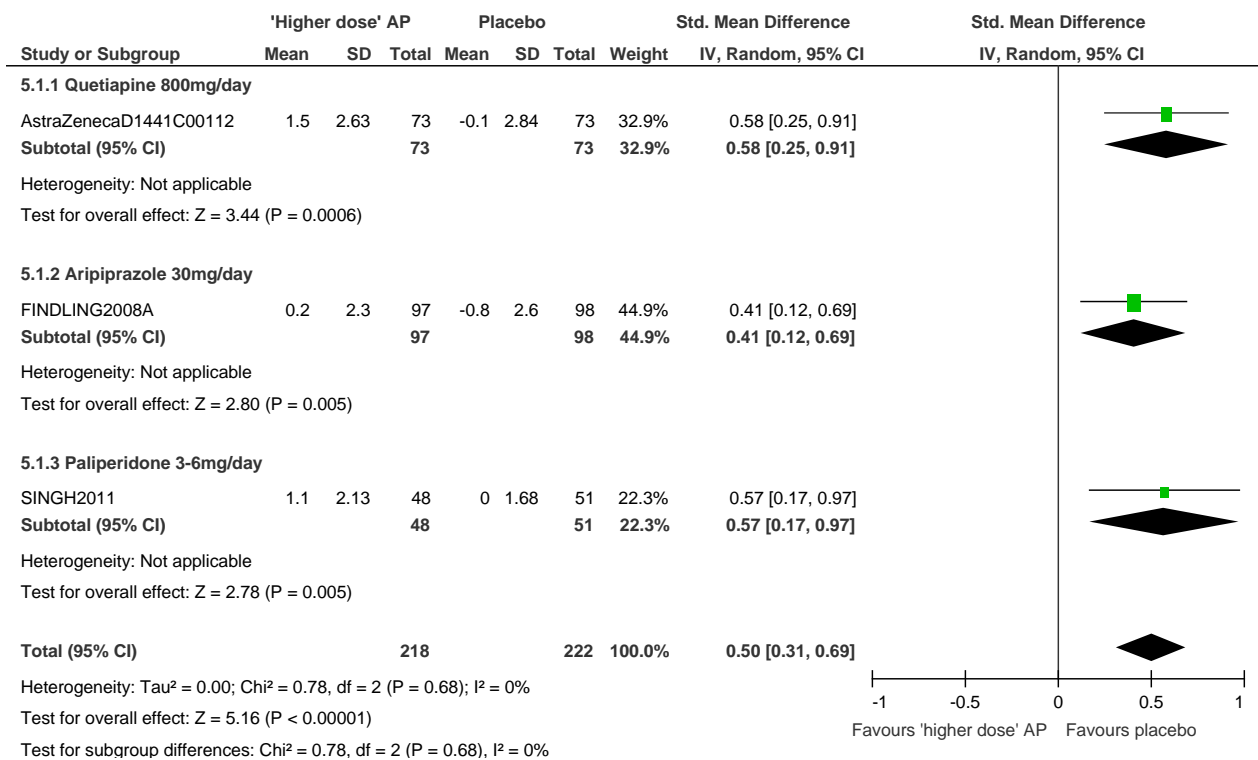


4.5 Mean change in psychosocial functioning (CGAS)

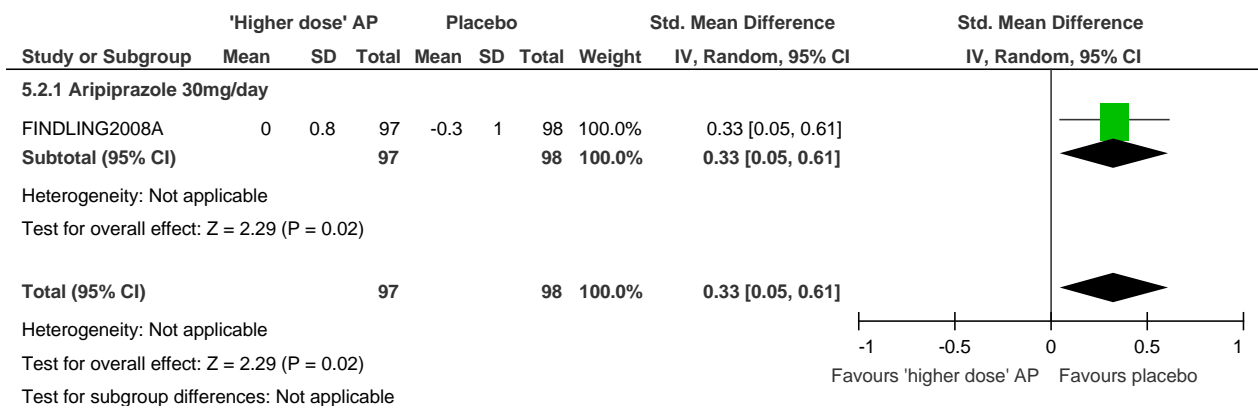


5. 'Higher dose' antipsychotic versus placebo: post-treatment side effect outcomes

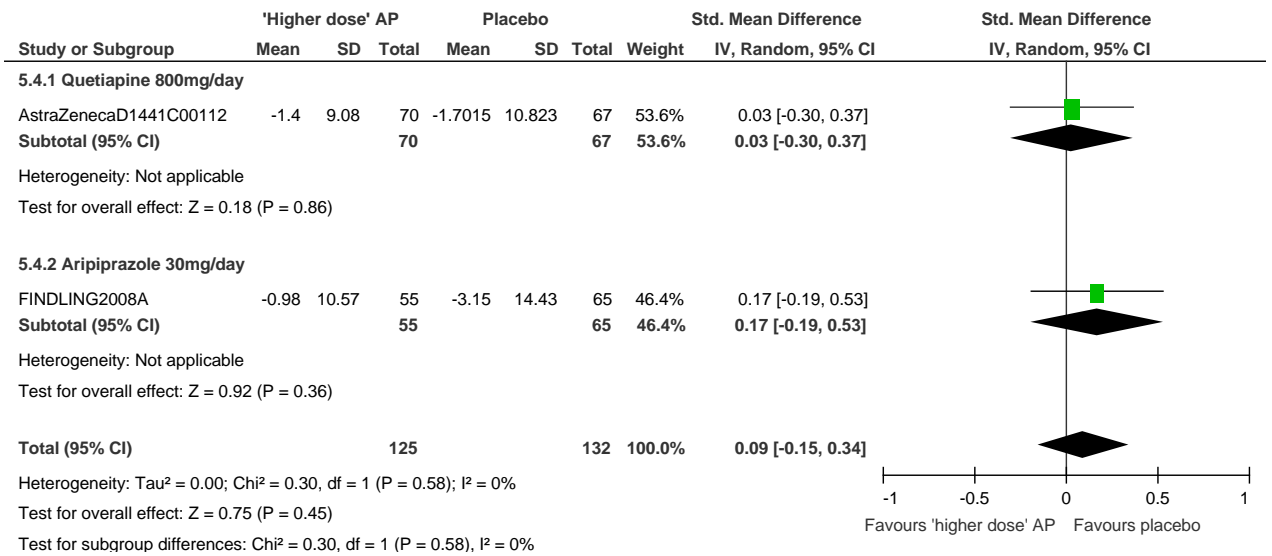
5.1 Mean change in weight (kg)



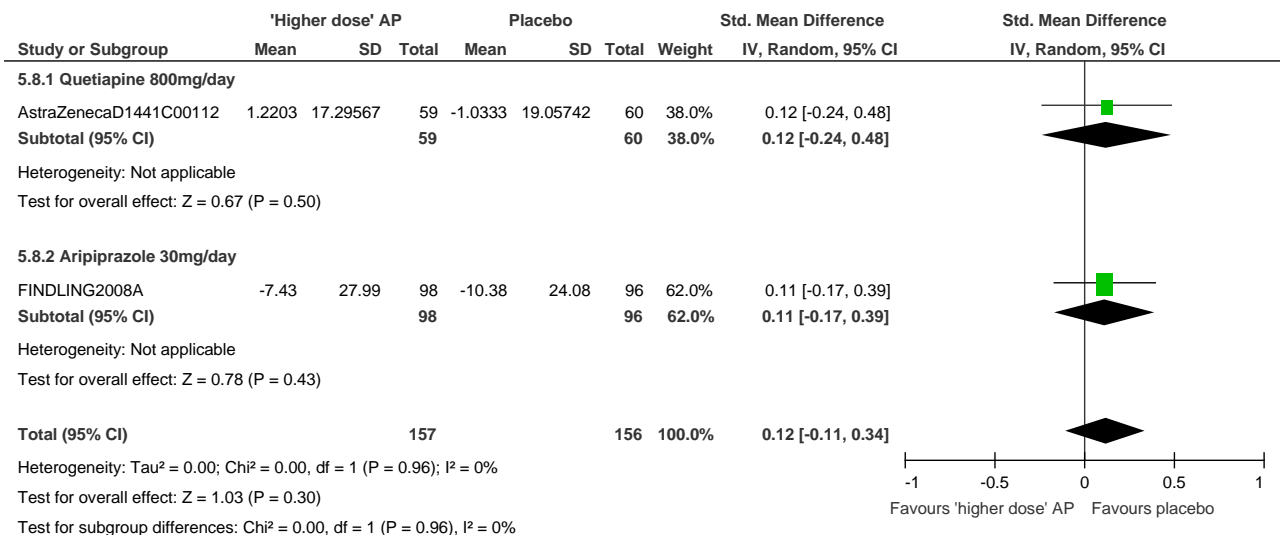
5.2 Mean change in BMI (kg/m²)



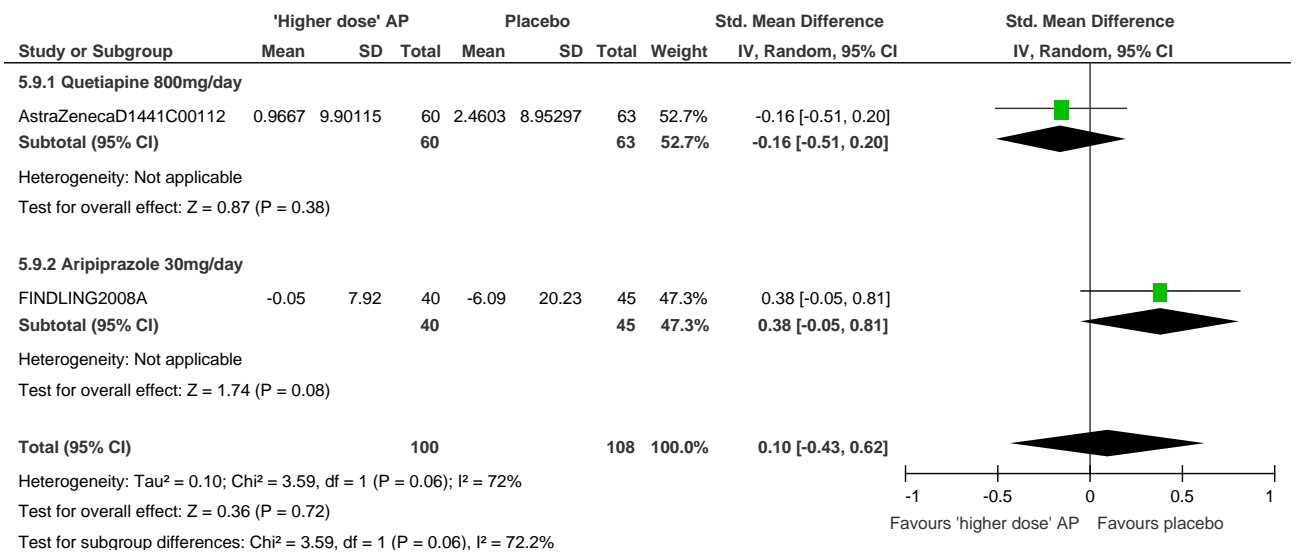
5.3 Mean change in fasting serum glucose level (mg/dl)



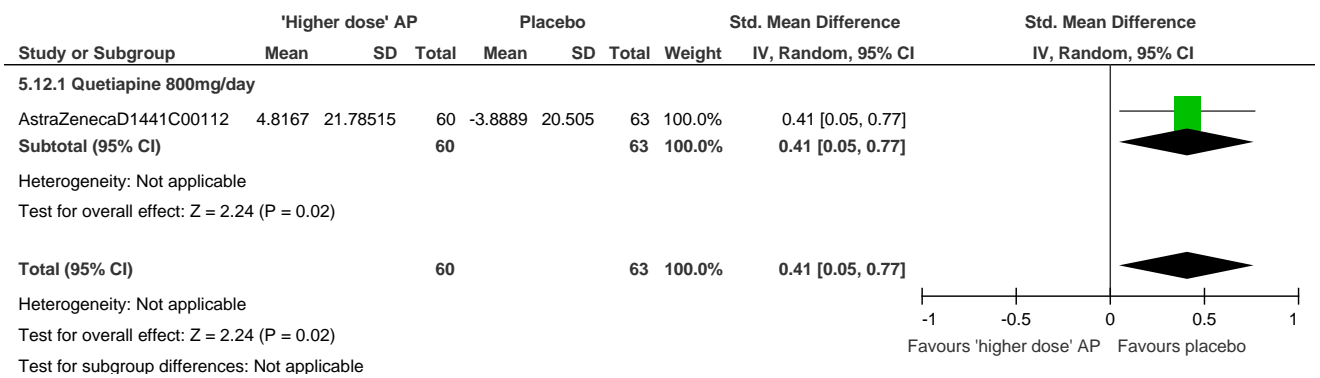
5.4 Mean change in fasting total cholesterol (mg/dl)



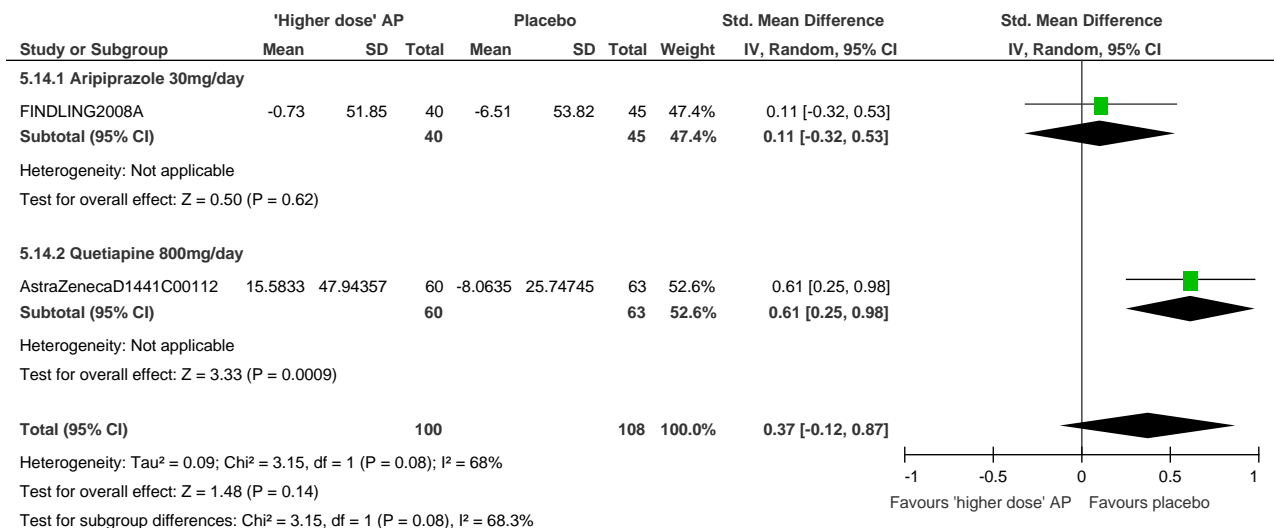
5.5 Mean change in fasting high-density lipoprotein cholesterol (mg/dl)



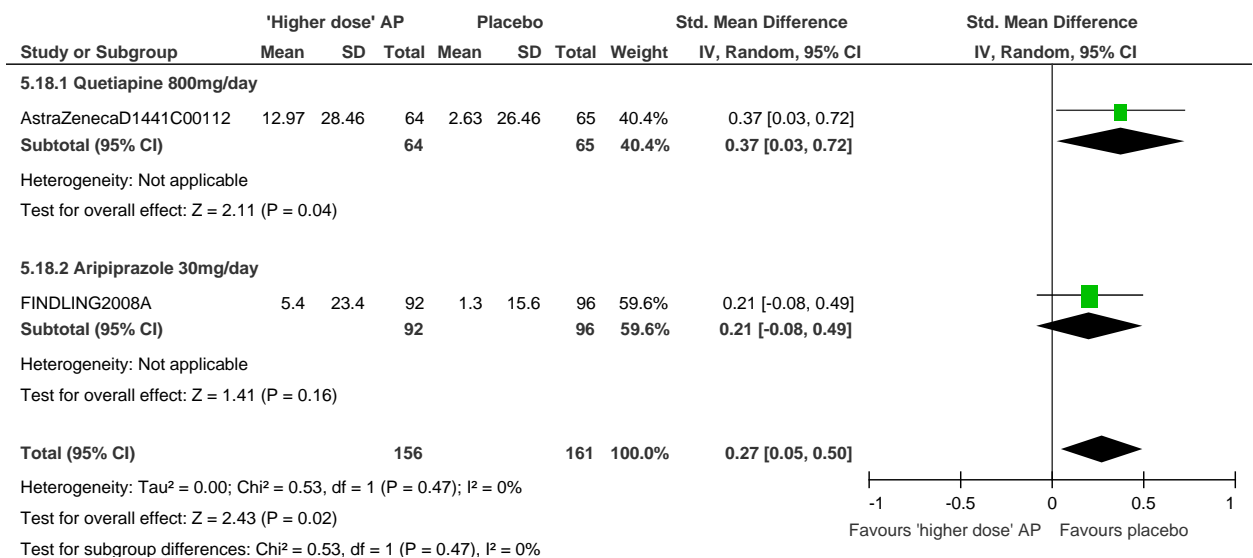
5.6 Mean change in fasting low-density lipoprotein cholesterol (mg/dl)



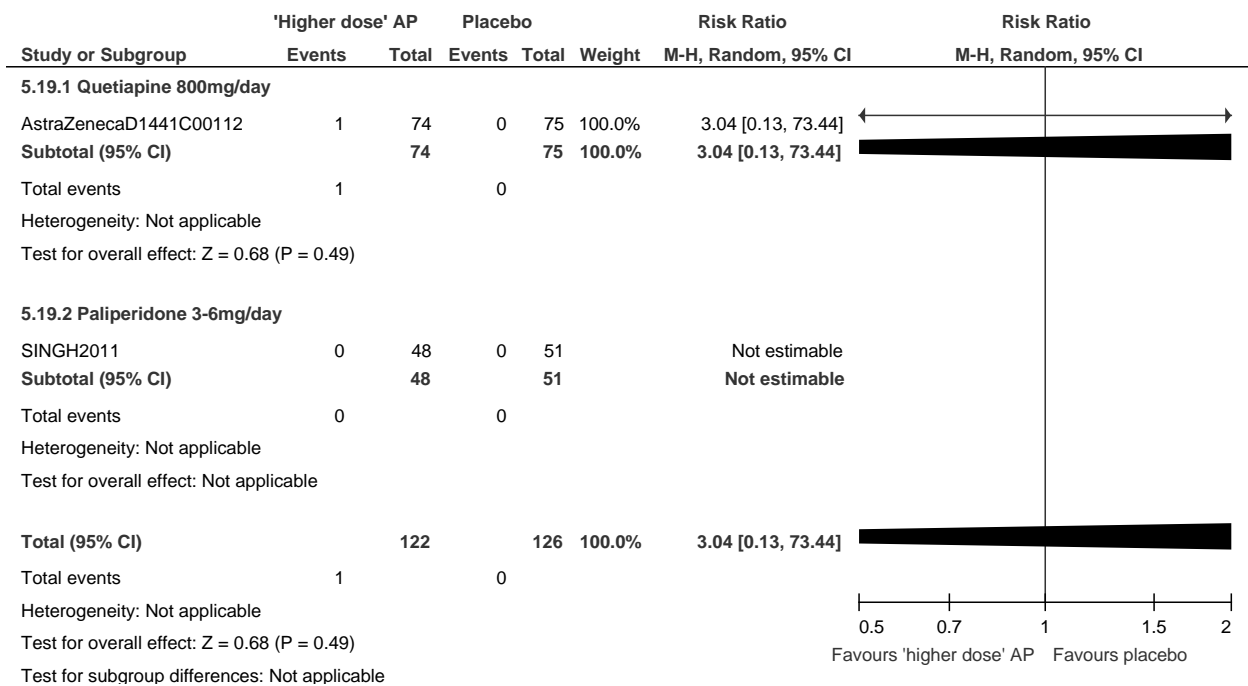
5.7 Mean change in fasting triglycerides (mg/dl)



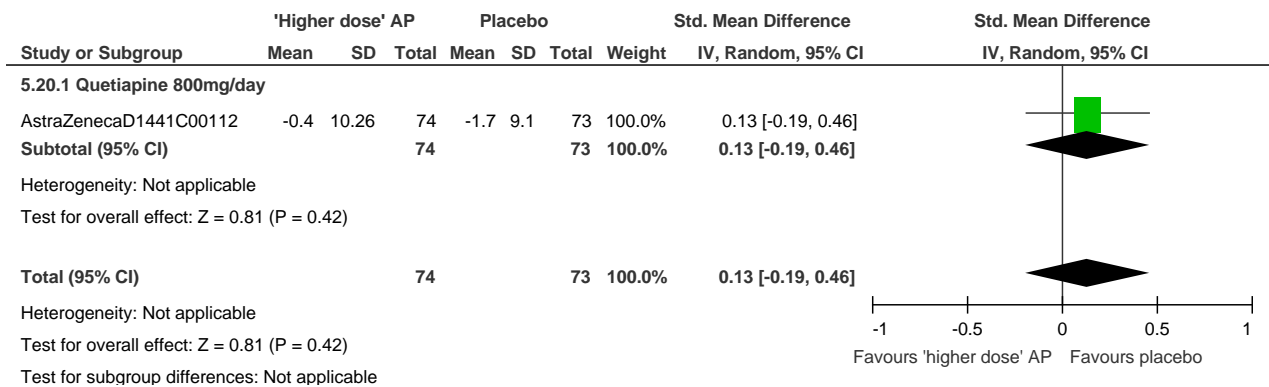
5.8 Mean change in QTcB interval (msec)



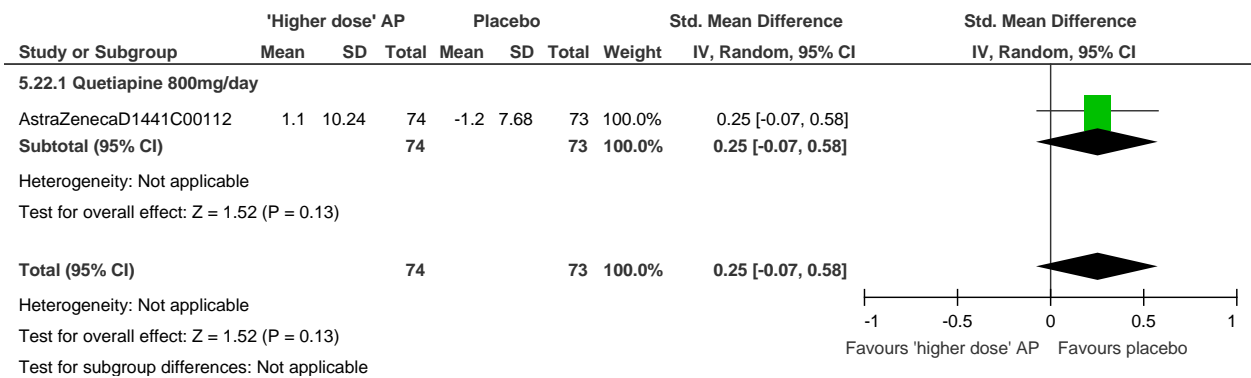
5.9 Prolonged QT interval (msec)



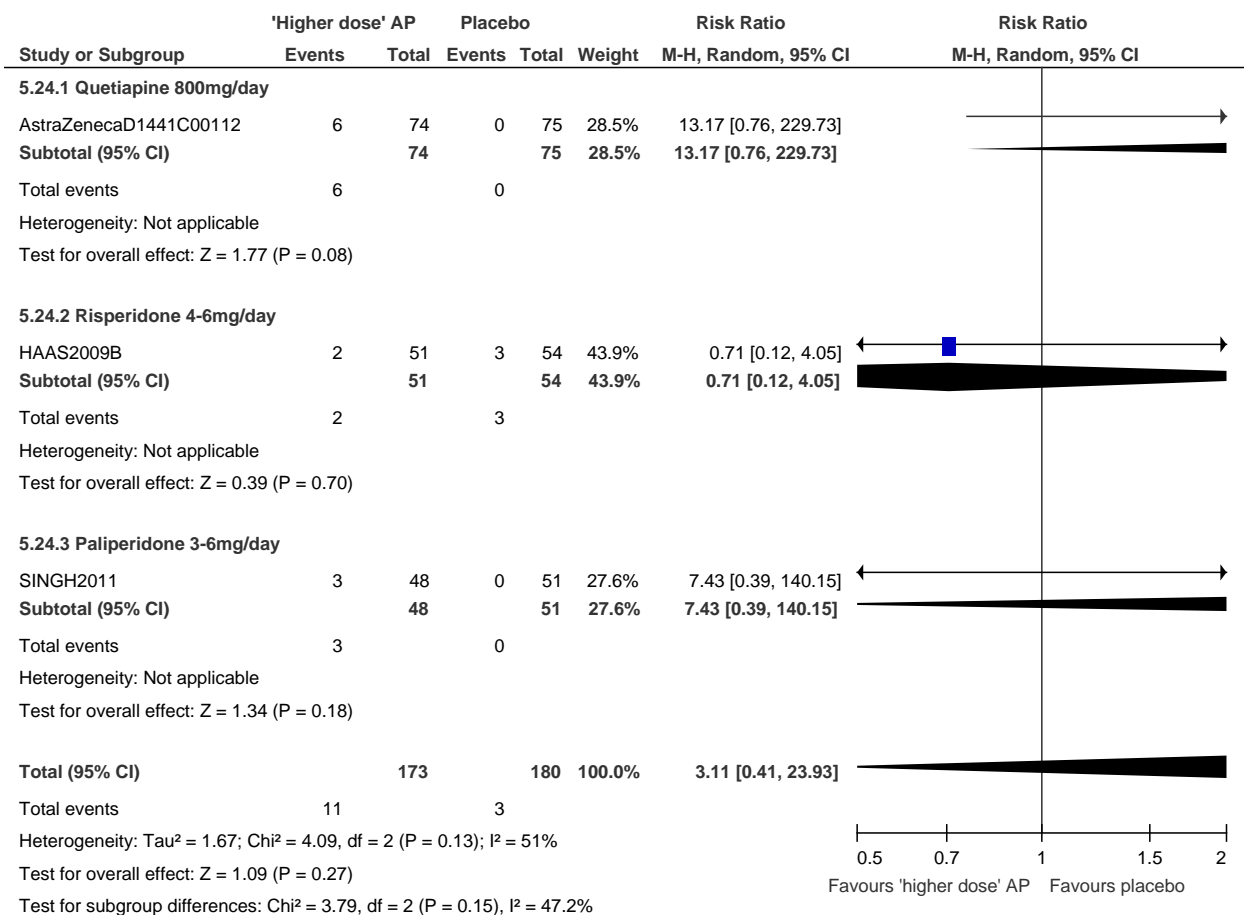
5.10 Mean change in systolic BP (mm Hg)



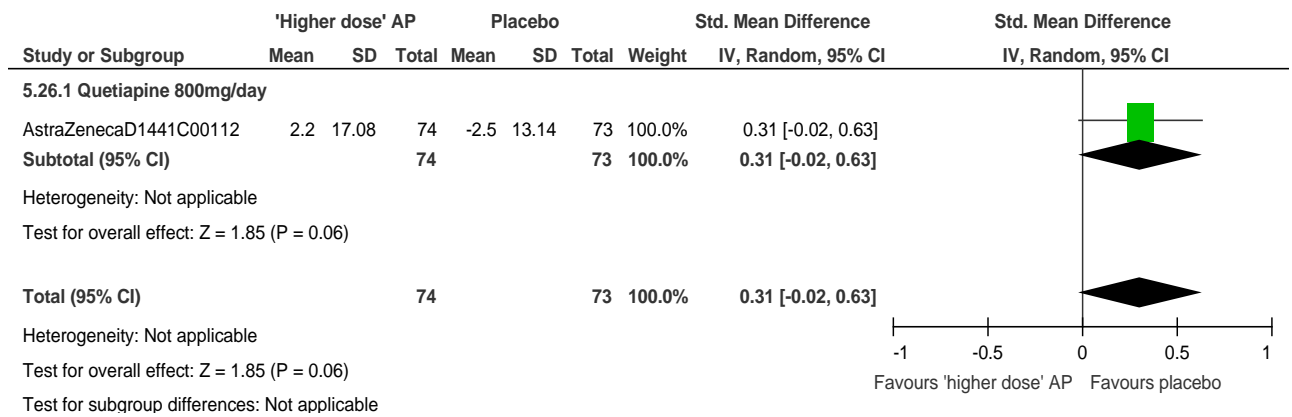
5.11 Mean change in diastolic BP (mm Hg)



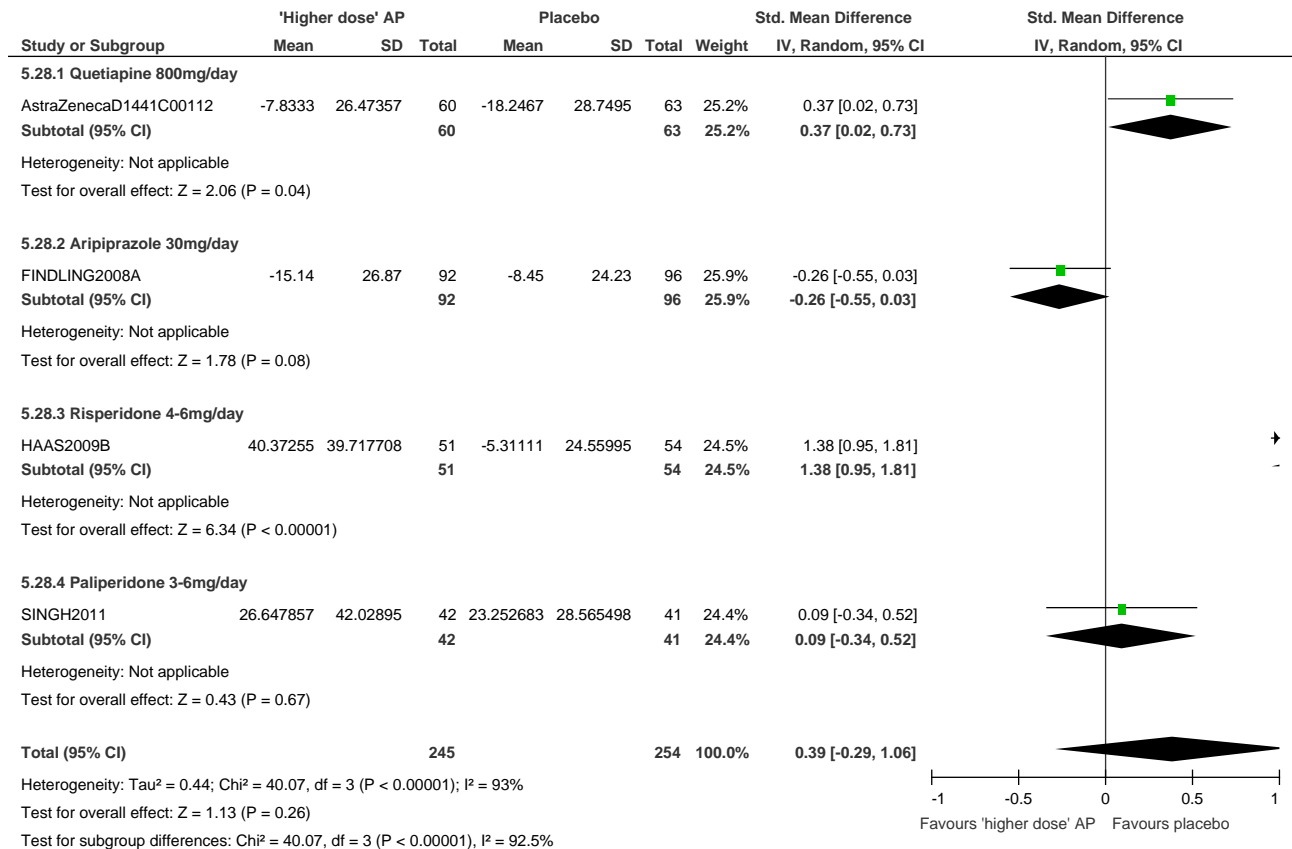
5.12 Tachycardia



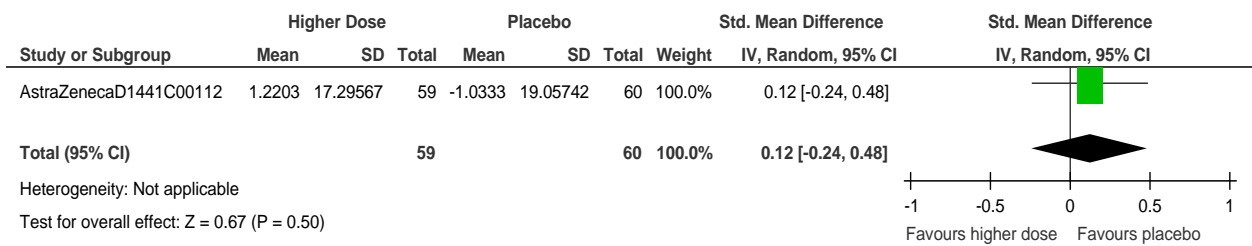
5.13 Mean change in standing pulse (BPM)



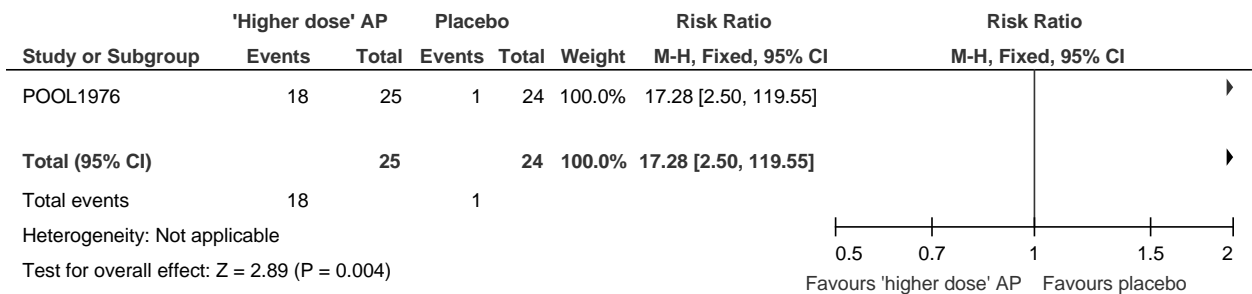
5.14 Mean change in prolactin (mg/dl)



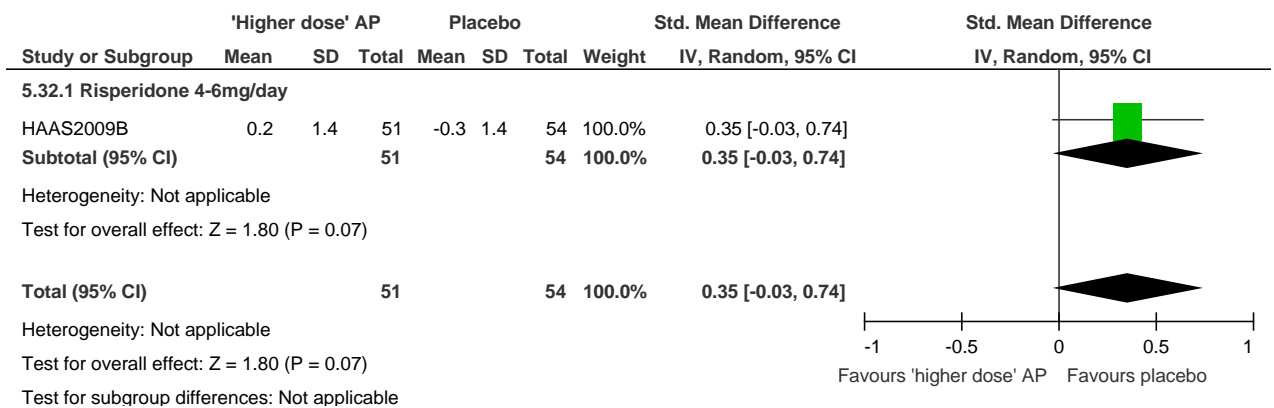
5.15 Mean change in insulin level (mg/dl)



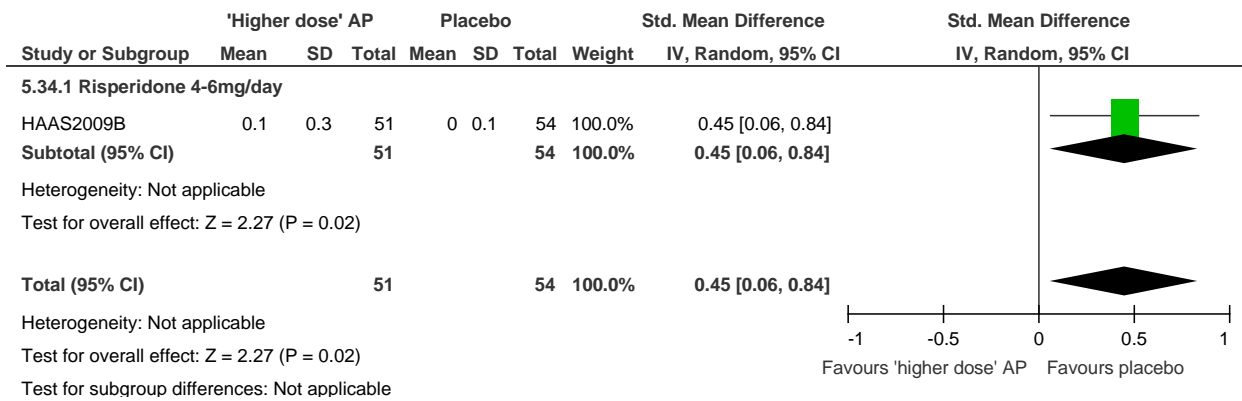
5.16 EPS



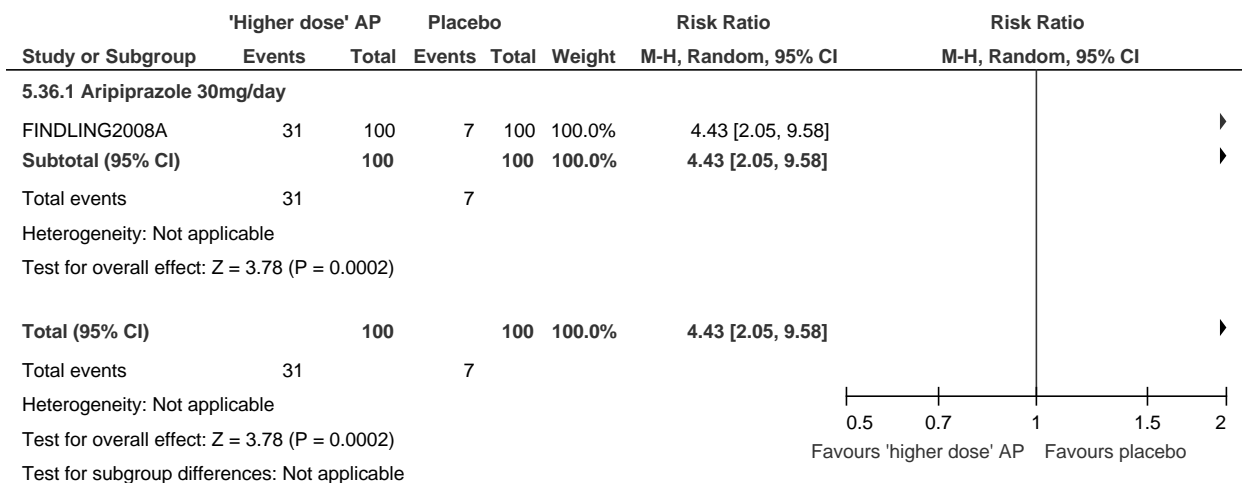
5.17 EPS (mean change in AIMS scores)



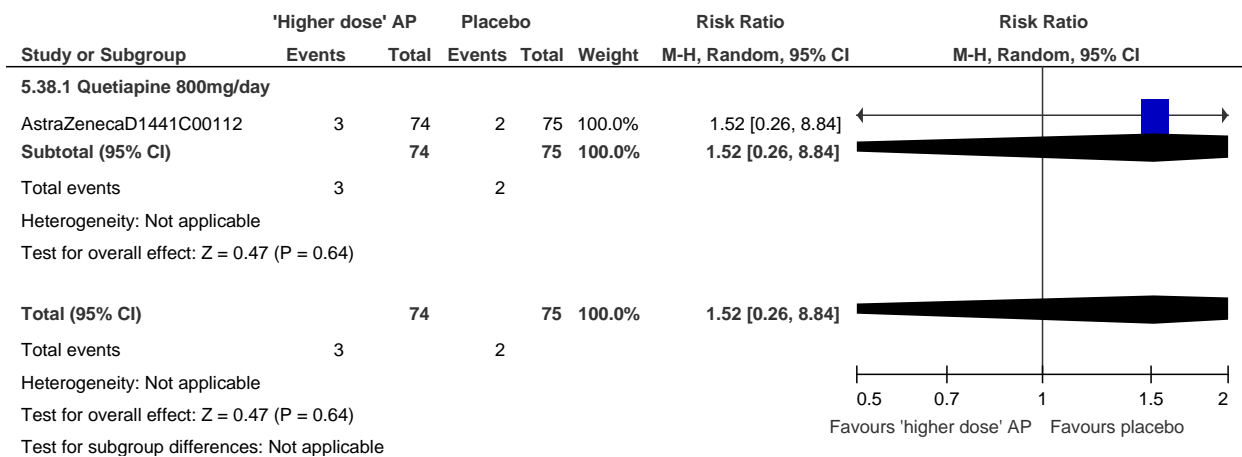
5.18 EPS (mean change in SAS scores)



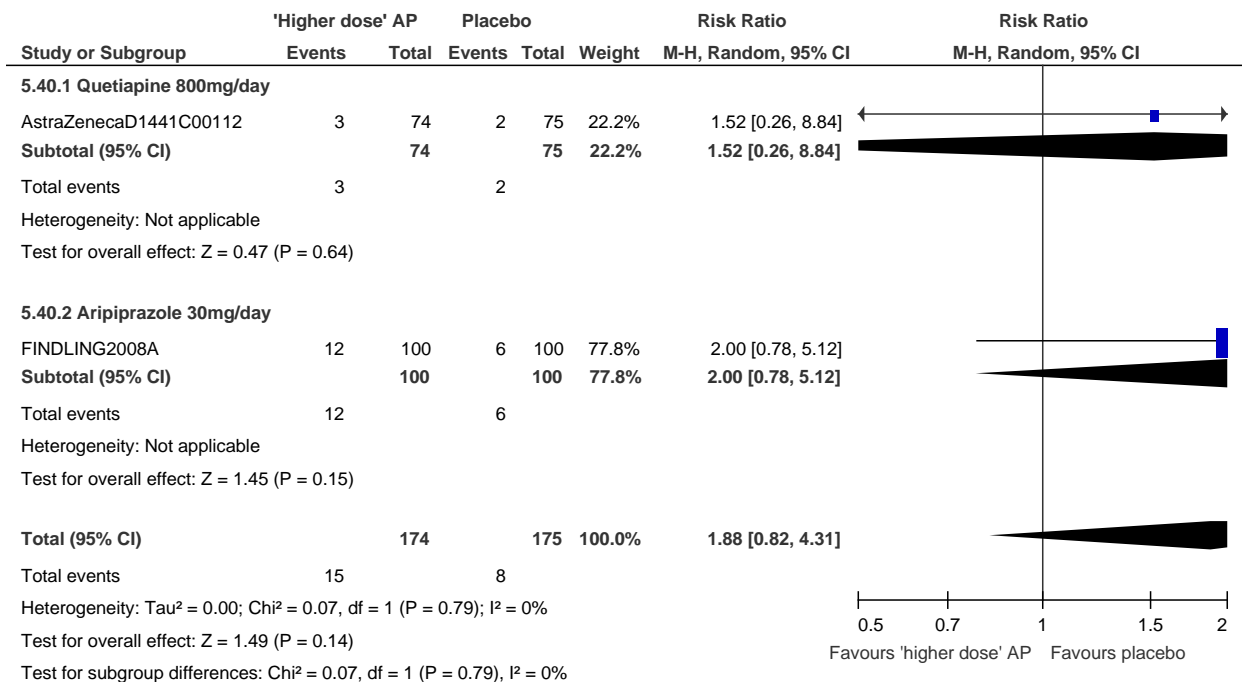
5.19 Parkinsonism



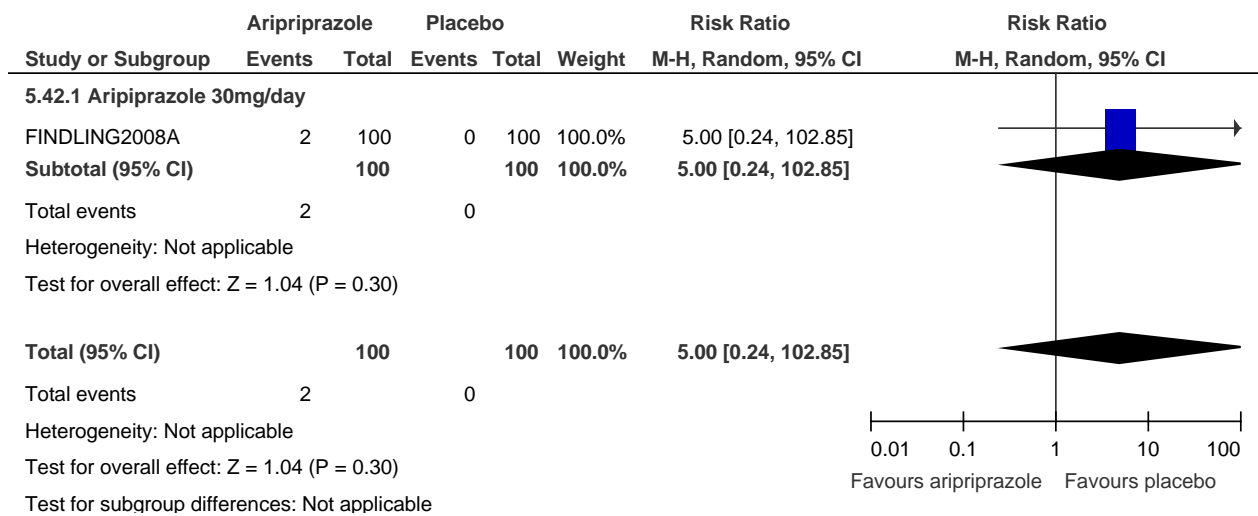
5.20 Tremor



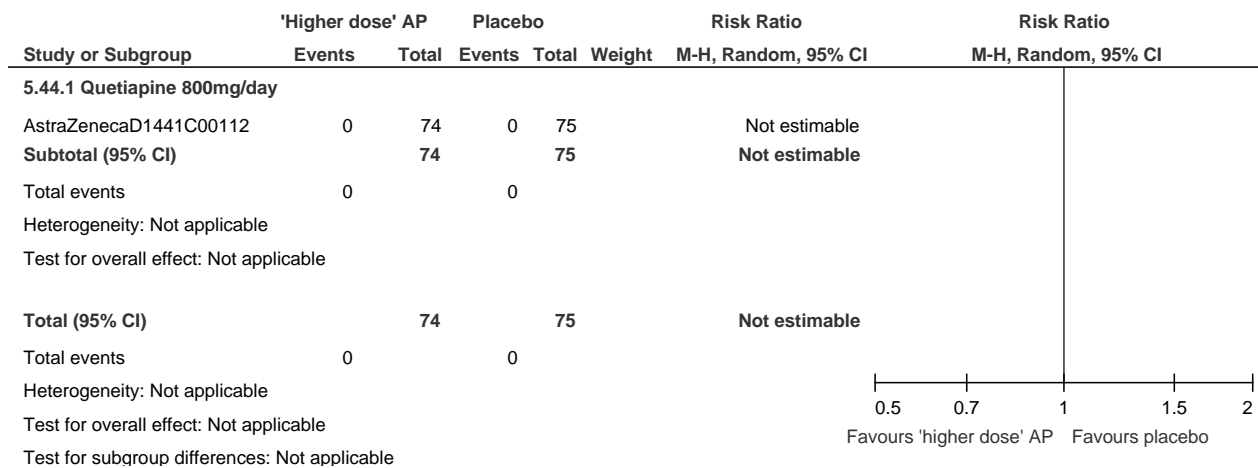
5.21 Akathisia



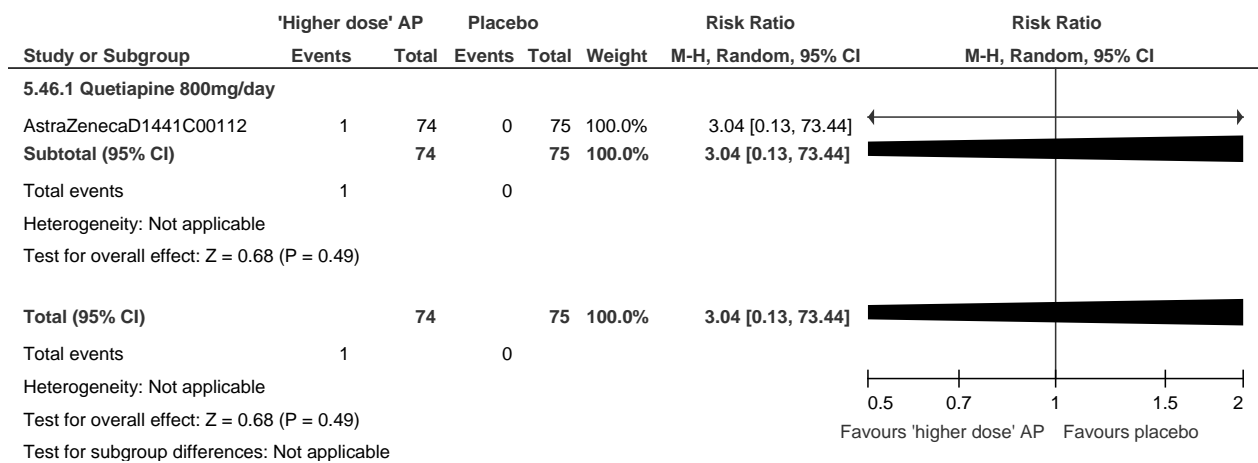
5.22 Dystonia



5.23 Dyskinesia



5.24 Extrapyramidal disorder

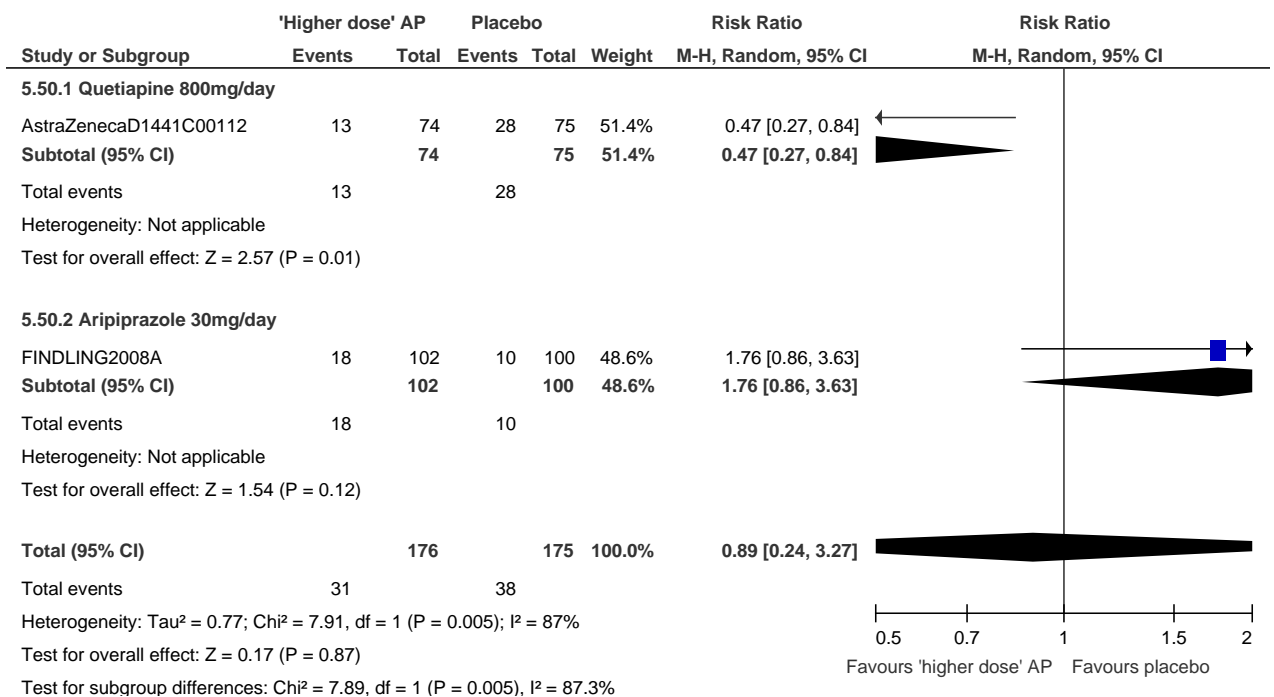


5.25 Mortality (including suicide)

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
5.48.1 Aripiprazole 30mg/day							
FINDLING2008A	0	100	0	100		Not estimable	
Subtotal (95% CI)		100		100		Not estimable	
Total events	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
5.48.2 Risperidone 4-6mg/day							
HAAS2009B	0	51	0	54		Not estimable	
Subtotal (95% CI)		51		54		Not estimable	
Total events	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Total (95% CI)		151		154		Not estimable	
Total events	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							

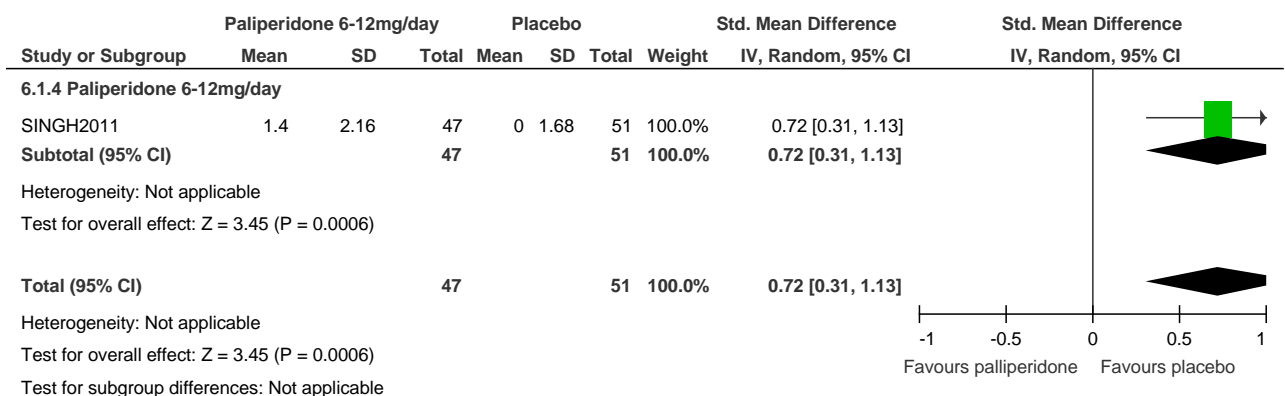
0.5 0.7 1 1.5 2
 Favours 'higher dose' AP Favours placebo

5.26 Leaving the study early for any reason

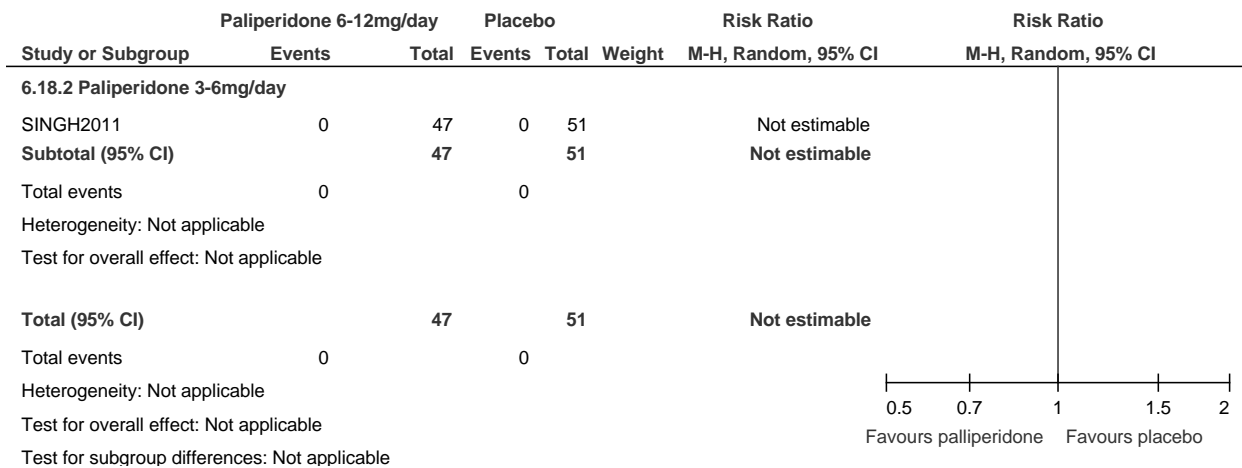


6. Additional (high) dose paliperidone versus placebo: post-treatment side effect outcomes

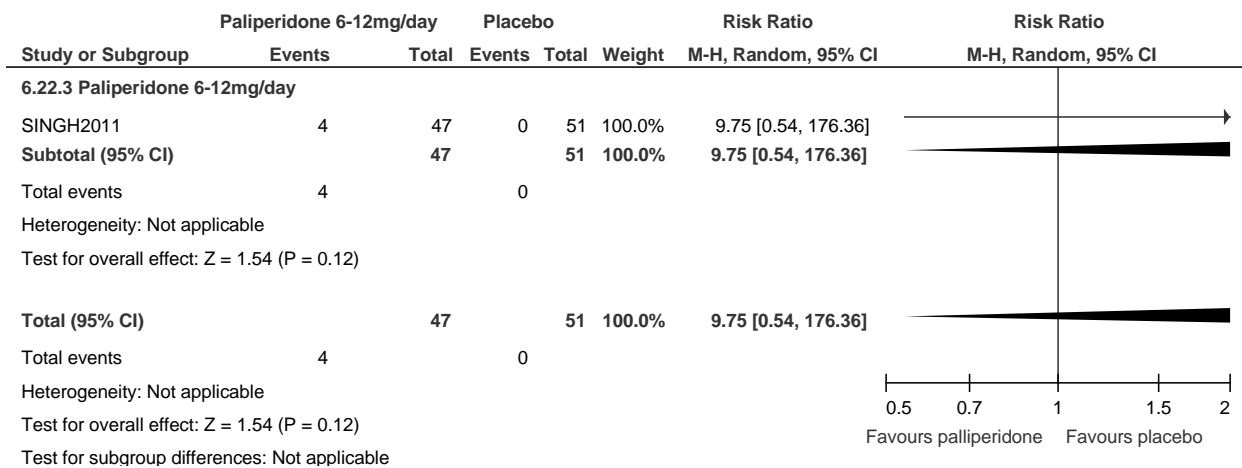
6.1 Mean change in weight (kg)



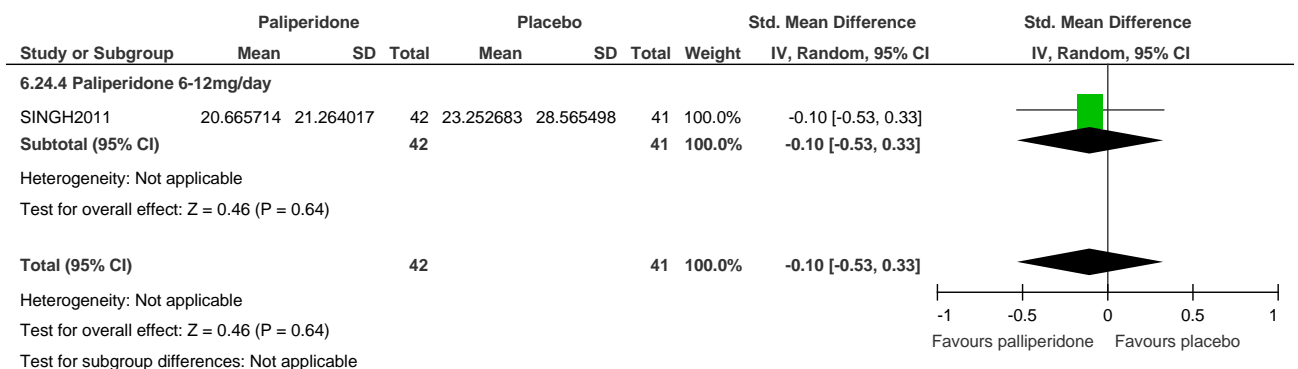
6.2 Prolonged QT interval



6.3 Tachycardia

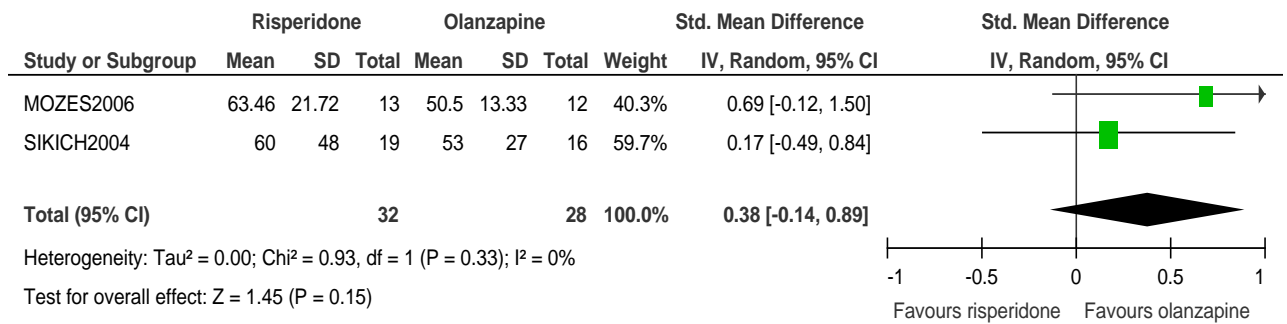


6.4 Prolactin (mg/dl)

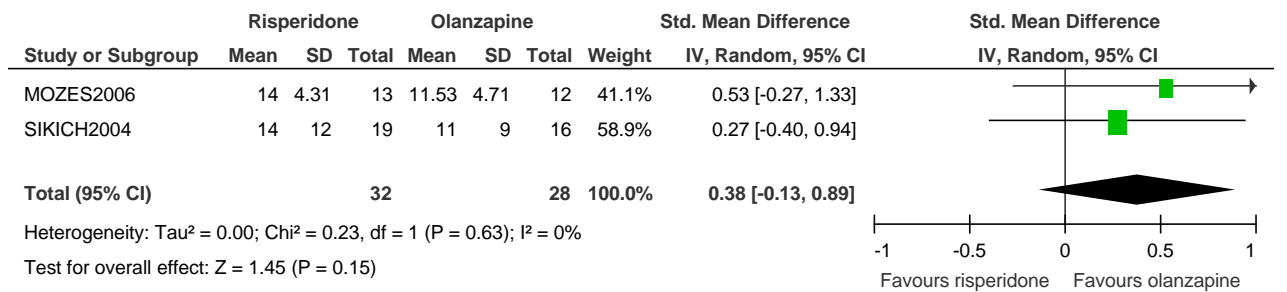


7. Risperidone versus olanzapine: post-treatment efficacy outcomes

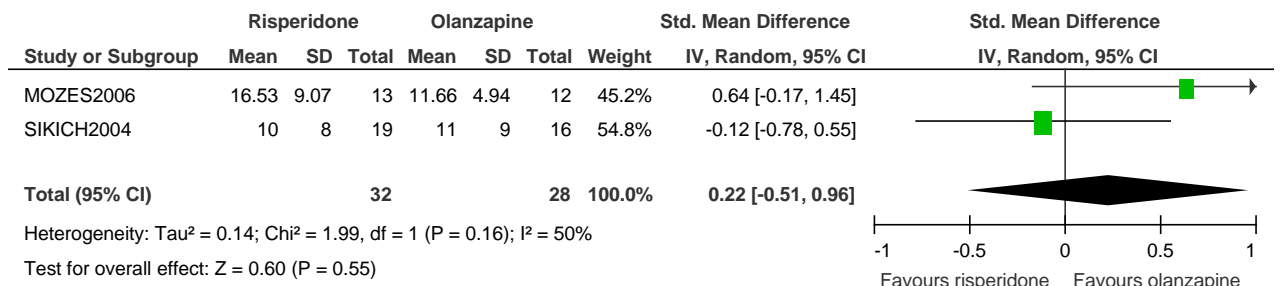
7.1 Mental state: mean endpoint total symptoms (PANSS, BPRS-C)



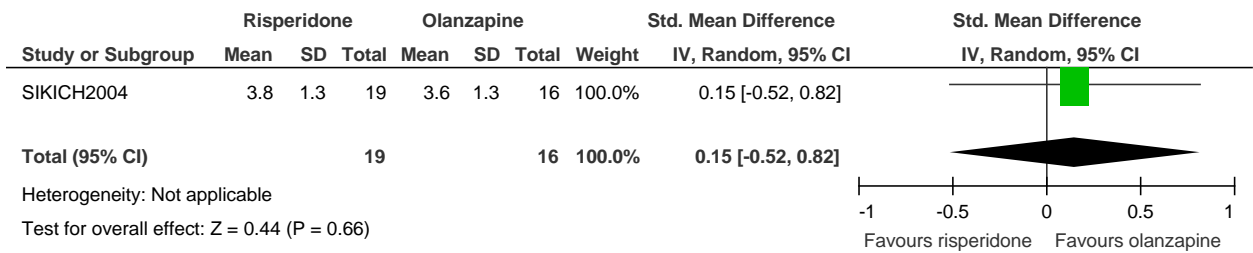
7.2 Mental state: mean endpoint positive symptoms (PANSS Positive, CPRS Positive)



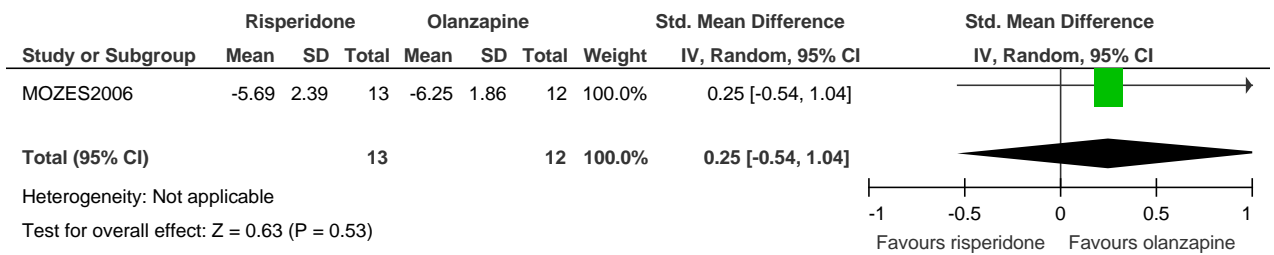
7.3 Mental state: mean endpoint negative symptoms (PANSS Negative, CPRS Negative)



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

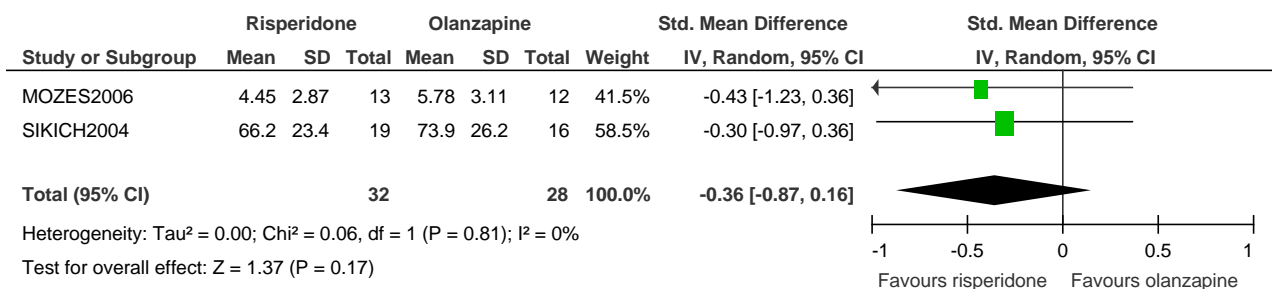


7.5 Mean endpoint psychosocial functioning (CGAS)

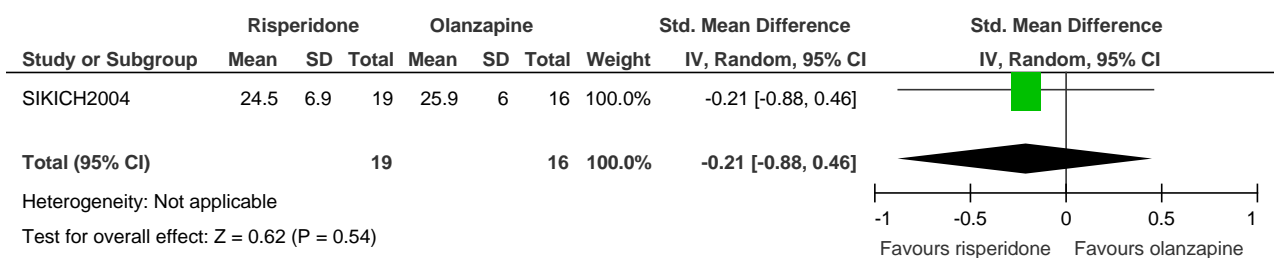


8. Risperidone versus olanzapine: post-treatment side effect outcomes

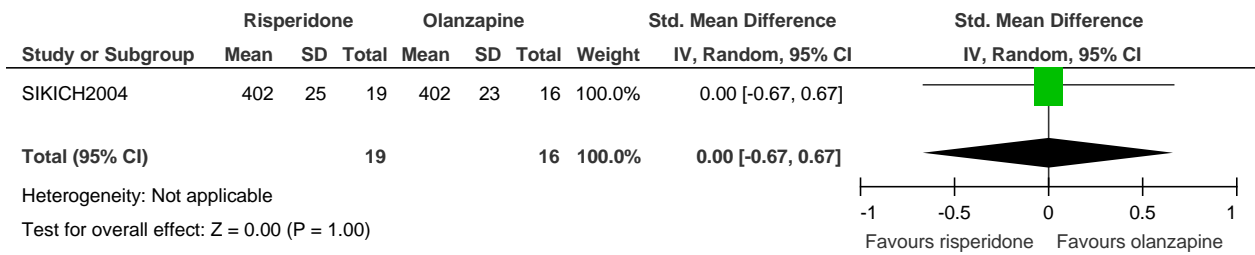
8.1 Weight (kg)



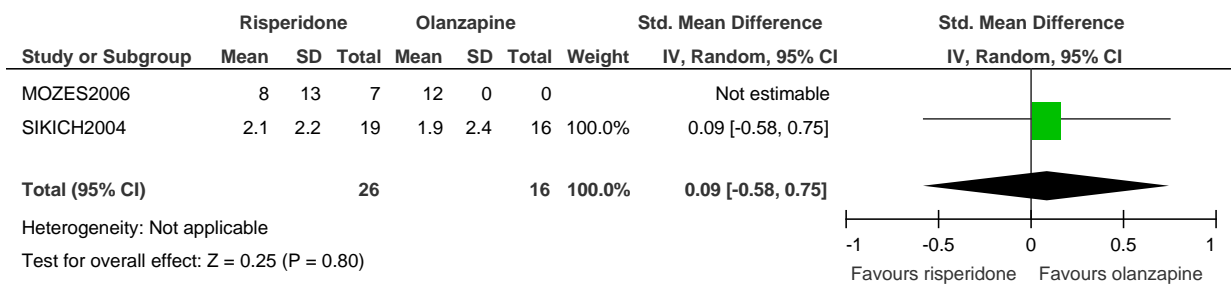
8.2 Mean endpoint BMI (kg/m²)



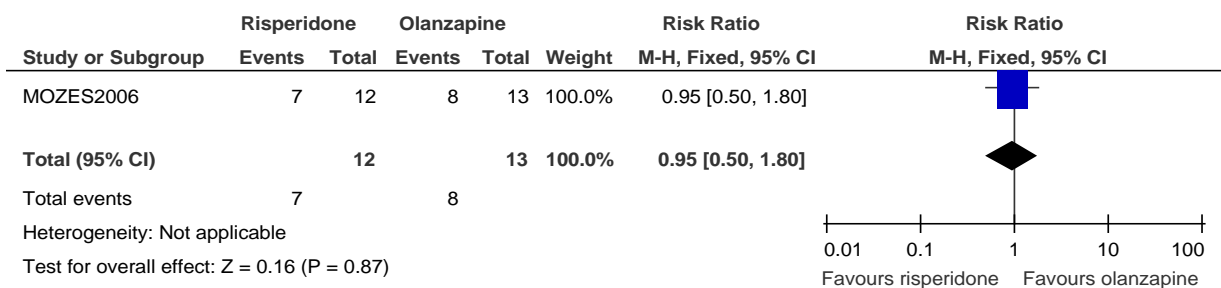
8.3 Mean endpoint QT interval (msec)



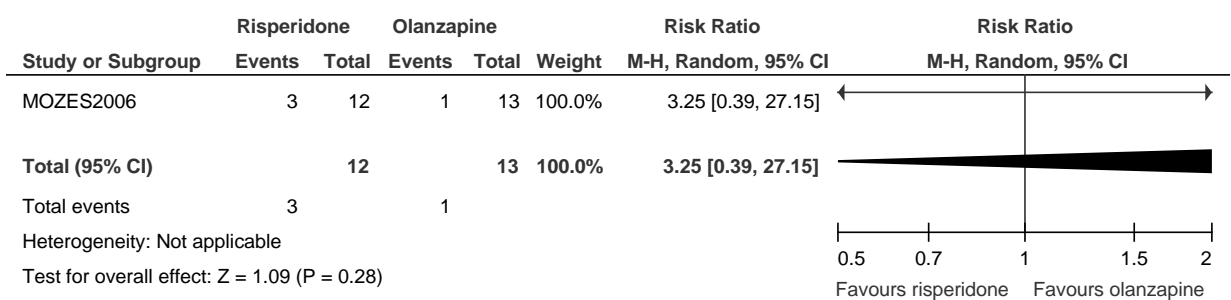
8.4 Mean endpoint EPS (SAS scores)



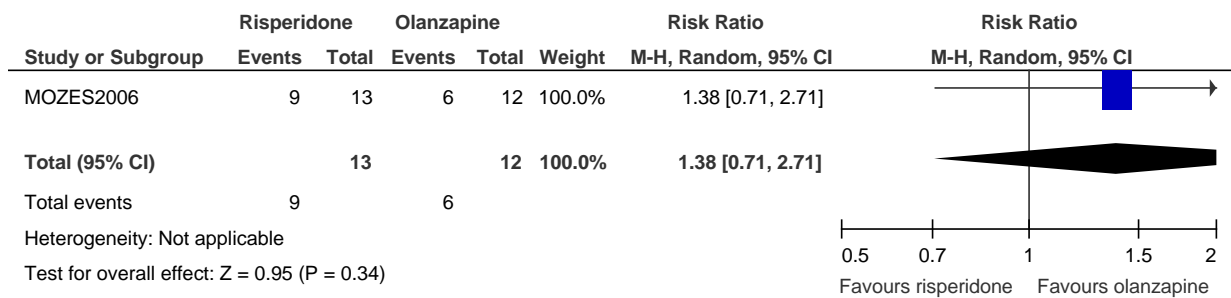
8.5 EPS (number of participants who developed EPS measured using SAS)



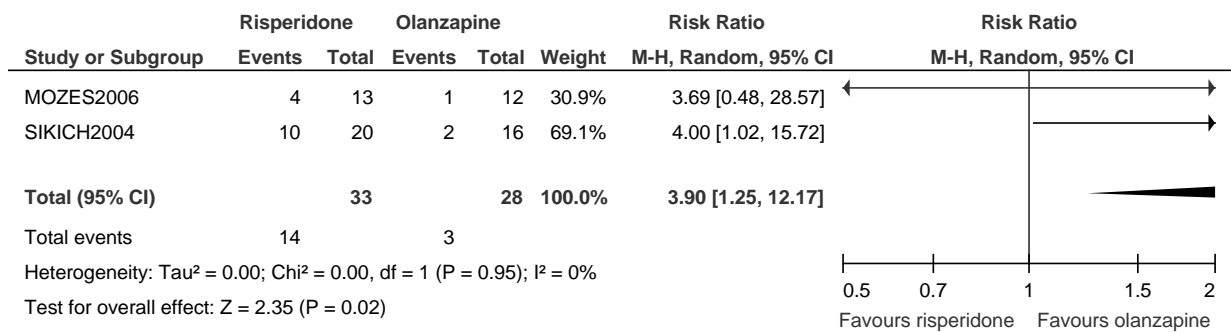
8.6 Mean endpoint EPS (BARS scores)



8.7 Tremor

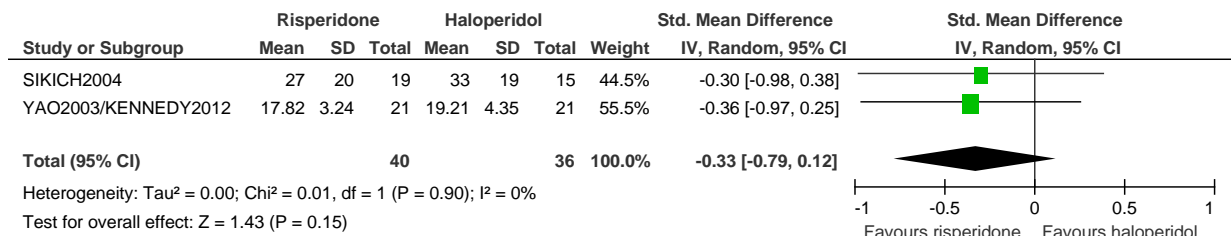


8.8 Leaving the study early for any reason

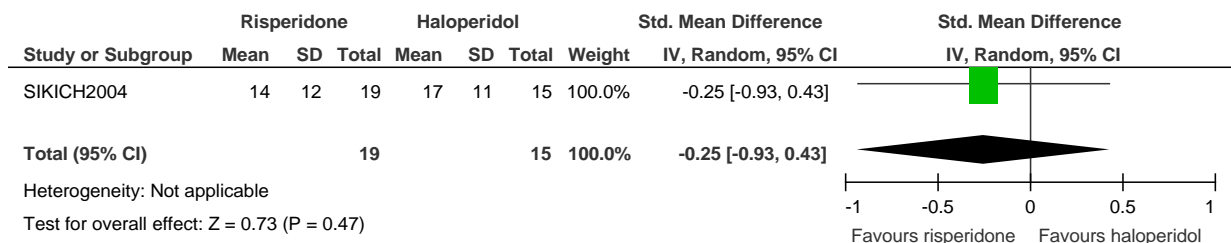


9. Risperidone versus haloperidol: post-treatment efficacy outcomes

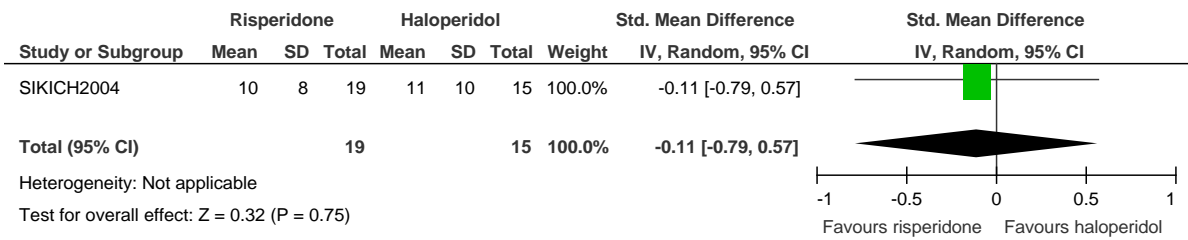
9.1 Mental state: mean endpoint total symptoms (BPRS)



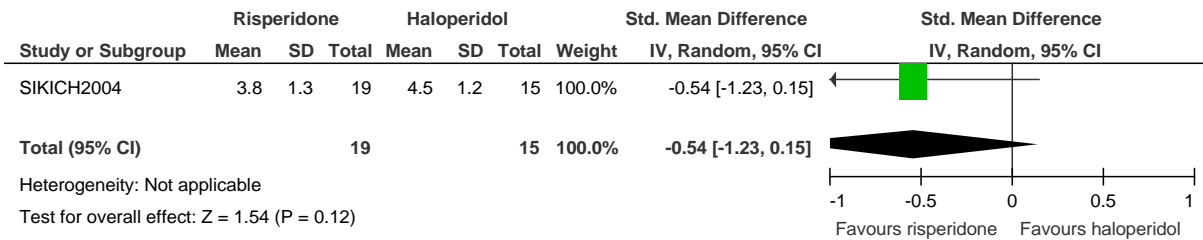
9.2 Mental state: mean endpoint positive symptoms (CPRS-Positive)



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

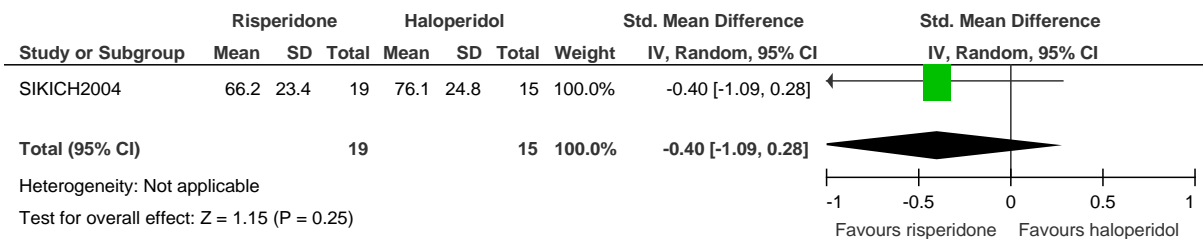


9.4 Mean endpoint global state: severity (CGI-S)

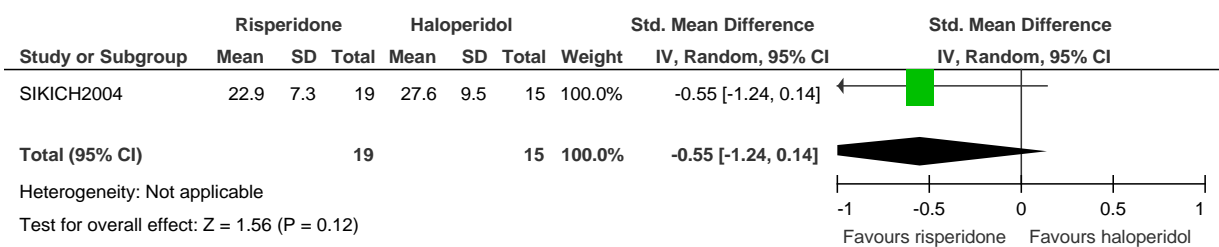


10. Risperidone versus haloperidol: post-treatment side effect outcomes

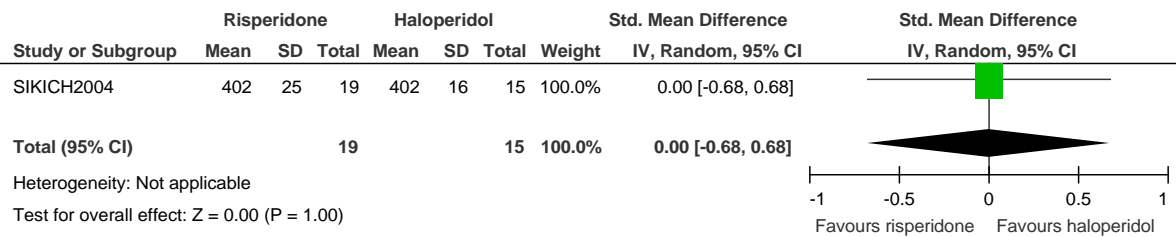
10.1 Mean endpoint weight (kg)



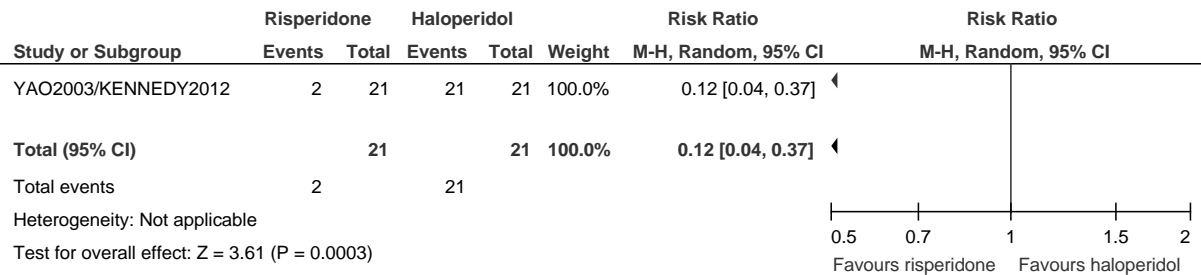
10.2 Mean endpoint BMI (kg/m²)



10.3 Mean endpoint QT interval (msec)



10.4 EPS

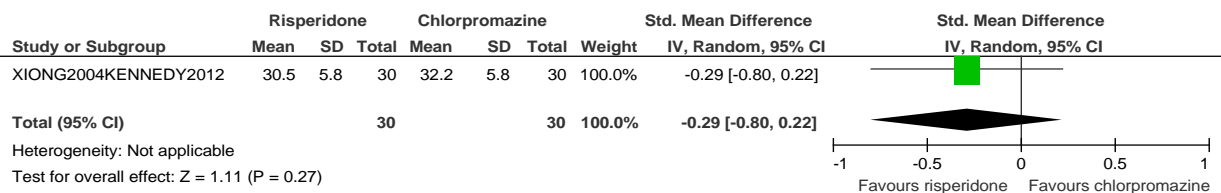


10.5 Leaving the study early for any reason



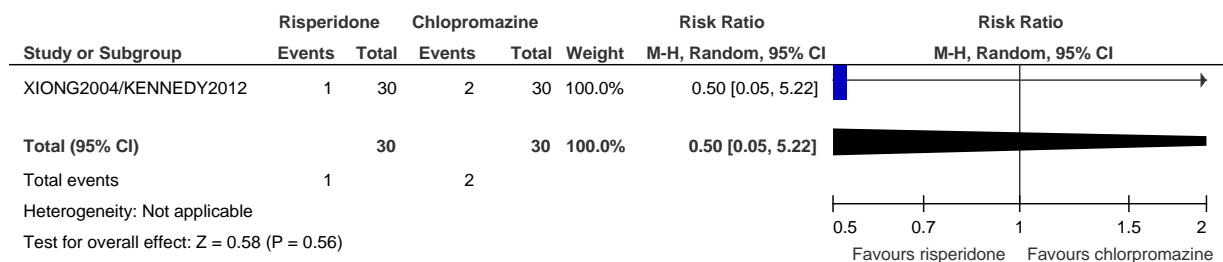
11. Chlorpromazine versus risperidone: post-treatment efficacy outcomes

11.1 Mental state: total symptoms (BPRS)



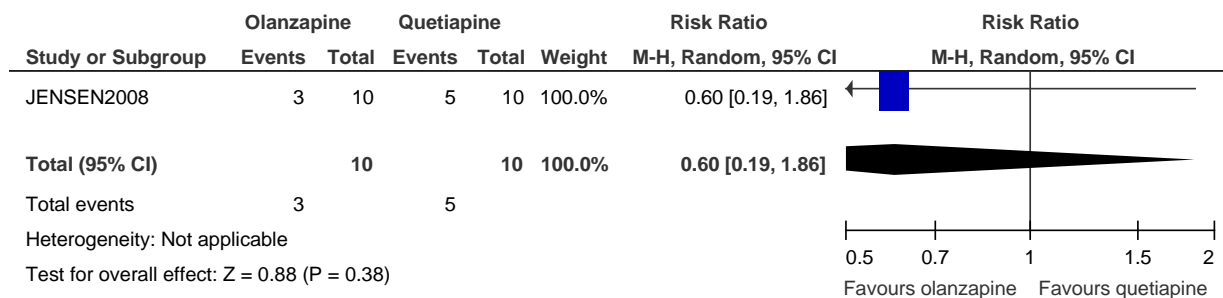
12. Chlorpromazine versus risperidone: post-treatment side effect outcomes

12.1 Tremor



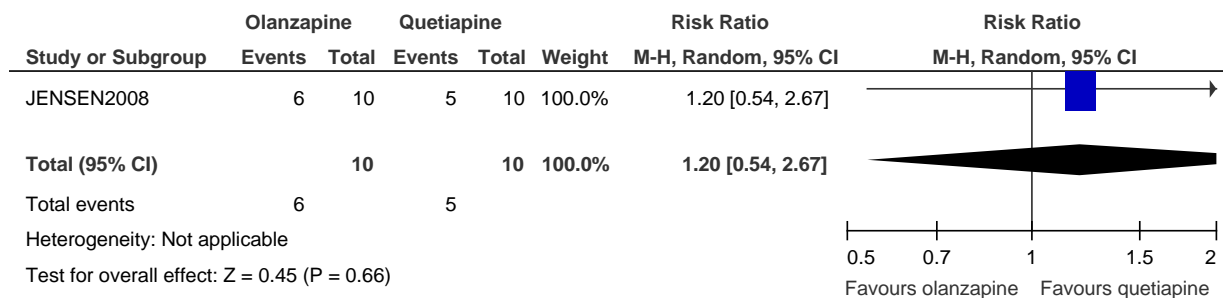
13. Olanzapine versus quetiapine: post-treatment efficacy outcomes

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

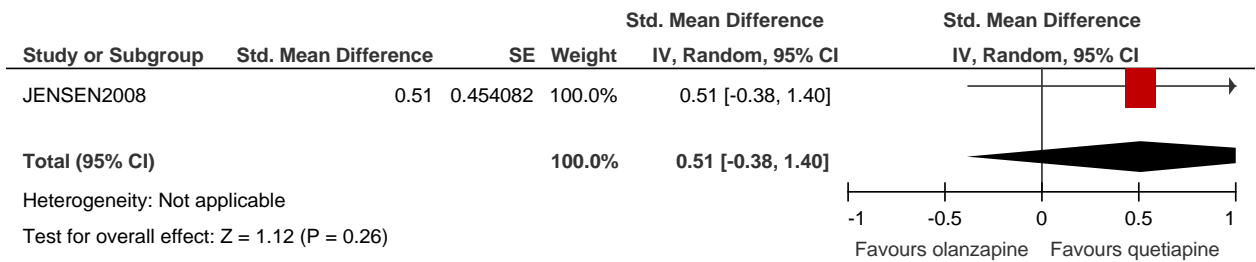


14. Olanzapine versus quetiapine: post-treatment side effect outcomes

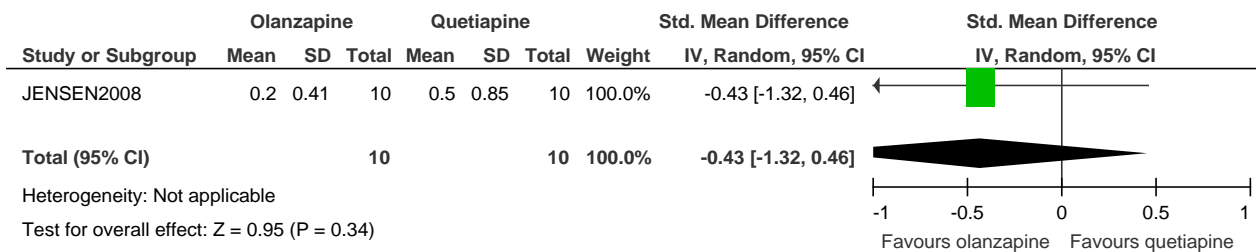
14.1 Weight gain (number of participants with kg gain of >7% from baseline)



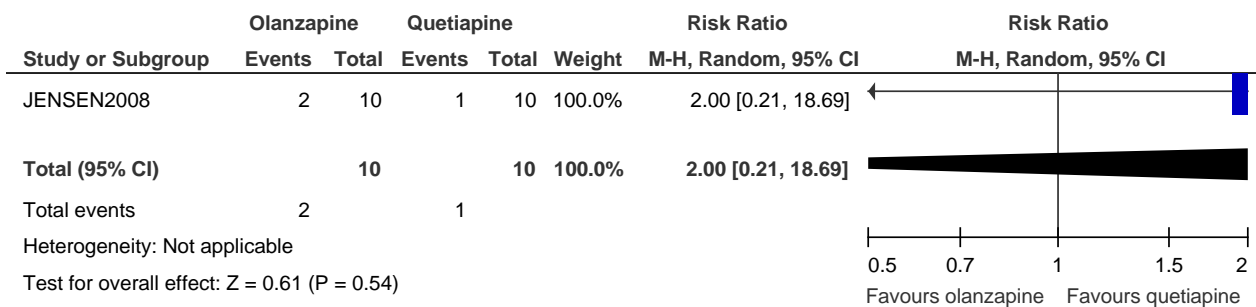
14.2 Mean endpoint BMI (kg/m²)



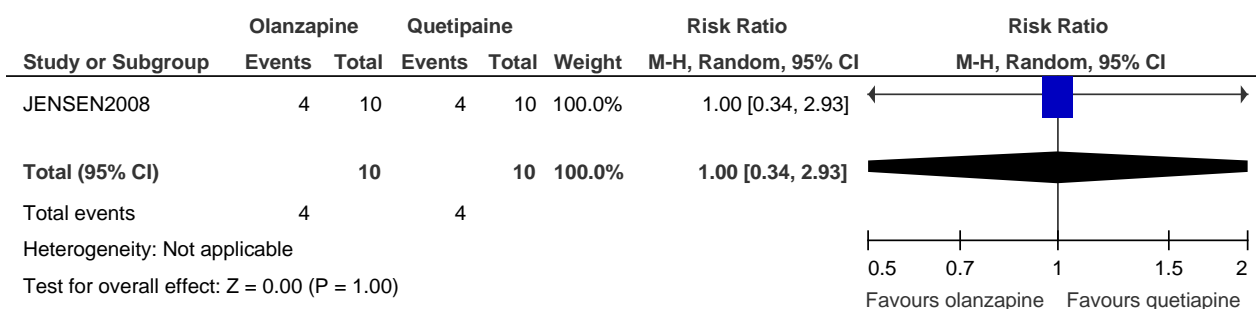
14.3 Mean endpoint EPS (SAS scores)



14.4 Akathisia

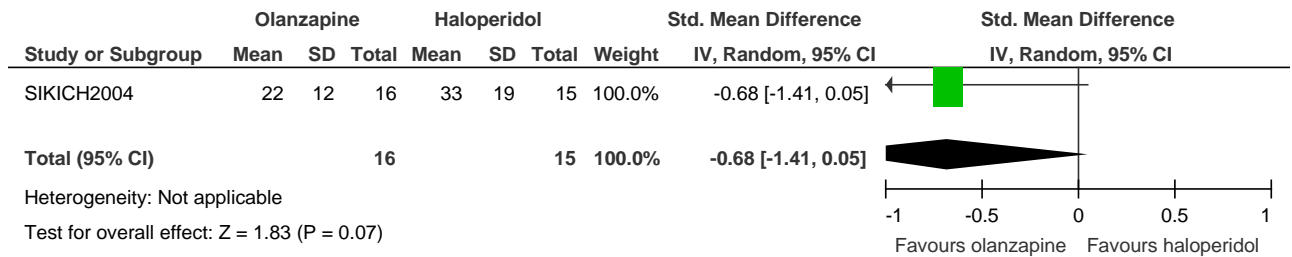


14.5 Leaving the study early for any reason

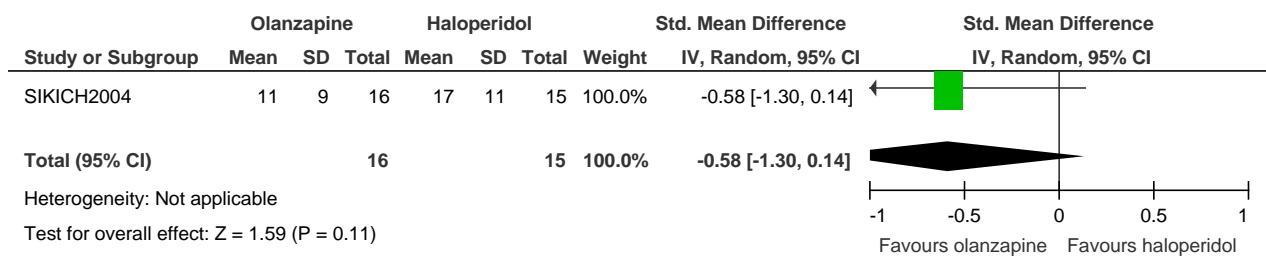


15. Olanzapine versus haloperidol: post-treatment efficacy outcomes

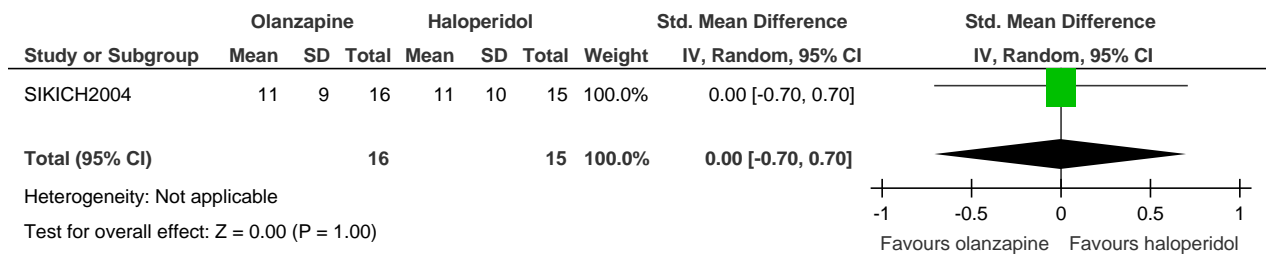
15.1 Mental state: mean endpoint total symptoms (BPRS-C)



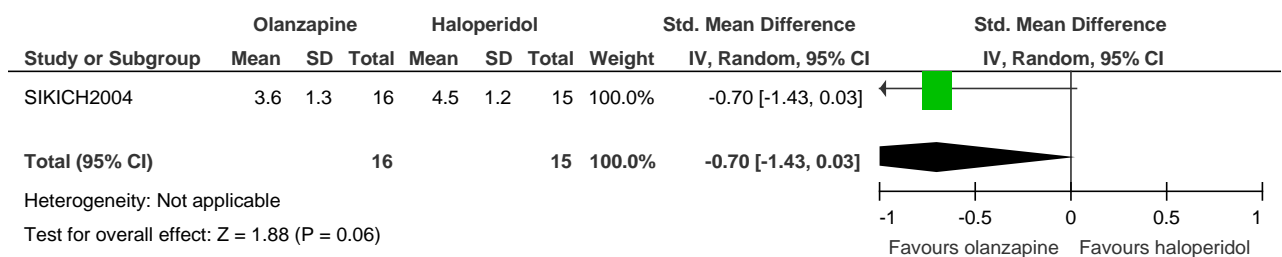
15.2 Mental state: mean endpoint in positive symptoms (CPRS Positive)



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

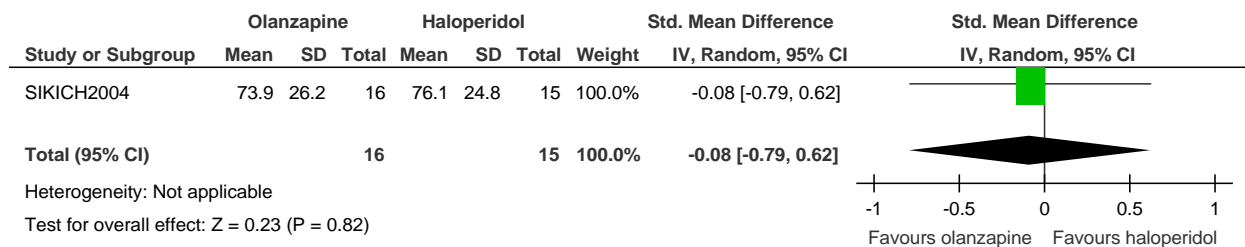


15.4 Mean endpoint in global state: severity (CGI-S)

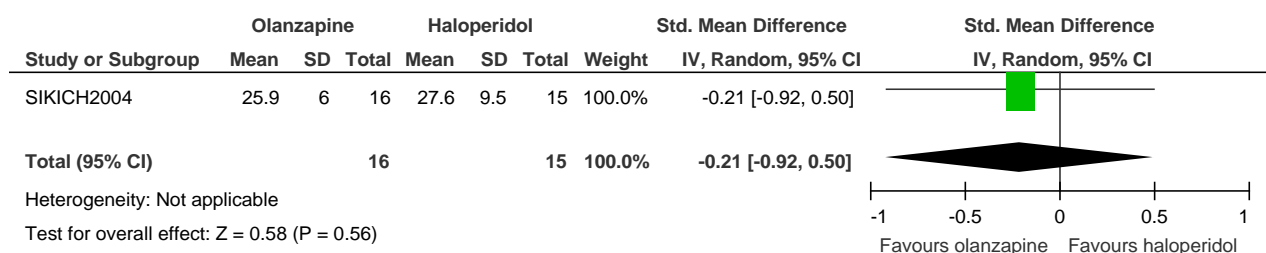


16. Olanzapine versus haloperidol: post-treatment side effect outcomes

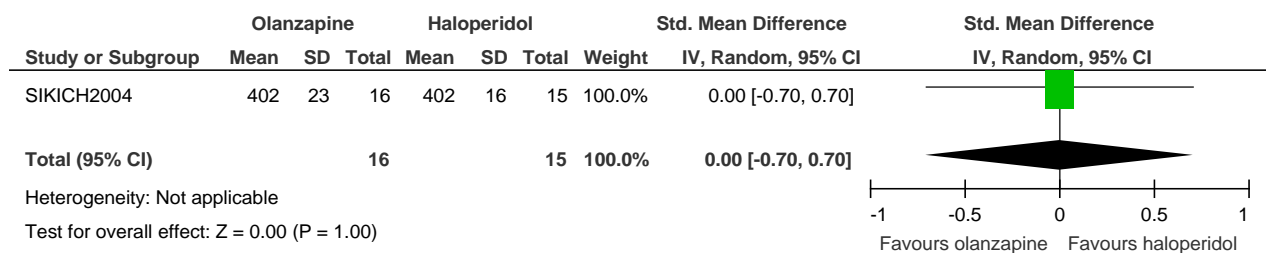
16.1 Mean endpoint in weight (kg)



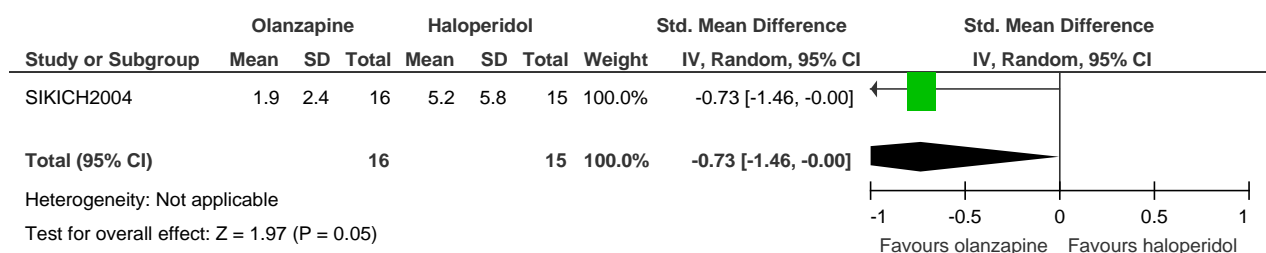
16.2 Mean endpoint BMI (kg/m²)



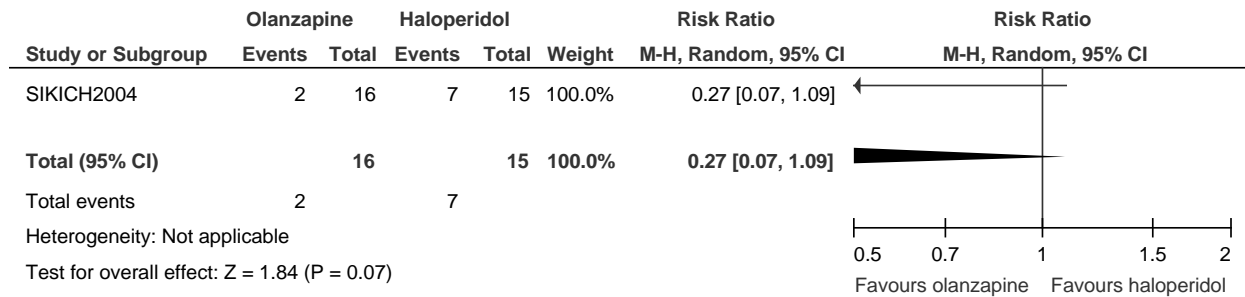
16.3 Mean endpoint QT interval (msec)



16.4 Mean endpoint EPS (SAS scores)

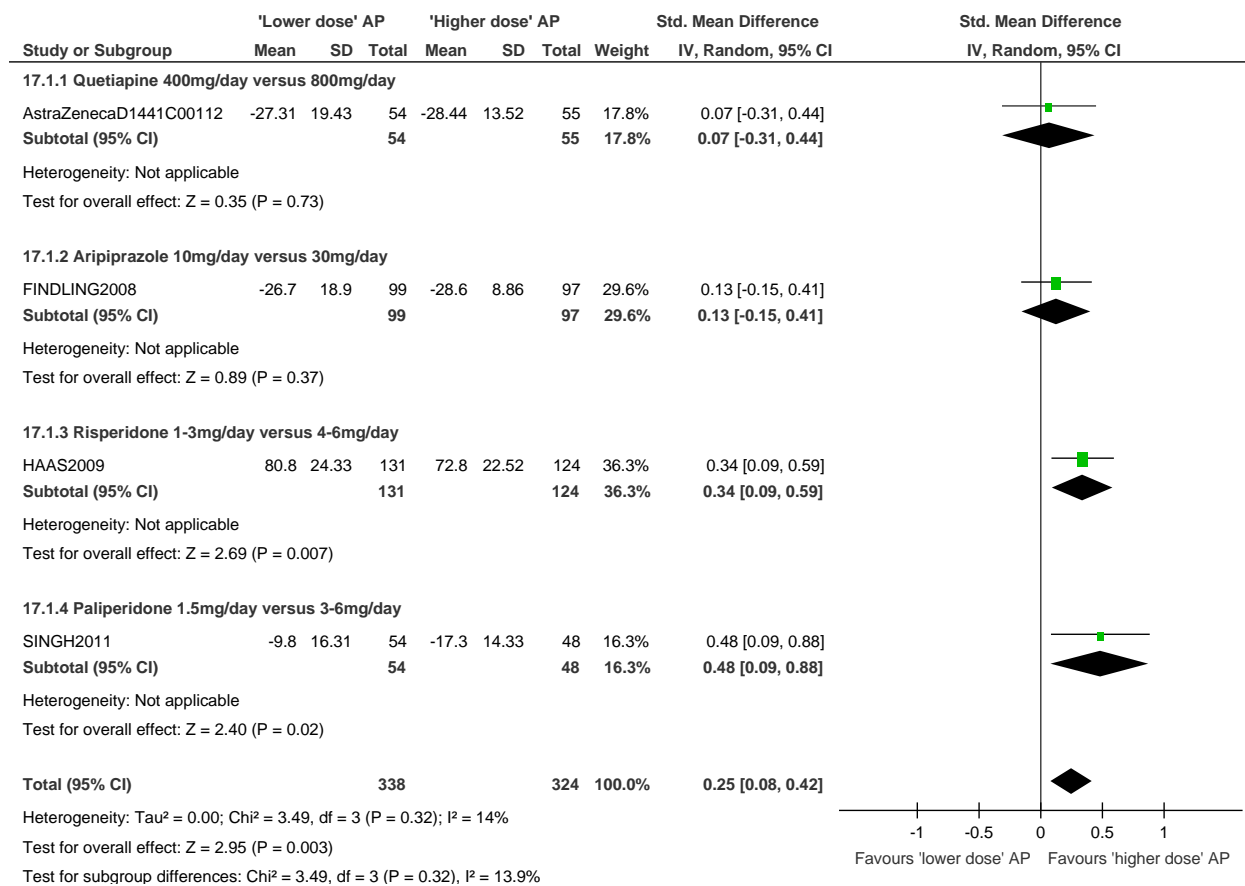


16.5 Leaving the study early for any reason

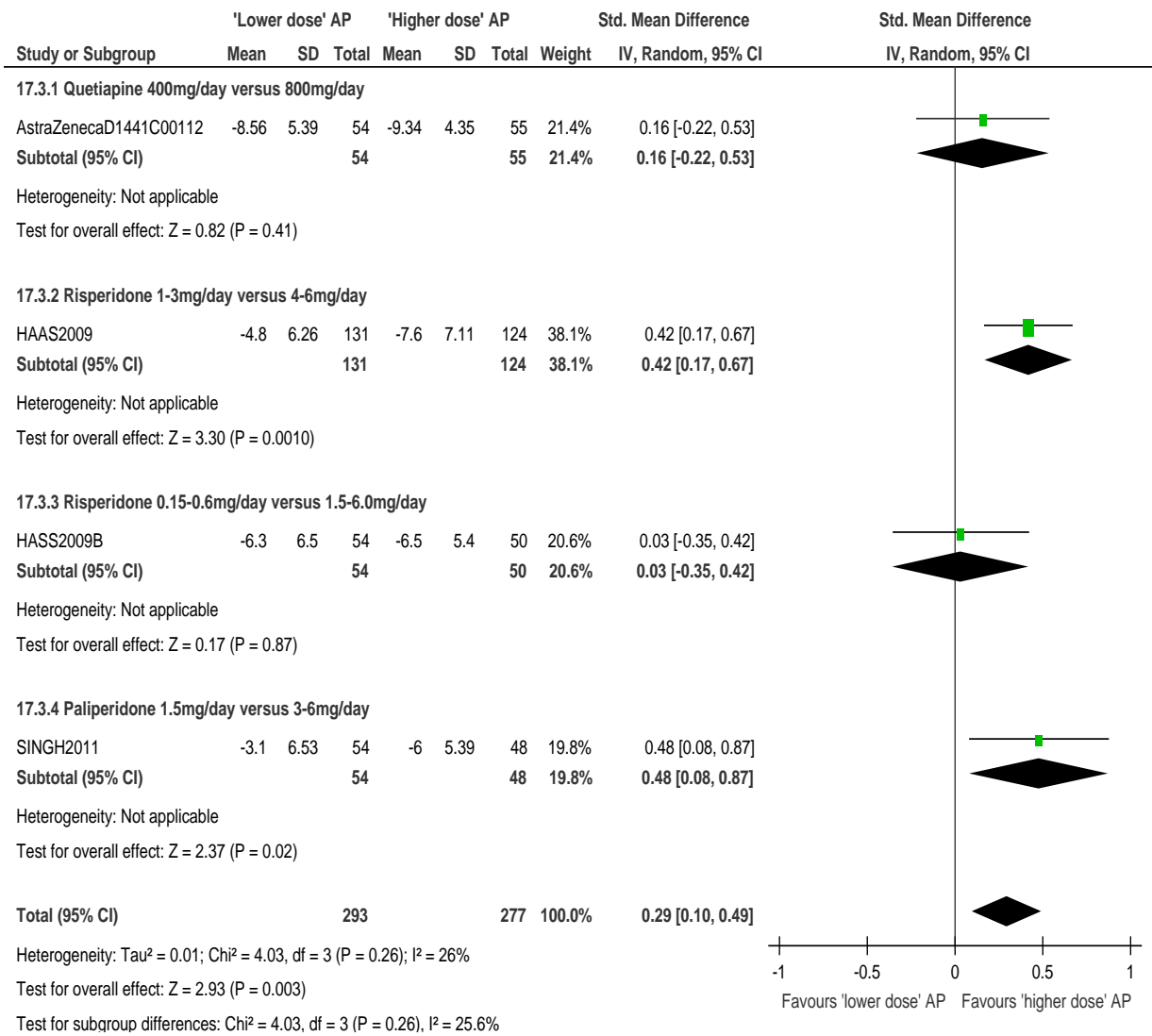


17. 'Lower dose' antipsychotic medication versus 'higher dose' antipsychotic medication: post-treatment efficacy outcomes

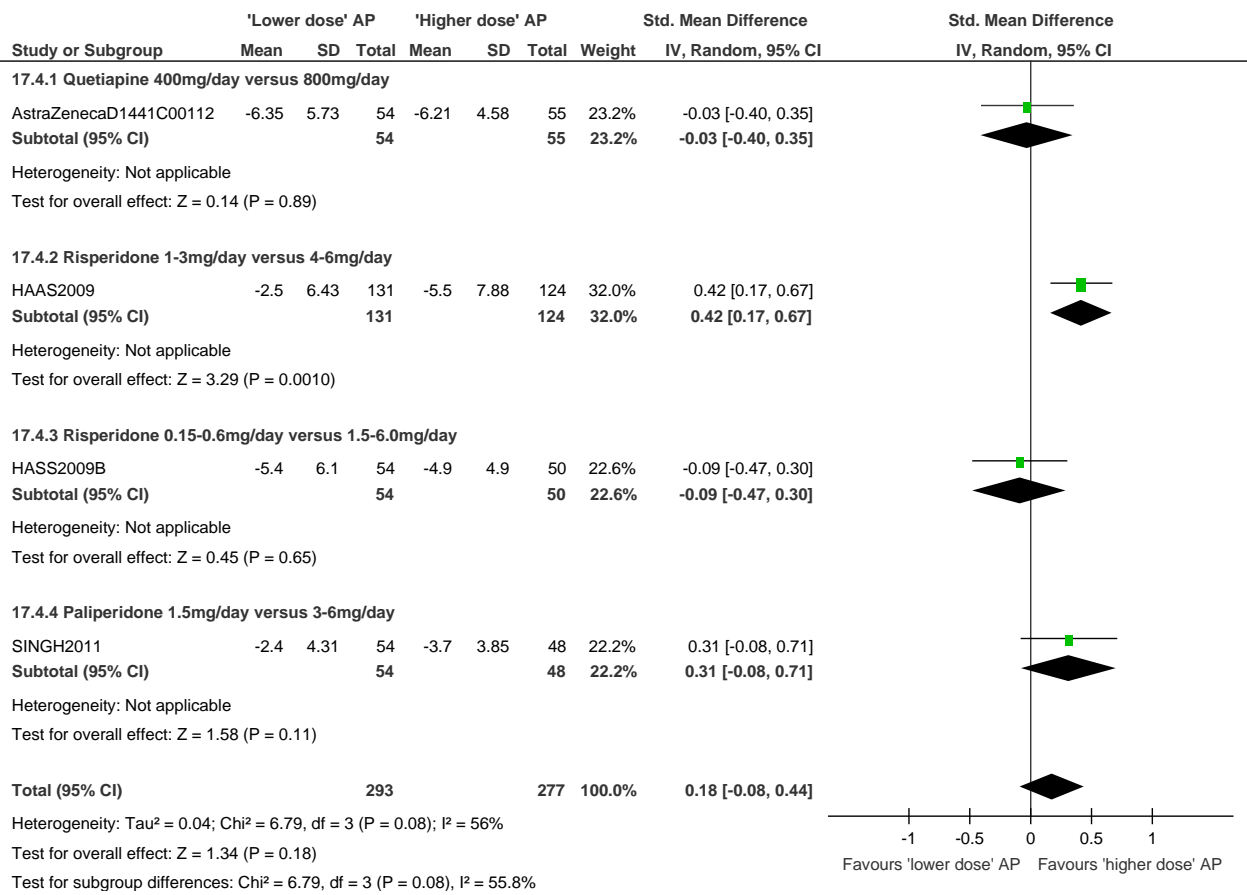
17.1 Mental state: mean change in total symptoms (PANSS)



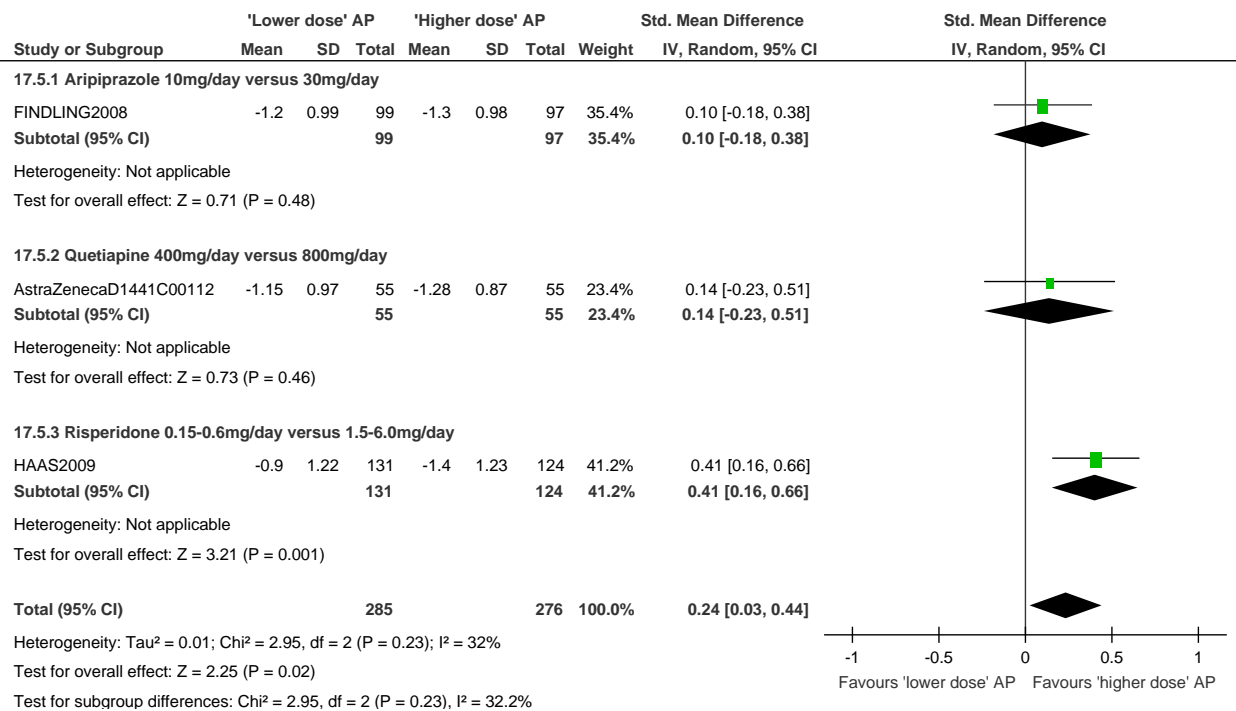
17.2 Mental state: mean change in positive symptoms (PANSS positive)



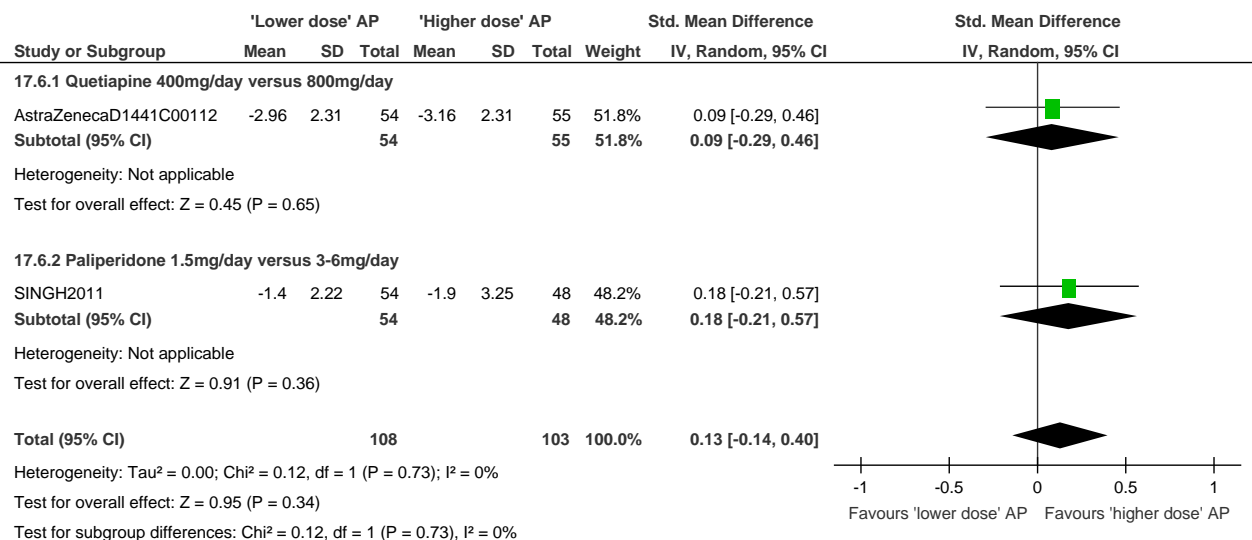
17.3 Mental state: mean change in negative symptoms (PANSS Negative)



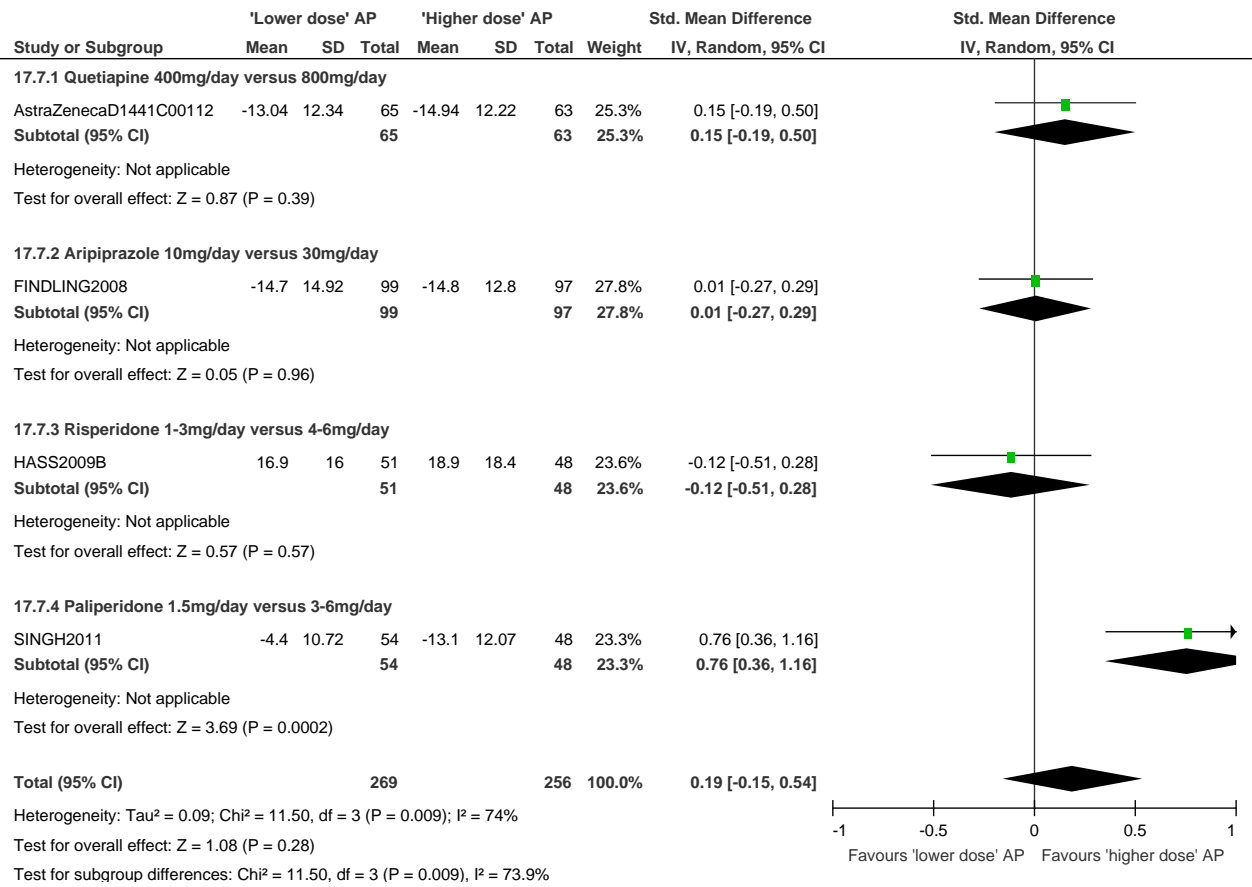
17.4 Global state (CGI-S)



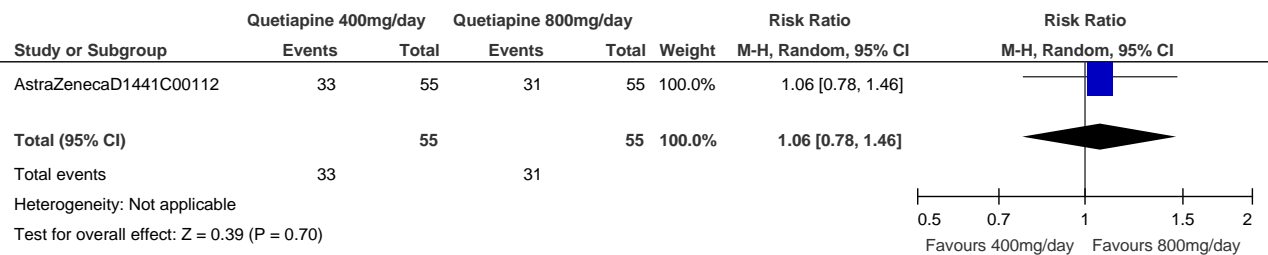
17.5 Depression (PANSS Depression; Anxiety and Depression)



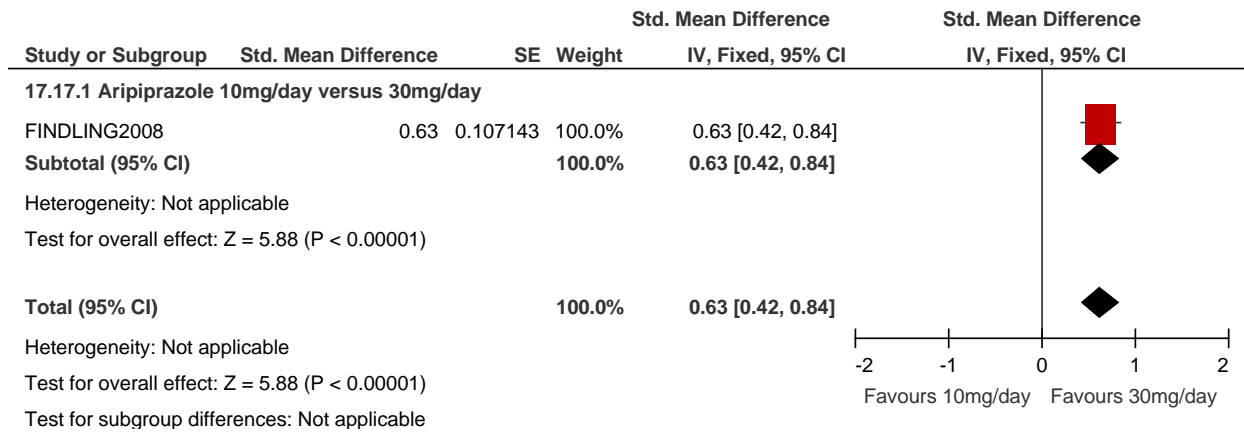
17.6 Psychosocial functioning (CGAS)



17.7 Response (CGI-I)

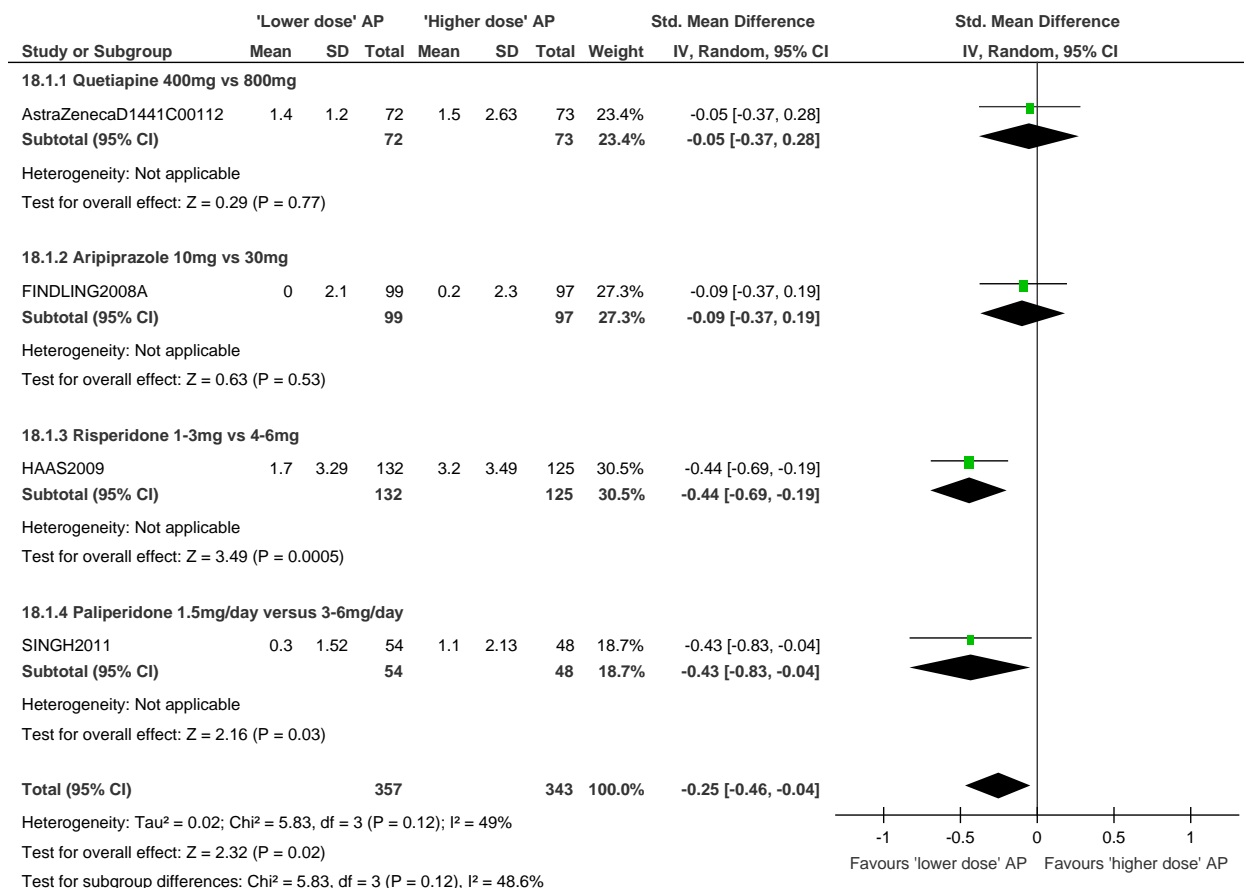


17.8 Quality of life (calculated using total and overall scores from the Paediatric Quality of Life Enjoyment and Satisfaction Questionnaire)

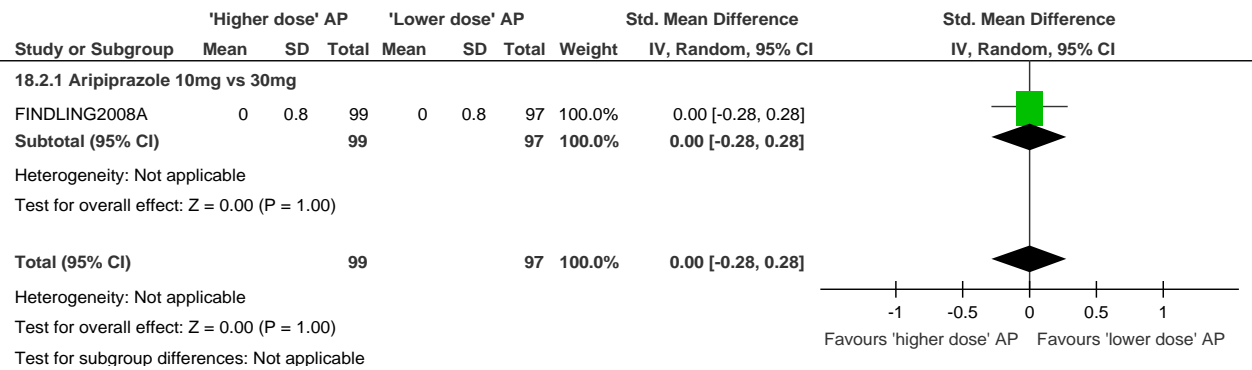


18. 'Lower dose' antipsychotic medication versus 'higher dose' antipsychotic medication: post-treatment side effect outcomes

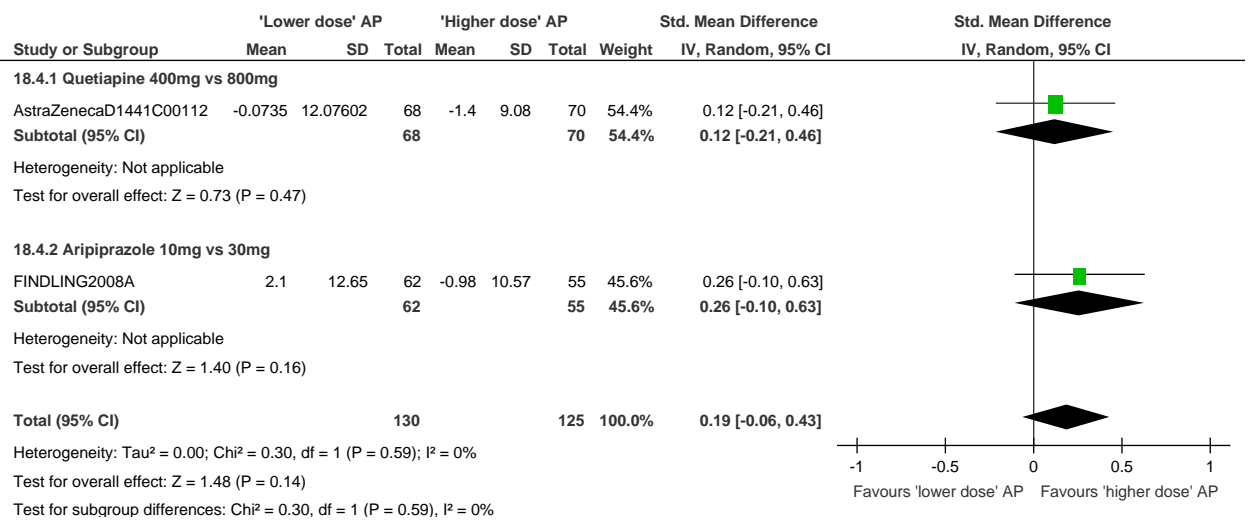
18.1 Mean change in weight (kg)



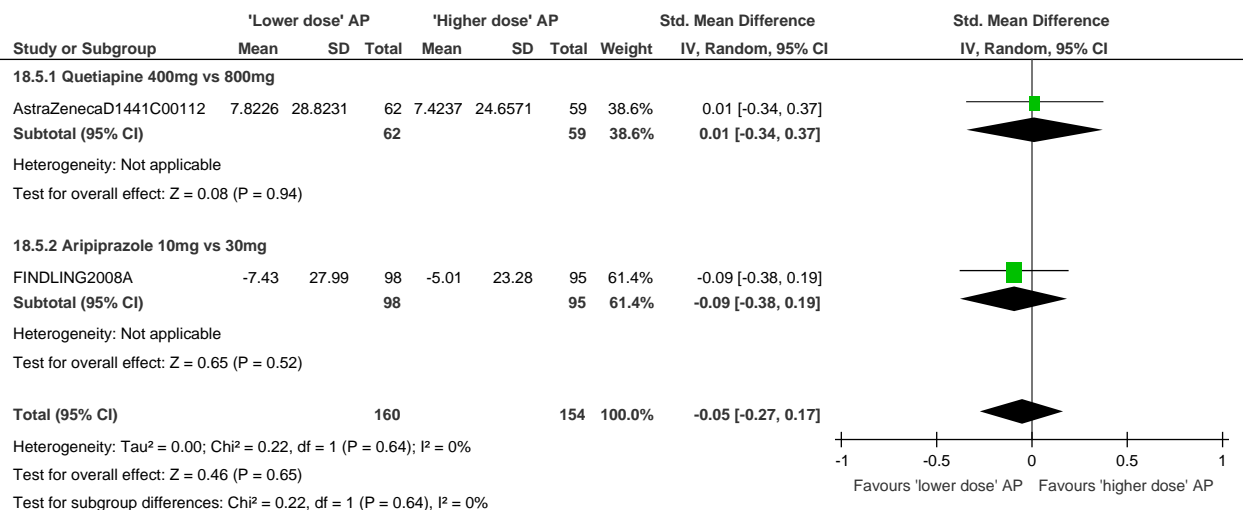
18.2 Mean change in BMI (kg/m²)



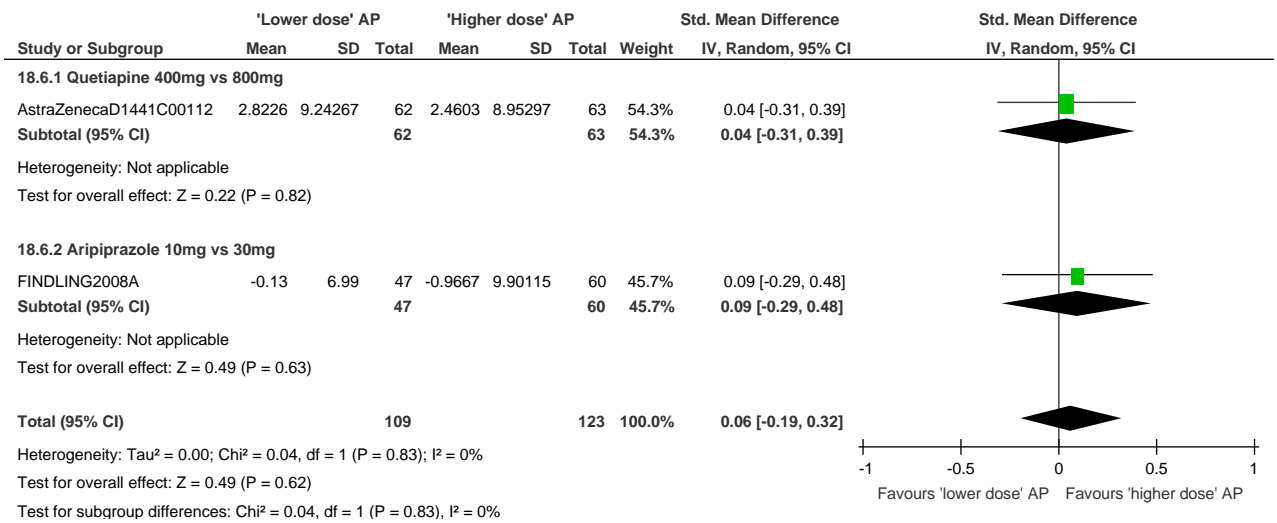
18.3 Mean change in fasting serum glucose level (mg/dl)



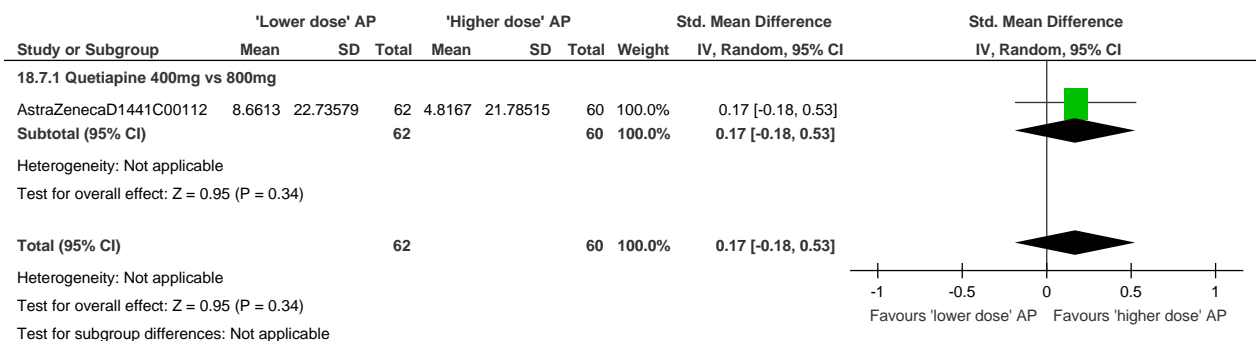
18.4 Mean change in fasting total cholesterol (mg/dl)



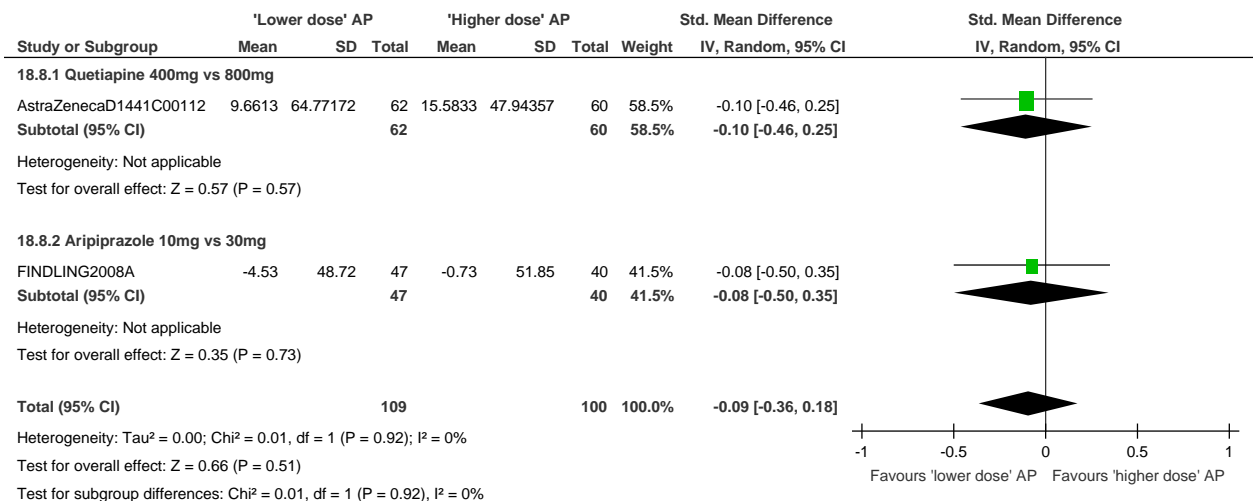
18.5 Mean change in fasting high-density lipoprotein cholesterol level (mg/dl)



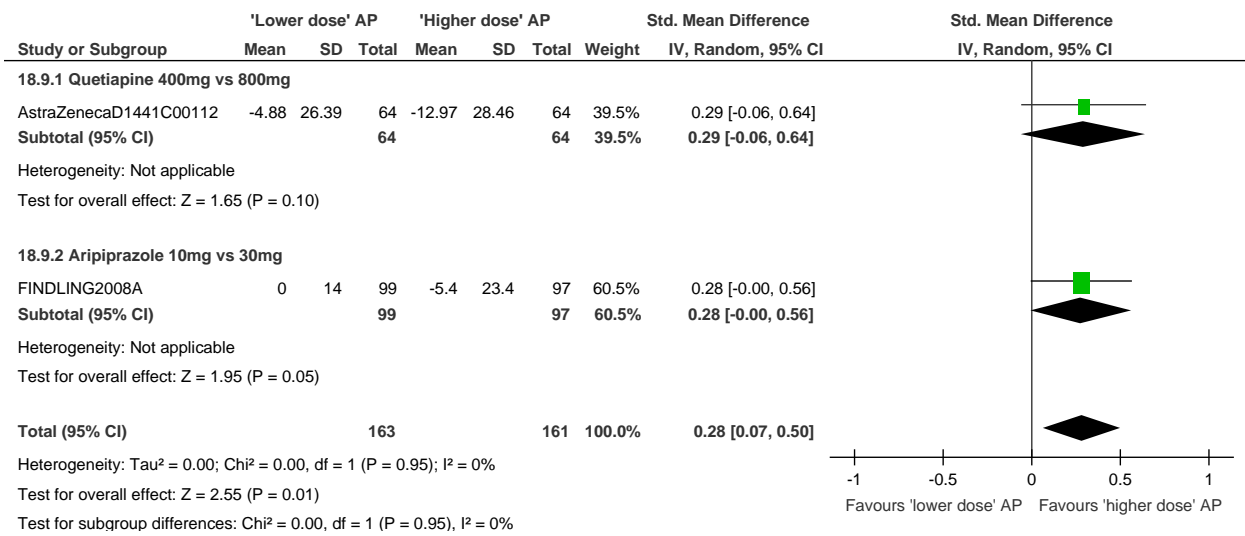
18.6 Mean change in low-density lipoprotein cholesterol level (mg/dl)



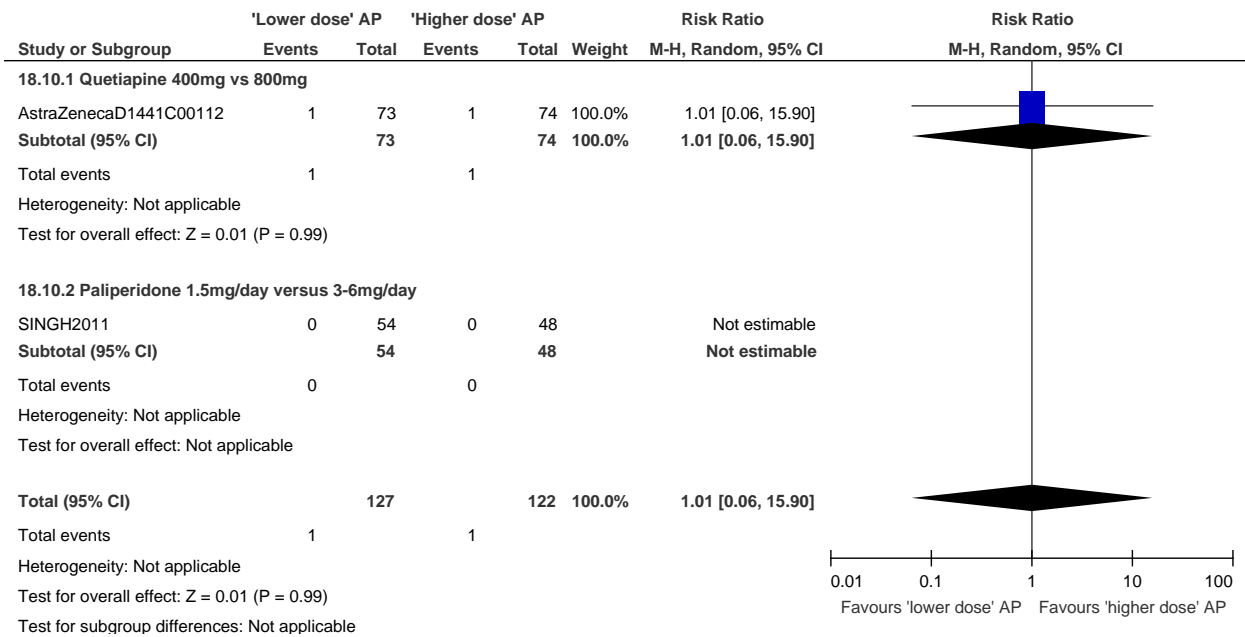
18.7 Mean change in fasting triglycerides (mg/dl)



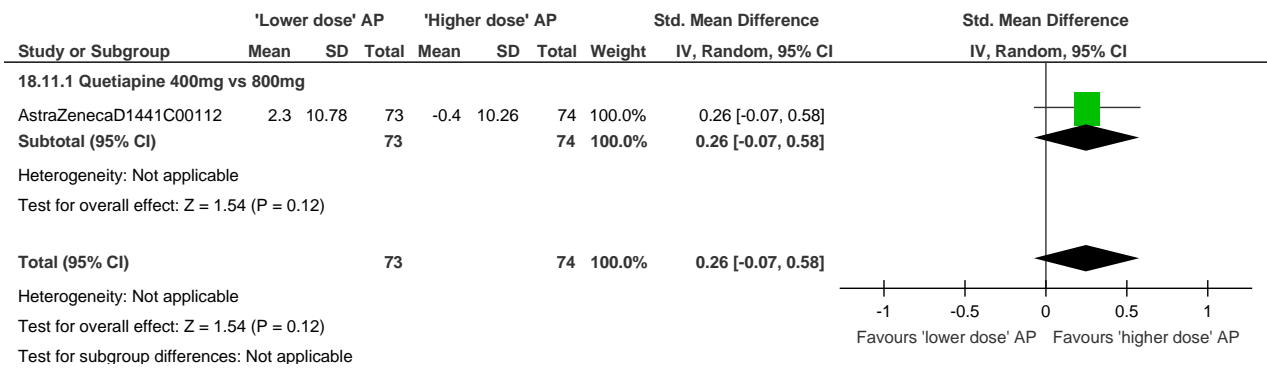
18.8 Mean change in QT interval (msec)



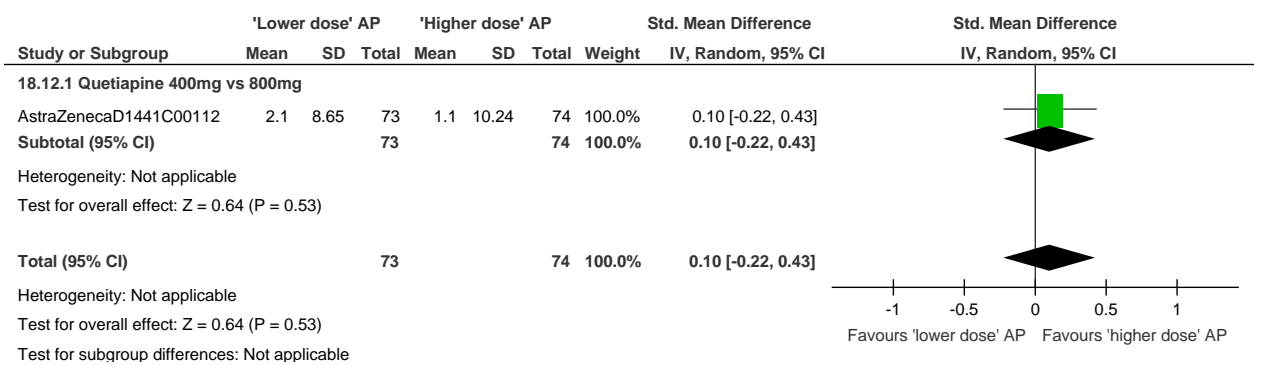
18.9 Mean change in prolonged QT interval (msec)



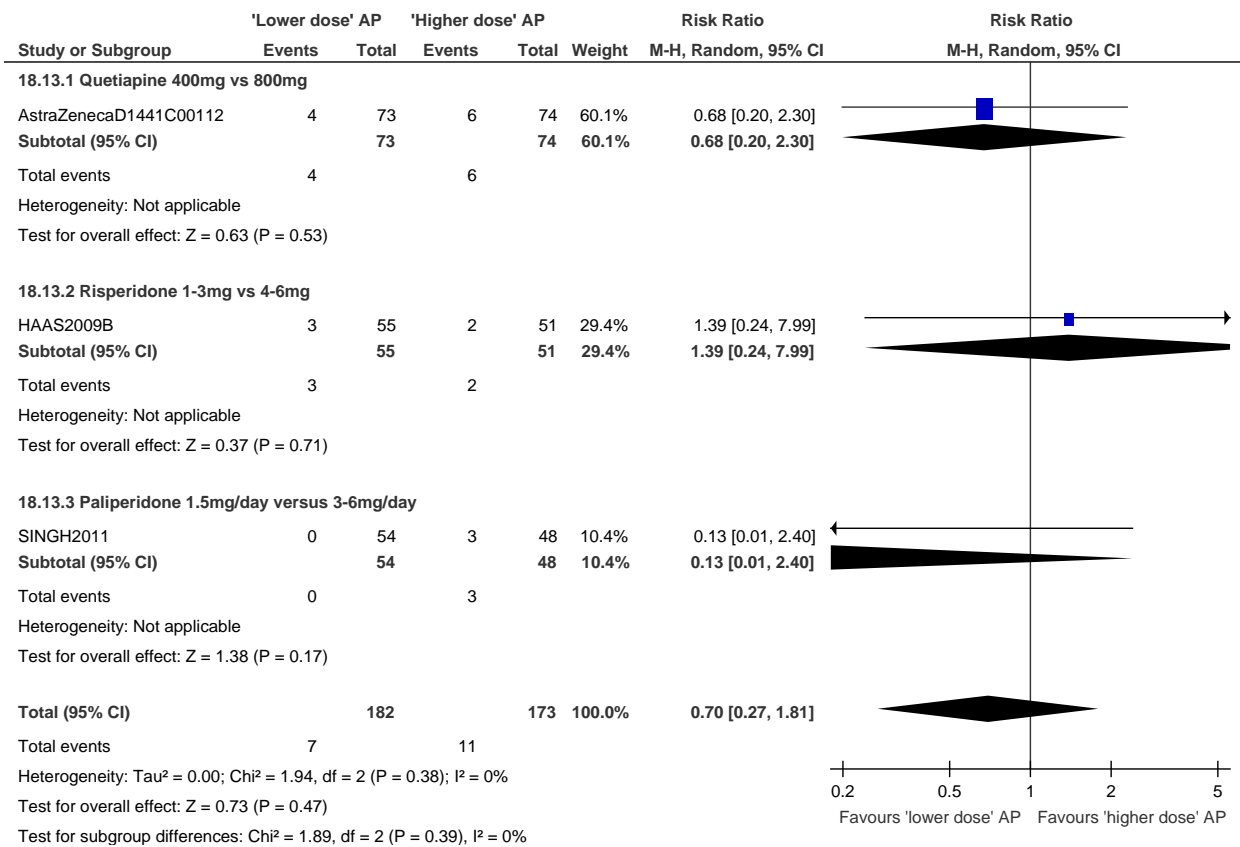
18.10 Mean change in systolic BP (mm Hg)



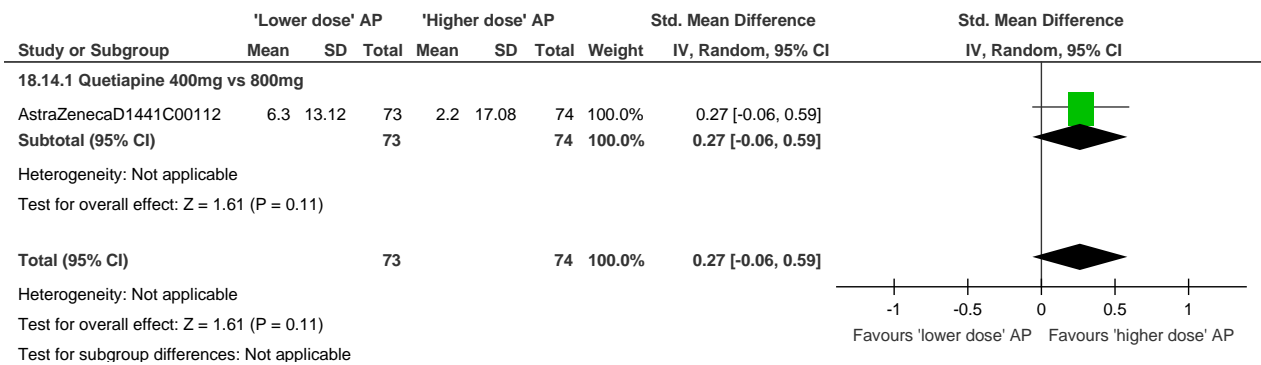
18.11 Mean change in diastolic BP (mm Hg)



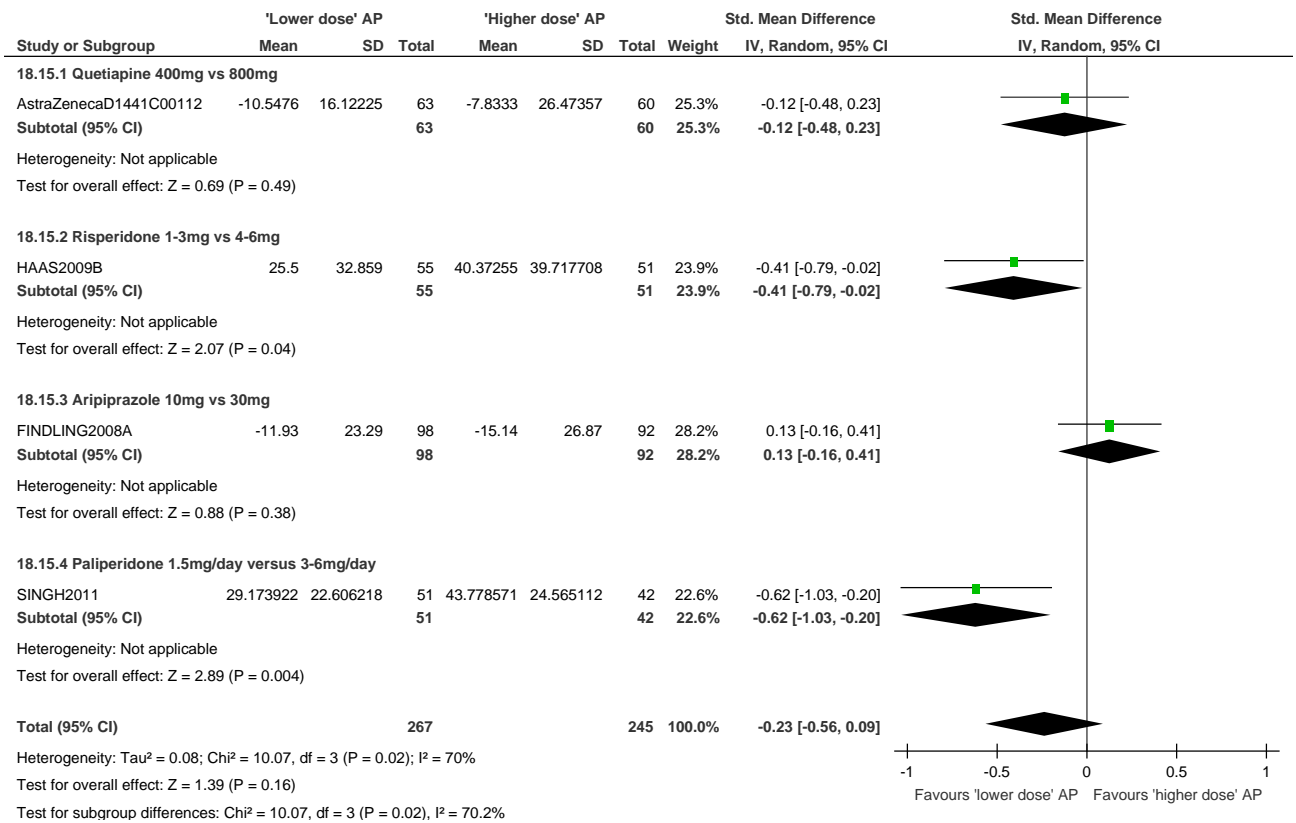
18.12 Tachycardia



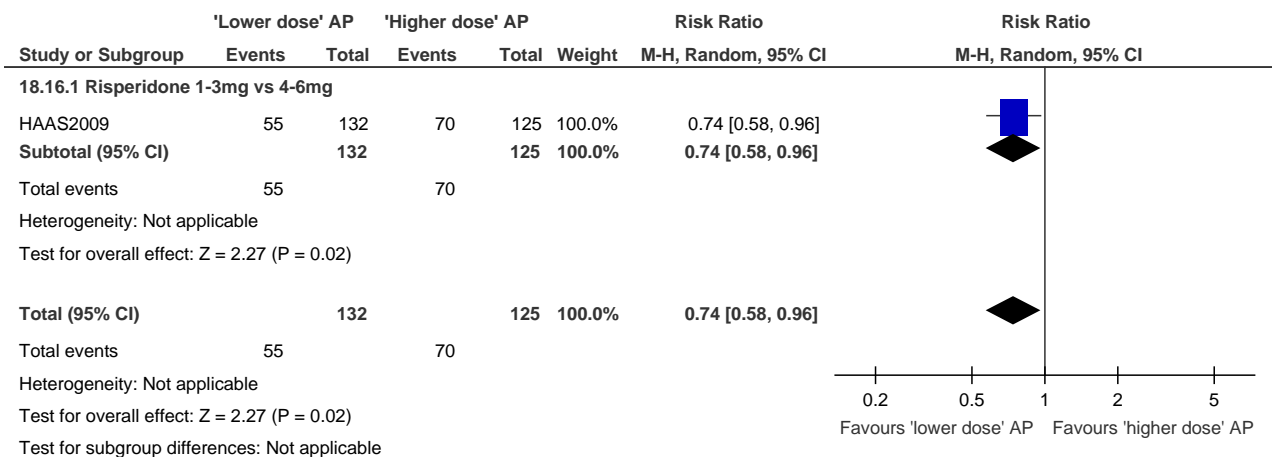
18.13 Mean change in standing pulse (BPM)



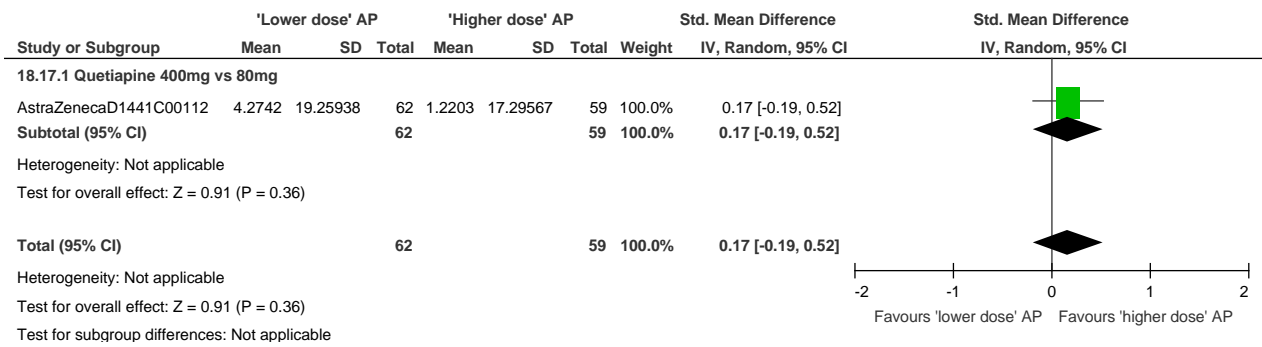
18.14 Mean change in prolactin level (mg/dl)



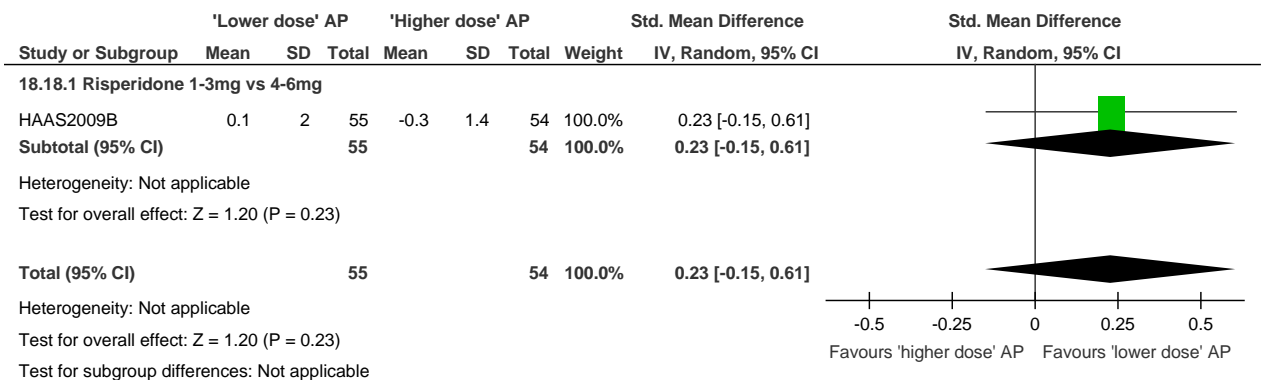
18.15 Elevated prolactin level (mg/dl)



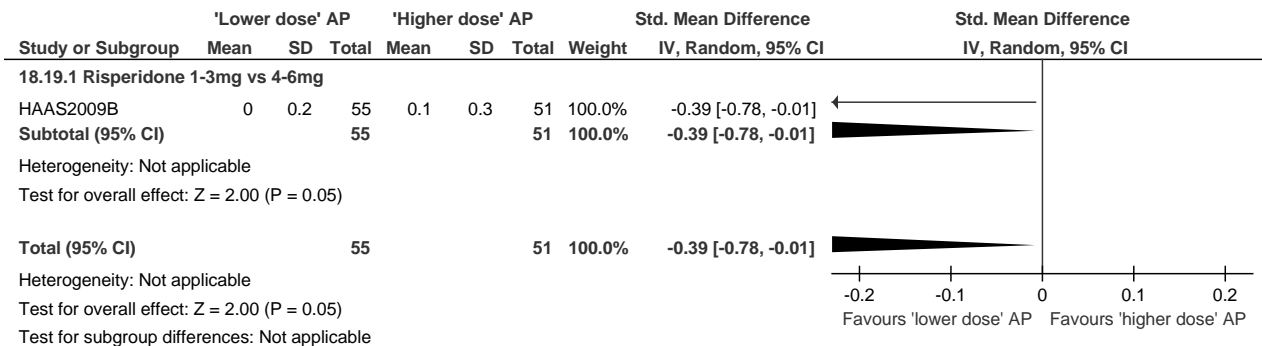
18.16 Mean change in insulin level (mg/dl)



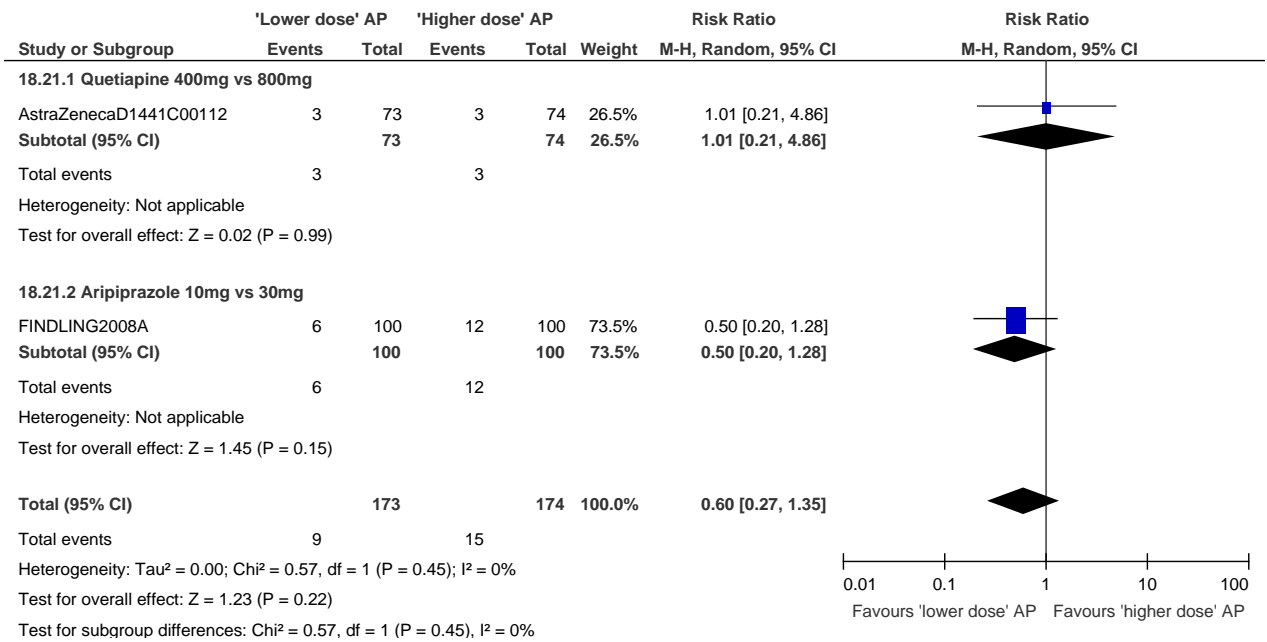
18.17 Mean change in EPS (AIMS scores)



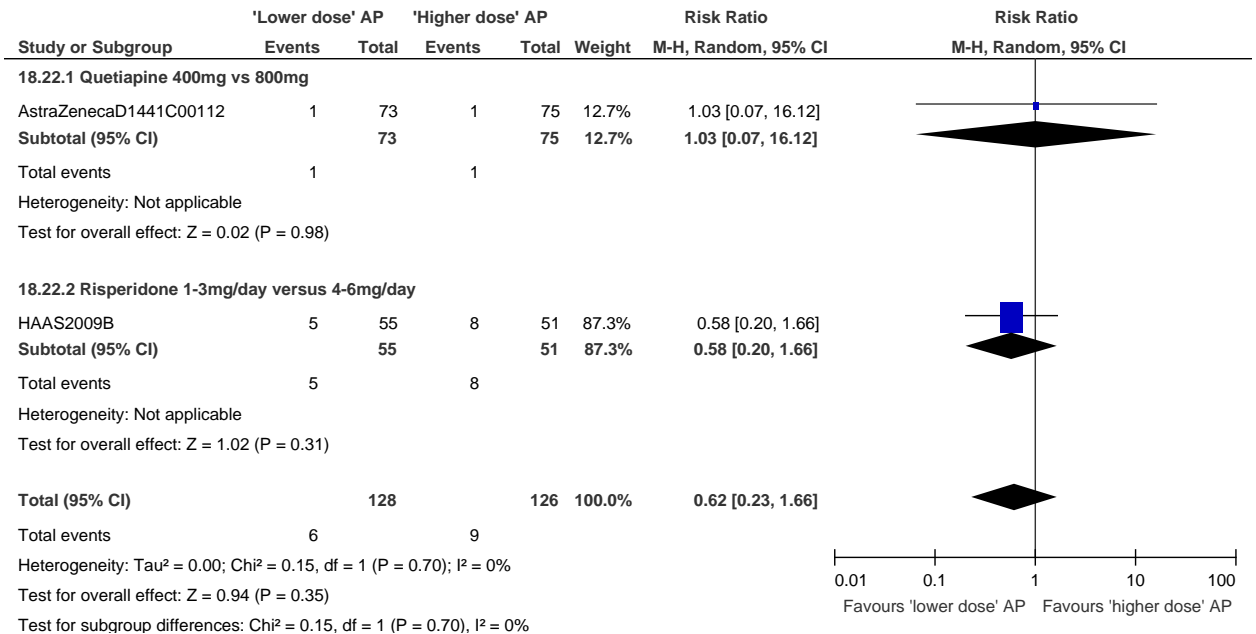
18.18 Mean change in EPS (SAS scores)



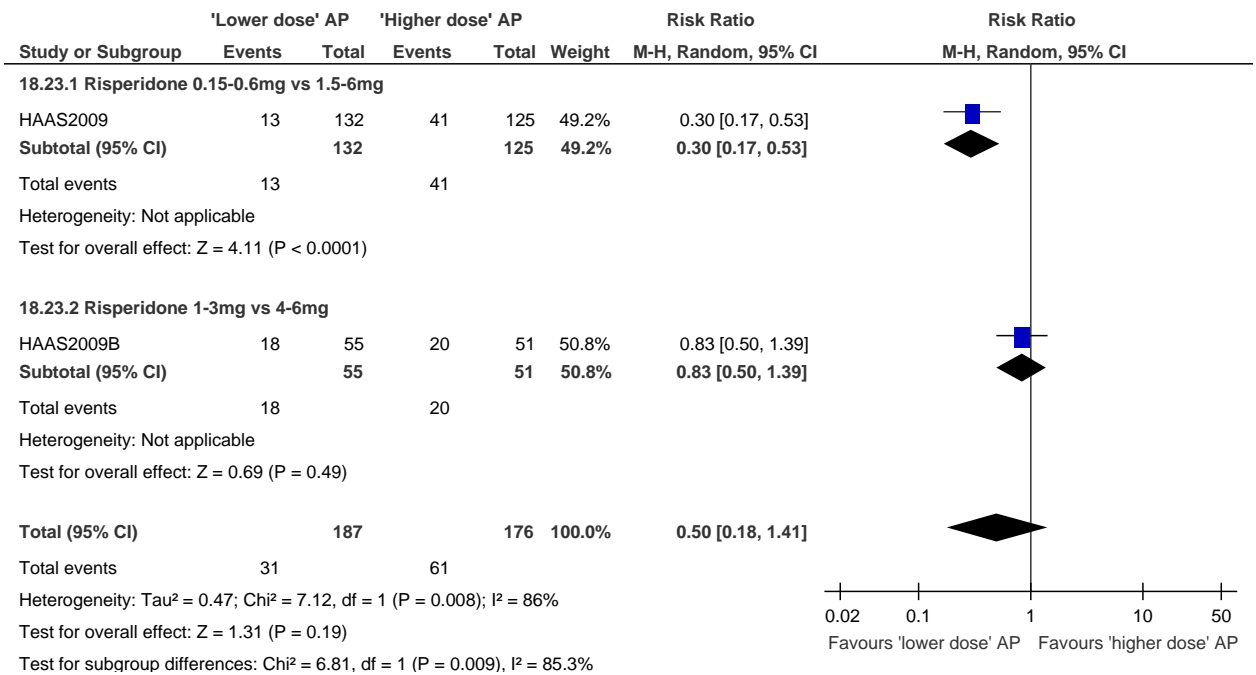
18.19 Akathisia



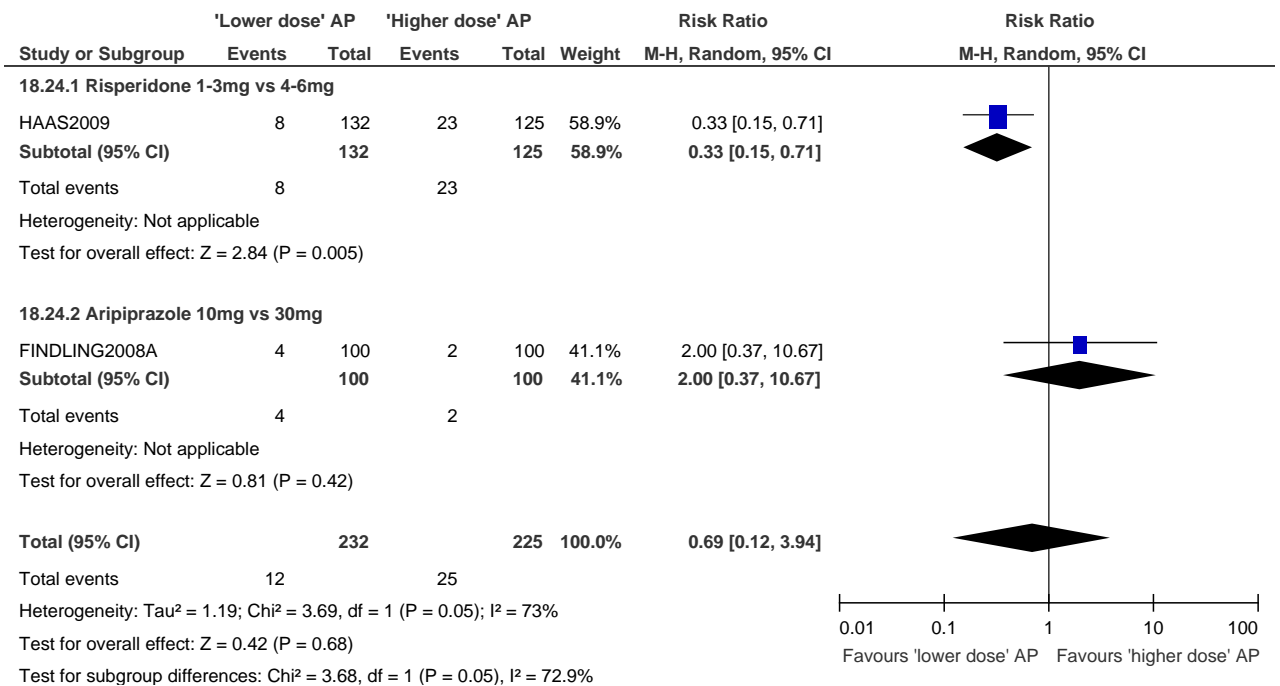
18.20 Extrapyramidal disorder



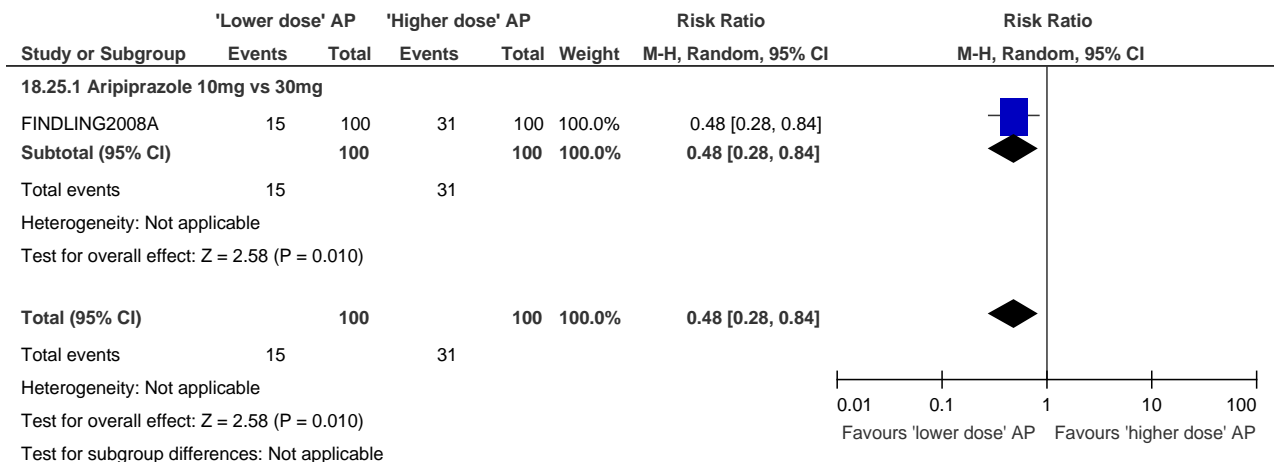
18.21 EPS



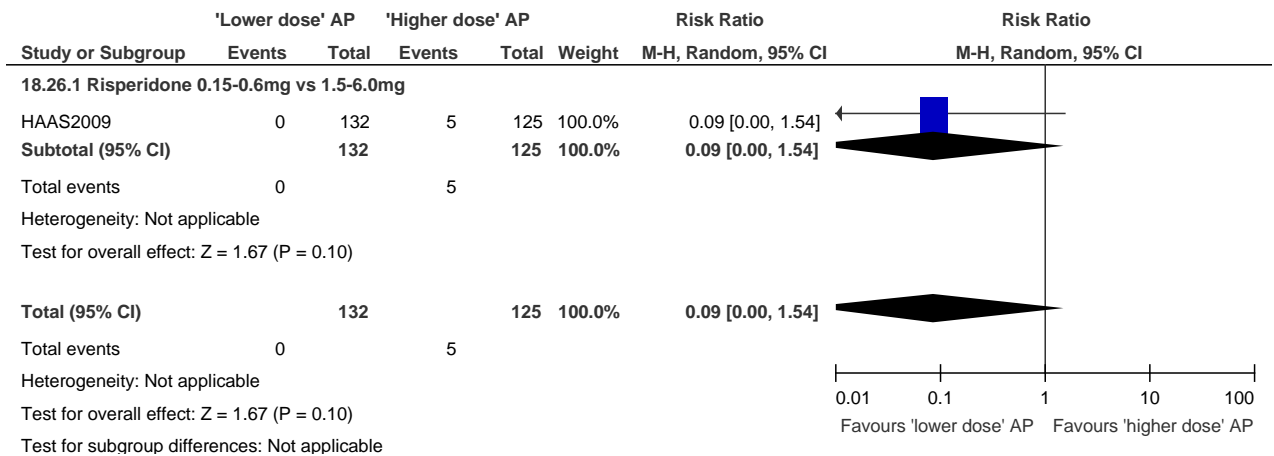
18.22 Dystonia



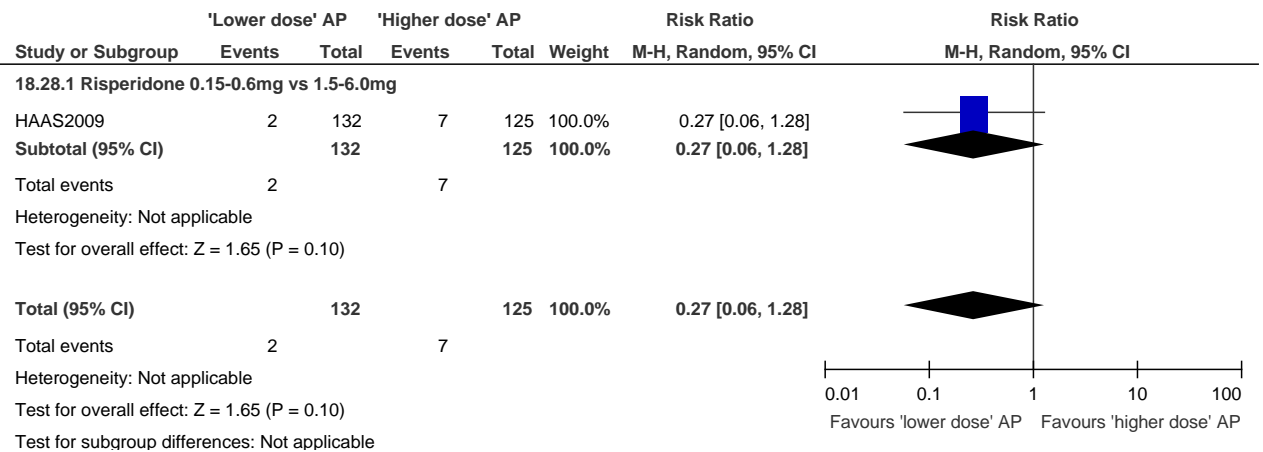
18.23 Parkinsonism



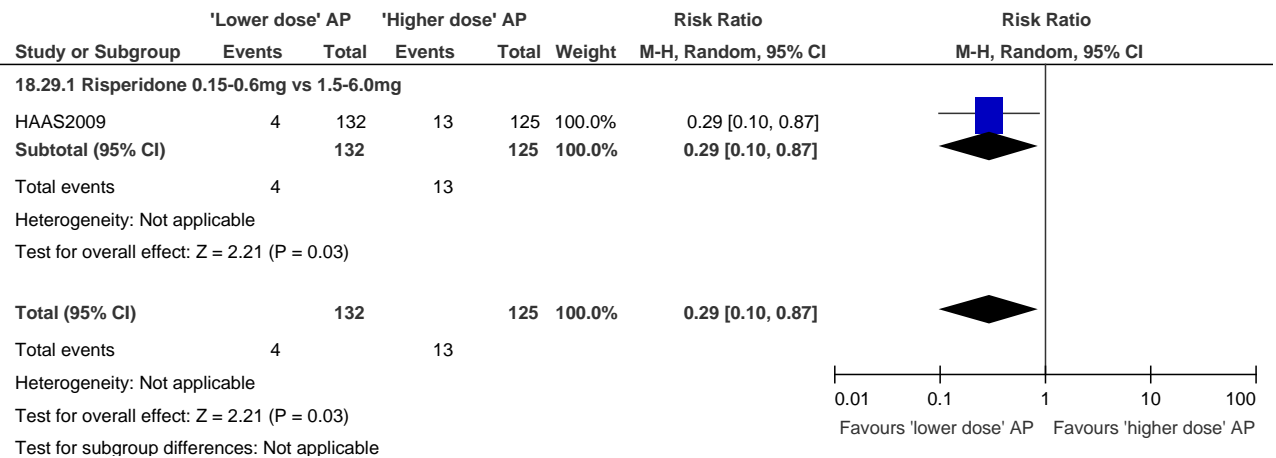
18.24 Parkinsonism symptoms



18.25 Dyskinesia



18.26 Tremor

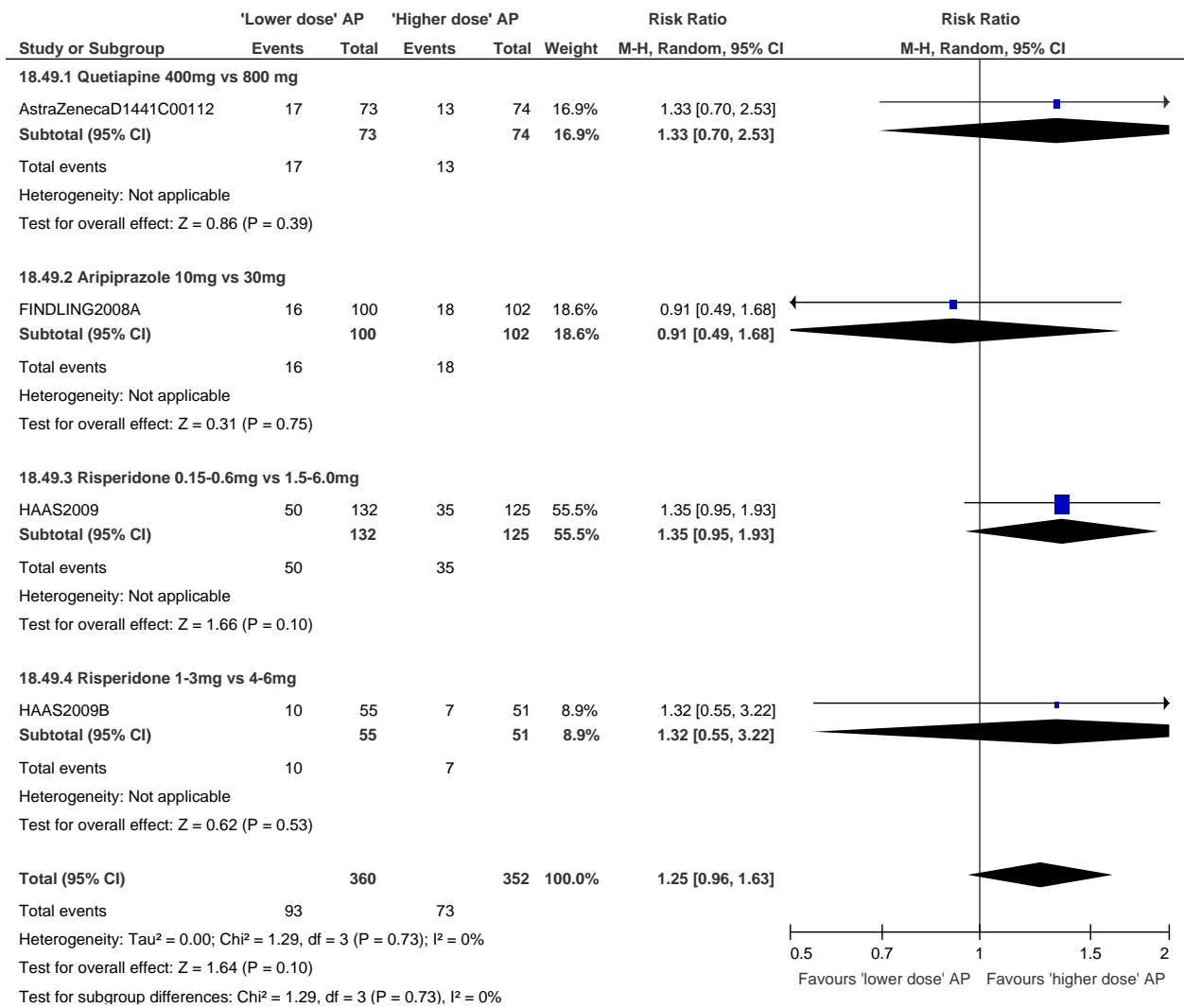


18.27 Mortality (including suicide)

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
18.30.1 Risperidone 1-3mg vs 4-6mg							
HAAS2009B	0	55	0	51		Not estimable	
Subtotal (95% CI)		55		51		Not estimable	
Total events	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
18.30.2 Aripiprazole 10mg vs 30mg							
FINDLING2008A	0	100	0	100		Not estimable	
Subtotal (95% CI)		100		100		Not estimable	
Total events	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Total (95% CI)		155		151		Not estimable	
Total events	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							

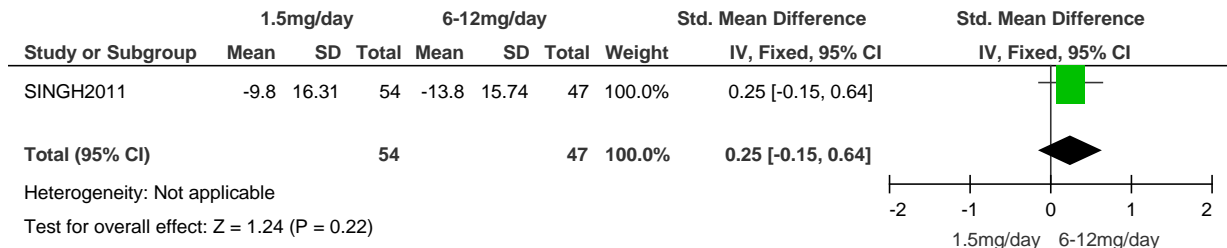
0.01 0.1 1 10 100
Favours 'Lower dose' AP Favours 'Higher dose' AP

18.28 Leaving the study early for any reason

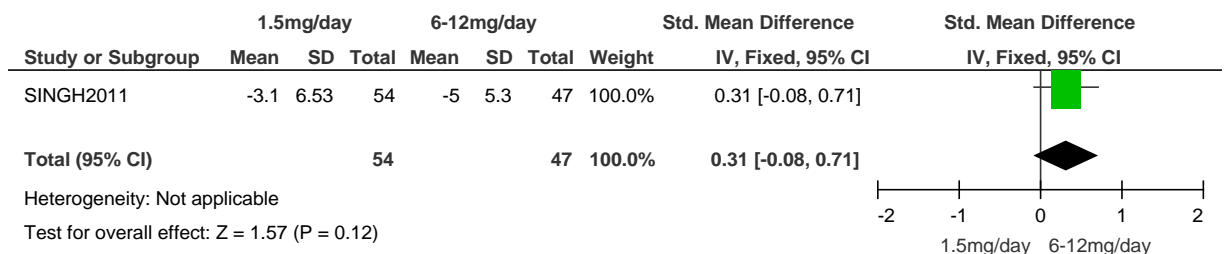


19. 'Lower dose' paliperidone (1.5mg/day) versus additional (high dose) paliperidone (6 to 12mg/day): post-treatment efficacy outcomes

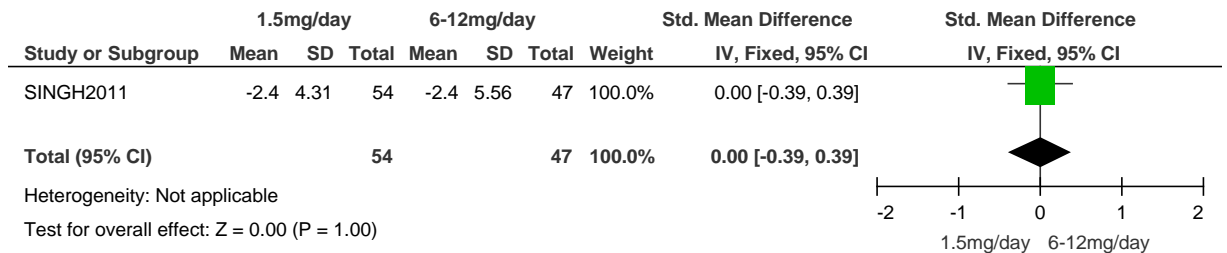
19.1 Mental state: mean change in total symptoms (PANSS)



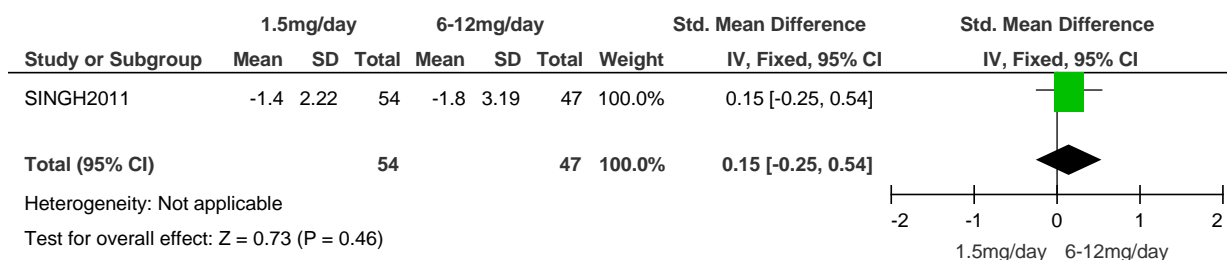
19.2 Mental state: mean change in positive symptoms (PANSS Positive)



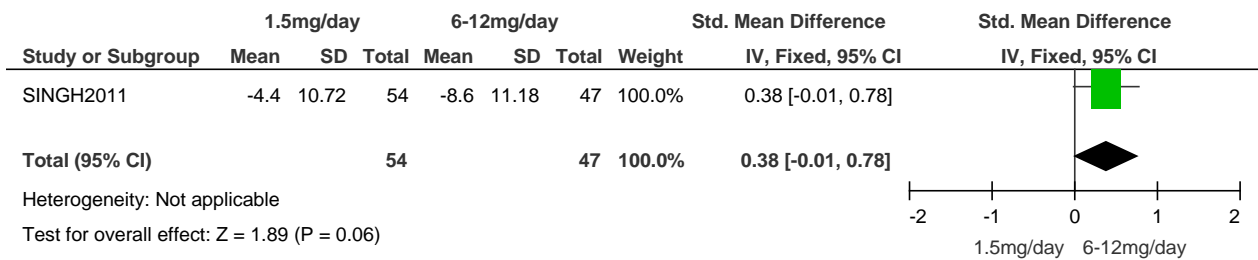
19.3 Mental state: mean change in negative symptoms (PANSS Negative)



19.4 Mean change in depression (PANSS Anxiety and Depression)

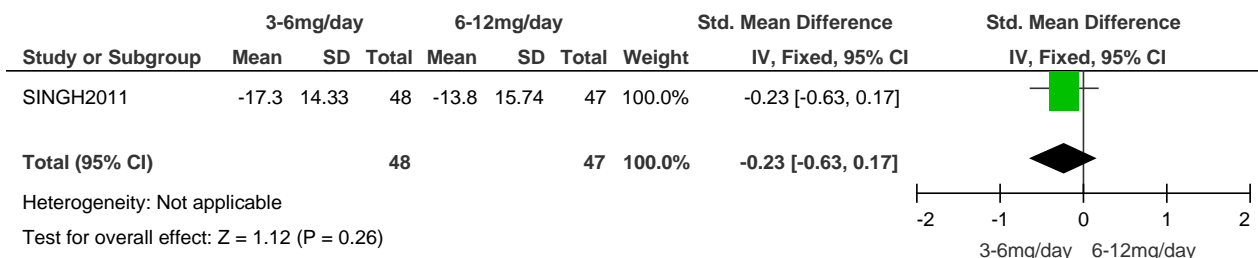


19.5 Mean change in psychosocial functioning (CGAS)

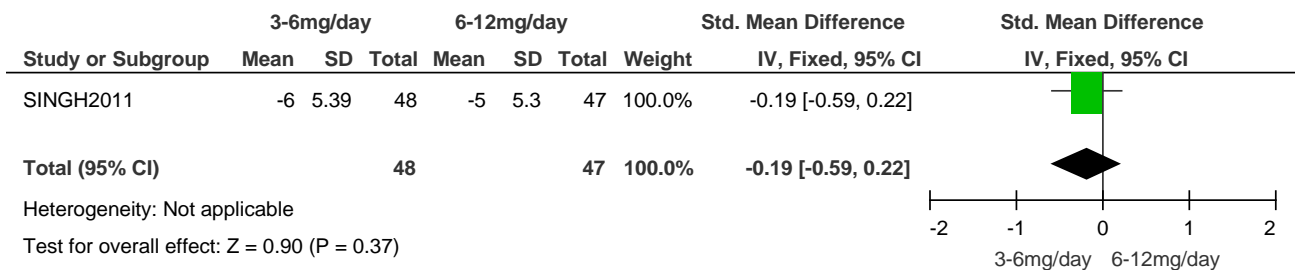


20. 'Higher dose' paliperidone (3 to 6mg/day) versus additional (high dose) paliperidone (6 to 12mg/day): post-treatment efficacy outcomes

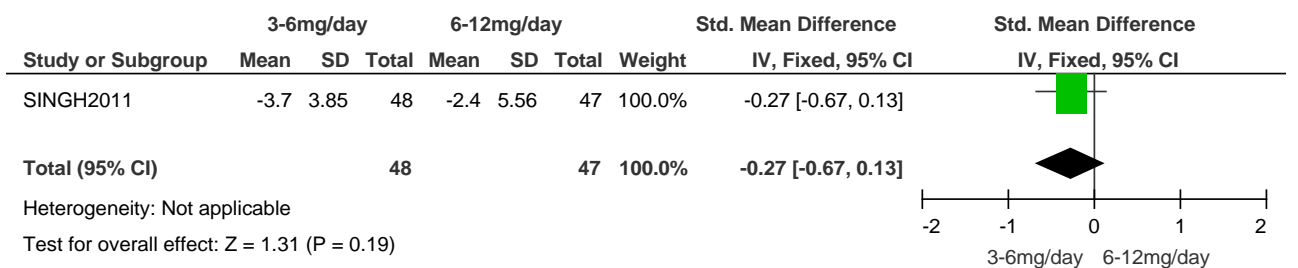
20.1 Mental state: mean change in total symptoms (PANSS)



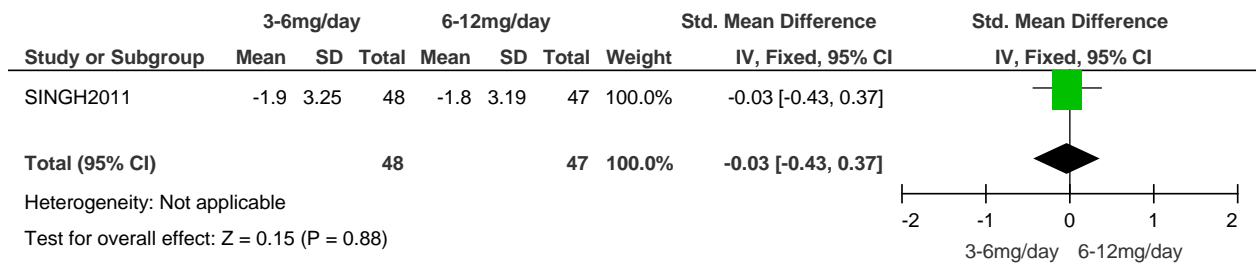
20.2 Mental state: mean change in positive symptoms (PANSS positive)



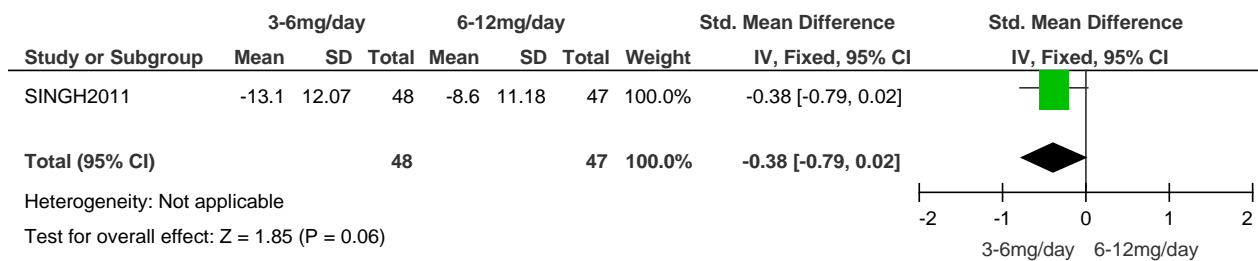
20.3 Mental state: mean change in negative symptoms (PANSS negative)



20.4 Mean change in depression (PANSS Anxiety and Depression)

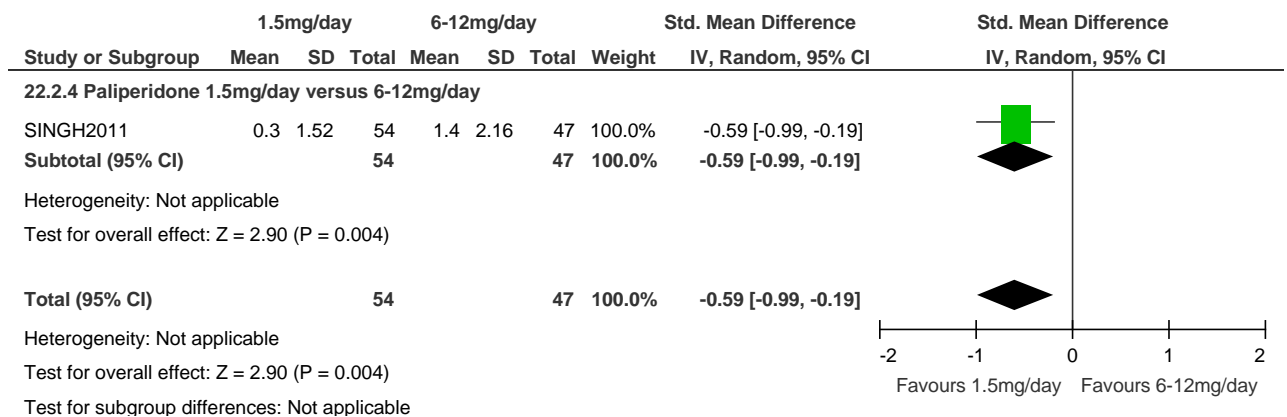


20.5 Mean change in psychosocial functioning (CGAS)

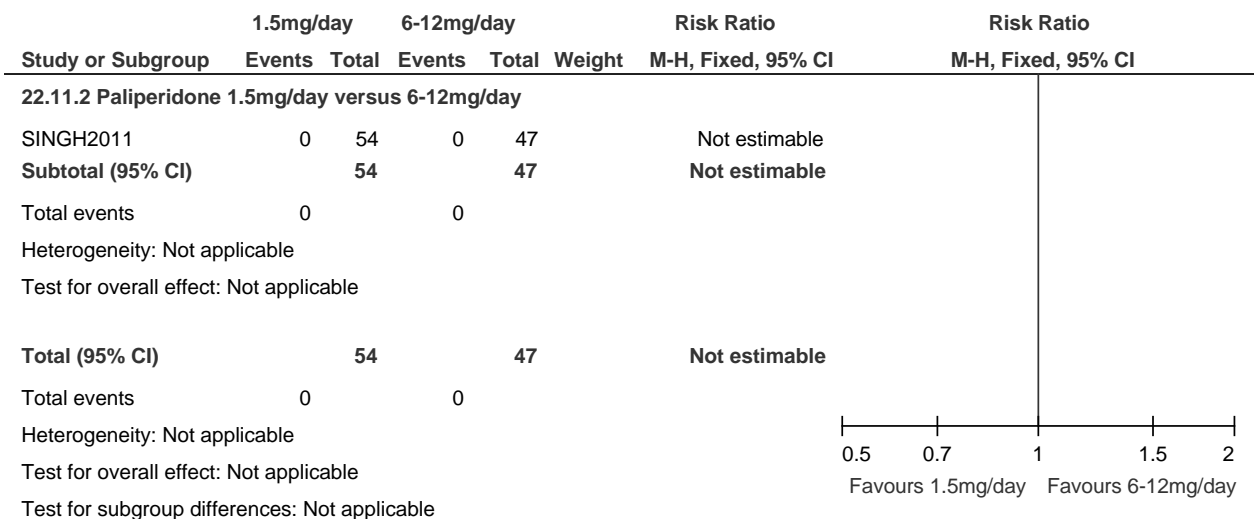


21. 'Lower dose' paliperidone (1.5mg/day) versus additional (high dose) paliperidone (6 to 12mg/day): post-treatment side effect outcomes

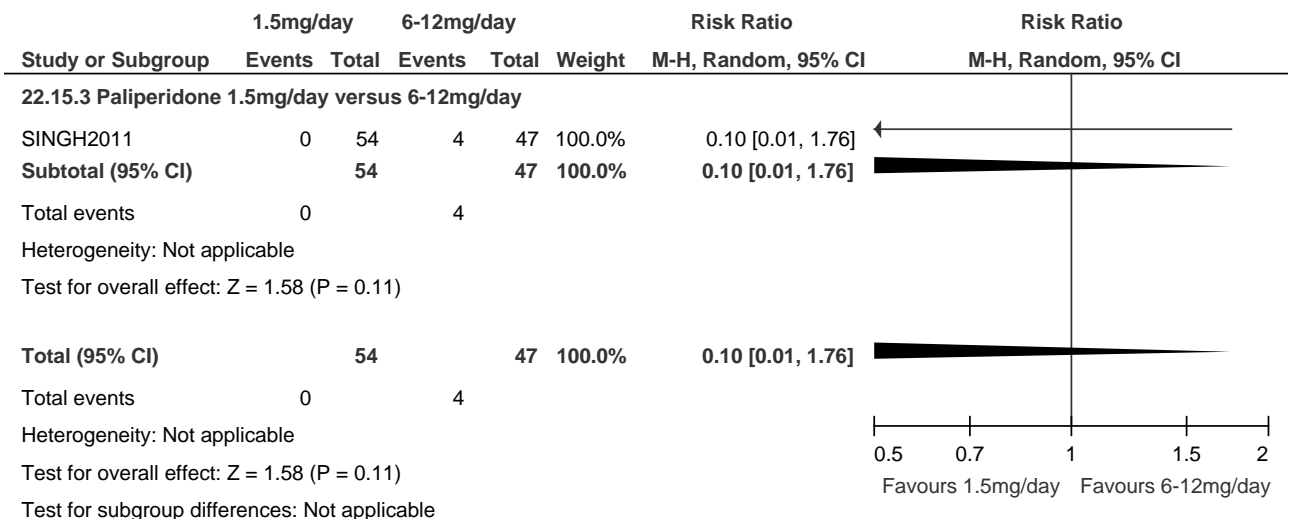
21.1 Mean change in weight (kg)



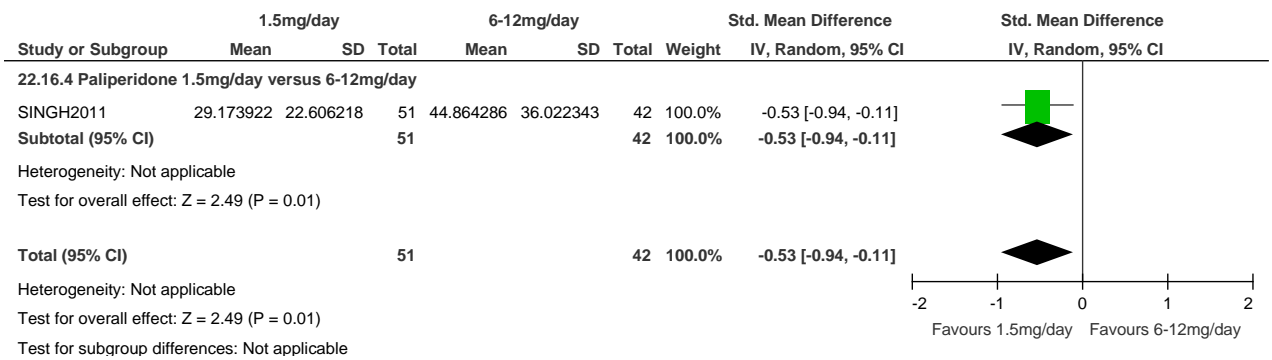
21.2 Prolonged QT interval (msec)



21.3 Tachycardia

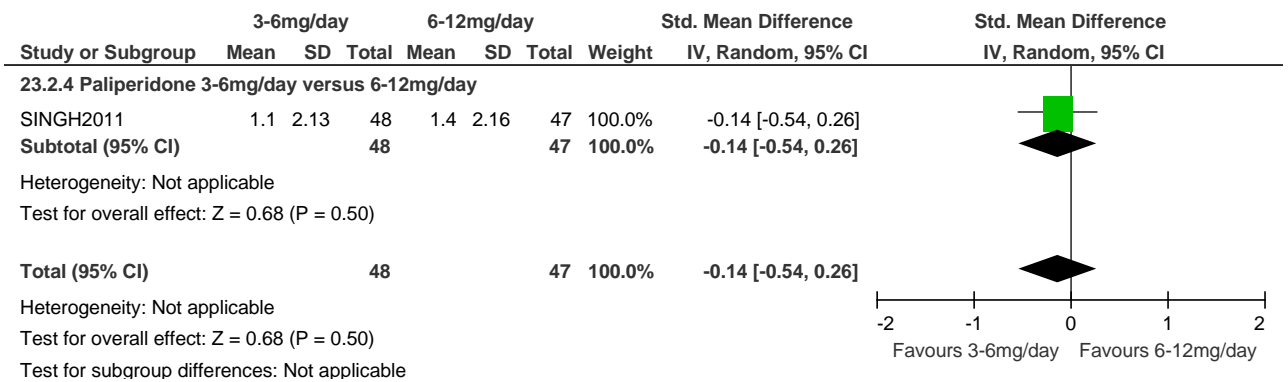


21.4 Mean change in prolactin level (mg/dl)

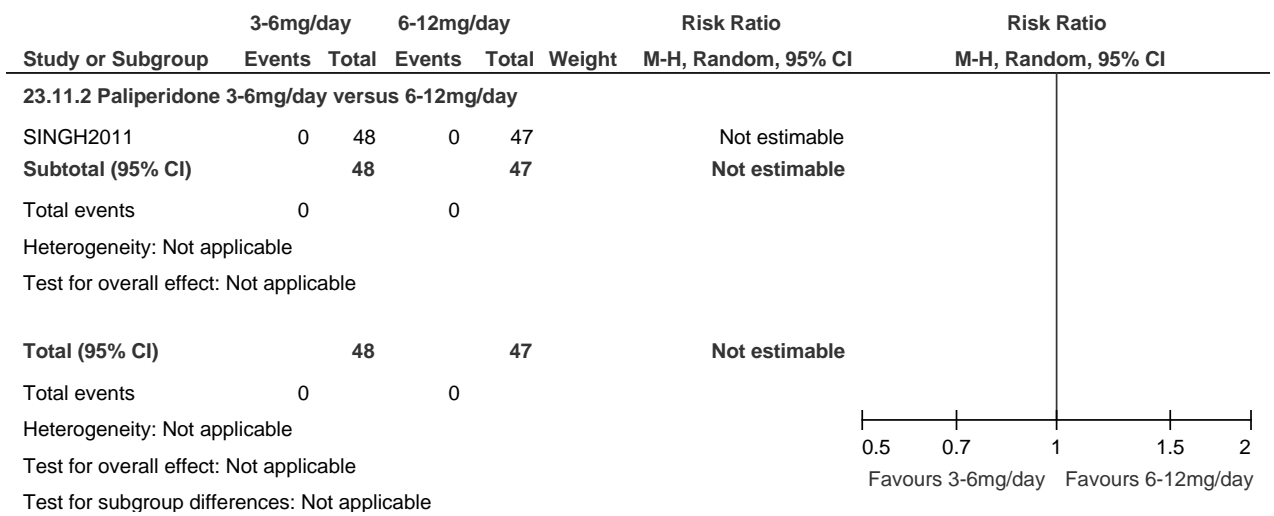


22. 'Higher dose' paliperidone (3 to 6mg/day) versus additional (high dose) paliperidone (6 to 12mg/day): post-treatment side effect outcomes

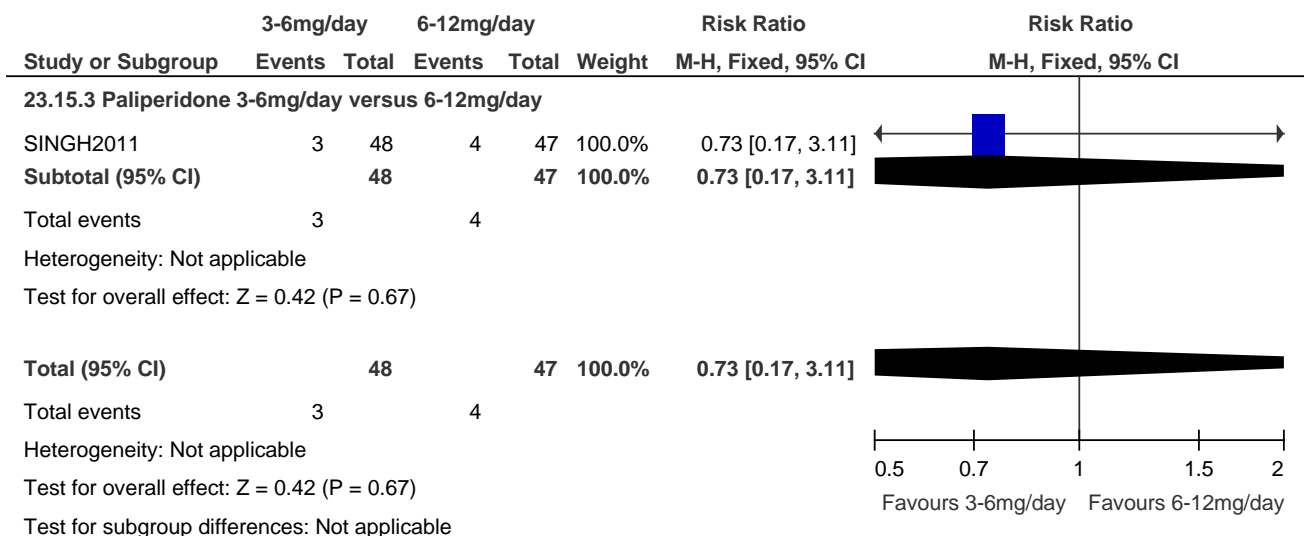
22.1 Mean change in weight (kg)



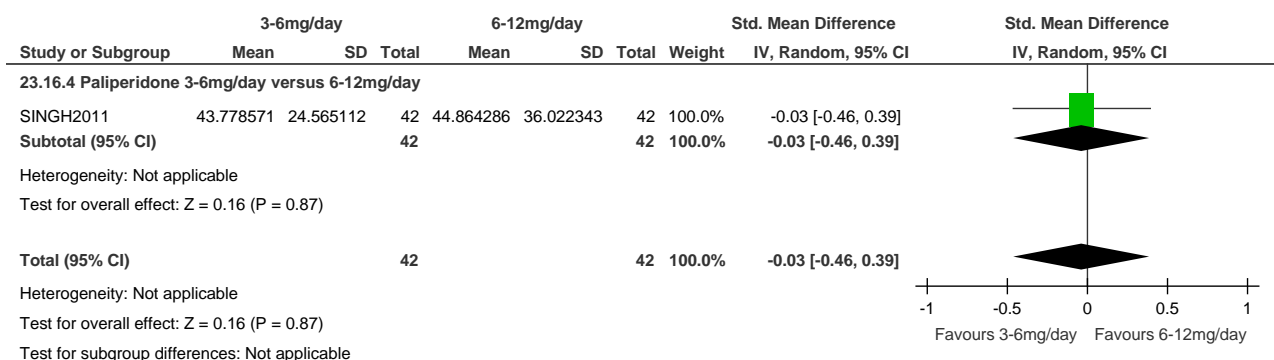
22.2 Prolonged QT interval (msec)



22.3 Tachycardia



22.4 Mean change in prolactin level (mg/dl)

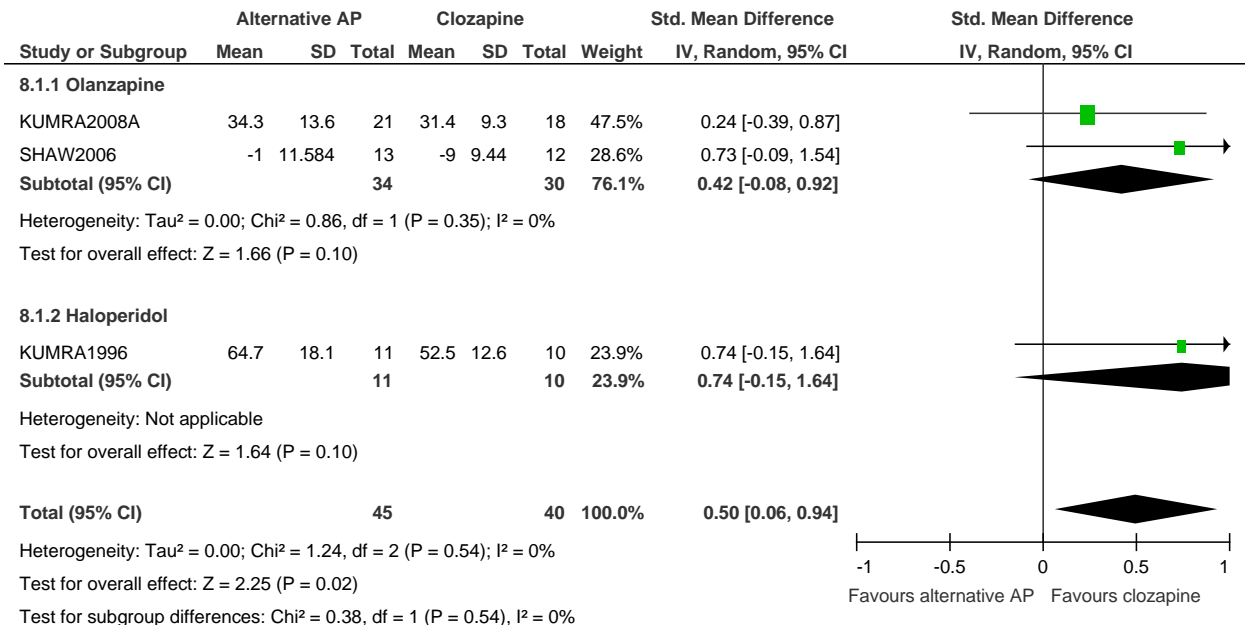


APPENDIX 14C (III): TREATMENT RESISTANT PSYCHOSIS AND SCHIZOPHRENIA

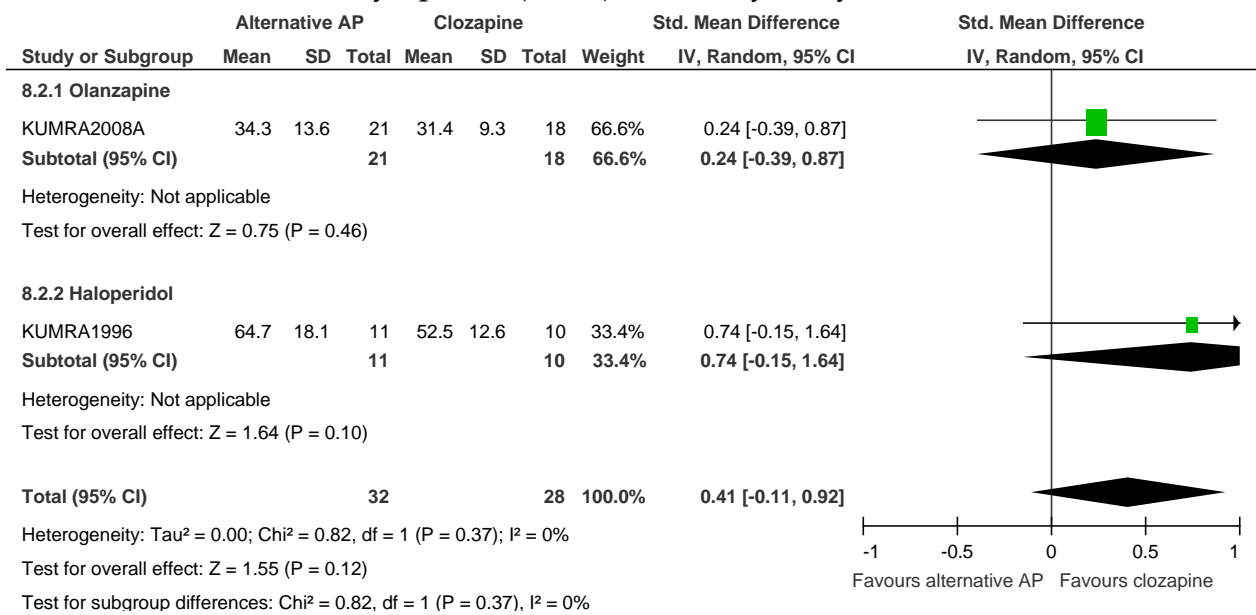
PHARMACOLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 18 YEARS AND YOUNGER

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

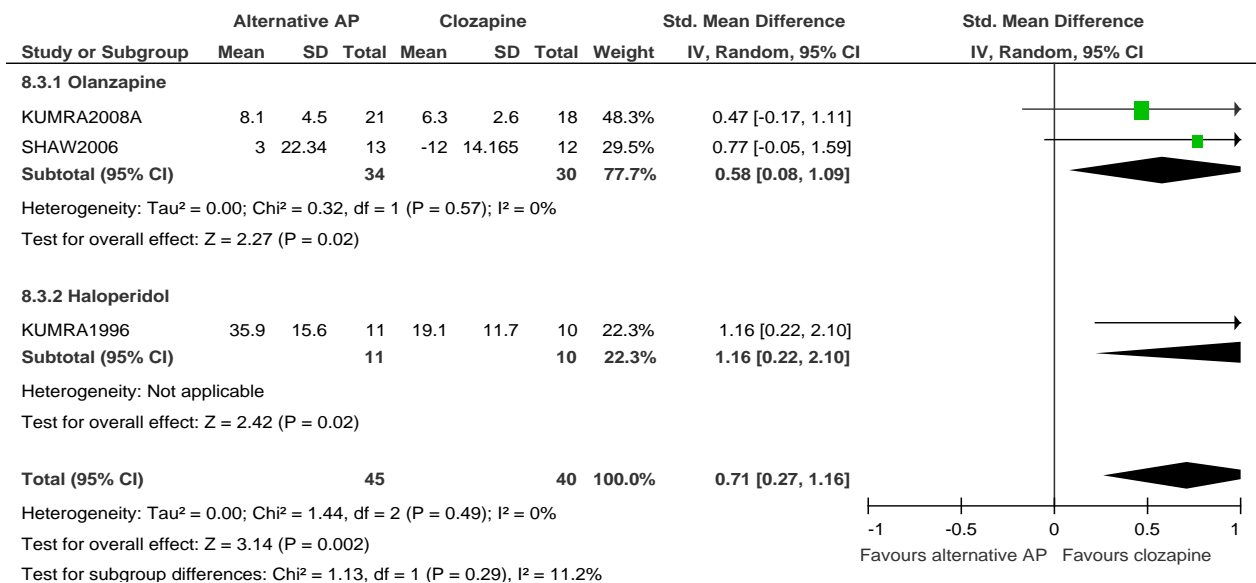
1.1 Mental state: total symptoms (BPRS)



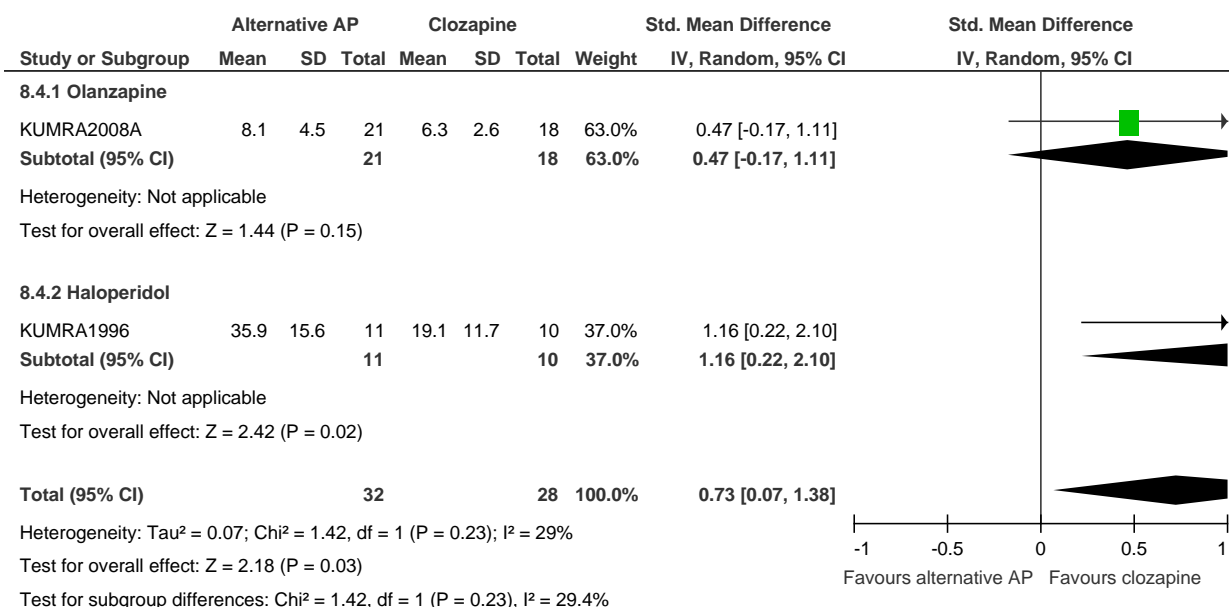
1.2 Mental state: total symptoms (BPRS) sensitivity analysis



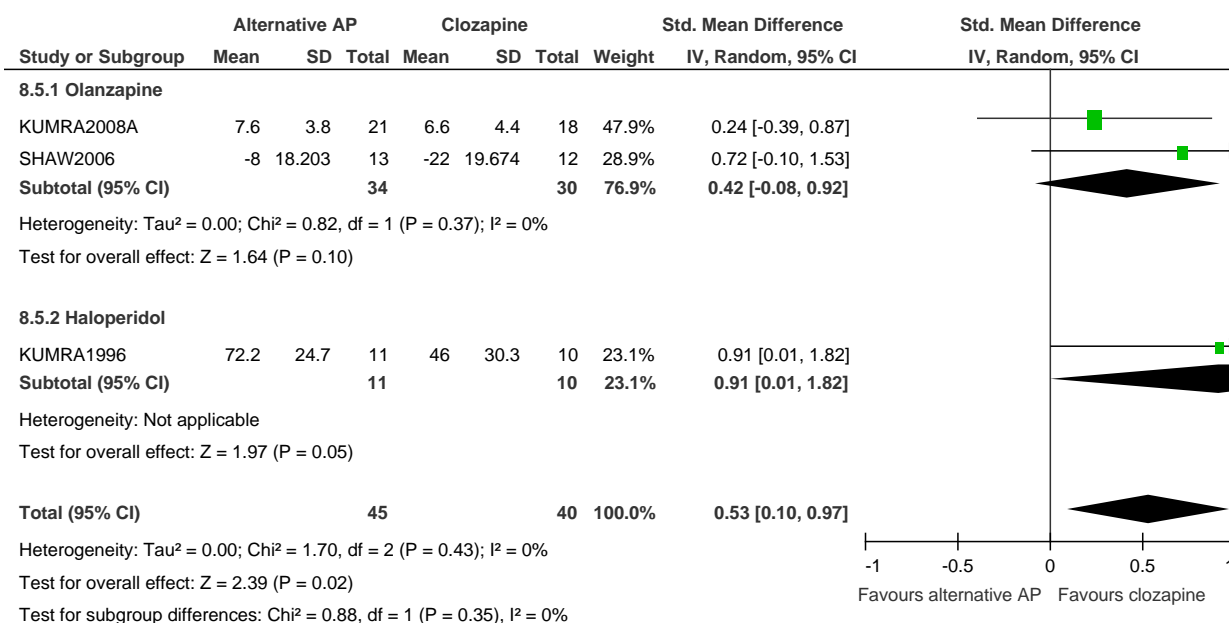
1.3 Mental state: positive symptoms (SAPS, BPRS Positive)



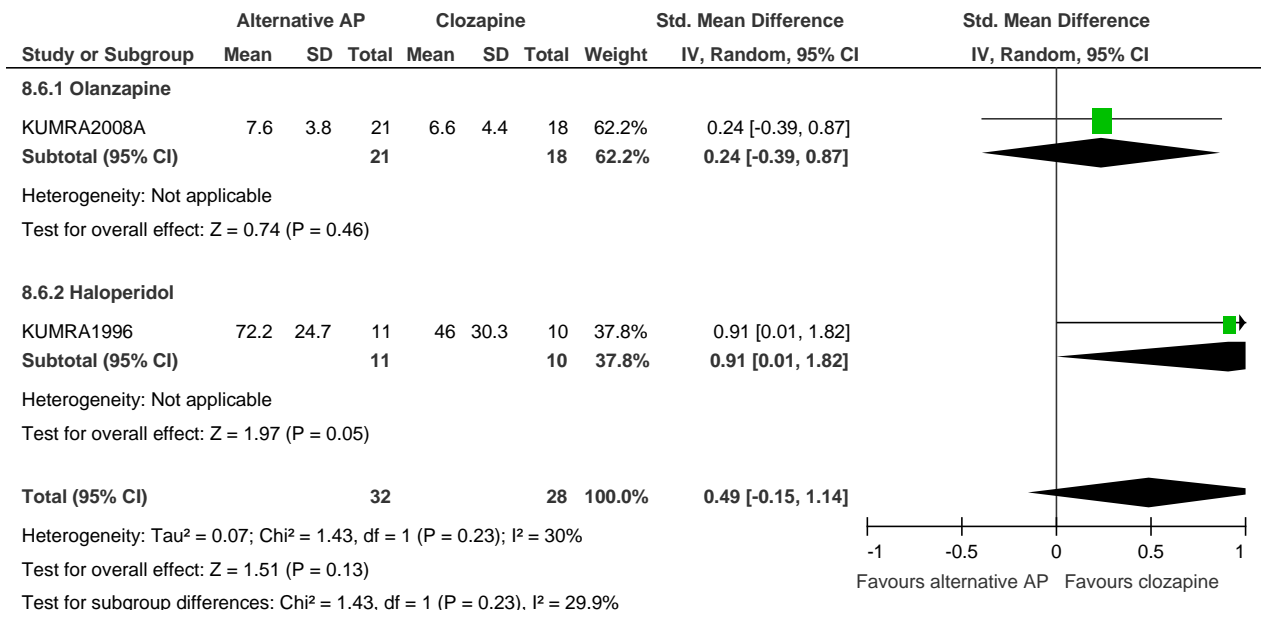
1.4 Mental state: positive symptoms (SAPS, BPRS Positive) sensitivity analyses



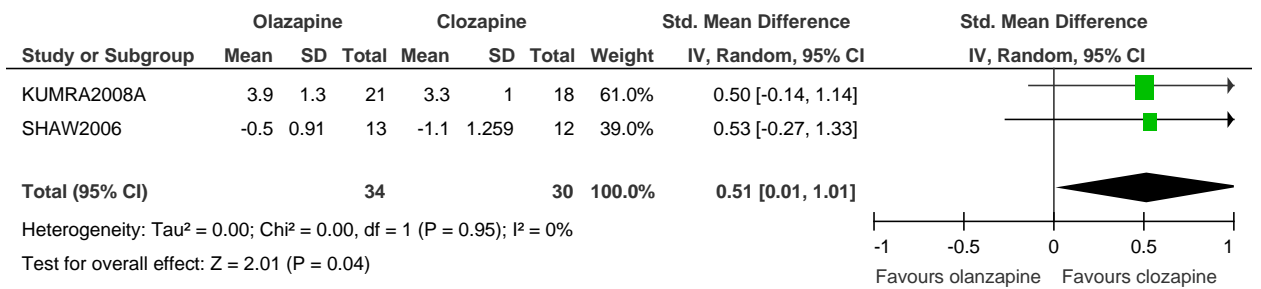
1.5 Mental state: negative symptoms (SANS)



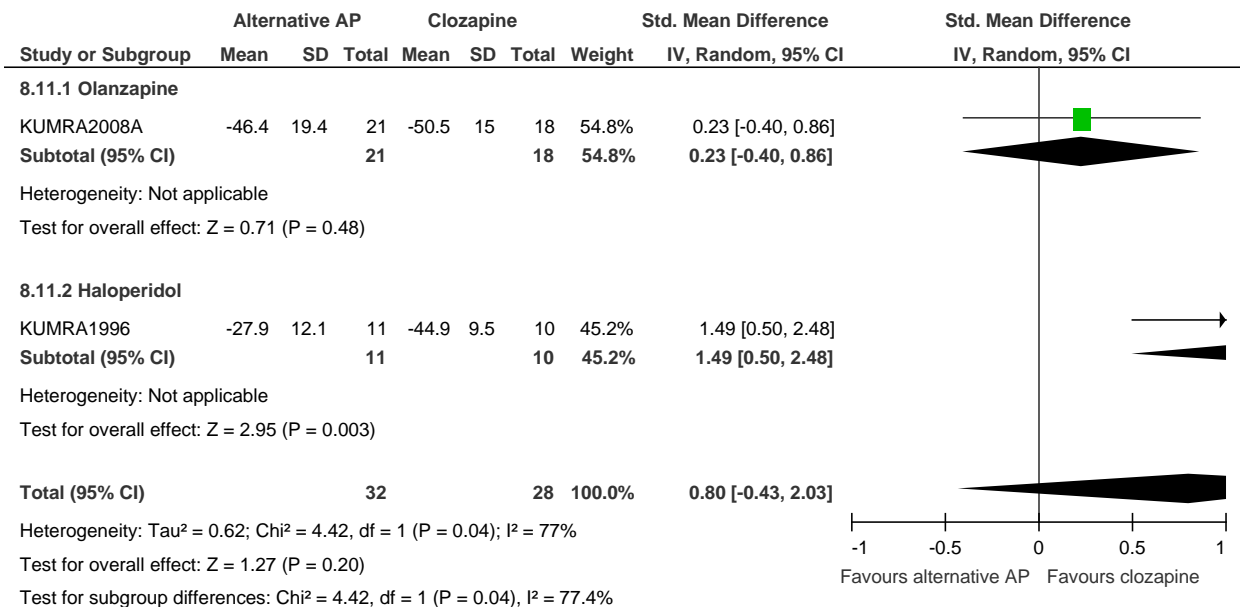
1.6 Mental state: negative symptoms (SANS) sensitivity analyses



1.7 Global state: severity (CGI-S)

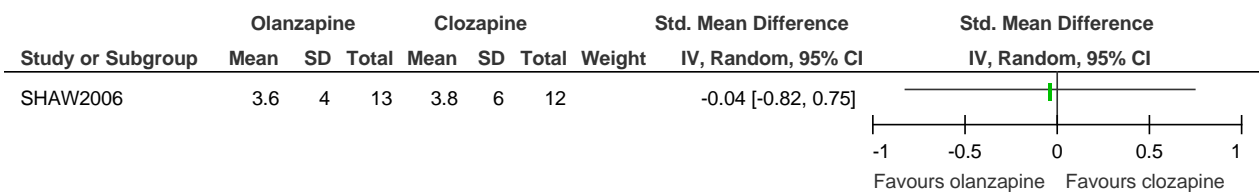


1.8 Functioning: psychosocial (CGAS)

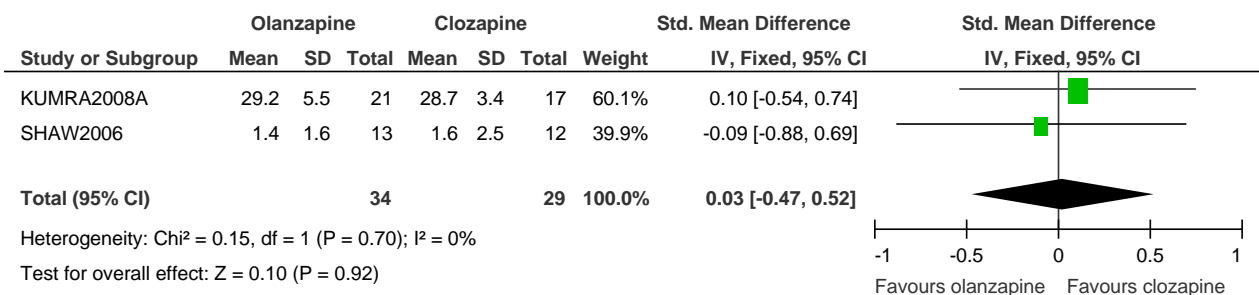


2. Clozapine versus another antipsychotic: post-treatment side effect outcomes

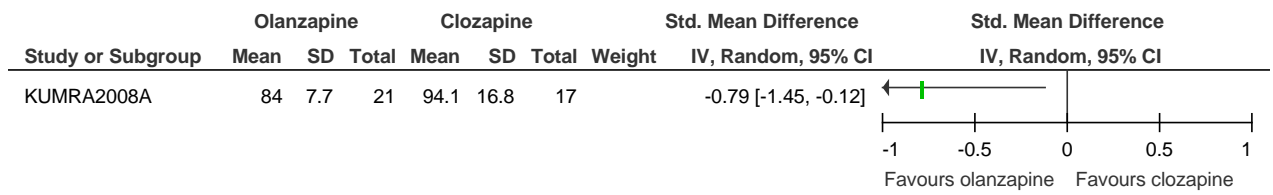
2.1 Weight (lbs)



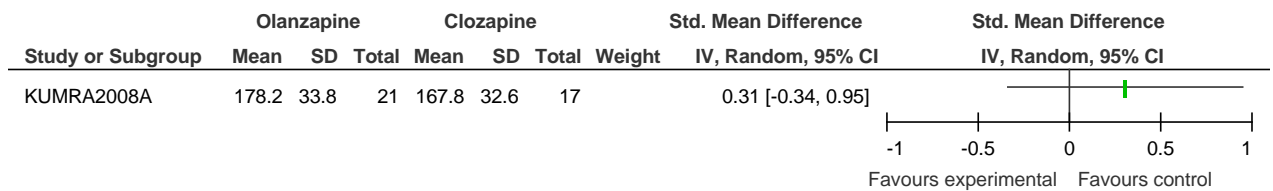
2.2 BMI (kg/m²)



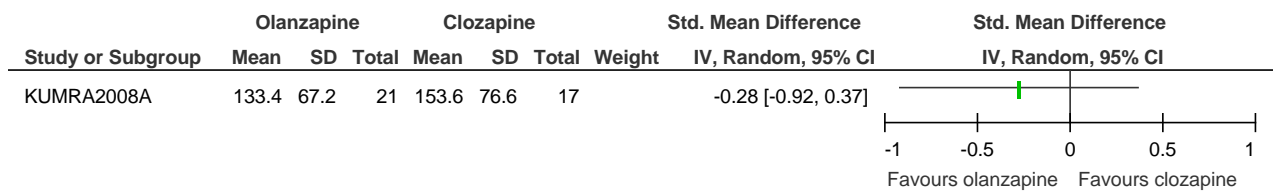
2.3 Fasting serum glucose level mg/dl



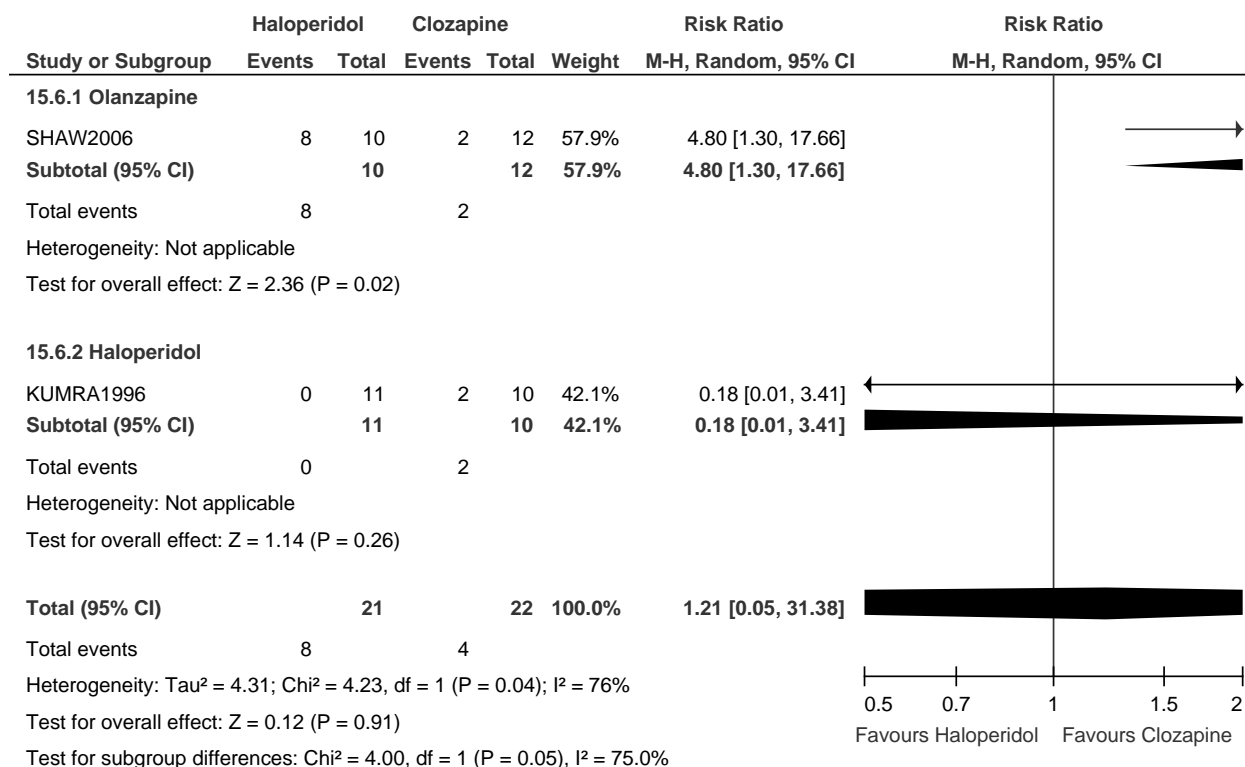
2.4 Fasting total cholesterol mg/dl



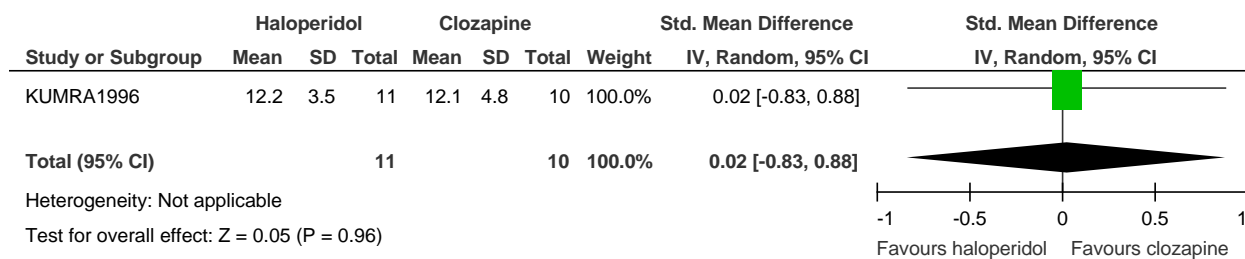
2.5 Fasting triglycerides mg/dl



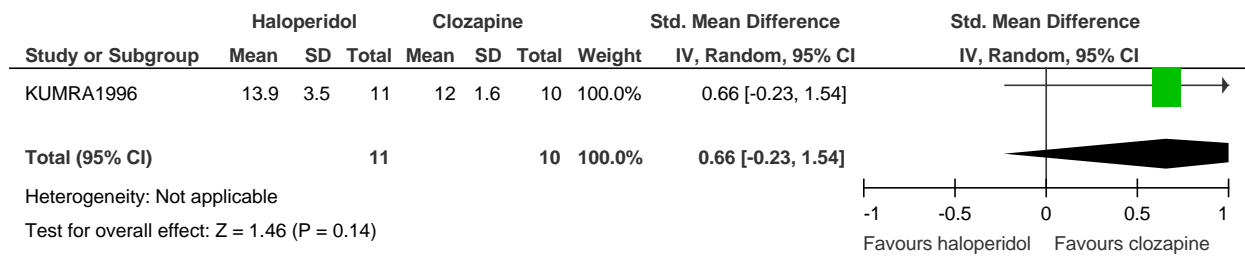
2.6 Tachycardia (number of participants)



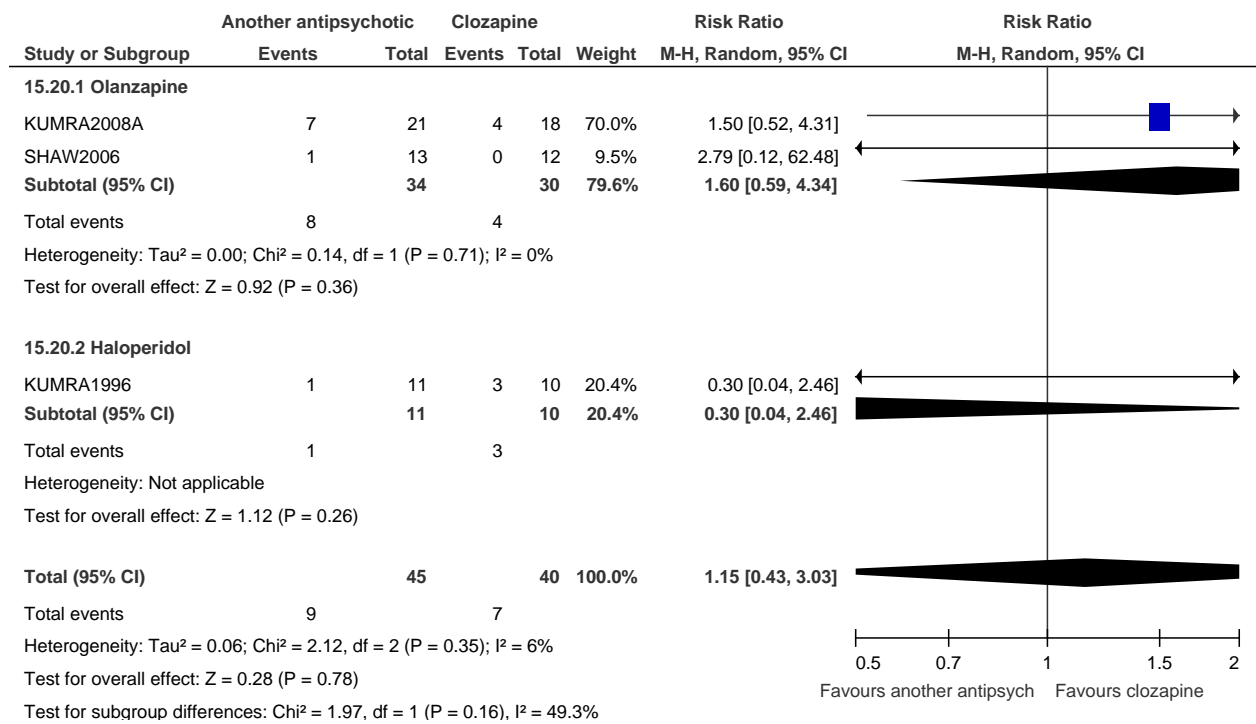
2.7 EPS (AIMS)



2.8 EPS (SAS)



2.9 Leaving the study early for any reason

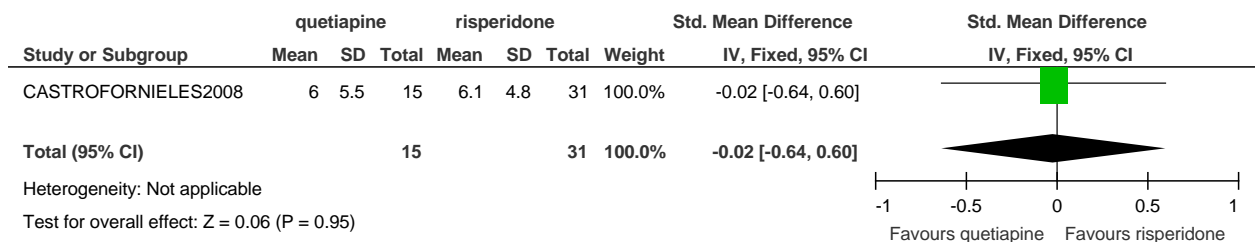


APPENDIX 14C (IV): OBSERVATIONAL STUDIES - SIDE EFFECTS

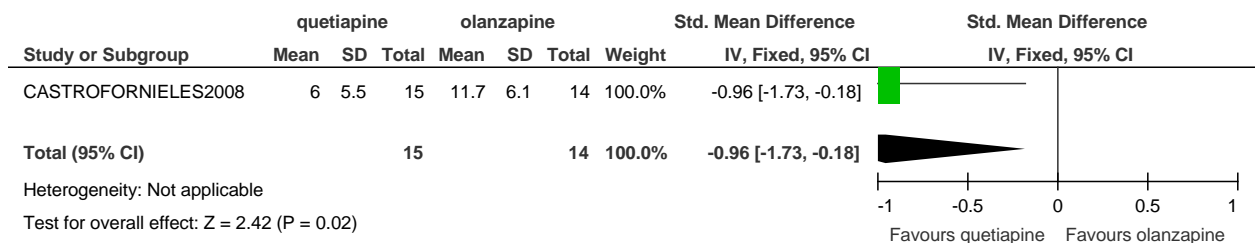
PHARMACOLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 18 YEARS AND YOUNGER

1. Weight change (kg)

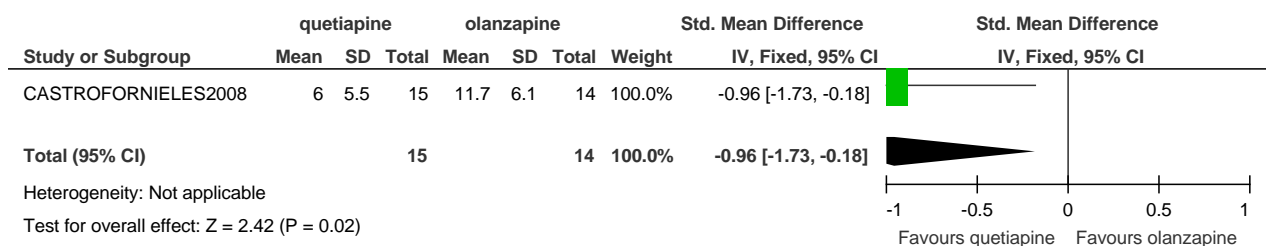
1.1 Quetiapine versus risperidone: post-treatment



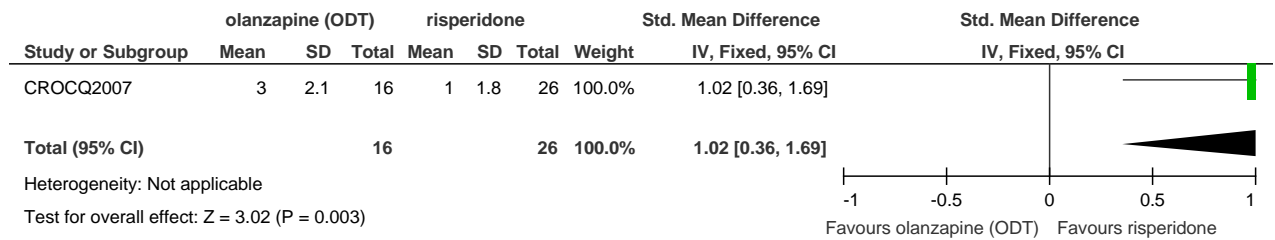
1.2 Quetiapine versus olanzapine: post-treatment



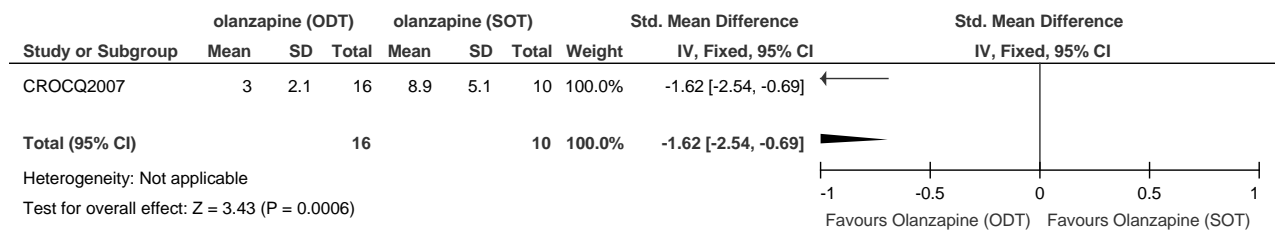
1.3 Olanzapine (standard oral tablet [SOT]) versus risperidone: post-treatment



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

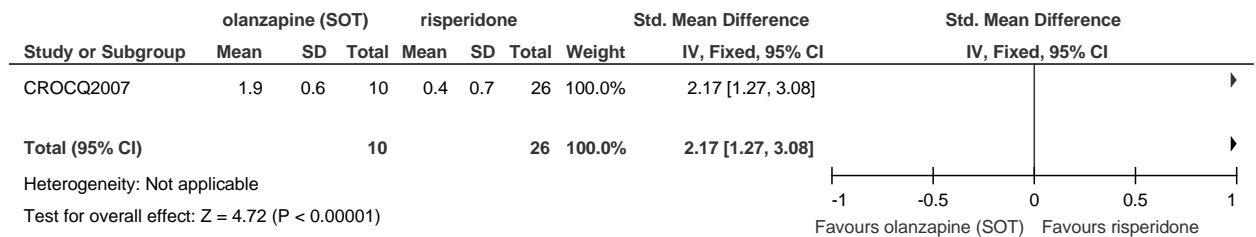


1.5 Olanzapine (SOT) versus olanzapine (ODT): post-treatment

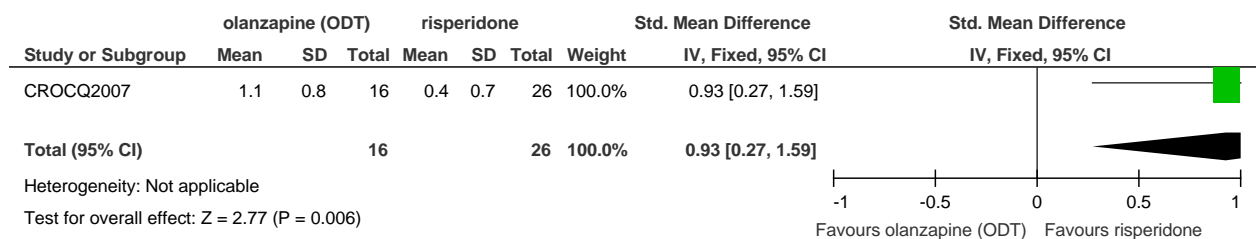


2. BMI change

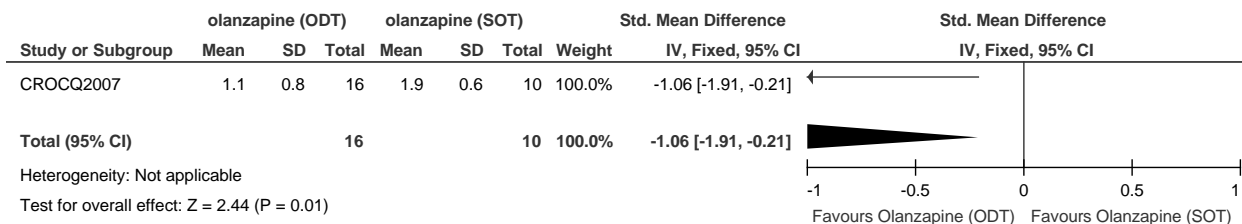
2.1 Olanzapine (SOT) versus risperidone: post-treatment



2.2 Olanzapine (ODT) versus risperidone: post-treatment

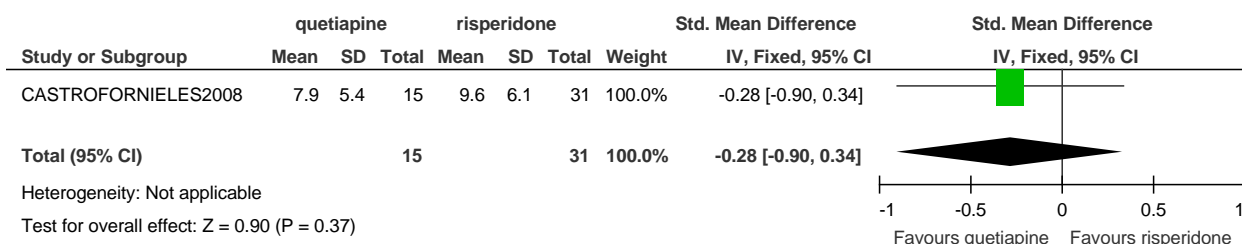


2.3 Olanzapine (SOT) versus olanzapine (ODT): post-treatment

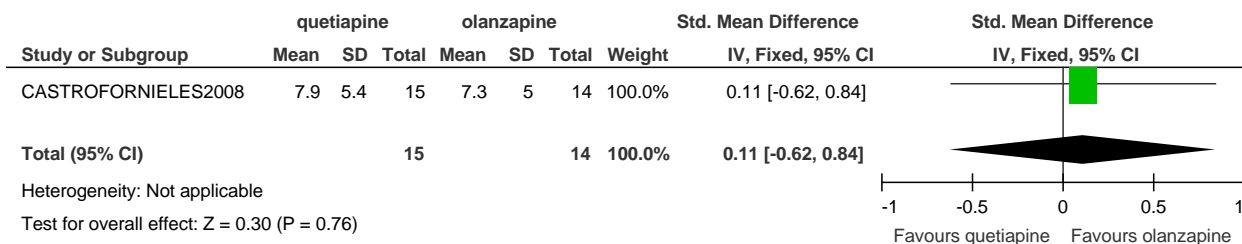


3. Neurological: UKU

3.1 Quetiapine versus risperidone: post-treatment



3.2 Quetiapine versus olanzapine: post-treatment



3.3 Olanzapine (SOT) versus risperidone: post-treatment

