

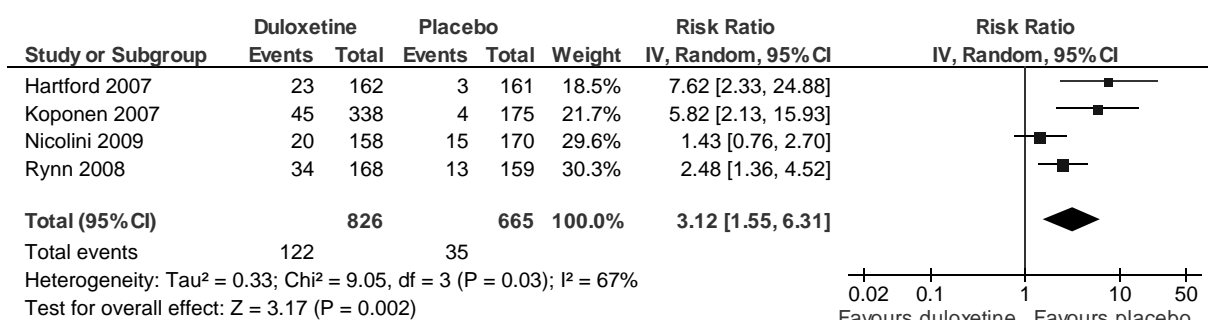
## Appendix 16c: Pharmacological interventions forest plots

Antidepressants versus placebo for GAD.....	2
Benzodiazepine versus placebo for GAD.....	18
Head-to-head trials of pharmacological interventions.....	32
Antidepressants versus other pharmacological interventions.....	36
Other pharmacological interventions (other than antidepressants).....	42
Comparing the effectiveness of different dosages.....	46
Maintenance treatment.....	66
Augmentation.....	70

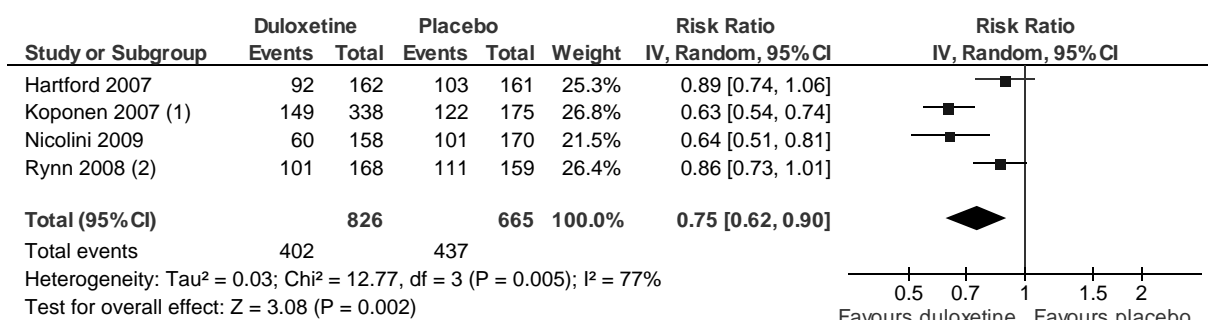
# 1 Antidepressants versus Placebo for GAD

## 1.1 Duloxetine versus Placebo

### 1.2 Discontinuation due to adverse events



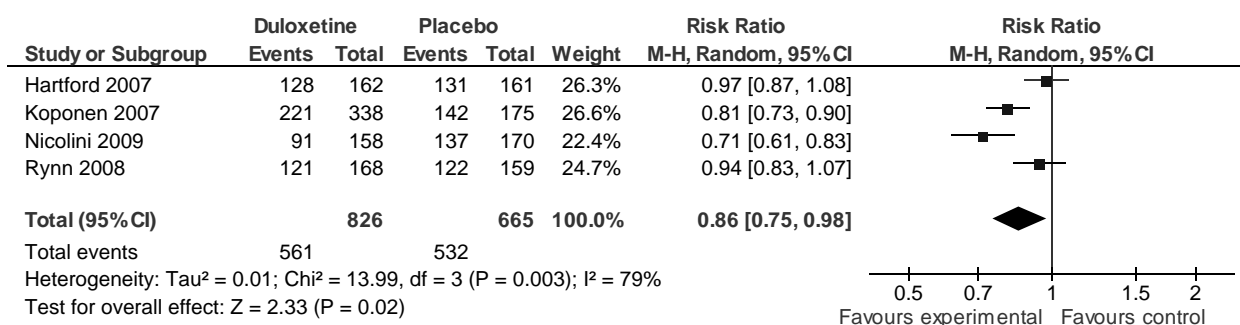
### 1.3 Non-Response



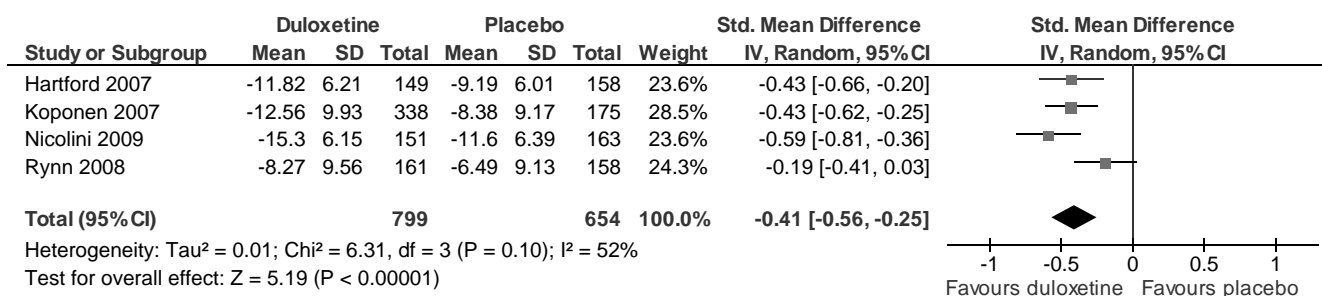
(1) changed

(2) changed

### 1.4 Non-remission

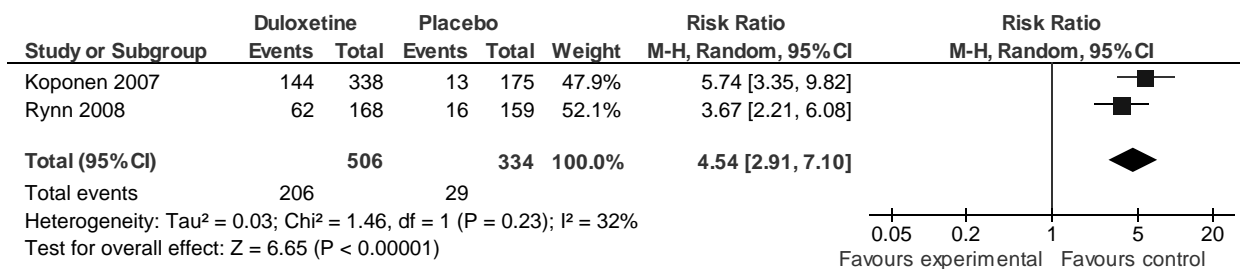


### 1.5 HAM-A Mean change from baseline

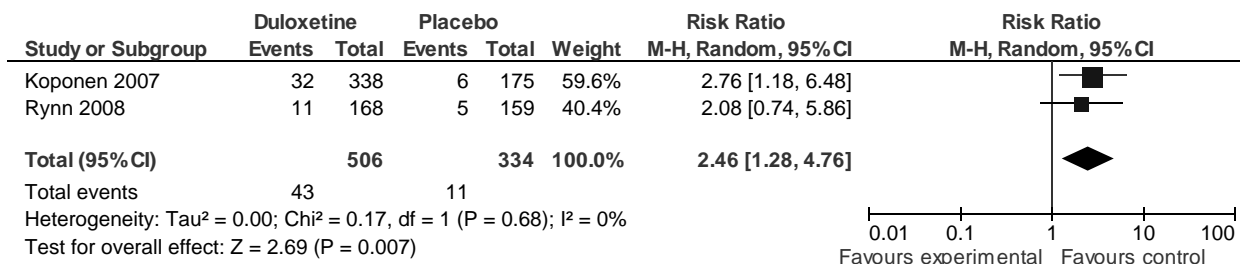


# 1 Antidepressants versus Placebo for GAD

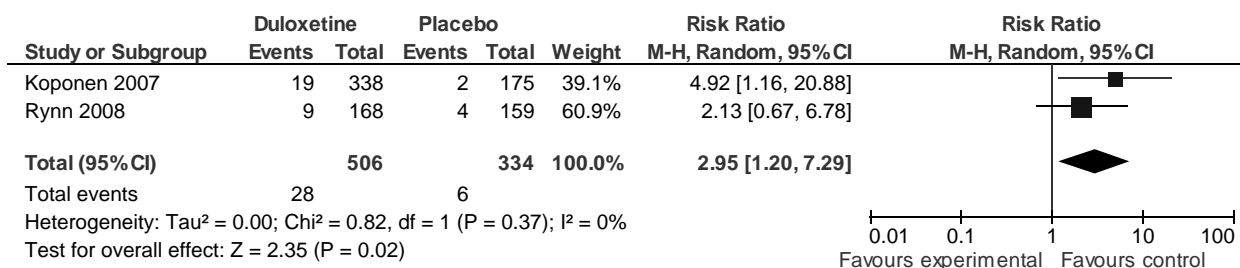
## 1.11 Nausea



## 1.12 Insomnia

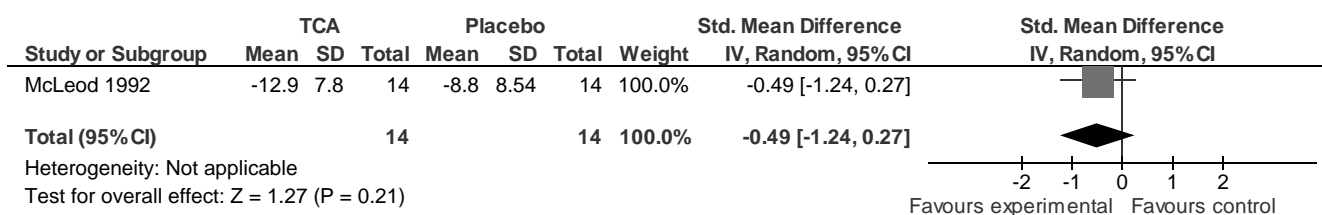


## 1.13 Sexual problems



## 2 Imipramine versus Placebo

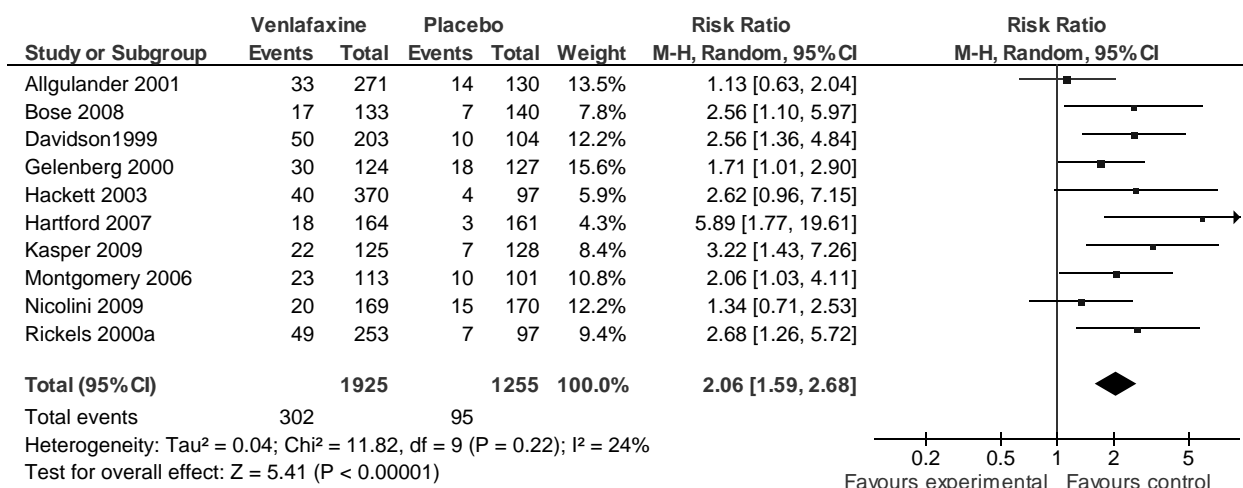
### 2.1 HAM-A



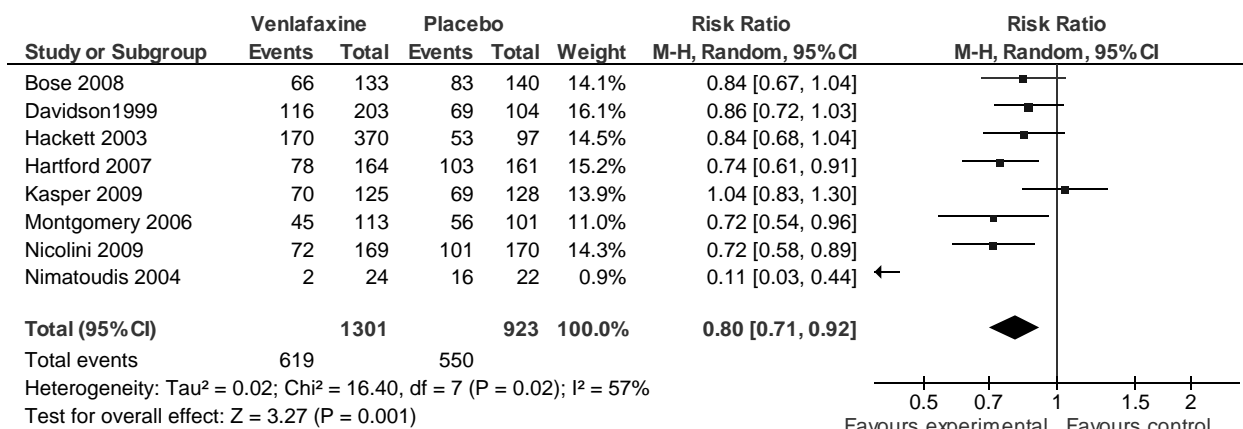
## 3 Venlafaxine versus Placebo

# 1 Antidepressants versus Placebo for GAD

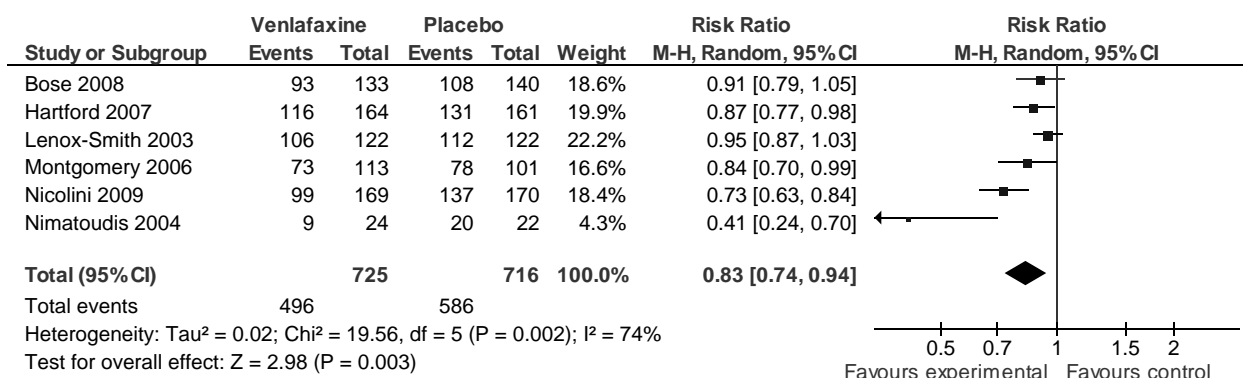
## 3.2 Discontinuation due to adverse events



## 3.3 Non-response

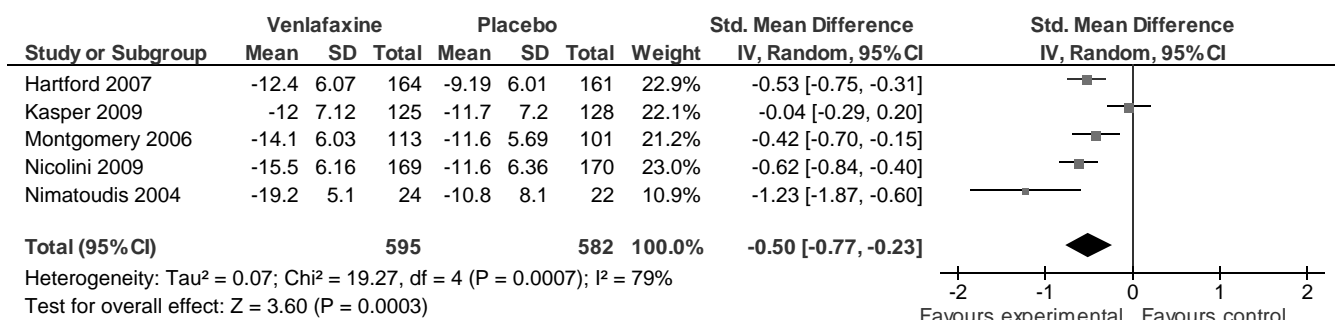


## 3.5 Non-remission

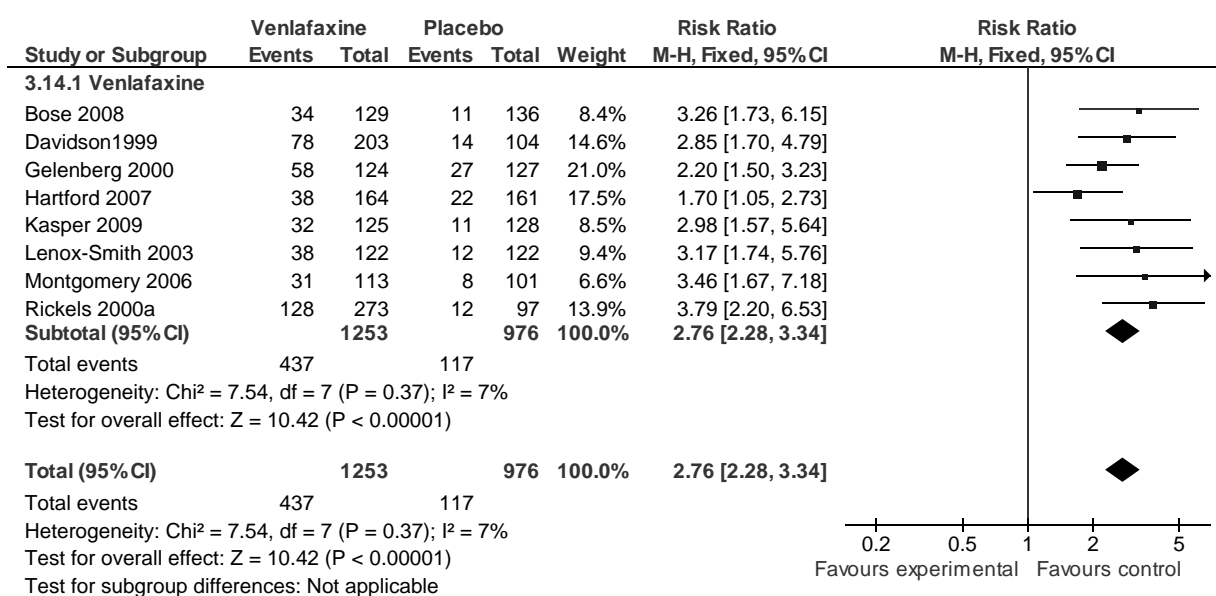


# 1 Antidepressants versus Placebo for GAD

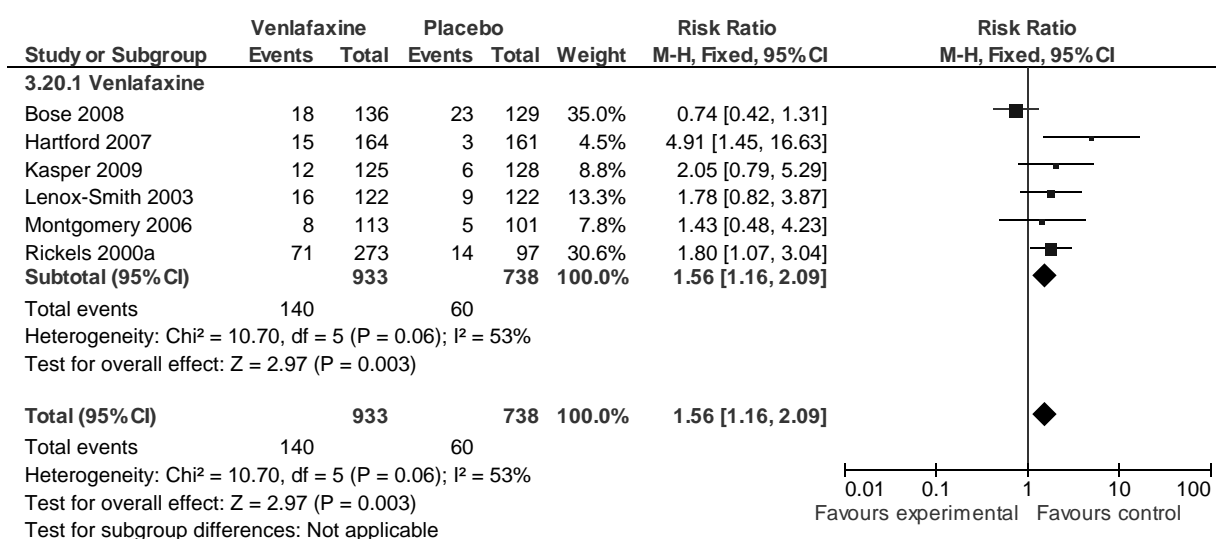
## 3.7 HAM-A



## 3.14 Nausea

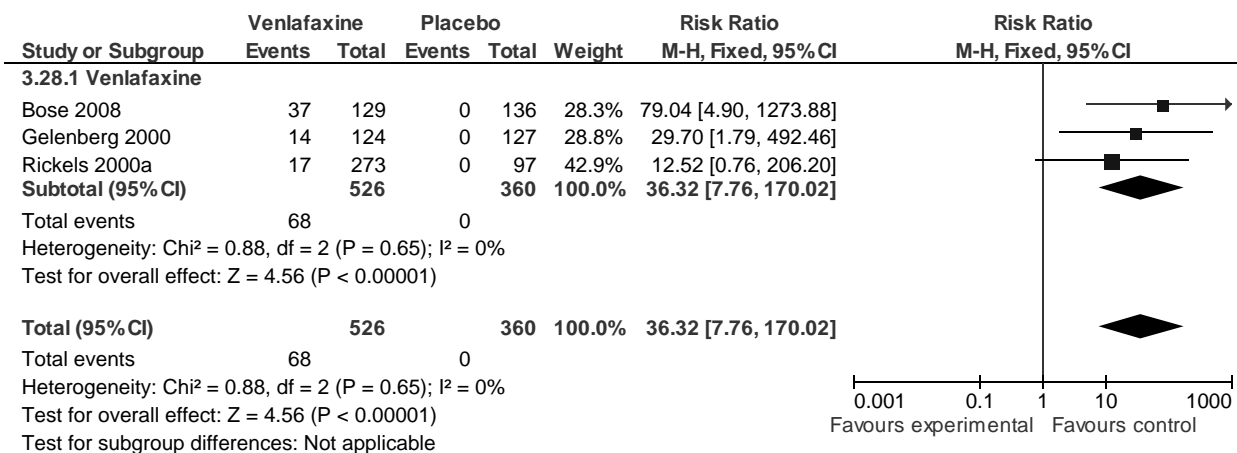


## 3.20 Insomnia



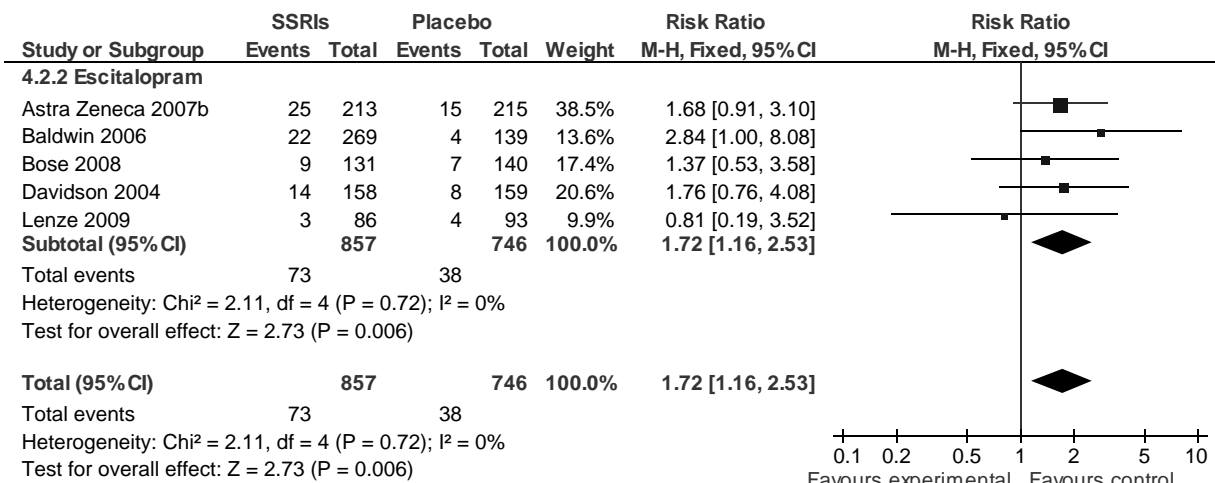
# 1 Antidepressants versus Placebo for GAD

## 3.28 Ejaculation disorder

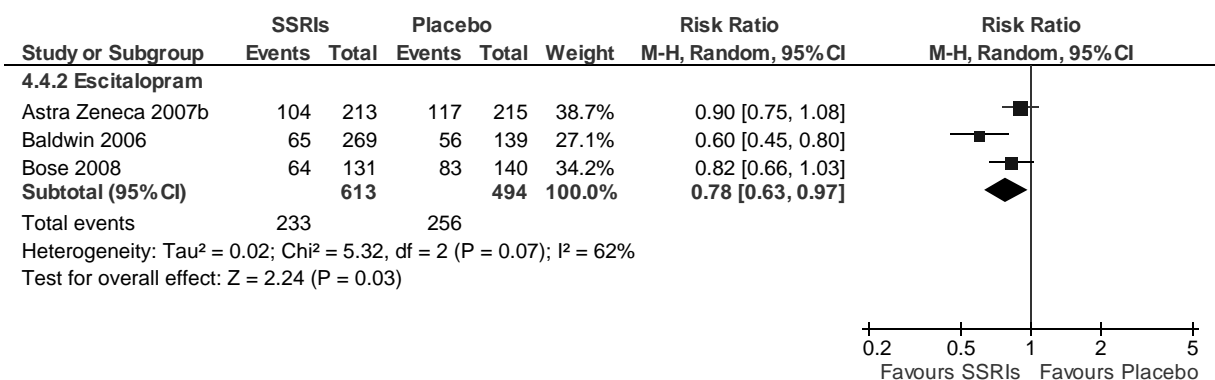


## 4 Escitalopram versus Placebo

### 4.2 Discontinuation due to adverse events

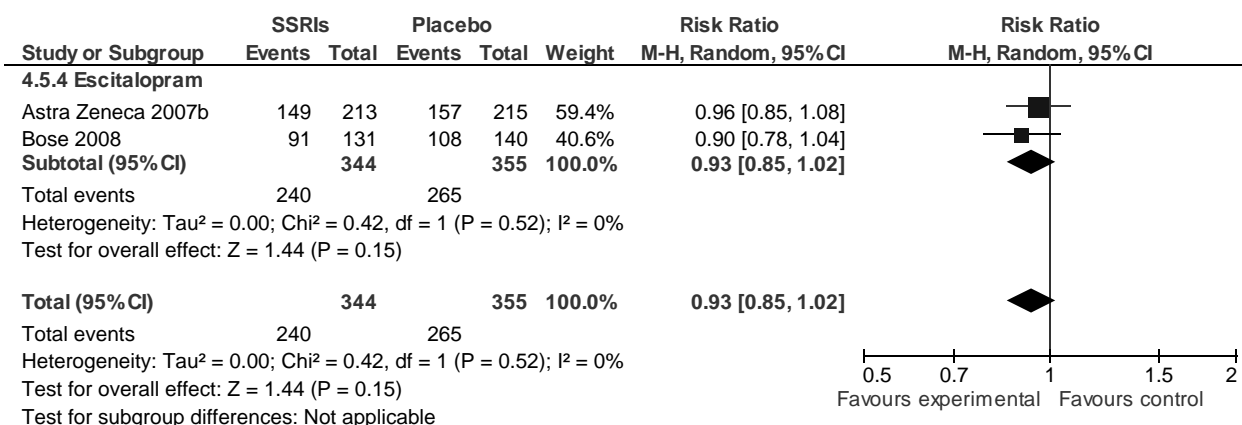


### 4.4 Non-response

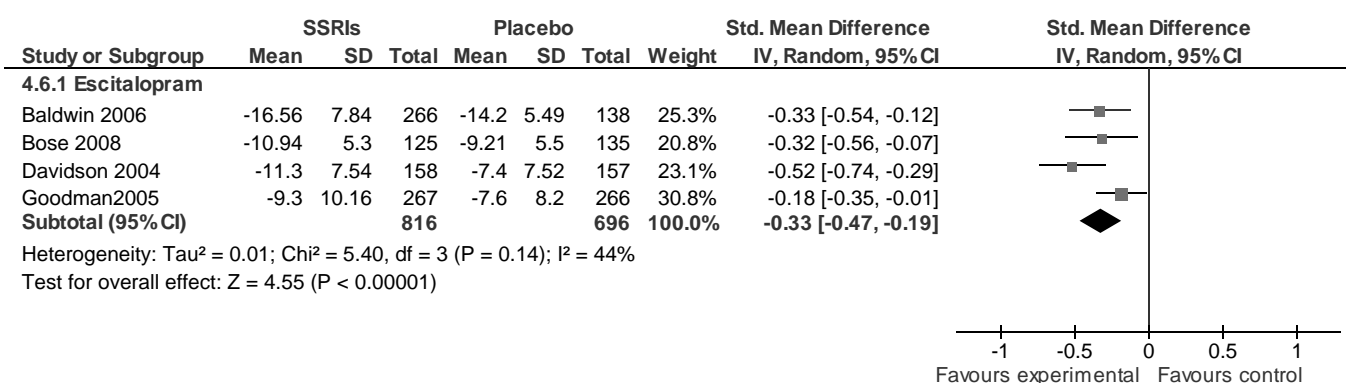


# 1 Antidepressants versus Placebo for GAD

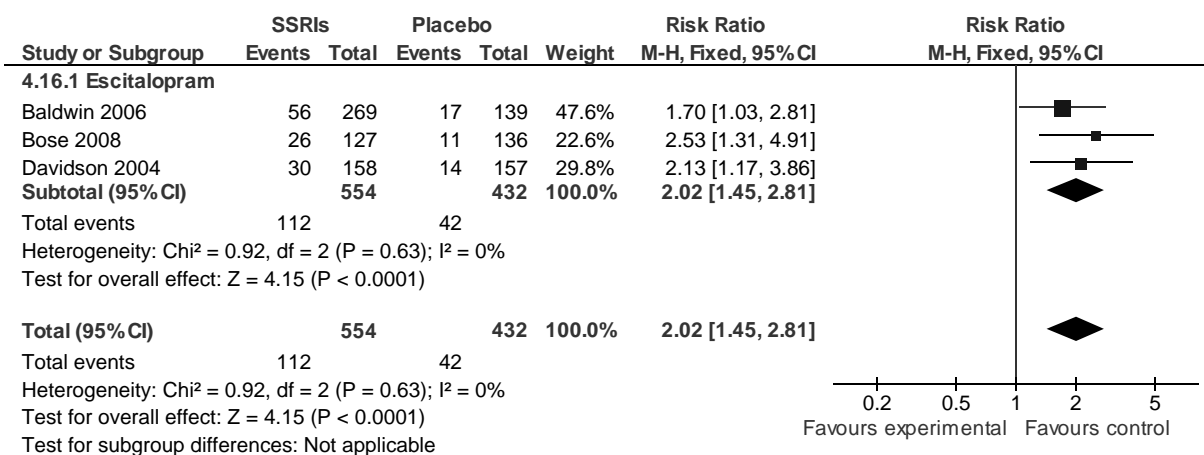
## 4.5 Non-remission



## 4.6 HAM-A (change from baseline)

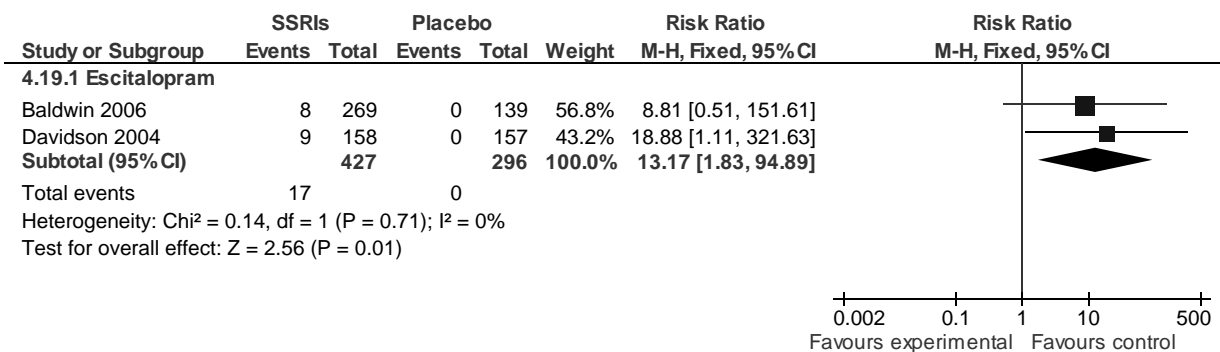


## 4.16 Nausea

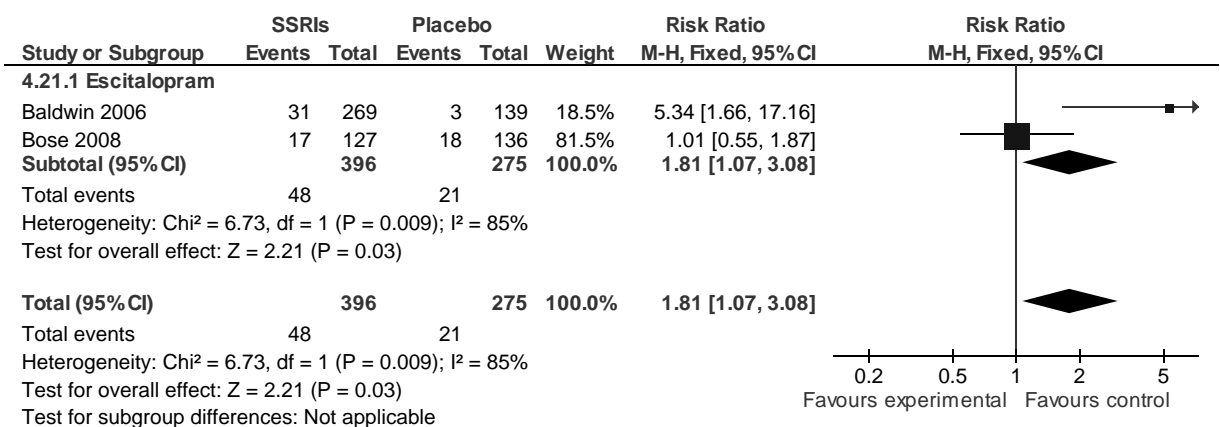


# 1 Antidepressants versus Placebo for GAD

## 4.19 Anorgasmia

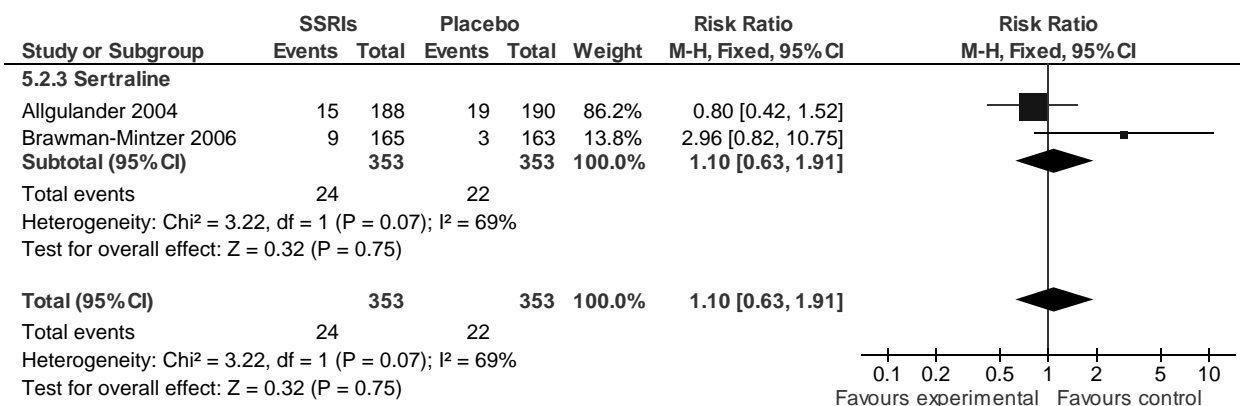


## 4.21 Insomnia



## 5 Sertraline versus Placebo

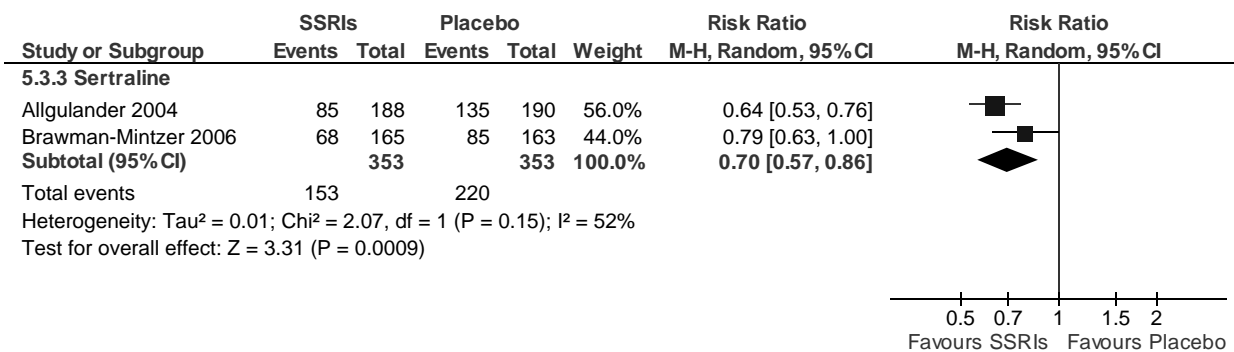
### 5.2 Discontinuation due to adverse events



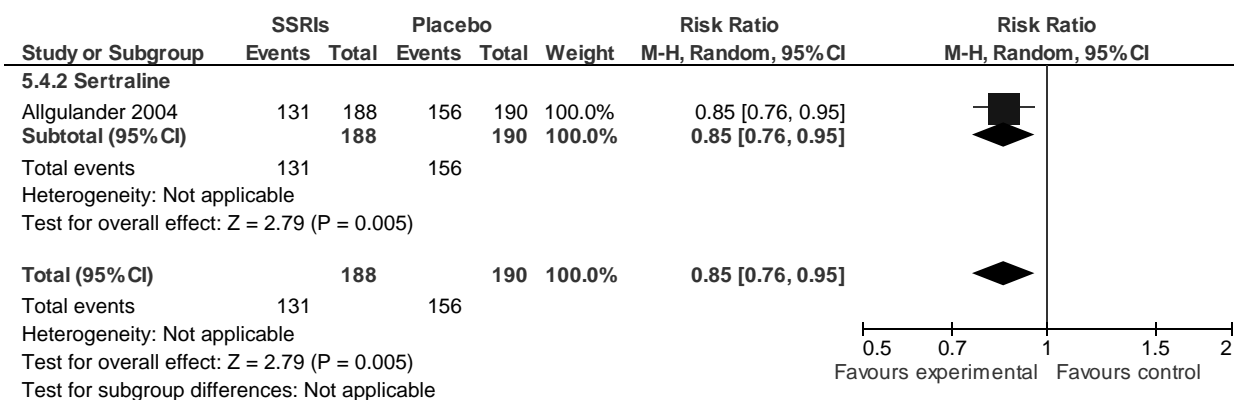


# 1 Antidepressants versus Placebo for GAD

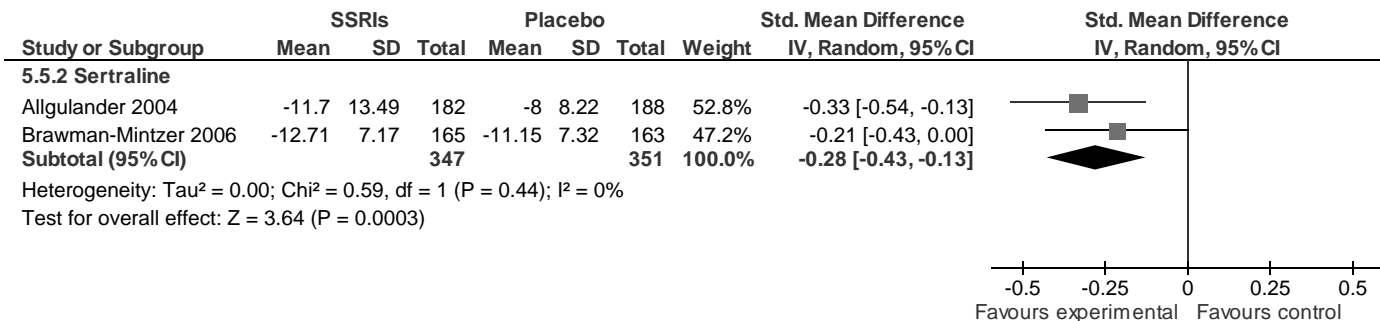
## 5.3 Non-response



## 5.4 Non-remission

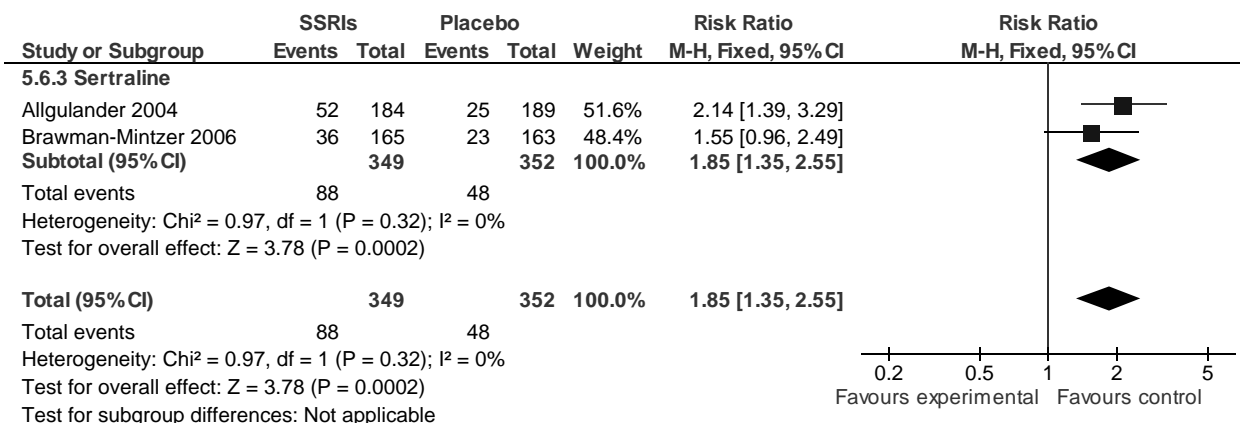


## 5.5 HAM-A (change from baseline)

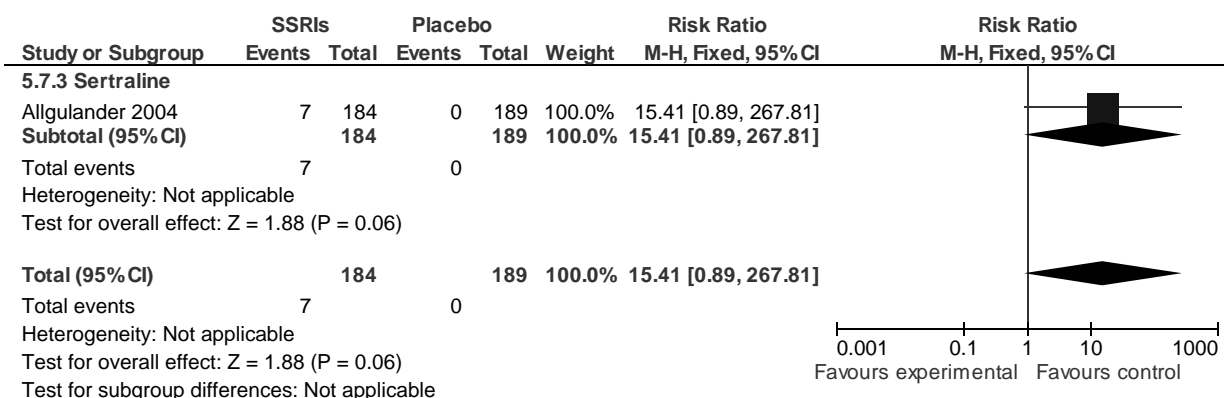


# 1 Antidepressants versus Placebo for GAD

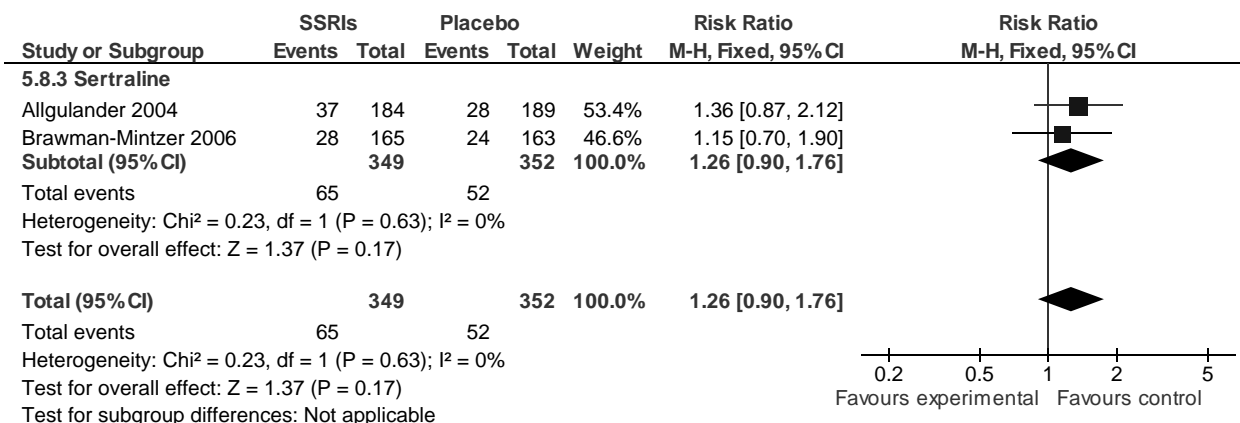
## 5.6 Nausea



## 5.7 Ejaculation disorder



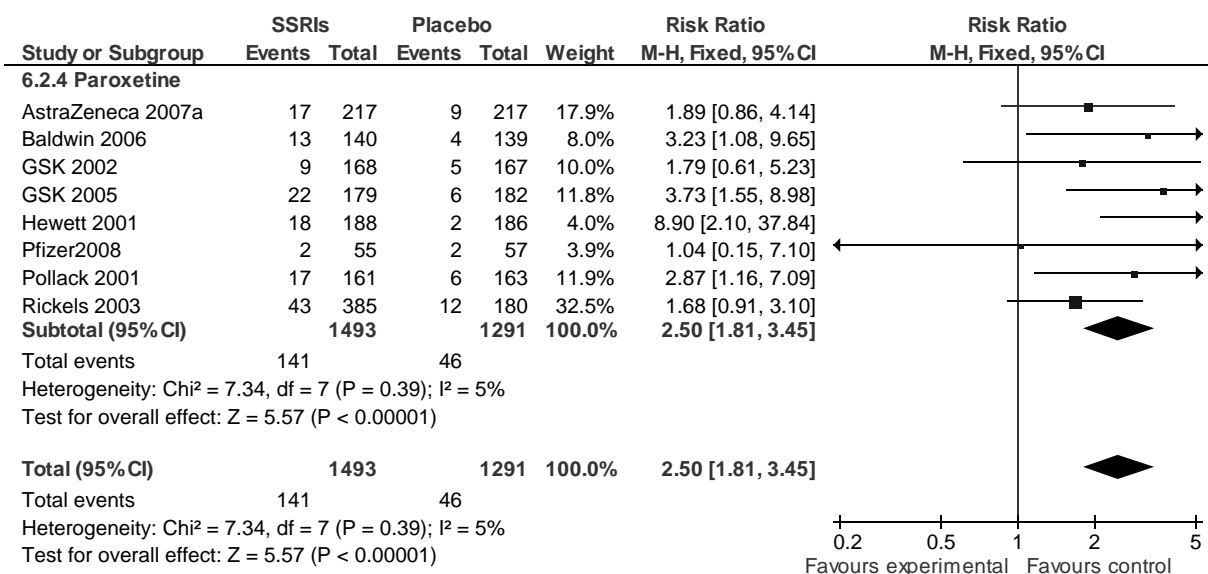
## 5.8 Insomnia



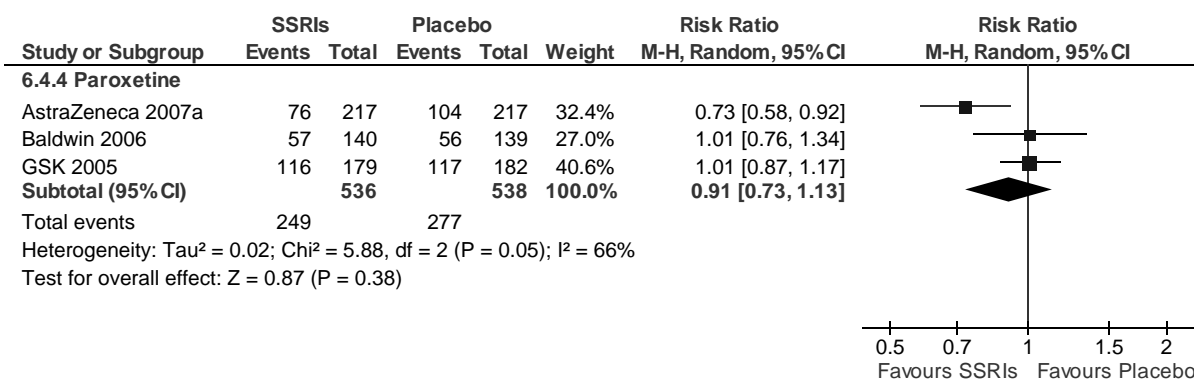
## 6 Paroxetine versus Placebo

# 1 Antidepressants versus Placebo for GAD

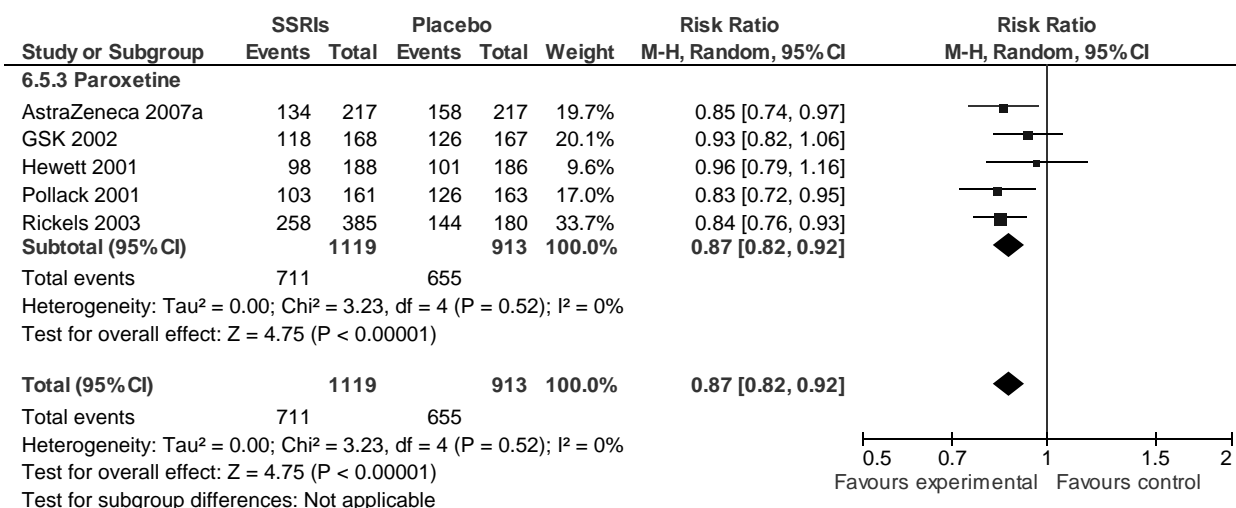
## 6.2 Discontinuation due to adverse events



## 6.4 Non-response

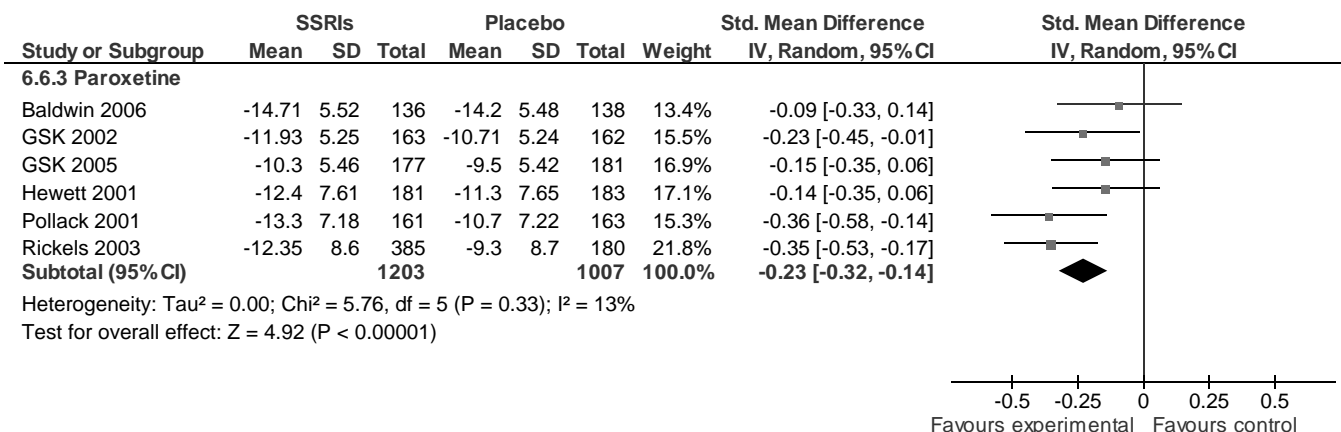


## 6.5 Non-remission

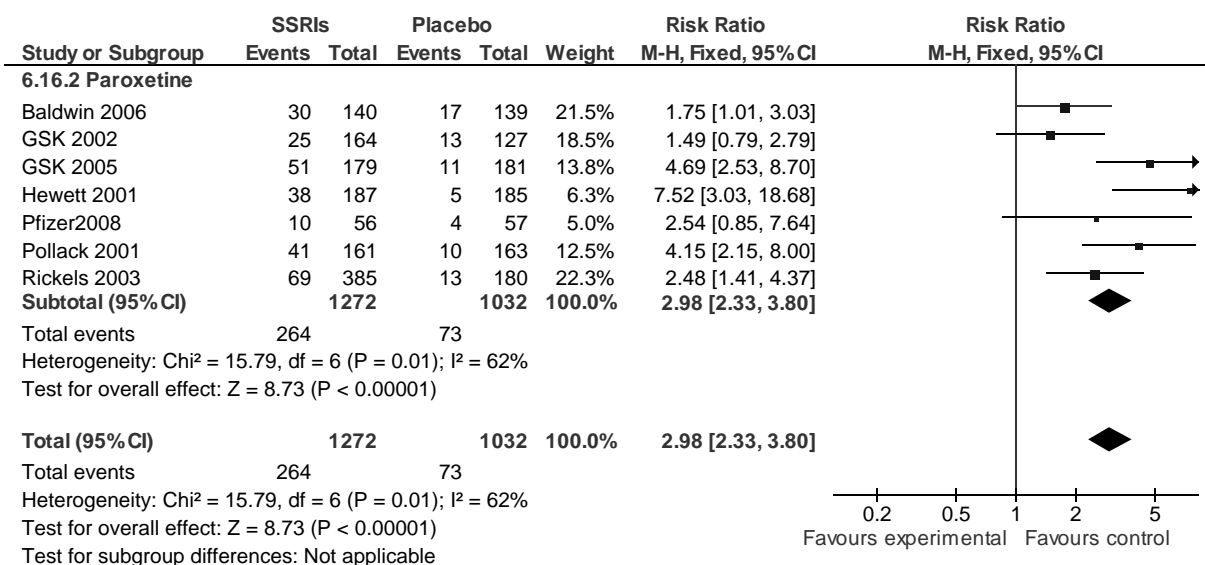


# 1 Antidepressants versus Placebo for GAD

## 6.6 HAM-A (change from baseline)

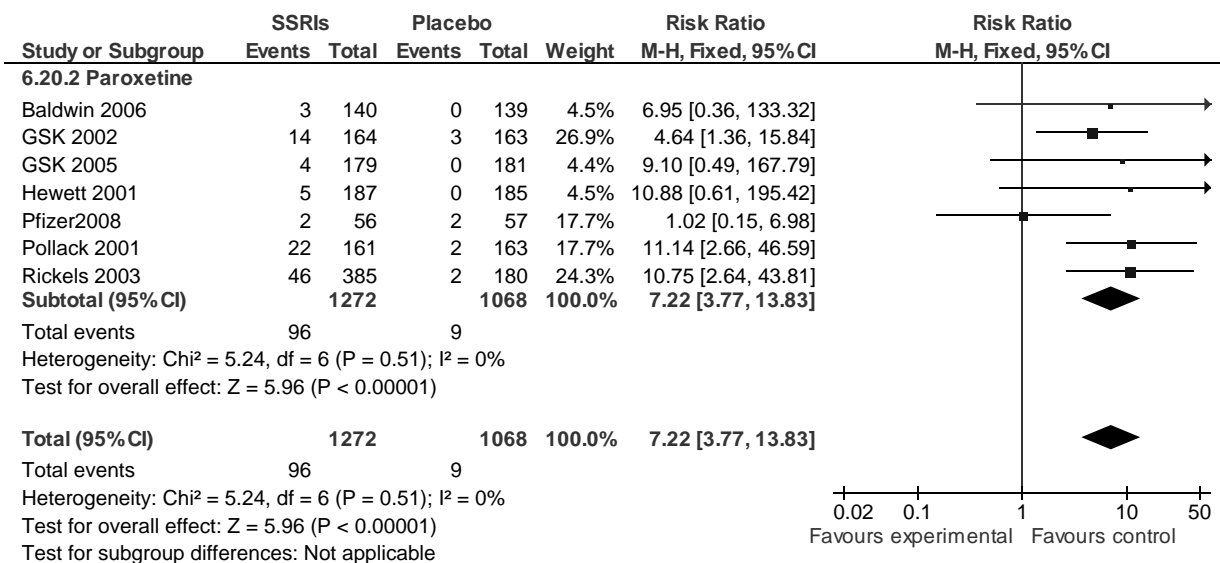


## 6.16 Nausea

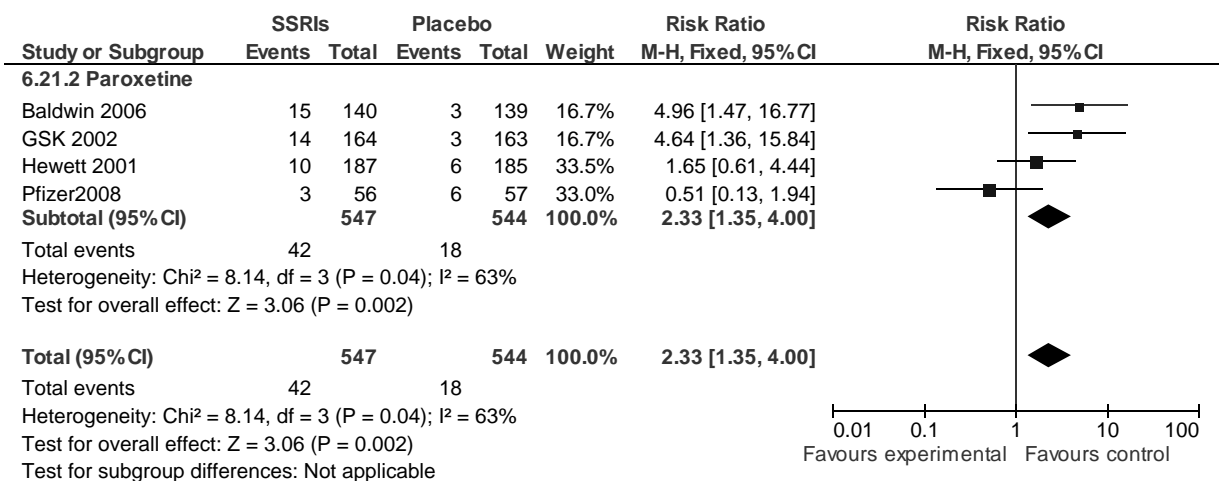


# 1 Antidepressants versus Placebo for GAD

## 6.20 Sexual problem



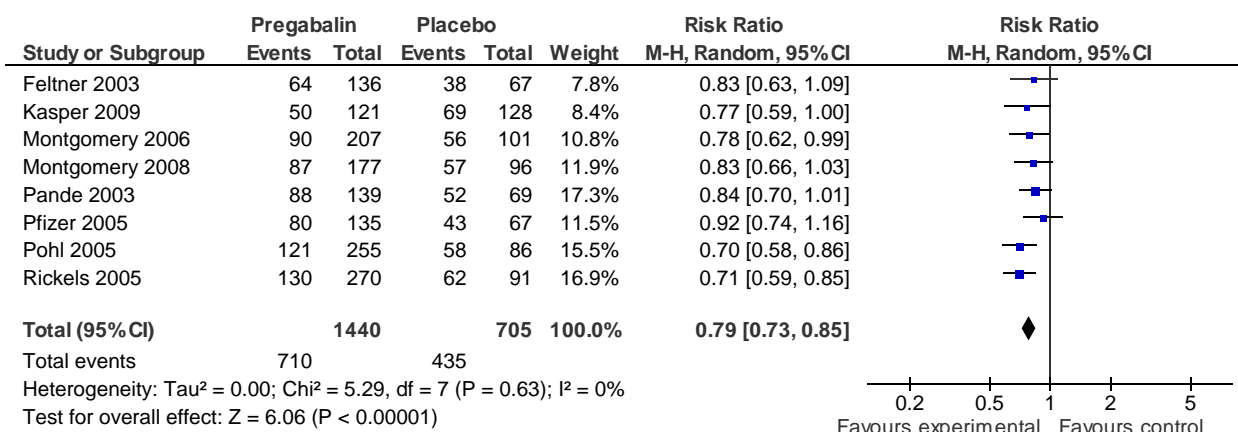
## 6.21 Insomnia



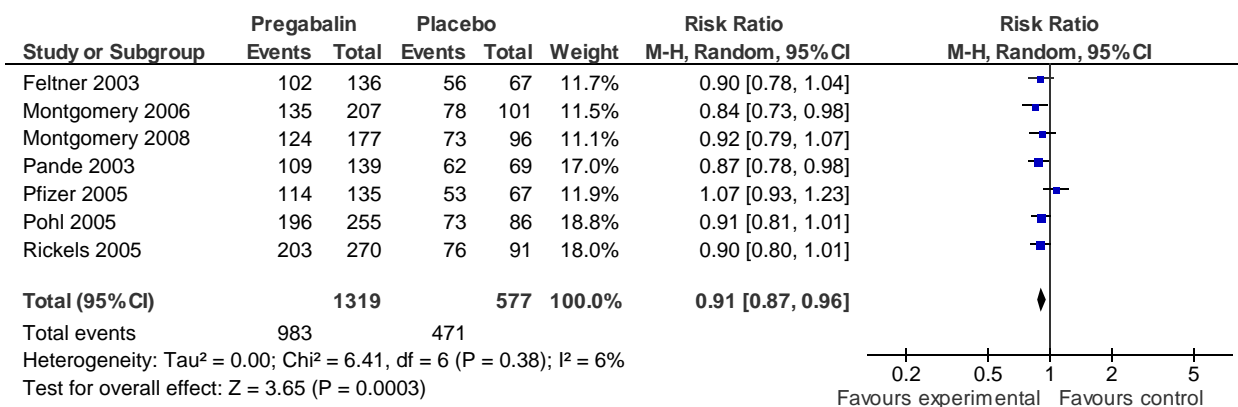
## 7 Pregabalin versus Placebo

## 7 Pregabalin vs Placebo

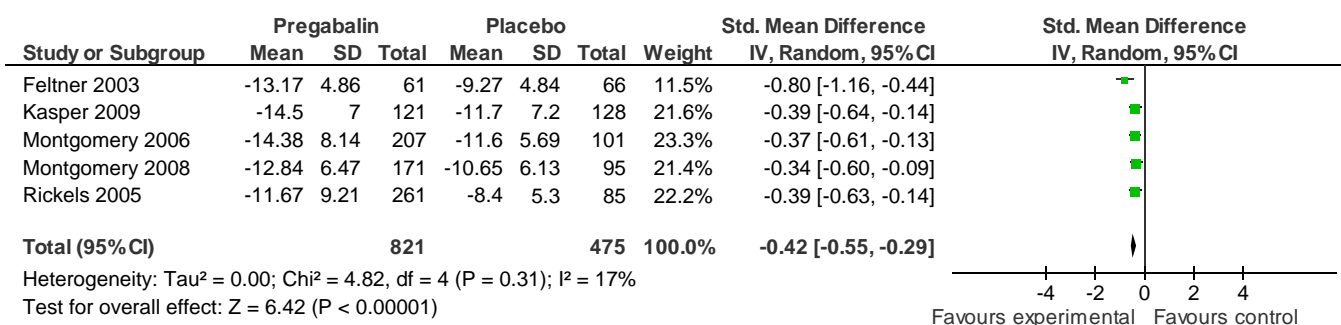
### 7.3 Non-response



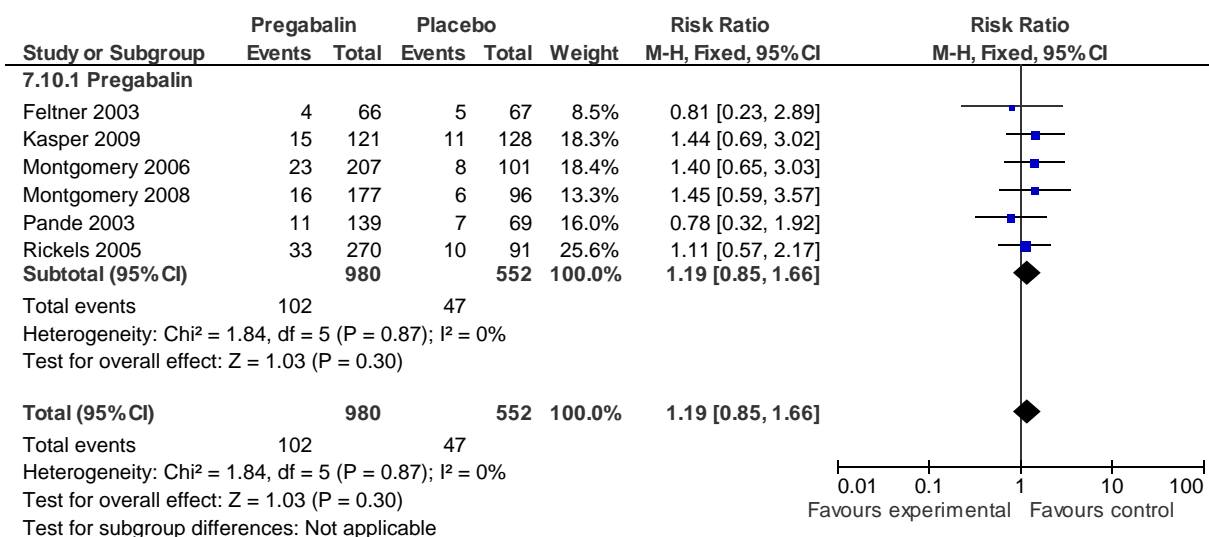
### 7.4 Non-remission



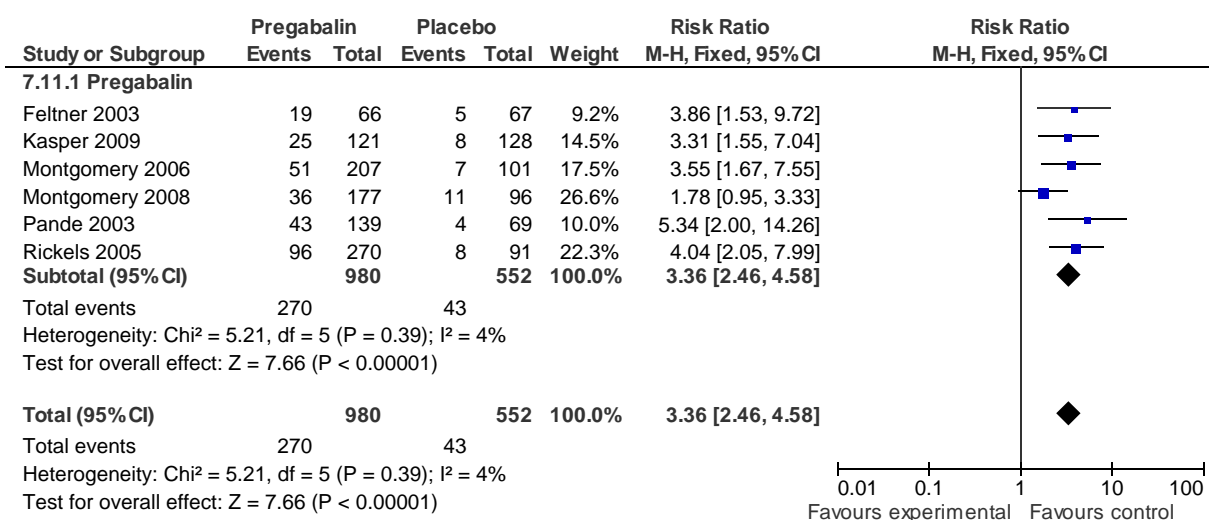
### 7.5 HAM-A



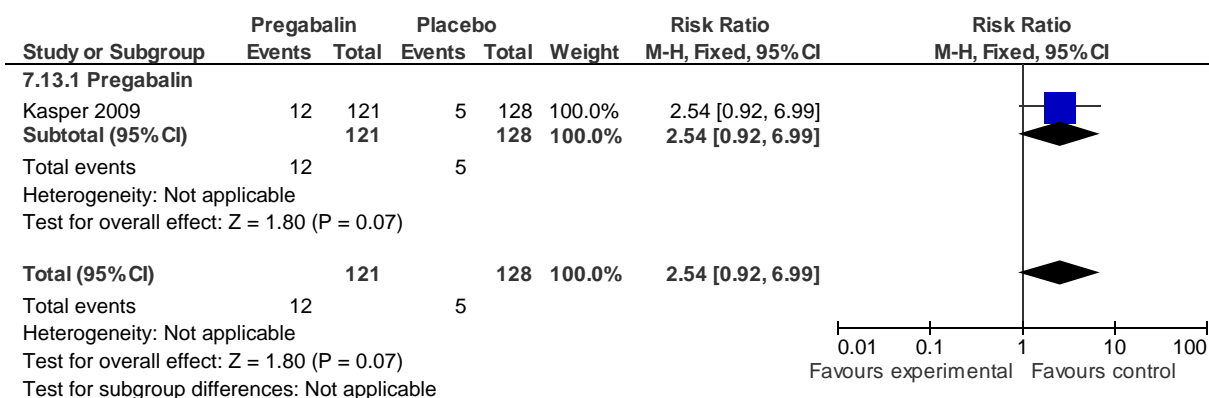
### 7.10 Nausea



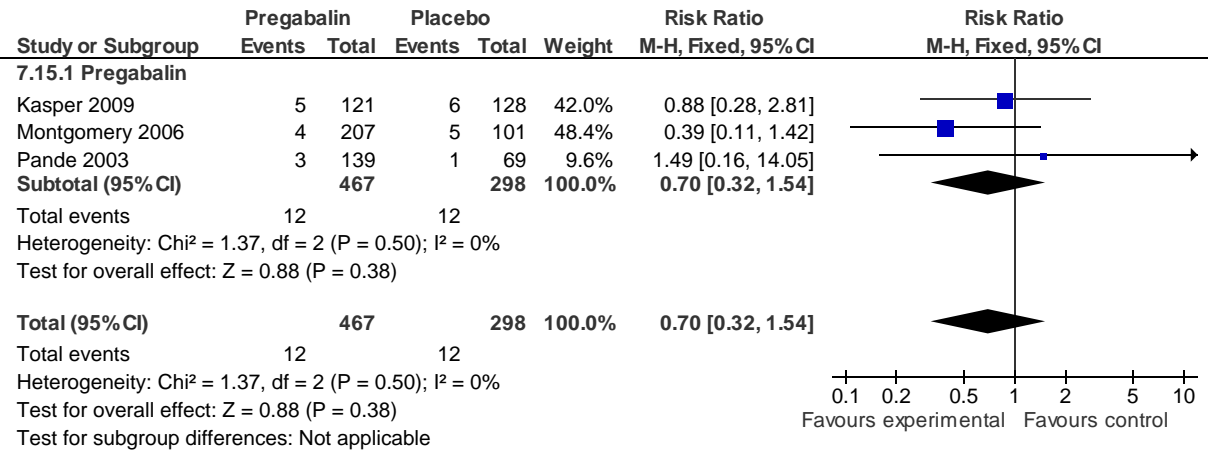
### 7.11 Dizziness



### 7.13 Fatigue



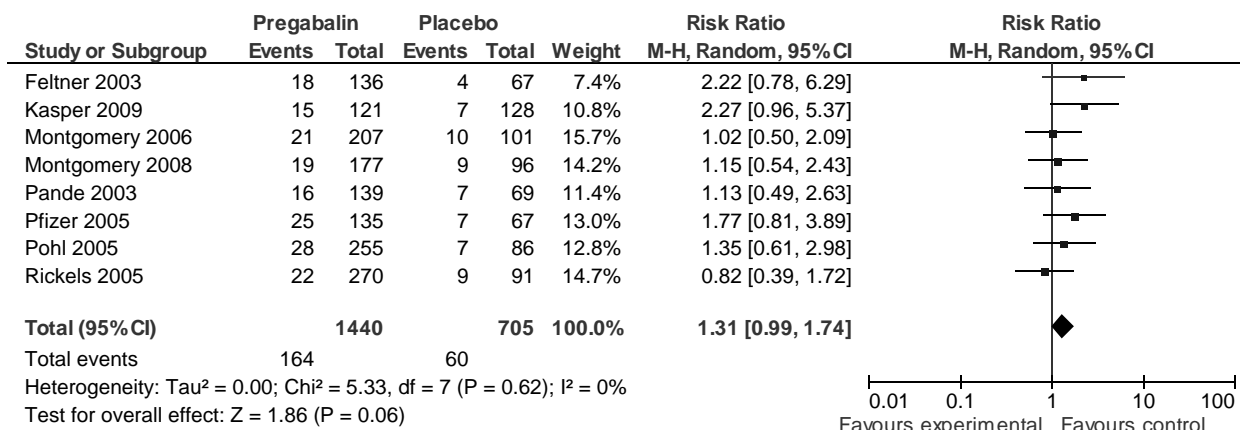
7.15 Insomnia





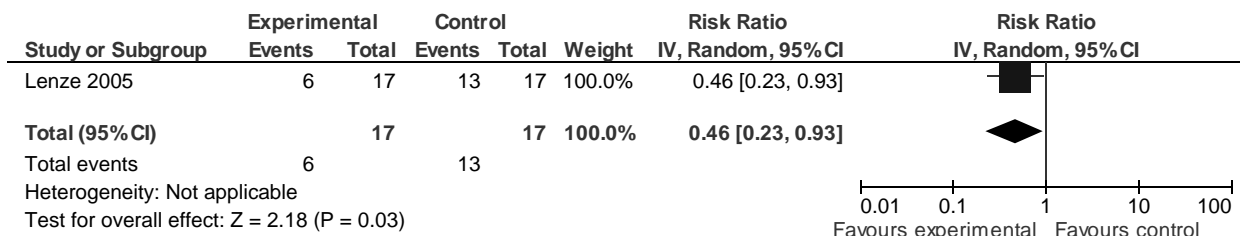
# 1 Antidepressants versus Placebo for GAD

## 7.2 Discontinuation due to adverse events

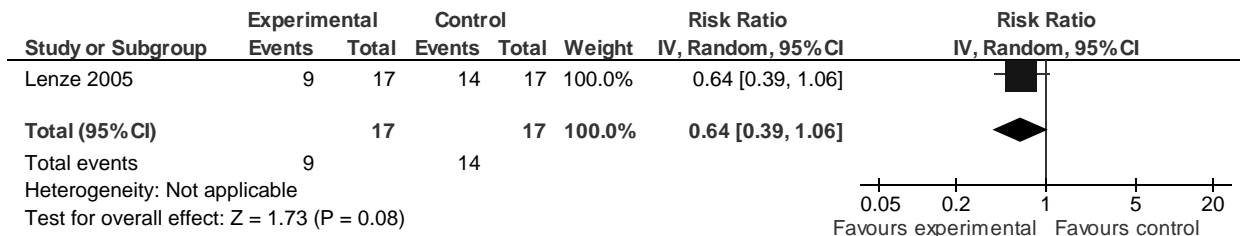


## 35 Citalopram versus Placebo

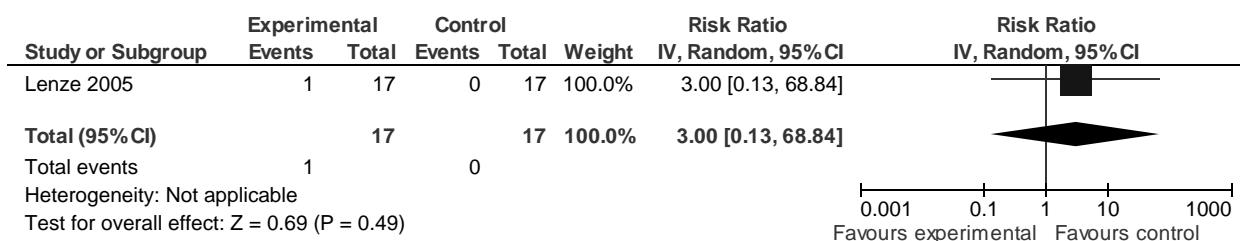
### 35.1 Non-response



### 35.2 Non-remission

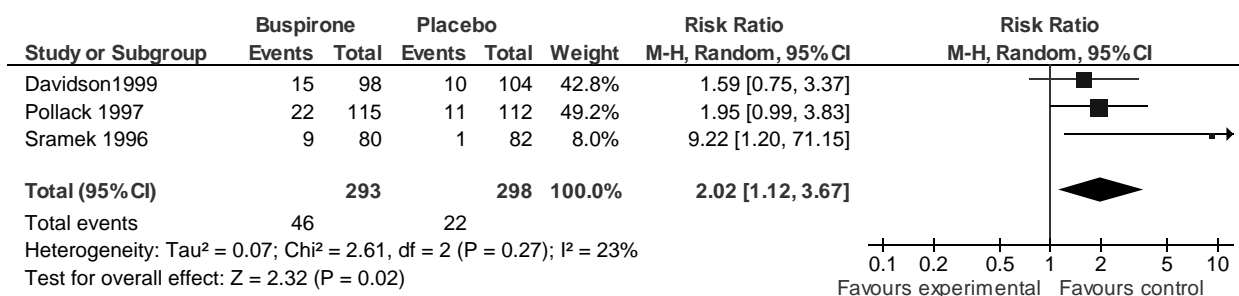


### 35.3 Discontinuation due to adverse events

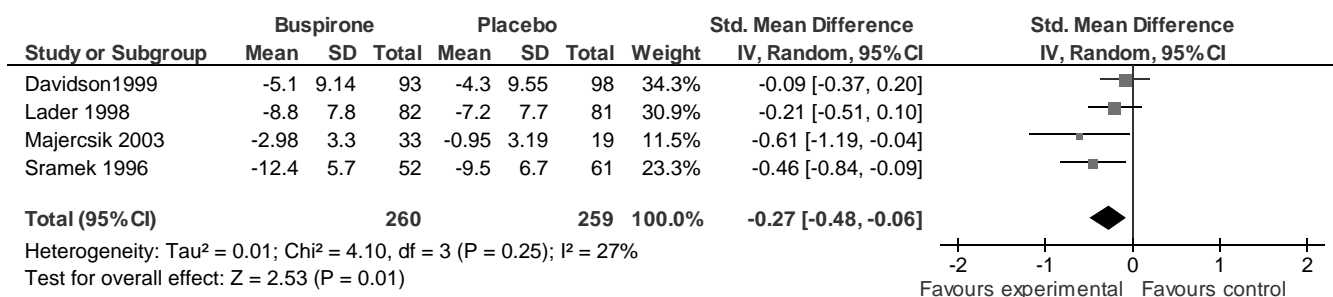


## 8 Buspirone vs Placebo

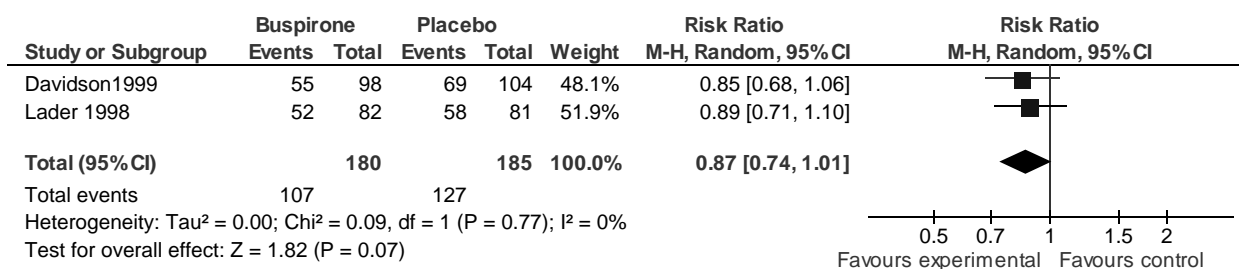
### 8.2 Discontinuation due to adverse events



### 8.3 HAM-A

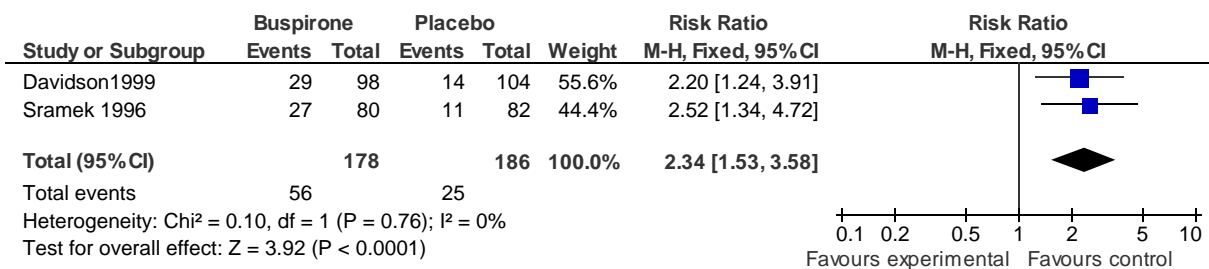


### 8.4 Non-response

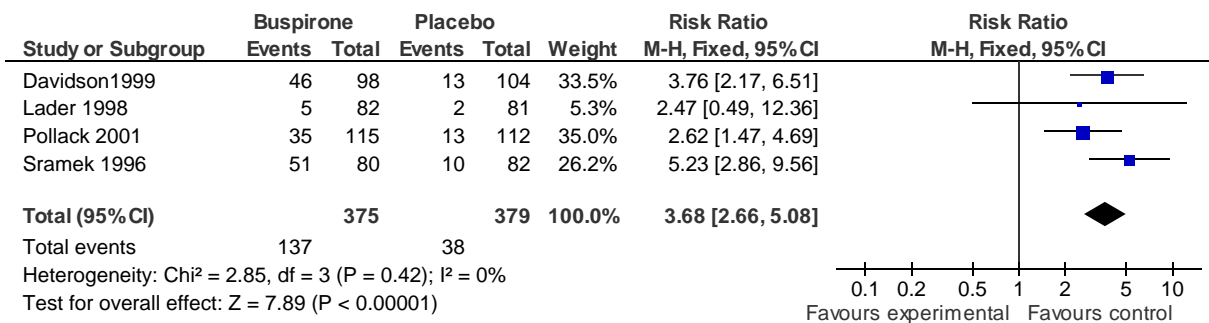


## 2 Benzodiazepine versus Placebo for GAD

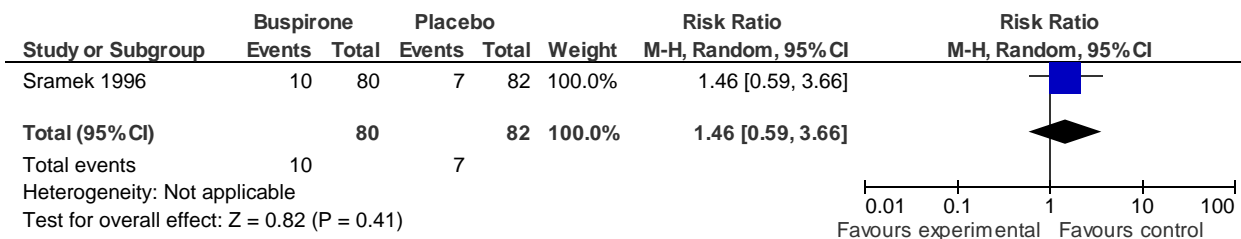
### 8.5 Nausea



### 8.6 Dizziness



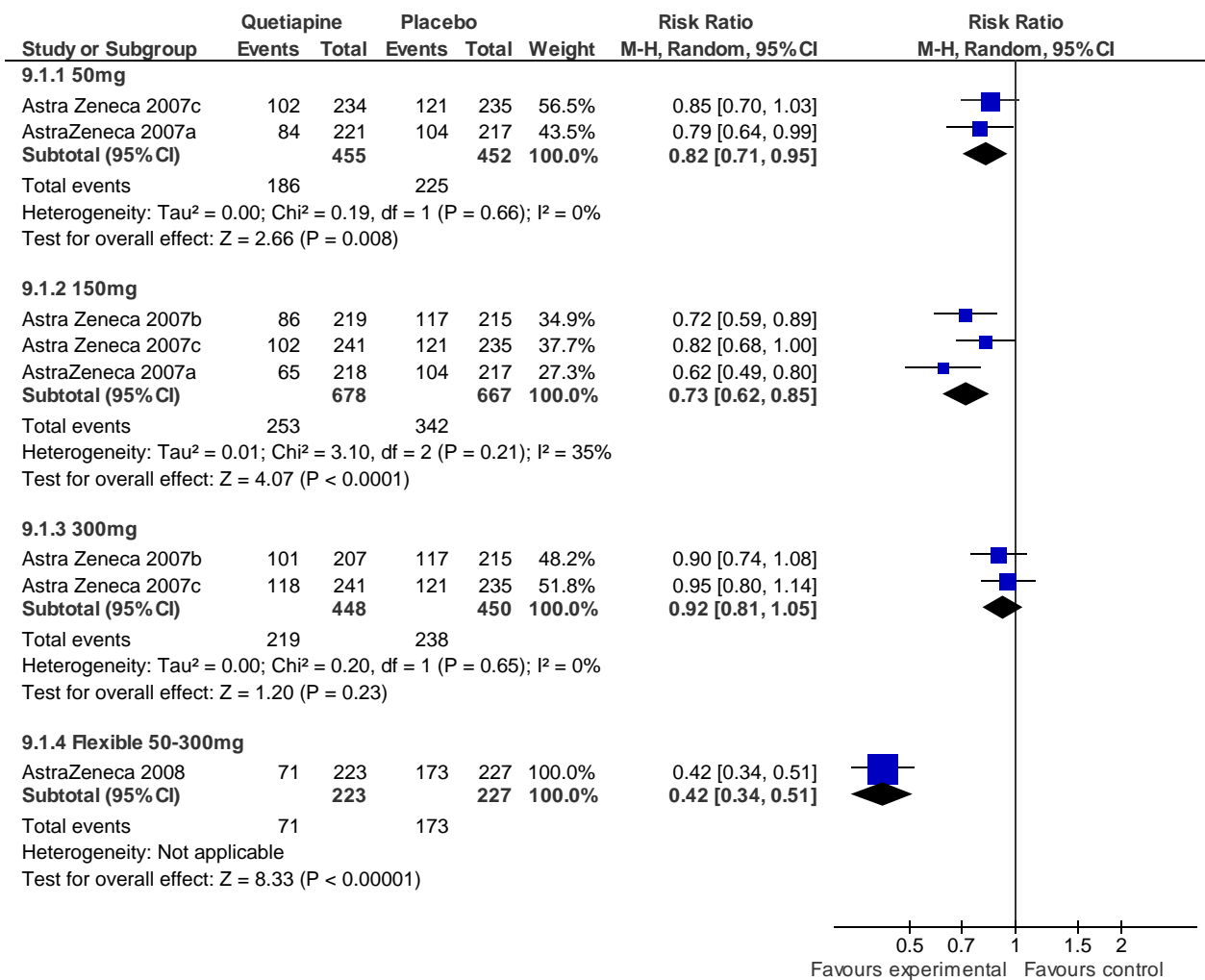
### 8.11 Insomnia



## 9 Quetiapine versus Placebo

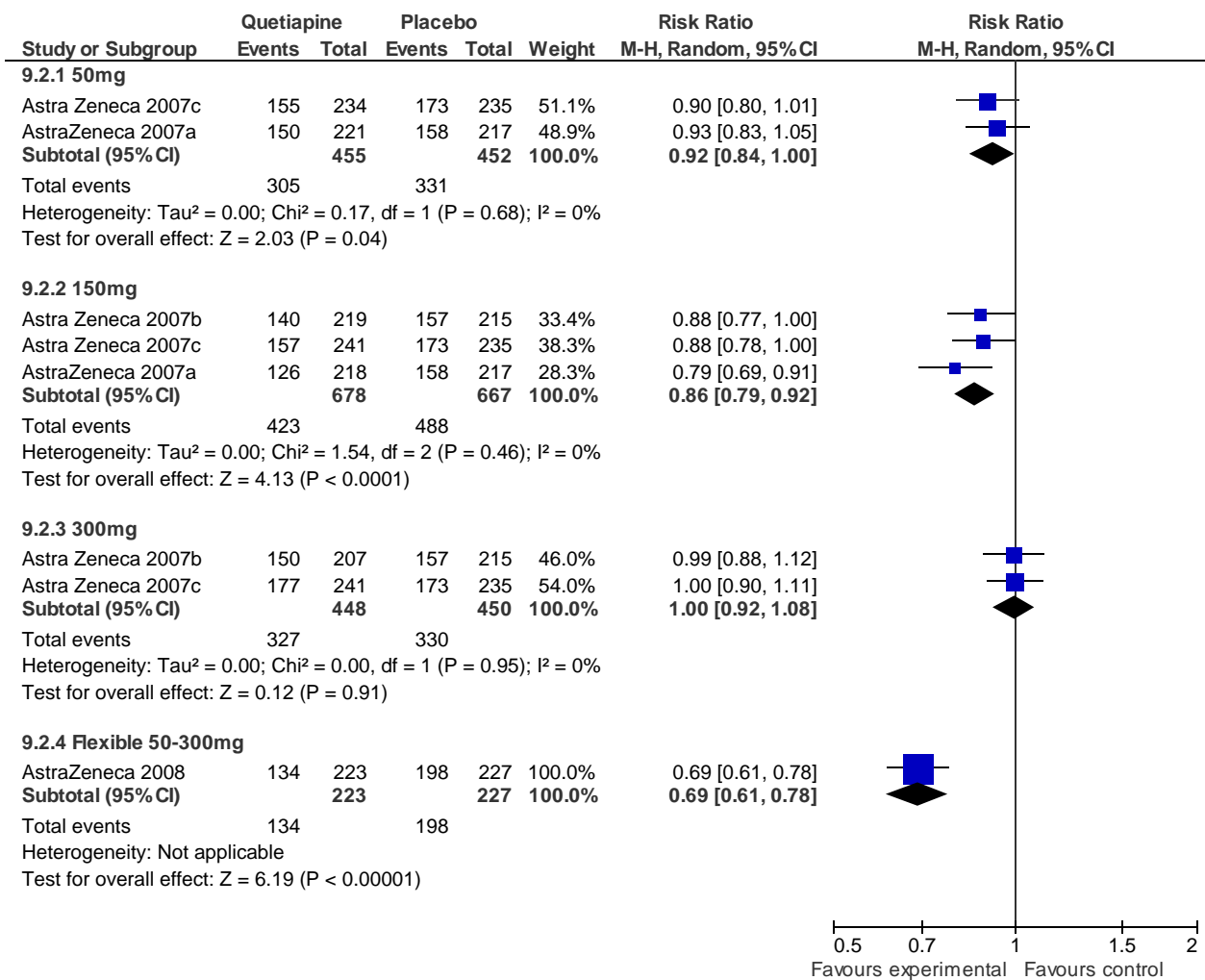
## 2 Benzodiazepine versus Placebo for GAD

### 9.1 Non-response



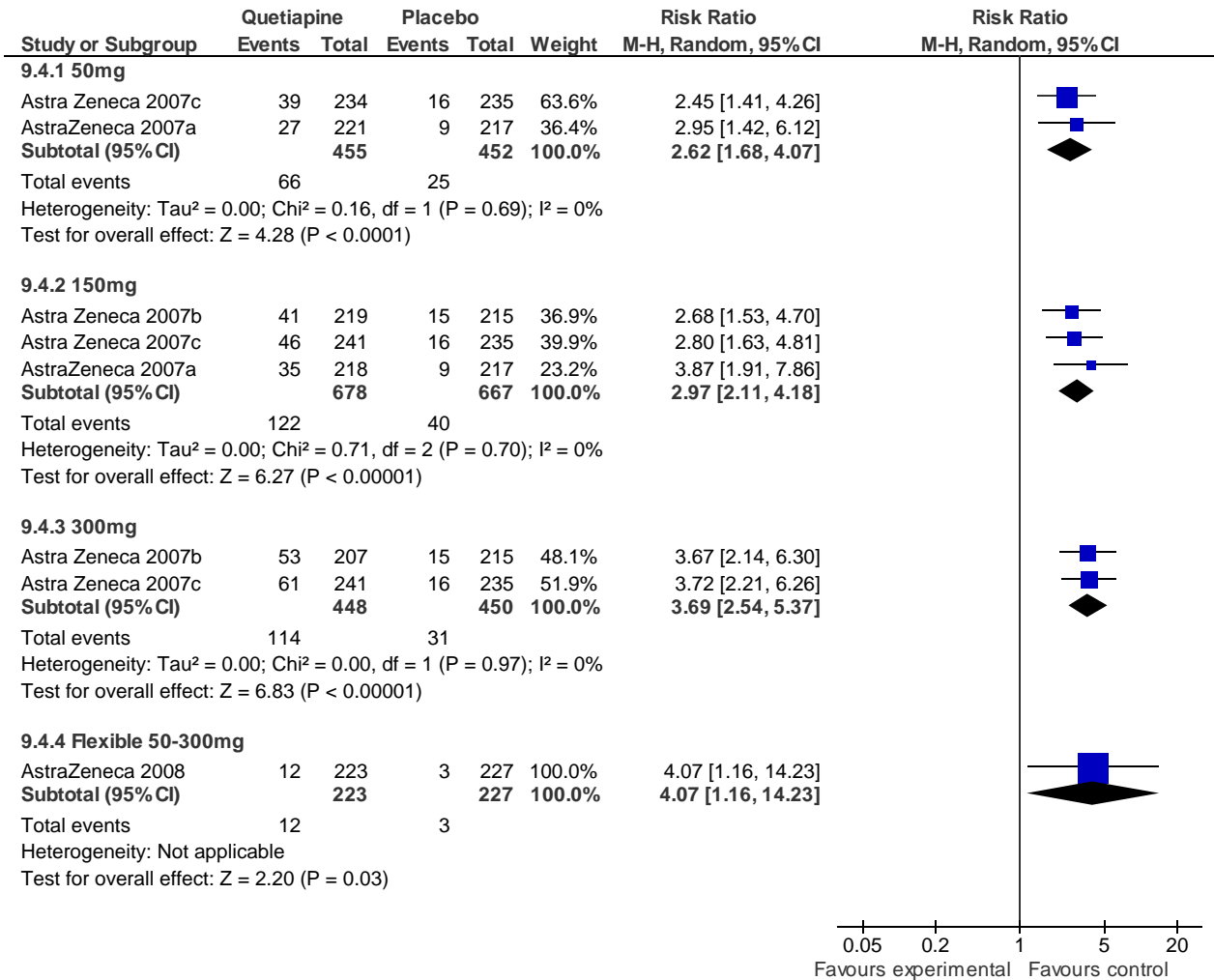
## 2 Benzodiazepine versus Placebo for GAD

### 9.2 Non-remission



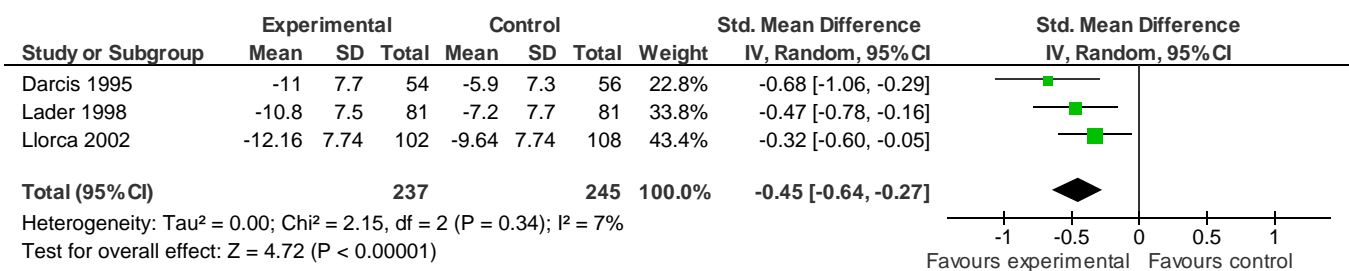
## 2 Benzodiazepine versus Placebo for GAD

### 9.4 Discontinuation due to adverse events



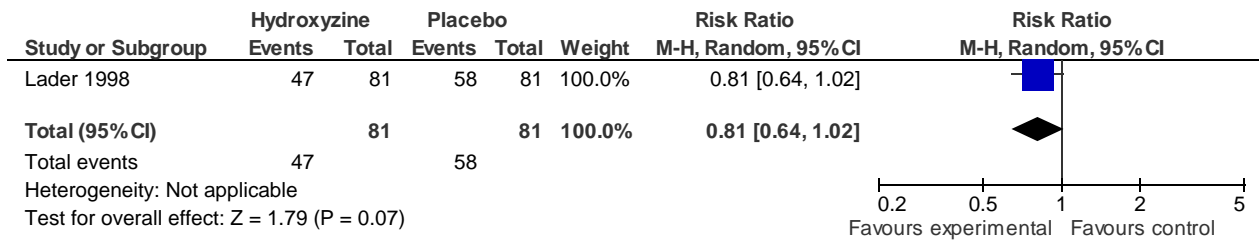
### 10 Hydroxyzine versus Placebo

#### 10.1 HAM-A

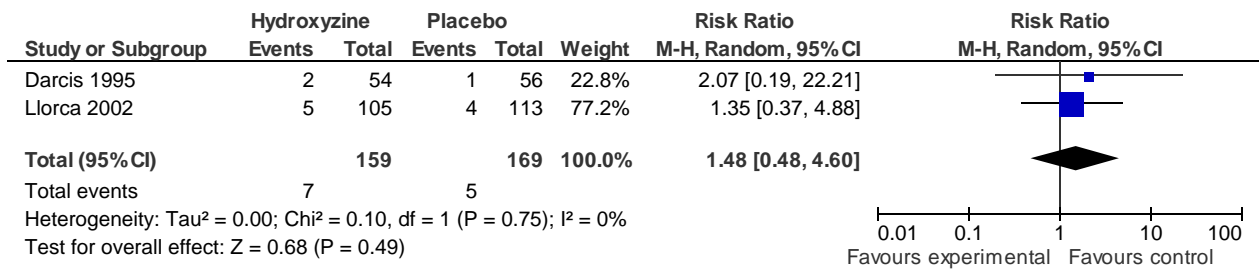


## 2 Benzodiazepine versus Placebo for GAD

### 10.2 Non-response

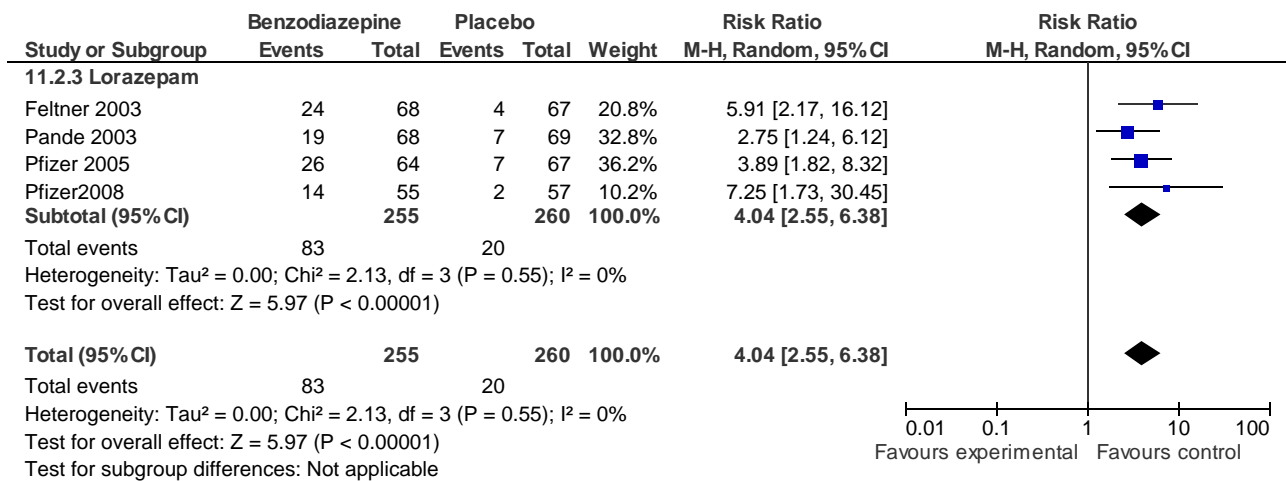


### 10.4 Discontinuation due to adverse events



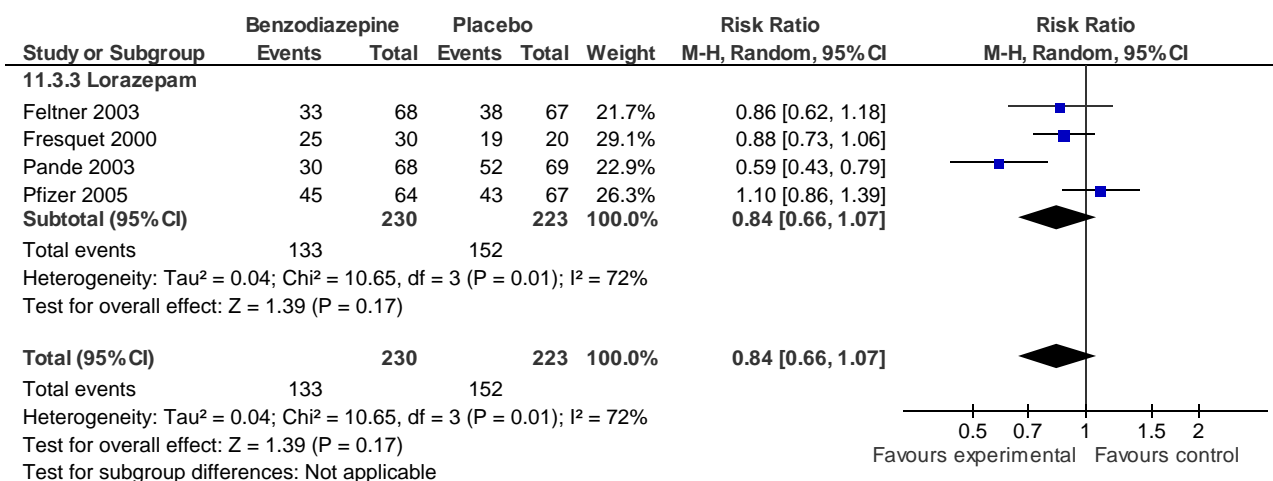
## 11 Lorazepam versus Placebo

### 11.2 Discontinuation due to adverse events

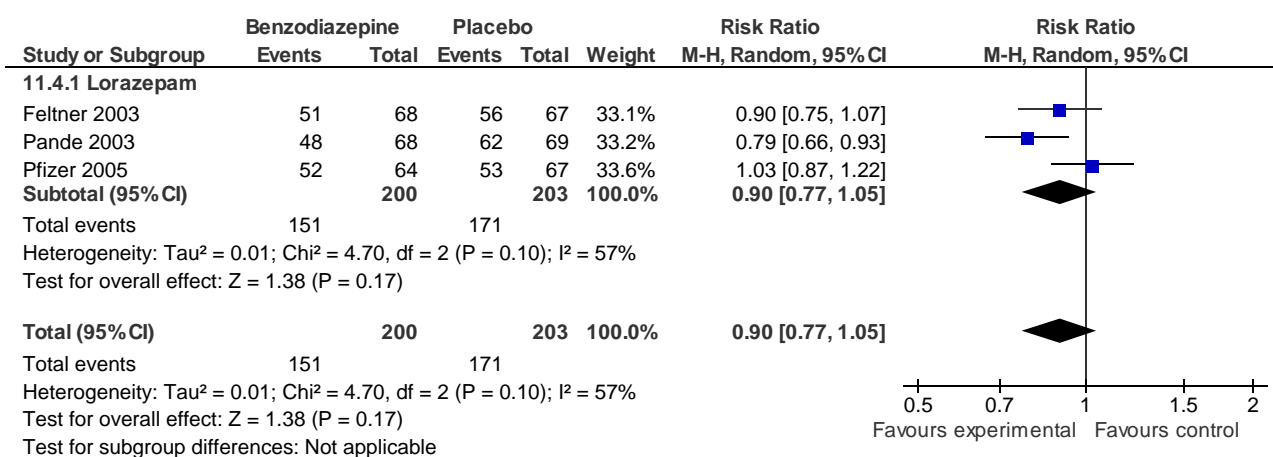


## 2 Benzodiazepine versus Placebo for GAD

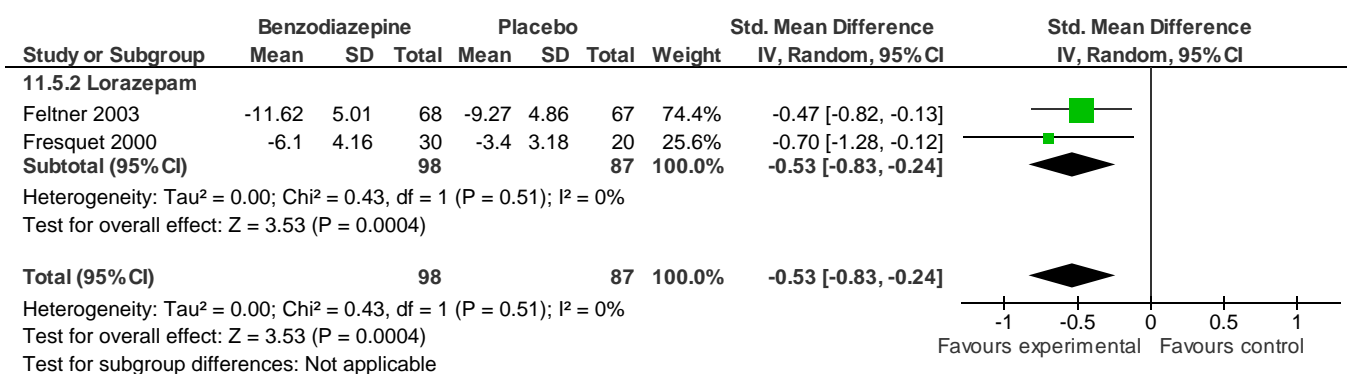
### 11.3 Non-response



### 11.4 Non-remission



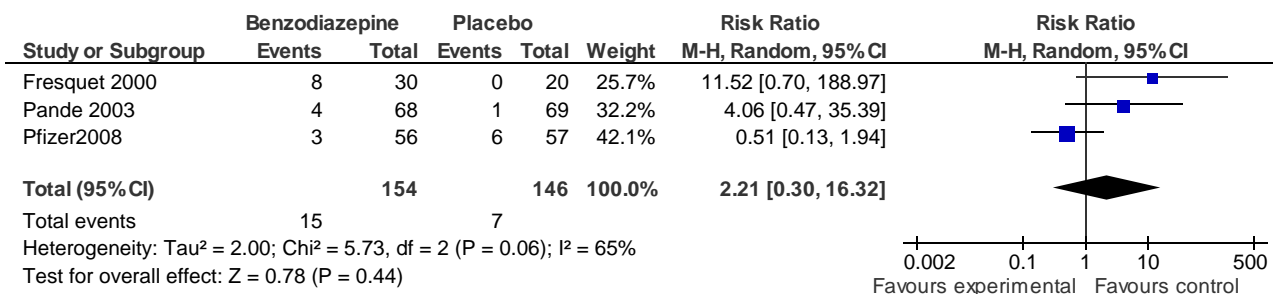
### 11.5 HAM-A



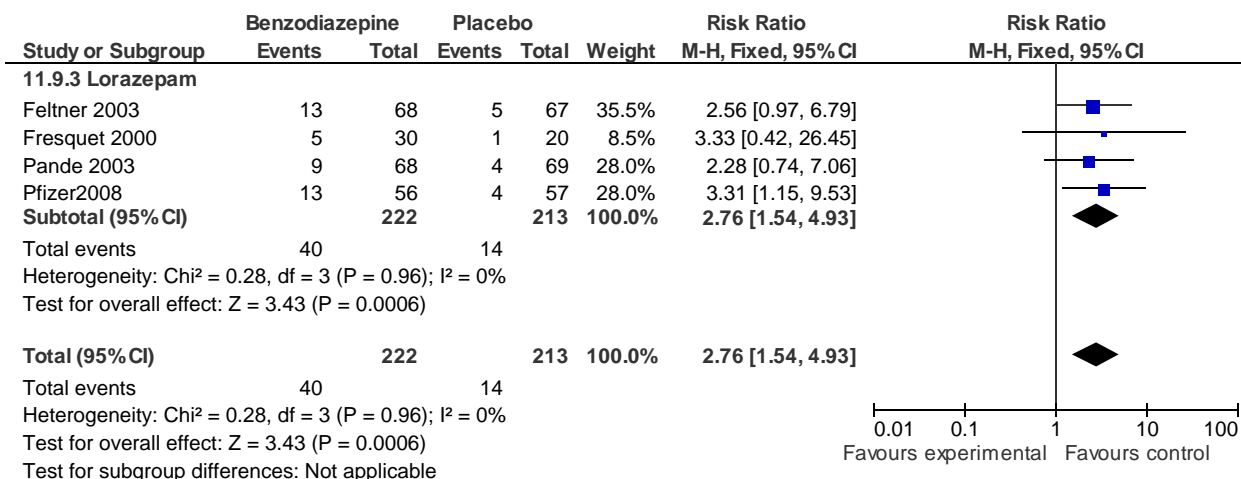


## 2 Benzodiazepine versus Placebo for GAD

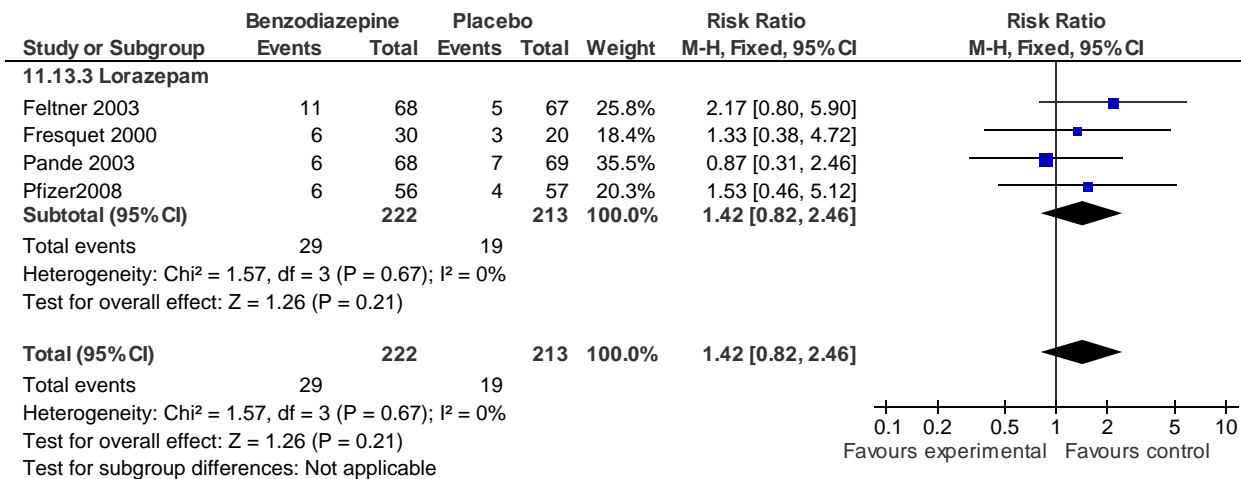
### 11.7 Insomnia



### 11.9 Dizziness



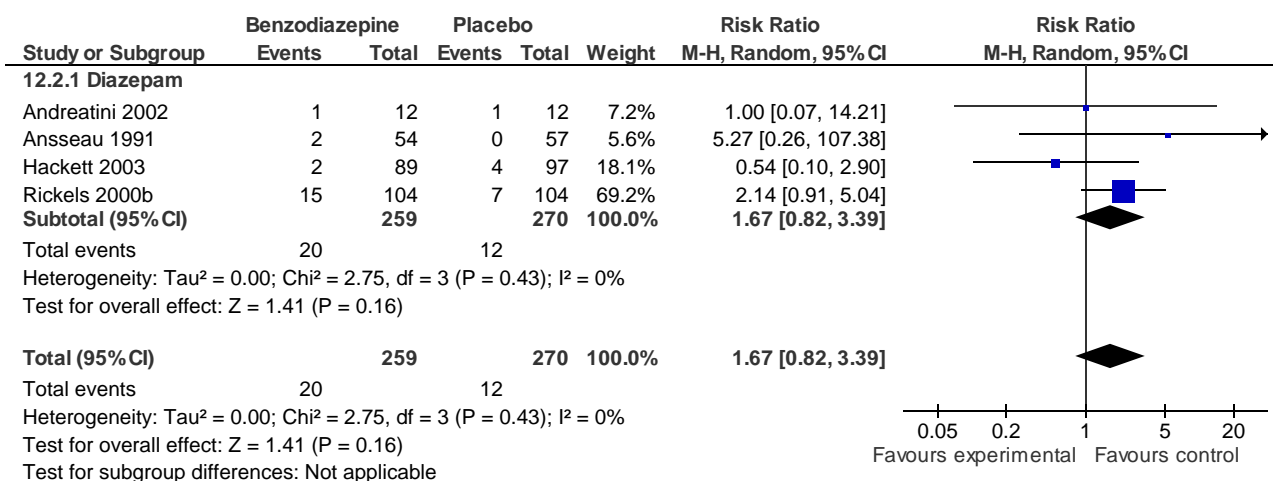
### 11.13 Nausea



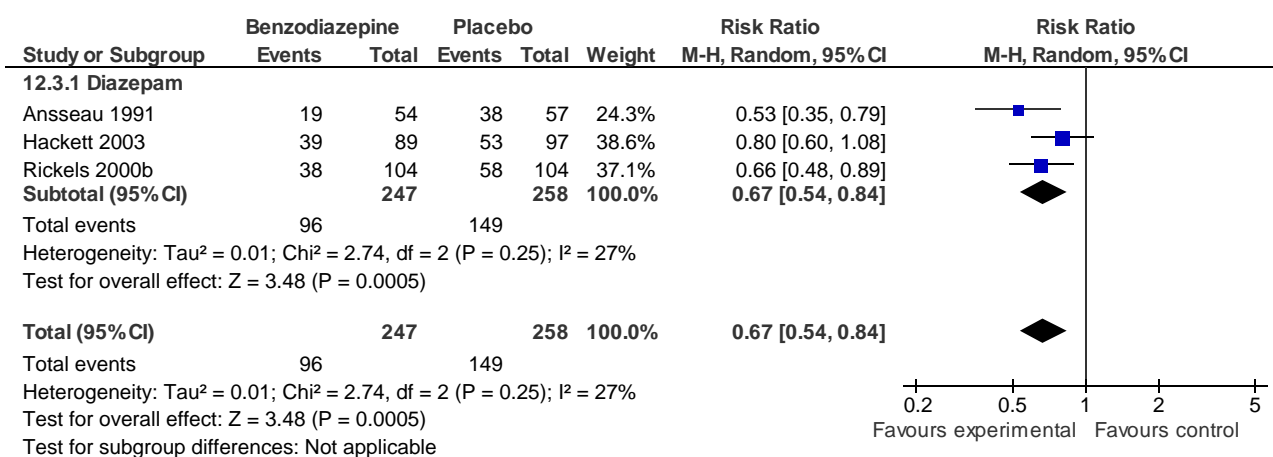
### 12 Diazepam versus Placebo

## 2 Benzodiazepine versus Placebo for GAD

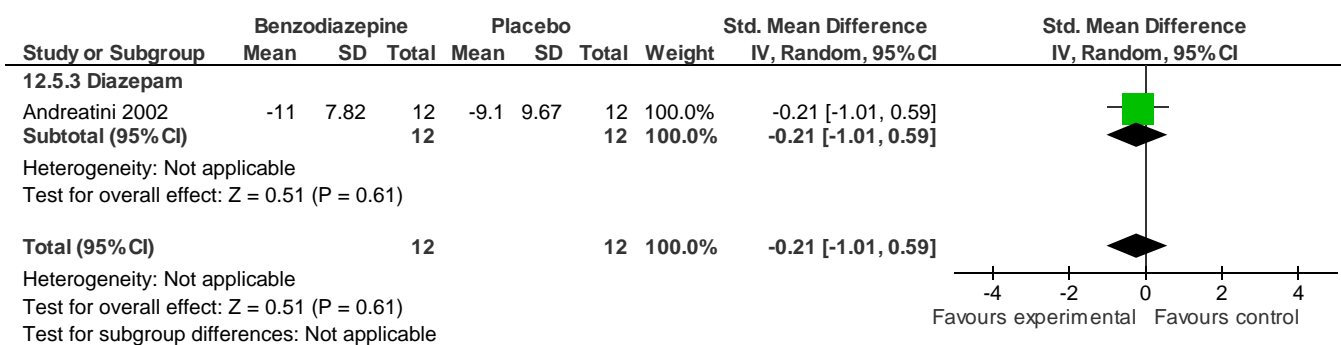
### 12.2 Discontinuation due to adverse events



### 12.3 Non-response

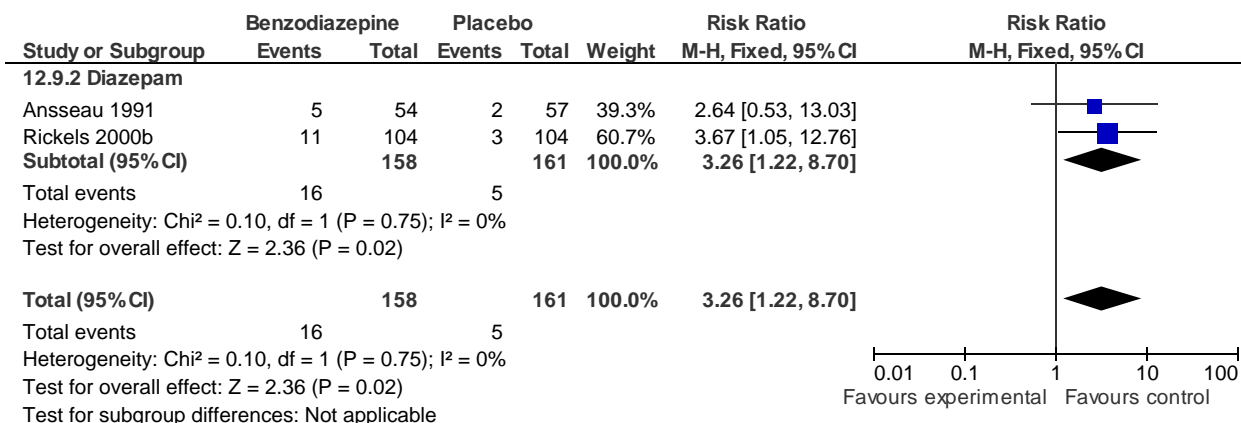


### 12.5 HAM-A

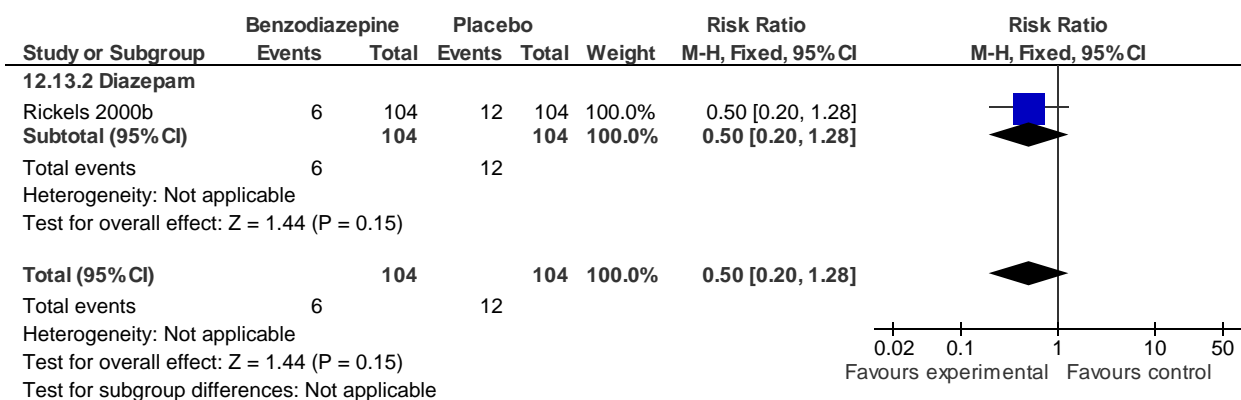


## 2 Benzodiazepine versus Placebo for GAD

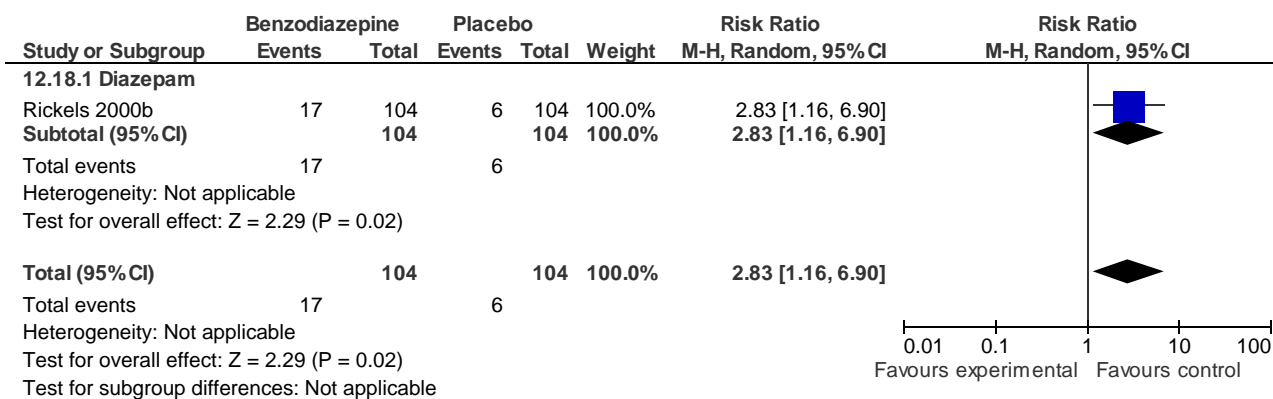
### 12.9 Dizziness



### 12.13 Nausea

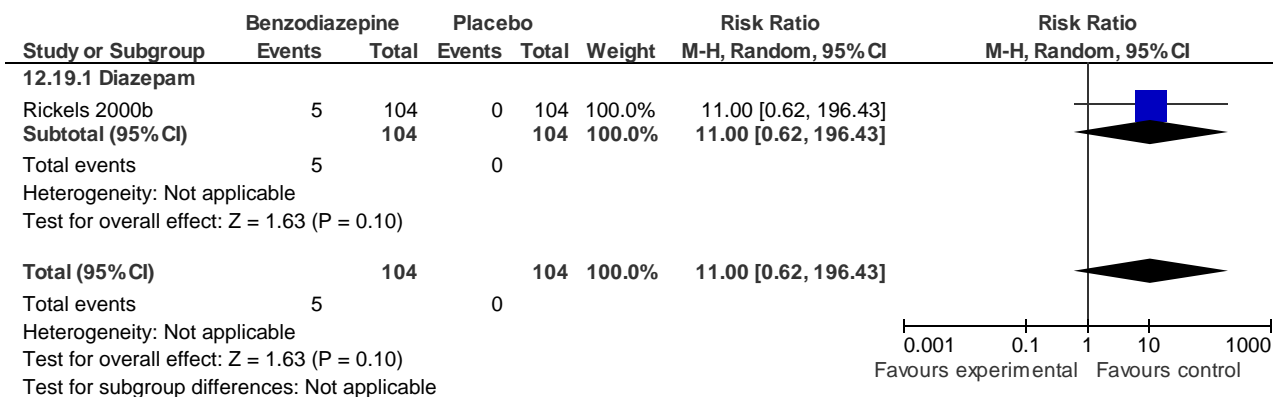


### 12.18 Fatigue



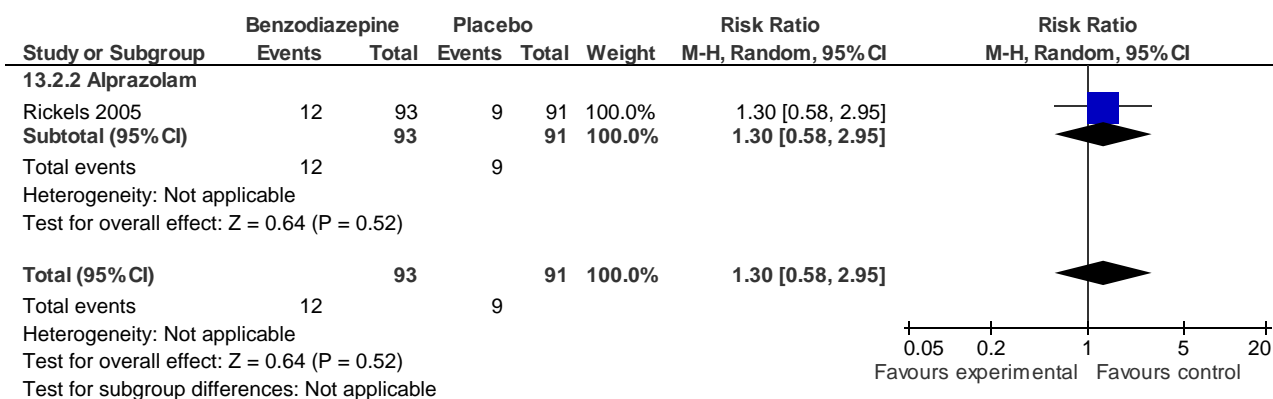
## 2 Benzodiazepine versus Placebo for GAD

### 12.19 Libido

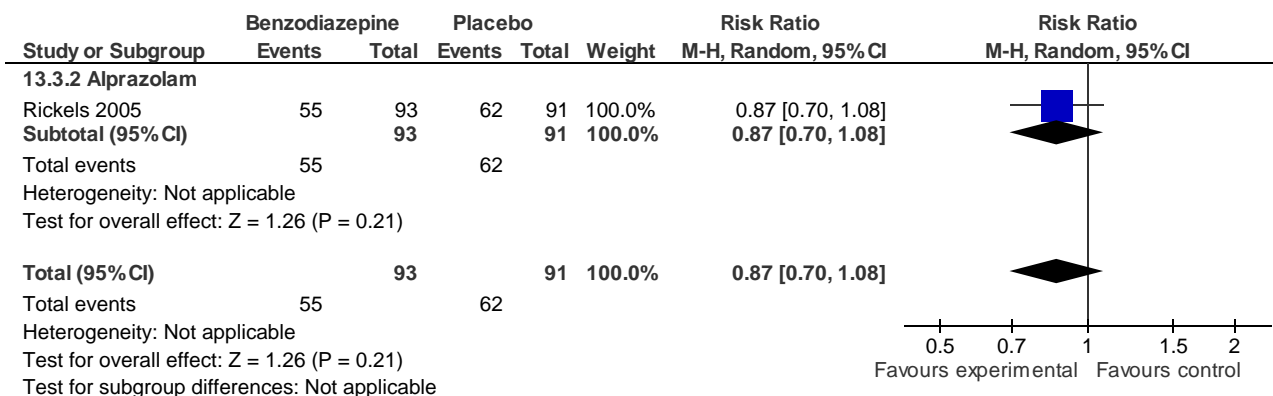


### 13 Alprazolam versus Placebo

#### 13.2 Discontinuation due to adverse events



#### 13.3 Non-response

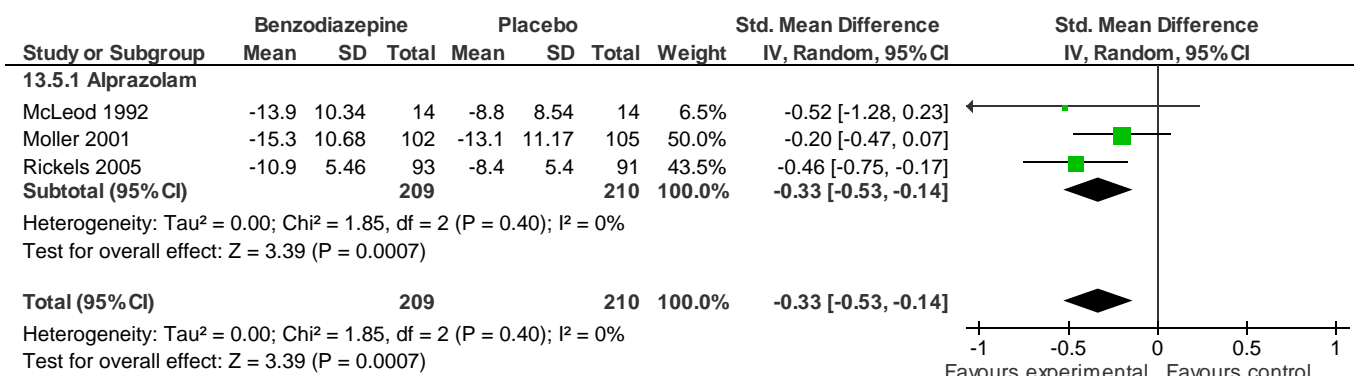


## 2 Benzodiazepine versus Placebo for GAD

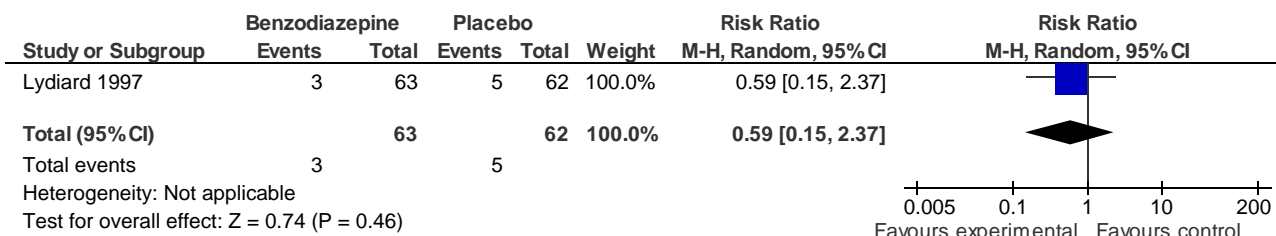
### 13.4 Non-remission



### 13.5 HAM-A

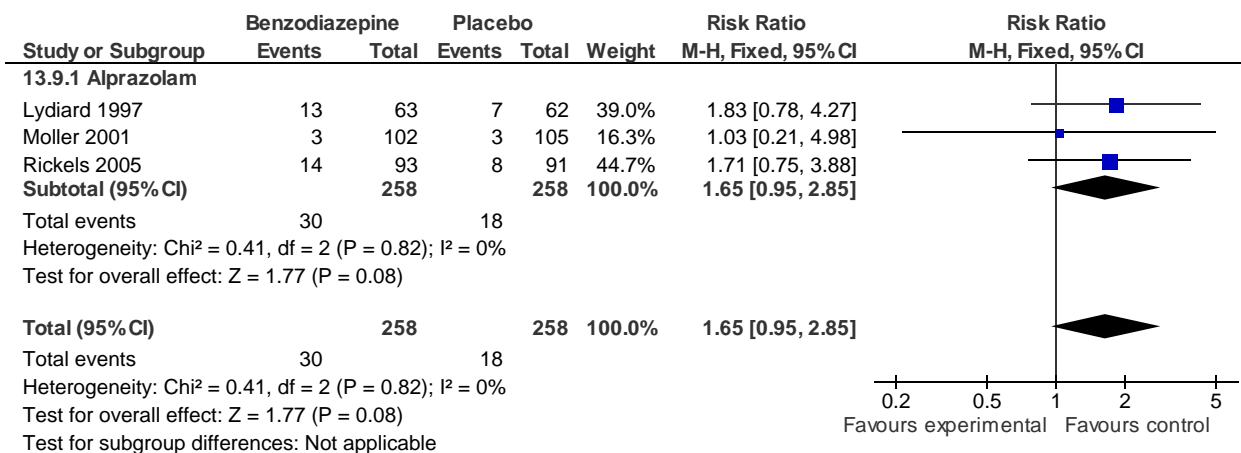


### 13.7 Insomnia

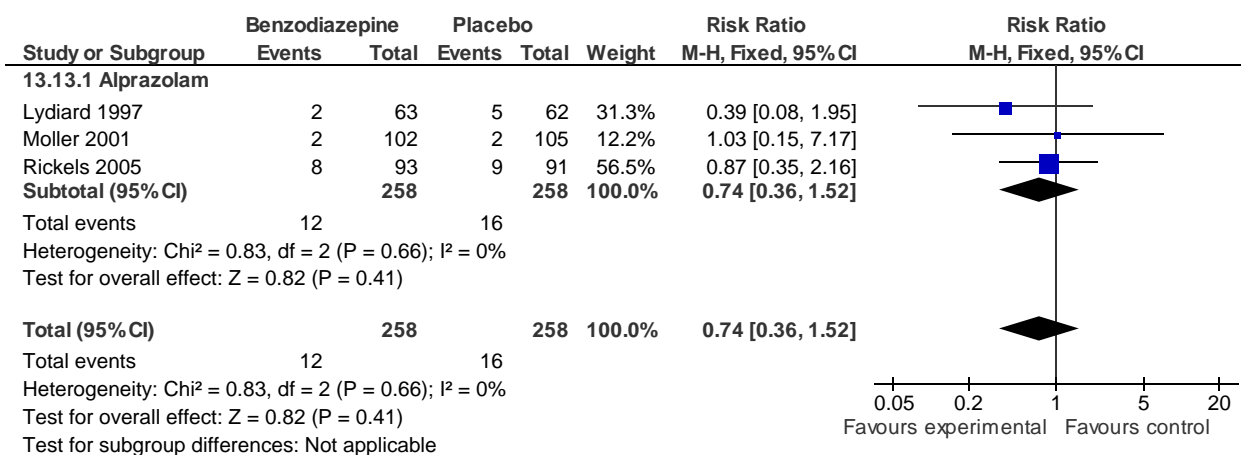


## 2 Benzodiazepine versus Placebo for GAD

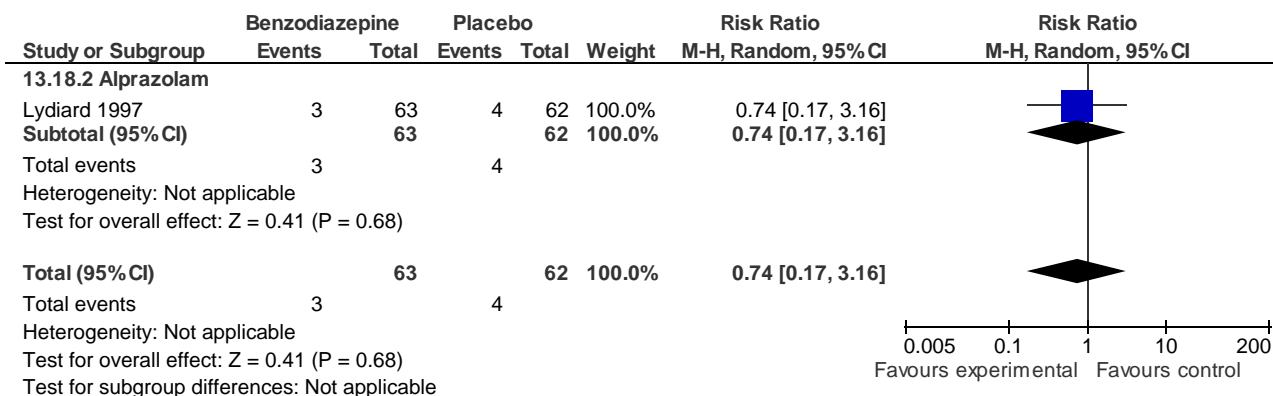
### 13.9 Dizziness



### 13.13 Nausea



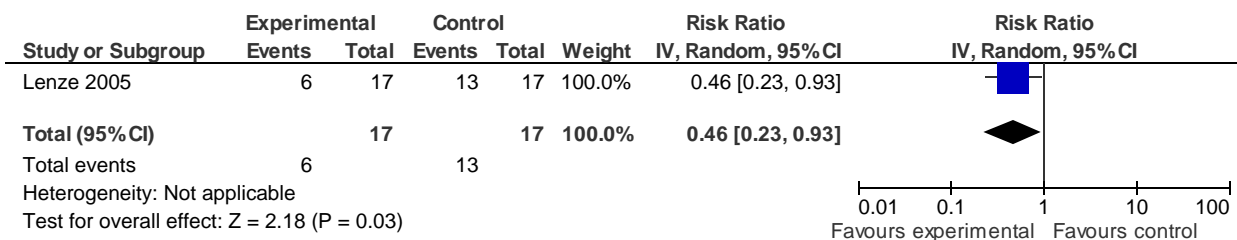
### 13.18 Fatigue



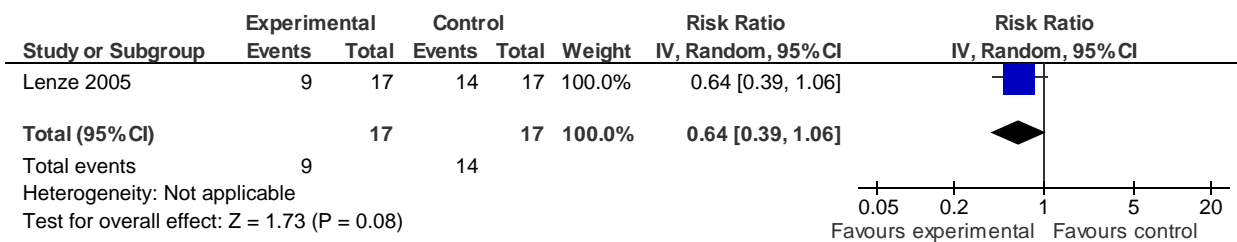
### 35 Citalopram versus Placebo

## 2 Benzodiazepine versus Placebo for GAD

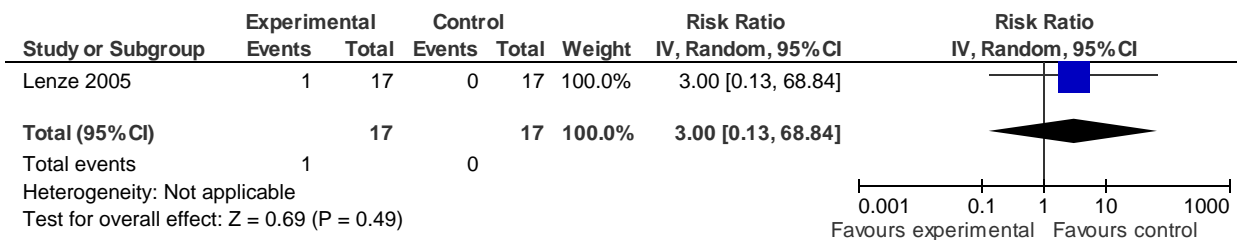
### 35.1 Non-response



### 35.2 Non-remission



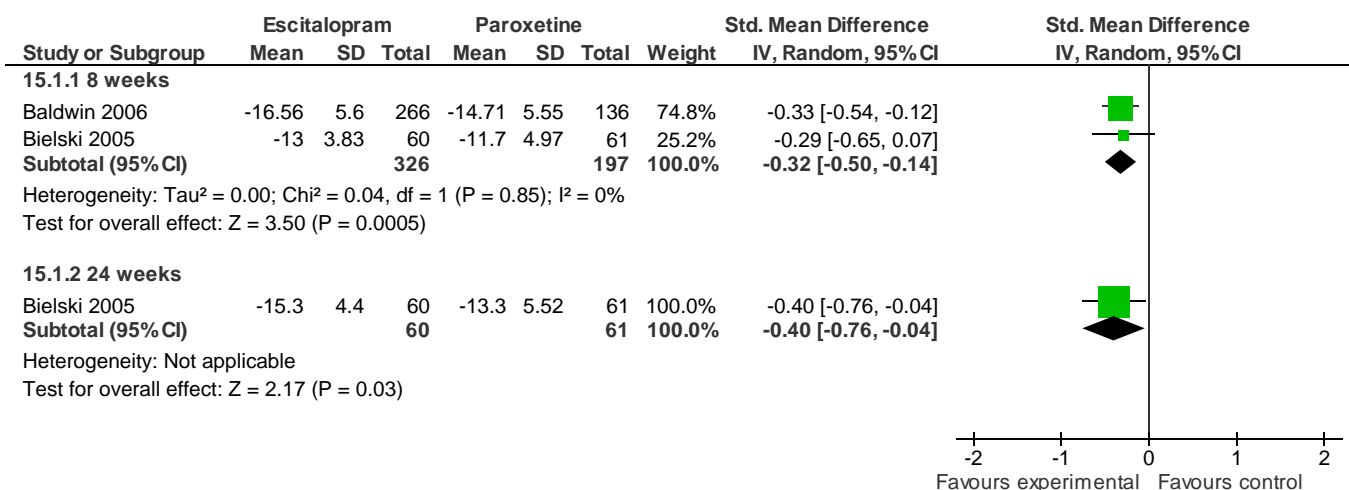
### 35.3 Discontinuation due to adverse events



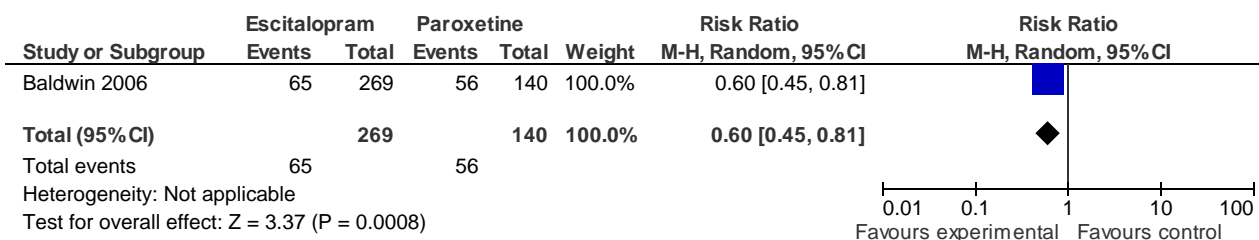
### 3 Head-to-Head trials of Pharmacological Interventions

#### 15 Escitalopram versus Paroxetine

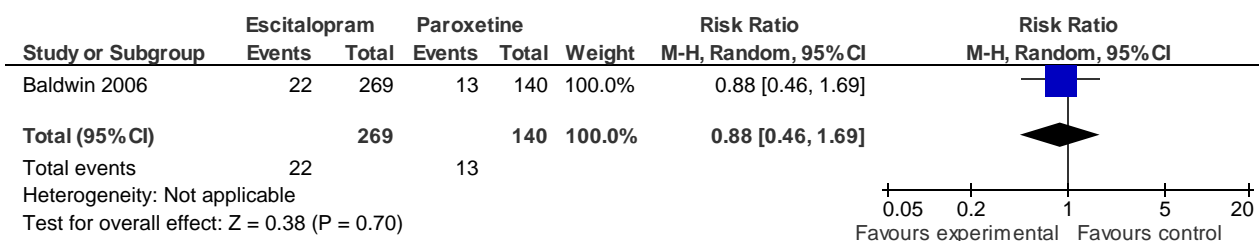
##### 15.1 HAM-A change from baseline



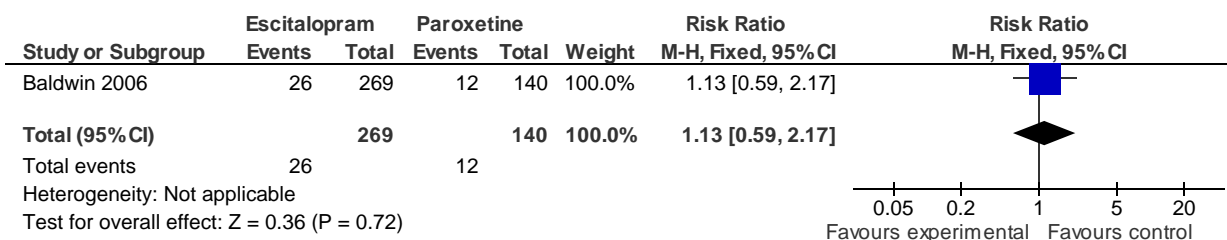
##### 15.2 Non-response



##### 15.7 Discontinuation due to adverse events



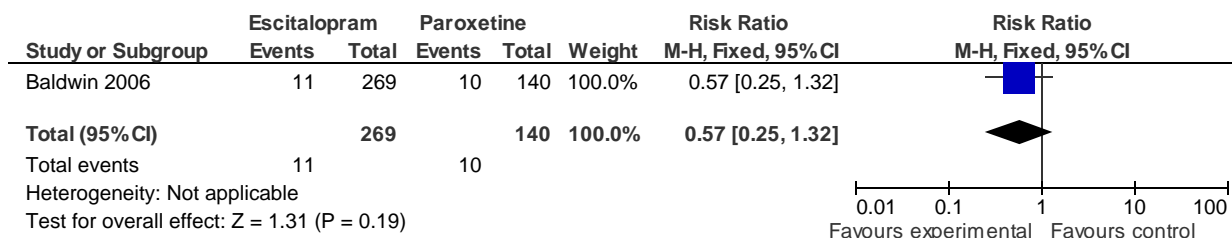
##### 15.8 Diarrhoea



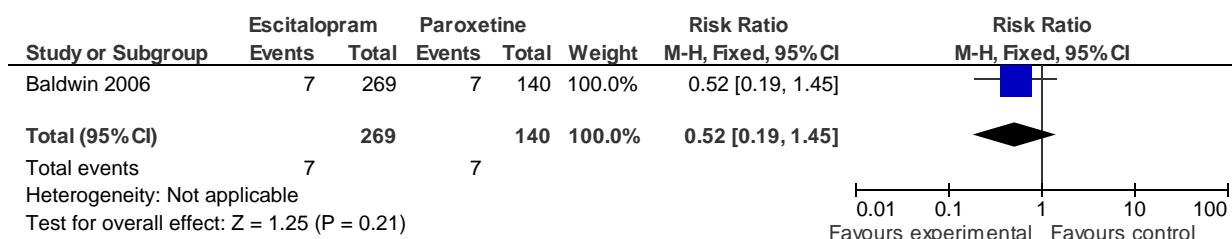


### 3 Head-to-Head trials of Pharmacological Interventions

#### 15.14 Decreased libido

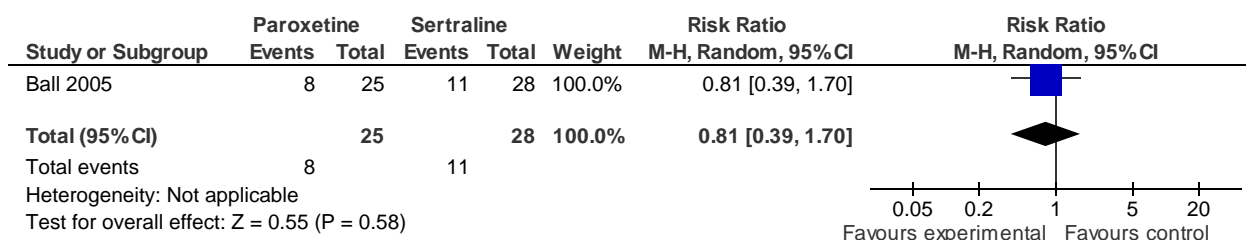


#### 15.17 Anxiety

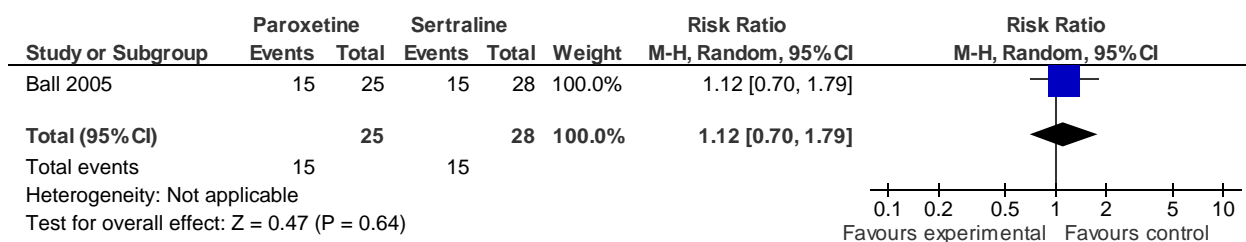


#### 16 Sertraline versus Paroxetine

##### 16.1 Non-response

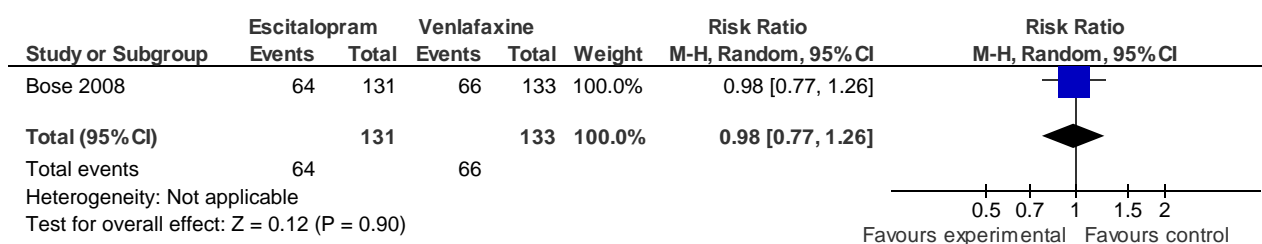


##### 16.2 Non-remission



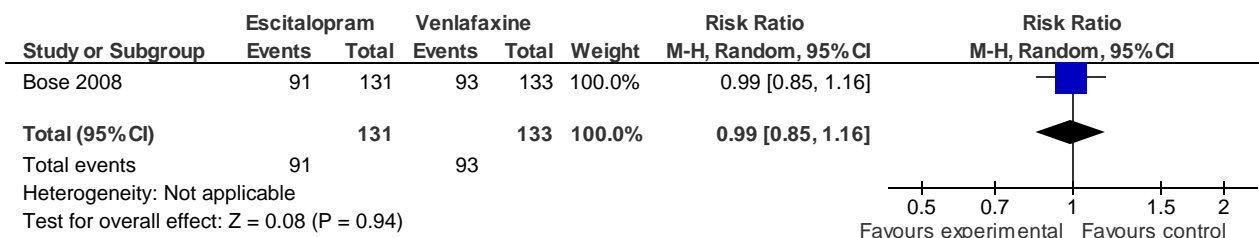
#### 17 Escitalopram versus Venlafaxine

##### 17.2 Non-response

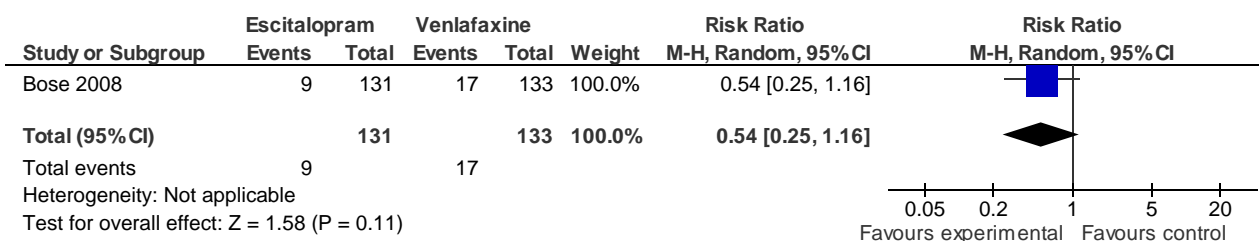


### 3 Head-to-Head trials of Pharmacological Interventions

#### 17.3 Non-remission

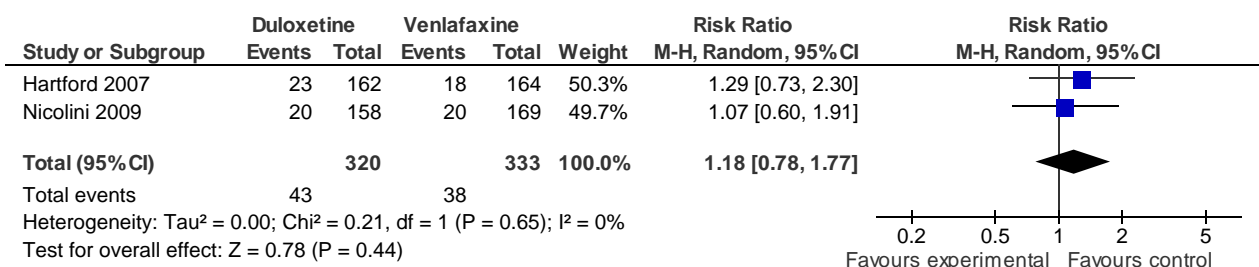


#### 17.4 Discontinuation due to adverse events

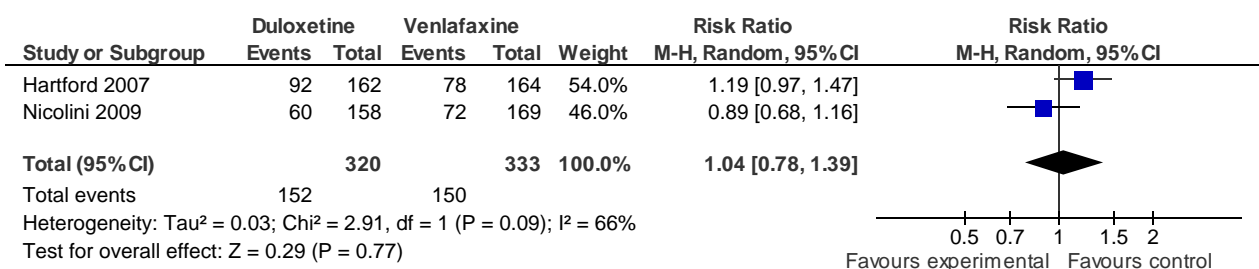


#### 21 Duloxetine versus Venlafaxine

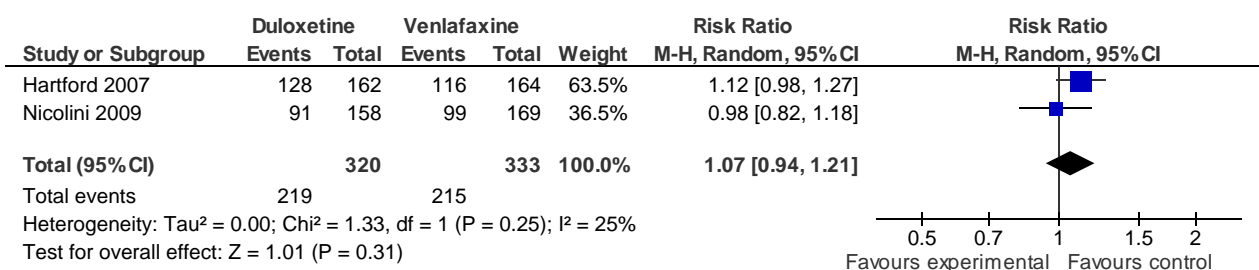
##### 21.2 Discontinuation due to adverse events



##### 21.3 Non-response

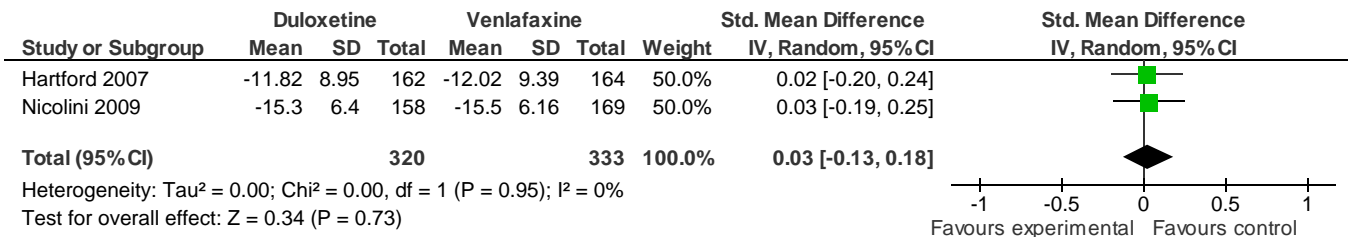


##### 21.4 Non-remission

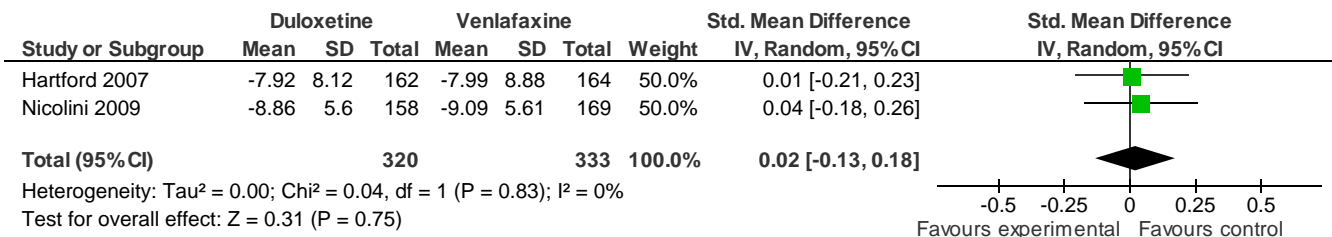


### 3 Head-to-Head trials of Pharmacological Interventions

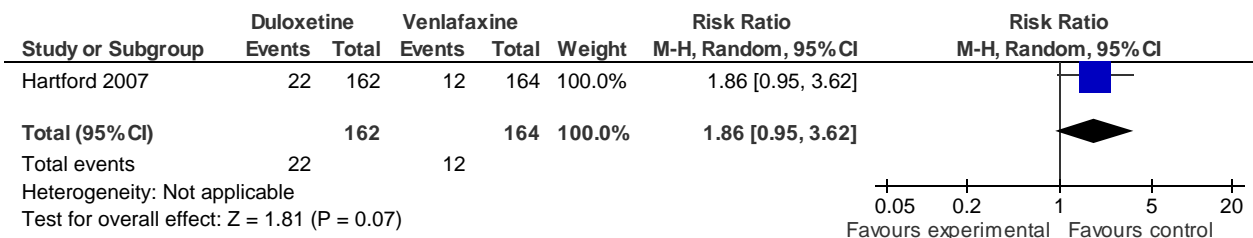
#### 21.5 HAM-A



#### 21.6 Sheehan Disability Scale



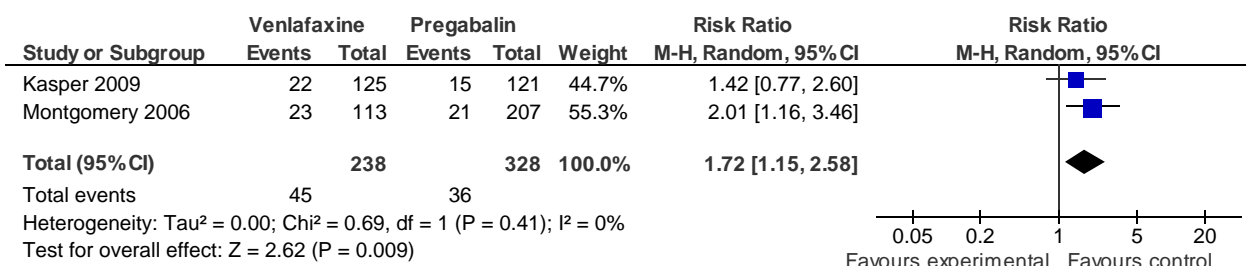
#### 21.9 Diarrhoea



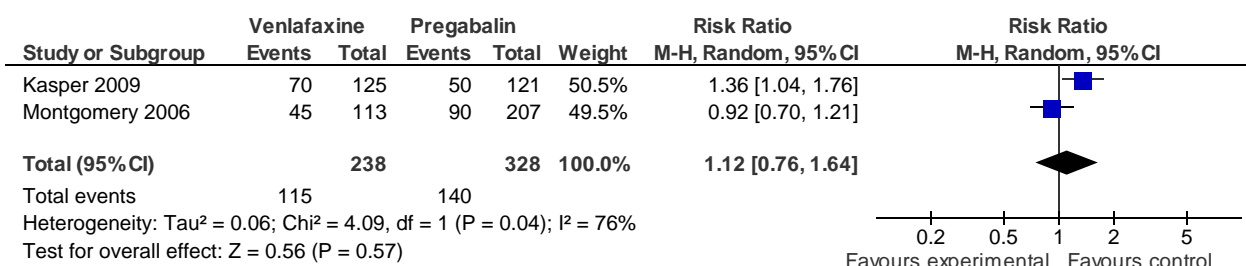
## 4 Antidepressants versus Other Pharmacological Interventions

### 14 Venlafaxine versus Pregabalin

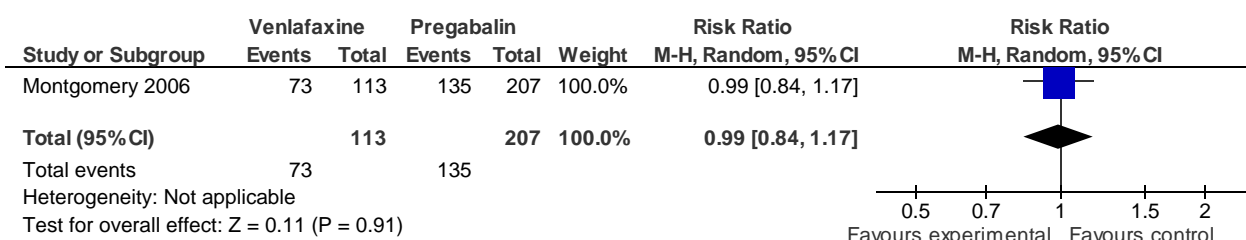
#### 14.2 Discontinuation due to adverse events



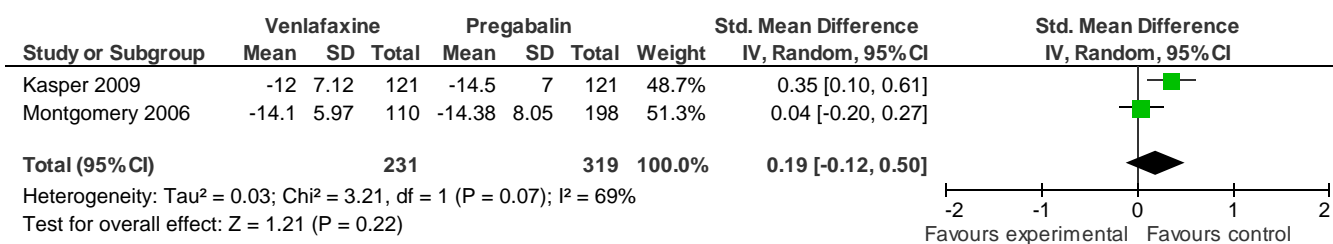
#### 14.3 Non-response



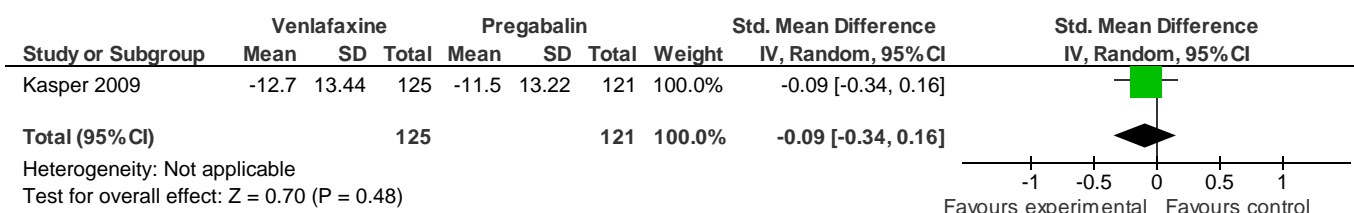
#### 14.4 Non-remission



#### 14.5 HAM-A

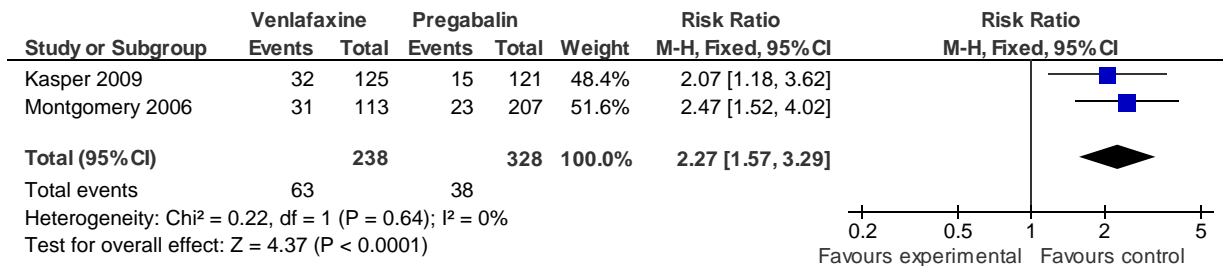


#### 14.7 Q-LES-Q

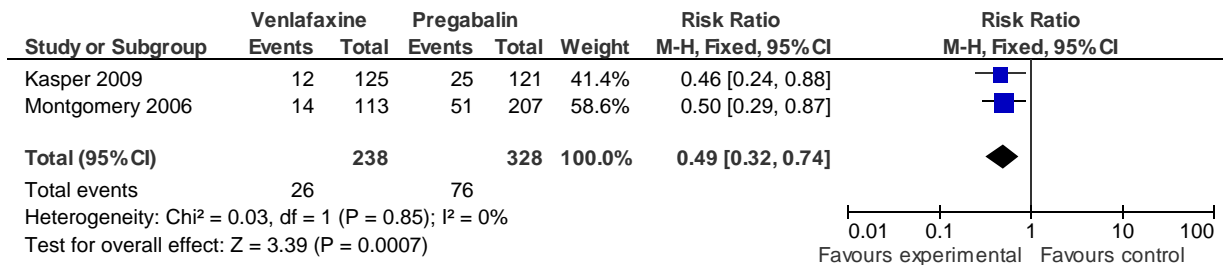


## 4 Antidepressants versus Other Pharmacological Interventions

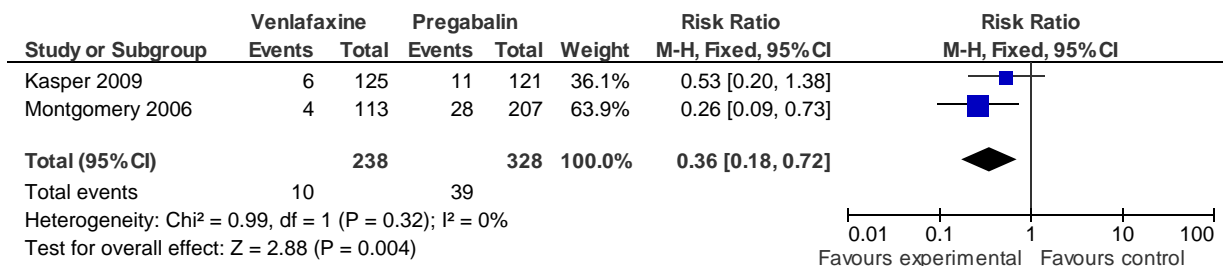
### 14.9 Nausea



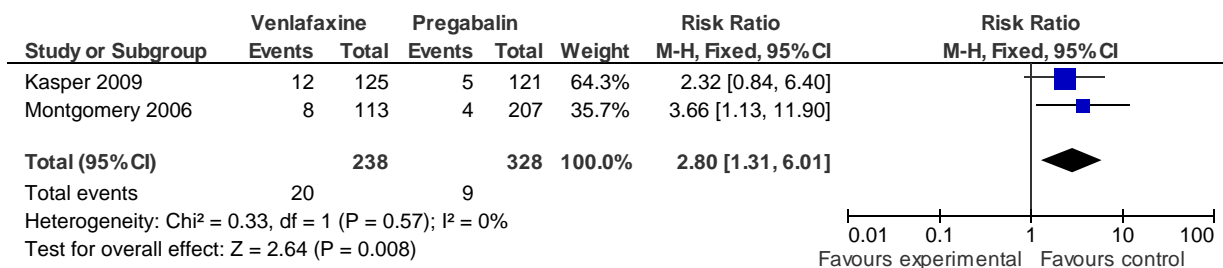
### 14.11 Dizziness



### 14.15 Somnolence

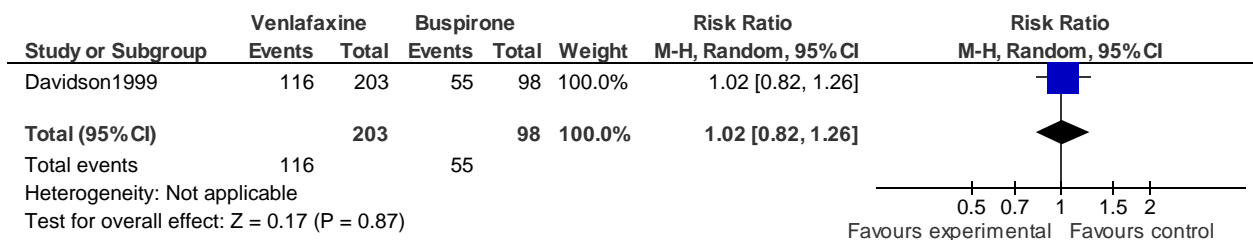


### 14.16 Insomnia



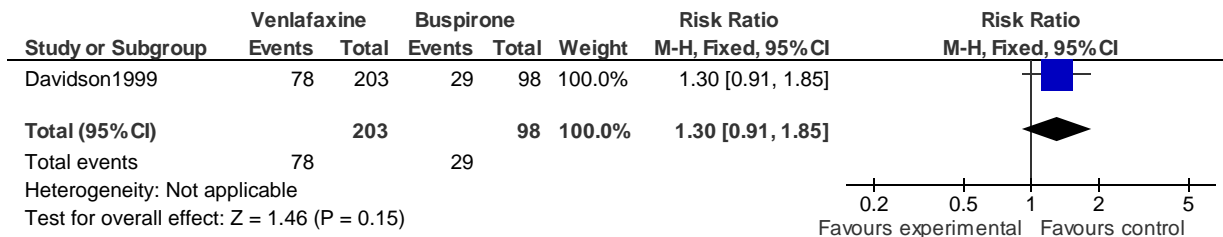
## 18 Venlafaxine versus Buspirone

### 18.1 Non-response

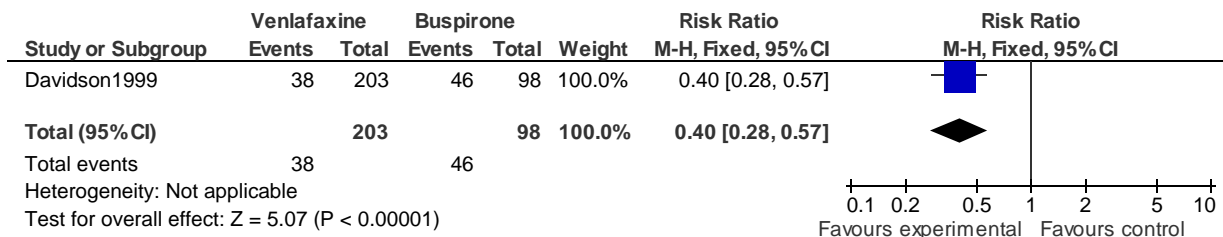


## 4 Antidepressants versus Other Pharmacological Interventions

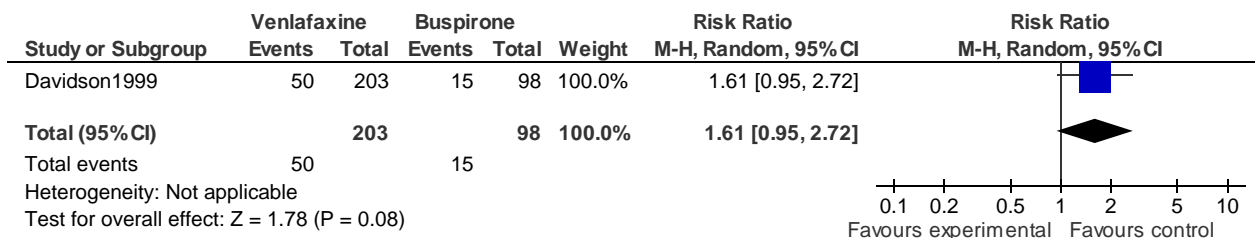
### 18.2 Nausea



### 18.3 Dizziness

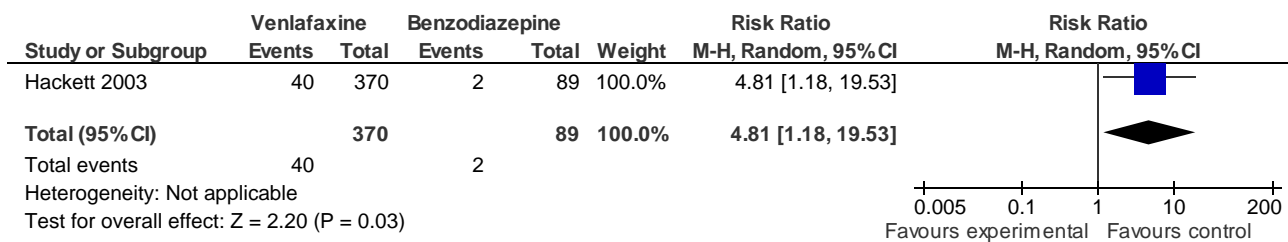


### 18.6 Discontinuation due to adverse events

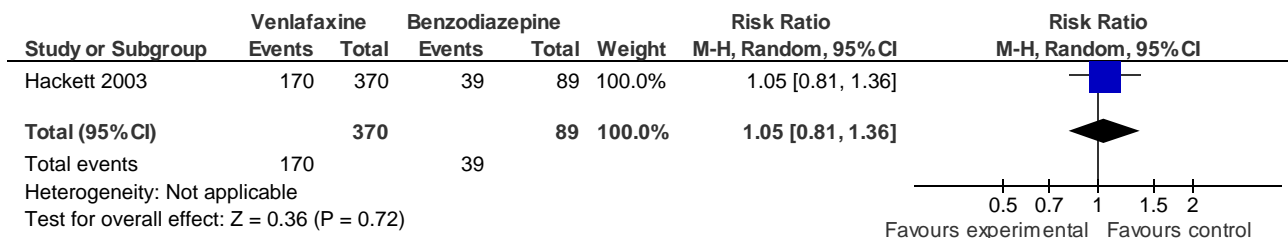


## 19 Venlafaxine versus Diazepam

### 19.2 Discontinuation due to adverse events



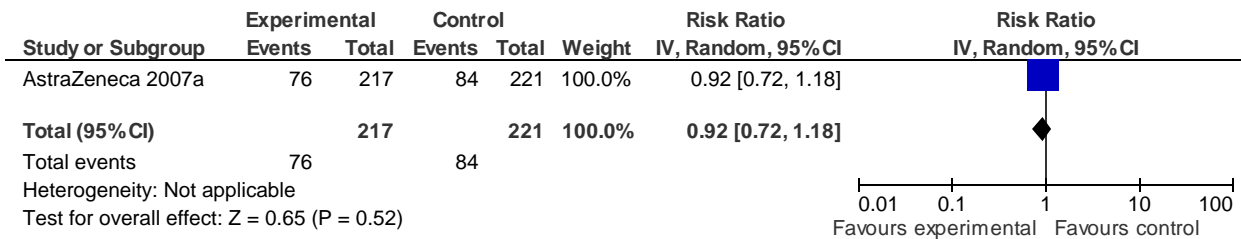
### 19.3 Non-response



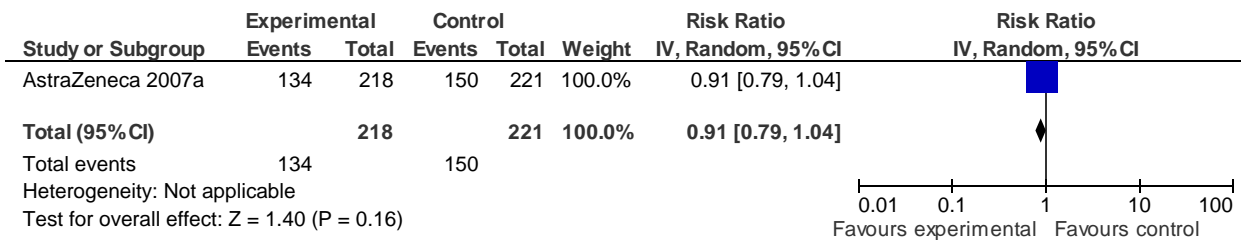
## 23 Quetiapine 50mg versus Paroxetine

## 4 Antidepressants versus Other Pharmacological Interventions

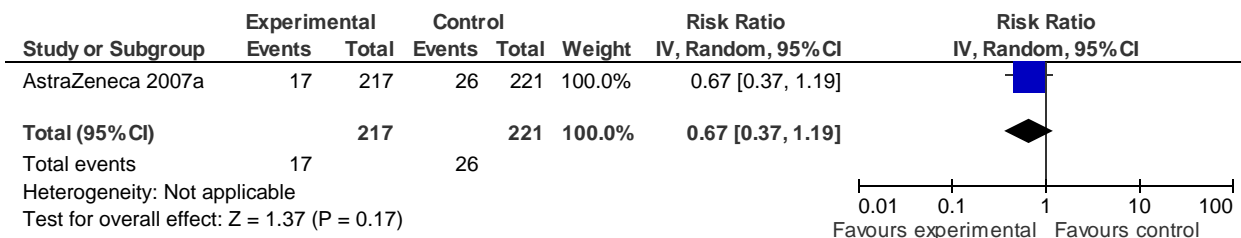
### 23.1 Non-response



### 23.2 Non-remission

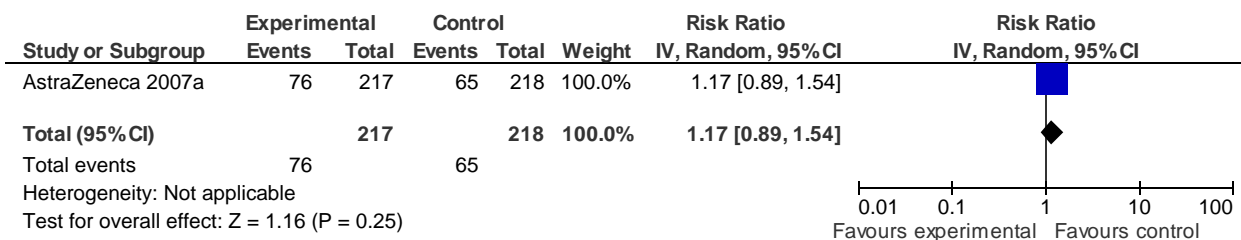


### 23.3 Discontinuation due to adverse events

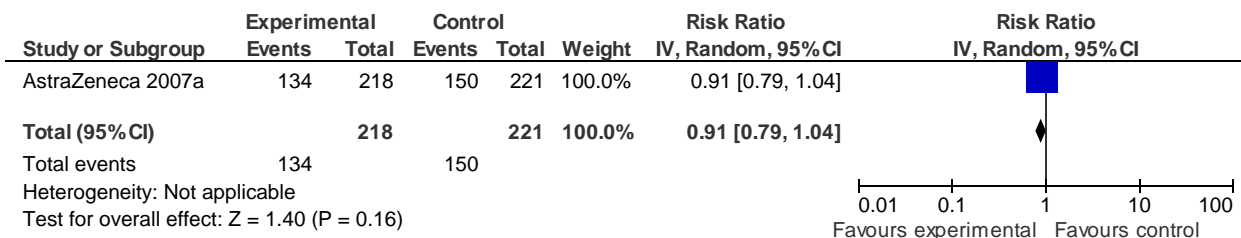


## 24 Quetiapine 150mg versus Paroxetine

### 24.1 Non-response

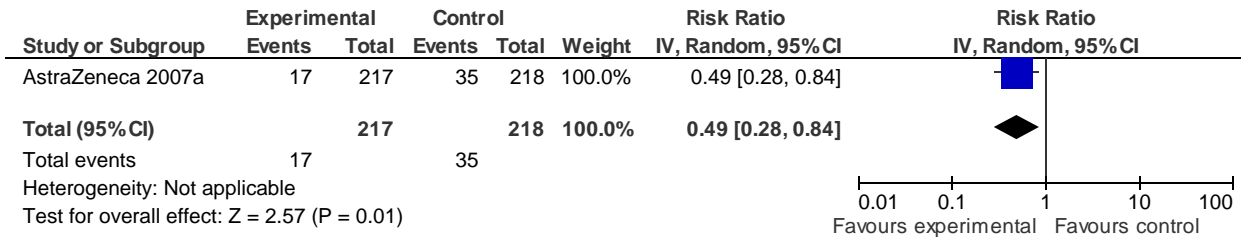


### 24.2 Non-remission



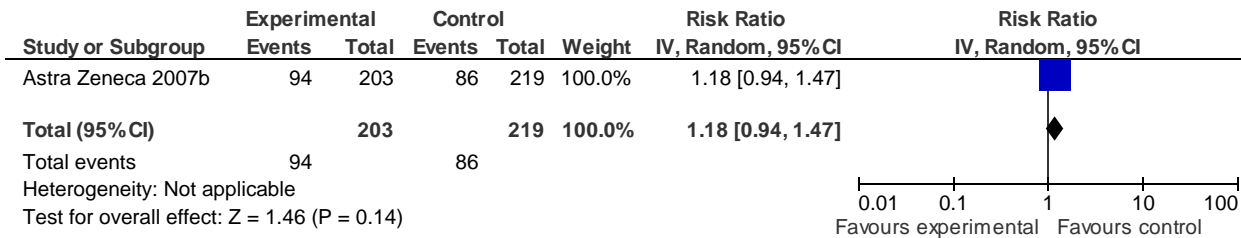
## 4 Antidepressants versus Other Pharmacological Interventions

### 24.3 Discontinuation due to adverse events

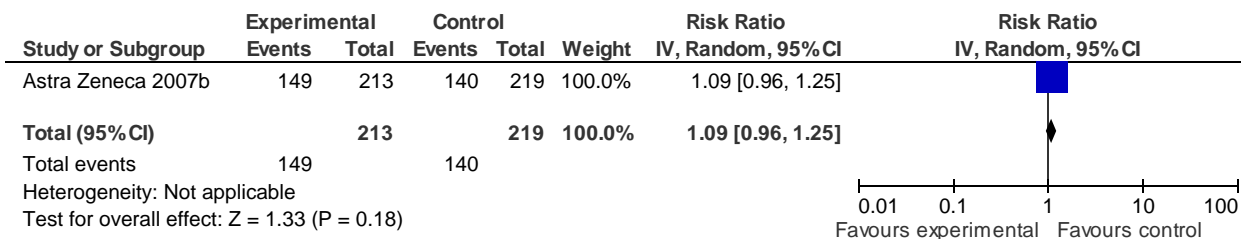


### 33 Quetiapine 150mg versus Escitalopram

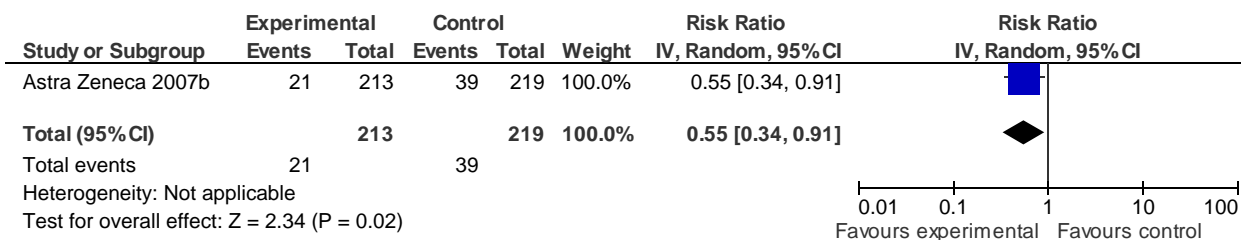
#### 33.1 Non-response



#### 33.2 Non-remission

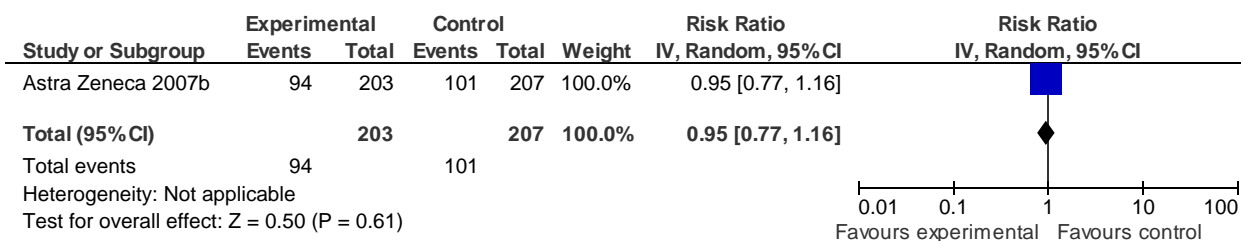


### 33.3 Discontinuation due to adverse events



### 34 Quetiapine 300mg versus Escitalopram

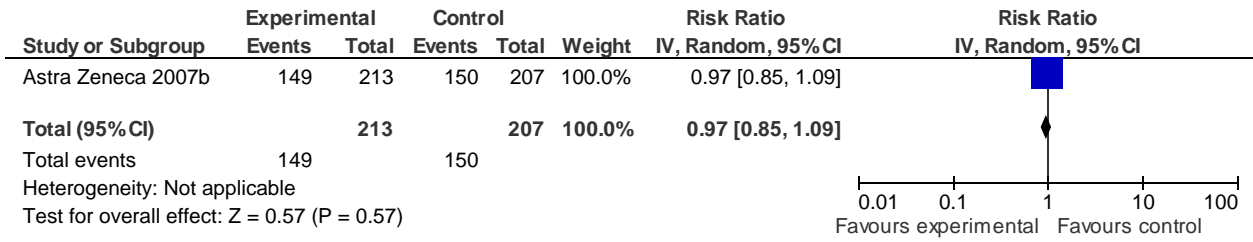
#### 34.1 Non-response



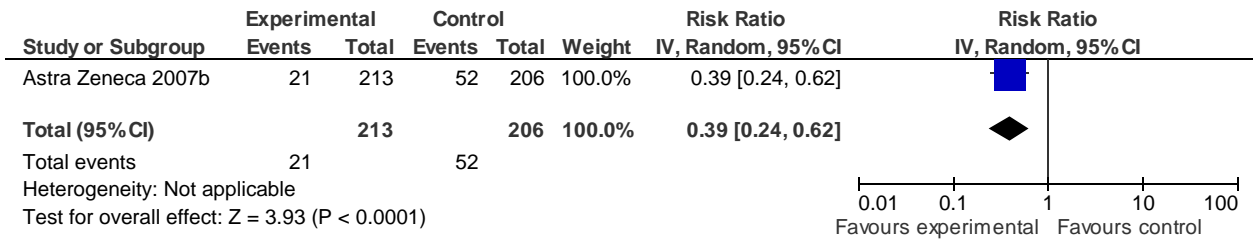


## 4 Antidepressants versus Other Pharmacological Interventions

### 34.2 Non-remission



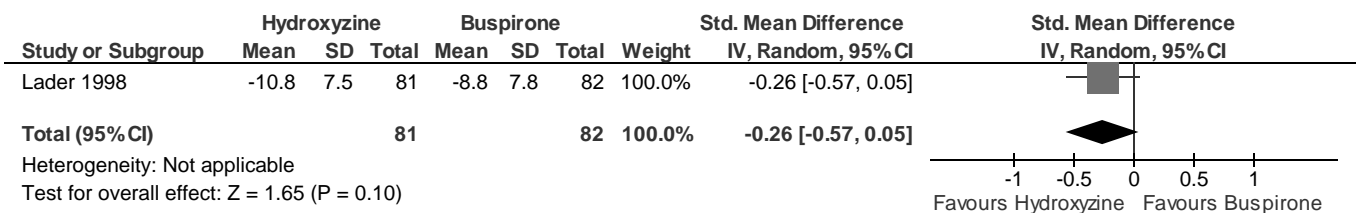
### 34.3 Discontinuation due to adverse events



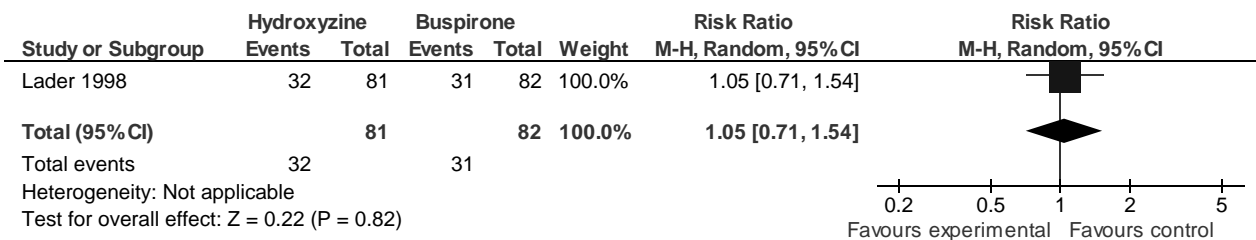
## 5 Other Pharmacological Interventions (other than antidepressants)

### 20 Hydroxyzine versus Buspirone

#### 20.2 HAM-A

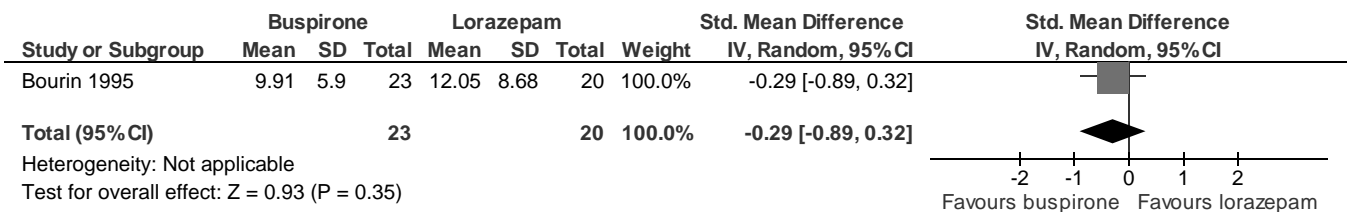


#### 20.4 At least one side effect



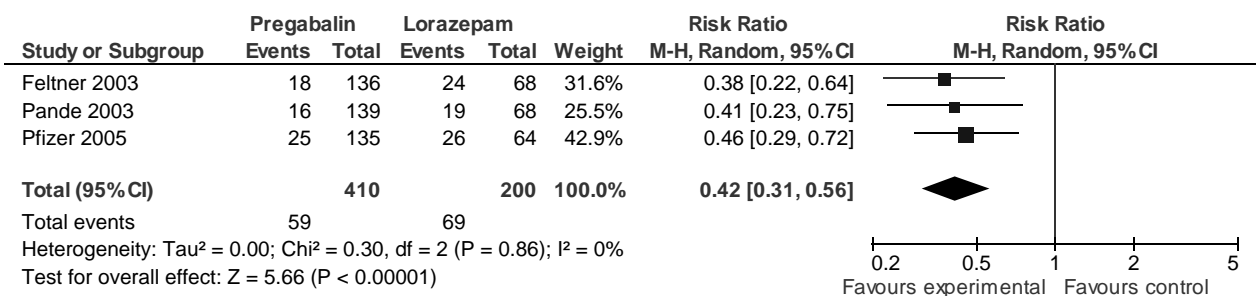
### 22 Buspirone versus Lorazepam

#### 22.1 HAM-A



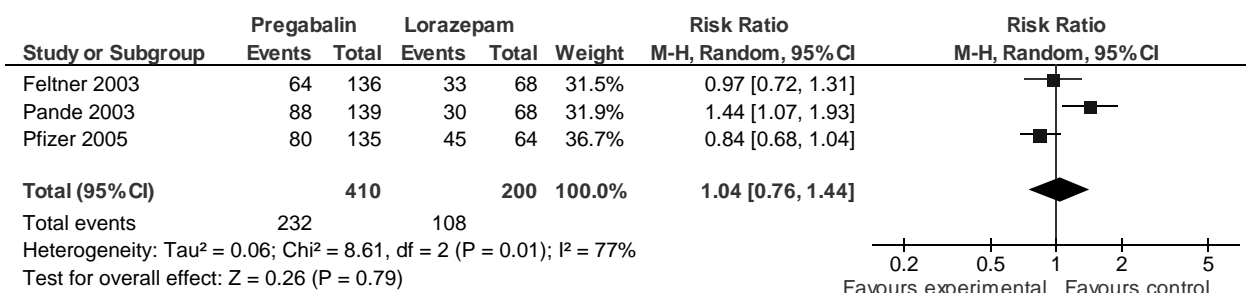
### 25 Pregabalin versus Lorazepam

#### 25.2 Discontinuation due to adverse events

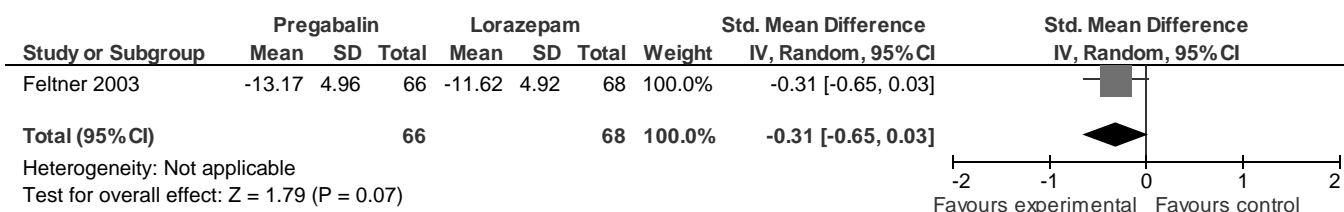


## 5 Other Pharmacological Interventions (other than antidepressants)

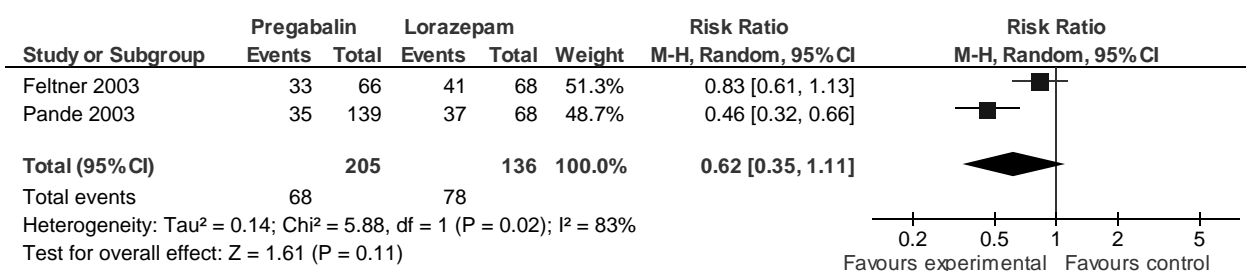
### 25.3 Non-response



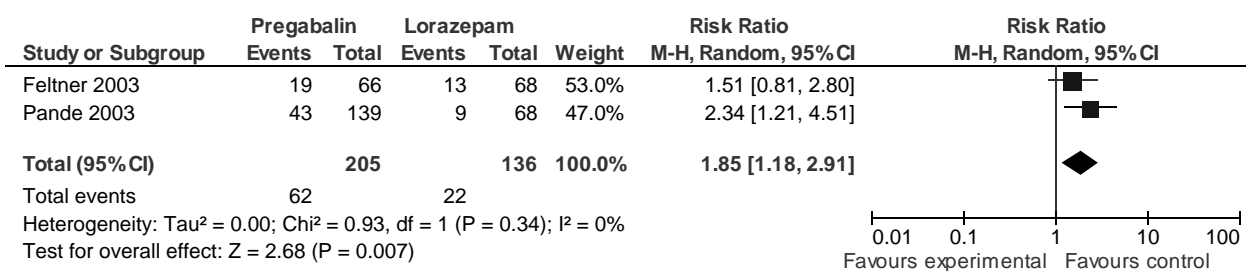
### 25.4 HAM-A



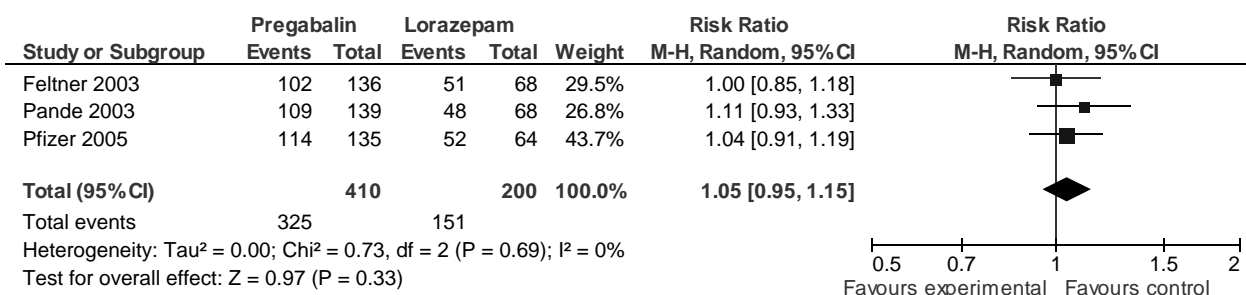
### 25.5 Somnolence



### 25.6 Dizziness



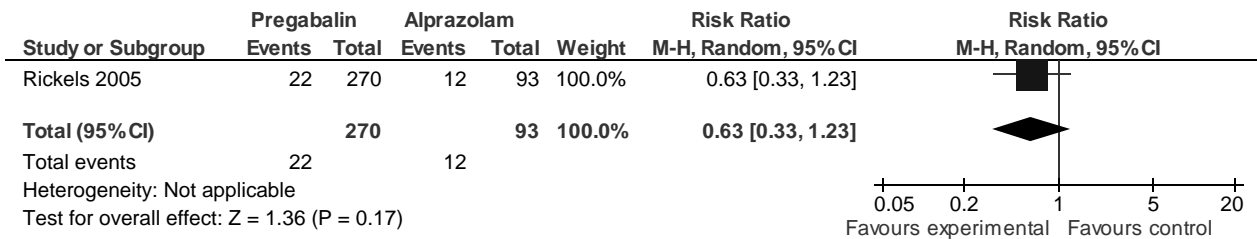
### 25.7 Non-remission



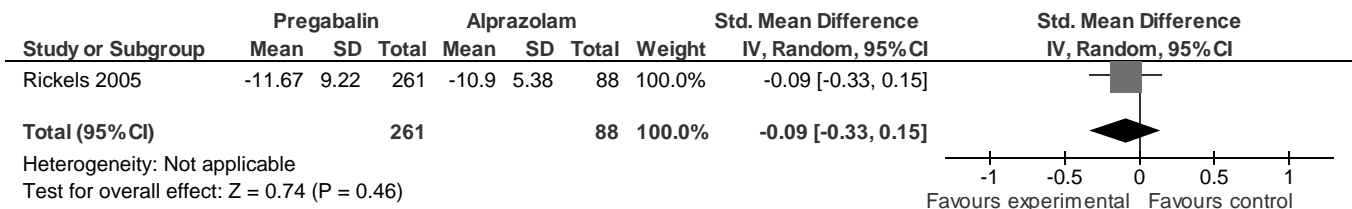
### 26 Pregabalin versus Alprazolam

## 5 Other Pharmacological Interventions (other than antidepressants)

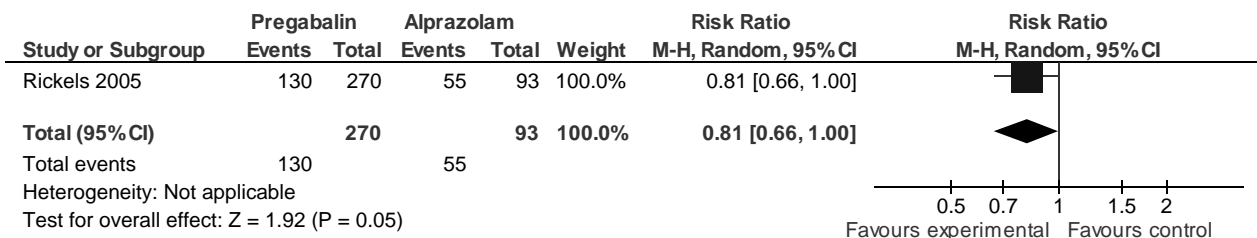
### 26.2 Discontinuation due to adverse events



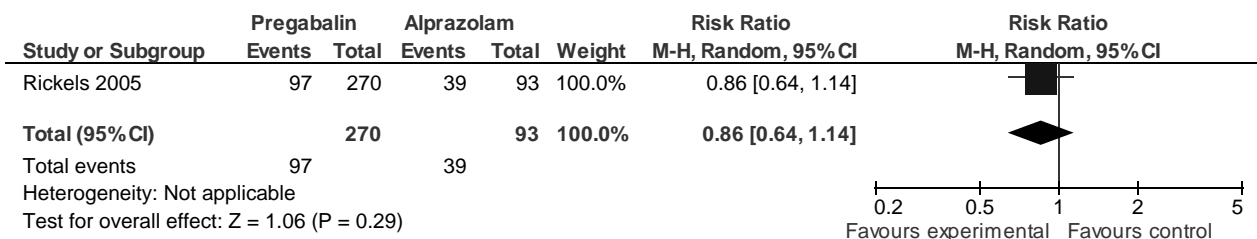
### 26.3 HAM-A



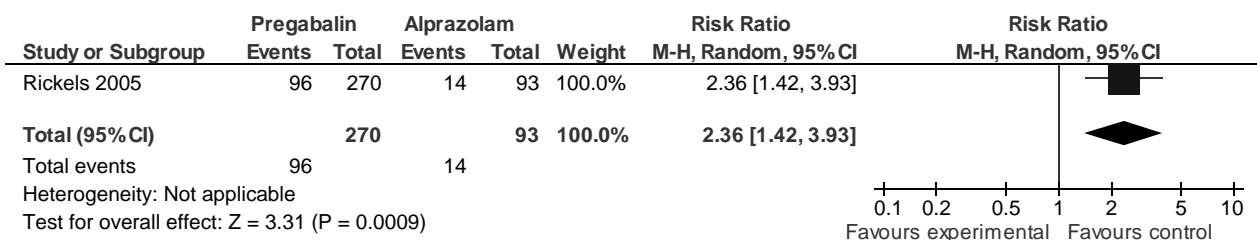
### 26.4 Non-response



### 26.5 Somnolence

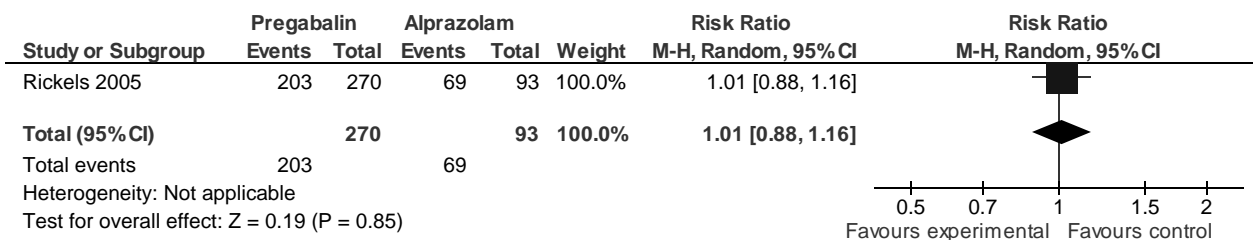


### 26.6 Dizziness



## 5 Other Pharmacological Interventions (other than antidepressants)

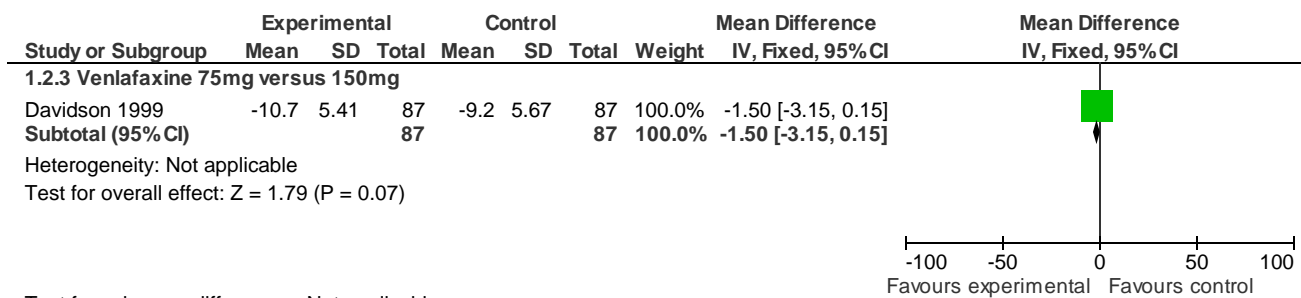
### 26.7 Non-remission



## 6 Comparing the Effectiveness of Different Dosages

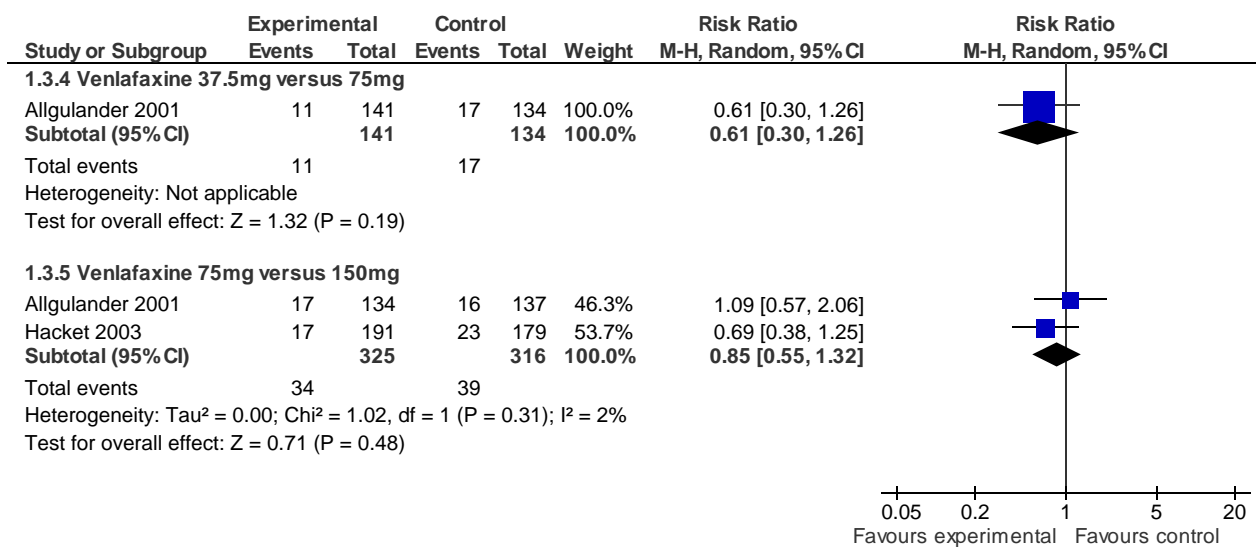
### 1 Venlafaxine

#### 1.2 HAM-A

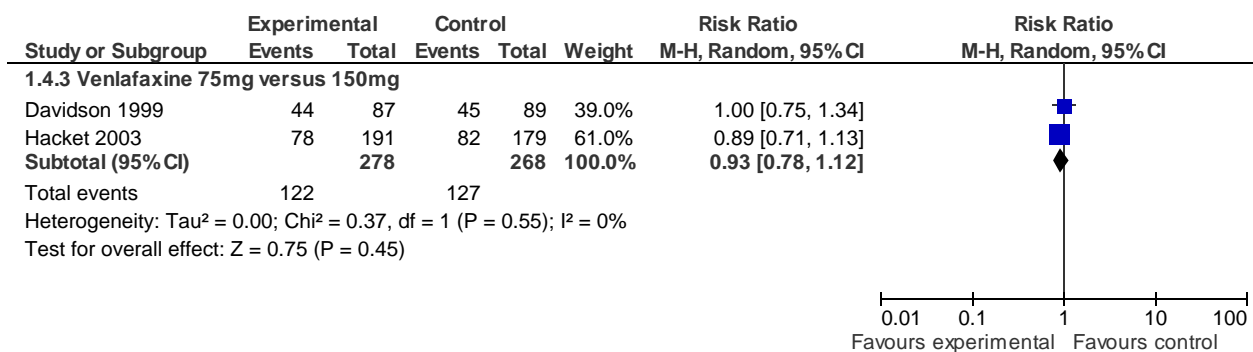


Test for subgroup differences: Not applicable

#### 1.3 Discontinuation due to Adverse Events

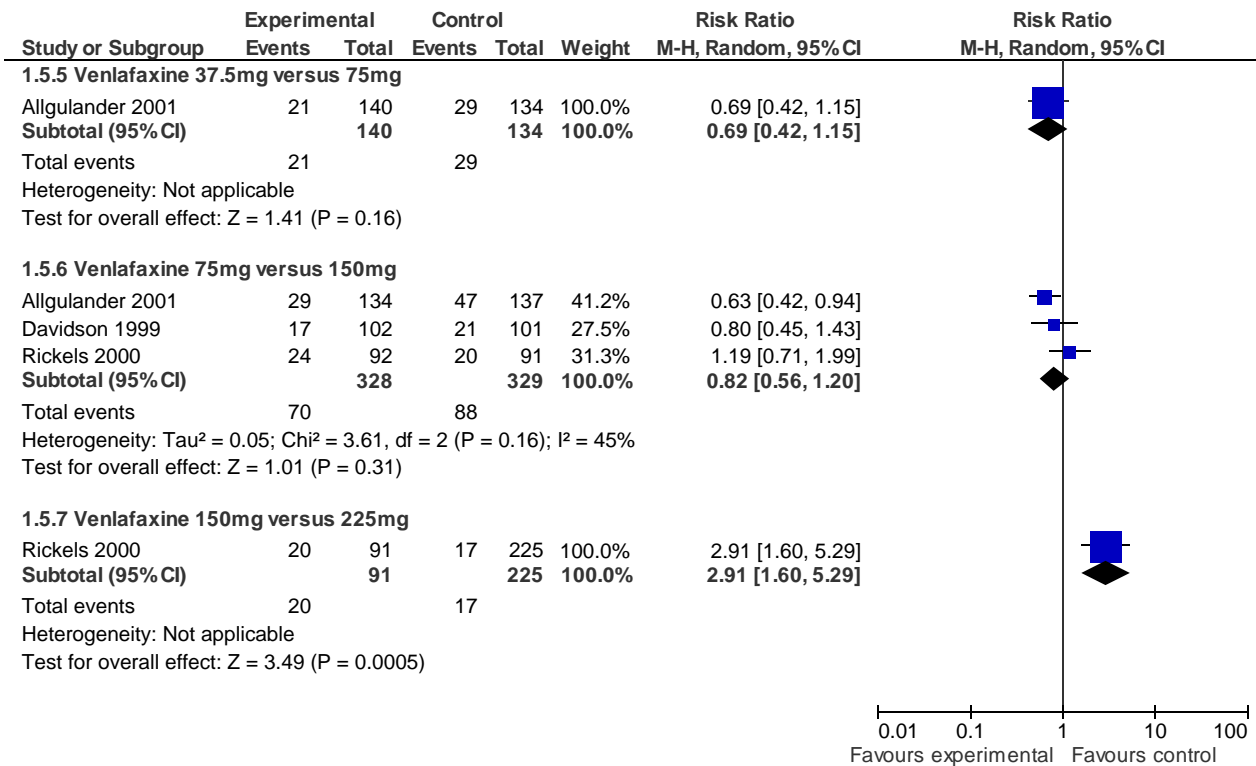


#### 1.4 Non Response



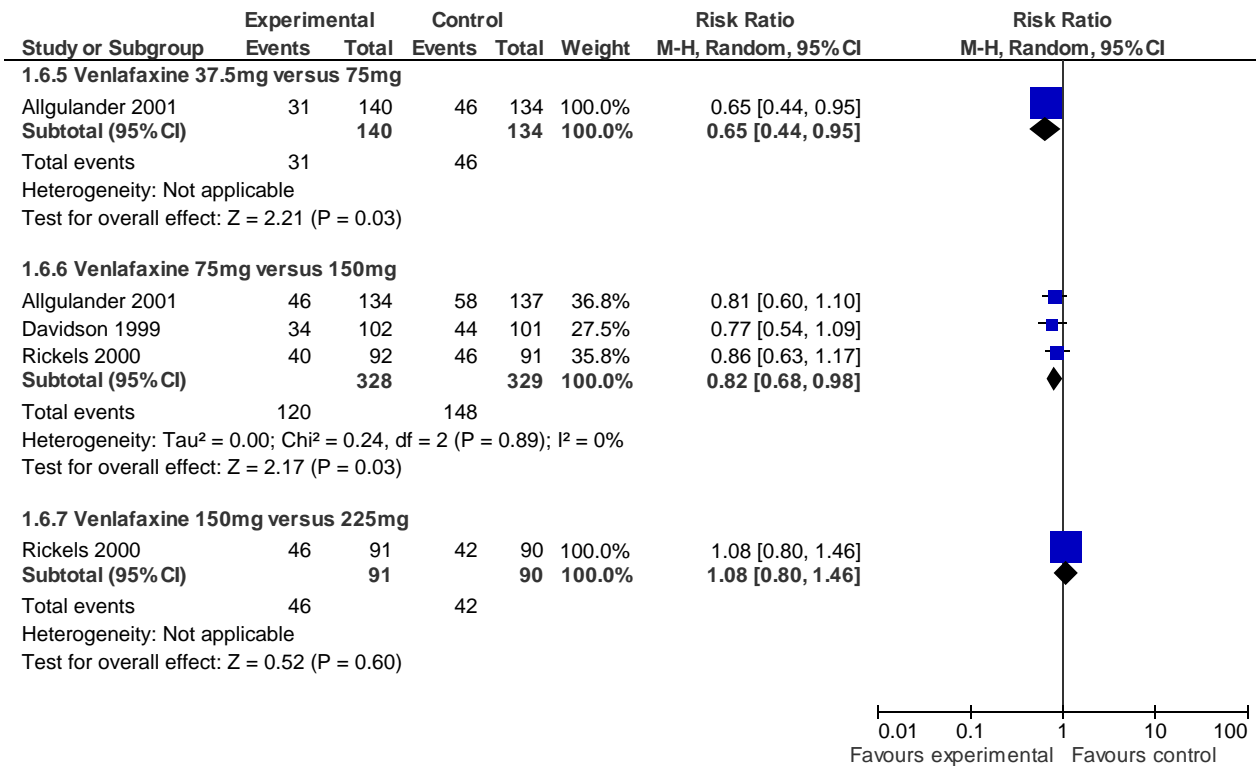
## 6 Comparing the Effectiveness of Different Dosages

### 1.5 Dizziness

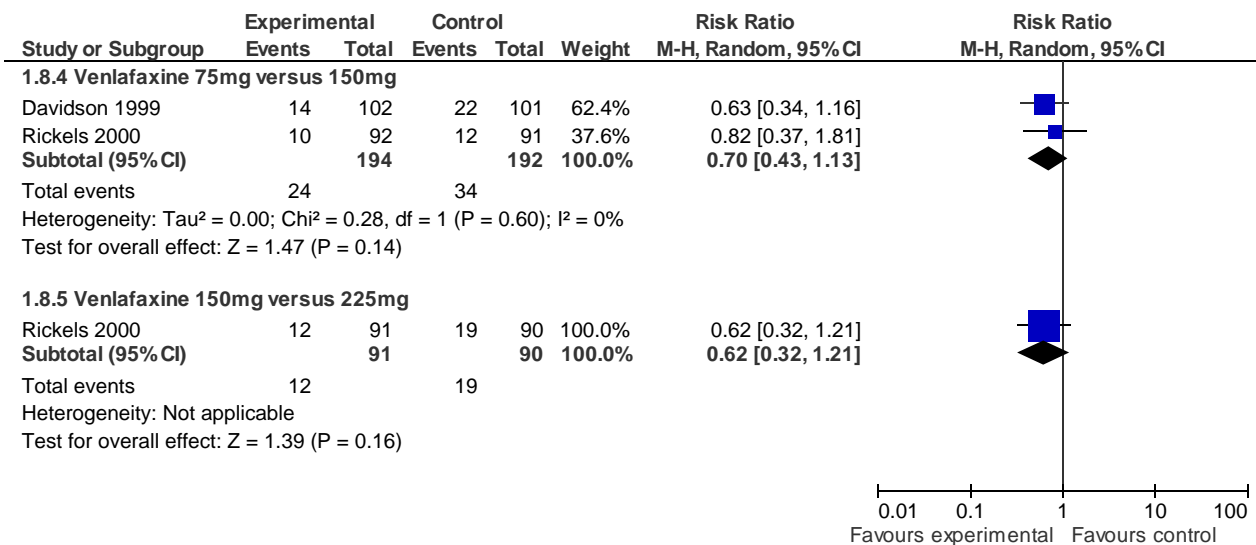


## 6 Comparing the Effectiveness of Different Dosages

### 1.6 Nausea



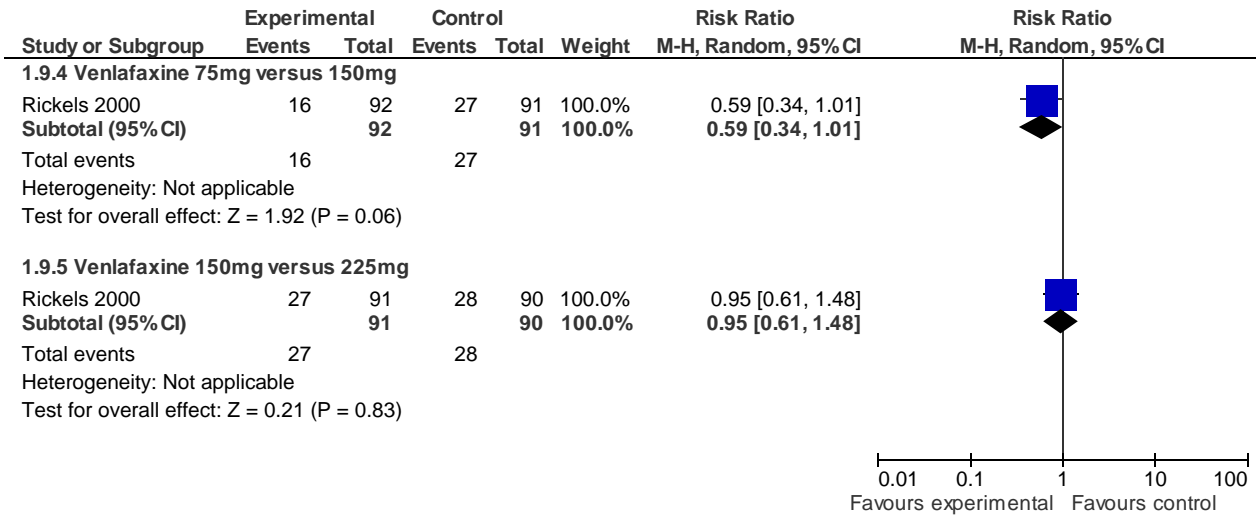
### 1.8 Asthenia



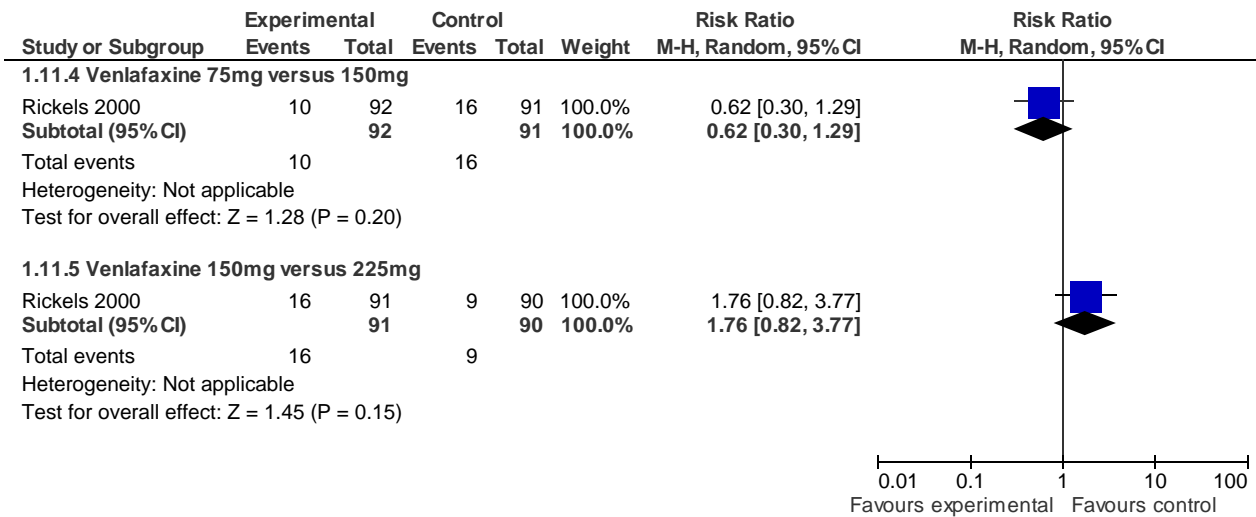


## 6 Comparing the Effectiveness of Different Dosages

### 1.9 Insomnia



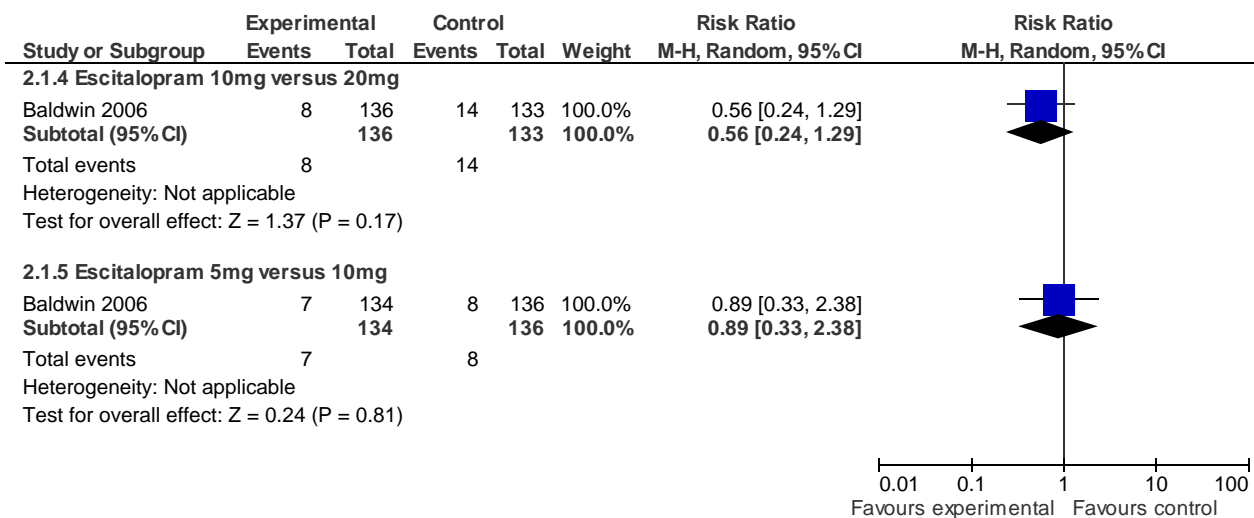
### 1.11 Nervousness



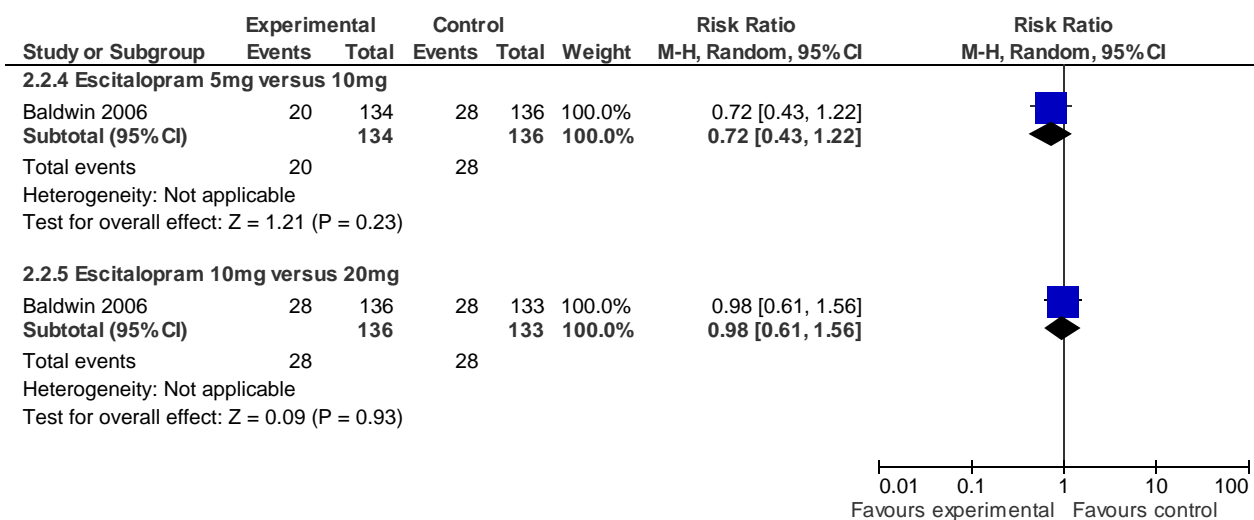
### 2 Escitalopram

## 6 Comparing the Effectiveness of Different Dosages

### 2.1 Discontinuation due to Adverse events

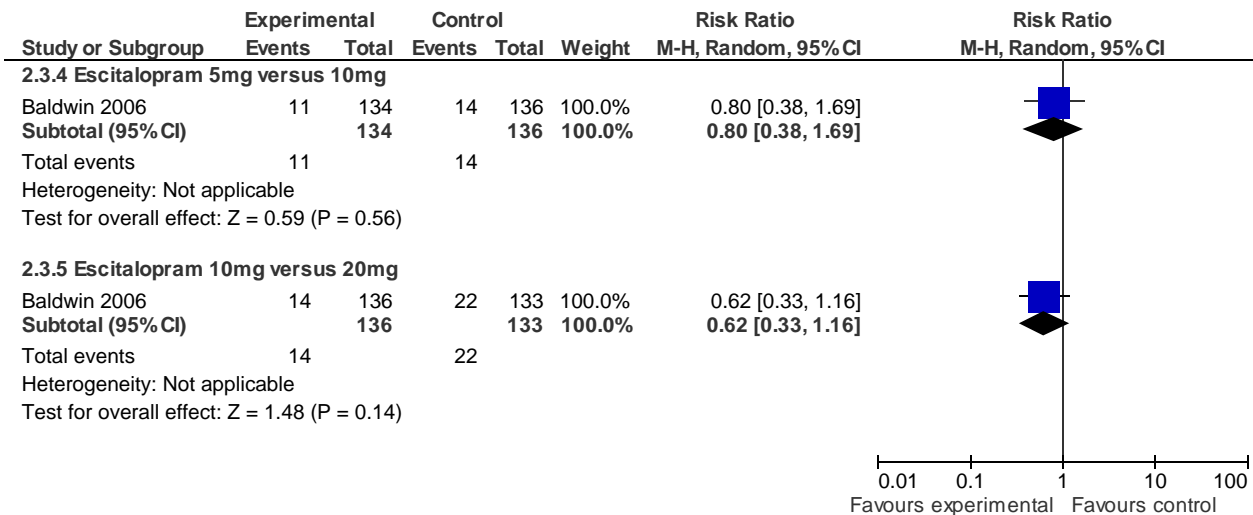


### 2.2 Nausea

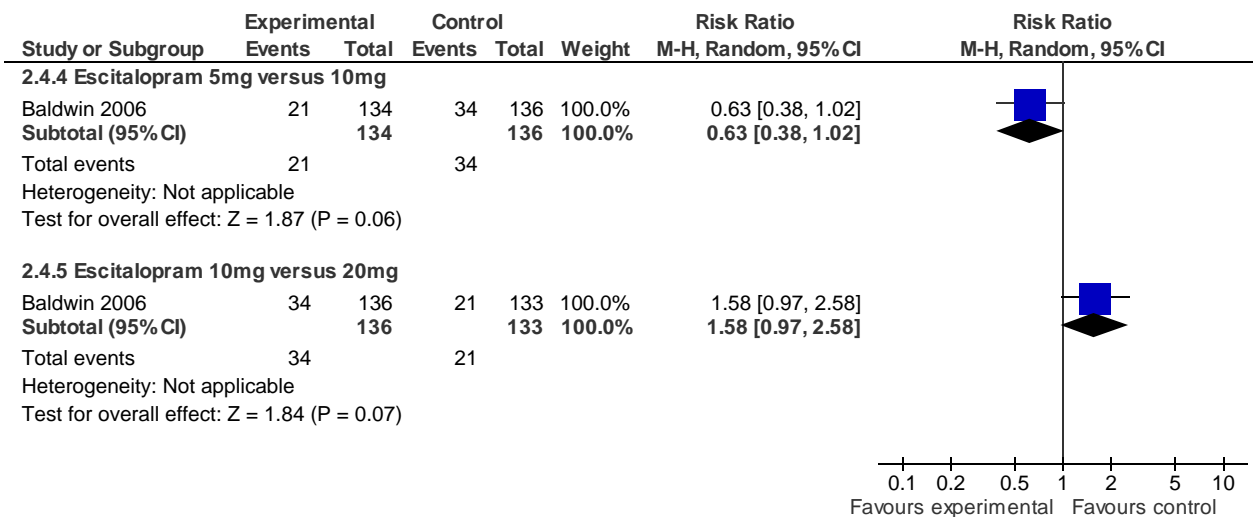


## 6 Comparing the Effectiveness of Different Dosages

### 2.3 Fatigue

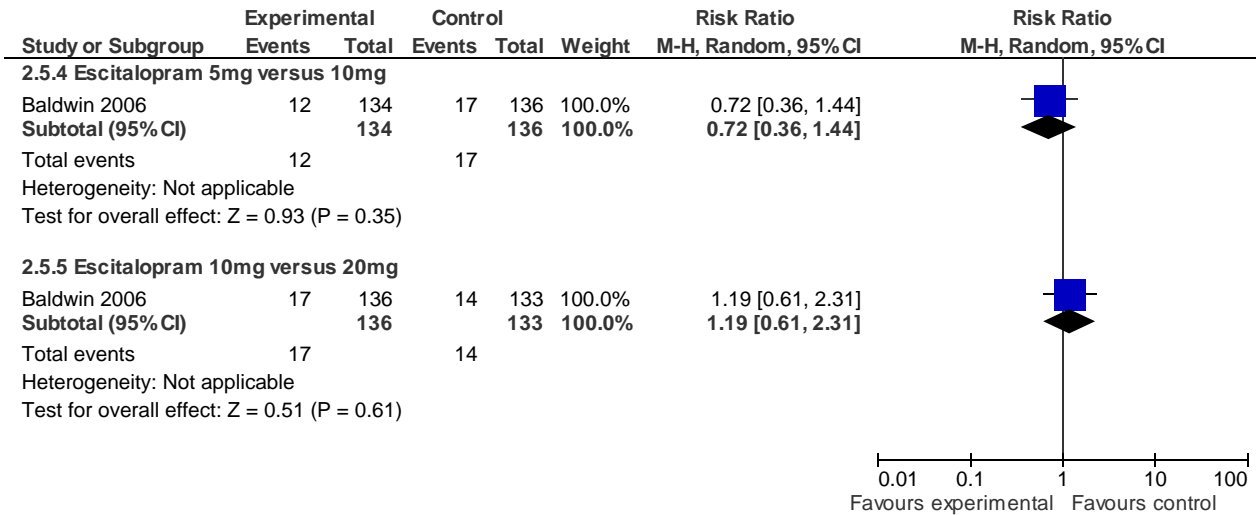


### 2.4 Headache

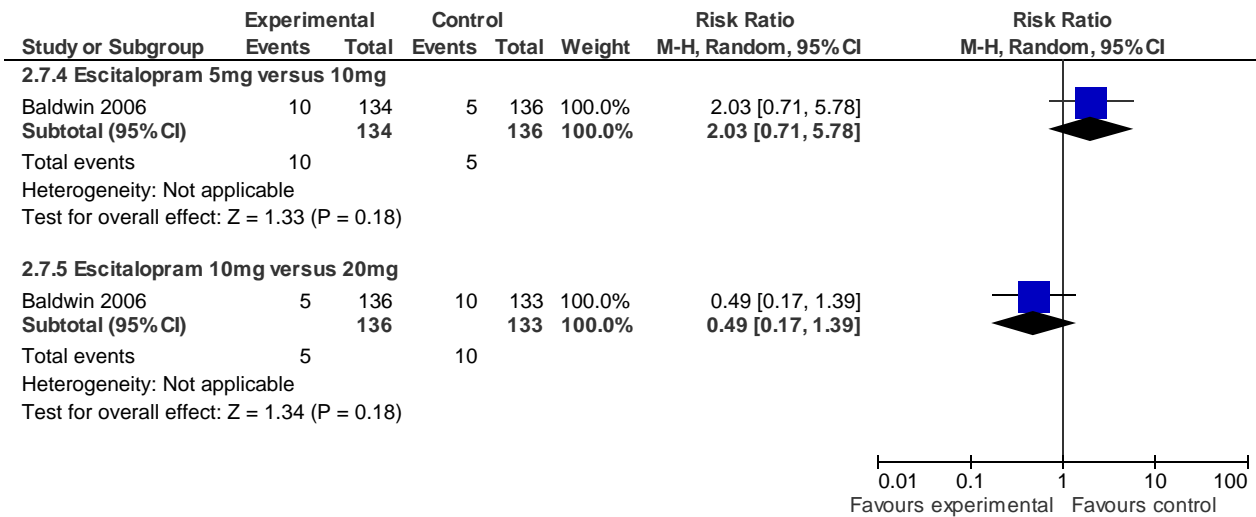


## 6 Comparing the Effectiveness of Different Dosages

### 2.5 Insomnia

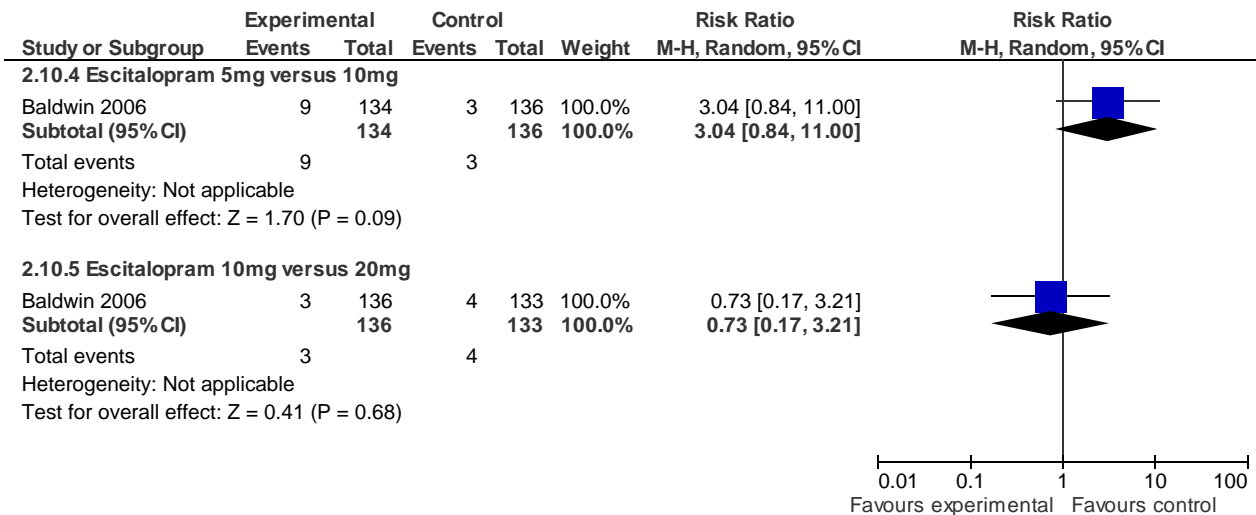


### 2.7 Somnolence

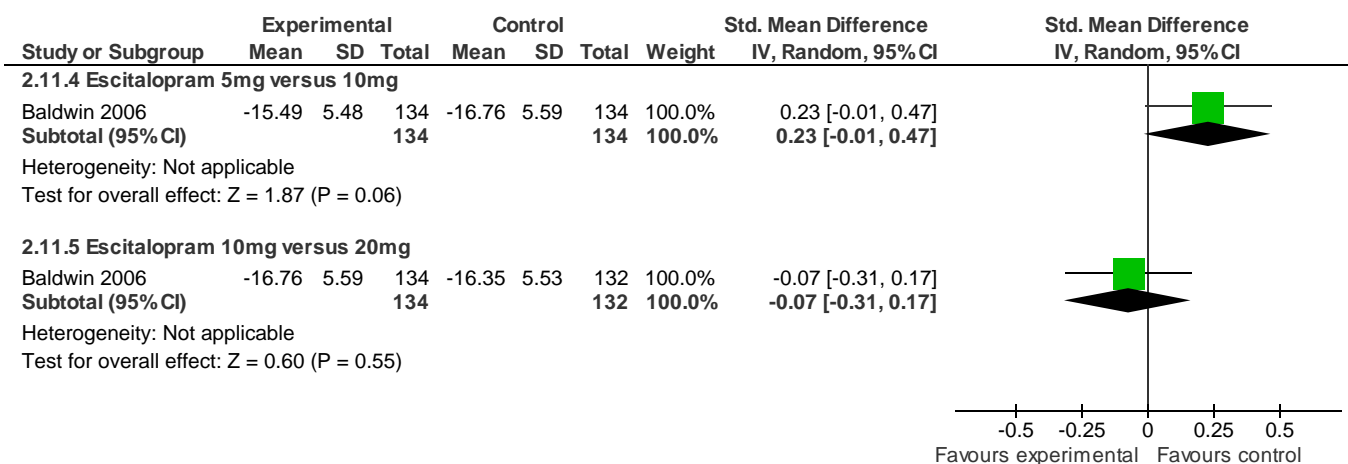


## 6 Comparing the Effectiveness of Different Dosages

### 2.10 Anxiety

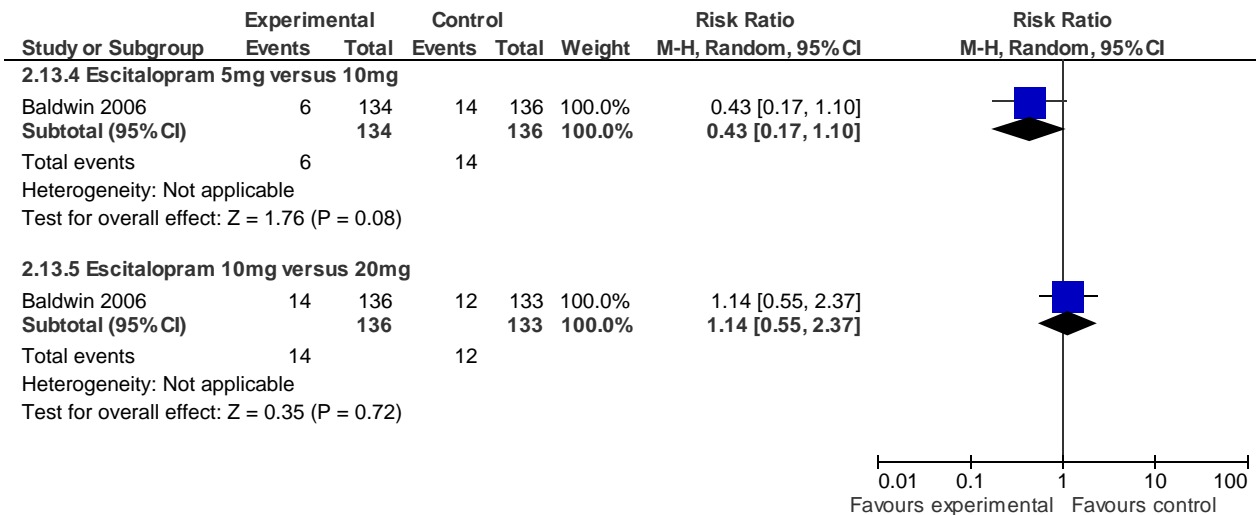


### 2.11 HAM-A



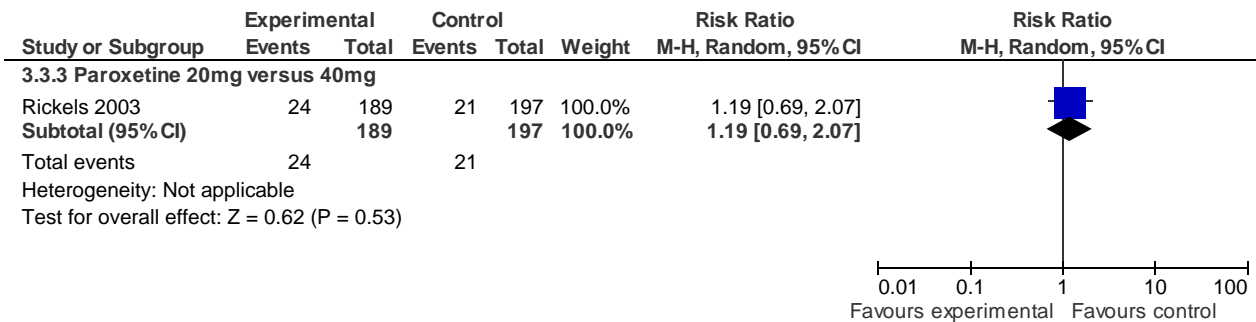
## 6 Comparing the Effectiveness of Different Dosages

### 2.13 Dizziness

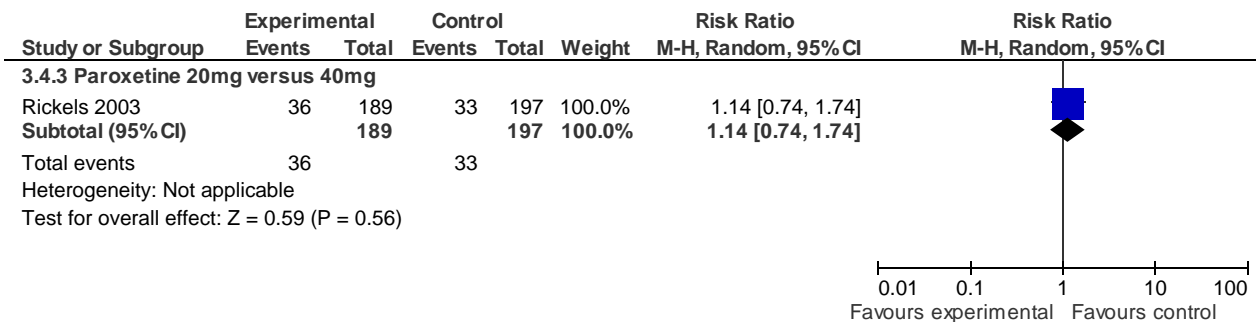


### 3 Paroxetine

#### 3.3 Decreased libido

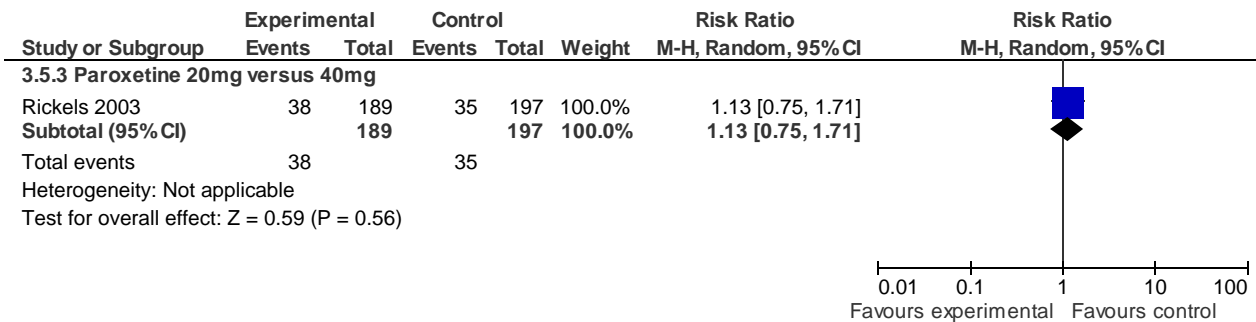


#### 3.4 Nausea

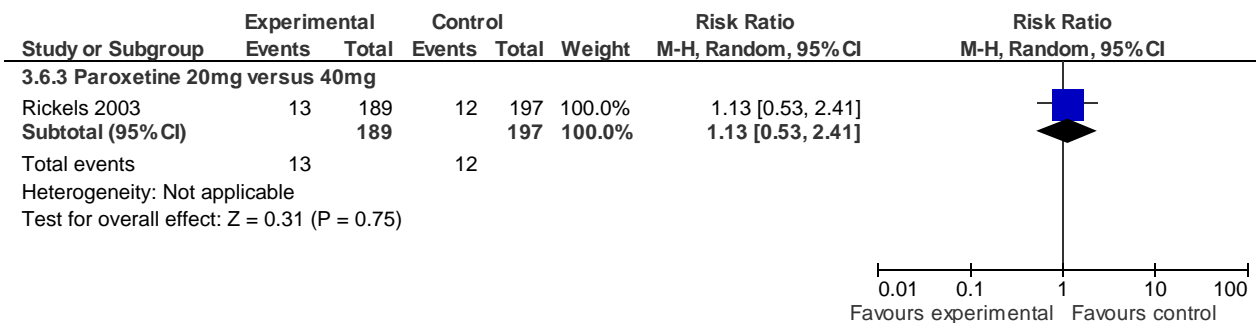


## 6 Comparing the Effectiveness of Different Dosages

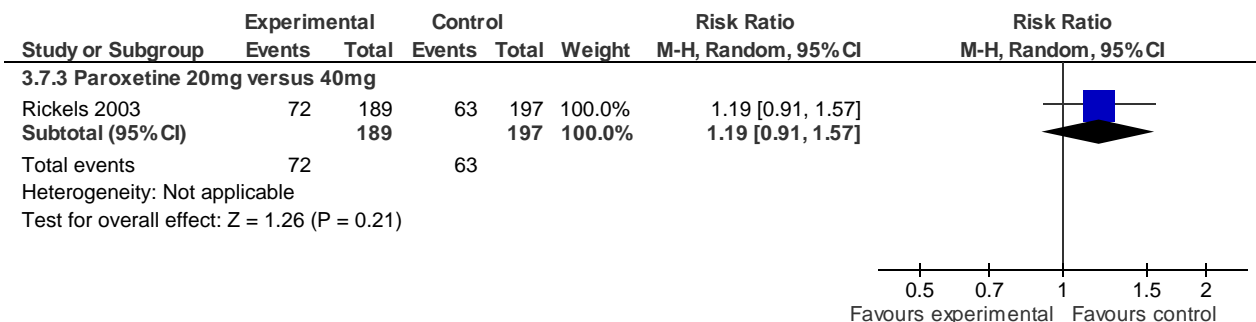
### 3.5 Somnolence



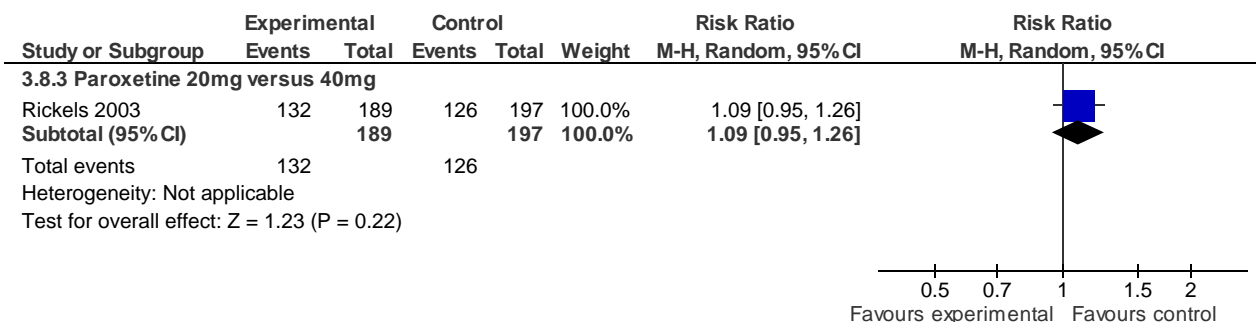
### 3.6 Decreased appetite



### 3.7 Non-response

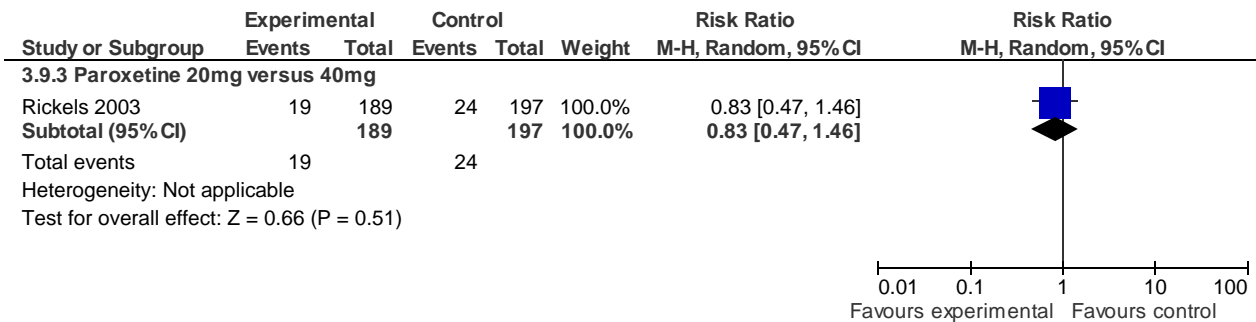


### 3.8 Non-remission

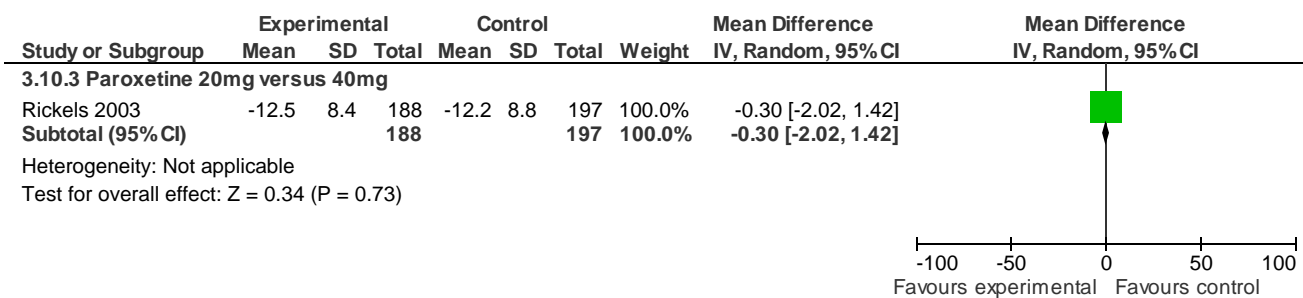


## 6 Comparing the Effectiveness of Different Dosages

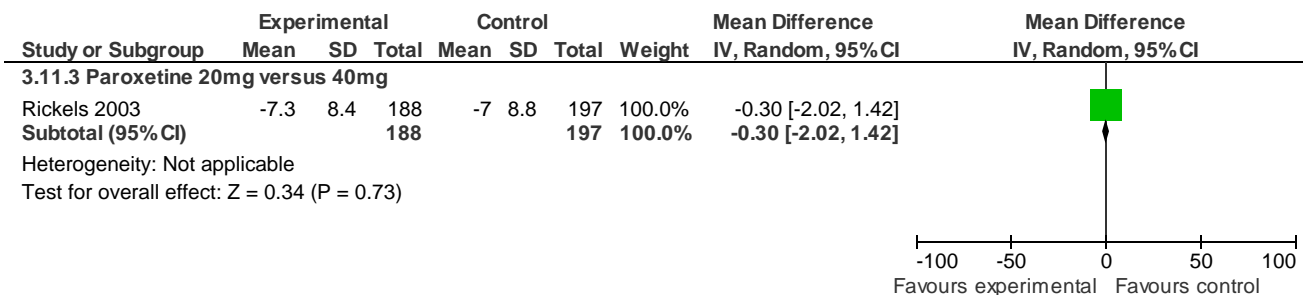
### 3.9 Discontinuation due to Adverse Events



### 3.10 HAM-A



### 3.11 HADS-A

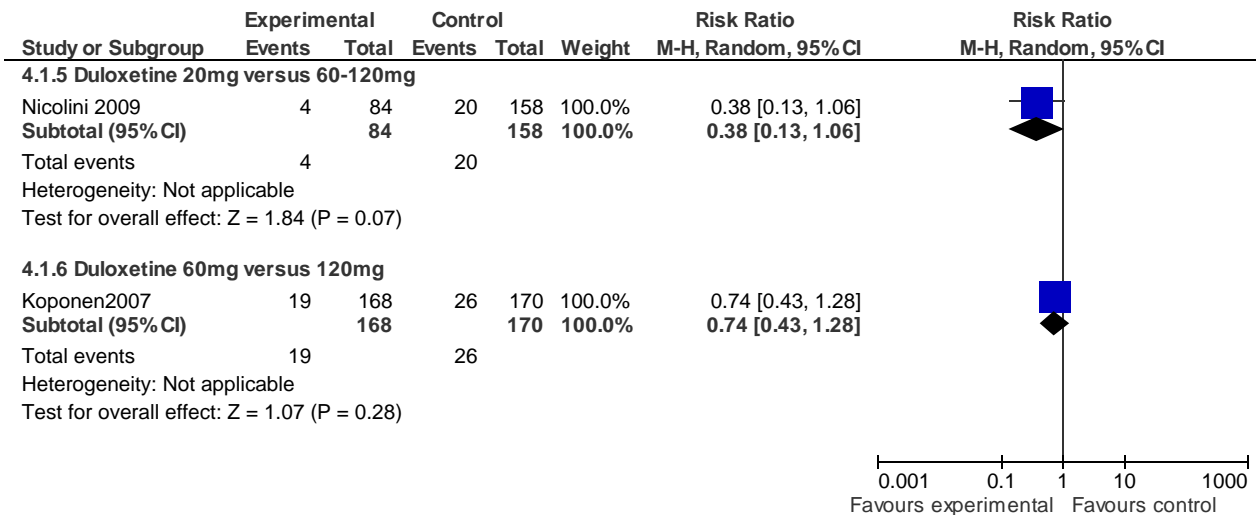


## 4 Duloxetine

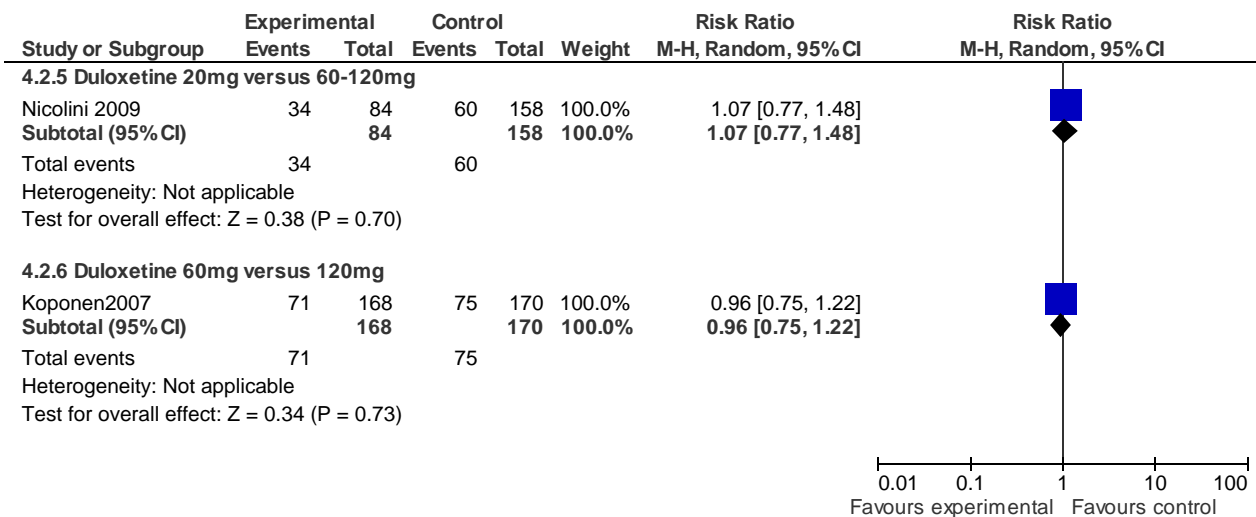


## 6 Comparing the Effectiveness of Different Dosages

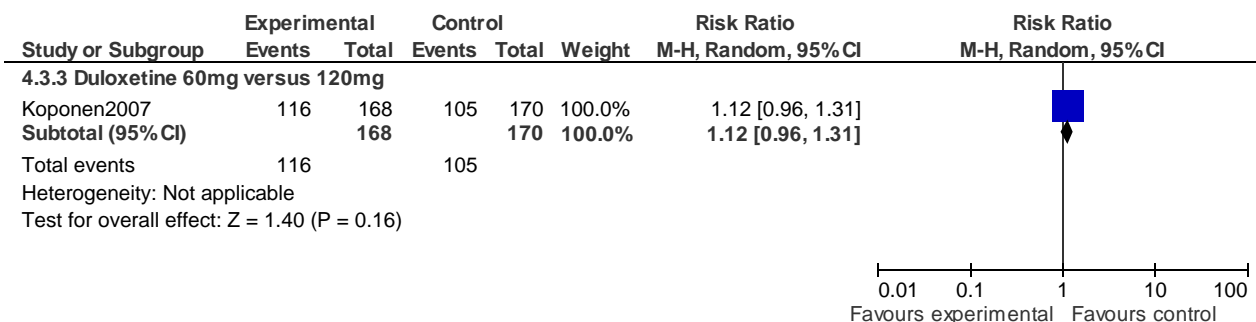
### 4.1 Discontinuation due to Adverse Events



### 4.2 Non-response

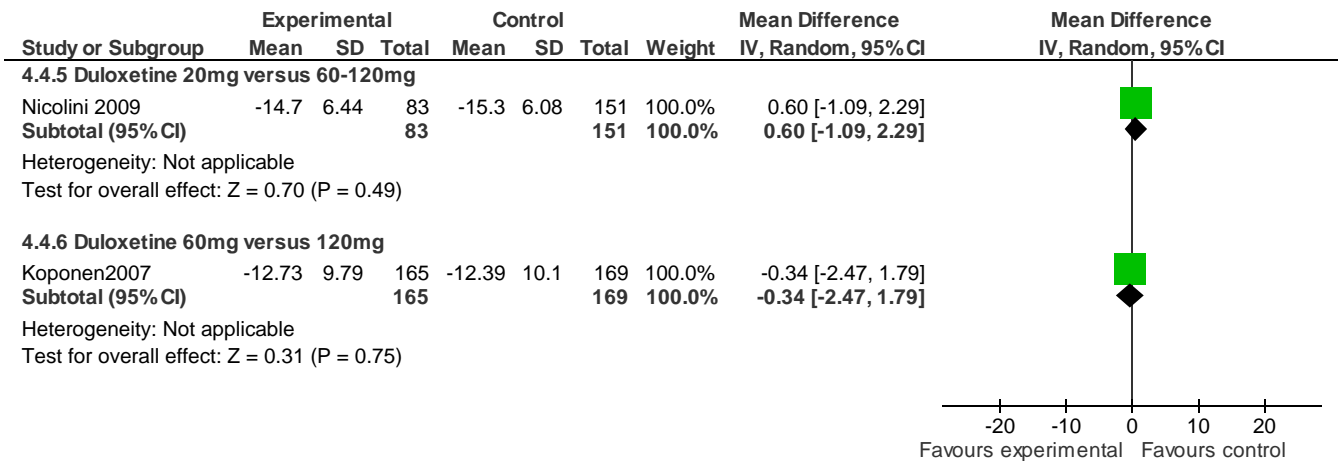


### 4.3 Non-remission

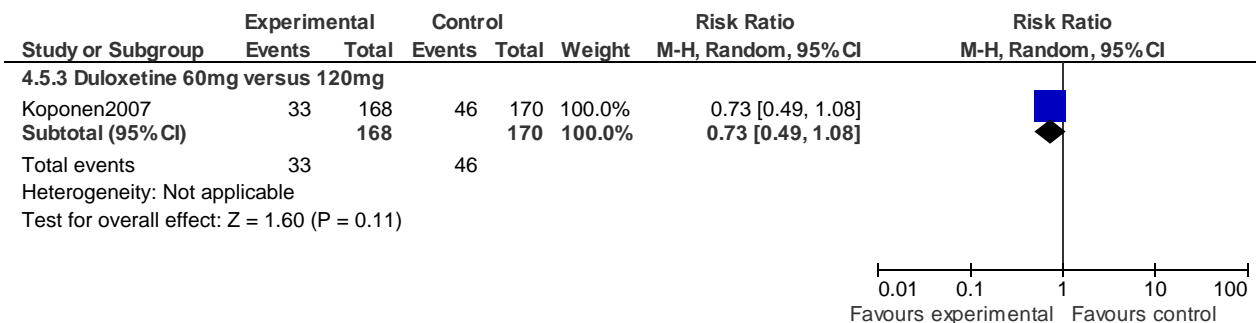


## 6 Comparing the Effectiveness of Different Dosages

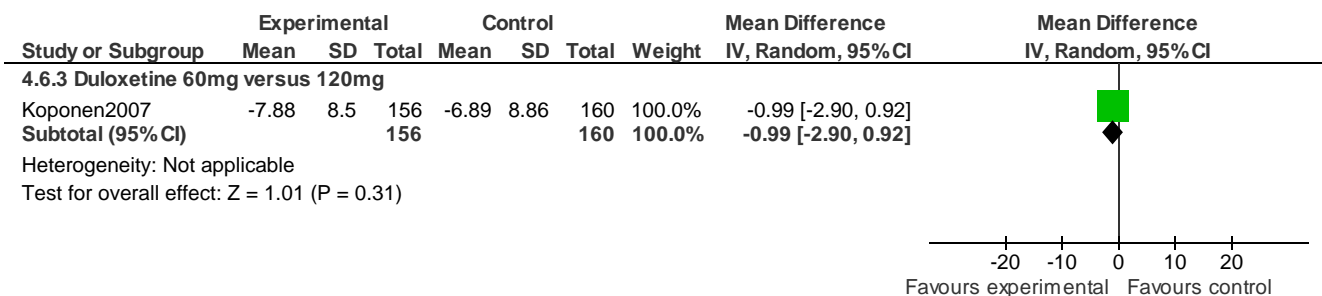
### 4.4 HAM-A



### 4.5 Discontinuation due to Any Reason

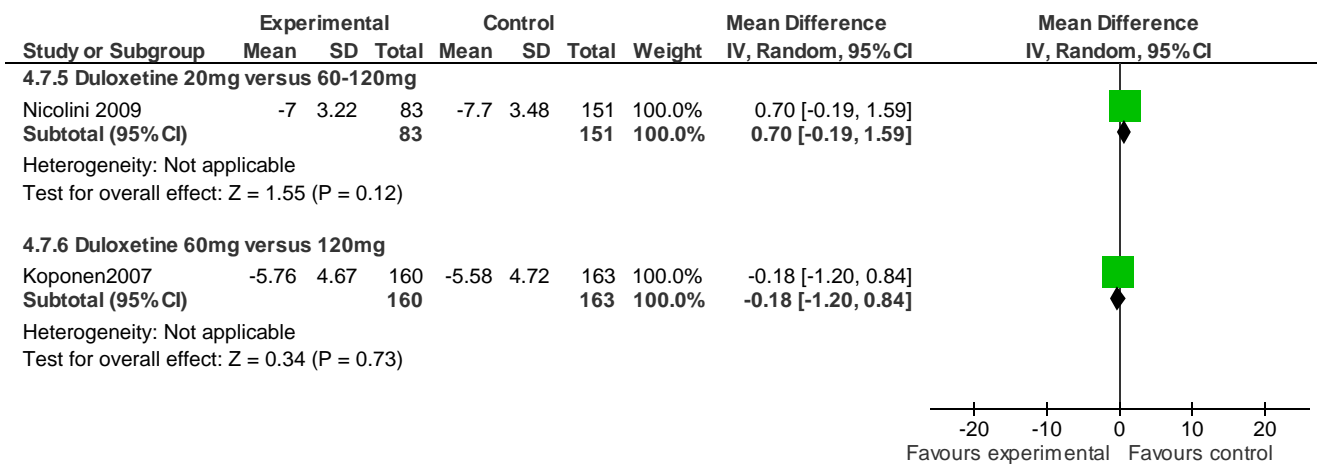


### 4.6 Sheehan Disability Scale

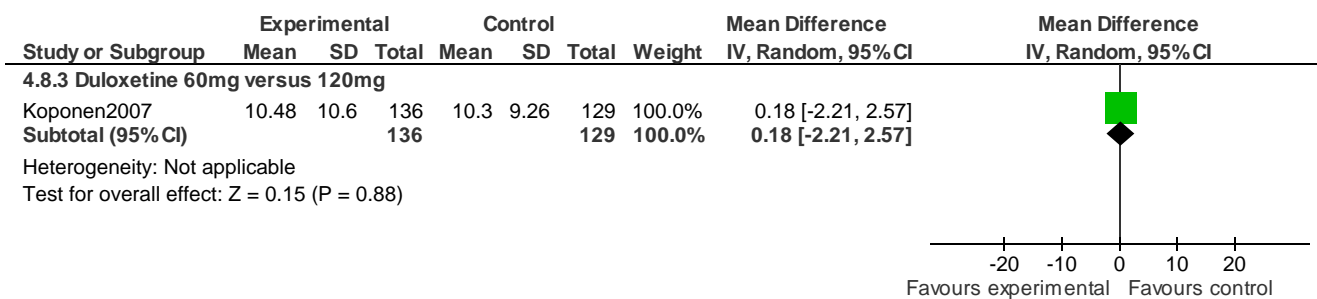


## 6 Comparing the Effectiveness of Different Dosages

### 4.7 HADS-A



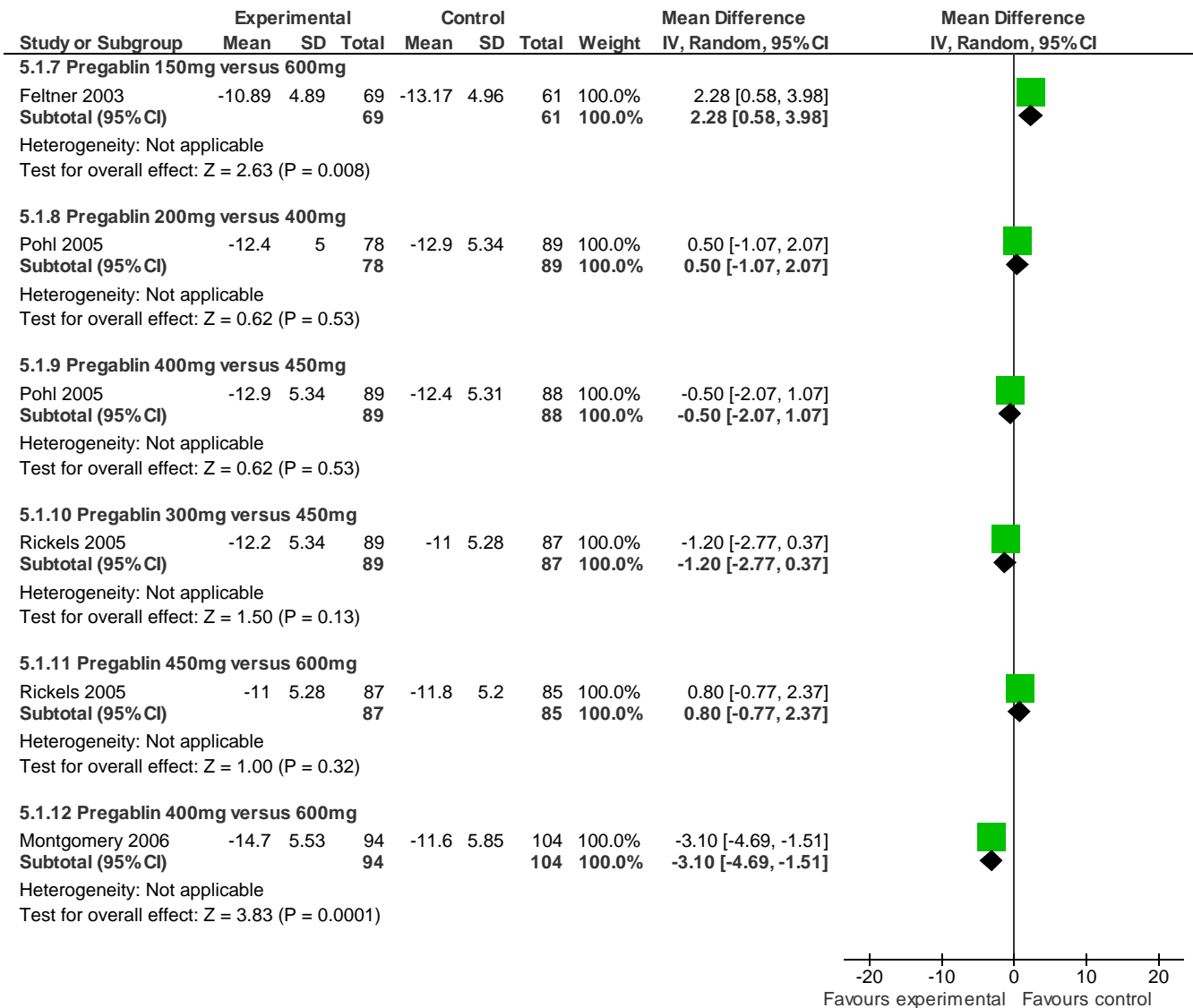
### 4.8 Q-LES-Q-SF



### 5 Pregablin

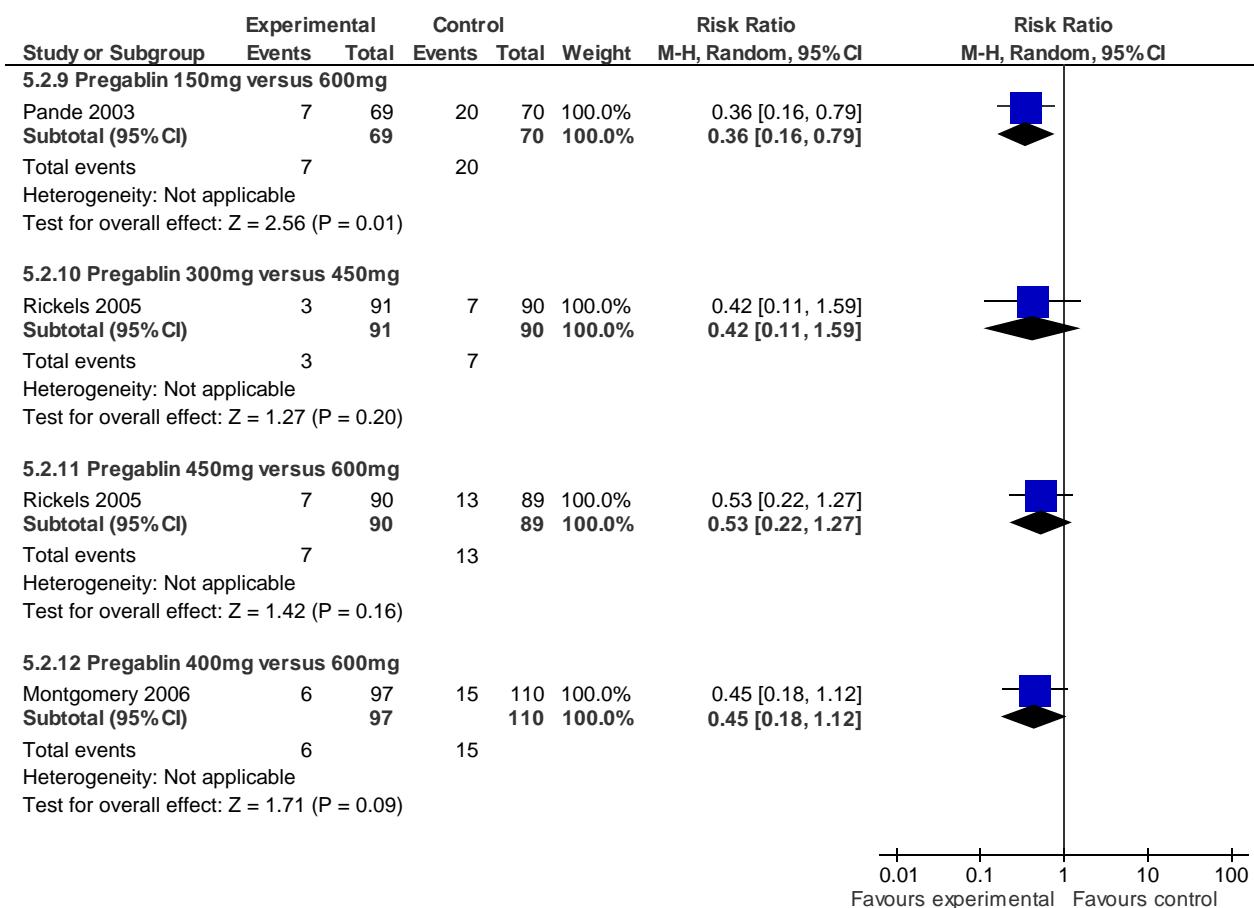
## 6 Comparing the Effectiveness of Different Dosages

### 5.1 HAM-A

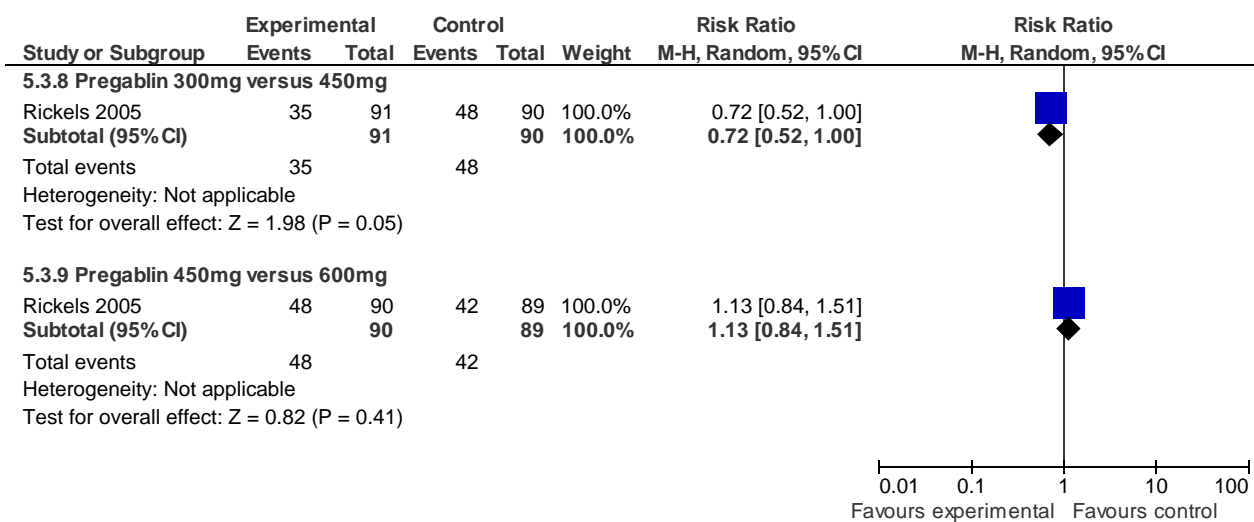


## 6 Comparing the Effectiveness of Different Dosages

### 5.2 Discontinuation due to Adverse Events

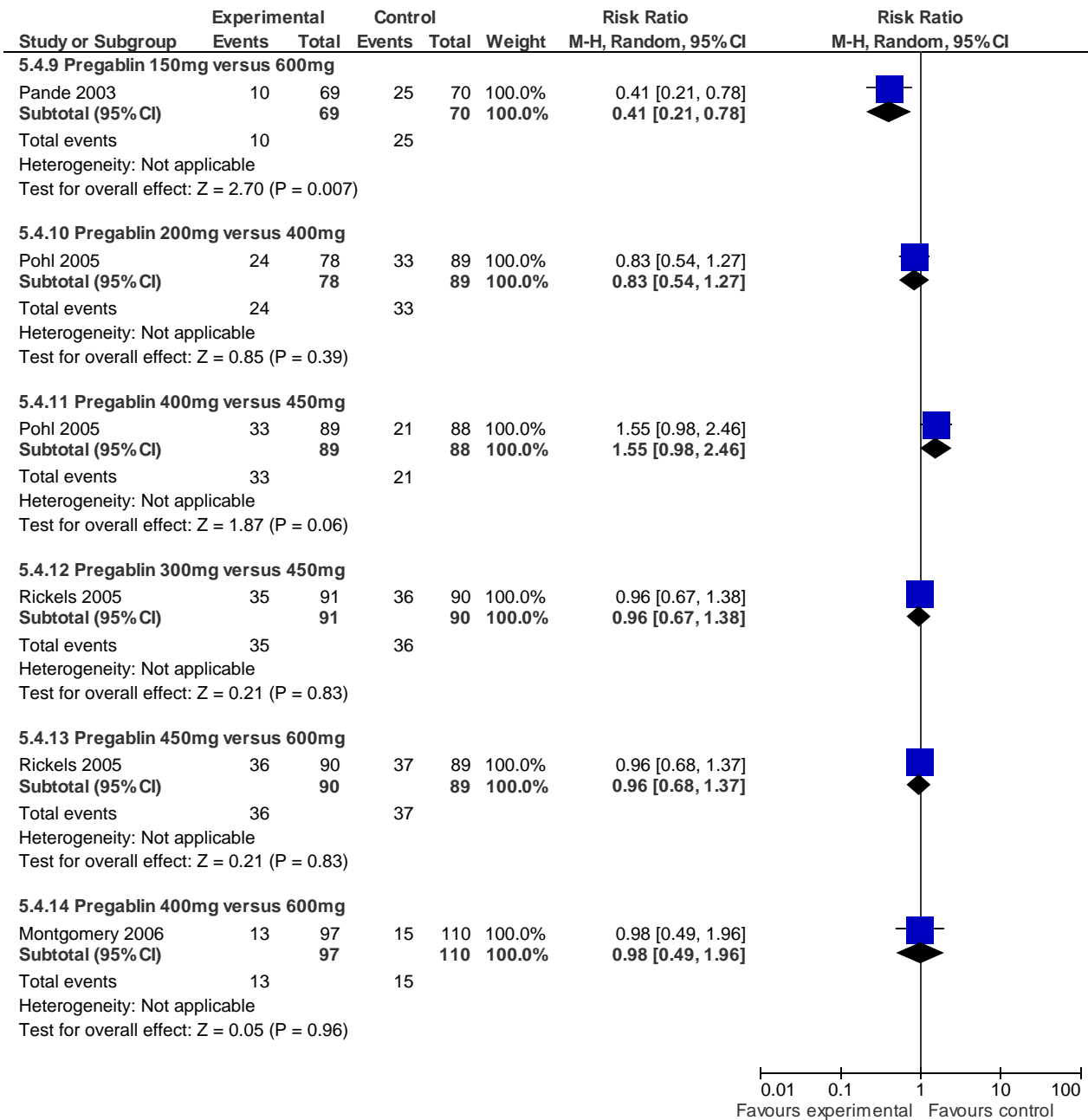


### 5.3 Non Response



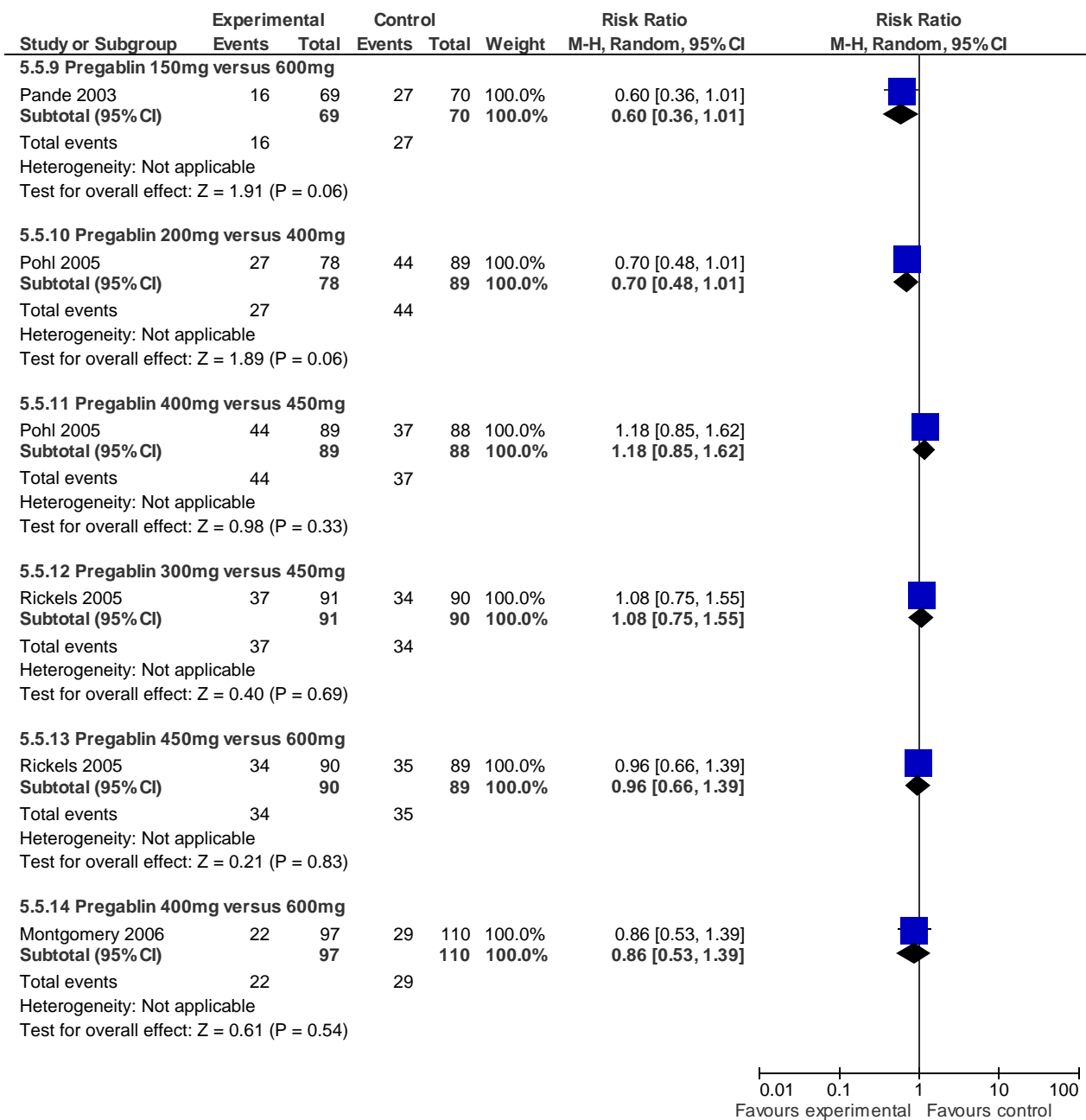
## 6 Comparing the Effectiveness of Different Dosages

### 5.4 Somnolence



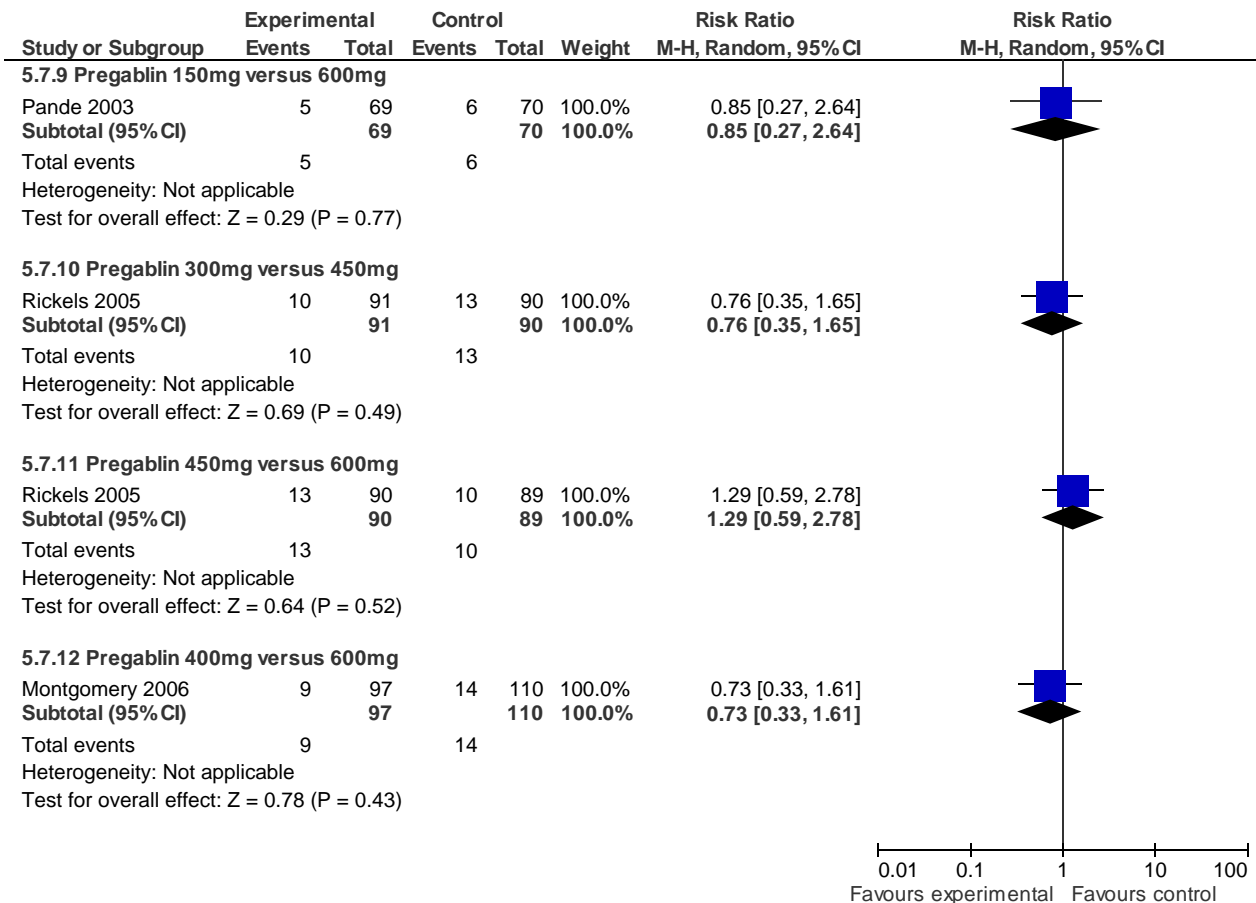
## 6 Comparing the Effectiveness of Different Dosages

### 5.5 Dizziness

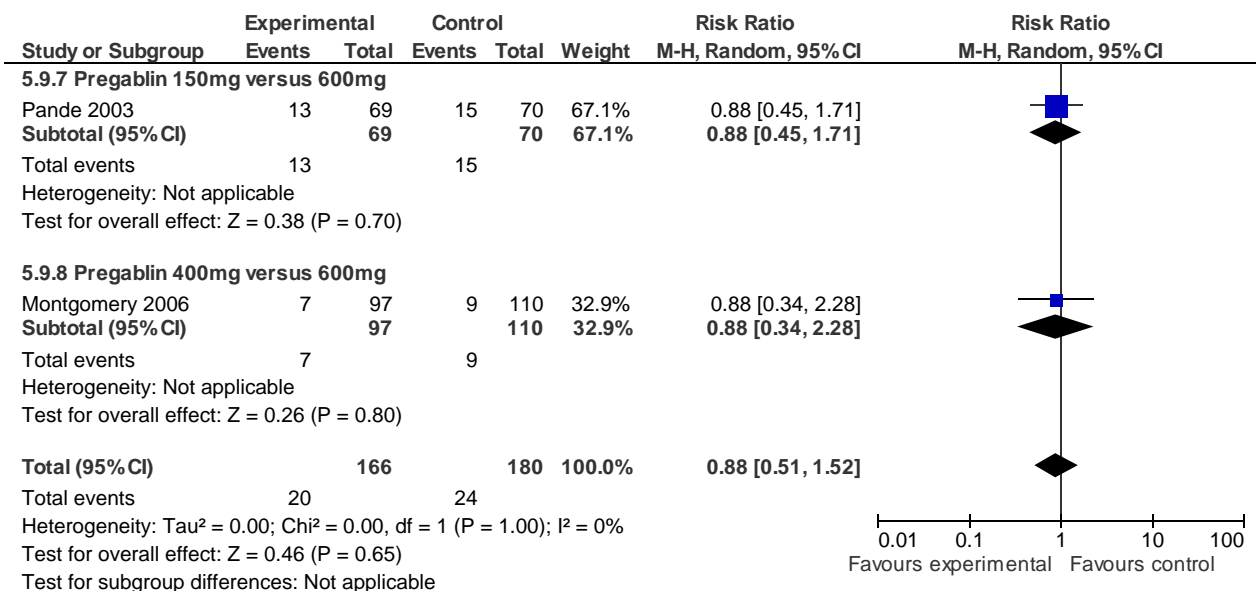


## 6 Comparing the Effectiveness of Different Dosages

### 5.7 Nausea



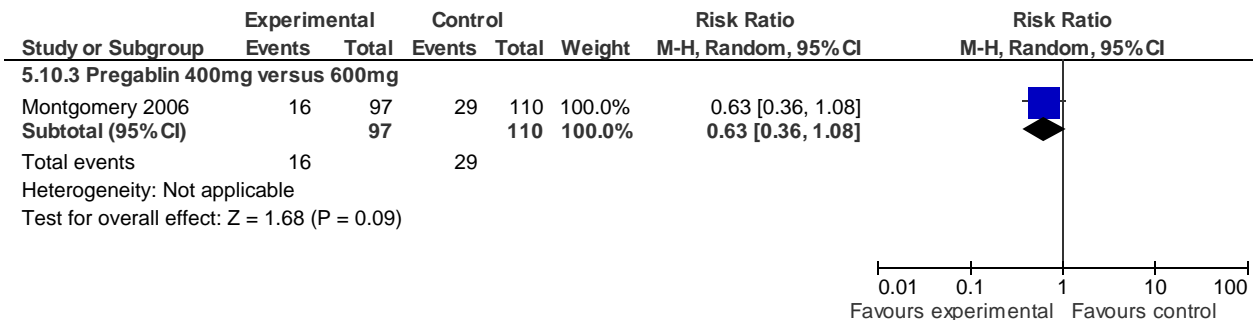
### 5.9 Headache



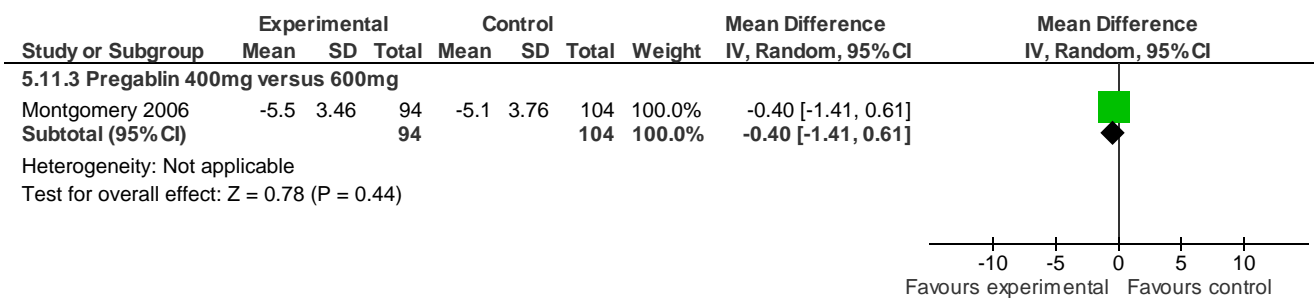


## 6 Comparing the Effectiveness of Different Dosages

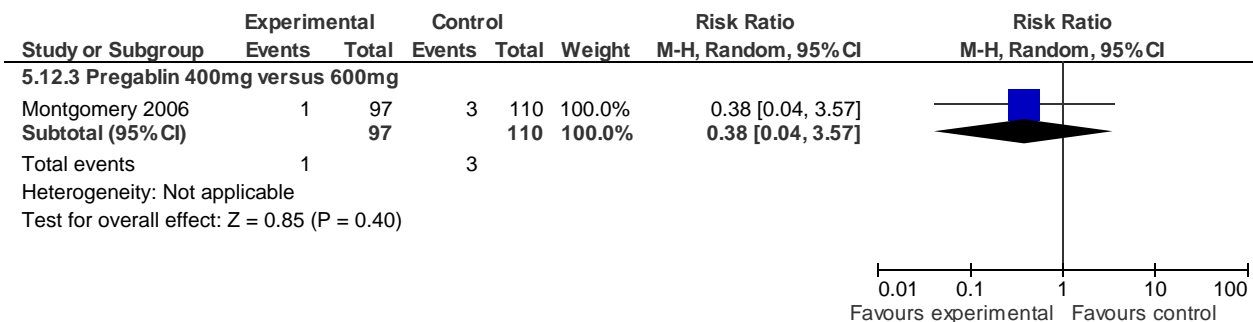
### 5.10 Discontinuation for any reason



### 5.11 HADS-A



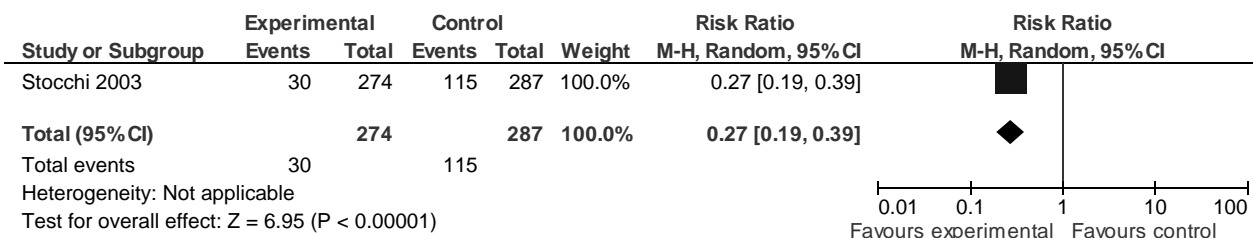
### 5.12 Insomnia



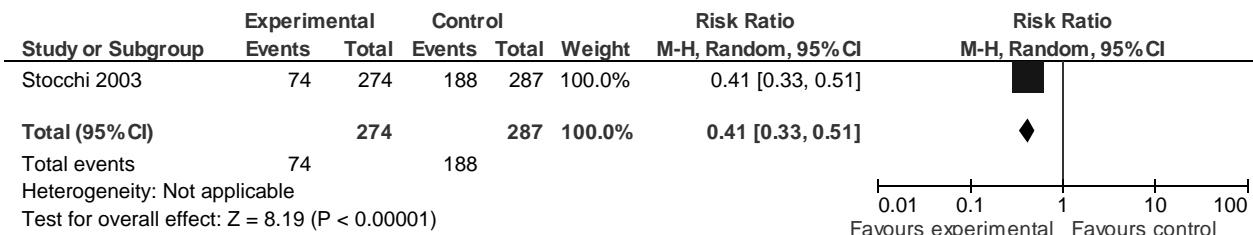
# 7 Maintenance Treatment

## 1 Paroxetine versus Placebo

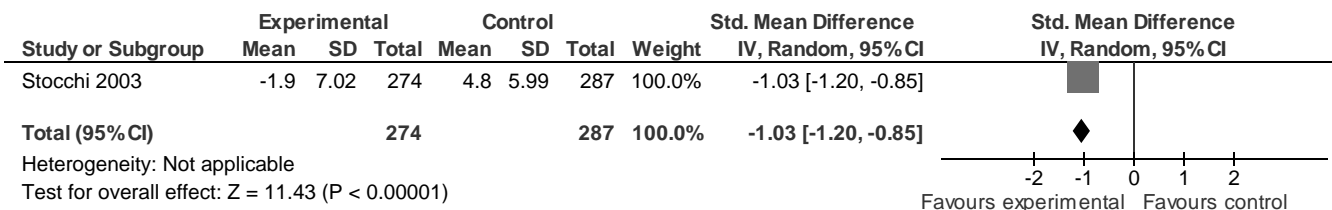
### 1.1 Relapse



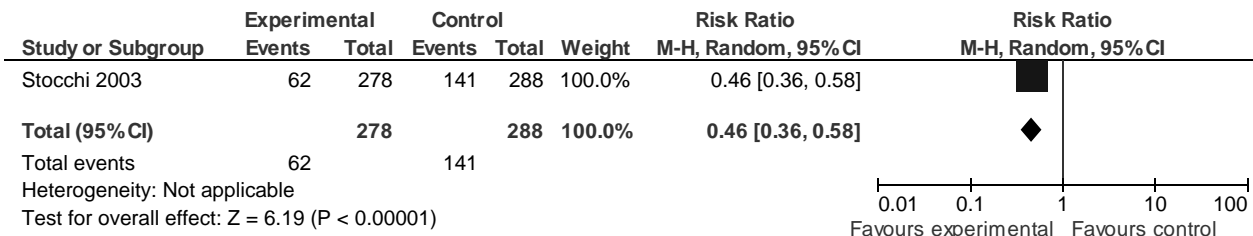
### 1.2 Non-remission



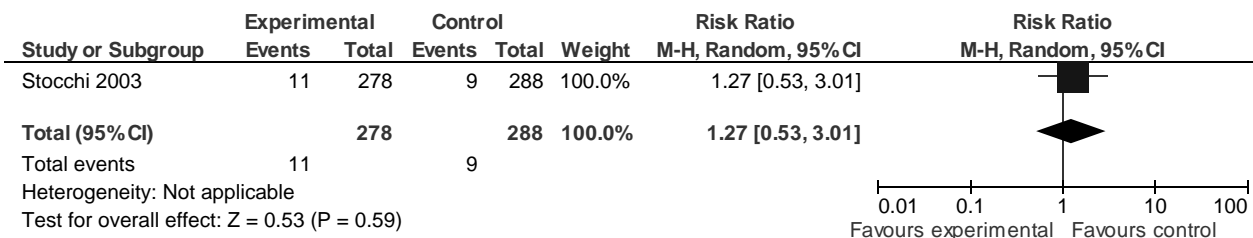
### 1.3 HAM-A



### 1.4 Discontinuation for any reason



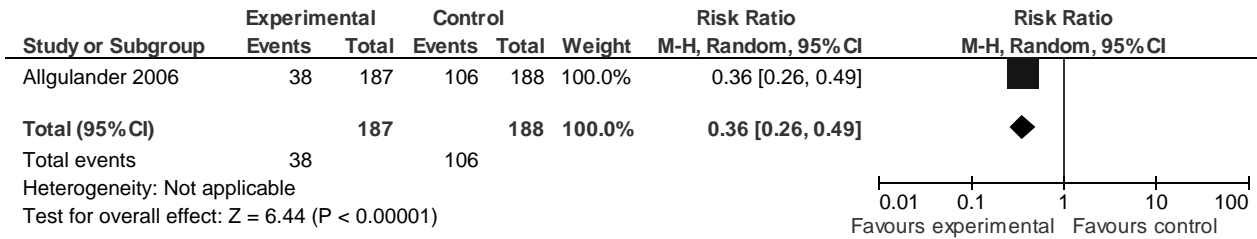
### 1.5 Discontinuation due to adverse events



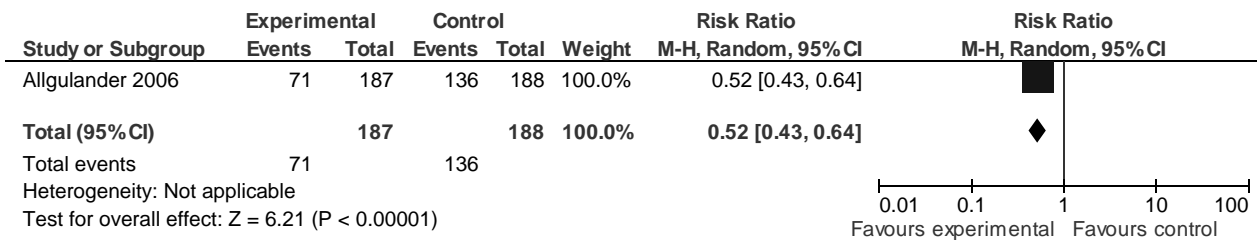
## 2 Escitalopram versus Placebo

## 7 Maintenance Treatment

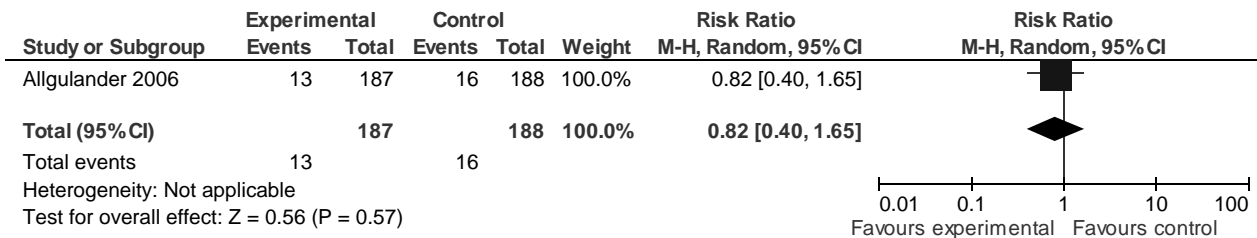
### 2.1 Relapse



### 2.2 Discontinuation for any reason

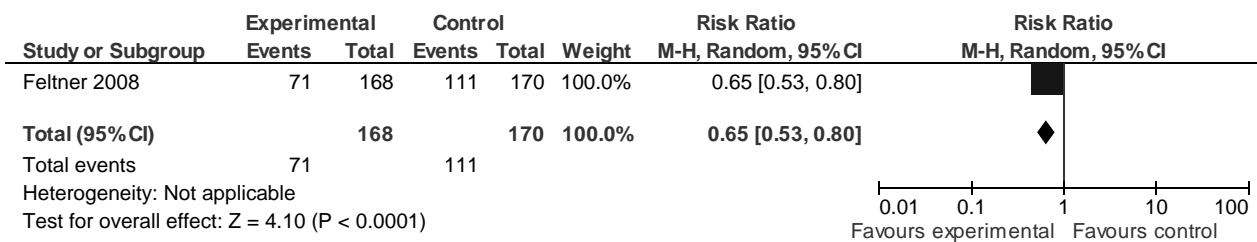


### 2.3 Discontinuation due to adverse events

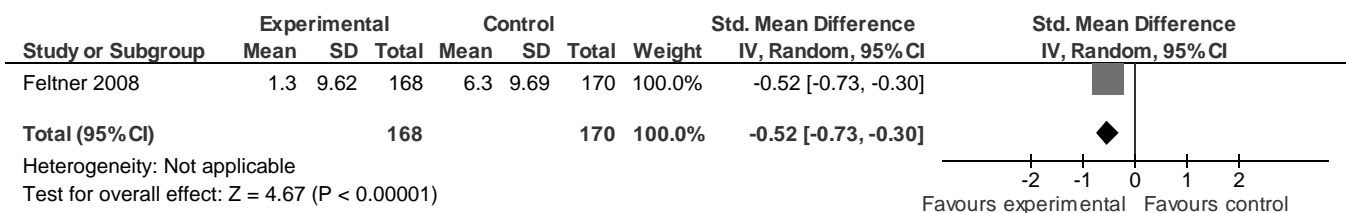


## 3 Pregabalin versus Placebo

### 3.1 Relapse

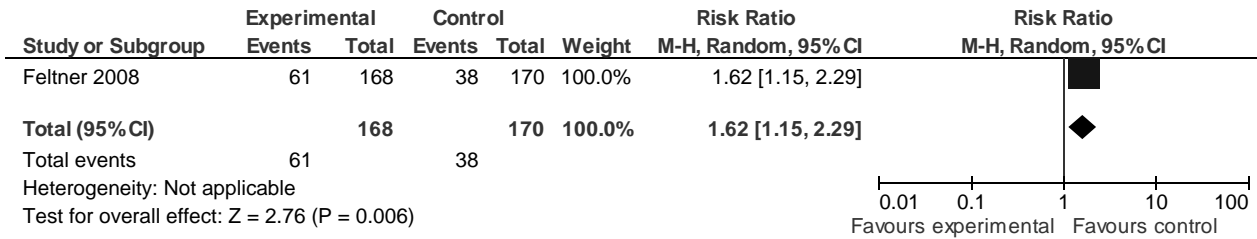


### 3.2 HAM-A

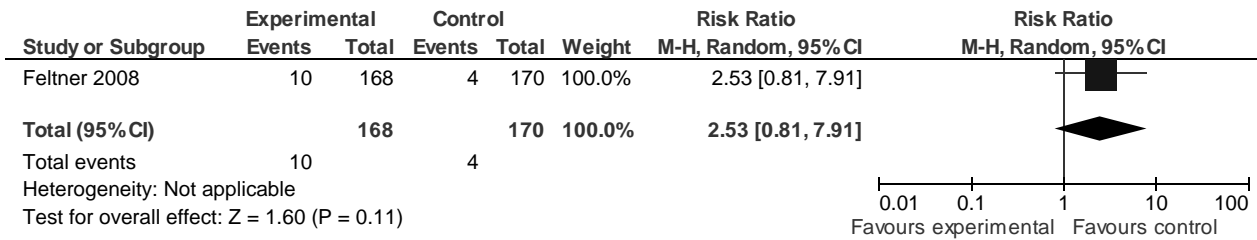


## 7 Maintenance Treatment

### 3.3 Discontinuation for any reason

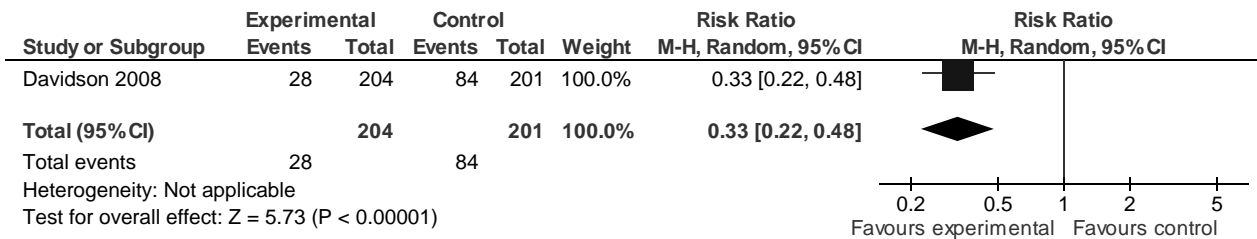


### 3.4 Discontinuation due to adverse events

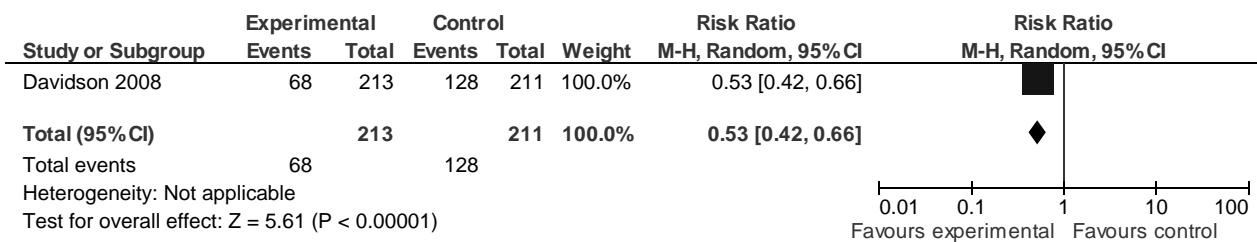


## 4 Duloxetine versus Placebo

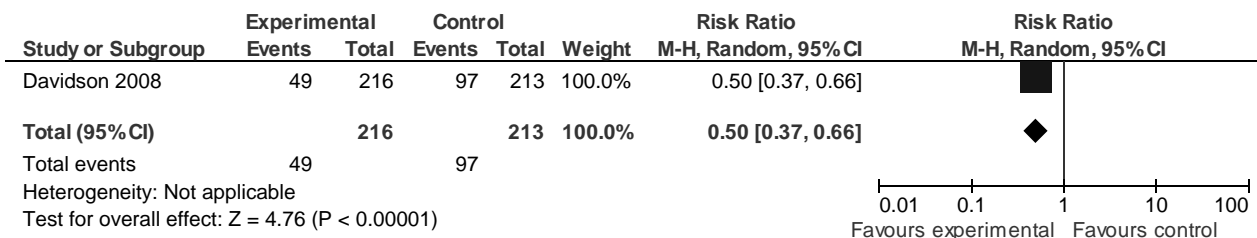
### 4.1 Relapse



### 4.2 Non-remission

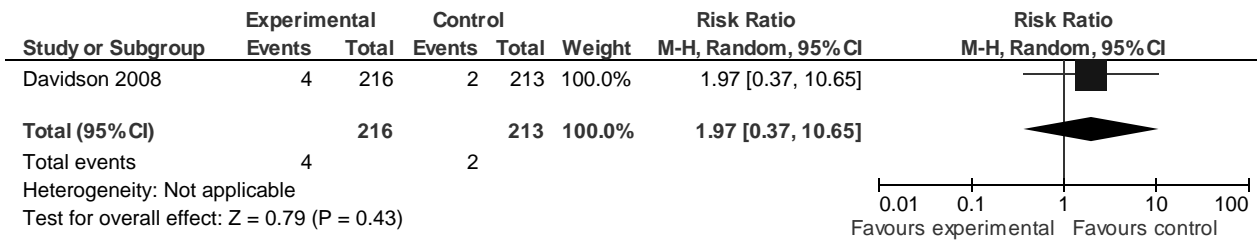


### 4.3 Discontinuation for any reason

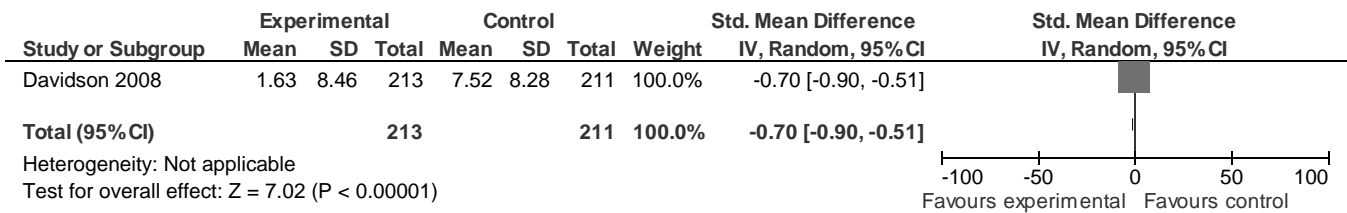


## 7 Maintenance Treatment

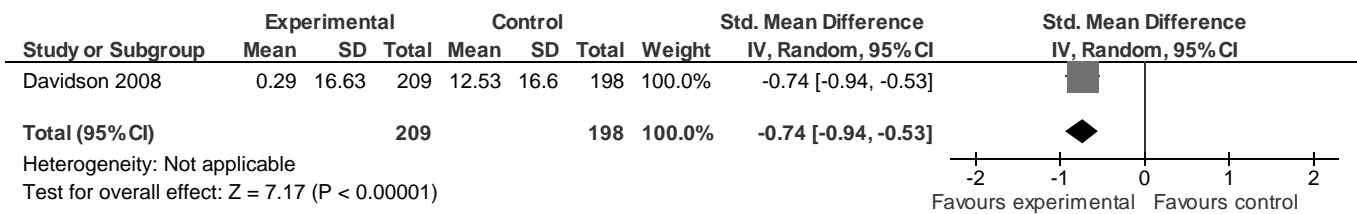
### 4.4 Discontinuation due to adverse events



### 4.5 HAM-A



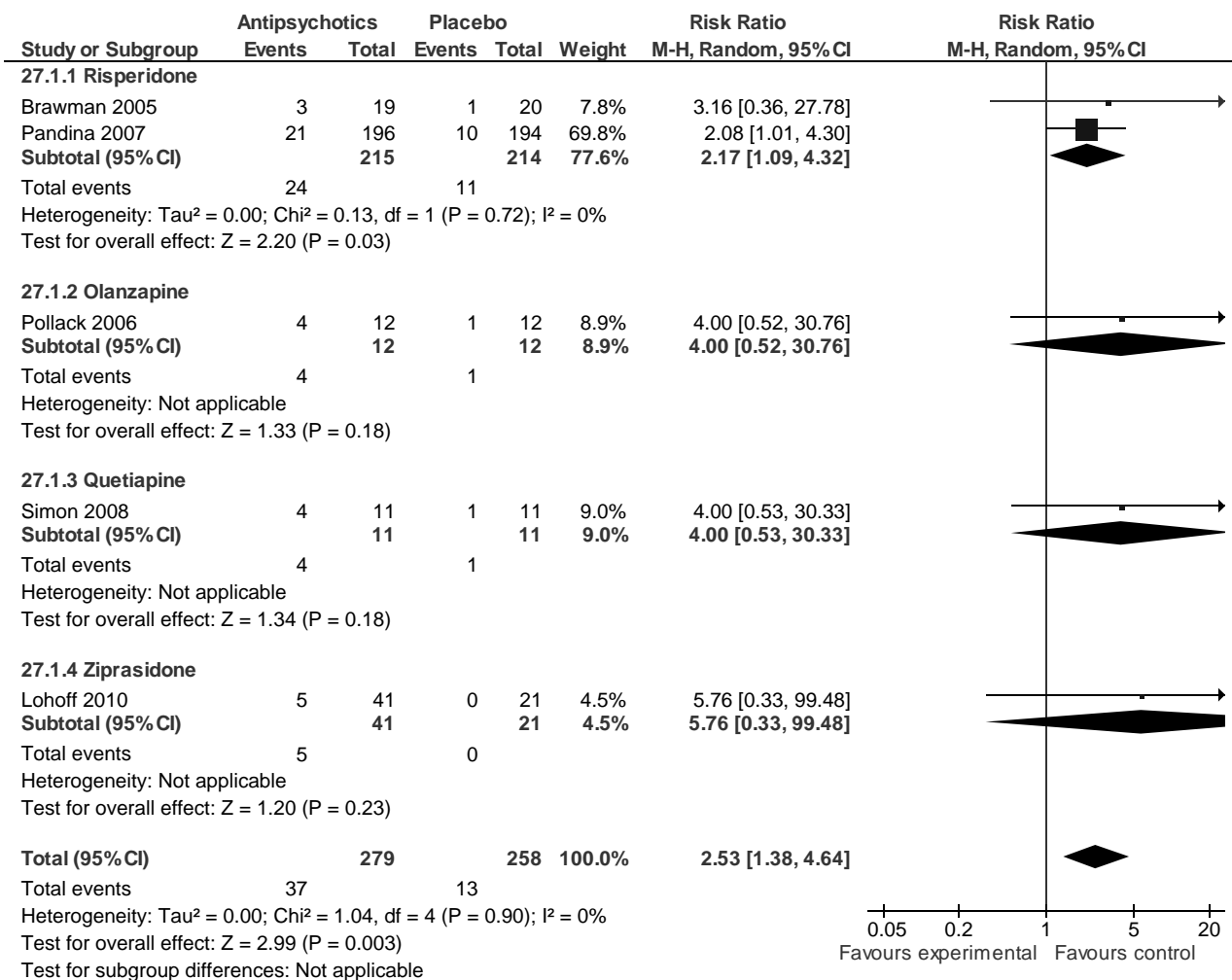
### 4.6 Q-LES-Q-SF



## 8 Augmentation

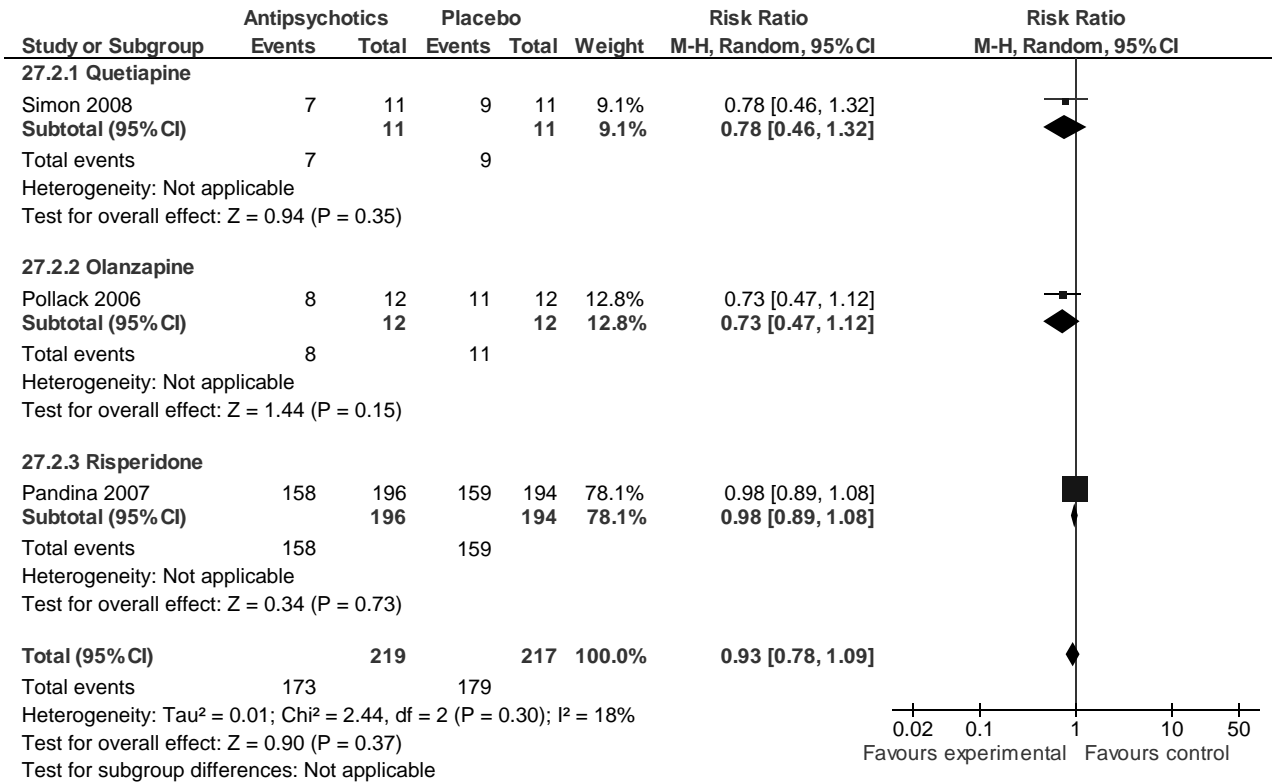
### 27 Augmentation: Antipsychotics versus Placebo

#### 27.1 Discontinuation due to adverse events

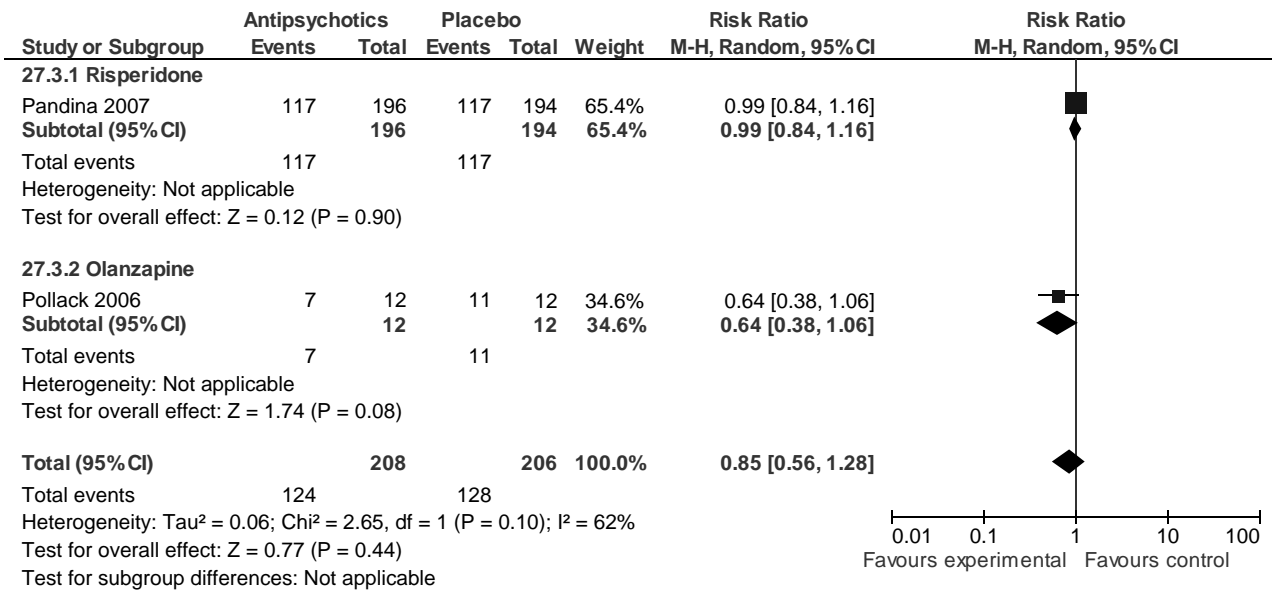


## 8 Augmentation

### 27.2 Non-remission

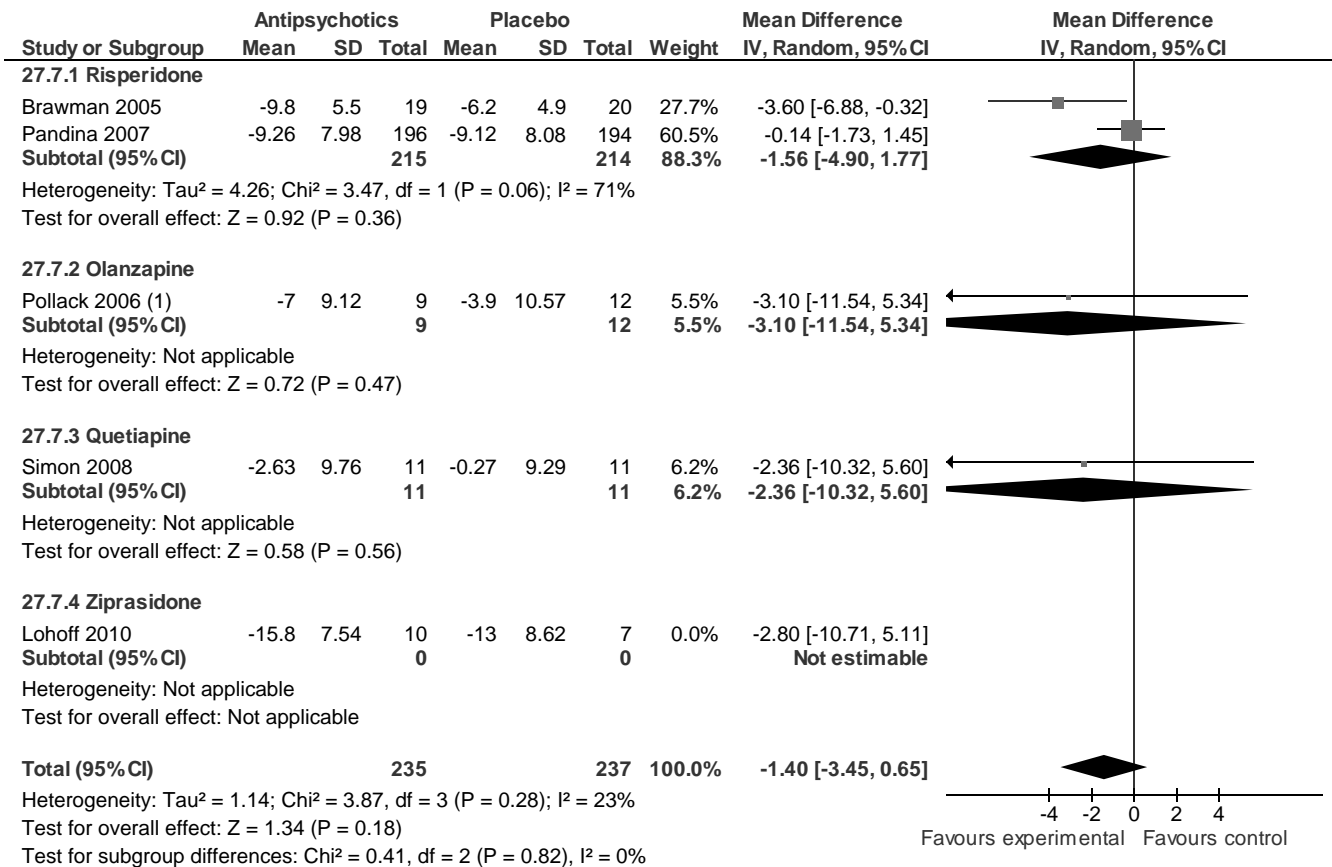


### 27.3 Non-response



# 8 Augmentation

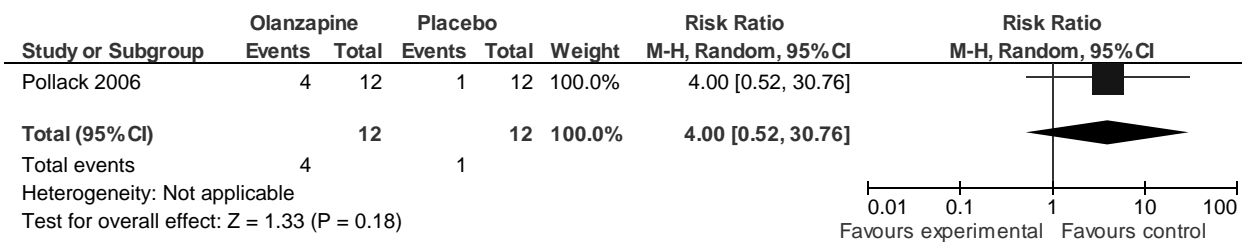
## 27.7 HAM-A



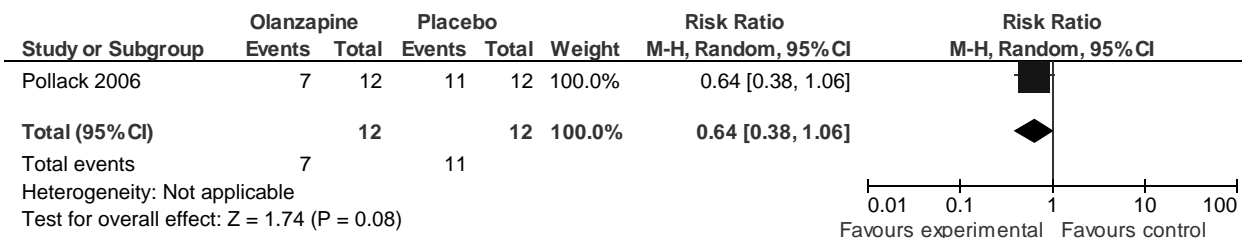
(1) change score

## 29 Augmentation: Olanzapine versus Placebo

### 29.2 Discontinuation due to adverse events



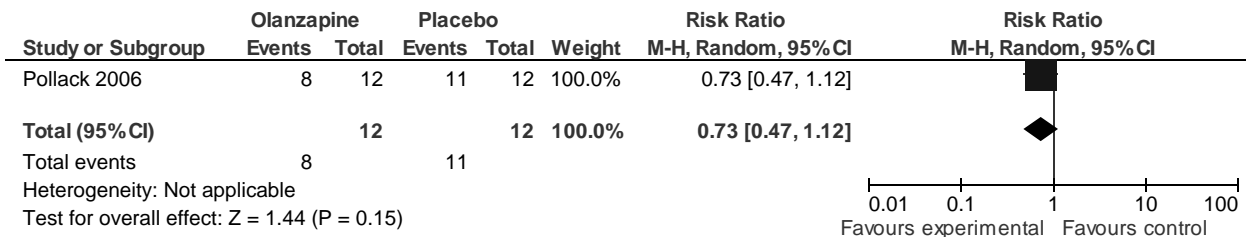
### 29.3 Non-response



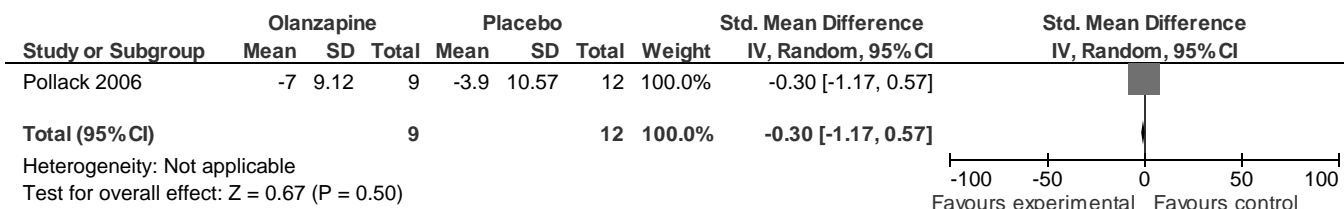


## 8 Augmentation

### 29.4 Non-remission

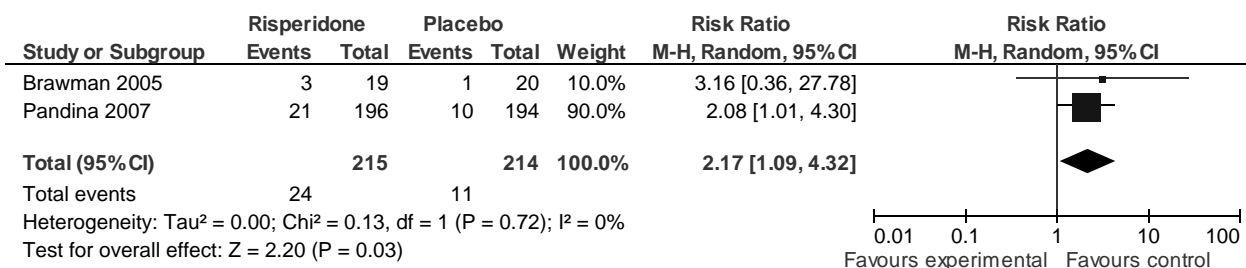


### 29.5 HAM-A



## 30 Augmentation: Risperidone versus Placebo

### 30.2 Discontinuation due to adverse events



### 30.6 HAM-A

