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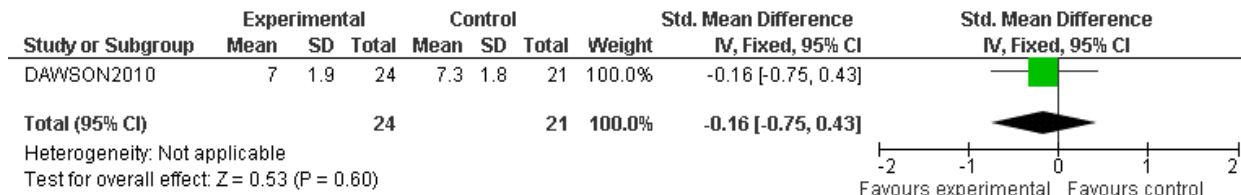
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## **1.1 PSYCHOSOCIAL INTERVENTIONS AIMED AT CORE FEATURES OF AUTISM (OVERALL AUTISTIC BEHAVIOURS)**

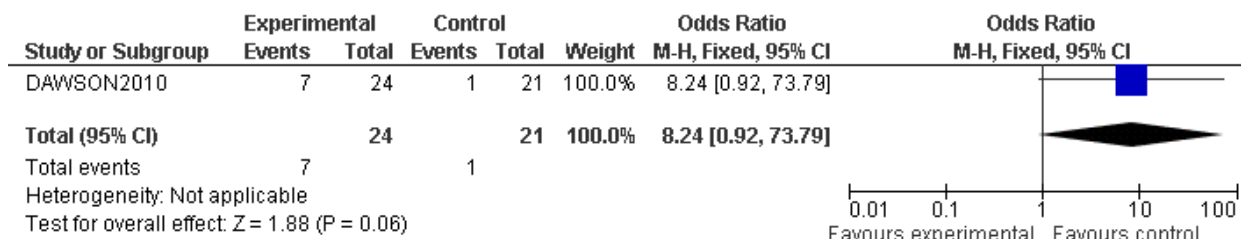
### **1.1.1 Behavioural interventions aimed at overall autistic behaviours as an indirect outcome**

*Early Start Denver Model versus treatment-as-usual for overall autistic behaviours as an indirect outcome*

## Overall autistic behaviours (ADOS severity)

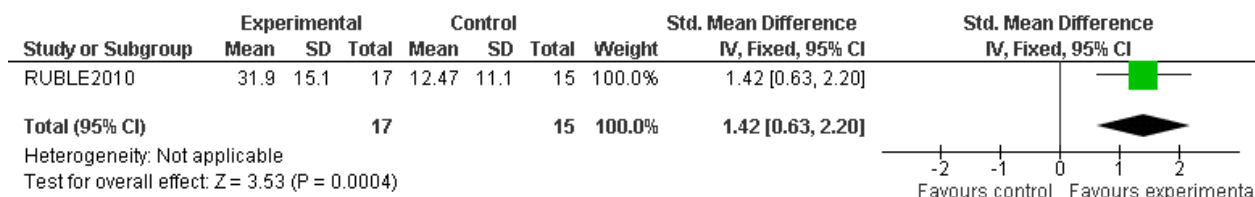


## Autism DSM-IV diagnosis (improvement in diagnosis from autistic disorder to PDD-NOS)

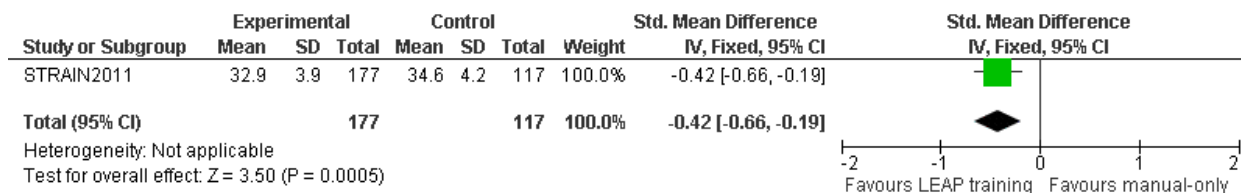


### 1.1.2 Educational interventions aimed at overall autistic behaviours as a direct outcome

#### *COMPASS versus treatment-as-usual for overall autistic behaviours as a direct outcome*



#### *LEAP training versus manual-only control for overall autistic behaviours as a direct outcome*

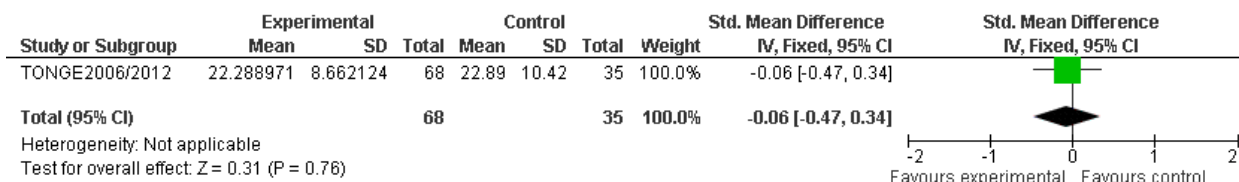




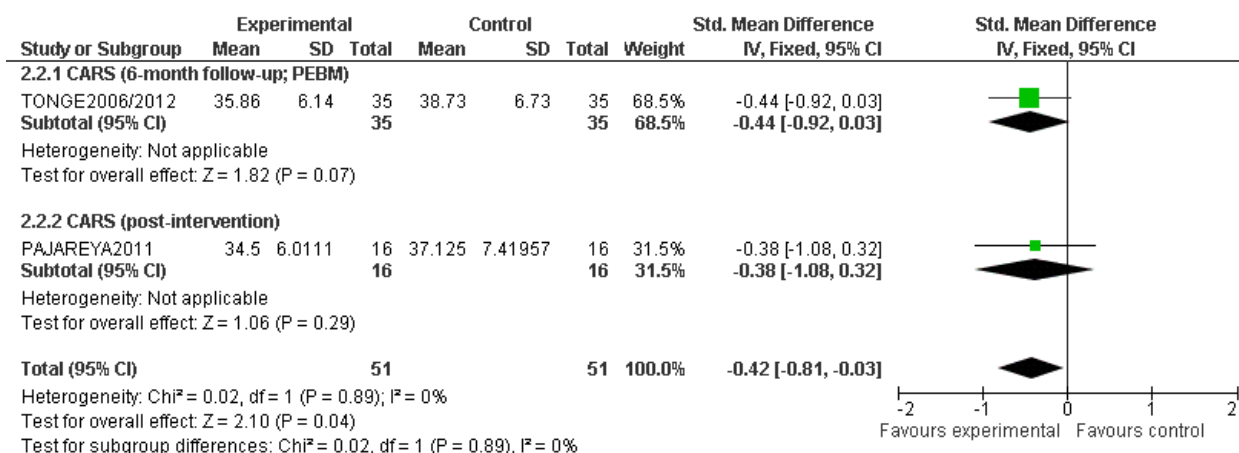
### 1.1.3 Parent training interventions aimed at overall autistic behaviours as a direct or indirect outcome

#### *Parent training versus treatment-as-usual for overall autistic behaviours as an indirect outcome*

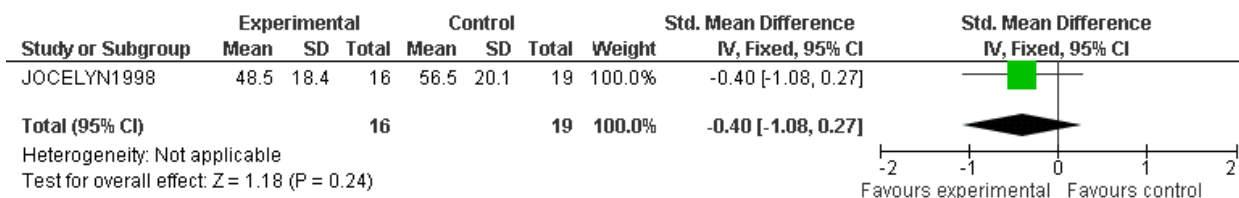
##### Overall autistic behaviours (DBC-ASA; 6-month follow-up; PEC+PEBM combined)



##### Overall autistic behaviours (CARS)

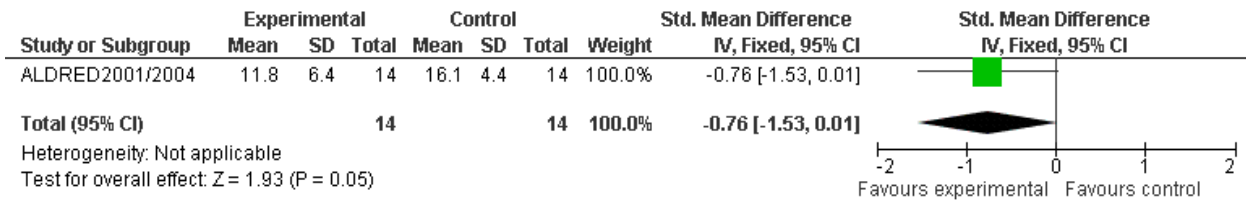


#### *Parent and day-care staff training versus standard day-care for overall autistic behaviours as a direct outcome*



### 1.1.4 Social-communication interventions aimed at overall autistic behaviours as an indirect outcome

#### *Child's Talk versus treatment-as-usual for overall autistic behaviours as an indirect outcome*

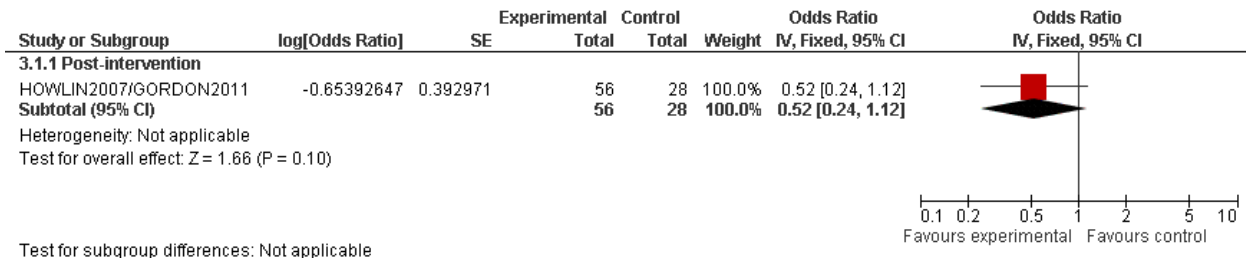


## 1.2 PSYCHOSOCIAL INTERVENTIONS AIMED AT THE CORE AUTISM FEATURE OF IMPAIRED RECIPROCAL SOCIAL COMMUNICATION AND INTERACTION

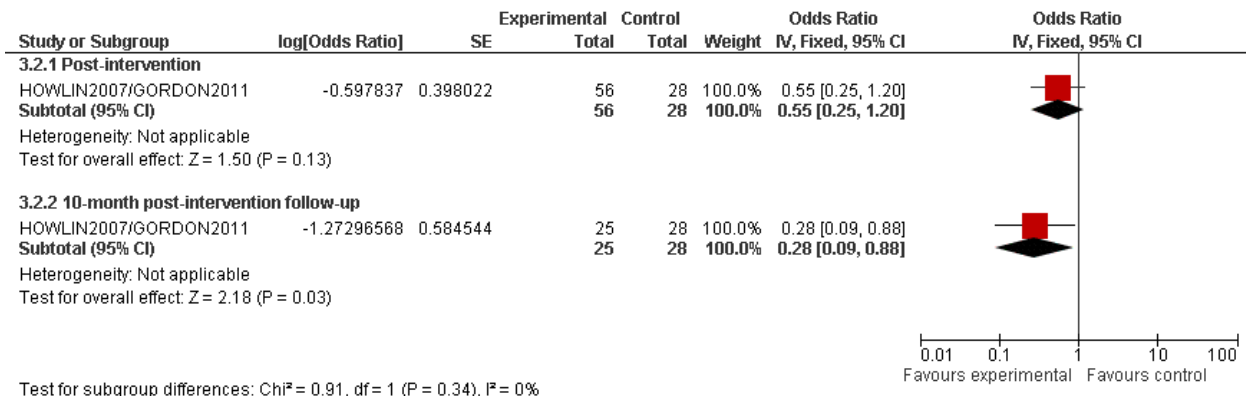
### 1.2.1 AAC intervention aimed at the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome

*PECS training for teachers versus treatment-as-usual for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome*

#### Communication (odds of being in a higher severity category on ADOS-G)

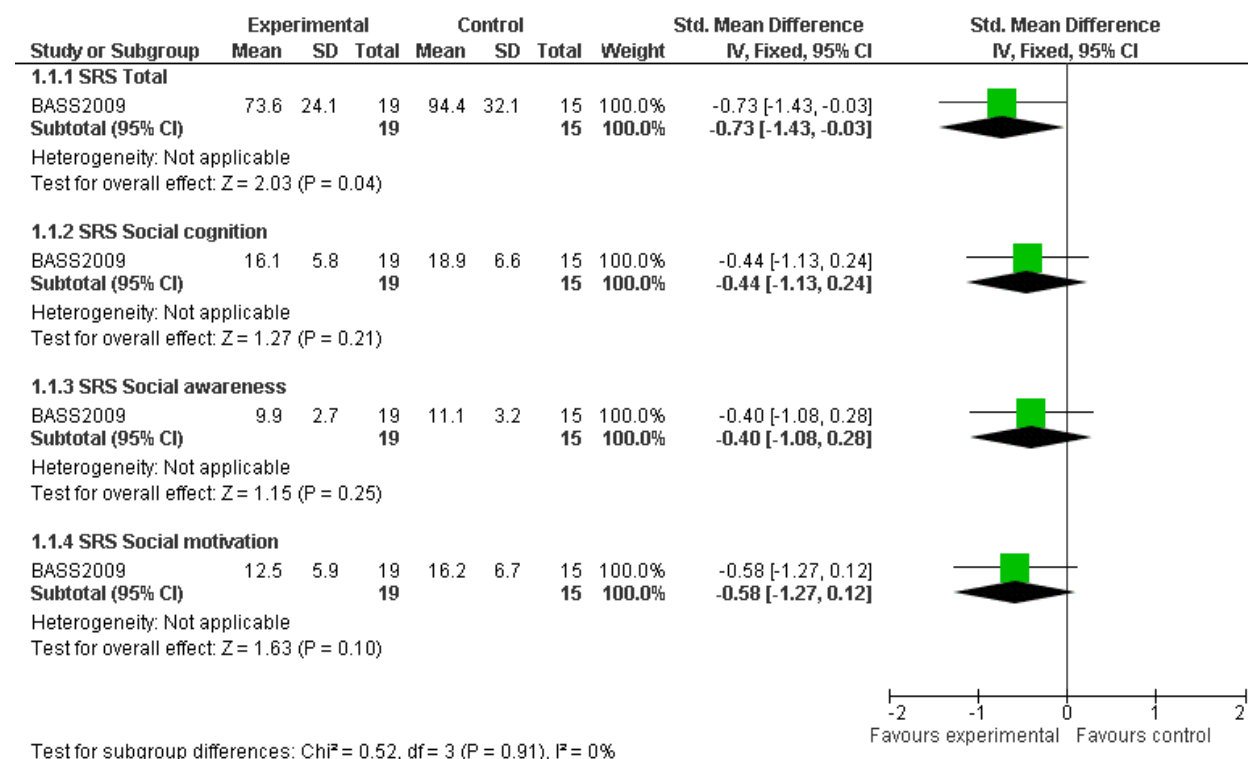


#### Social interaction (odds of being in a higher severity category on ADOS-G)



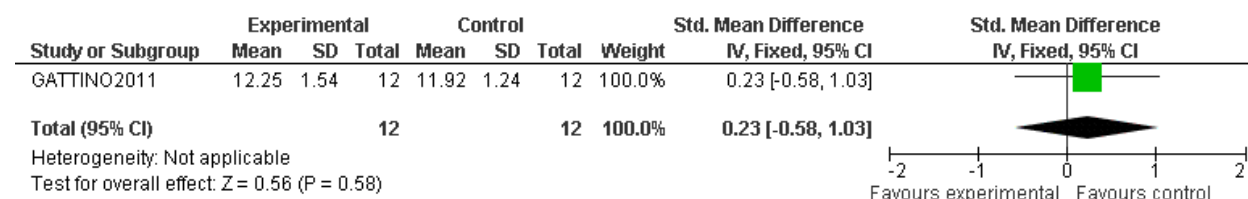
## 1.2.2 Animal-based intervention aimed at the core autism feature of impaired reciprocal social communication and interaction as a direct outcome

### *Horseback riding versus waitlist control for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome*



## 1.2.3 Arts-based intervention aimed at the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome

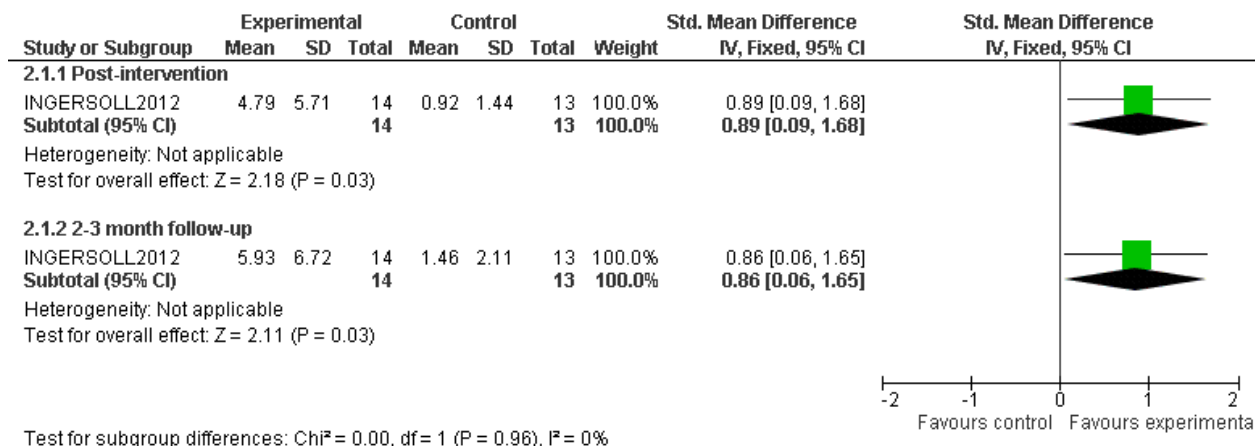
### *RMT versus waitlist control for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome*



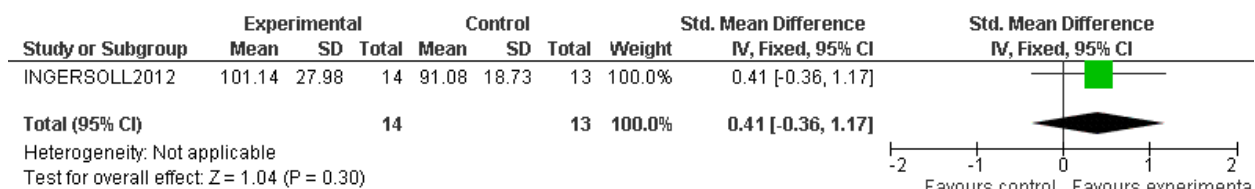
## 1.2.4 Behavioural intervention aimed at the core autism feature of impaired reciprocal social communication and interaction as a direct or indirect outcome

### *RIT versus treatment-as-usual for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome*

#### Examiner-child joint/shared attention (ESCS IJA)

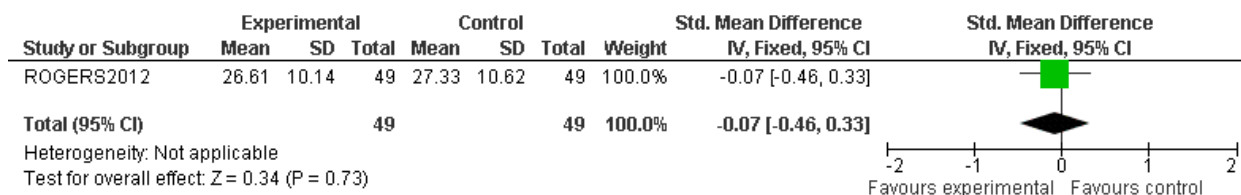


#### Social and emotional development (Bayley-Social-emotional subscale)

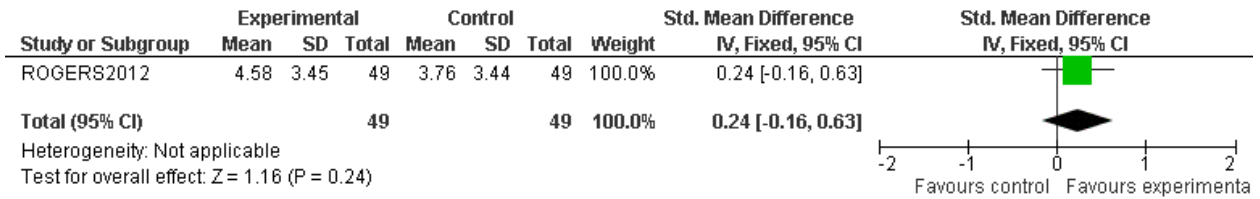


### *P-ESDM versus treatment-as-usual for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome*

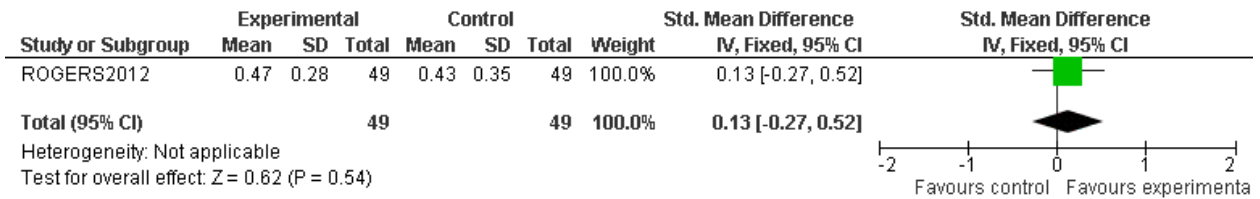
#### Social affect (ADOS-T)



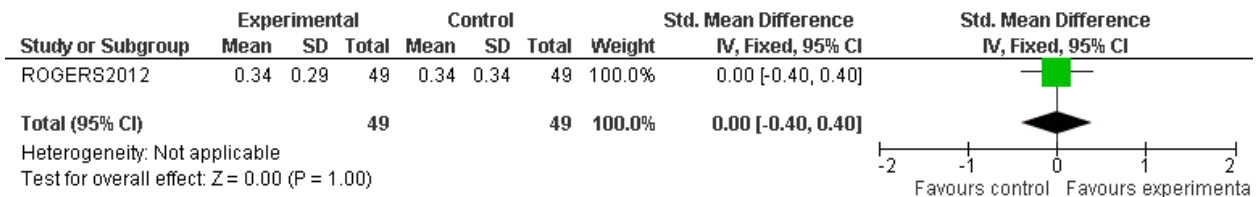
### Imitation



### Orienting to social stimuli



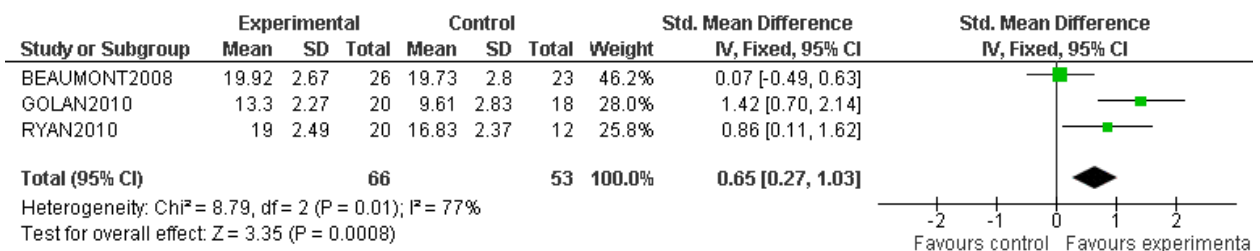
### Orienting to joint attention



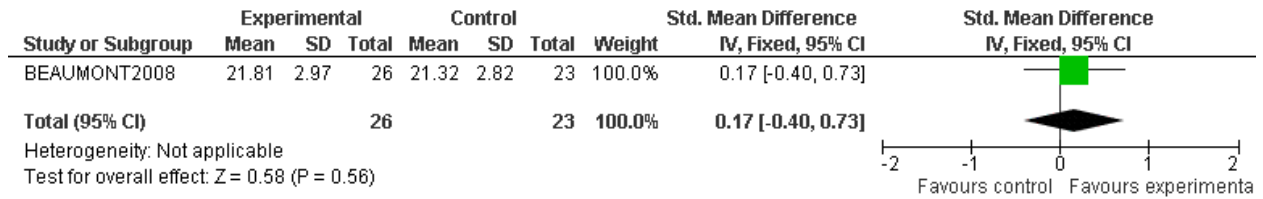
## 1.2.5 Cognitive interventions aimed at the core autism feature of impaired reciprocal social communication and interaction as a direct outcome

*ERT versus treatment-as-usual for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome*

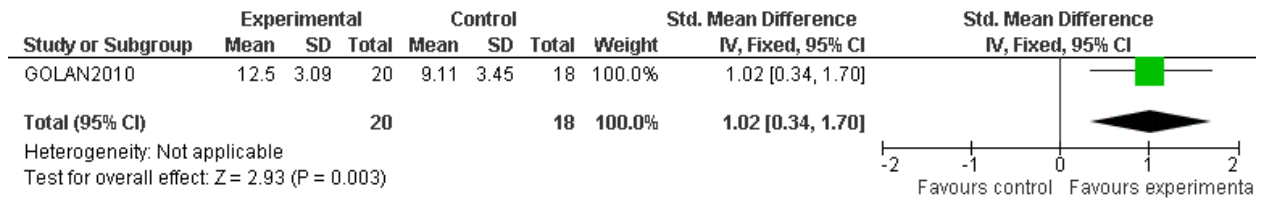
### Emotion recognition



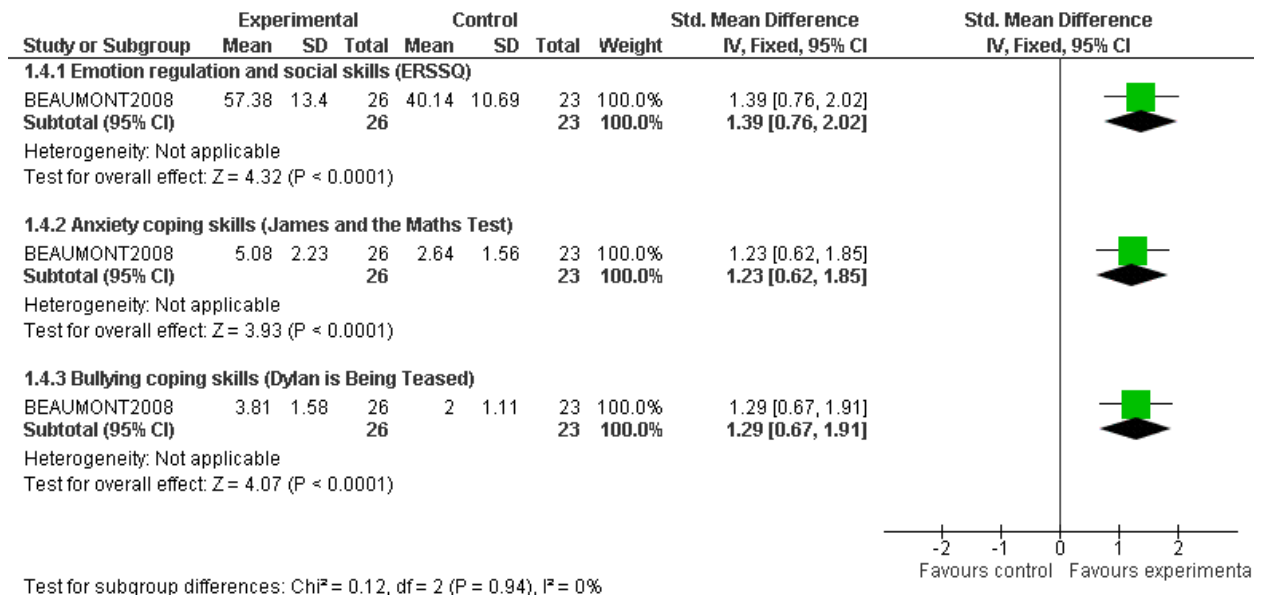
## Recognising emotion from posture



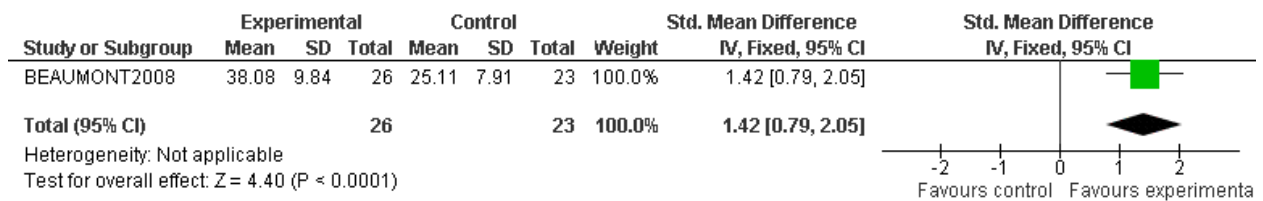
## Emotion understanding (EmoVoc)



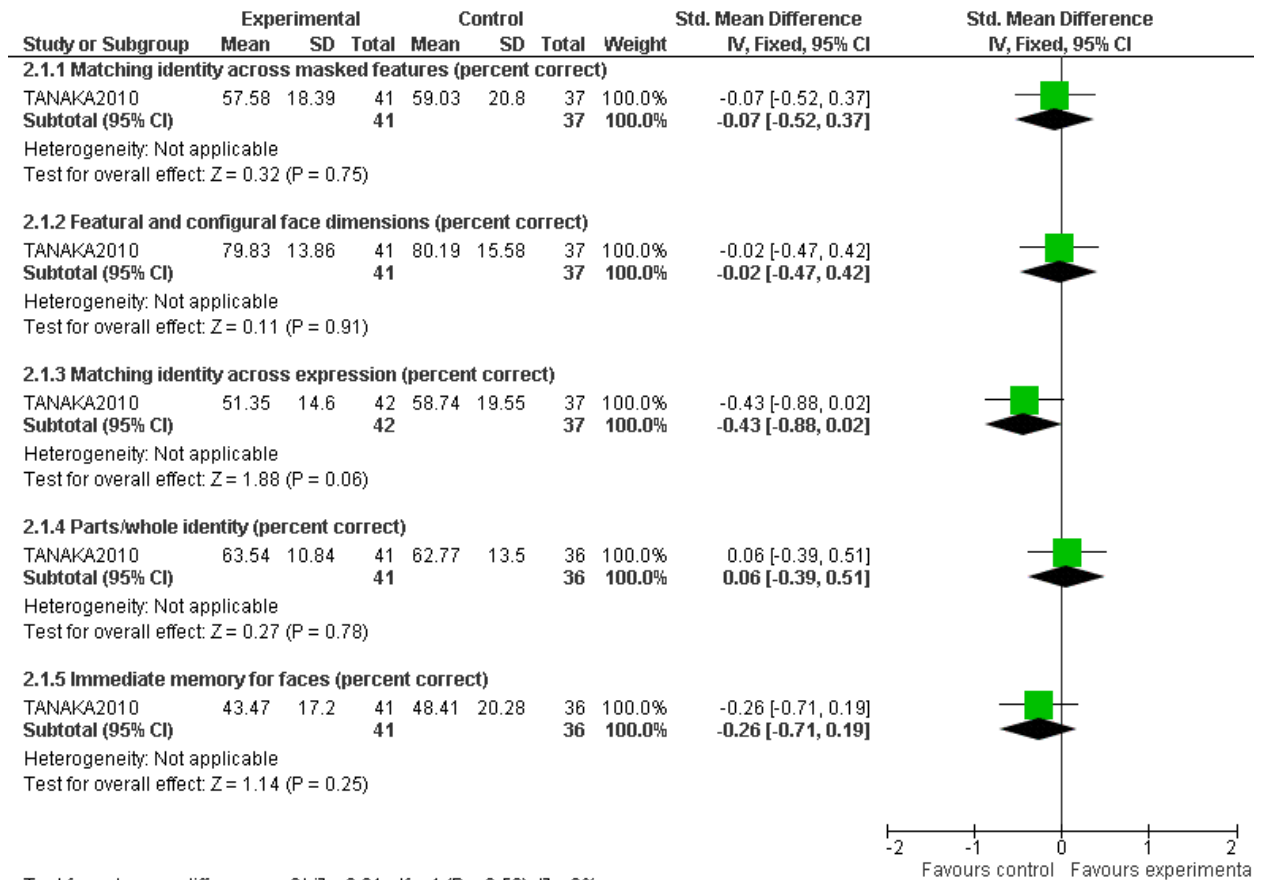
## Emotion regulation



## Social skills (SSQ)

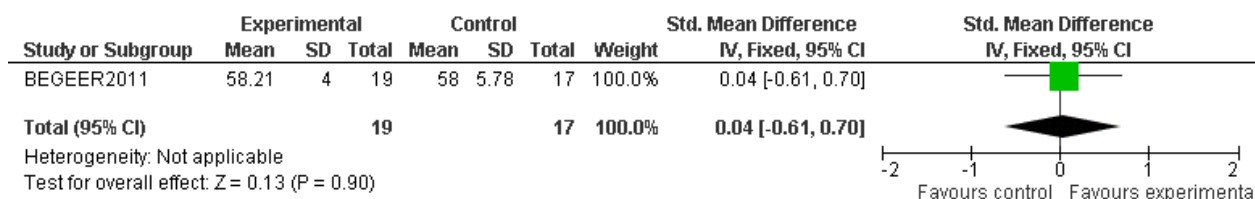


*FRT versus waitlist control for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome*

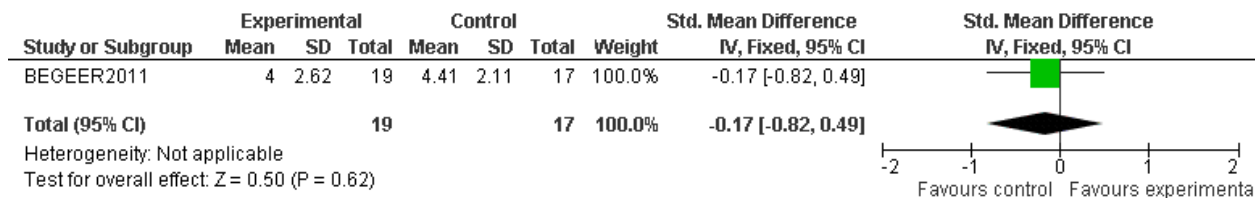


*ToM versus waitlist control for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome*

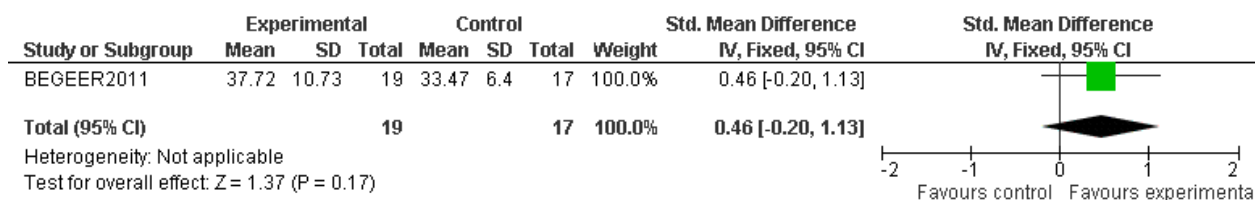
**Theory of Mind (ToM test, total score)**



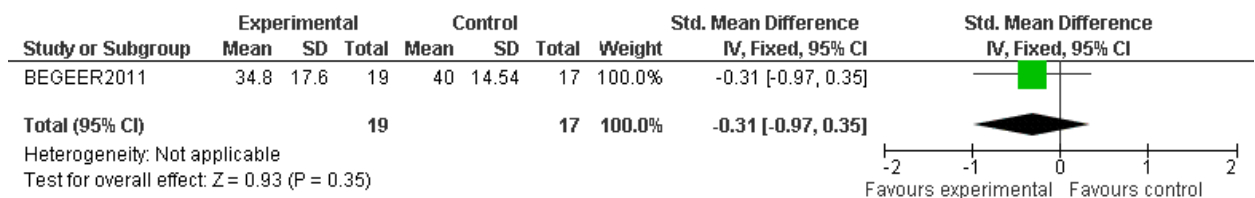
### Empathy (Index of Empathy for Children and Adolescents)



### Emotional awareness (LEAS-C)



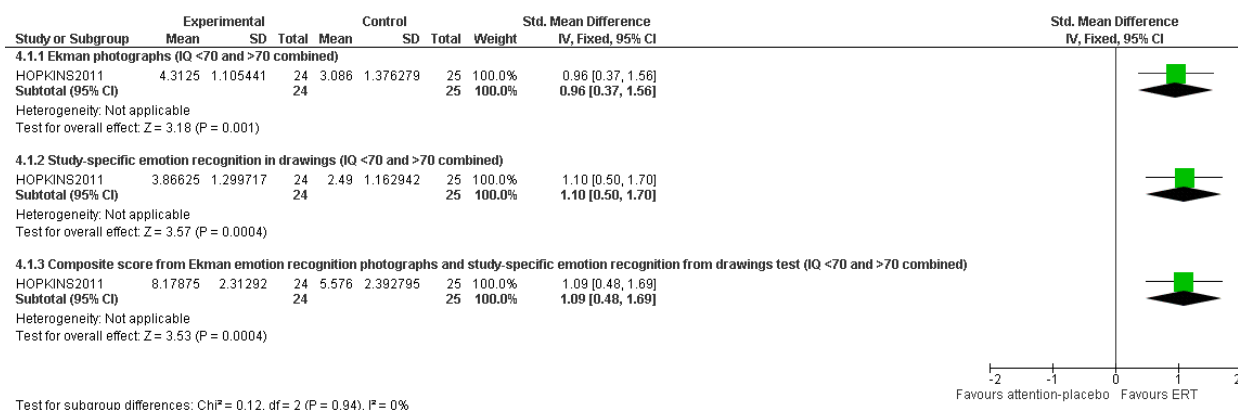
### Maladaptive social behaviour (CSBQ)



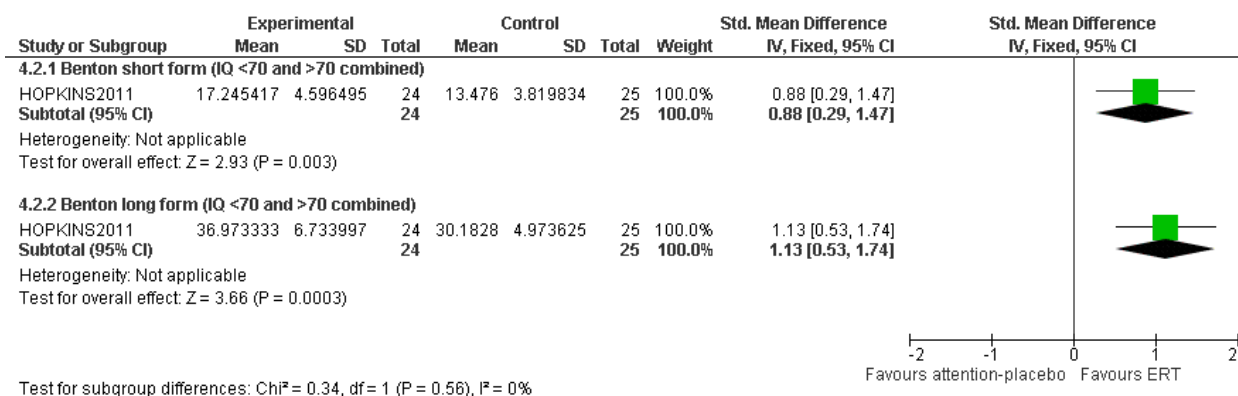
### *Computer-based ERT versus software training (attention-placebo) for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome*

#### Emotion recognition

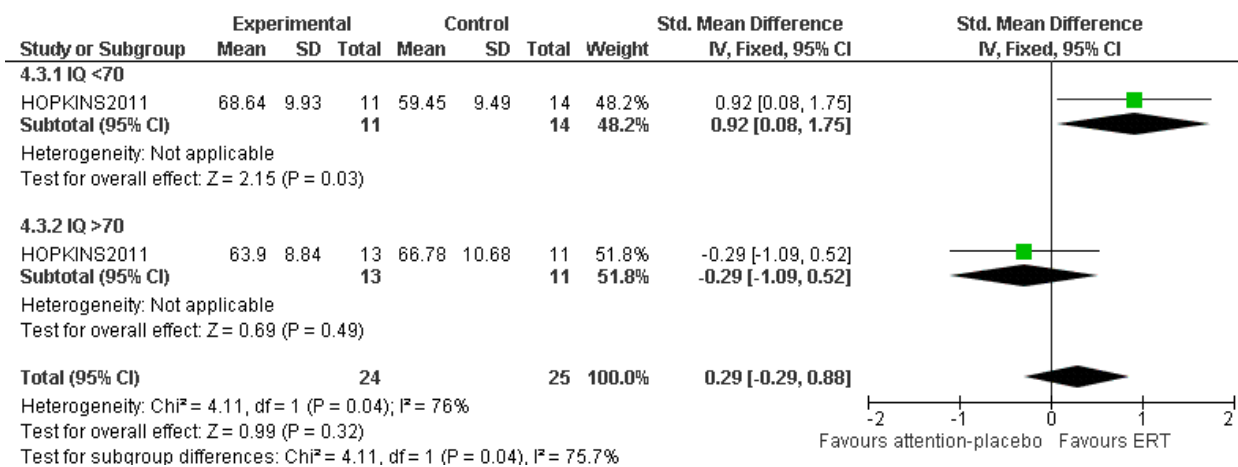




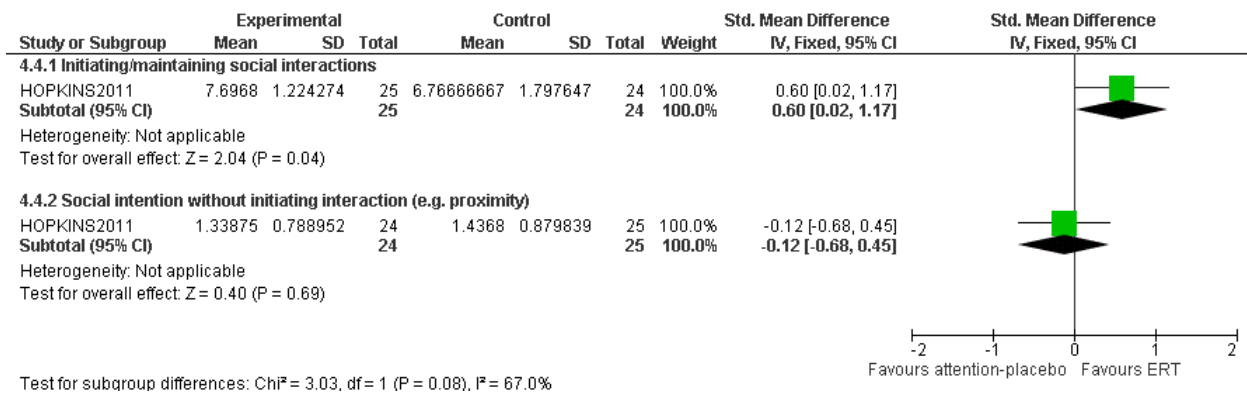
## Face recognition



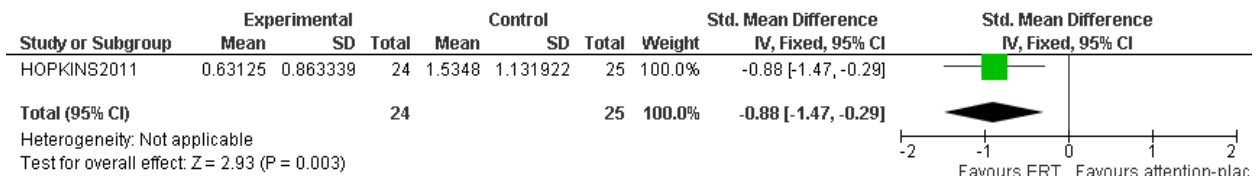
## Social skills (SSRS standardised score)



## Positive social interaction (behavioural observation)

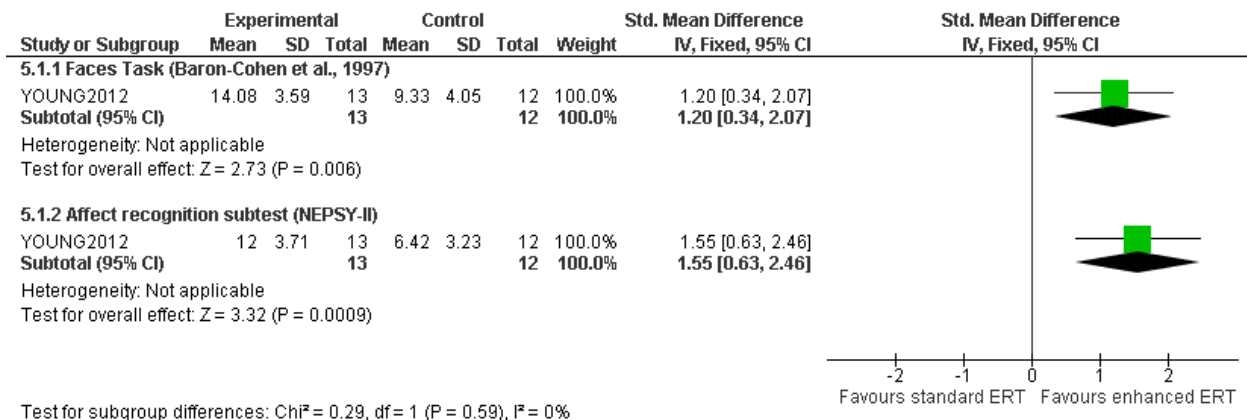


### Negative social interaction (behavioural observation)

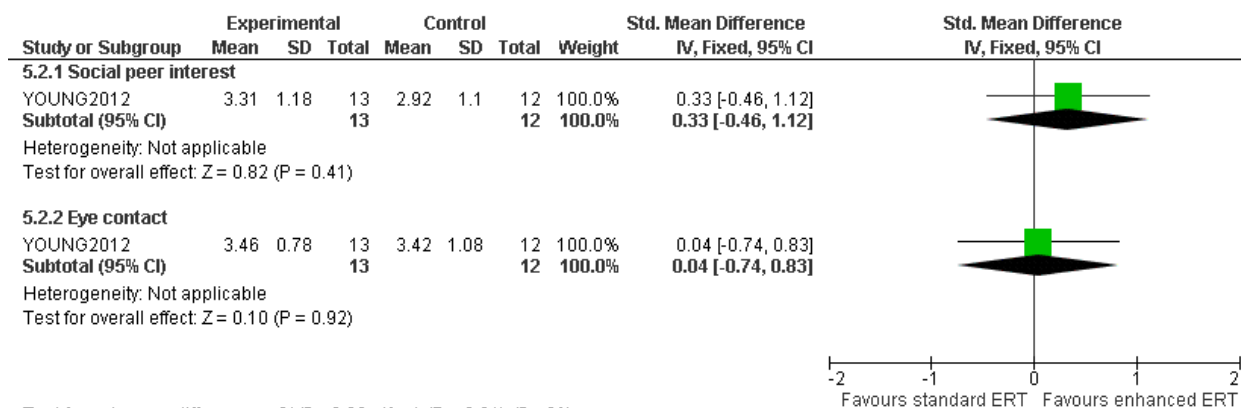


## *Enhanced ERT versus standard ERT for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome*

### Emotion recognition

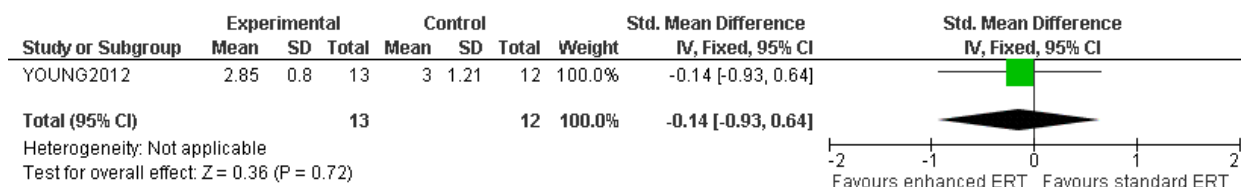


### Positive social behaviours



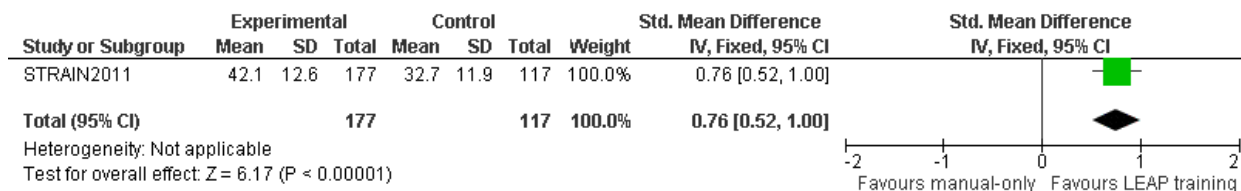
Test for subgroup differences: Chi<sup>2</sup> = 0.26, df = 1 (P = 0.61), I<sup>2</sup> = 0%

### Gaze aversion

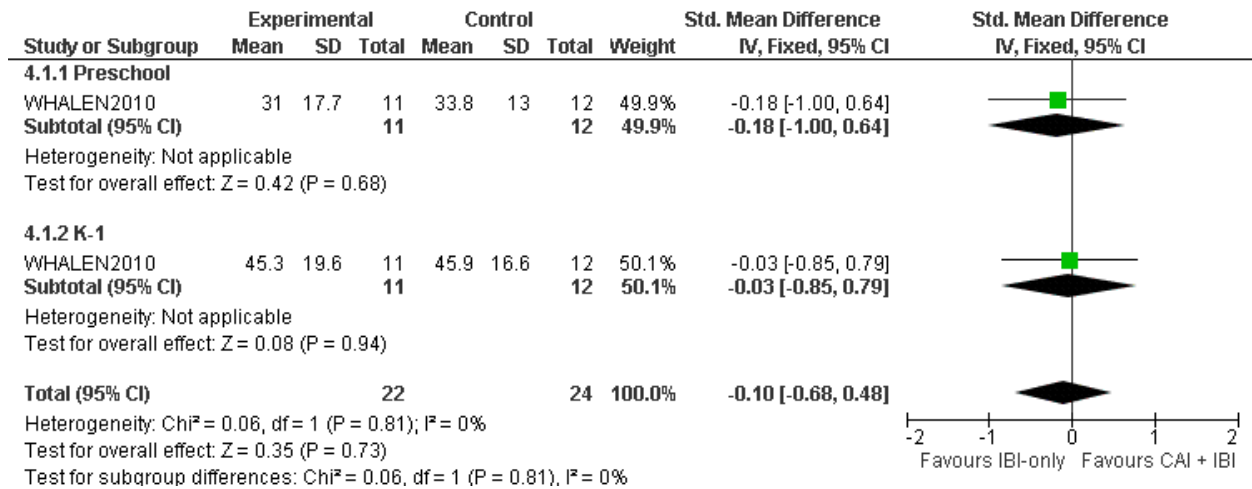


## 1.2.6 Educational interventions aimed at the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome

*LEAP training versus manual-only control for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome*



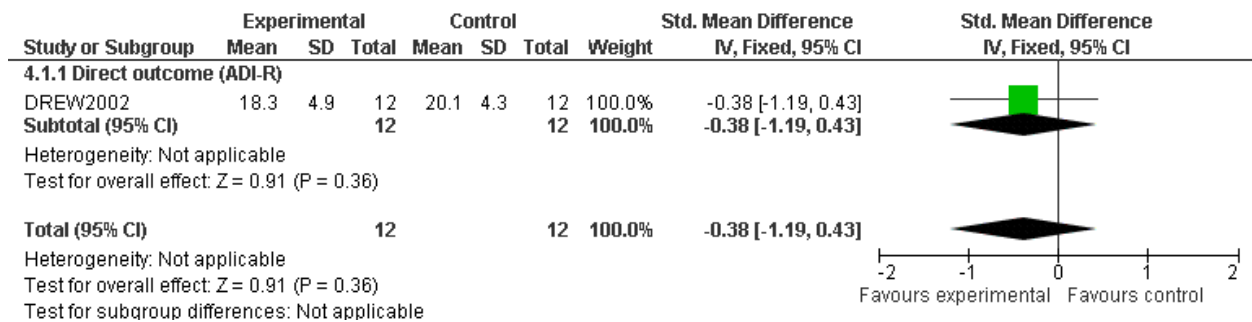
*Combined TeachTown and IBI versus IBI-only for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome*



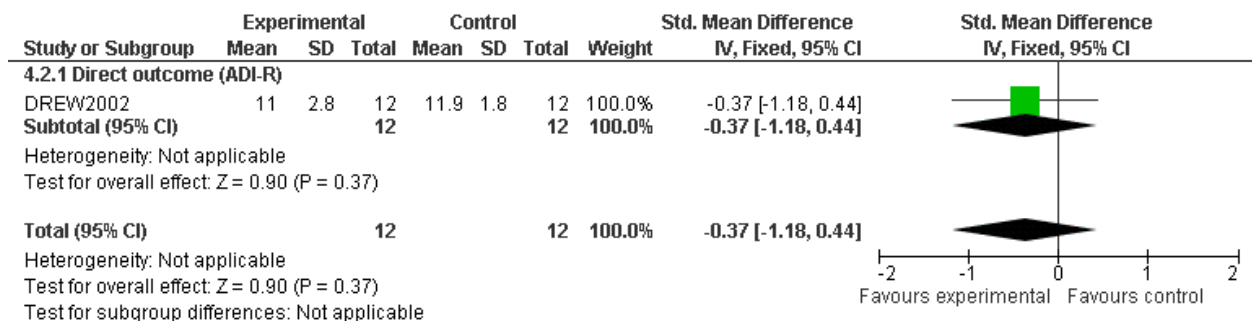
### 1.2.7 Parent training interventions aimed at the core autism feature of impaired reciprocal social communication and interaction as a direct or indirect outcome

#### *Parent training versus treatment-as-usual for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome*

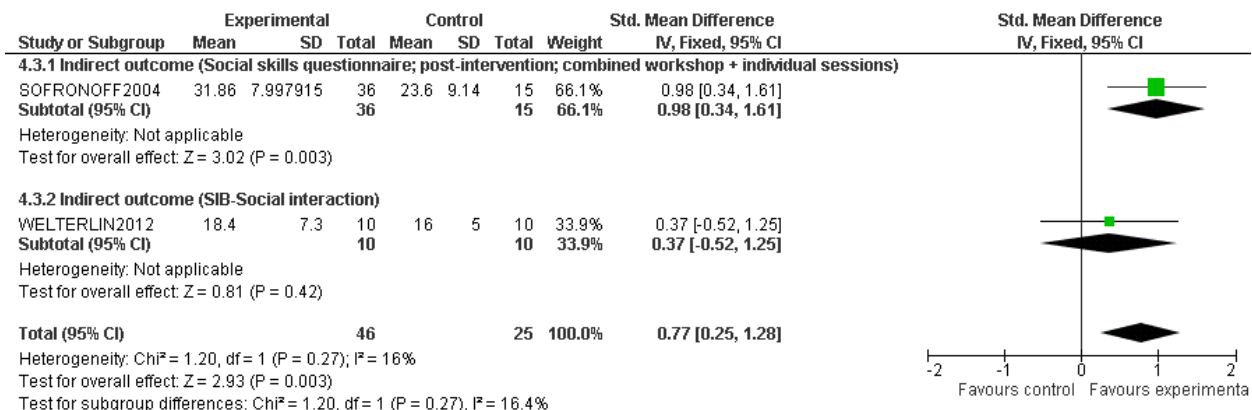
##### Reciprocal social interaction



##### Nonverbal communication



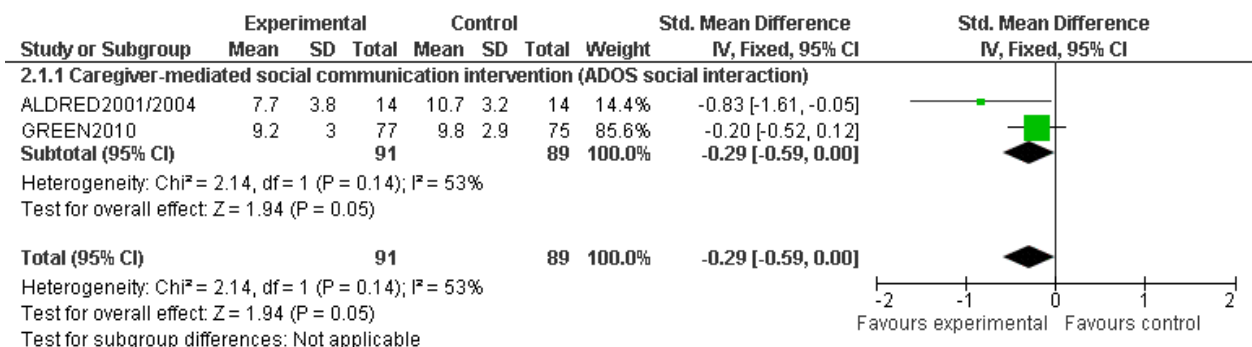
*Parent training versus treatment-as-usual for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome*



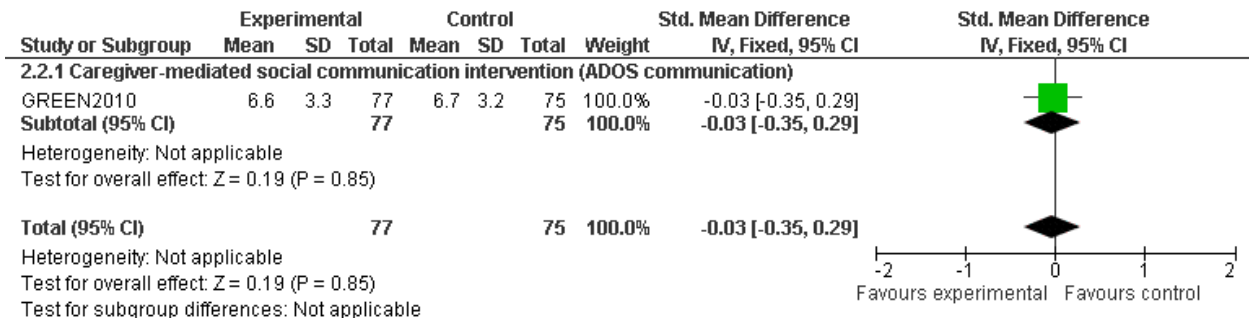
**1.2.8 Social-communication interventions aimed at the core autism feature of impaired reciprocal social communication and interaction as a direct outcome**

*Caregiver- or preschool-teacher- mediated social-communication interventions versus treatment-as-usual for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome*

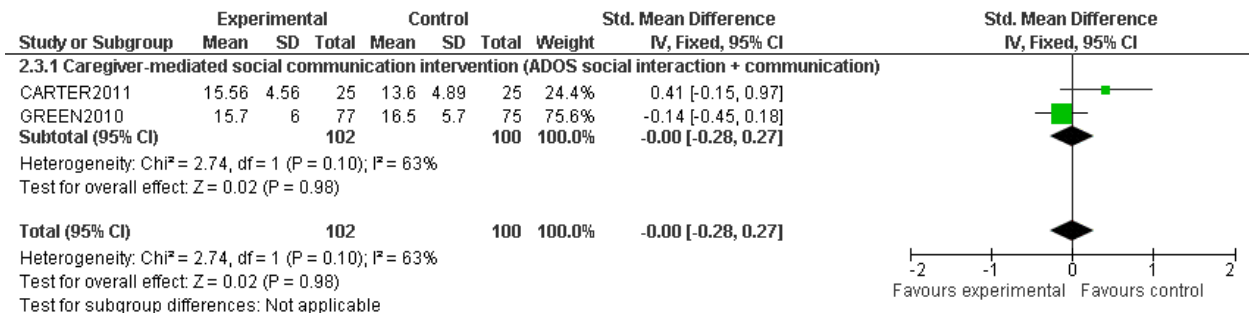
**Social interaction**



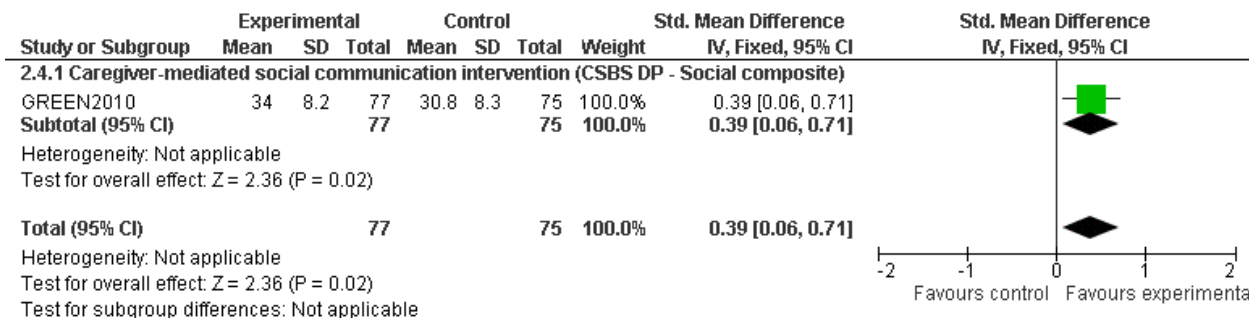
**Communication**



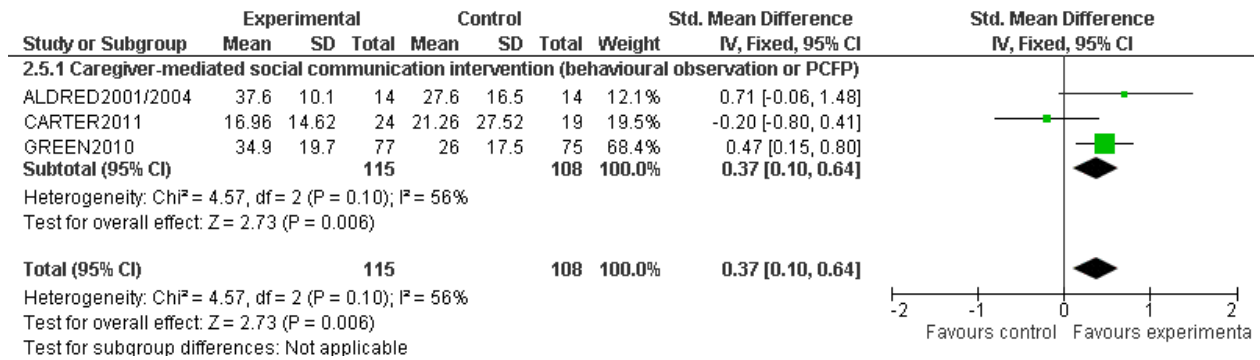
### Social interaction and communication



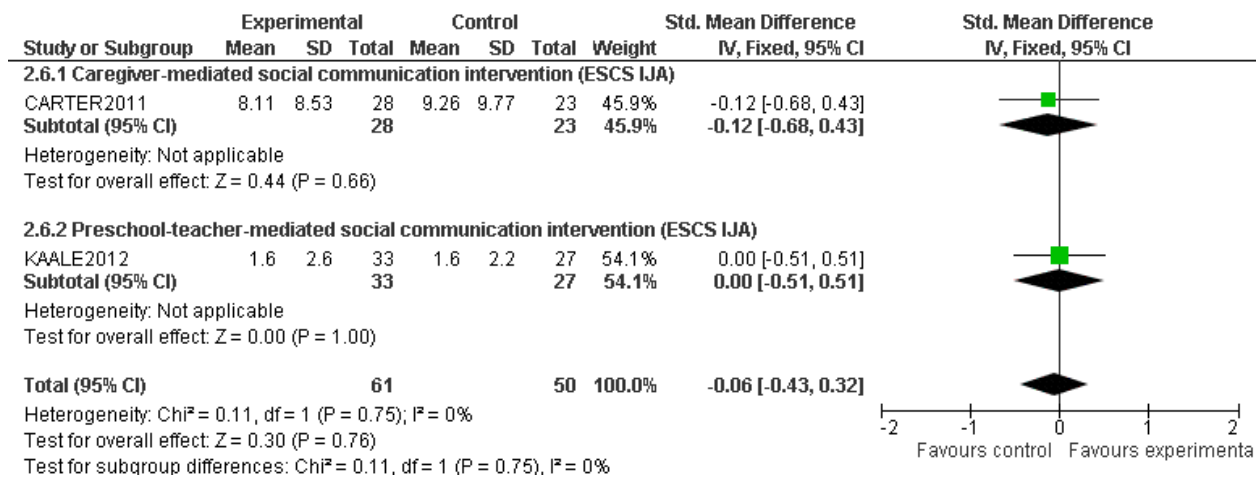
### Parent-rated social-communication



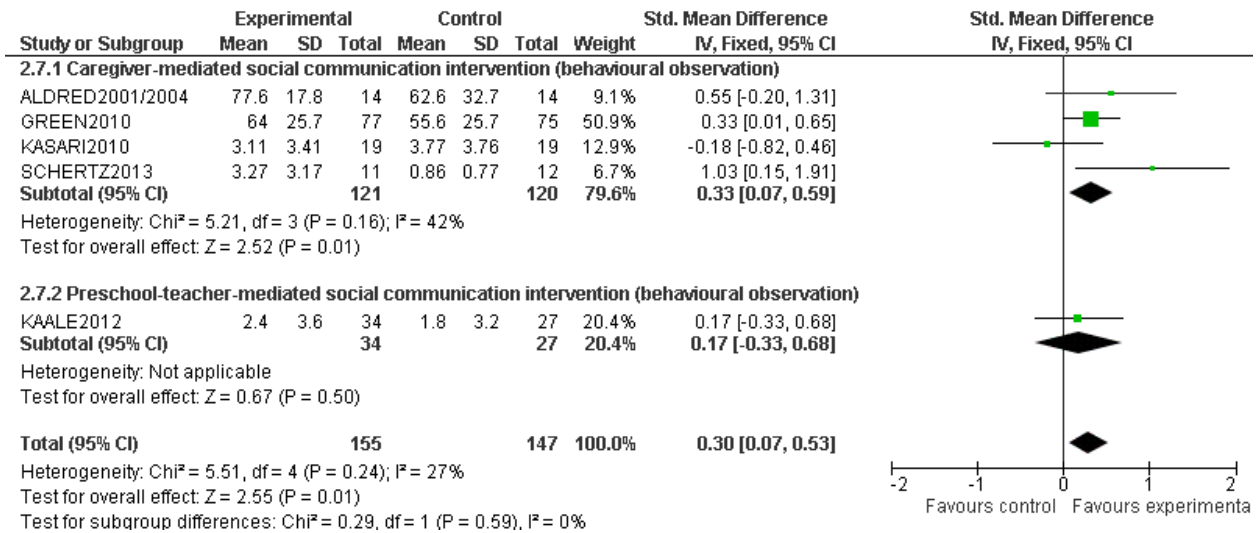
### Communication acts



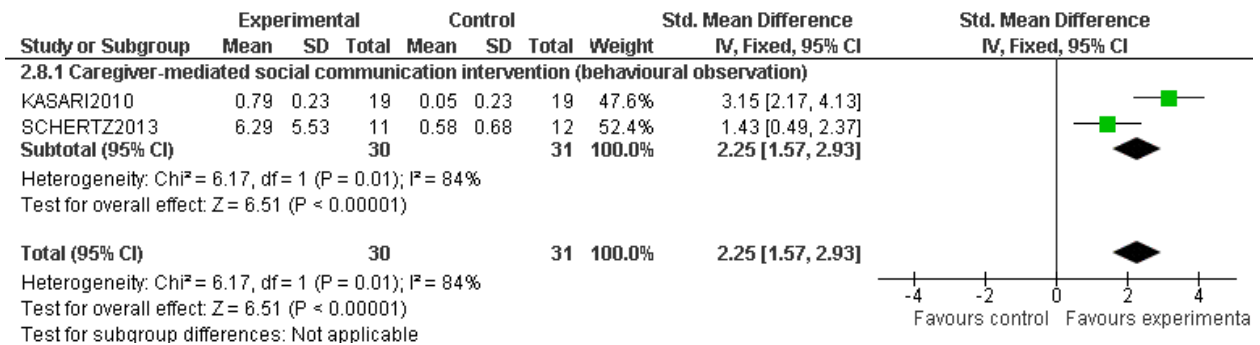
### Examiner-child joint/shared attention



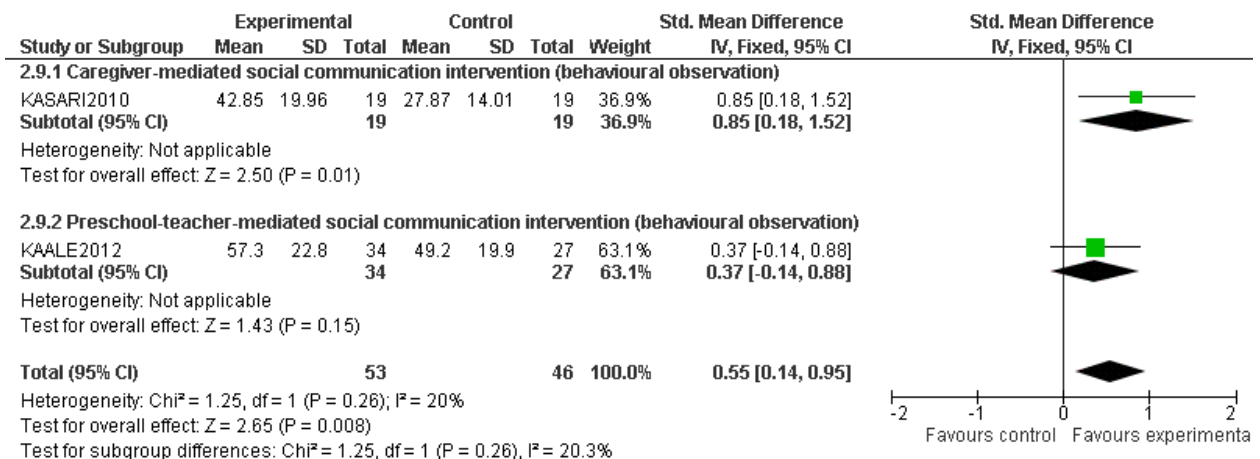
### Parent-child joint/shared attention



### Parent-child joint attention responses

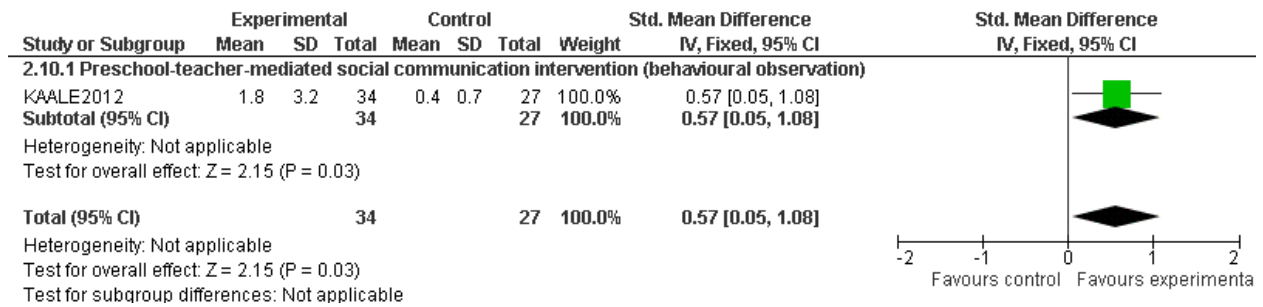


### Parent-child joint engagement

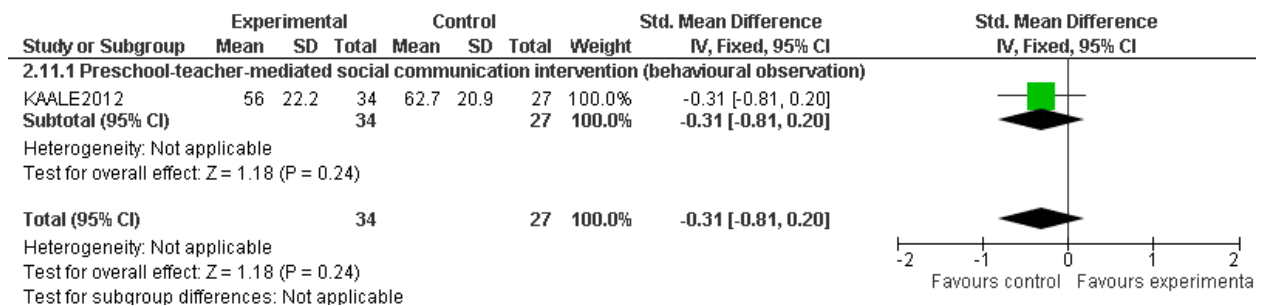




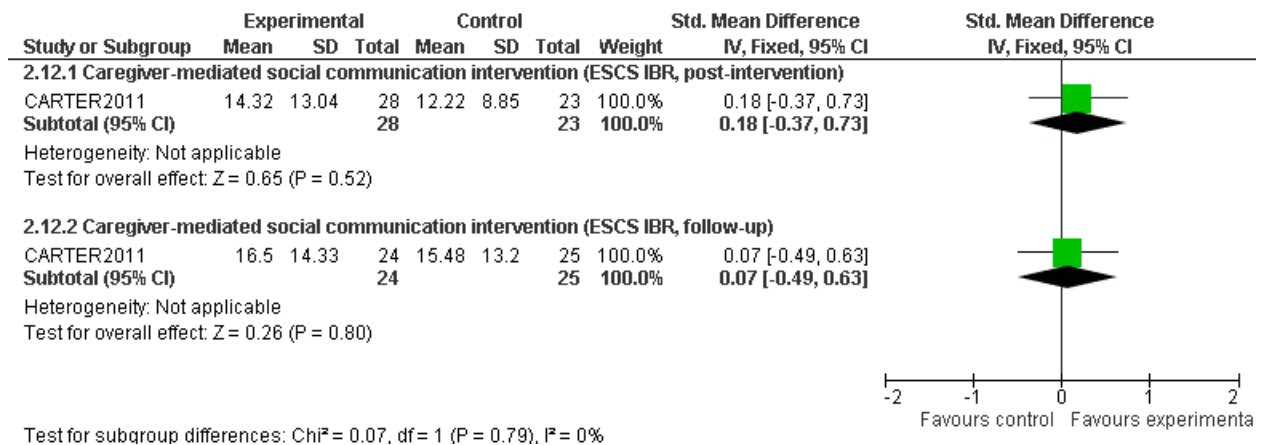
## Teacher-child joint/shared attention



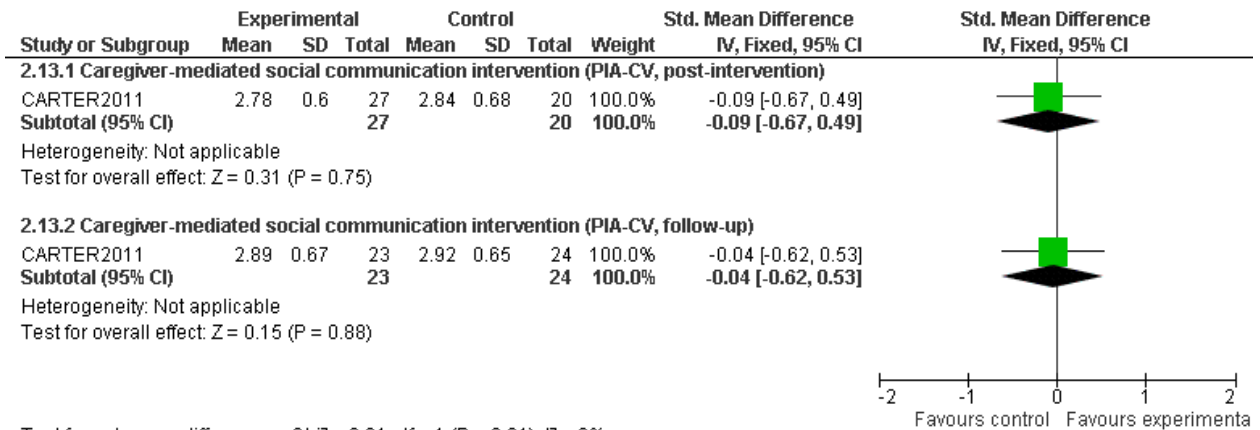
## Teacher-child joint engagement



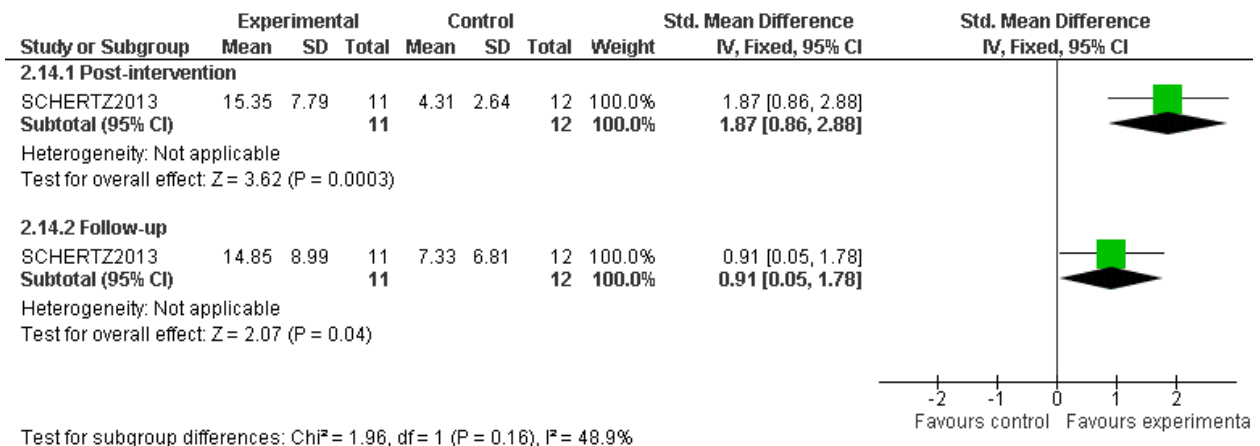
## Behaviour requests



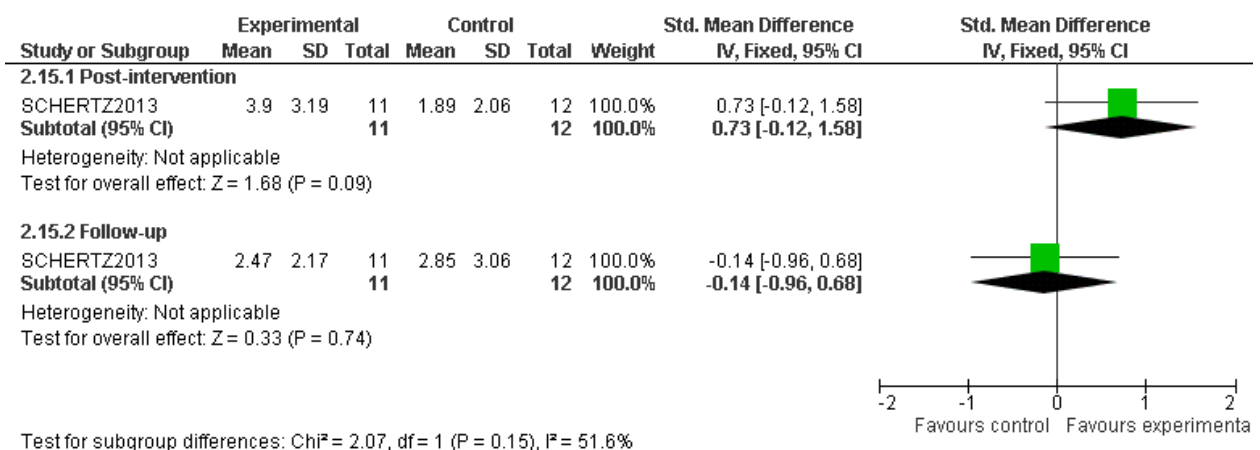
## Non-verbal communication



### Focusing on faces (behavioural observation; caregiver-mediated)

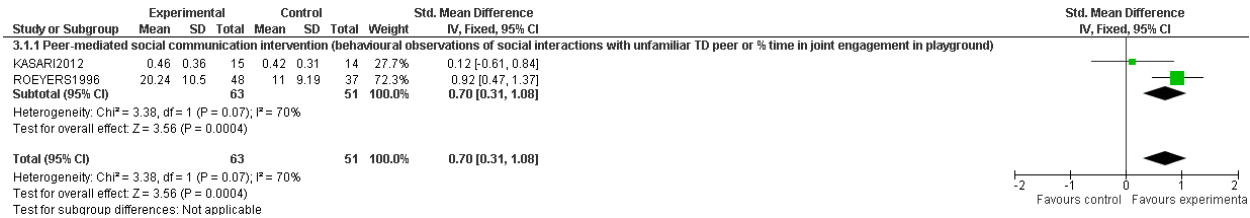


### Turn-taking (behavioural observation; caregiver-mediated)

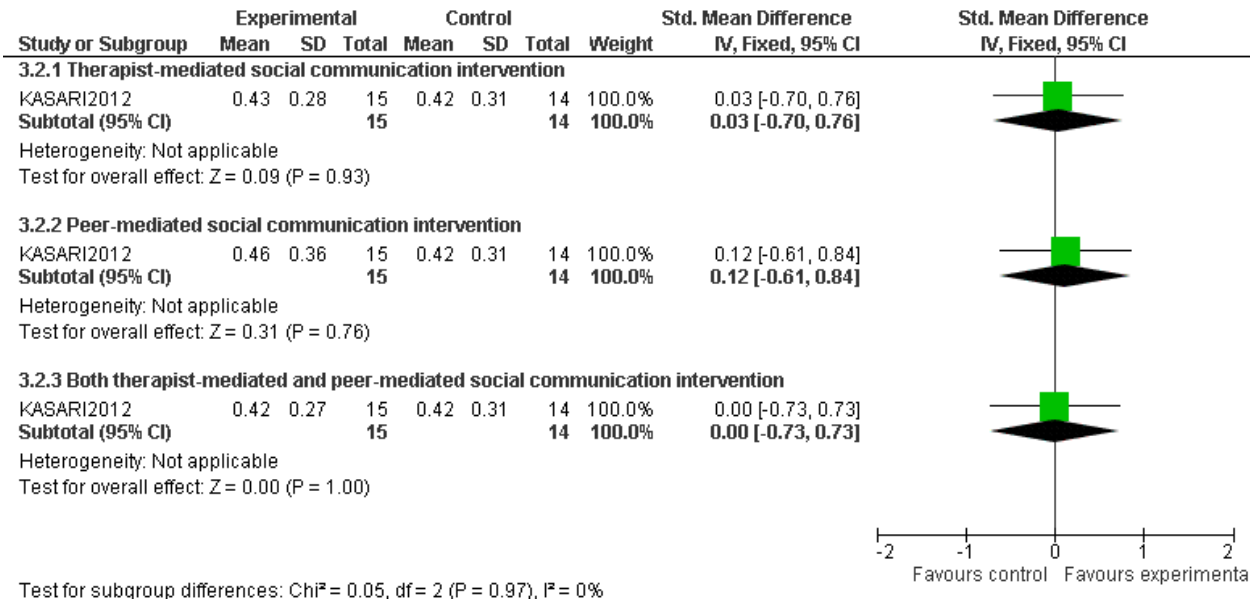


*Peer-mediated (and/or therapist-mediated) social-communication interventions versus treatment-as-usual for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome*

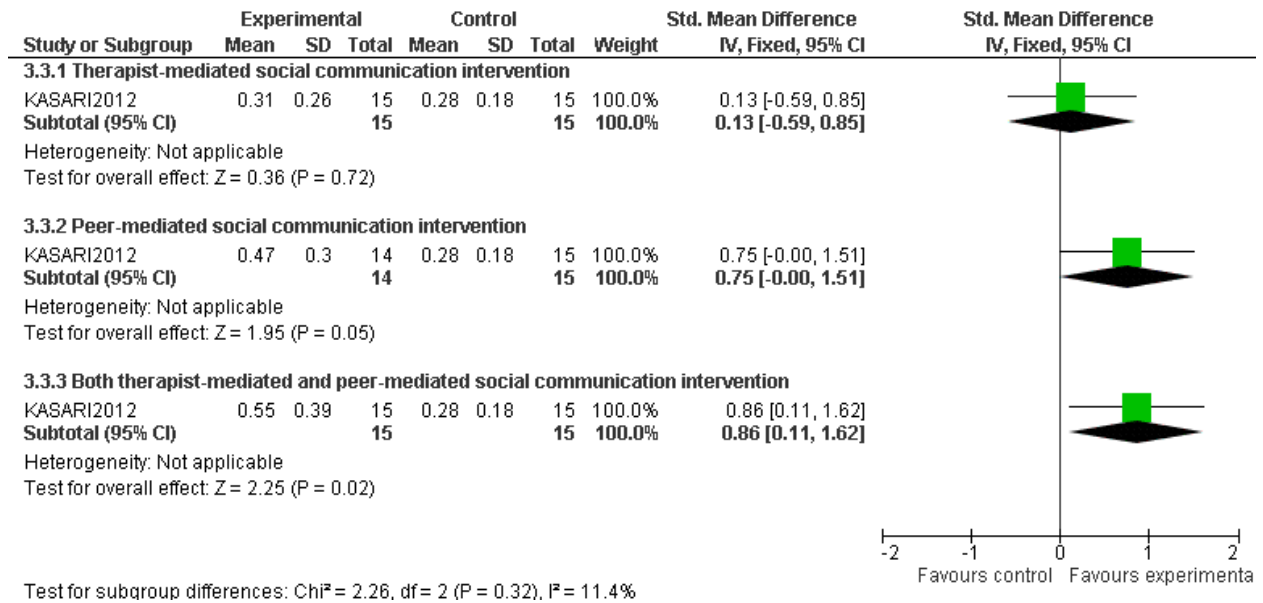
**Peer-child joint engagement**



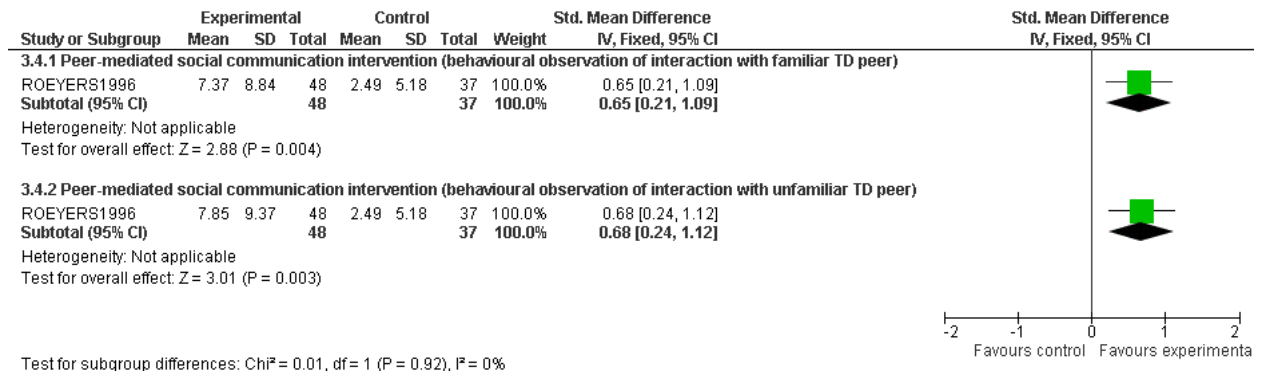
**Percentage of time jointly engaged during playground observations (post-intervention)**



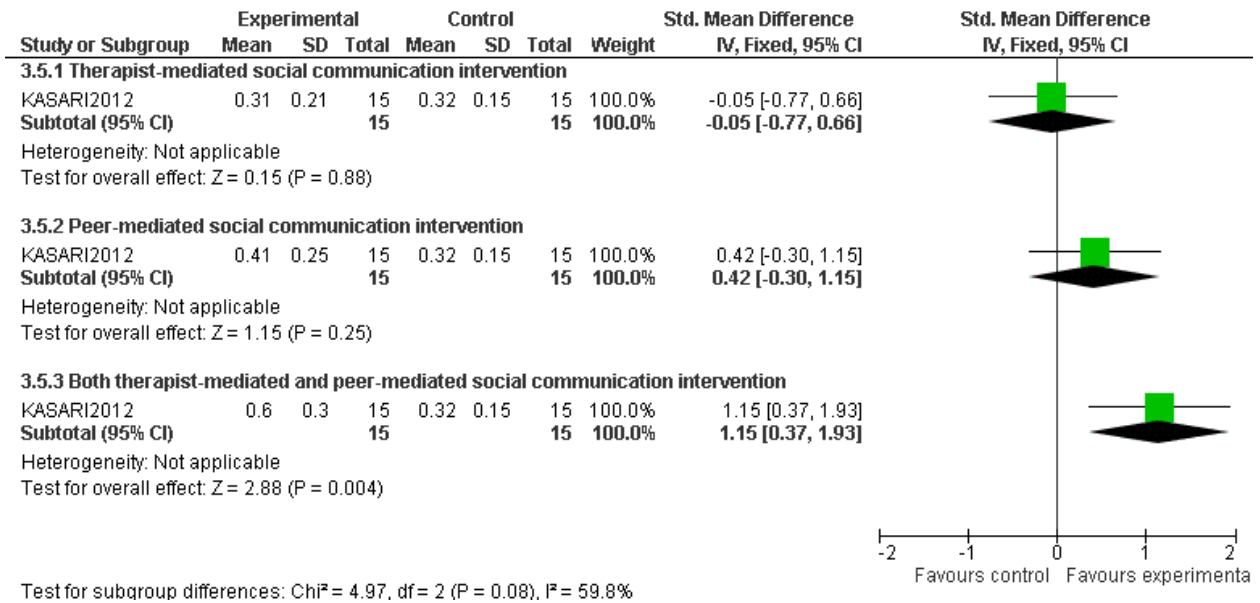
**Percentage of time jointly engaged during playground observations (follow-up)**



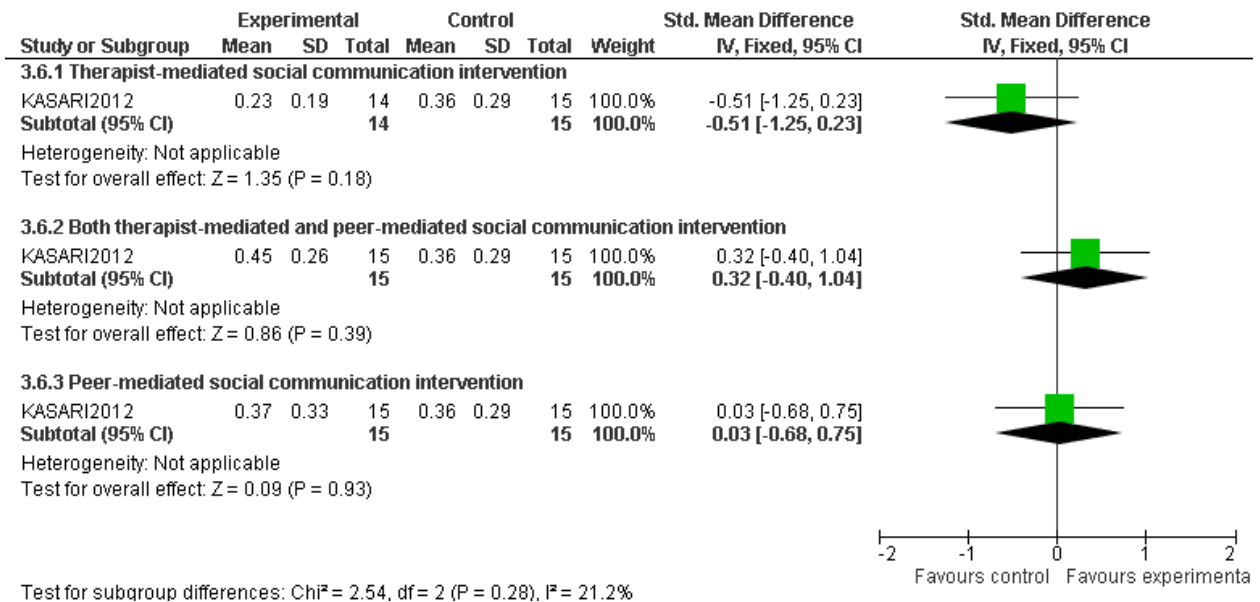
### Child-initiated social interactions



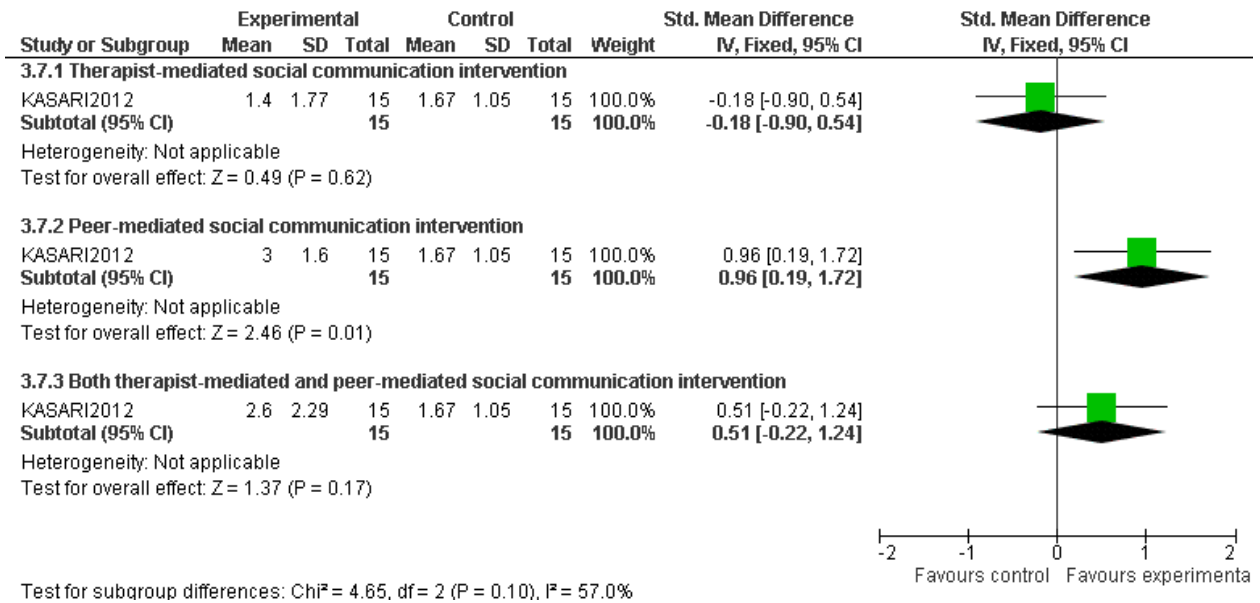
### Social network salience (SNS; post-intervention)



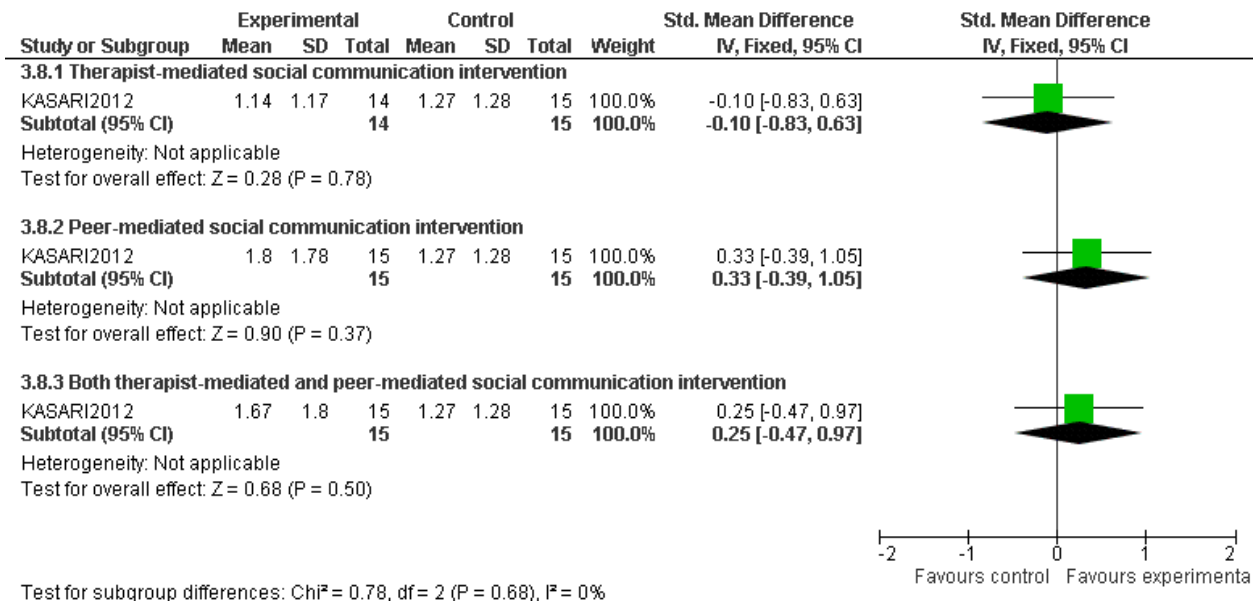
### Social network salience (SNS; follow-up)



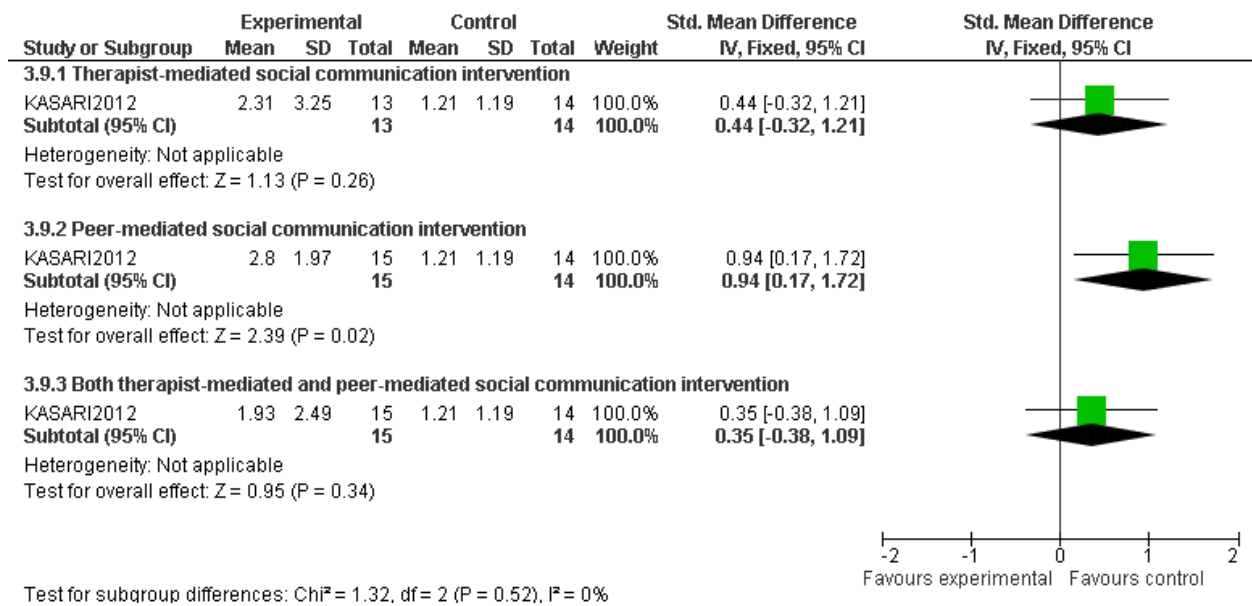
### Number of received friendship nominations (SNS; post-intervention)



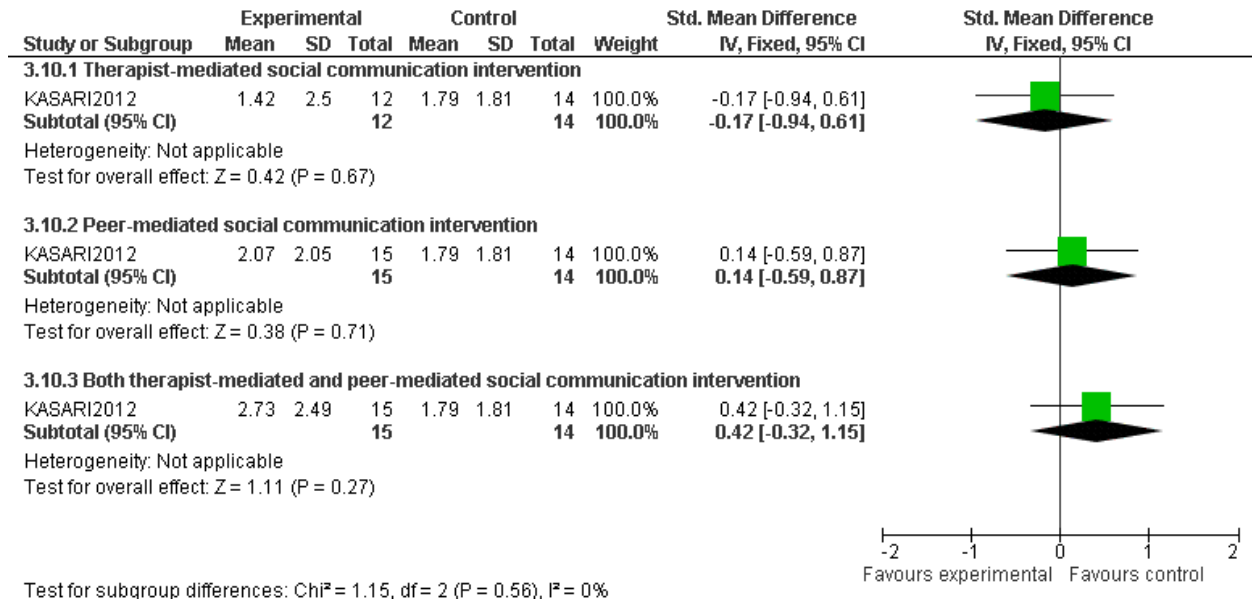
### Number of received friendship nominations (SNS; follow-up)



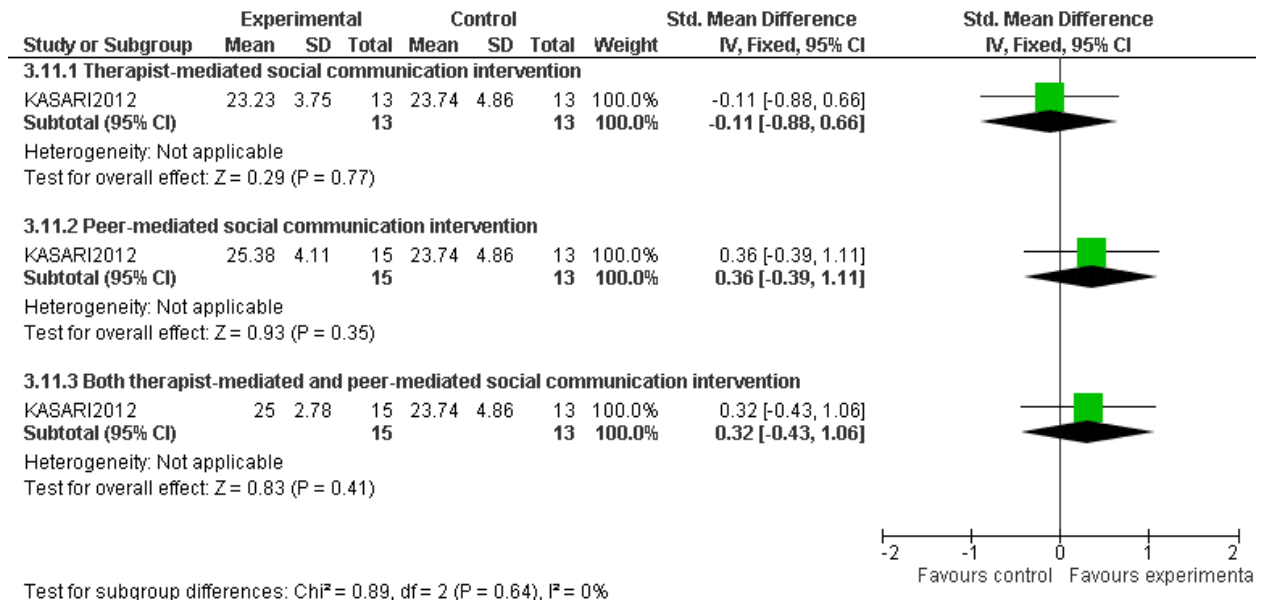
### Number of times child identified as someone other children don't like to 'hang out with' (SNS; post-intervention)



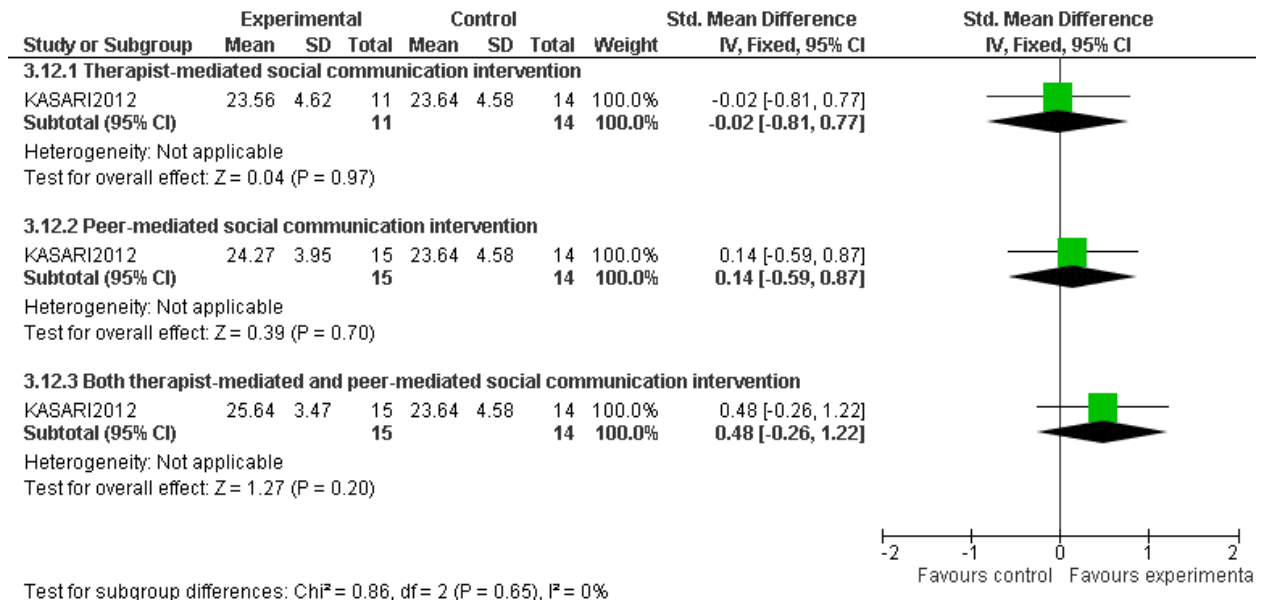
### Number of times child identified as someone other children don't like to 'hang out with' (SNS; follow-up)



### Teacher-rated social skills (post-intervention)



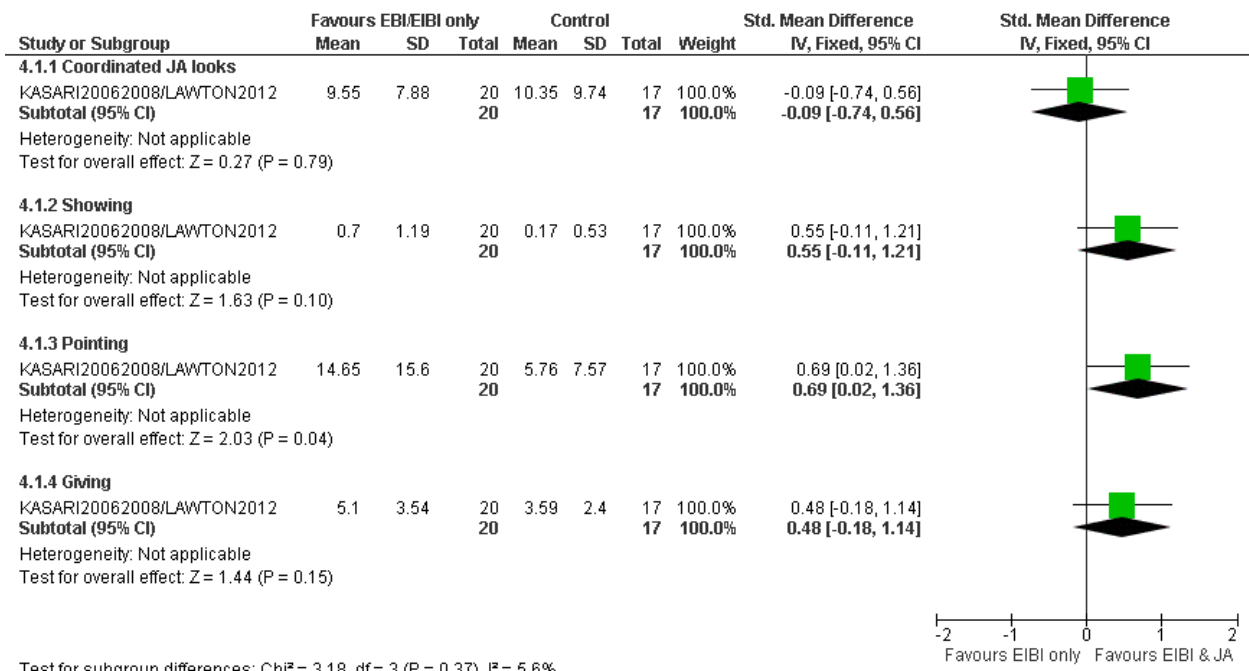
**Teacher-rated social skills (follow-up)**



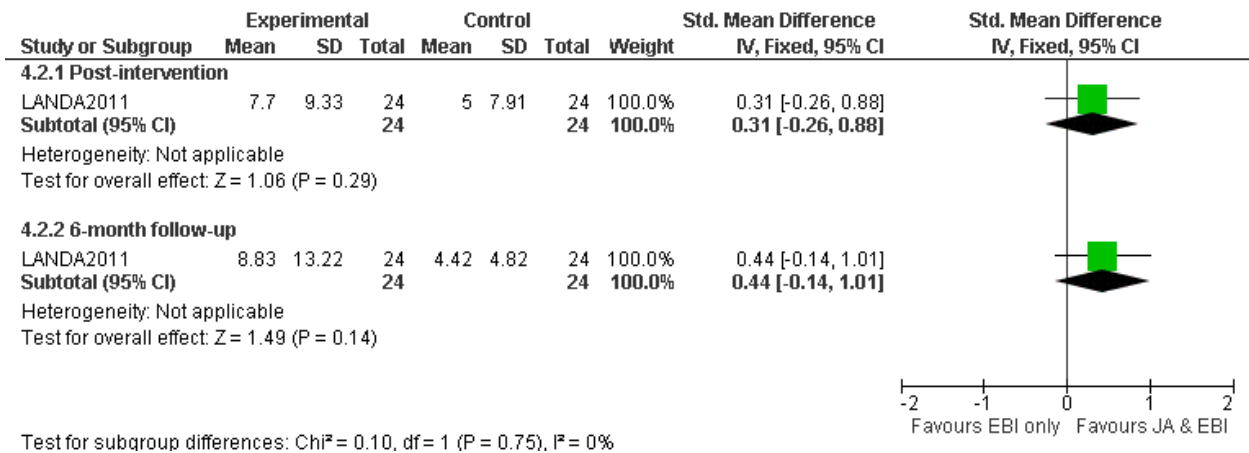
***Joint attention training and EBI/EIBI versus EBI/EIBI only for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome***

**Examiner-child joint attention - Child-initiated JA (ESCs, post-intervention)**

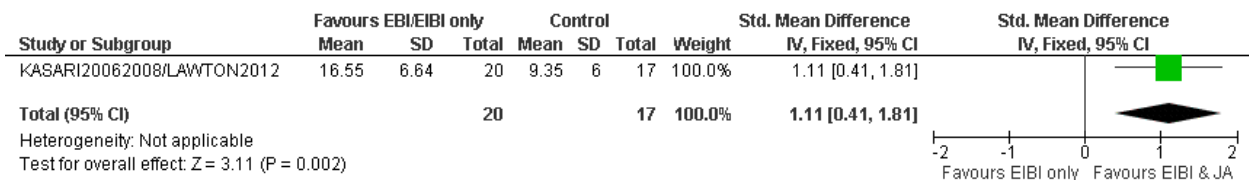




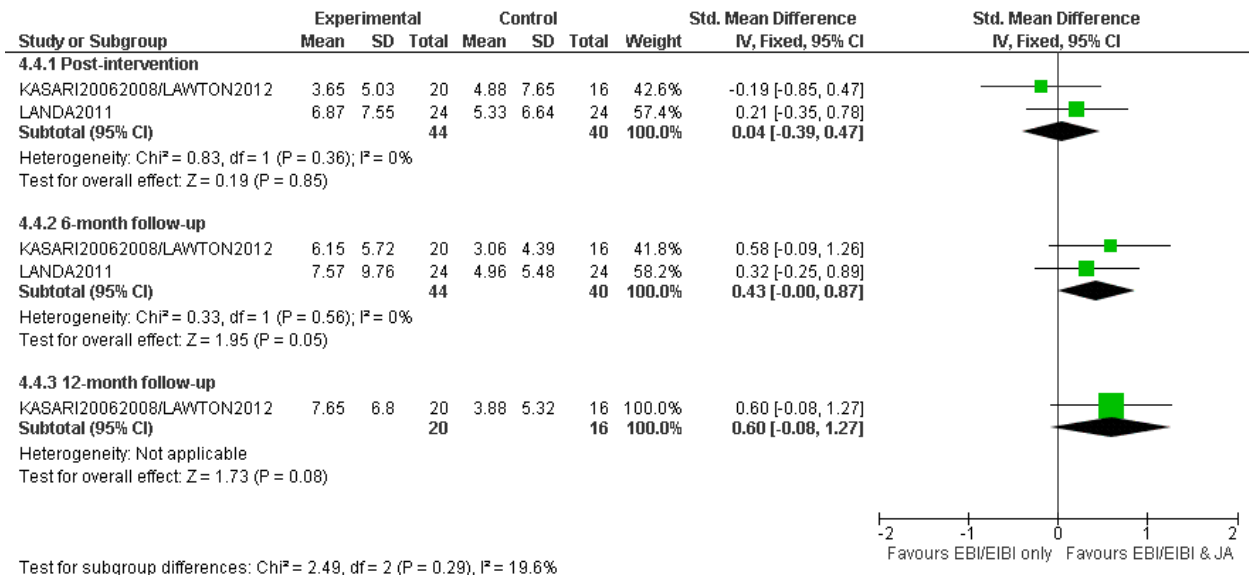
### Examiner-child joint attention- Child-initiated JA (CSBSDP)



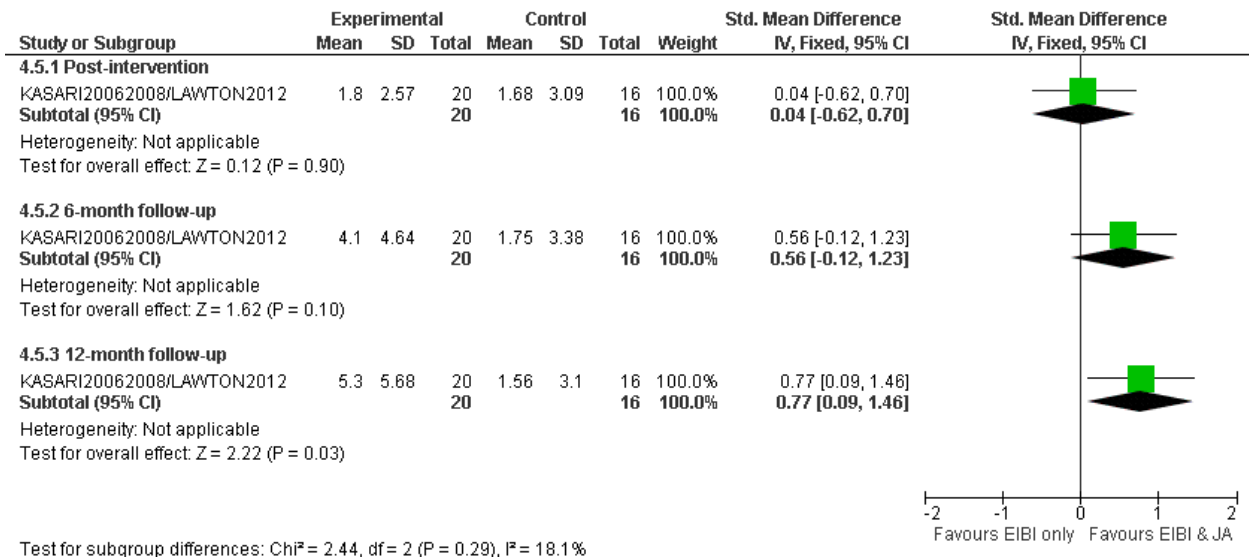
### Examiner-child joint attention - Child responding to JA (ESCs, post-intervention)



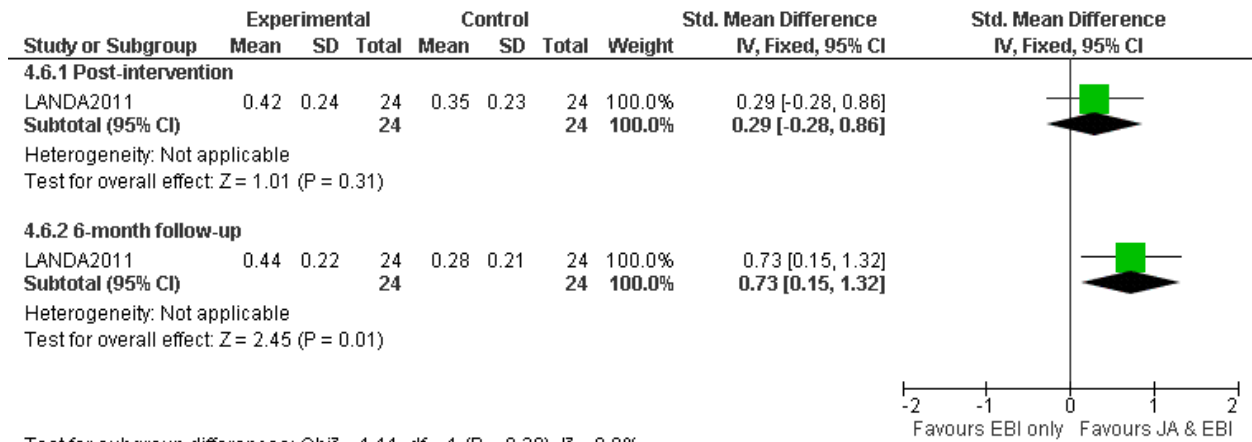
### Examiner-child shared positive affect



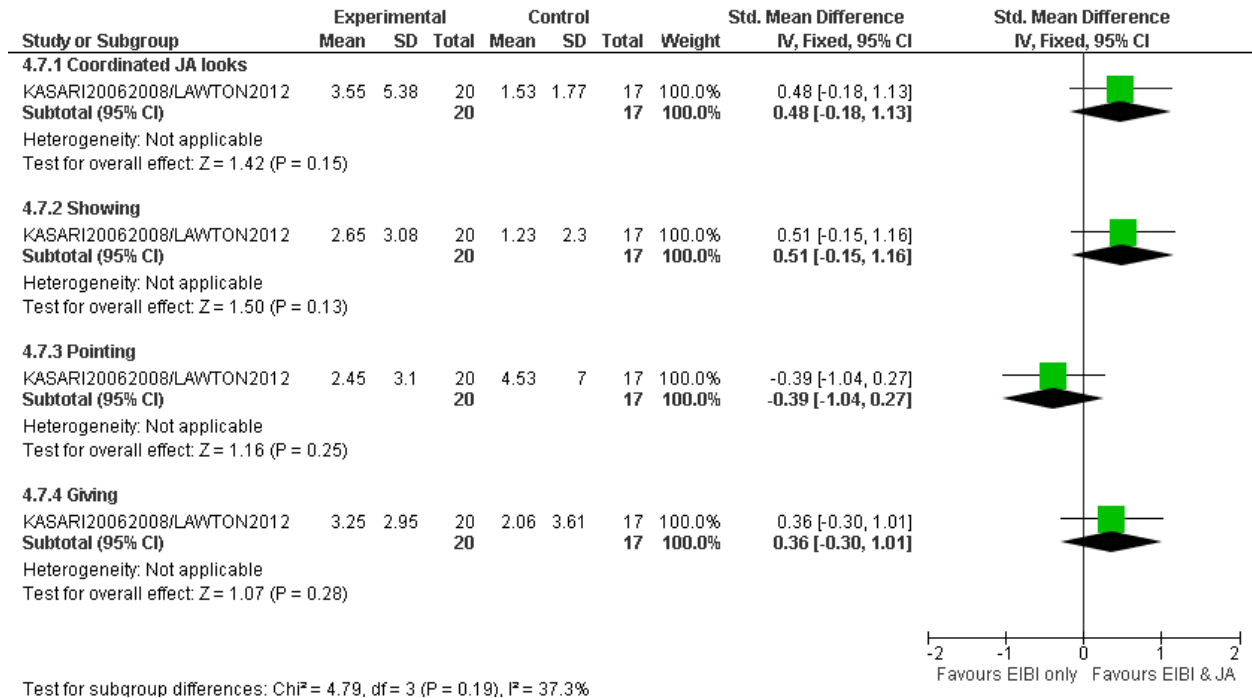
### Examiner-child joint attention, shared positive affect & utterance (ESCs)



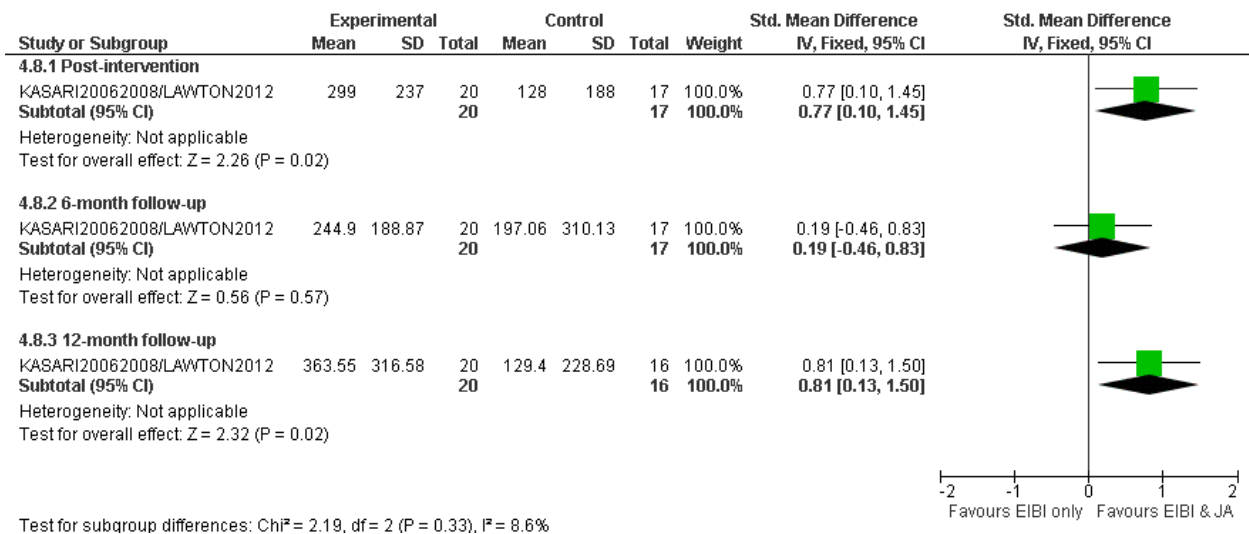
### Examiner-child socially engaged imitation (SEI)



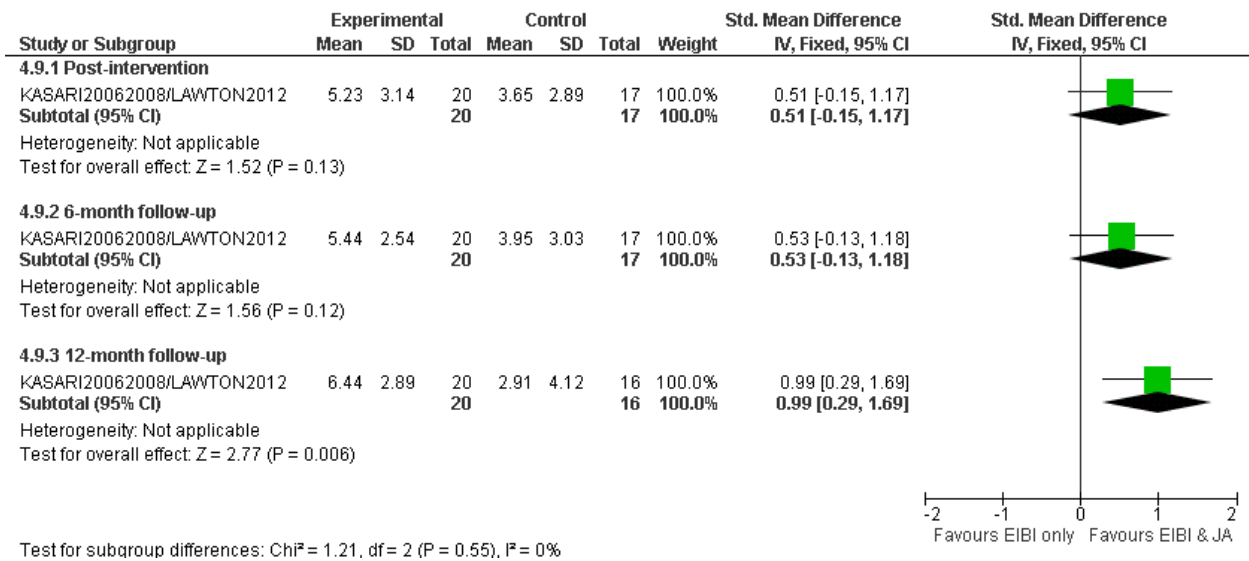
### Mother-child joint attention - Child-initiated JA (post-intervention)



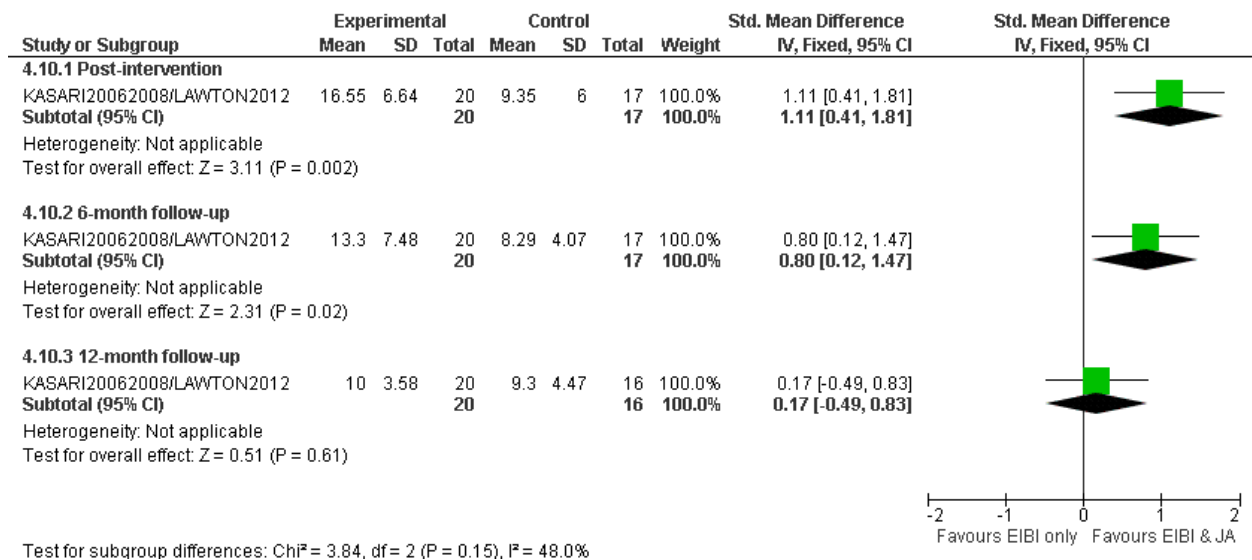
### Mother-child joint attention: Child-initiated JA (duration in seconds)



### Examiner-child and mother-child joint attention: JA initiation composite

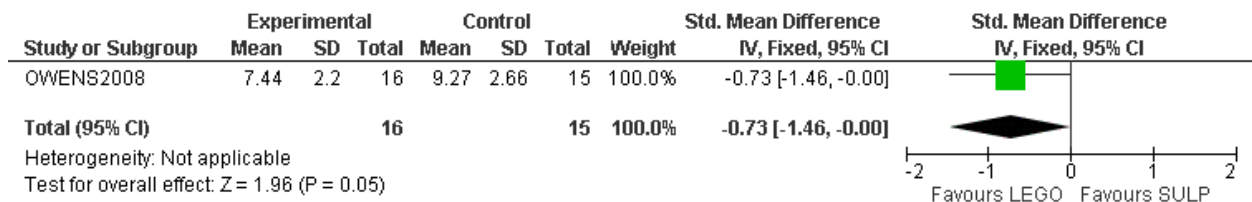


### Examiner-child and mother-child joint attention: JA responses composite

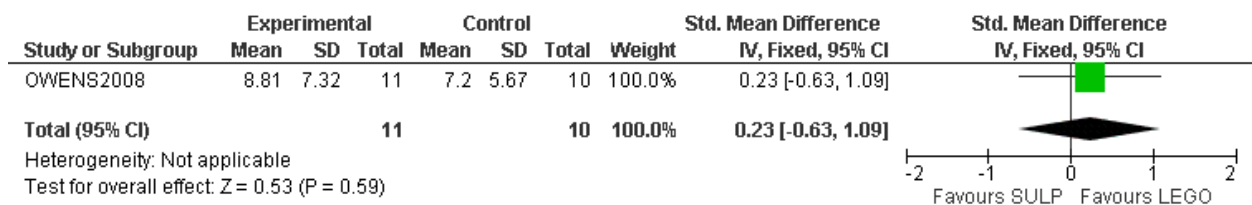


*LEGO® therapy versus Sulp for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome*

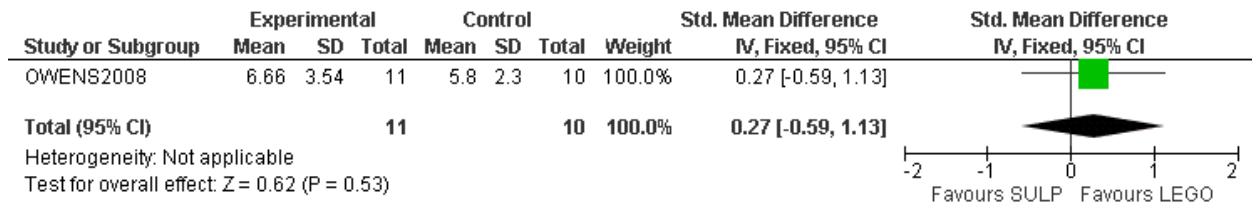
**Social interaction (GARS)**



**Frequency of child-initiated social interactions with TD peers (behavioural observation)**

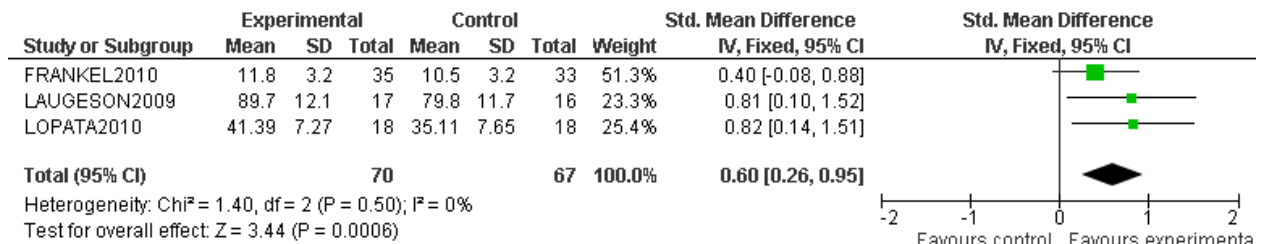


**Duration of all social interactions with TD peers (behavioural observation)**

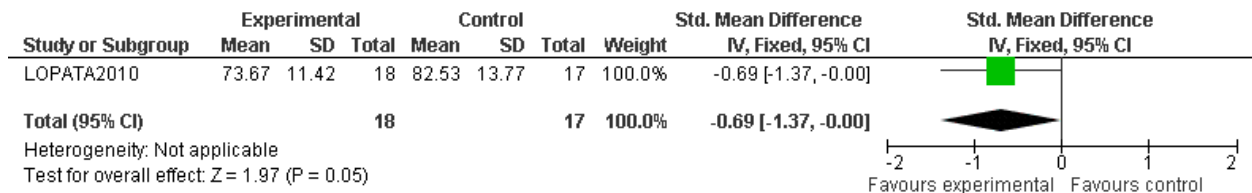


*Social skills group versus treatment-as-usual for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome*

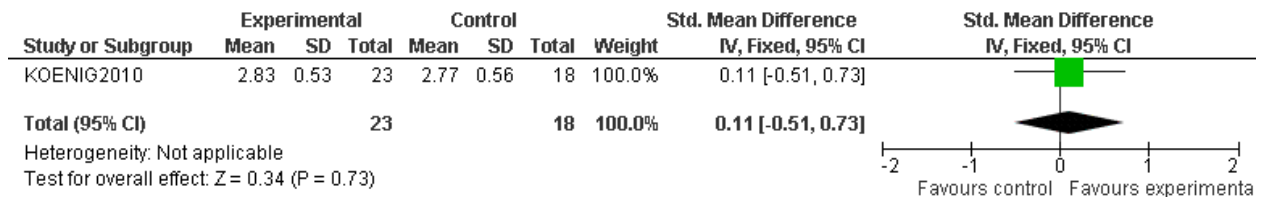
**Social skills (SSRS Assertion/Social skills standardized score or BASC-2-PRS)**



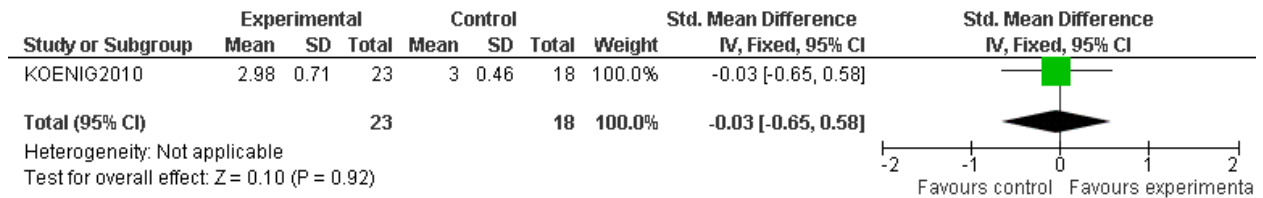
**Social impairment (SRS total)**



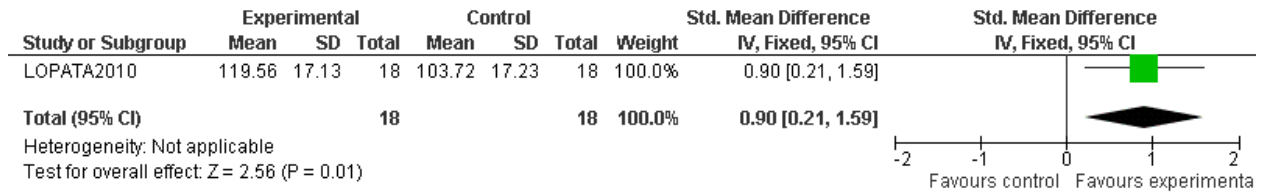
**Adaptive social behaviour (SCI Pro-social index)**



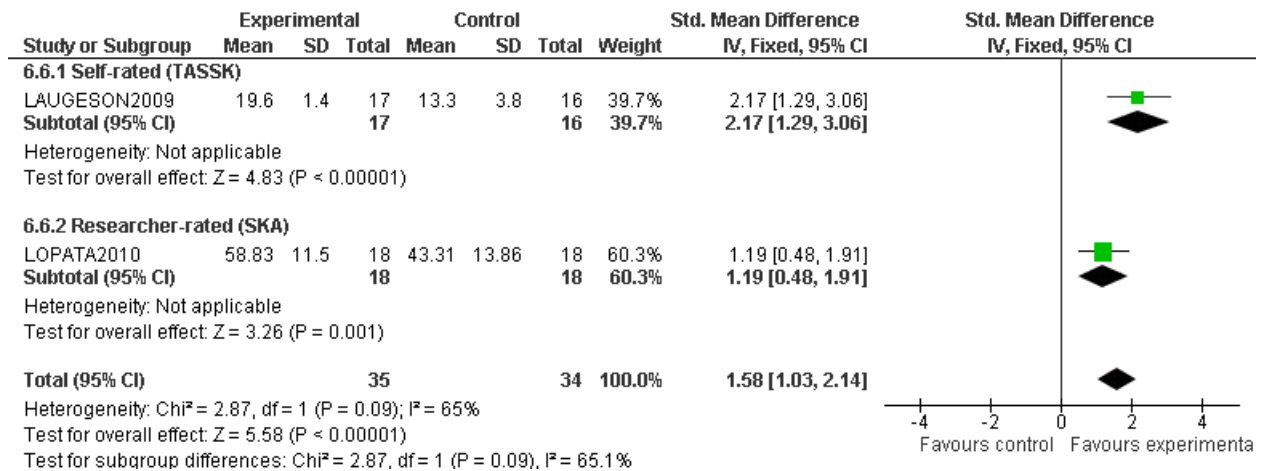
**Capacity for social interactions (SCI Social initiation index)**



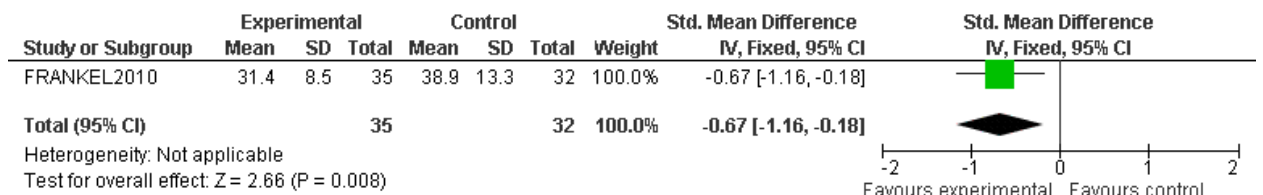
### Study-specific targeted social skills (ASC)



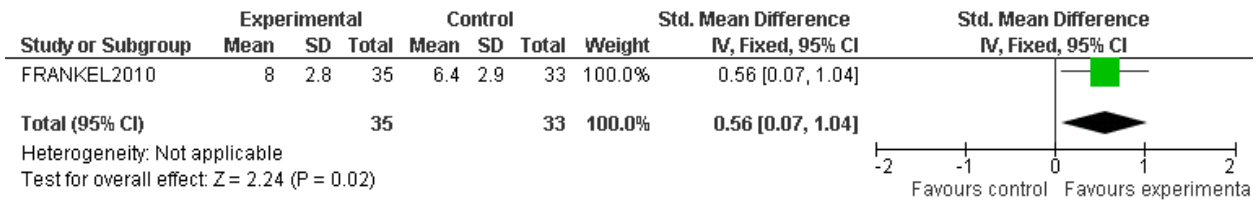
### Social skills knowledge



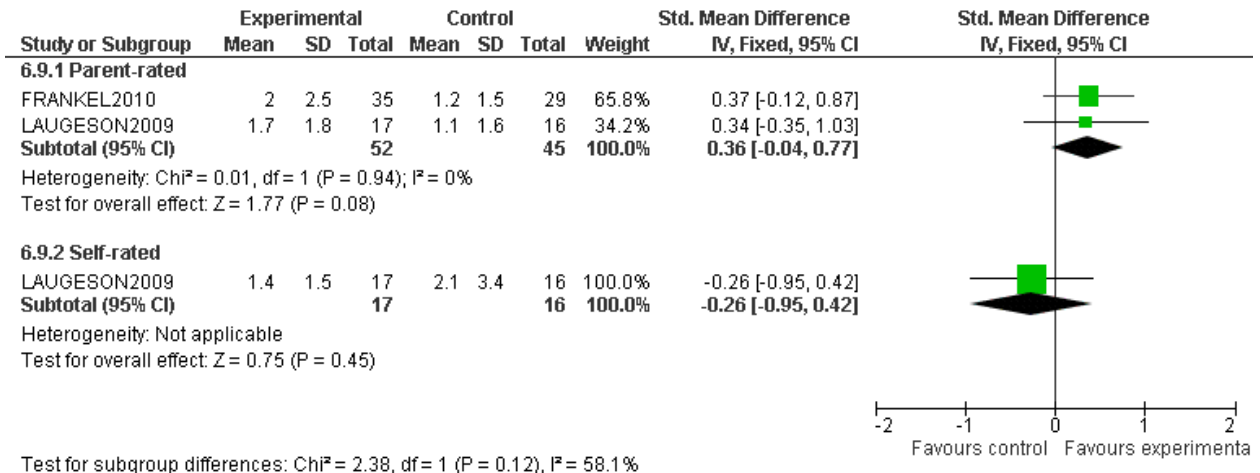
### Feelings of loneliness (Loneliness Scale)



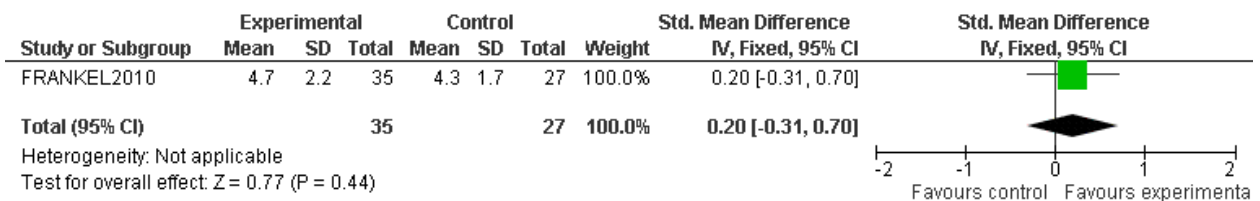
### Popularity (self-rated PHS popularity)



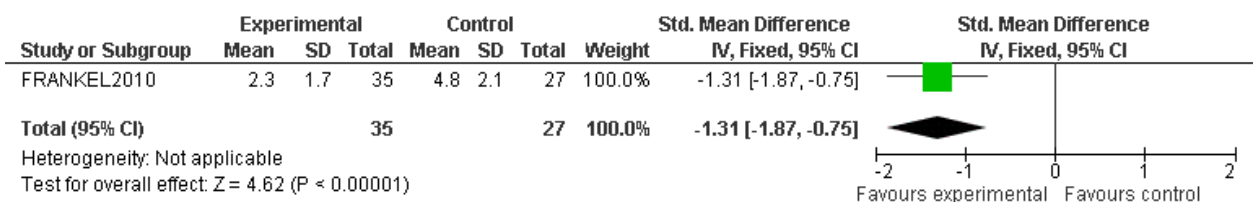
### Number of times child invited to a play date (QPQ Guest)



### Time spent in interactive activities (QPQ Engage)

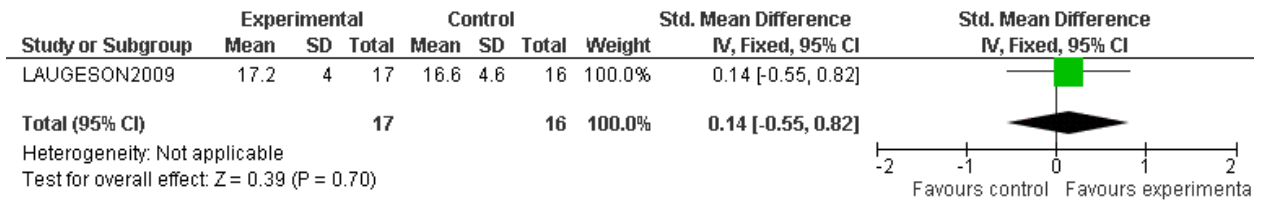


### Time spent in minimally interactive activities (QPQ Disengage)

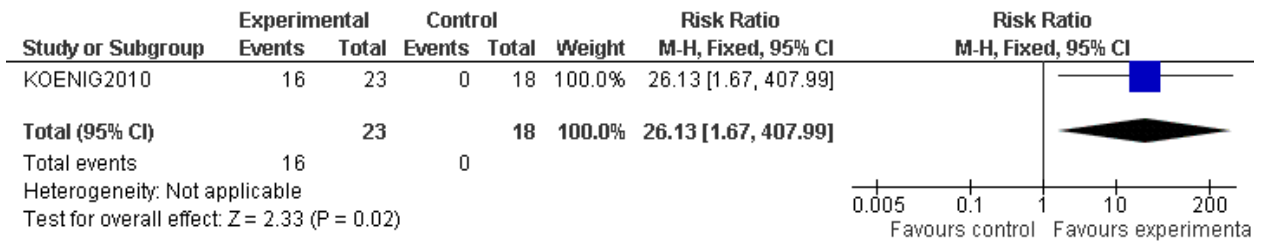


### Quality of friendships (self-rated FQS)

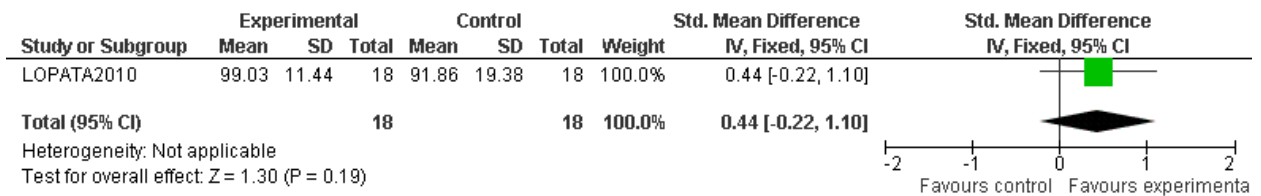




**Positive treatment response ( 'much improved/very improved' on CGI-improvement)**

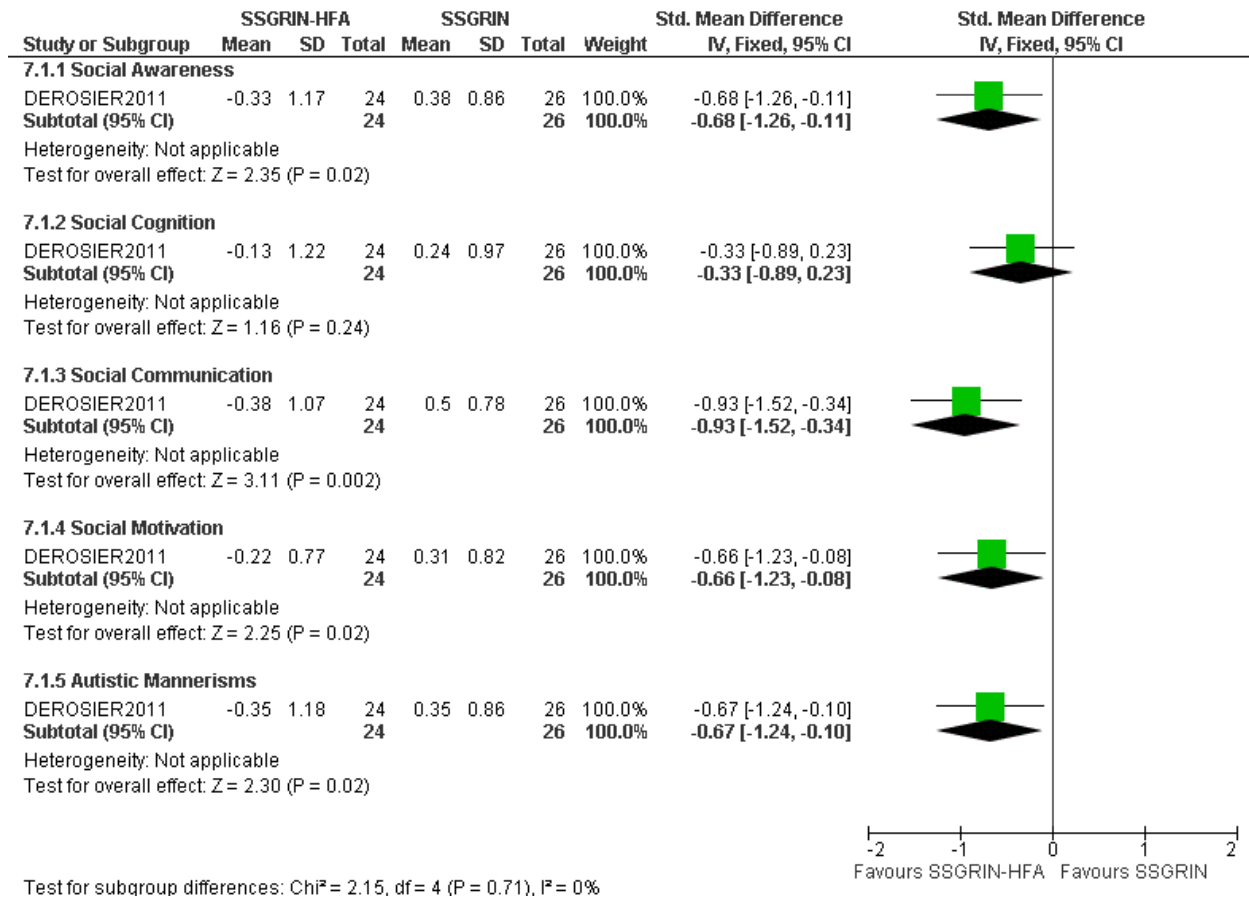


**Emotion recognition (DANVA2)**

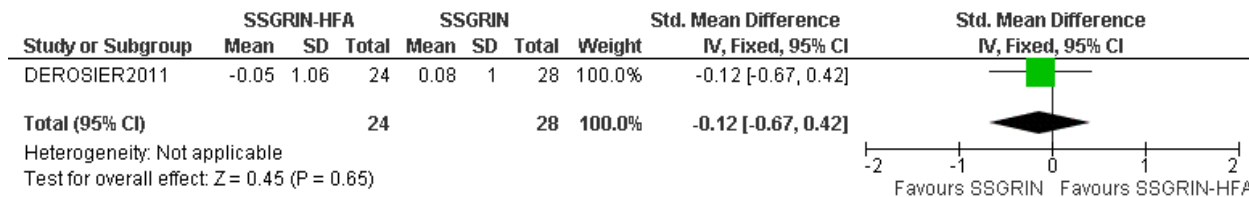


*Social skills group modified for autism versus standard social skills group for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome*

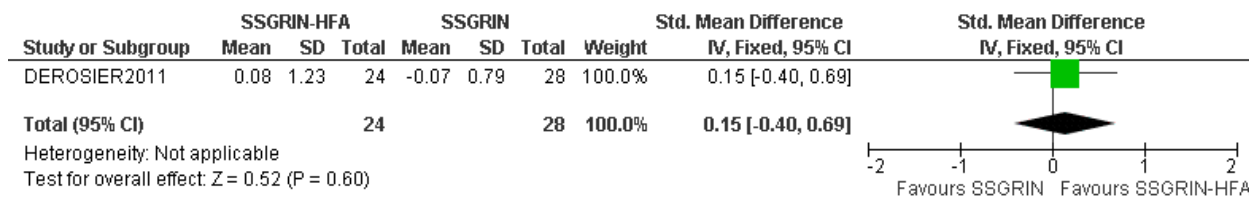
**Social skills (SRS standardized change score)**



**Social self-efficacy (self-rated Social Self-efficacy Scale; standardized change score)**



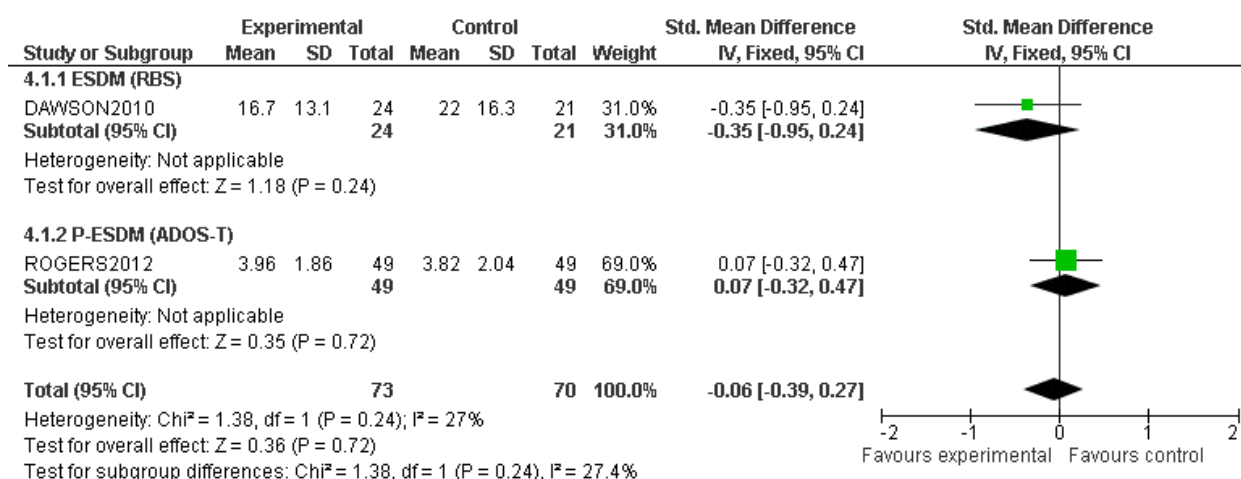
**Feelings of loneliness (Social Dissatisfaction Questionnaire; standardized change score)**



## 1.3 PSYCHOSOCIAL INTERVENTIONS AIMED AT THE CORE AUTISM FEATURE OF RESTRICTED INTERESTS AND RIGID AND REPETITIVE BEHAVIOURS

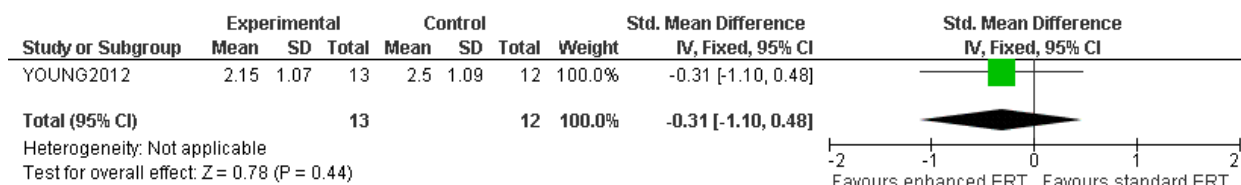
### 1.3.1 Behavioural interventions aimed at the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome

*ESDM or P-ESDM versus treatment-as-usual for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome*



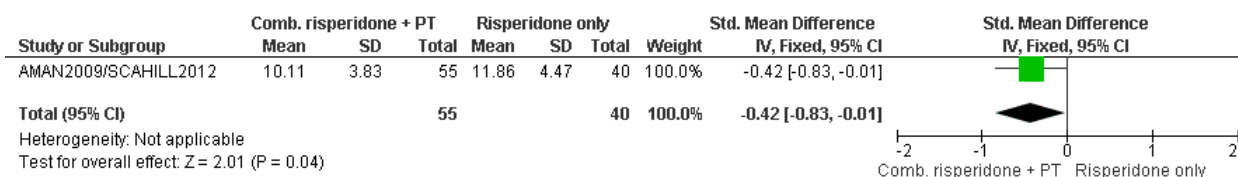
### 1.3.2 Cognitive intervention aimed at the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome

*Enhanced ERT versus standard ERT for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome*



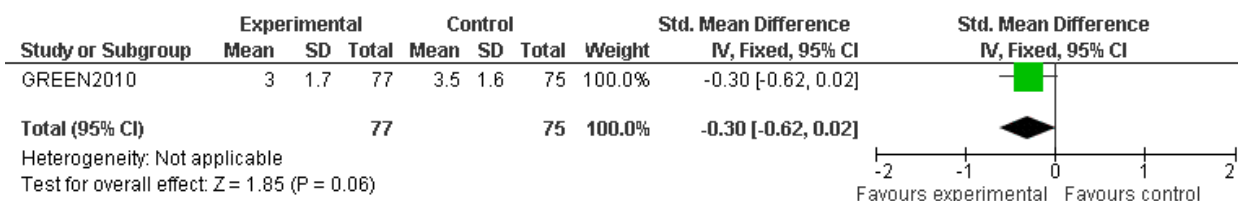
### 1.3.3 Parent training intervention aimed at the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome

*Combined parent training and antipsychotic versus antipsychotic-only for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome*



### 1.3.4 Social-communication intervention aimed at the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome

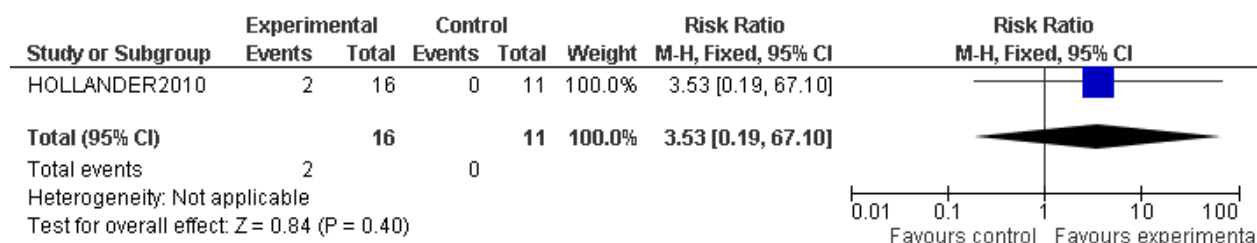
*Caregiver-mediated social-communication intervention (PACT) versus treatment-as-usual for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome*



## 1.4 PHARMACOLOGICAL INTERVENTIONS AIMED AT CORE FEATURES OF AUTISM (OVERALL AUTISTIC BEHAVIOURS)

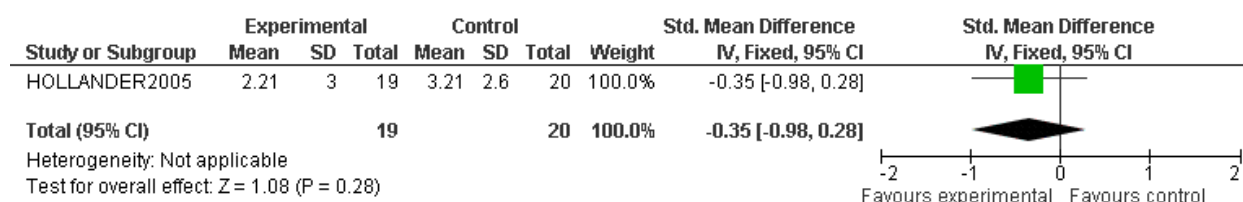
### 1.4.1 Anticonvulsants for overall autistic behaviours as an indirect outcome

*Divalproex sodium versus placebo for overall autistic behaviours as an indirect outcome*



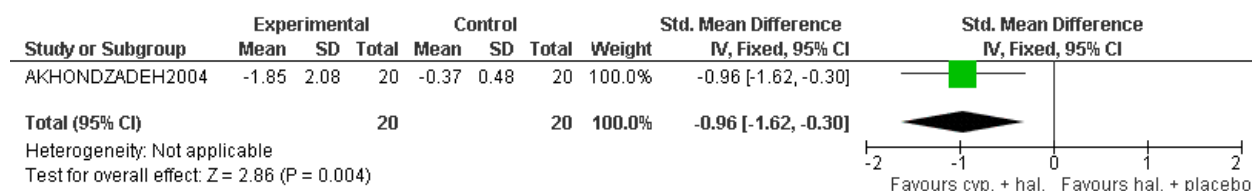
### 1.4.2 Antidepressants for overall autistic behaviours as an indirect outcome

#### *Fluoxetine versus placebo for overall autistic behaviours as an indirect outcome*



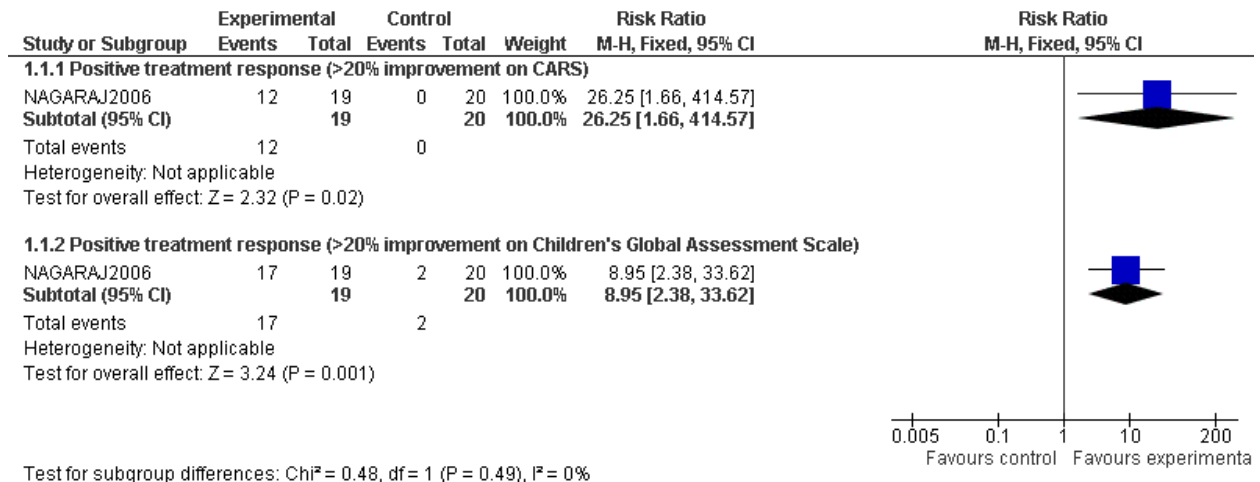
### 1.4.3 Antihistamines for overall autistic behaviours as an indirect outcome

#### *Cyproheptadine and haloperidol versus placebo and haloperidol for overall autistic behaviours as an indirect outcome*

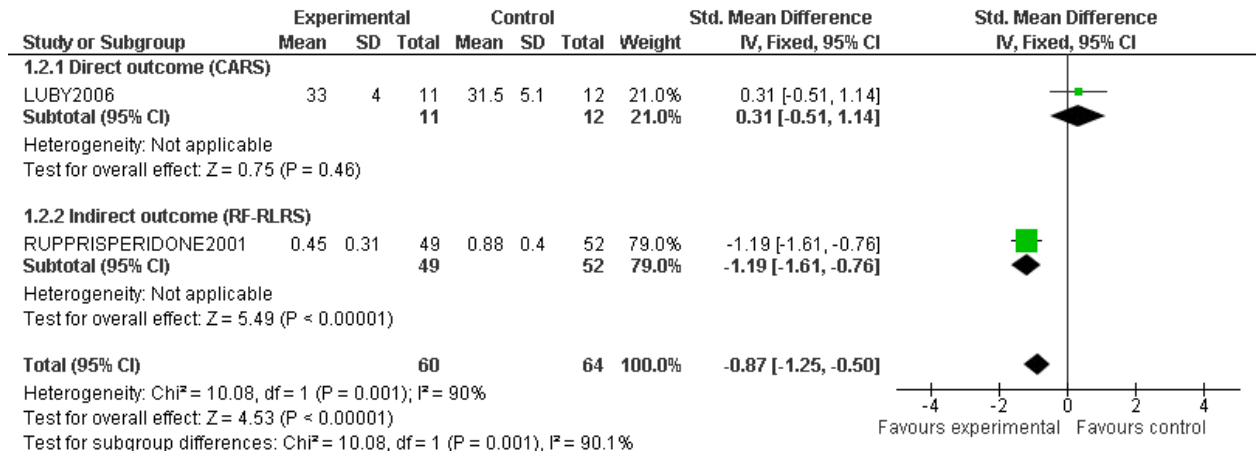


### 1.4.4 Antipsychotics for overall autistic behaviours as a direct or indirect outcome

#### *Risperidone versus placebo for overall autistic behaviours as a direct outcome*

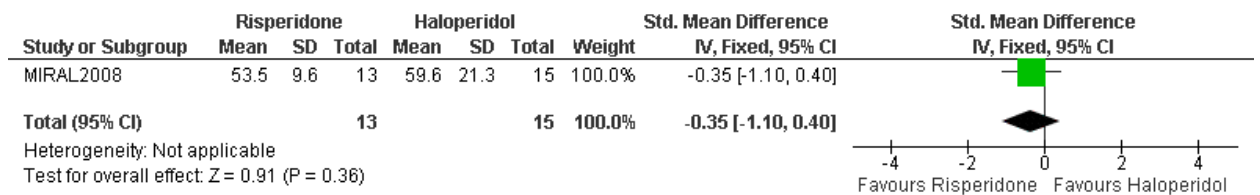


**Risperidone versus placebo for overall autistic behaviours as a direct or indirect outcome**

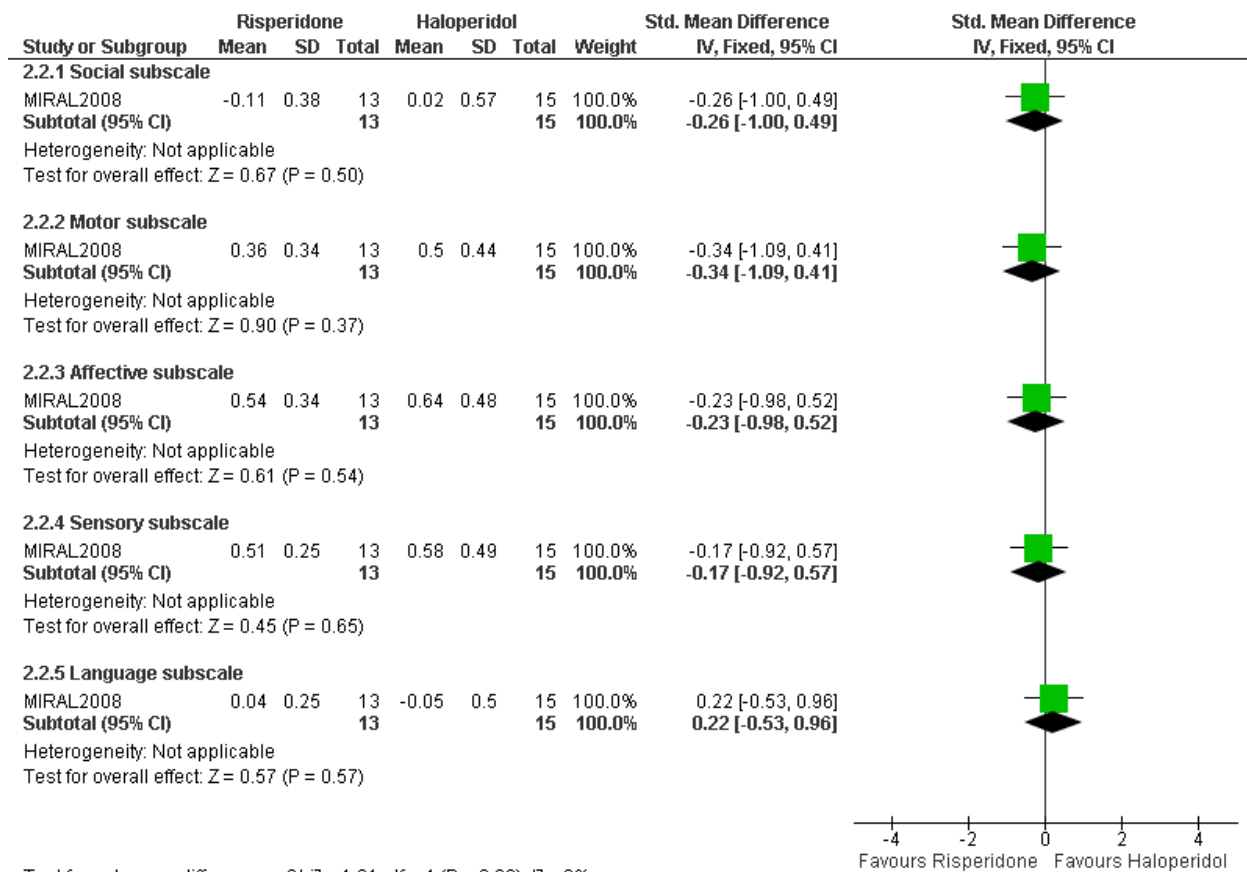


**Risperidone versus haloperidol for overall autistic behaviours as a direct outcome**

**Overall autistic behaviours (Turgay DSM-IV PDD Rating Scale)**

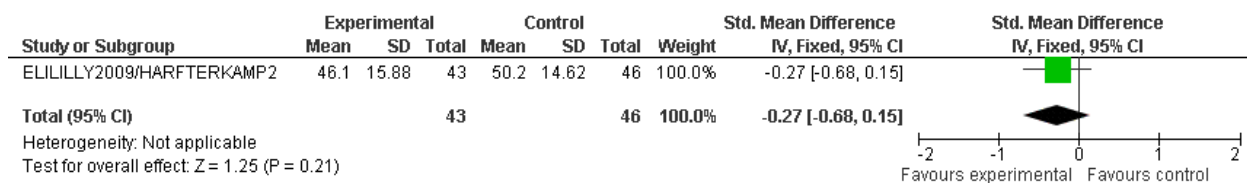


**Overall autistic behaviours (RF-RLRS)**



### 1.4.5 SNRIs for overall autistic behaviours as an indirect outcome

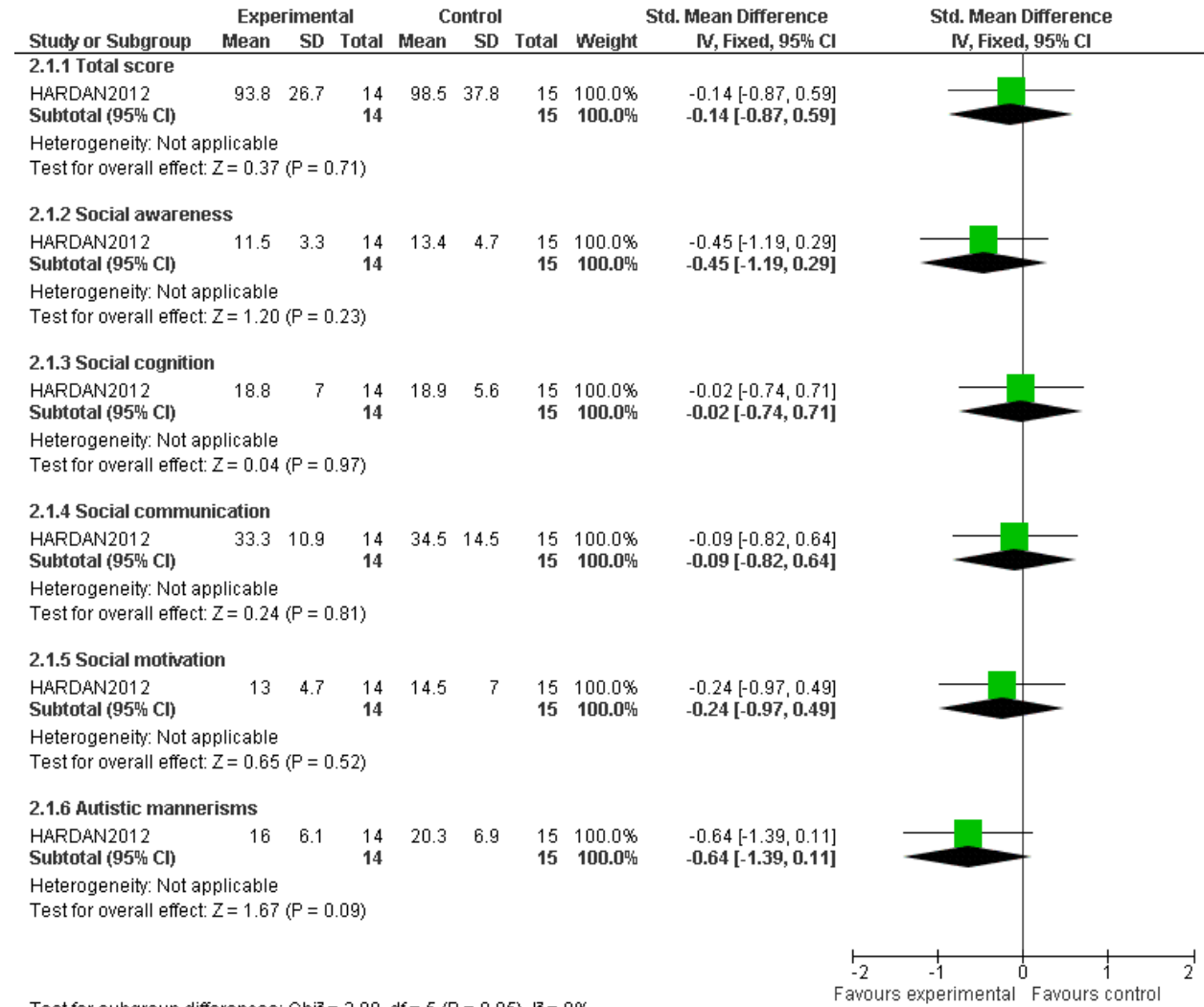
#### *Atomoxetine versus placebo for overall autistic behaviours as an indirect outcome*



## 1.5 PHARMACOLOGICAL INTERVENTIONS AIMED AT THE CORE AUTISM FEATURE OF IMPAIRED RECIPROCAL SOCIAL COMMUNICATION AND INTERACTION

### 1.5.1 Antioxidants for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome

#### *N-acetylcysteine versus placebo for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome*



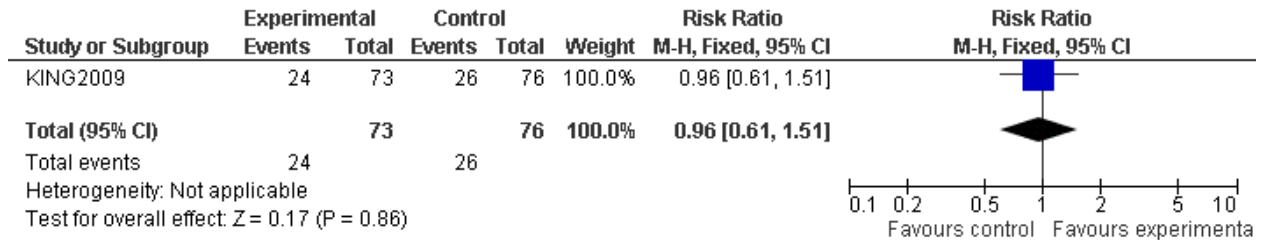
## 1.6 PHARMACOLOGICAL INTERVENTIONS AIMED AT THE CORE AUTISM FEATURE OF RESTRICTED INTERESTS AND RIGID AND REPETITIVE BEHAVIOURS



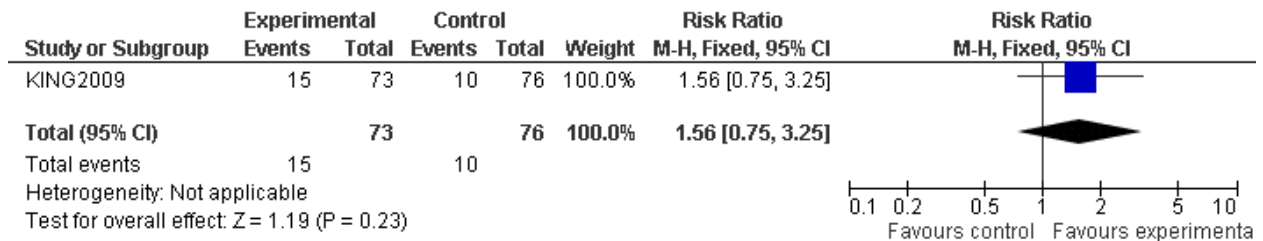
### 1.6.1 Antidepressants for the core autism feature of restricted interests and rigid and repetitive behaviours as a direct outcome

*SSRIs versus placebo for the core autism feature of restricted interests and rigid and repetitive behaviours as a direct outcome*

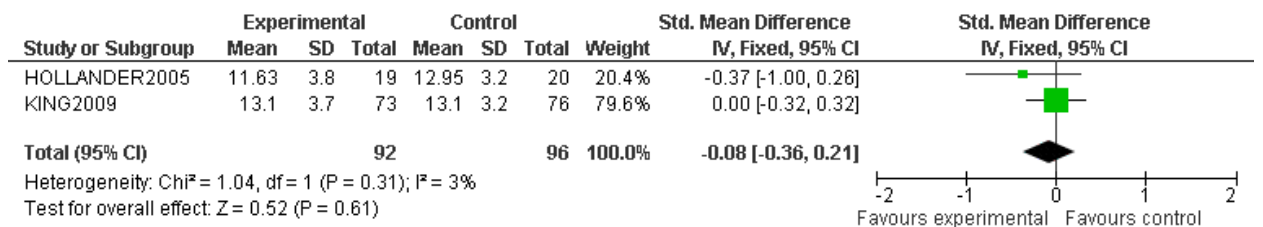
**Global positive treatment response ('much improved/very improved' on CGI-improvement)**



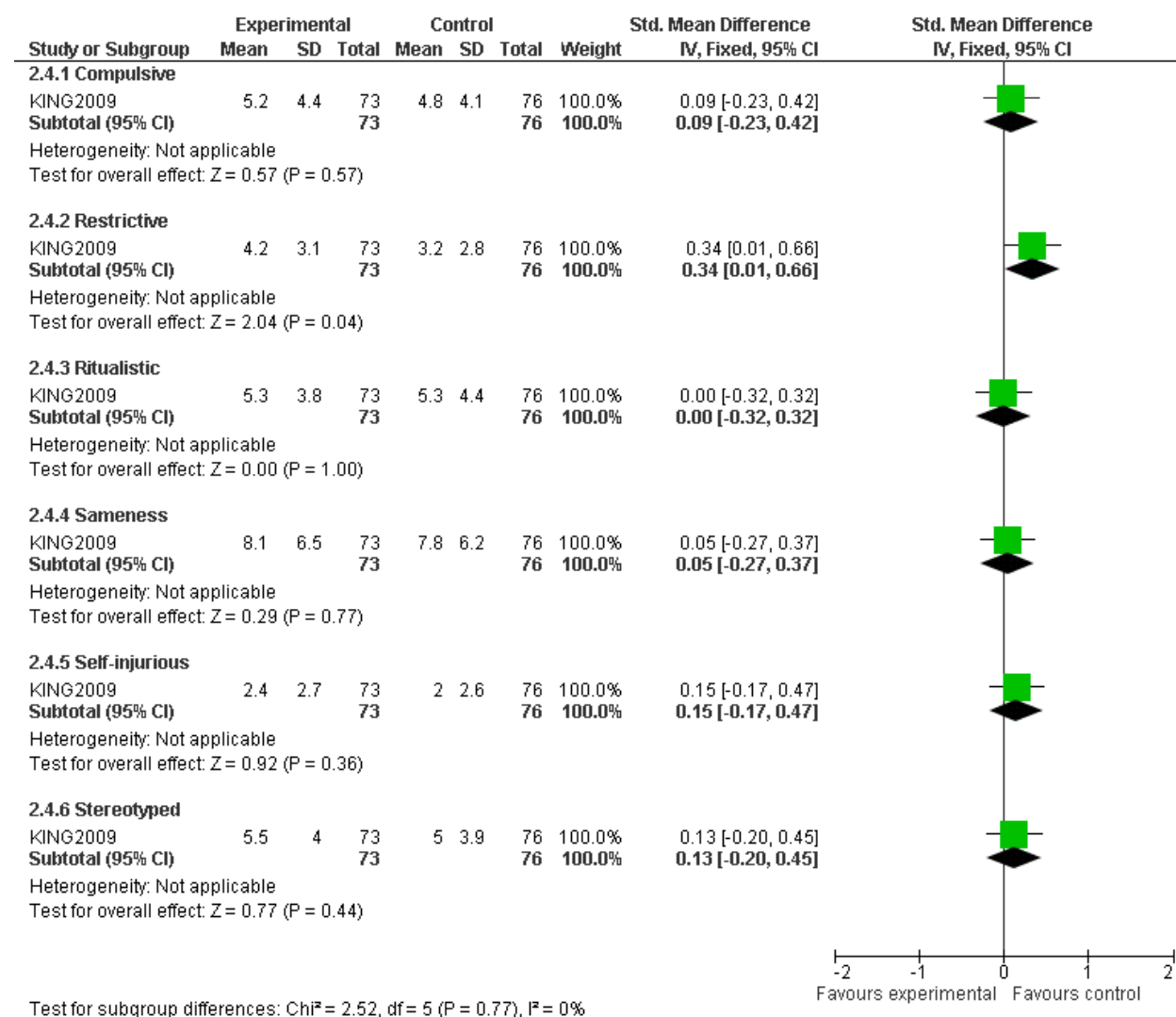
**Global positive treatment response (>25% improvement on CYBOCS-PDD & 'much improved/very improved' on CGI-improvement)**



#### Compulsions (CYBOCS-PDD)

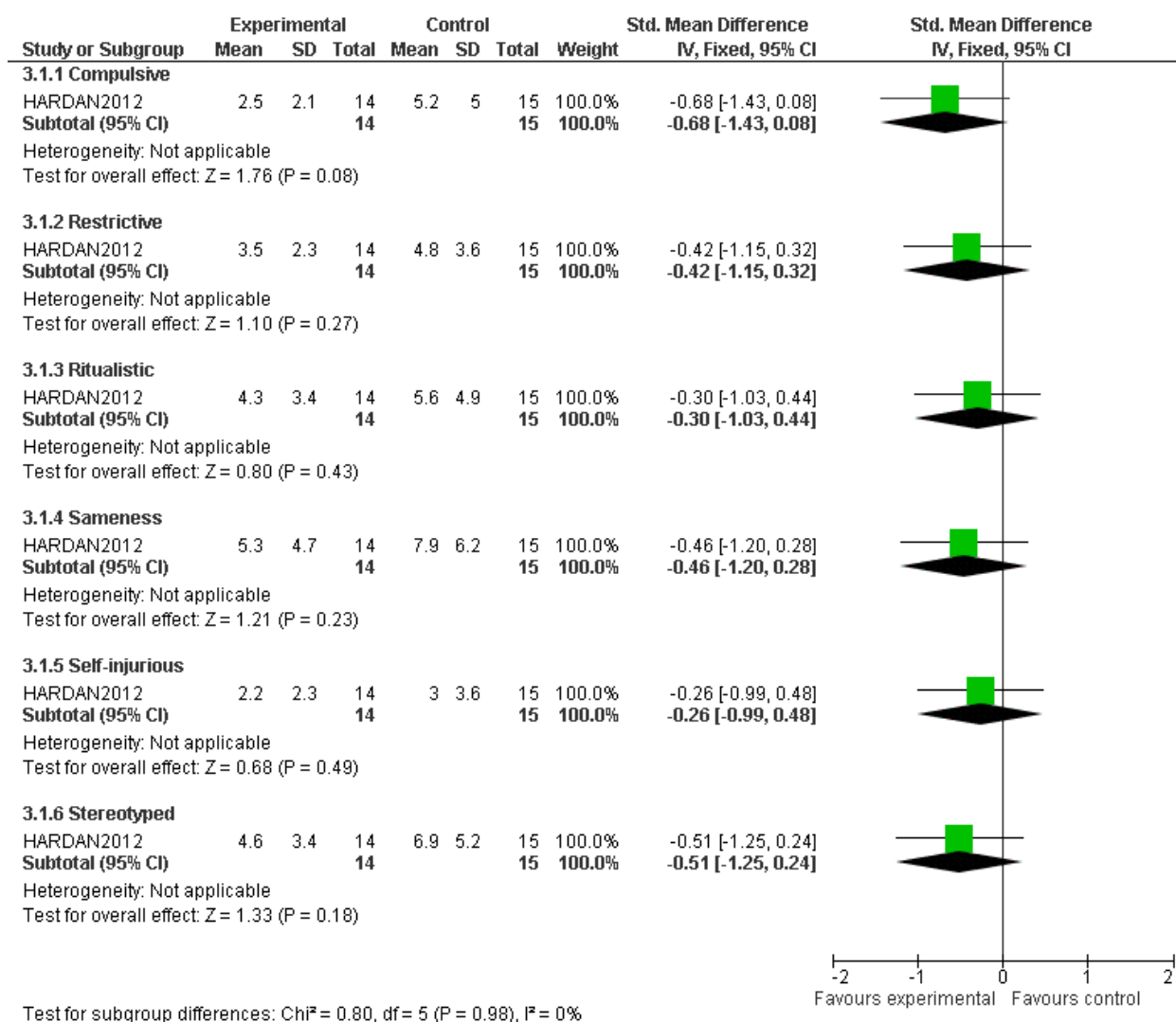


#### Repetitive behaviour (RBS)



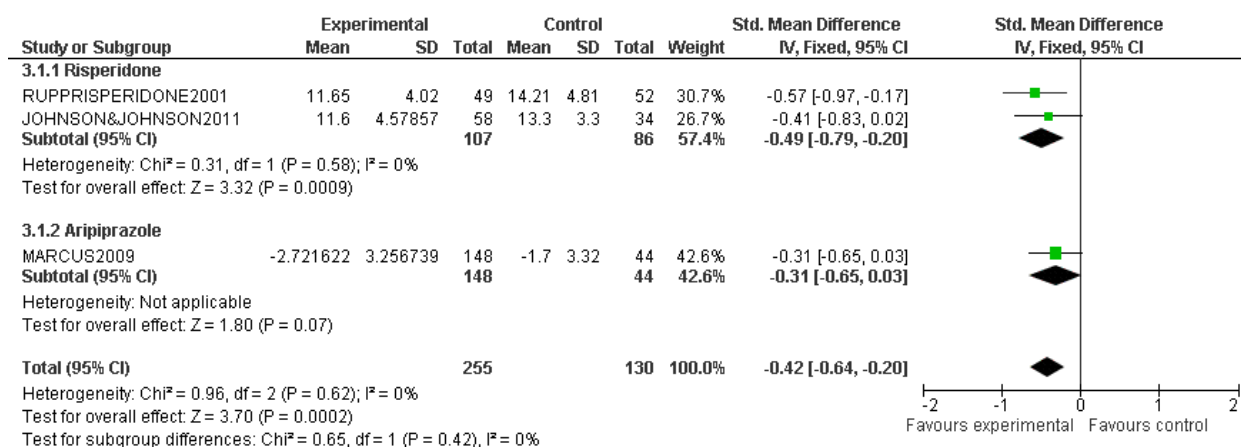
## 1.6.2 Antioxidants for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome

*N-acetylcysteine versus placebo for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome*

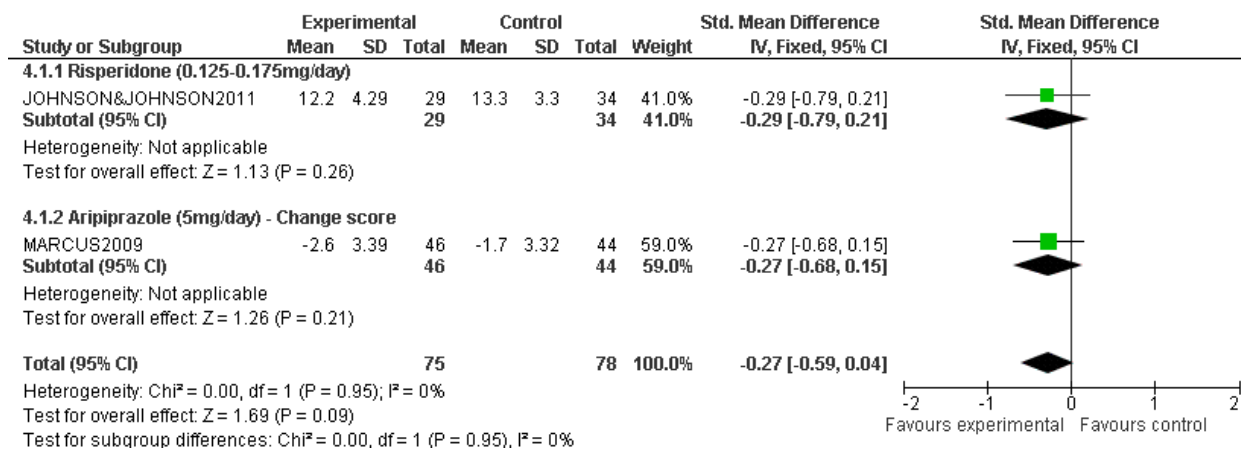


### 1.6.3 Antipsychotics for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome

*Antipsychotics versus placebo for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome*



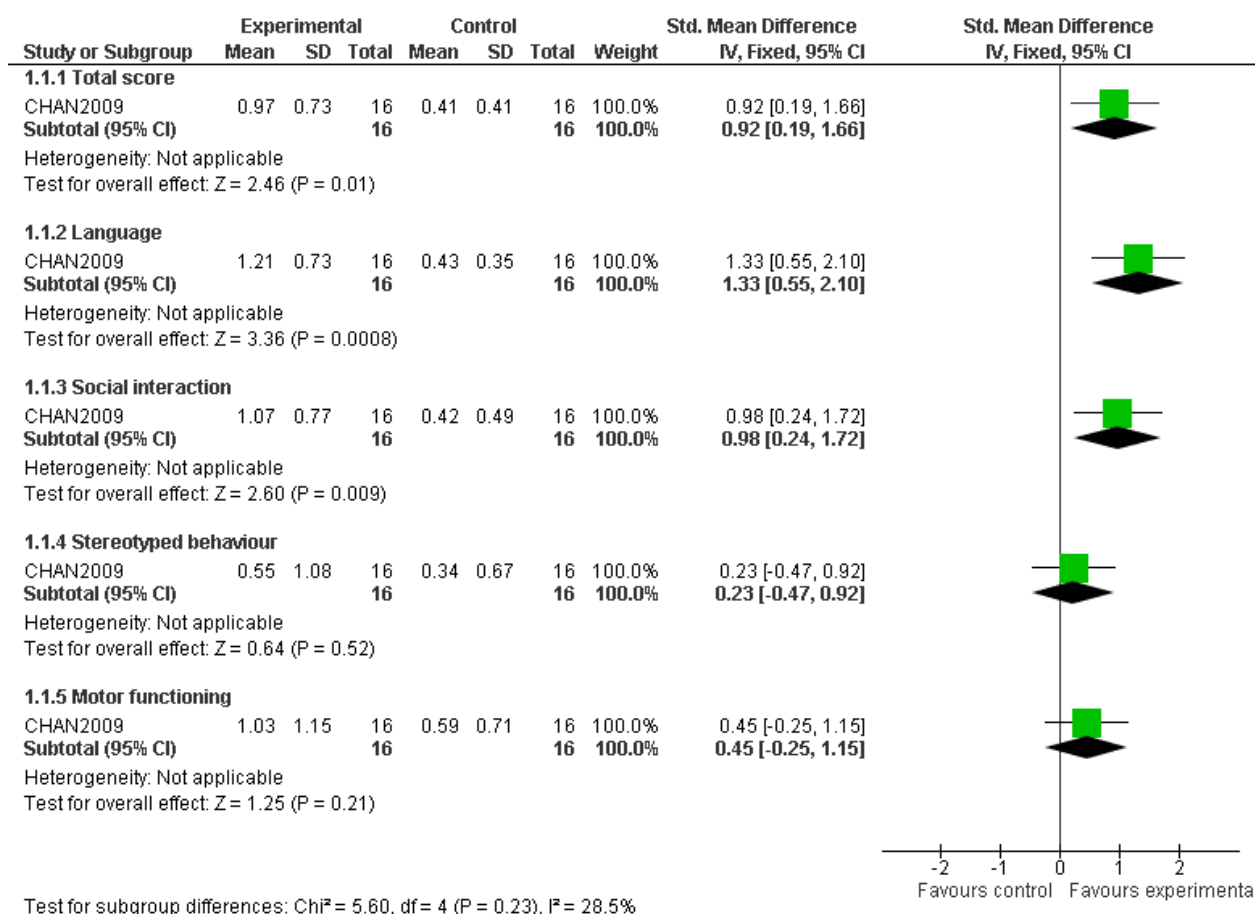
*Low-dose antipsychotics versus placebo for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome*



## 1.7 BIOMEDICAL INTERVENTIONS AIMED AT CORE FEATURES OF AUTISM (OVERALL AUTISTIC BEHAVIOURS)

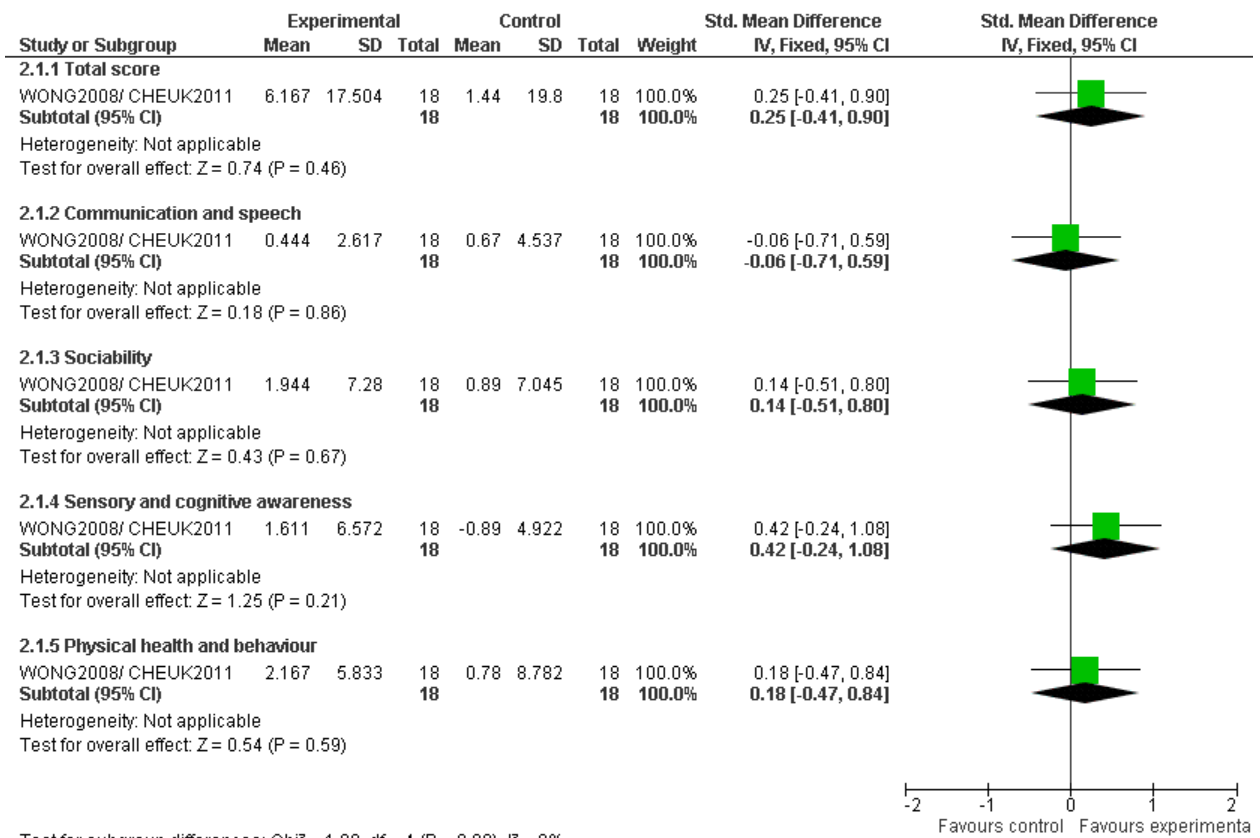
### 1.7.1 Complementary therapies for overall autistic behaviours as a direct or indirect outcome

*Acupressure versus waitlist for overall autistic behaviours as a direct outcome*

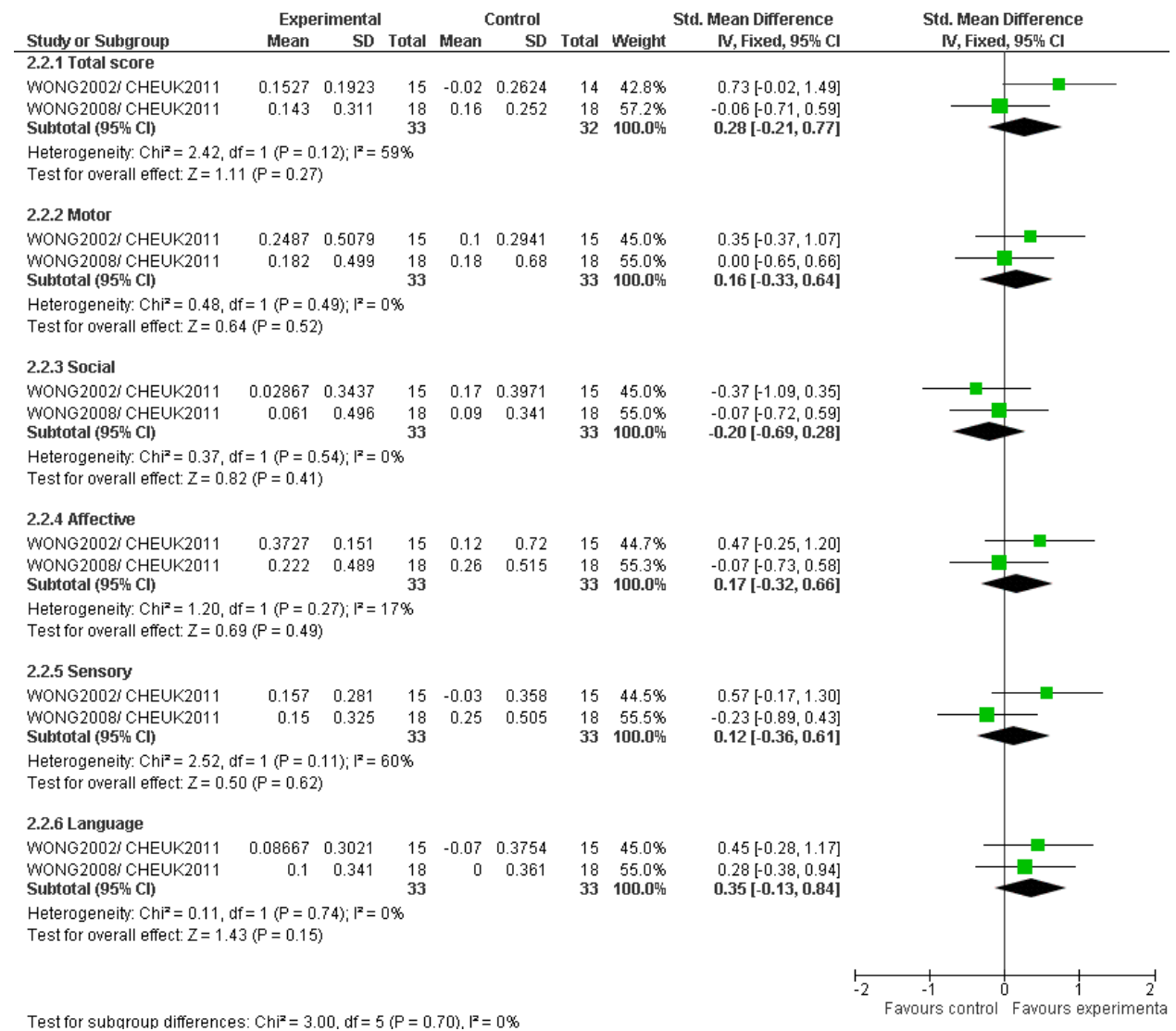


*Acupuncture/electro-acupuncture and conventional educational programme versus conventional educational programme only for overall autistic behaviours as a direct outcome*

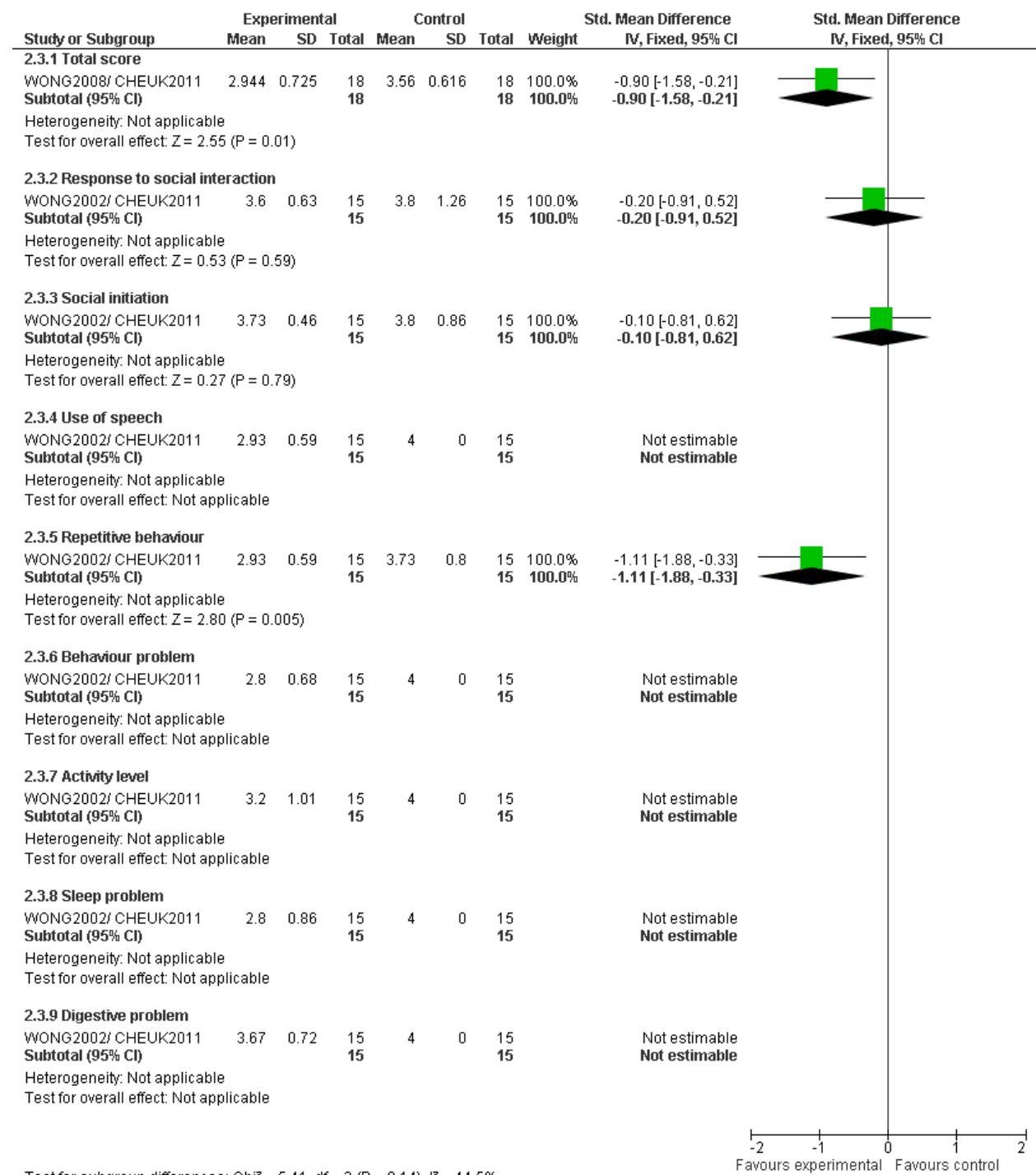
**Overall autistic behaviours (ATEC)**



**Overall autistic behaviours (RLRS)**



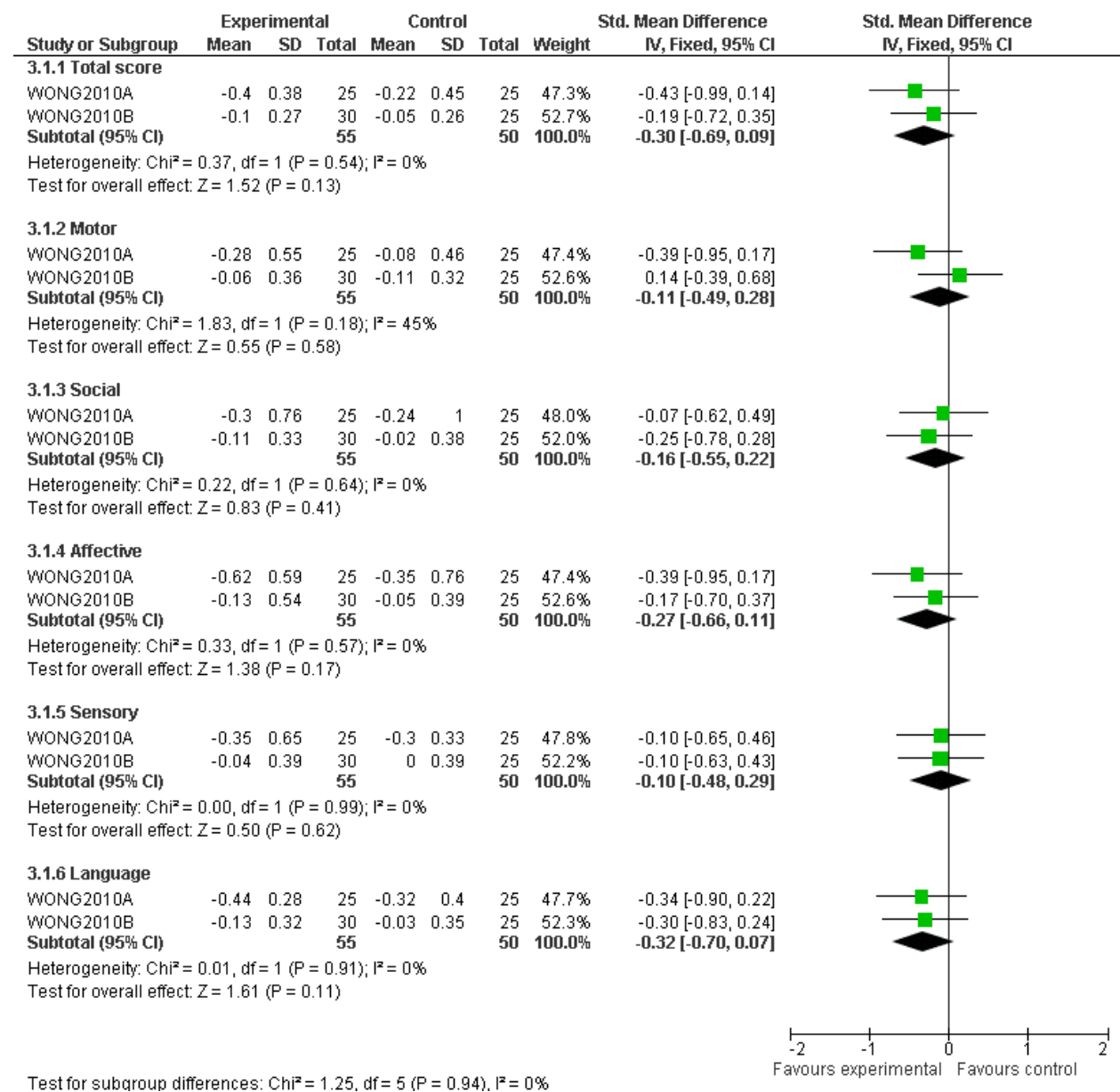
**Overall autistic behaviours (CGI)**



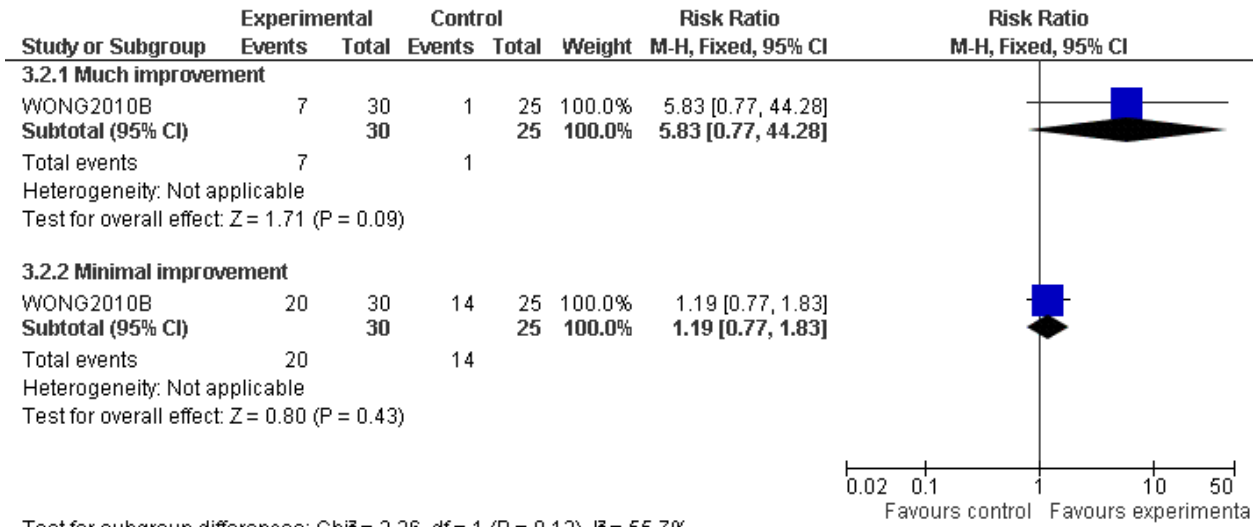
*Acupuncture/electro-acupuncture versus sham acupuncture/electro-acupuncture for overall autistic behaviours as an indirect outcome*

**Overall autistic behaviours (RLRS; change scores)**

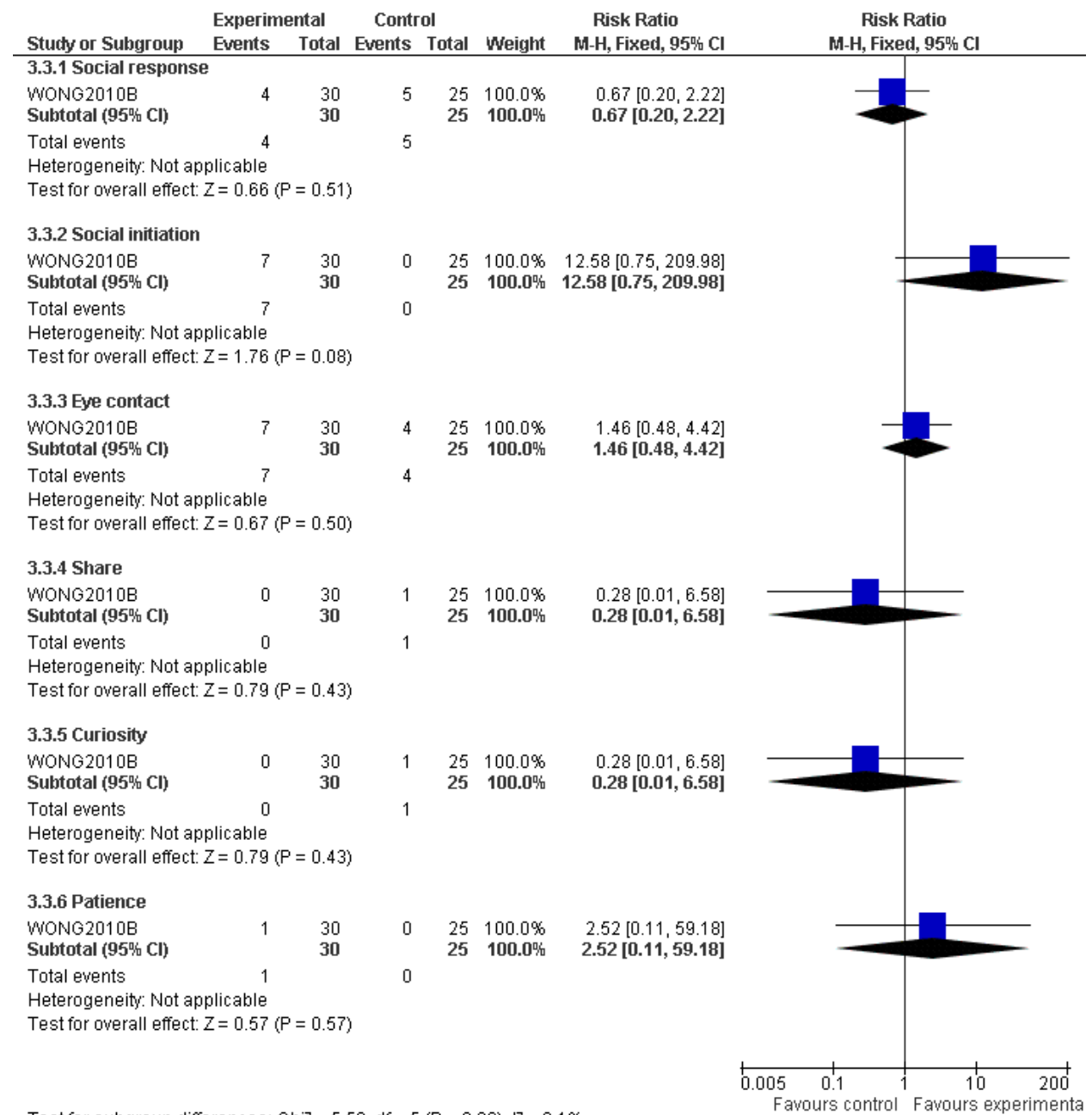




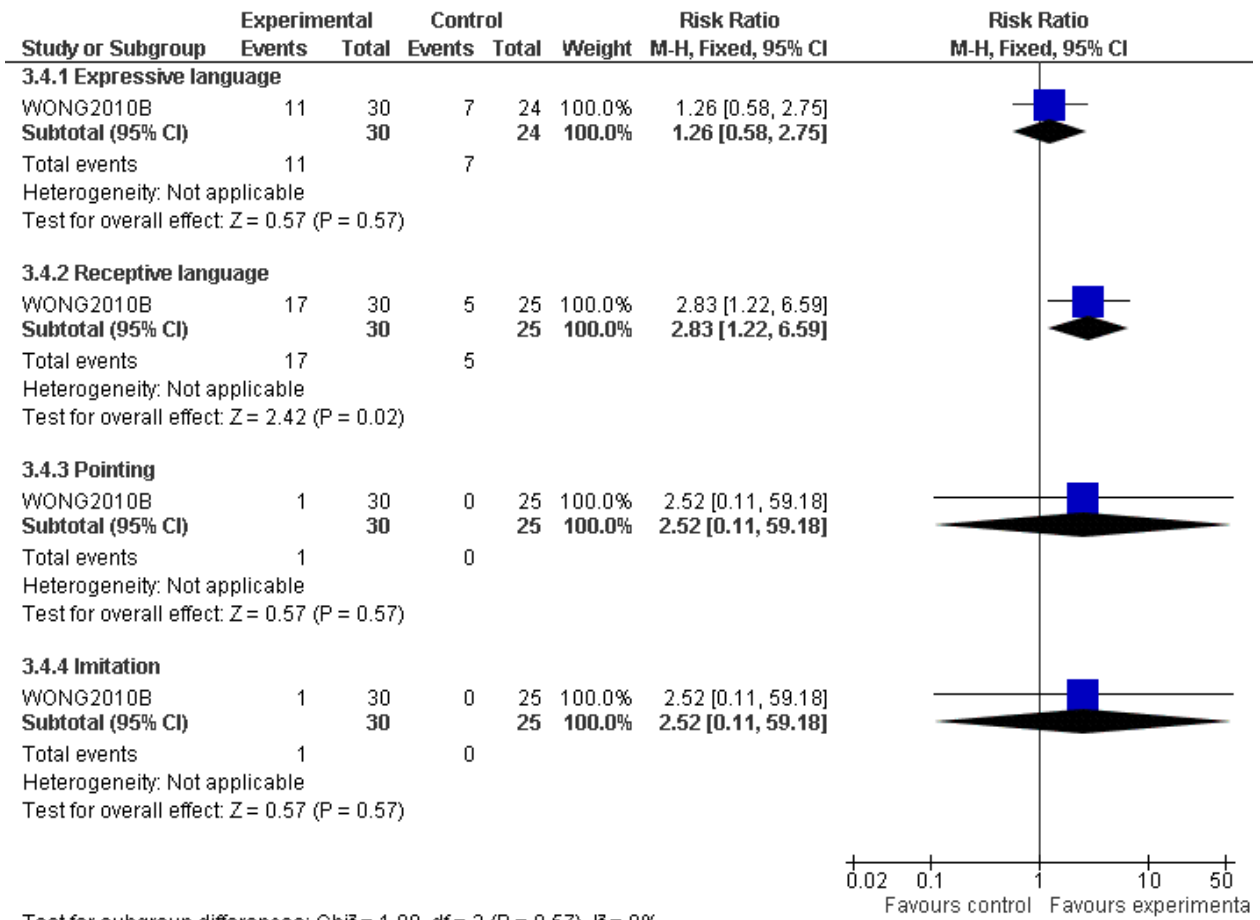
**Positive treatment response (improvement in autistic behaviours; CGI-I)**



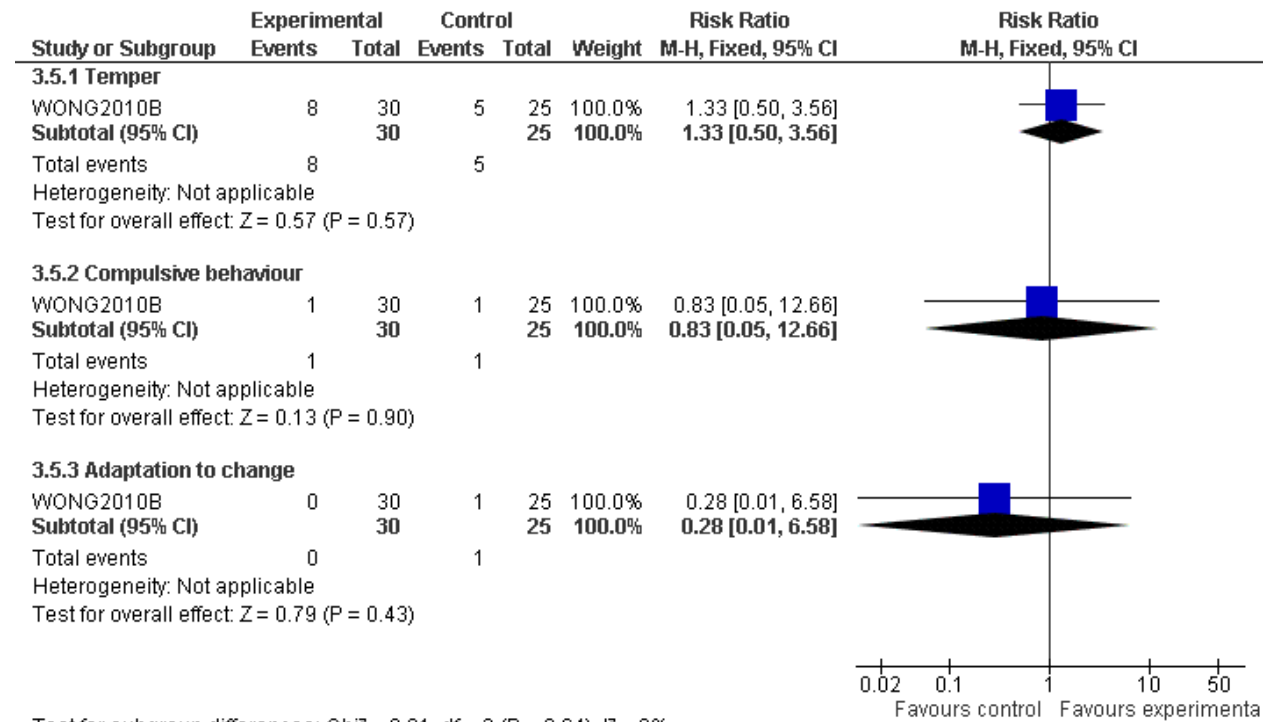
**Positive treatment response for social relatedness (study-specific parent-reported 'better than before')**



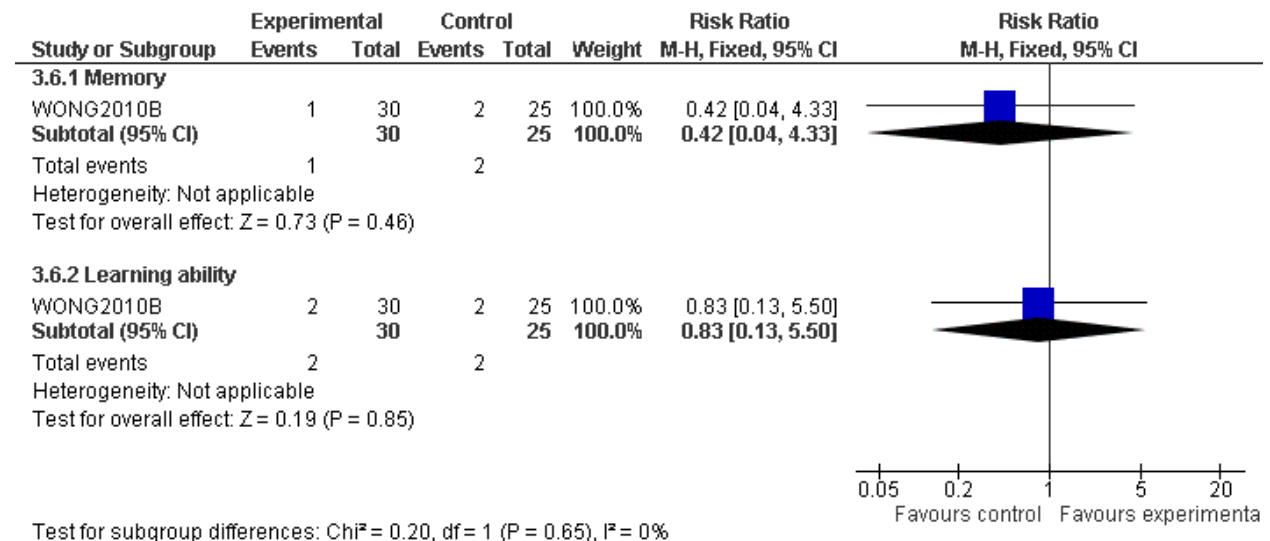
**Positive treatment response for non-verbal and verbal communication (study-specific parent-reported 'better than before')**



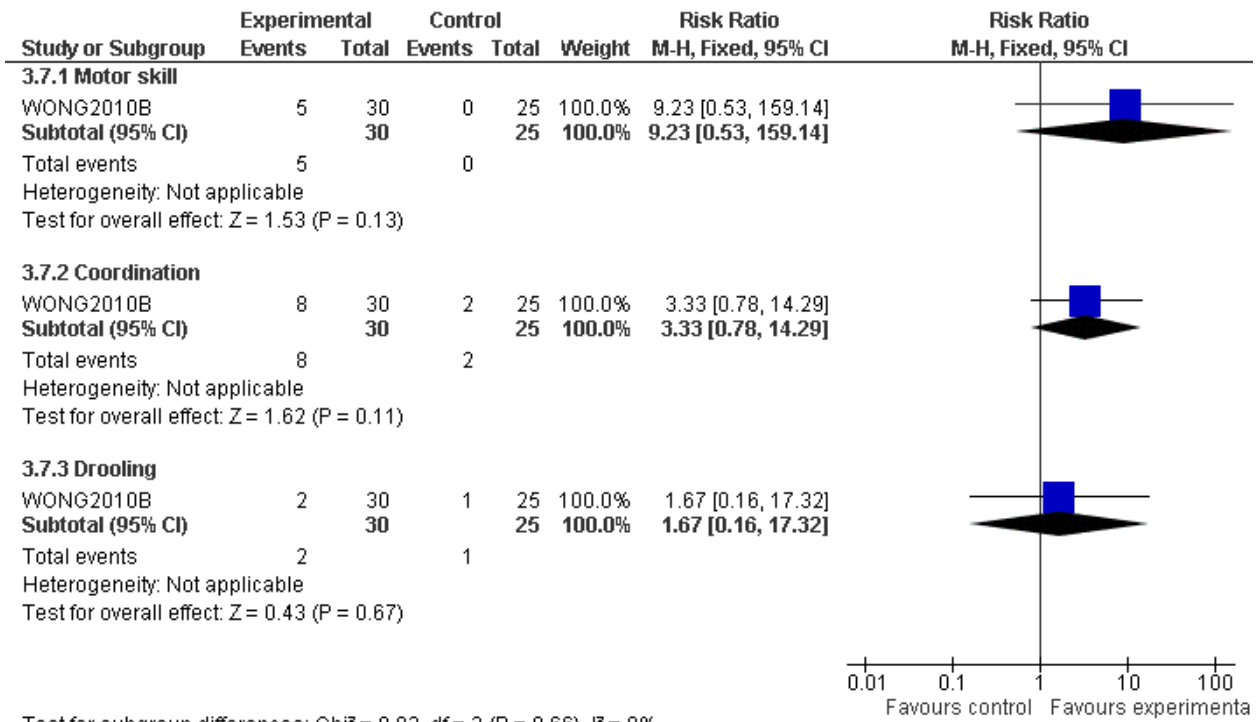
**Positive treatment response for stereotypy interest and behaviour (study-specific parent-reported 'better than before')**



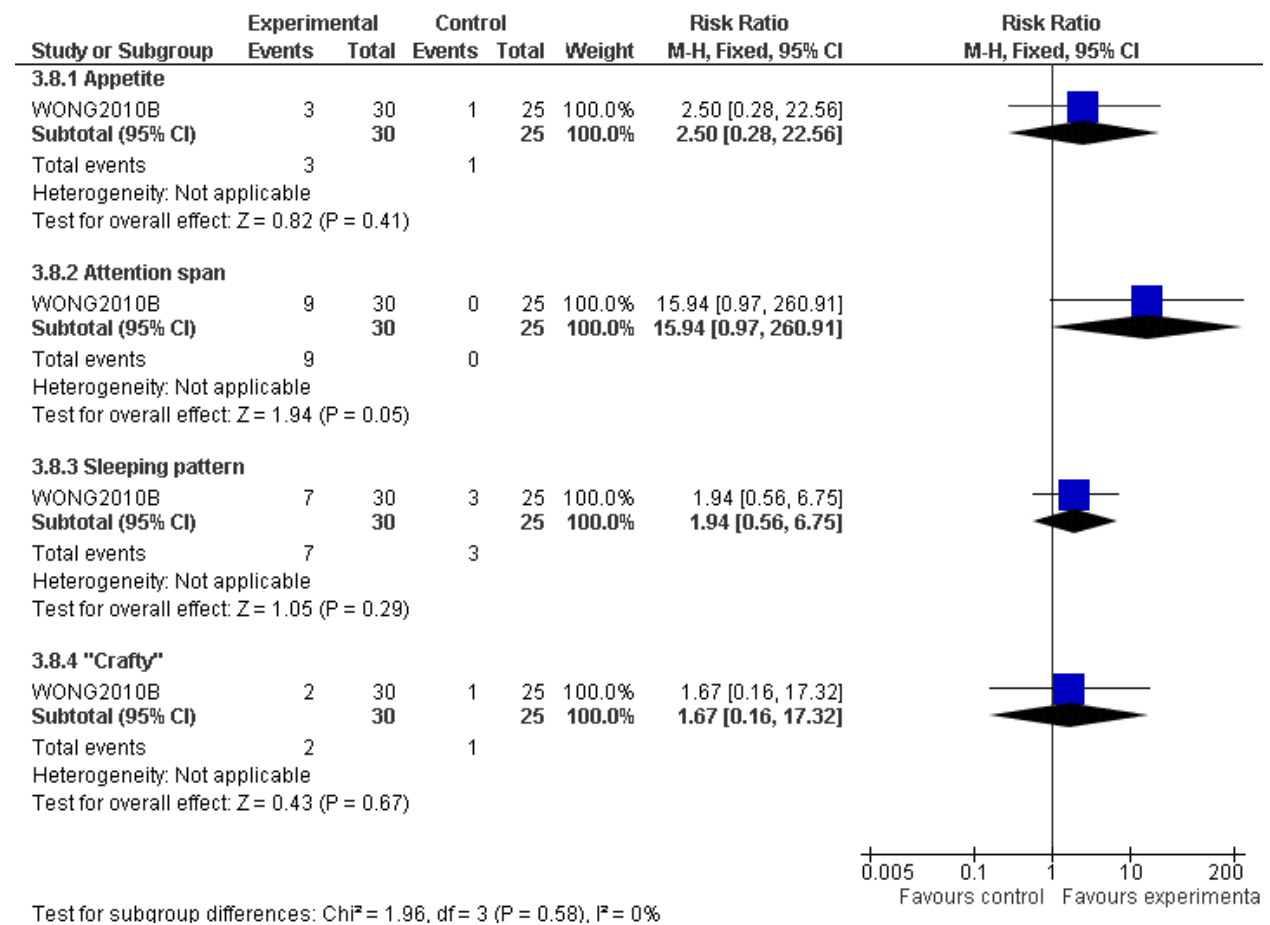
**Positive treatment response for cognition (study-specific parent-reported 'better than before')**



**Positive treatment response for motor abnormalities (study-specific parent-reported 'better than before')**

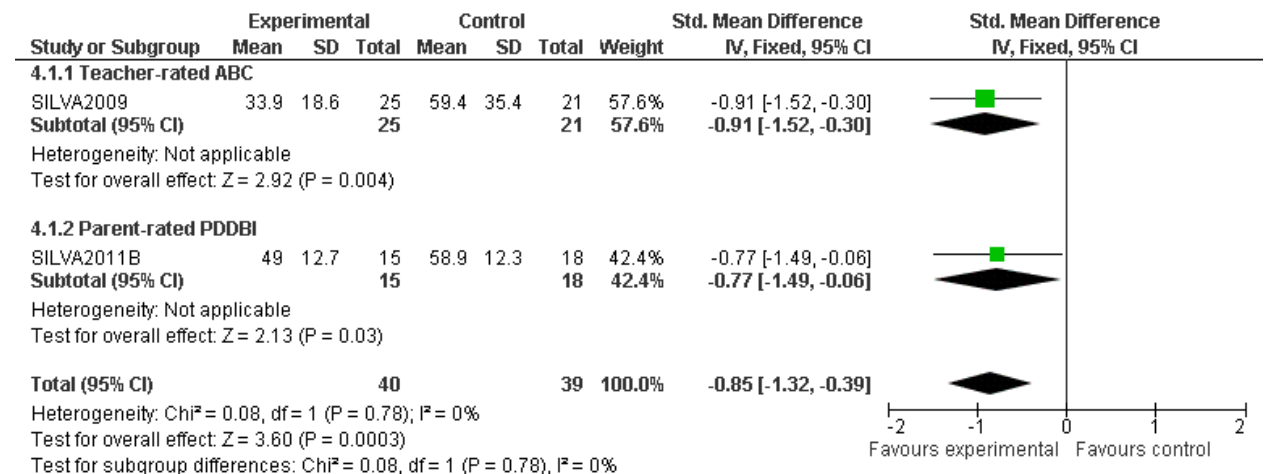


**Positive treatment response for other parent-reported changes (study-specific parent-reported 'better than before')**

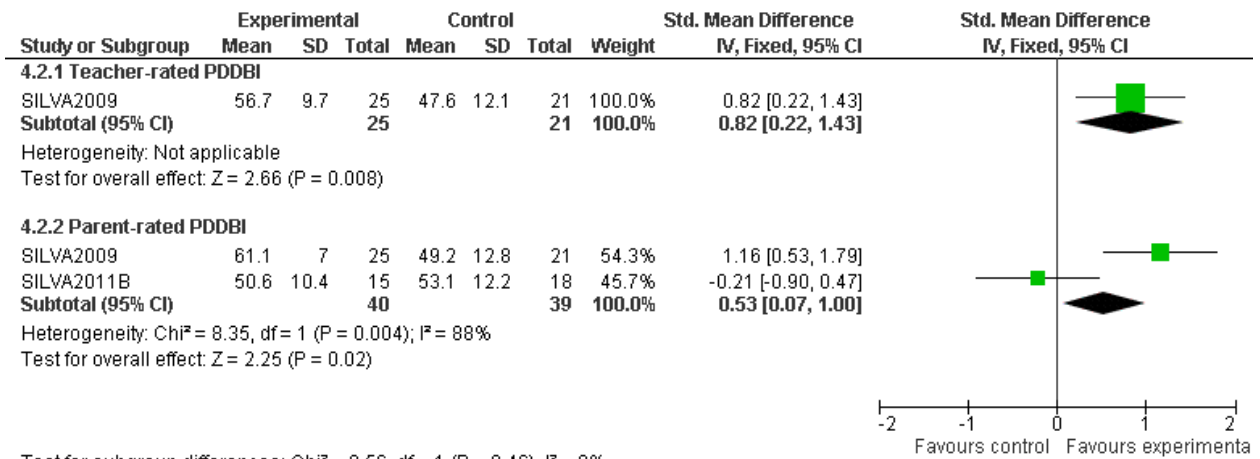


*Qigong massage training versus waitlist for overall autistic behaviours as an indirect outcome*

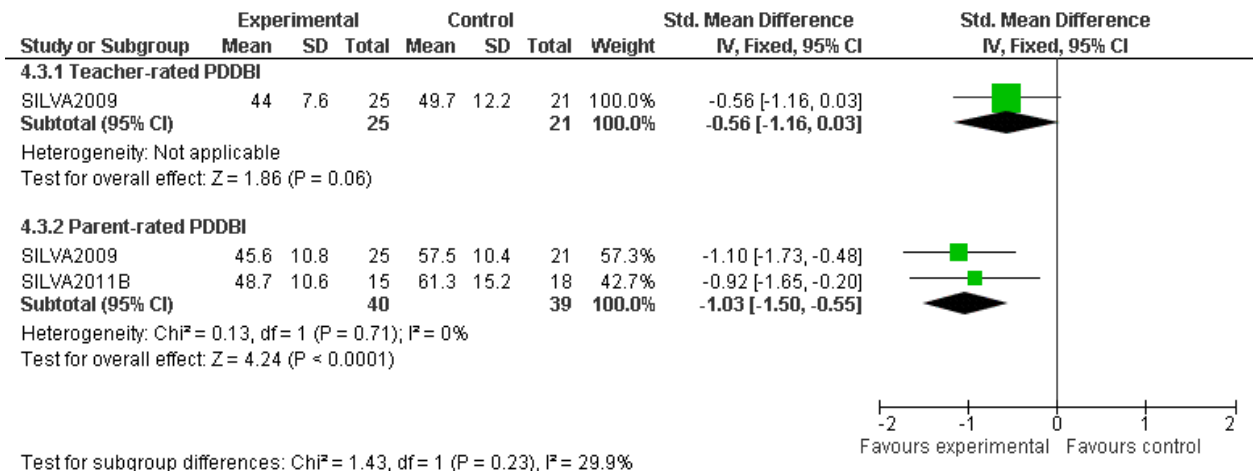
**Overall autistic behaviours**



## Social, language, and communication abilities



## Maladaptive behaviour

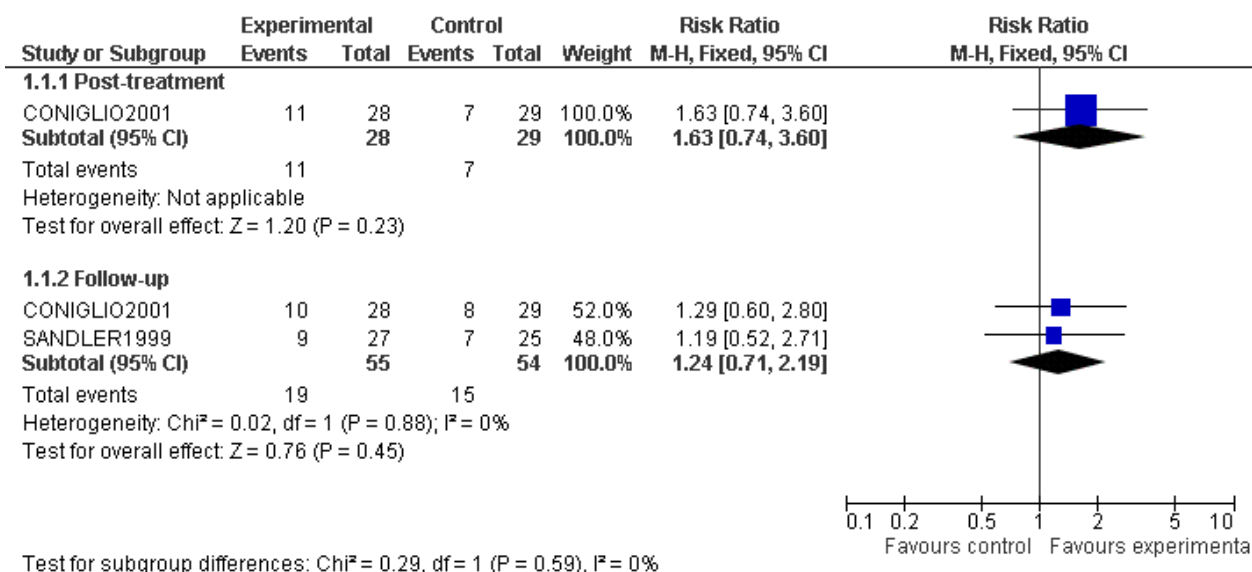


## 1.7.2 Hormones for overall autistic behaviours as a direct or indirect outcome

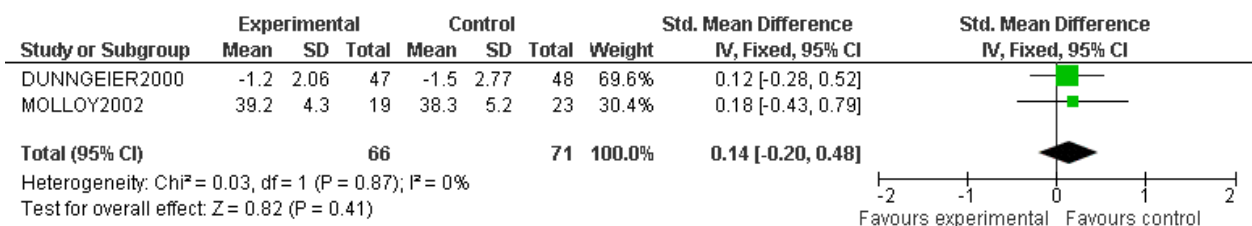
*Secretin versus placebo for overall autistic behaviours as a direct or indirect outcome*

Positive treatment response (decrease of >4.07 points CARS or parent-rated CGI 'much/very much improved')

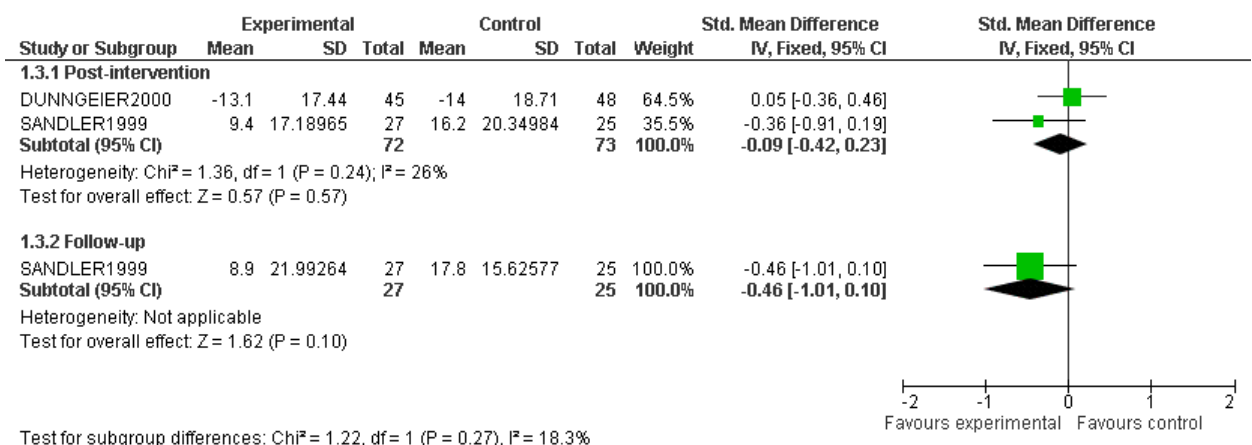




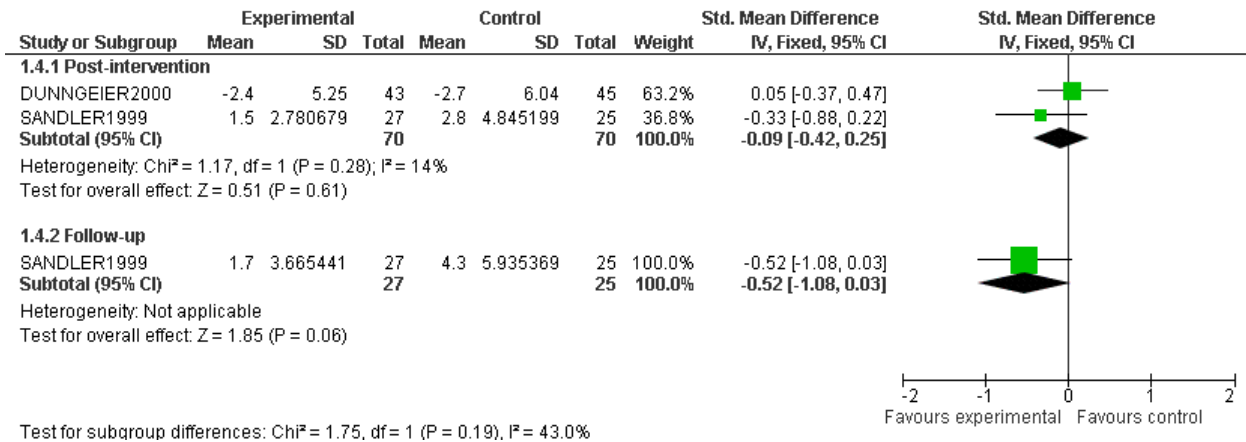
### Overall autistic behaviours (CARS; endpoint or change scores)



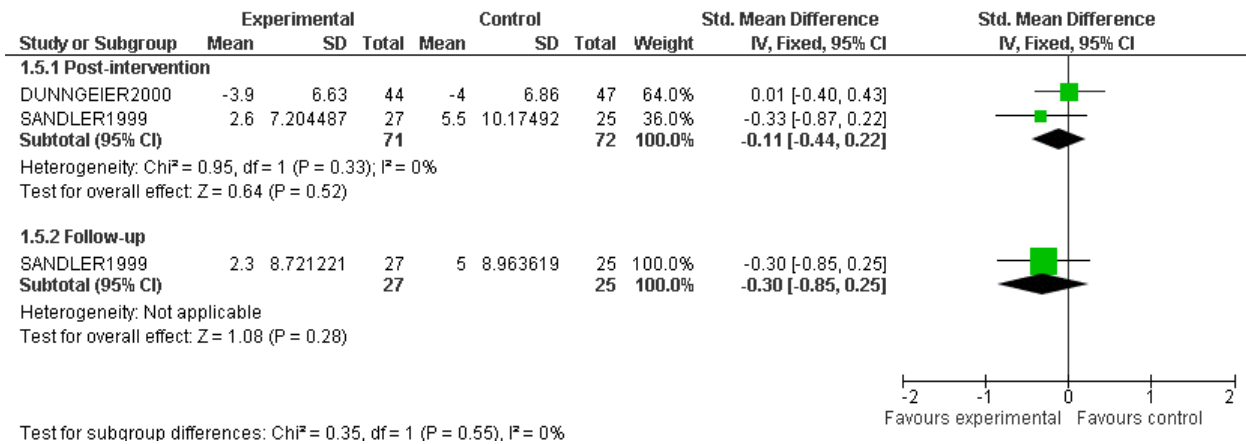
### Overall autistic behaviours (ABC Total; change score)



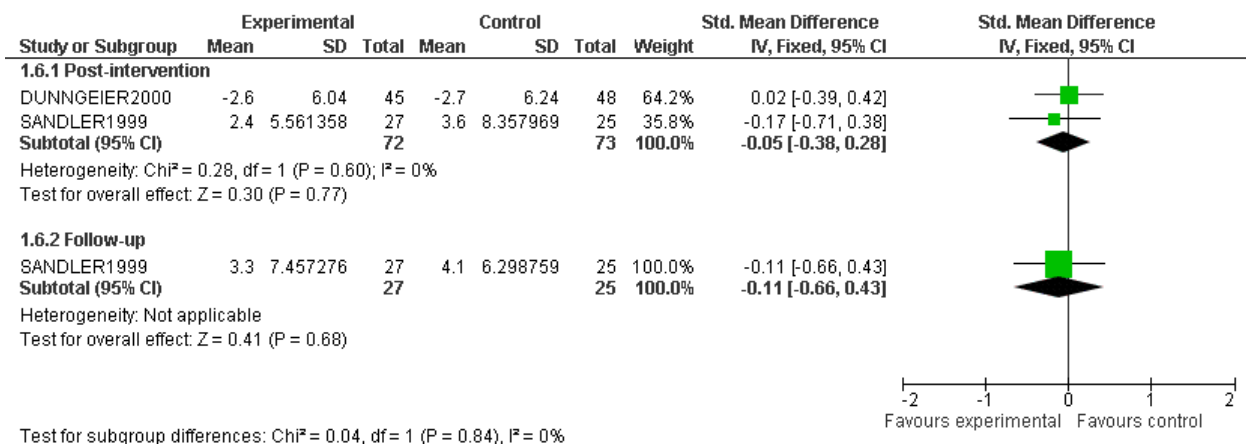
### Sensory function (ABC sensory; change scores)



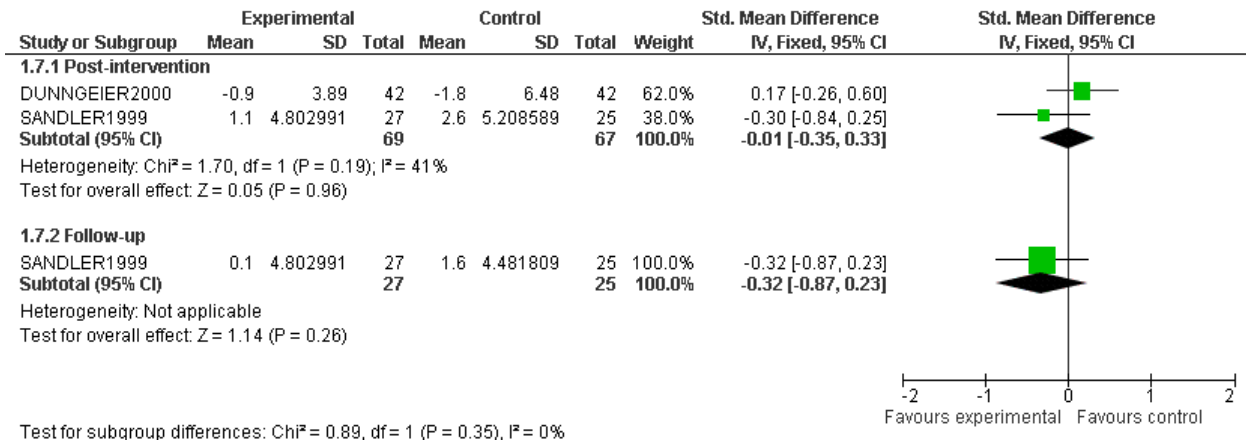
**Social relatedness (ABC social relatedness; change scores)**



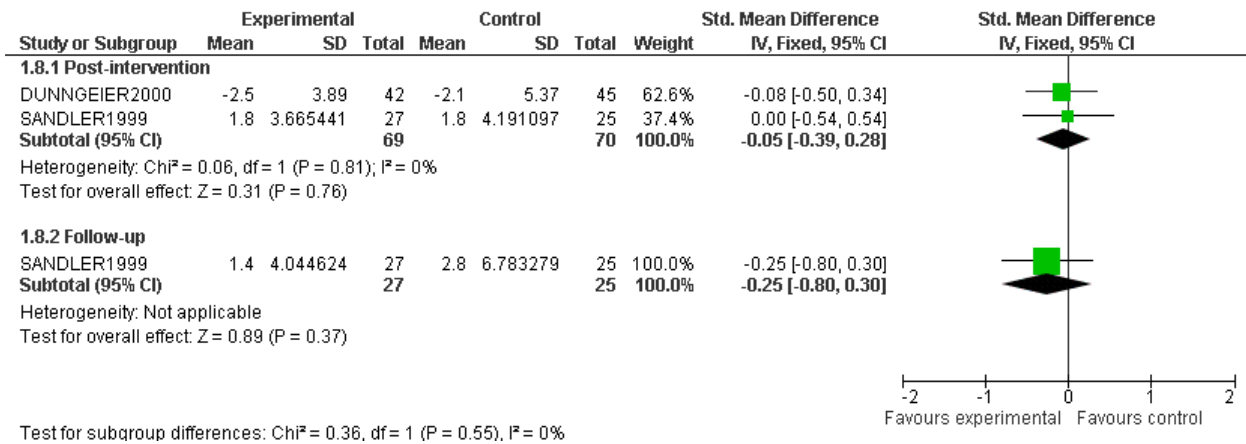
**Body and object use (ABC body and object use; change scores)**



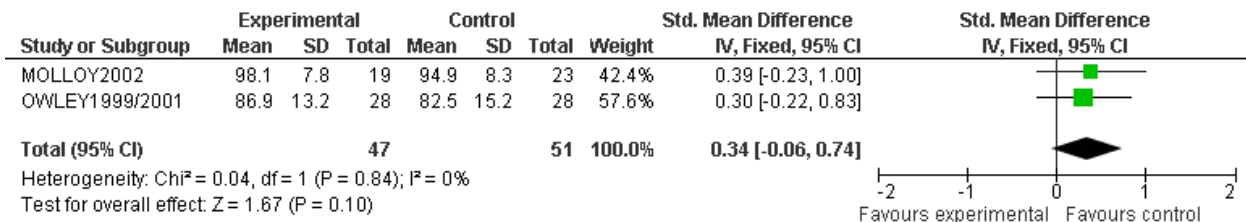
**Language (ABC language; change scores)**



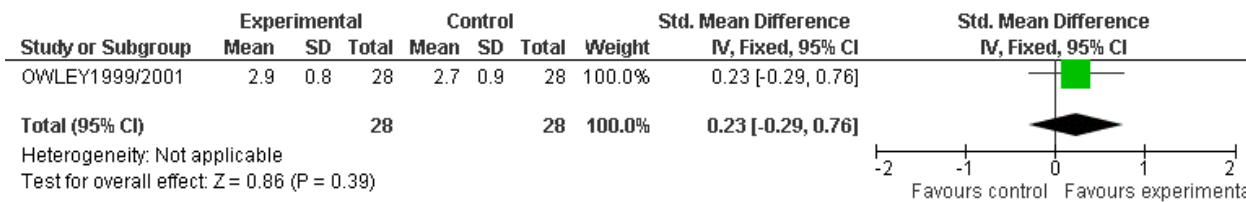
### Socialization (ABC socialization; change scores)



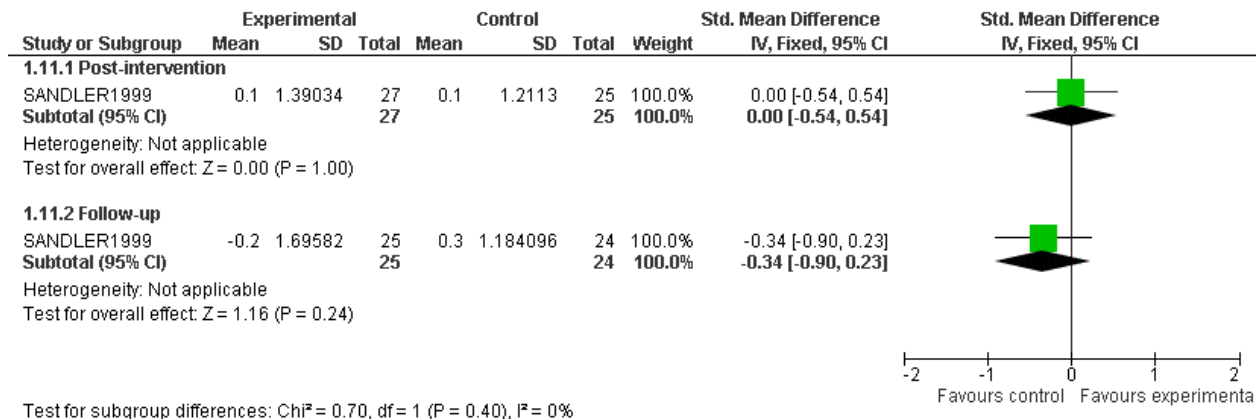
### Overall autistic behaviours (GARS)



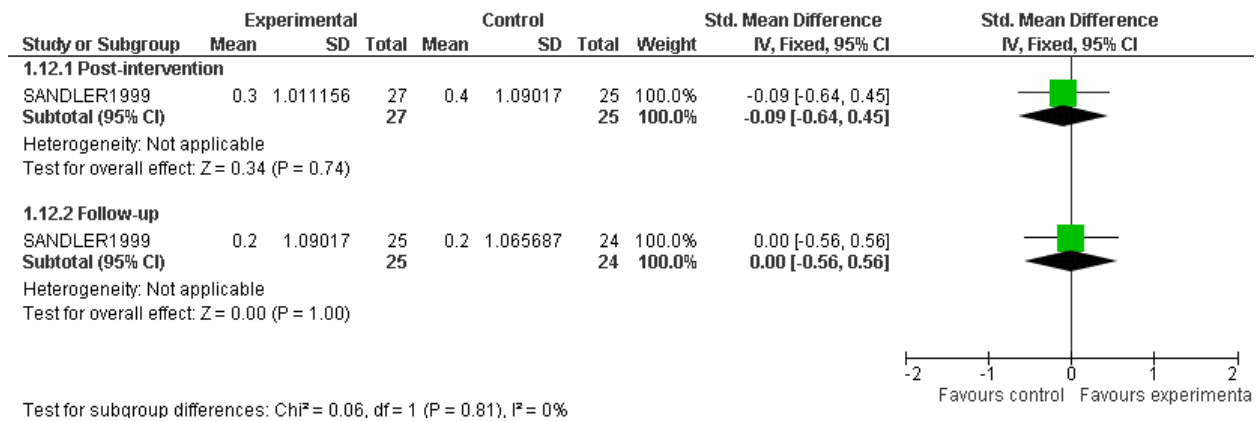
### Overall autistic behaviours (CGI)



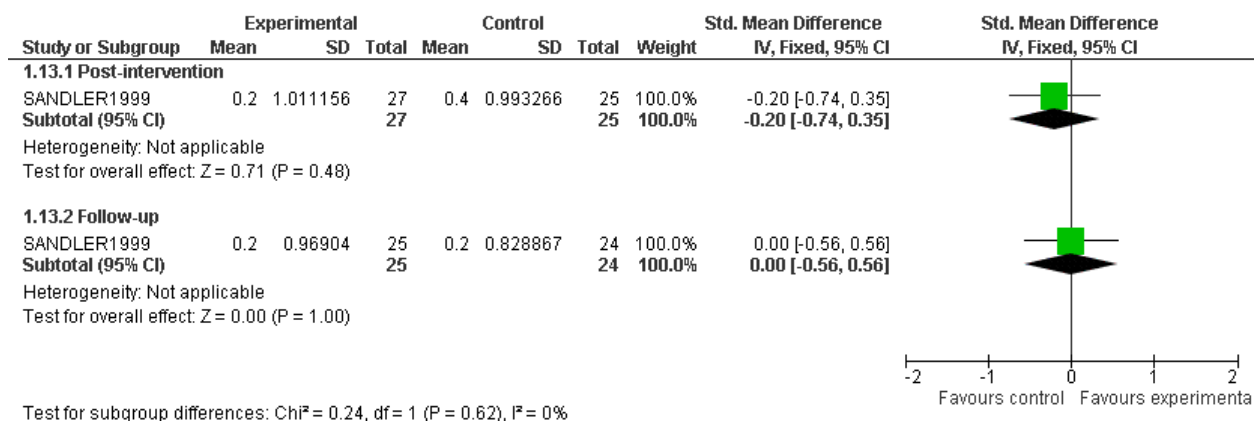
### Response to social interaction (CGI; change scores)



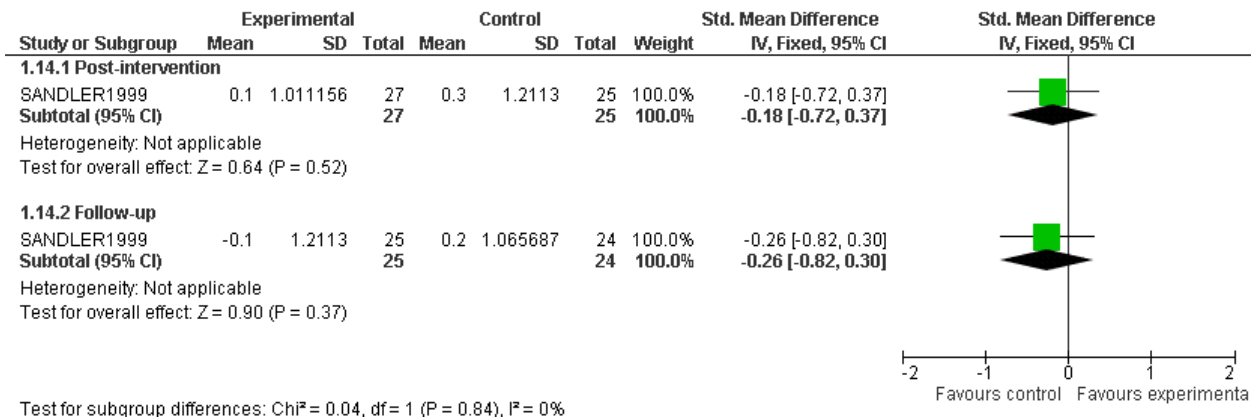
### Social initiation (CGI; change scores)



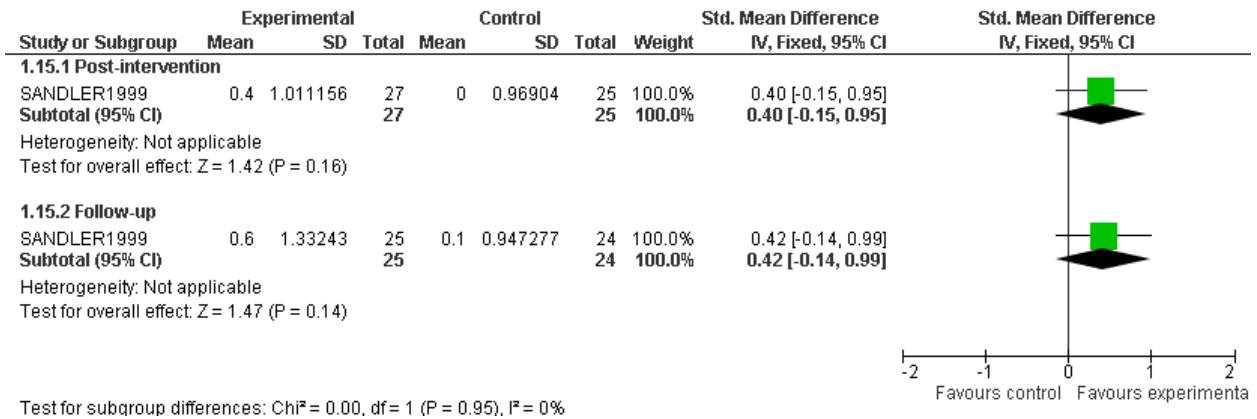
### Use of speech (CGI; change scores)



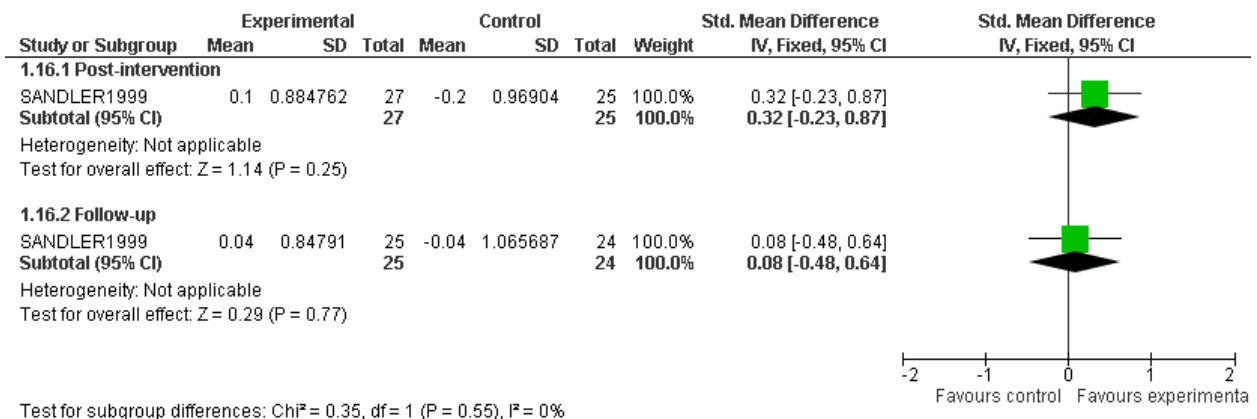
### Types of repetitive behaviour (CGI; change scores)



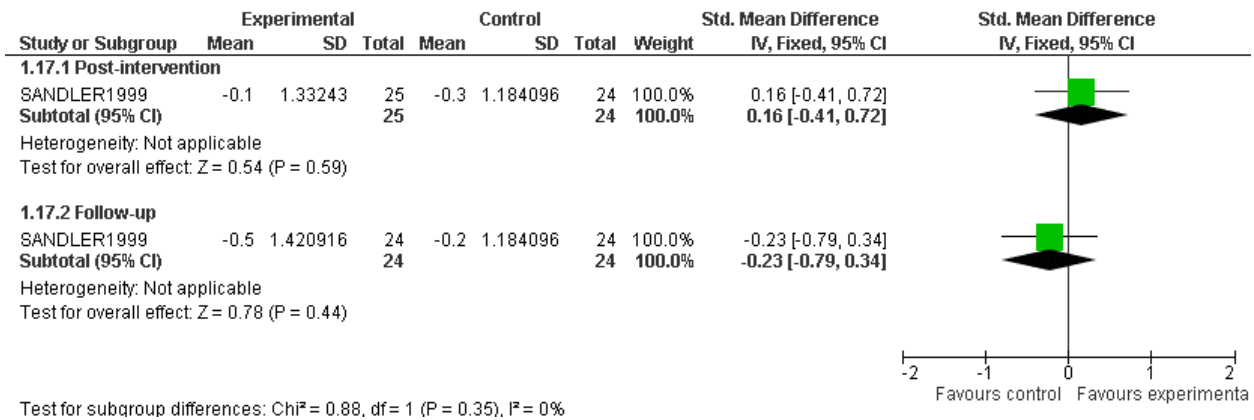
### Behaviour problems (CGI; change scores)



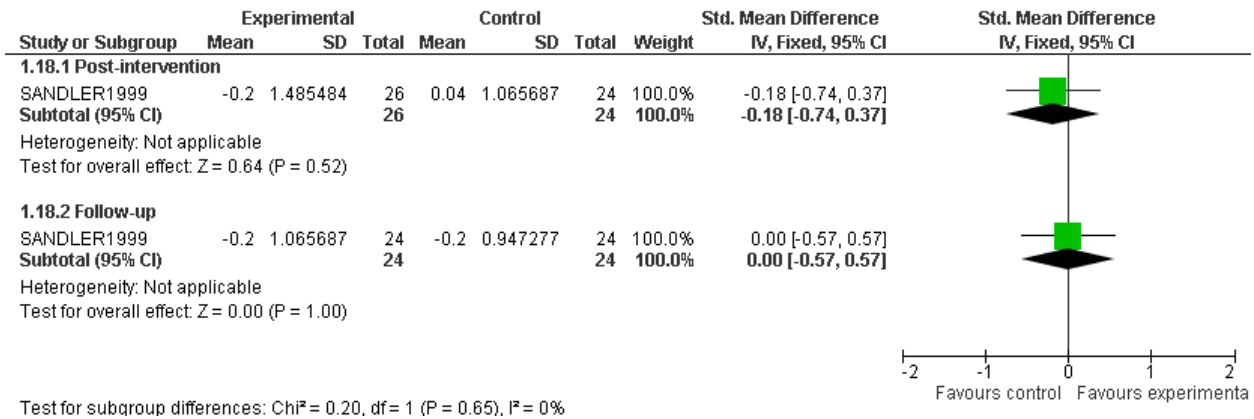
### Activity level (CGI; change scores)



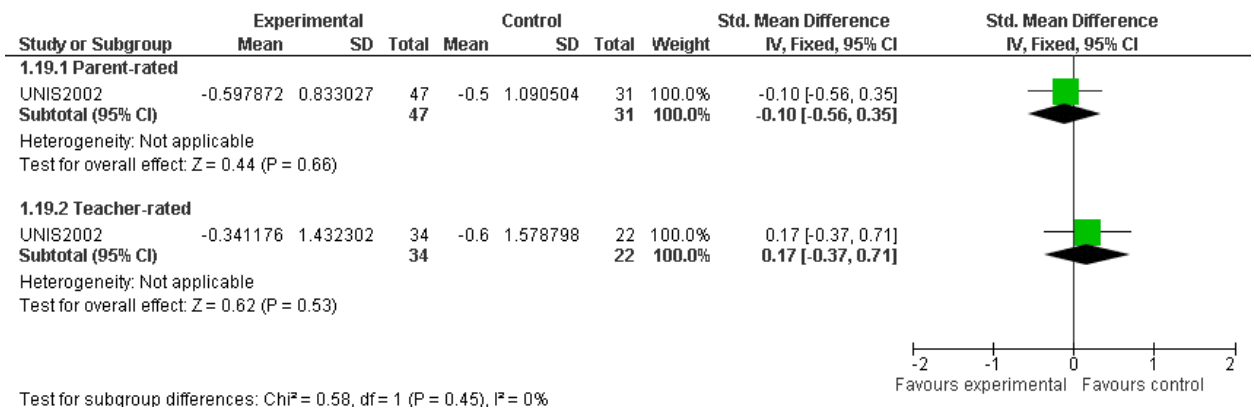
### Sleep problems (CGI; change scores)



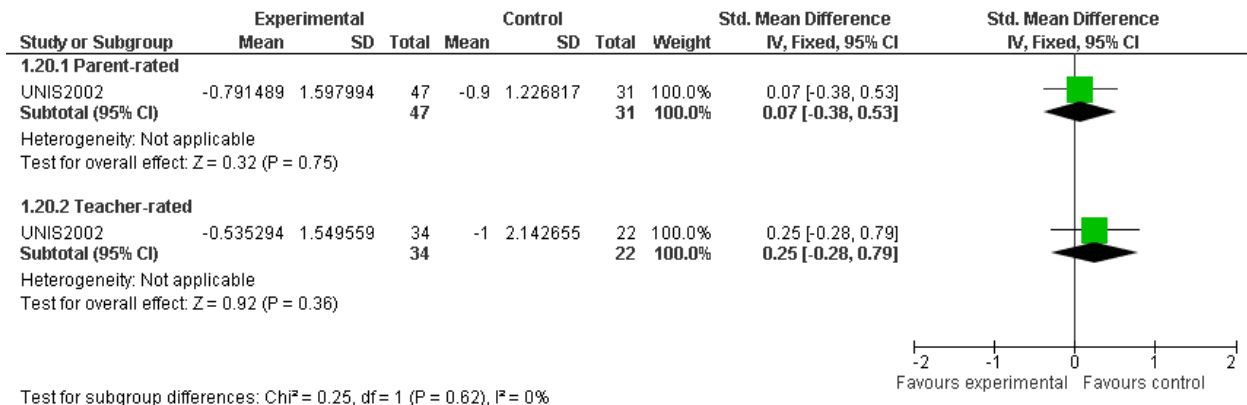
### Digestive problems (CGI; change scores)



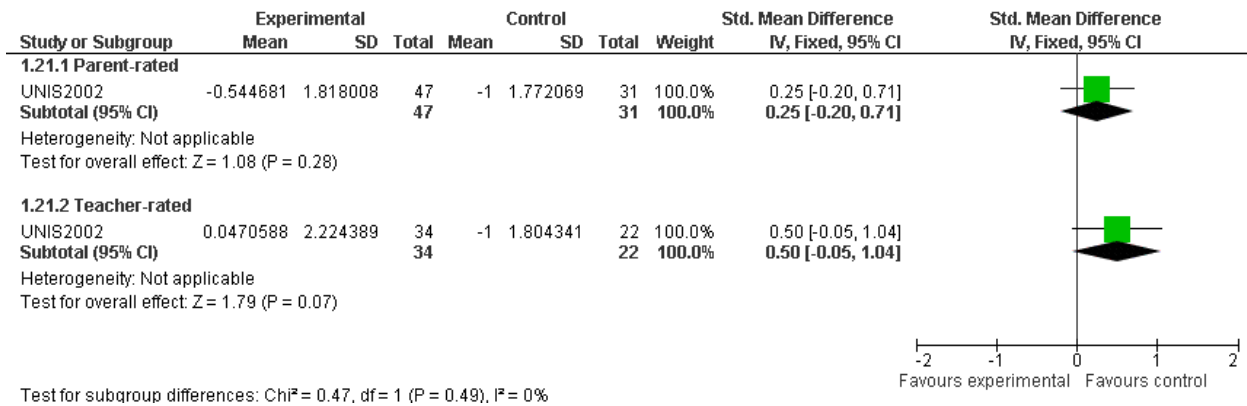
### Overall autistic behaviours (SOS total change score; porcine+synthetic groups combined)



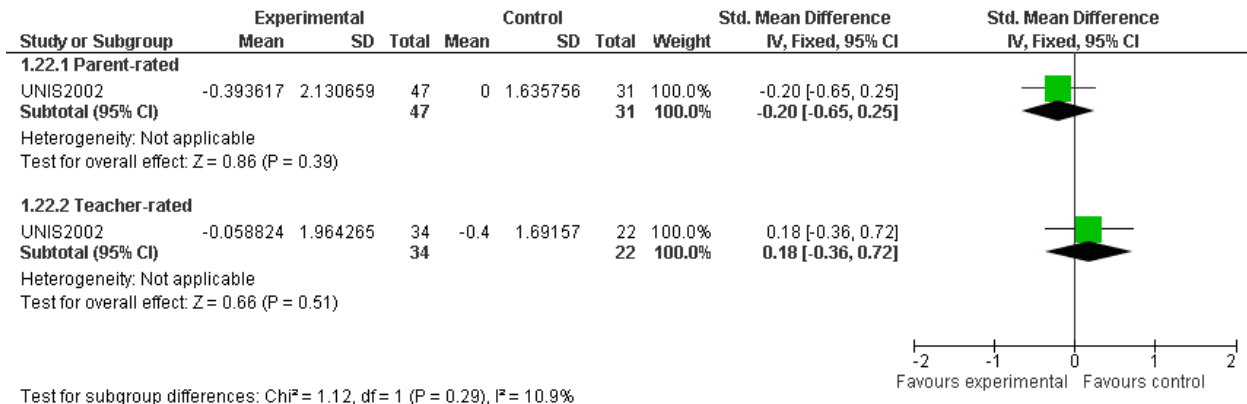
**Social (SOS change score; porcine+synthetic groups combined)**



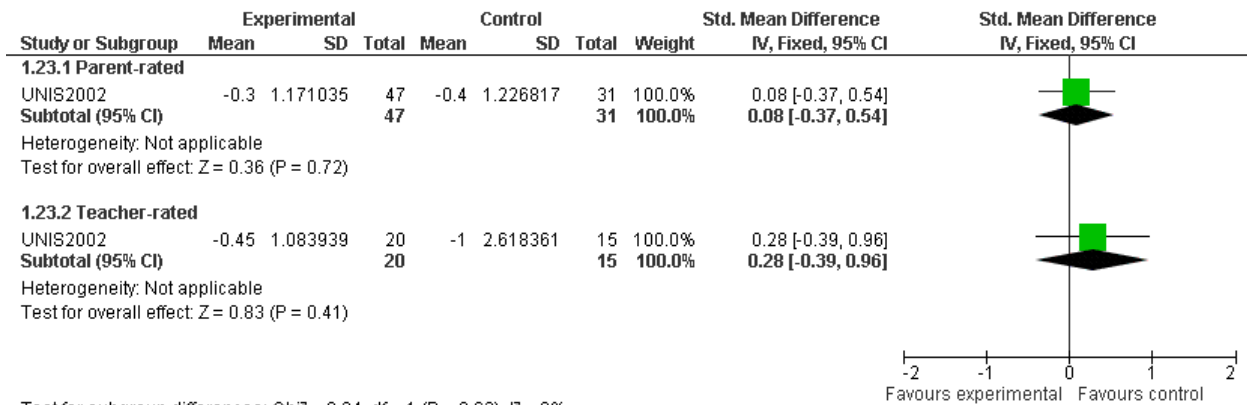
**Communication (SOS change score; porcine+synthetic groups combined)**



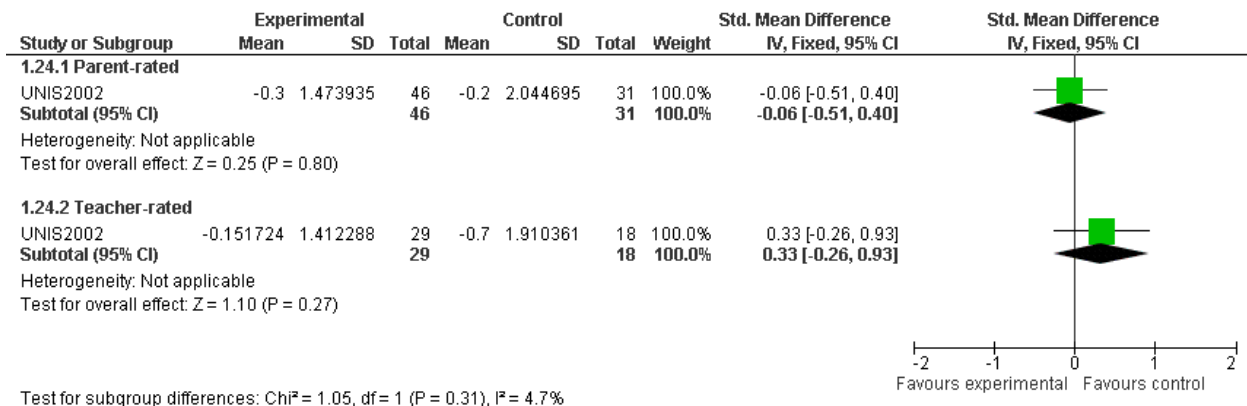
**Repetitive behaviour (SOS change score; porcine+synthetic groups combined)**



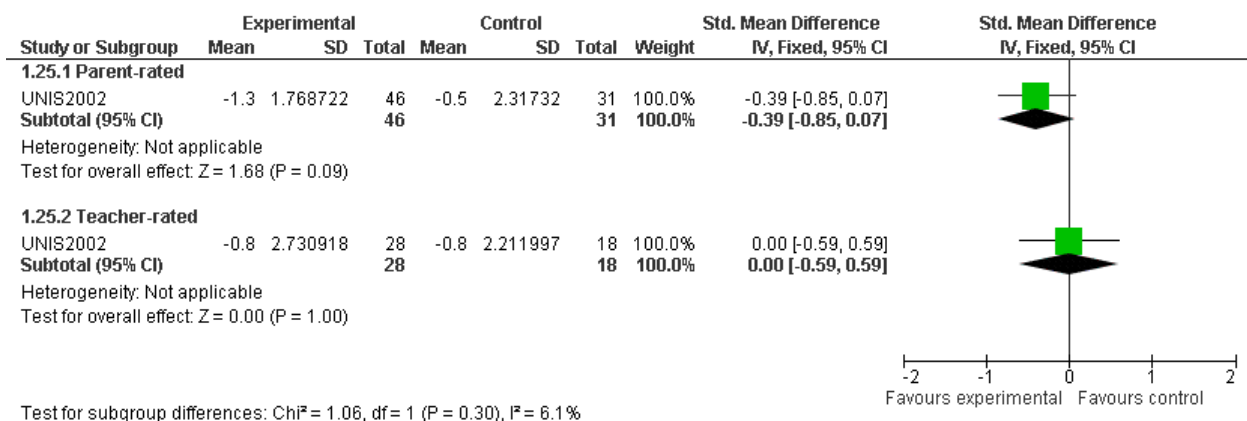
### Digestive (SOS change score; porcine+synthetic groups combined)



### Mood (SOS change score; porcine+synthetic groups combined)

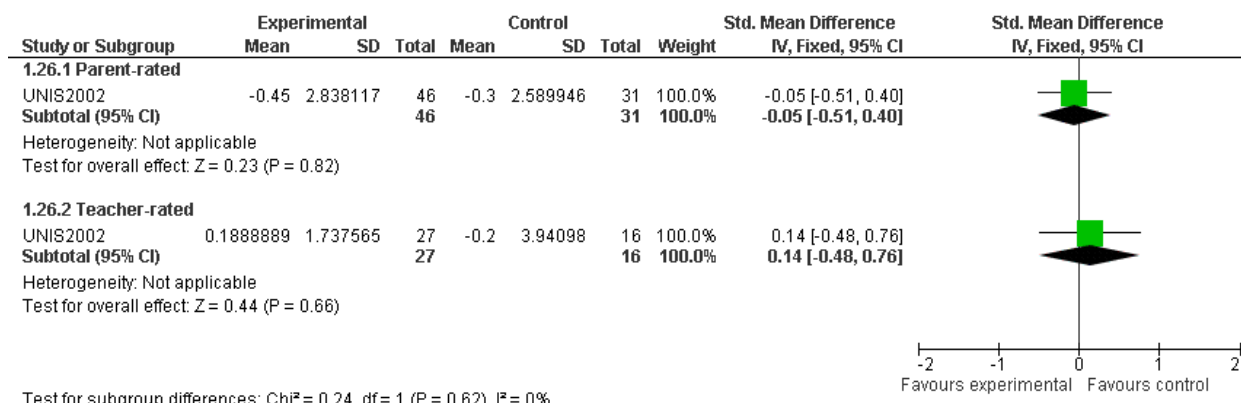


### Sensory (SOS change score; porcine+synthetic groups combined)

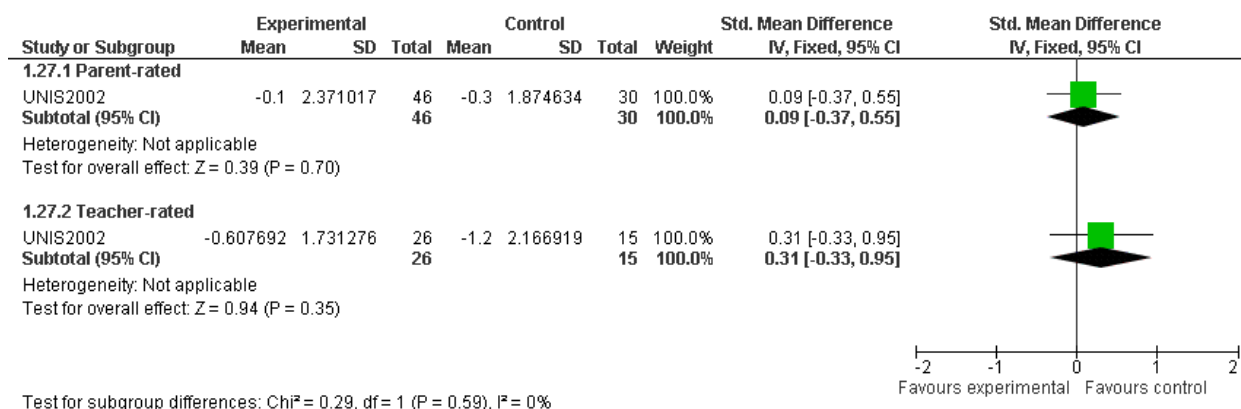




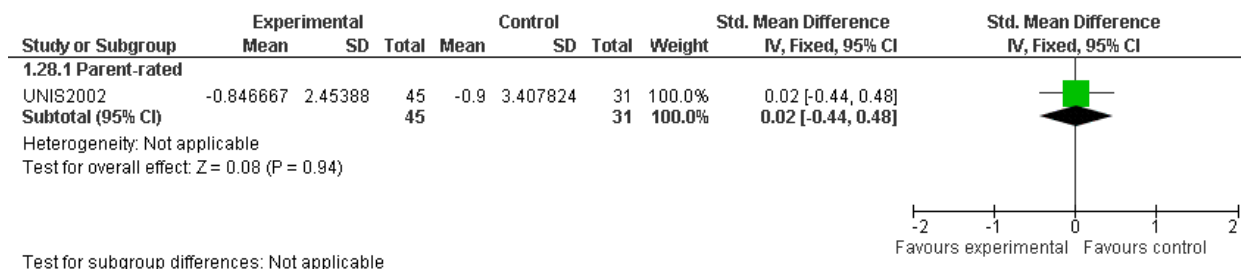
### Hyperactivity (SOS change score; porcine+synthetic groups combined)



### Lethargy (SOS change score; porcine+synthetic groups combined)



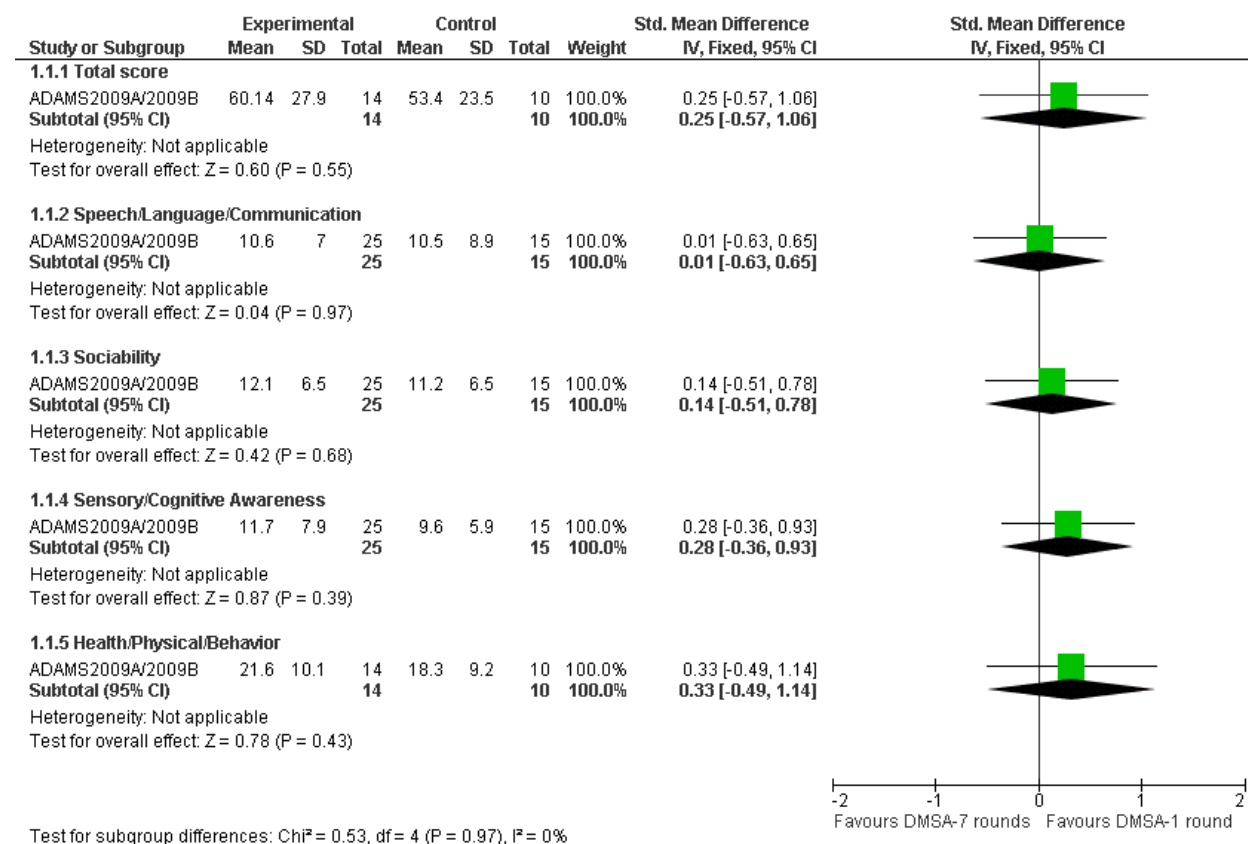
### Sleep (SOS change score; porcine+synthetic groups combined)



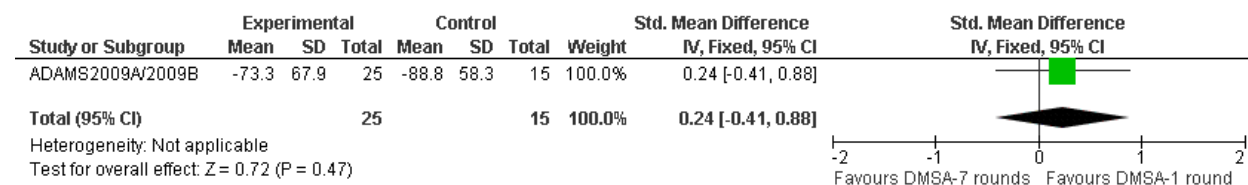
### 1.7.3 Medical procedures for overall autistic behaviours as a direct or indirect outcome

*Long-term chelation (7-rounds of DMSA therapy) versus short-term chelation (1-round of DMSA therapy and 6-rounds of placebo) for overall autistic behaviours as a direct outcome*

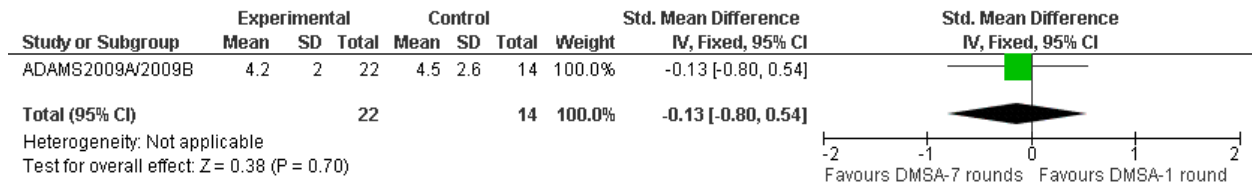
#### Overall autistic behaviours (ATEC)



#### Overall autistic behaviours (PDDBI)

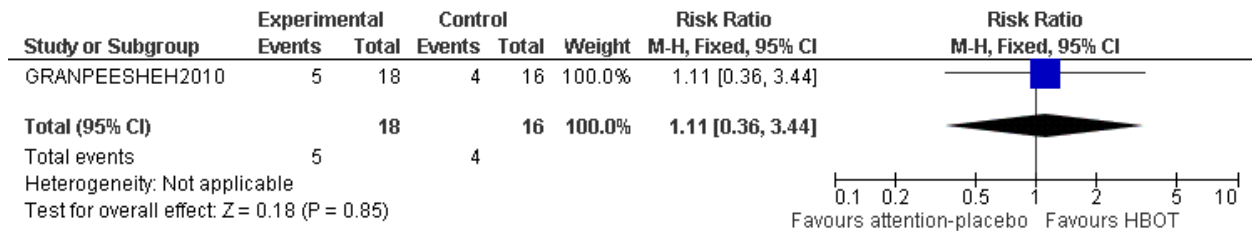


#### Overall autistic behaviours (SAS)

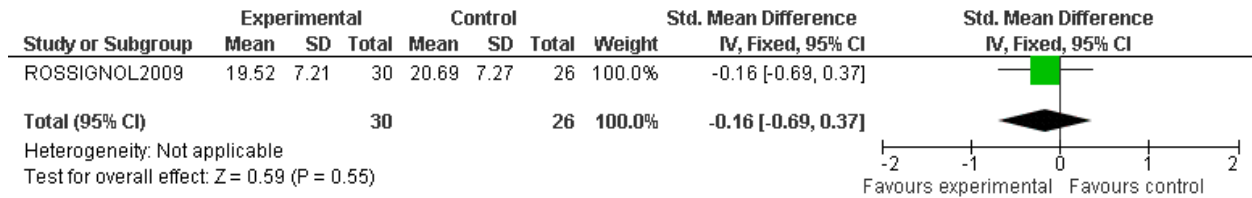


*HBOT versus placebo for overall autistic behaviours as a direct or indirect outcome*

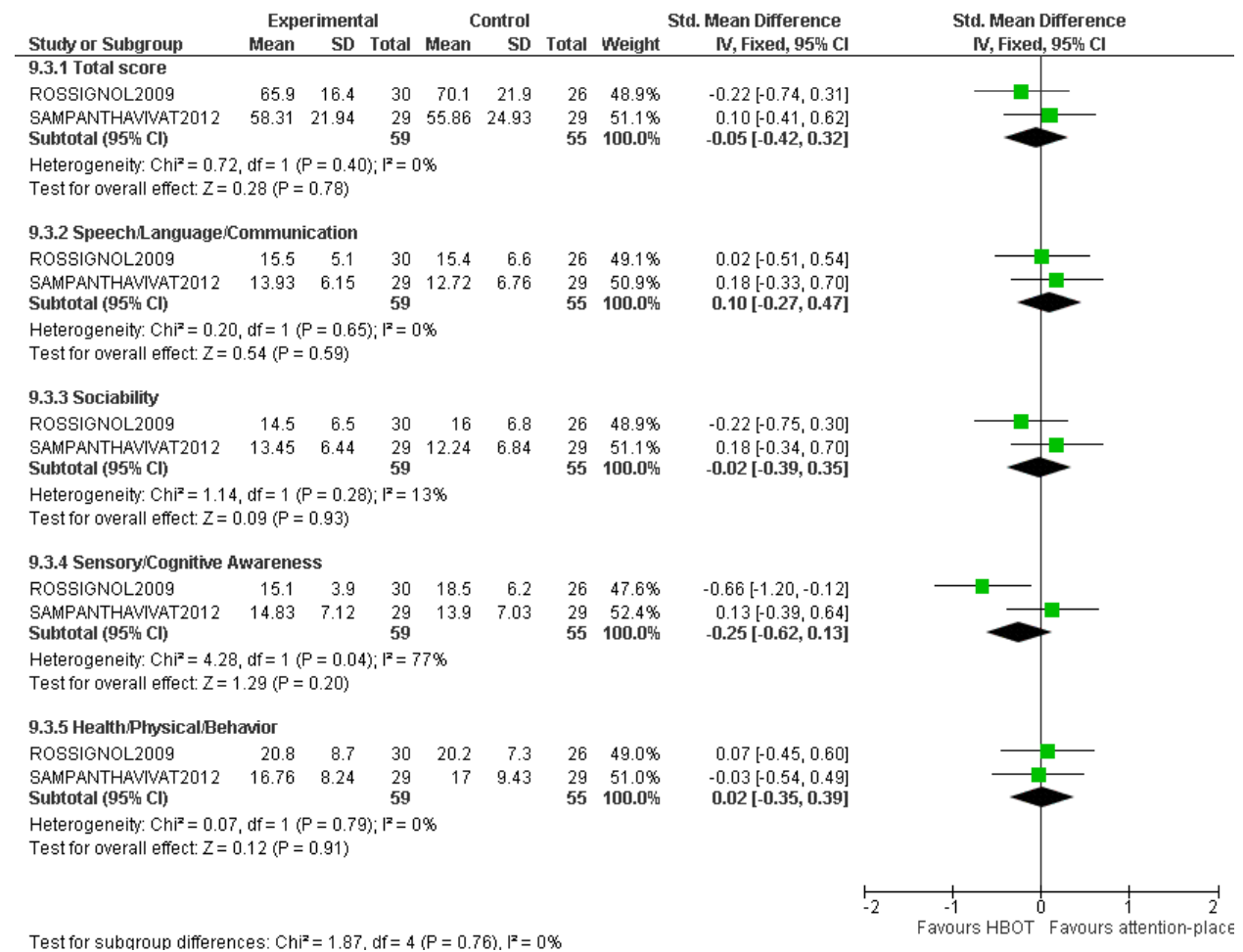
**Positive treatment response (improvement in ADOS diagnostic classification based on total score)**



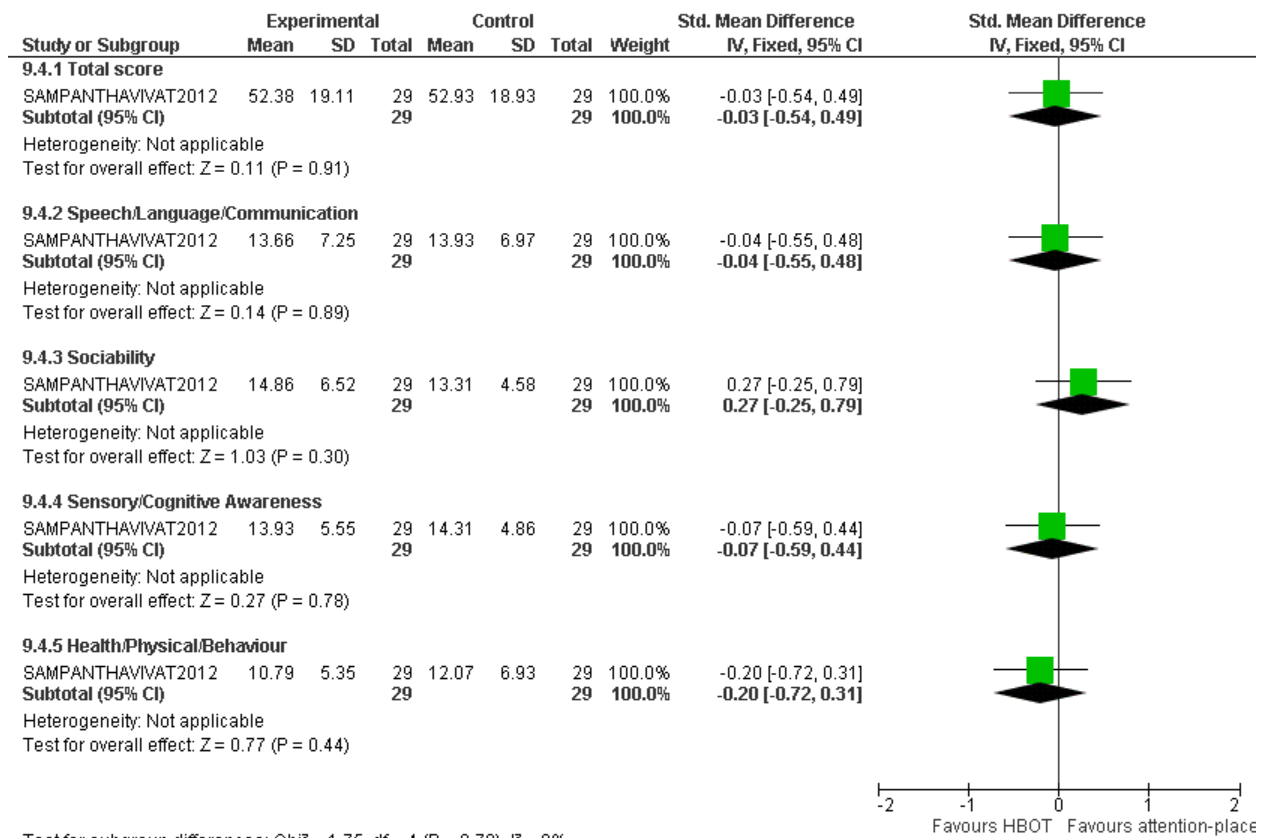
**Overall autistic behaviours (ADOS total)**



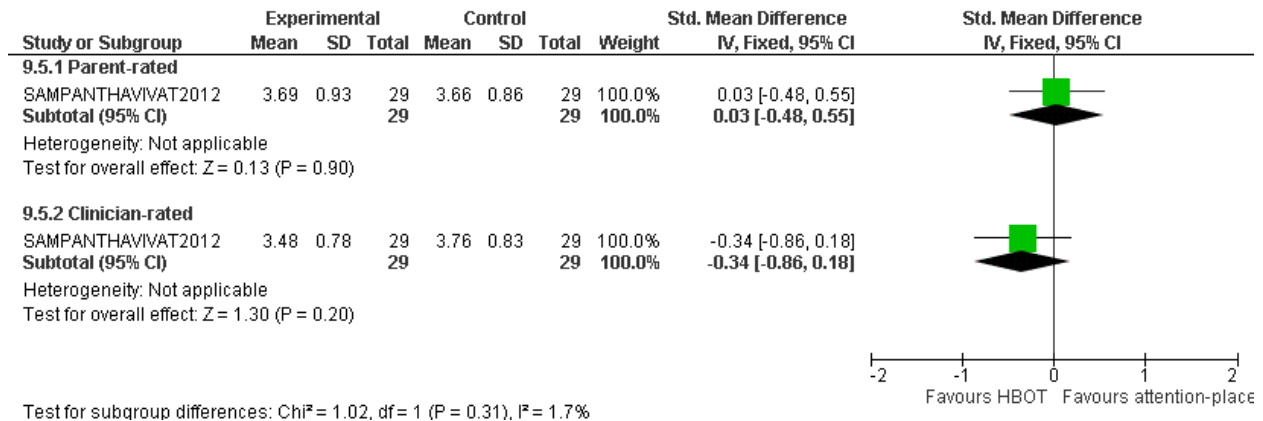
**Overall autistic behaviours (parent-rated ATEC)**



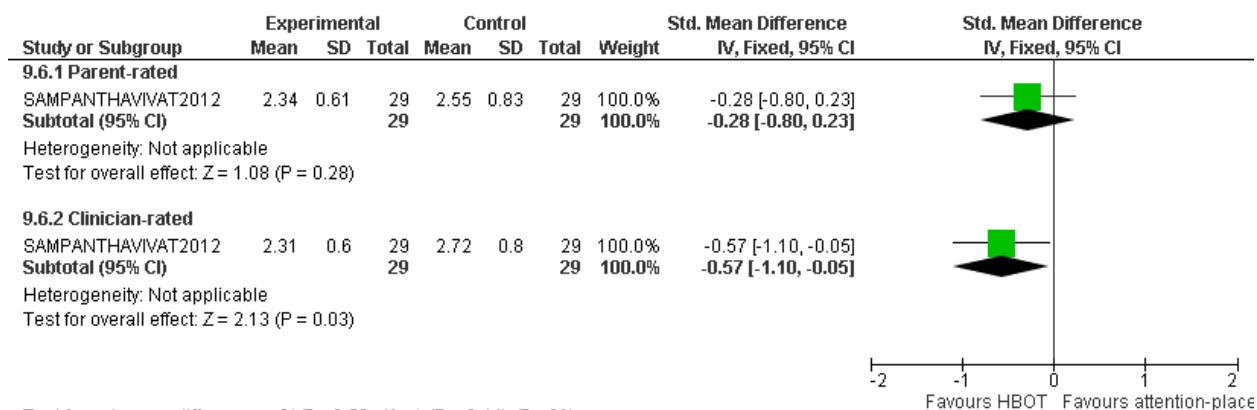
**Overall autistic behaviours (clinician-rated ATEC)**



### Global severity (CGI-S)



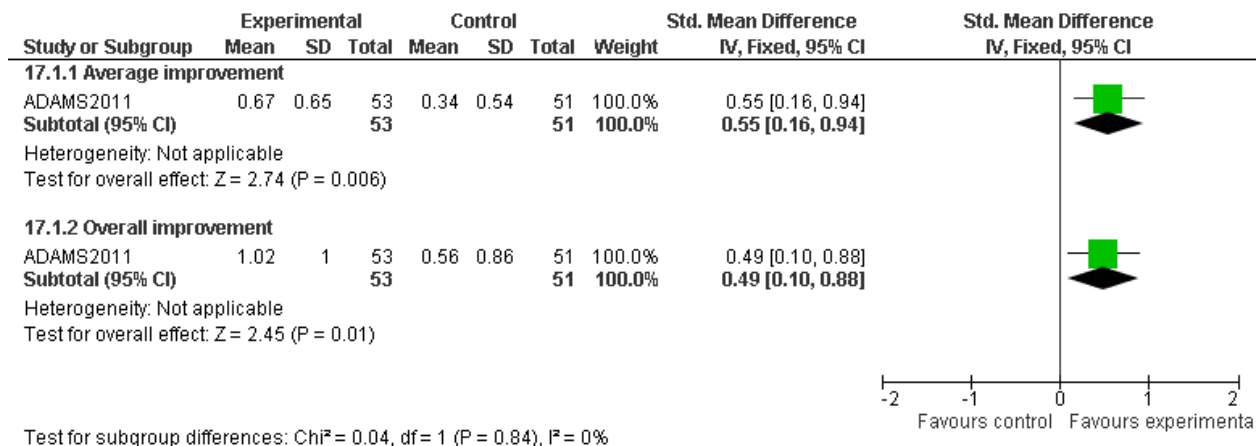
### Global improvement (CGI-I)



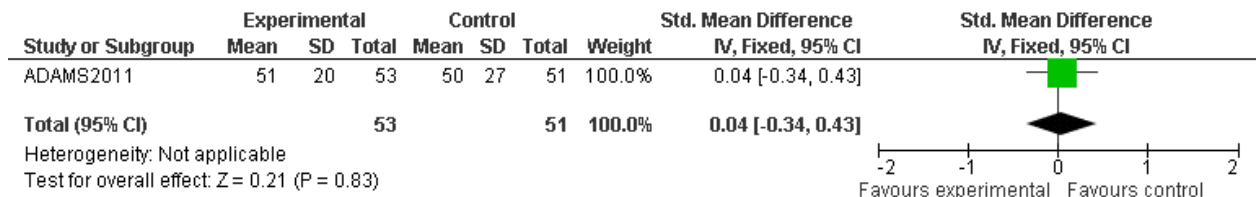
### 1.7.4 Nutritional interventions for overall autistic behaviours as a direct or indirect outcome

#### *Multivitamin/mineral supplement versus placebo for overall autistic behaviours as a direct outcome*

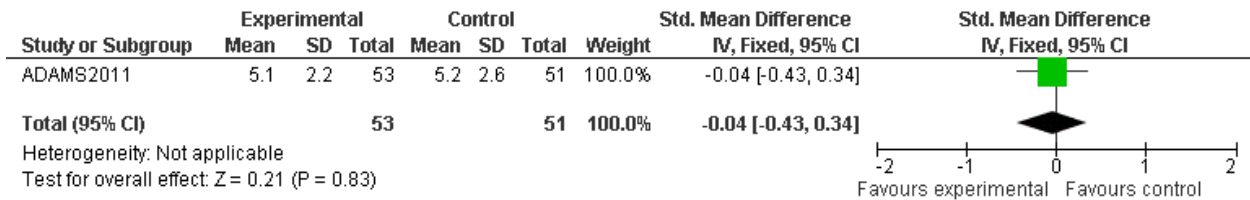
##### Overall autistic behaviours (PGI-R)



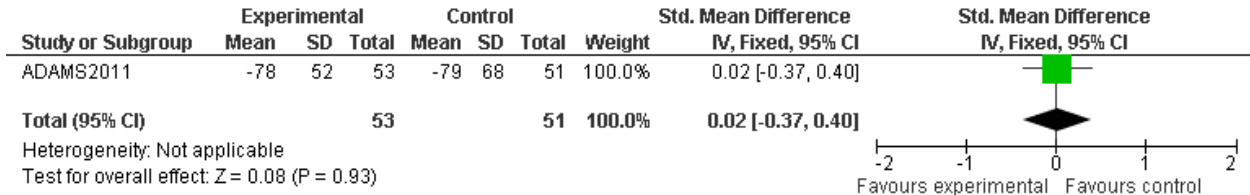
##### Overall autistic behaviours (ATEC)



##### Overall autistic behaviours (SAS)

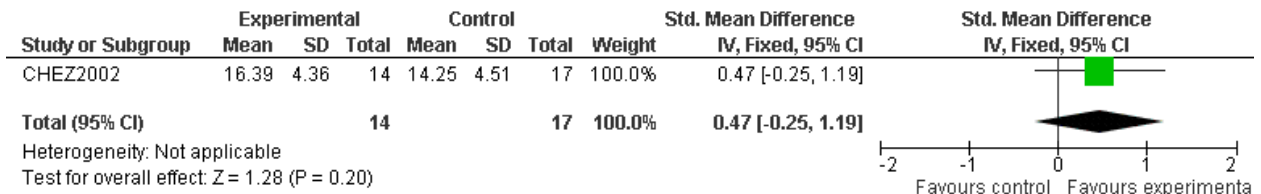


### Overall autistic behaviours (PDDBI)

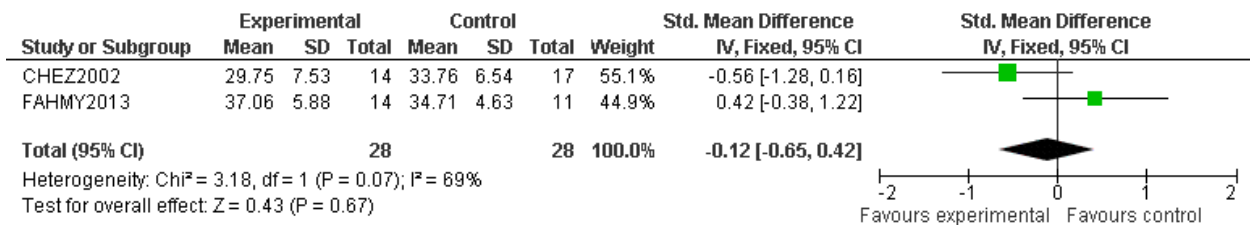


### *L-carnosine or L-carnitine supplement versus placebo for overall autistic behaviours as a direct outcome*

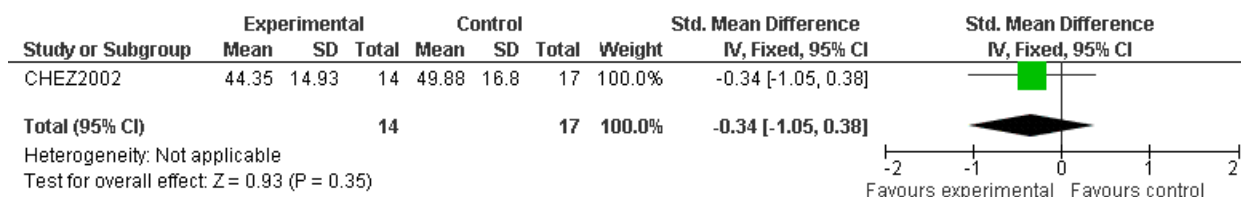
#### Global improvement (PGI-I)



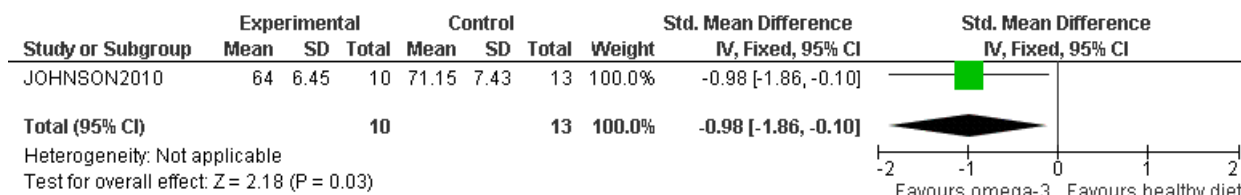
#### Overall autistic behaviours (CARS)



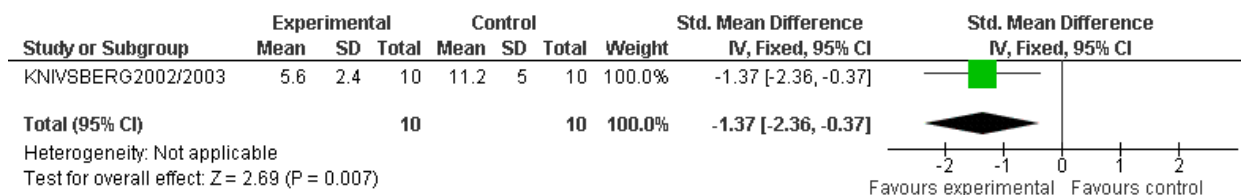
#### Overall autistic behaviours (GARS)



*Omega-3 fatty acids versus placebo for overall autistic behaviours as an indirect outcome*



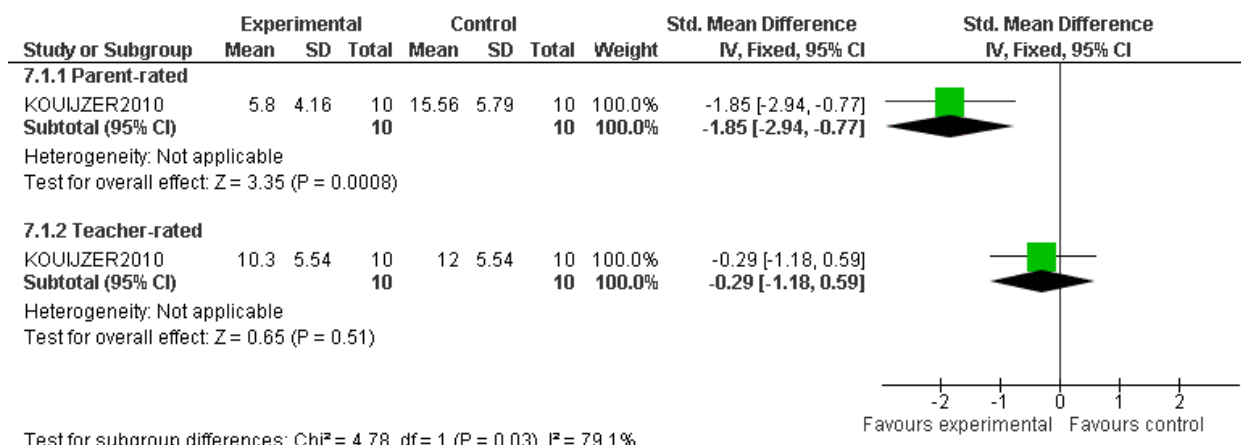
*Gluten-free and casein-free diet versus treatment-as-usual for overall autistic behaviours as a direct outcome*



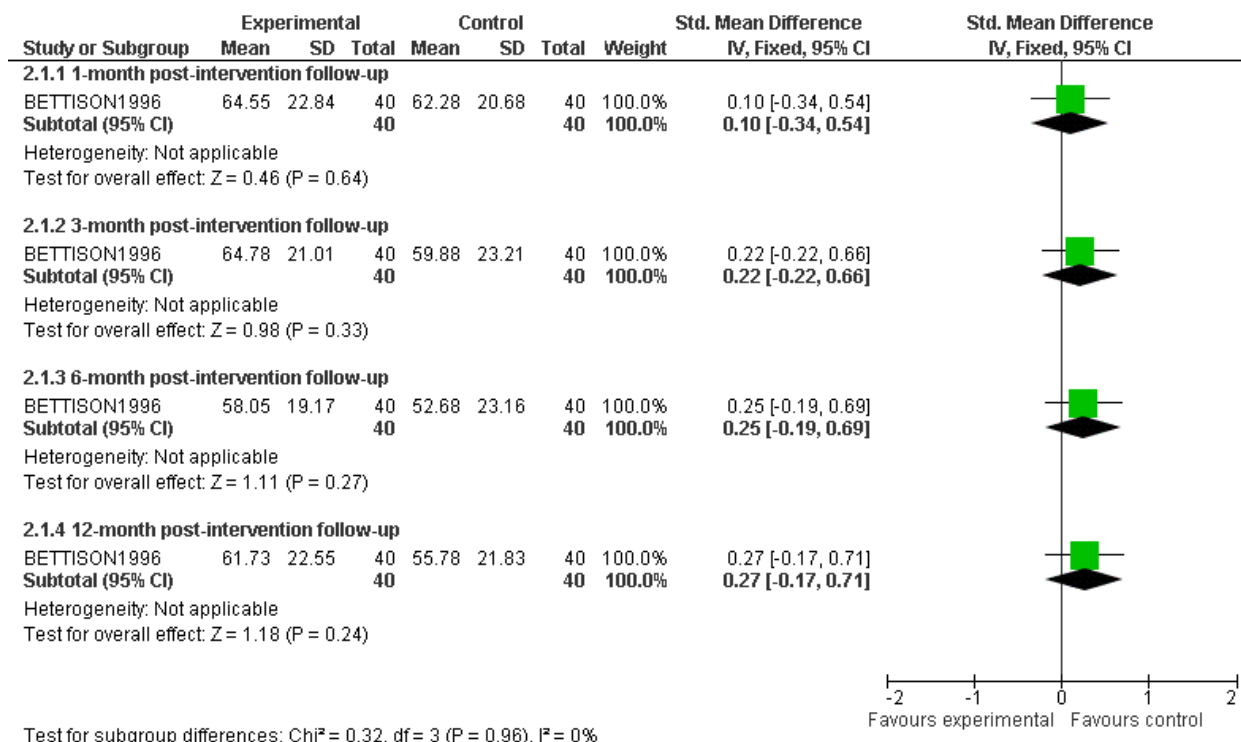
**1.7.5 Sensory interventions for overall autistic behaviours as a direct or indirect outcome**

*Neurofeedback versus treatment-as-usual for overall autistic behaviours as a direct outcome*





*Auditory integration training versus attention-placebo (structured listening) for overall autistic behaviours as an indirect outcome*

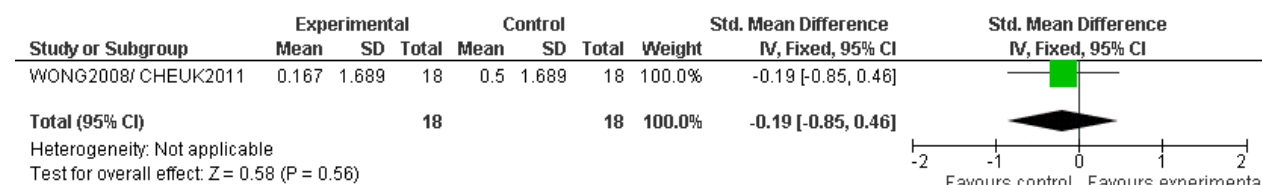


## 1.8 BIOMEDICAL INTERVENTIONS AIMED AT THE CORE AUTISM FEATURE OF IMPAIRED RECIPROCAL SOCIAL COMMUNICATION AND INTERACTION

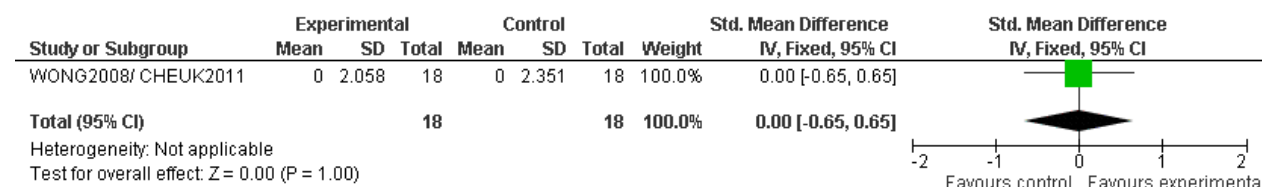
### 1.8.1 Complementary therapies for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome

*Electro-acupuncture and conventional educational programme versus conventional educational programme only for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome*

#### Communication (ADOS change score)



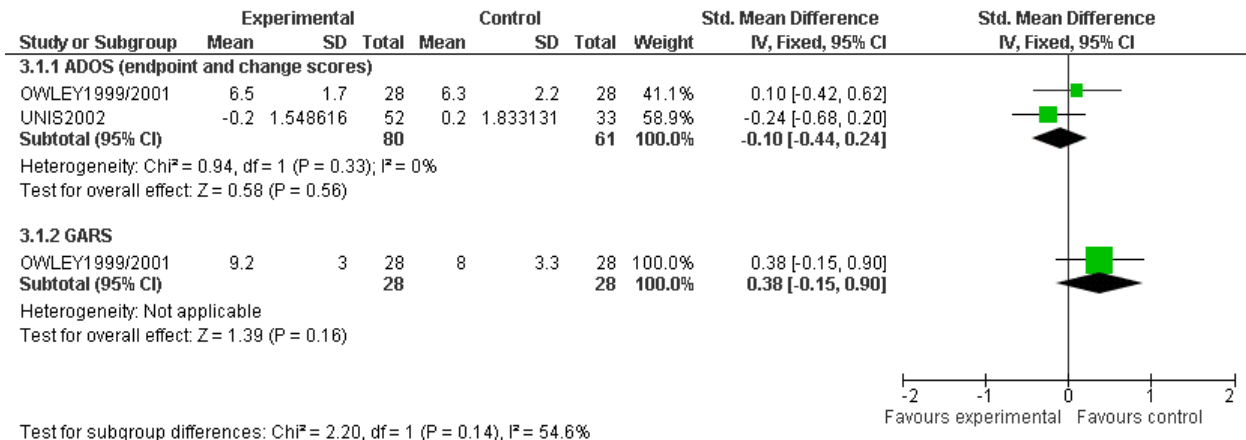
#### Social interaction (ADOS change score)



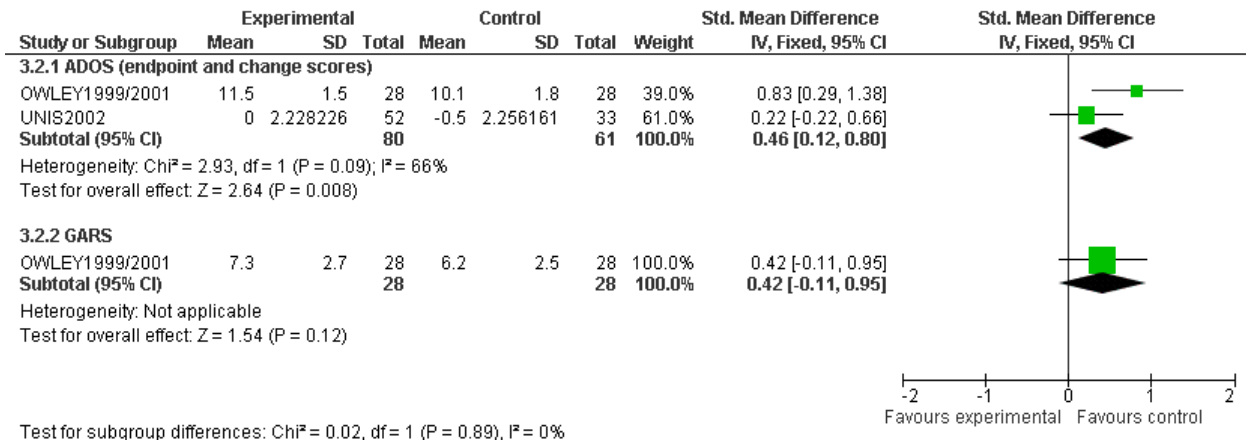
### 1.8.2 Hormones for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome

*Secretin versus placebo for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome*

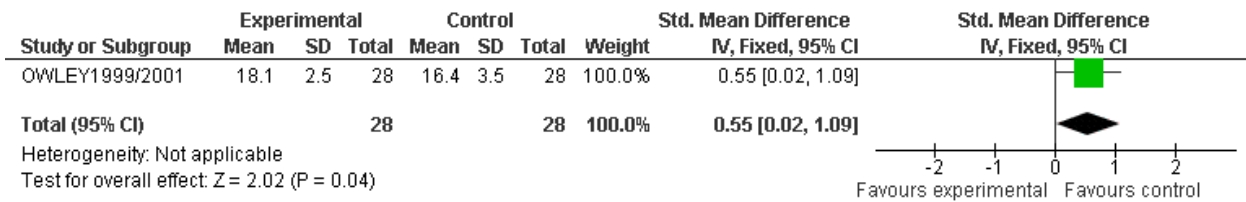
#### Communication



### Social interaction



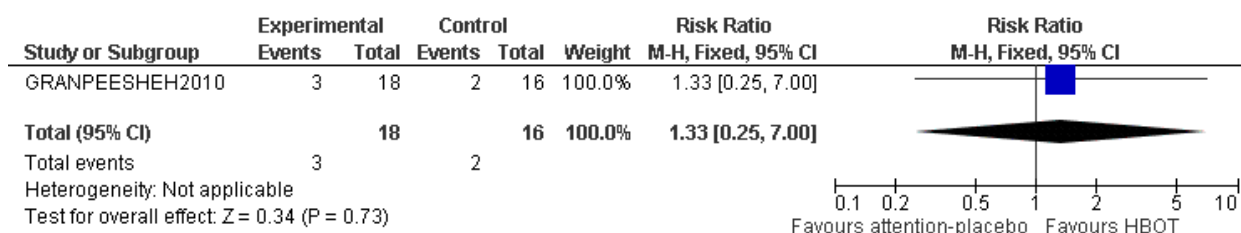
### Communication and Social Interaction (ADOS; change score)



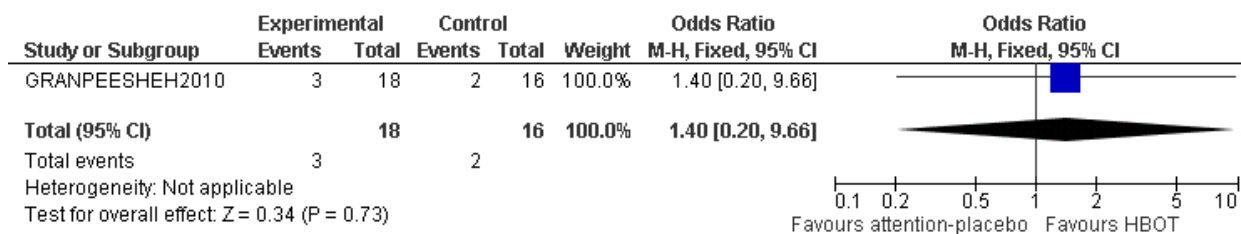
### 1.8.3 Medical procedures for the core autism feature of impaired reciprocal social communication and interaction as a direct or indirect outcome

*Hyperbaric oxygen treatment (HBOT) versus attention-placebo for the core autism feature of impaired reciprocal social communication and interaction as a direct outcome*

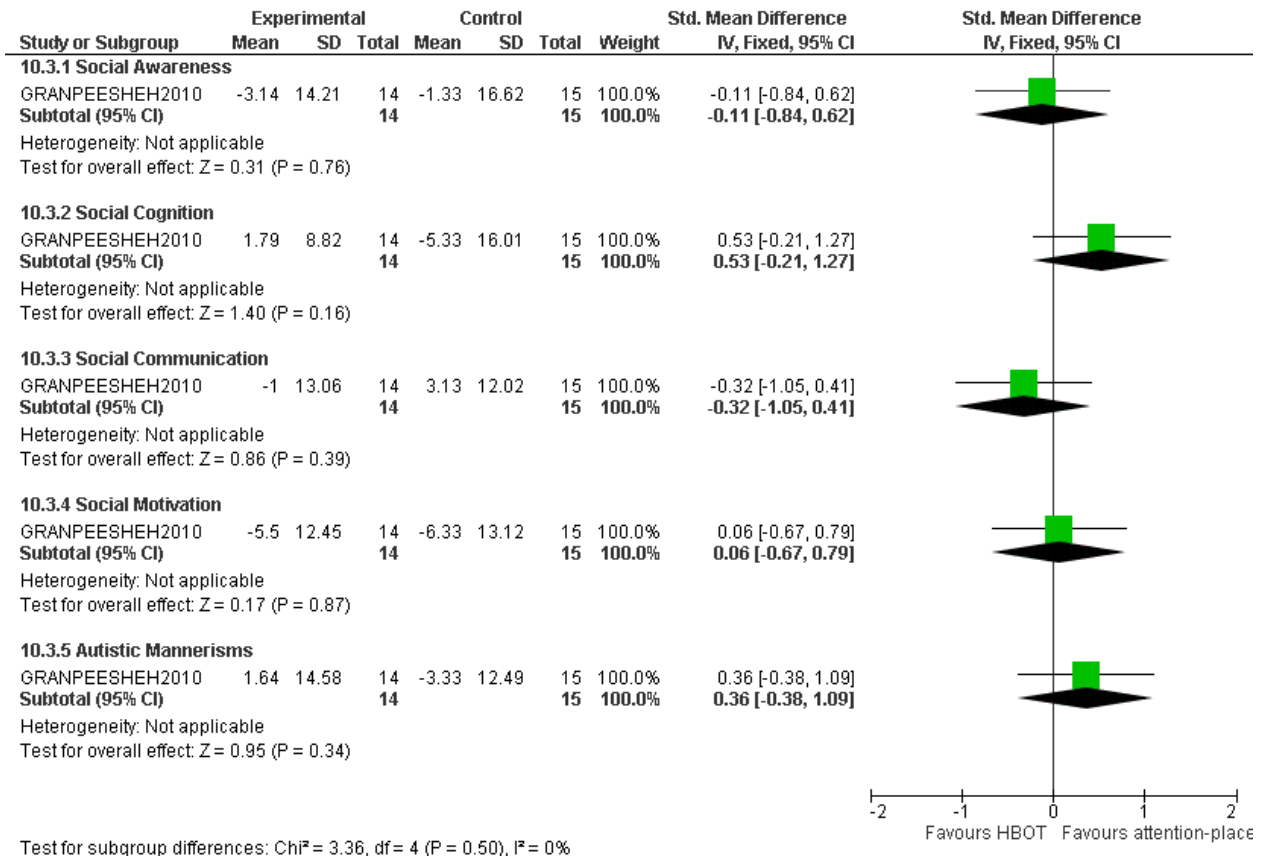
**Positive treatment response (improvement in ADOS diagnostic classification based on Communication domain)**



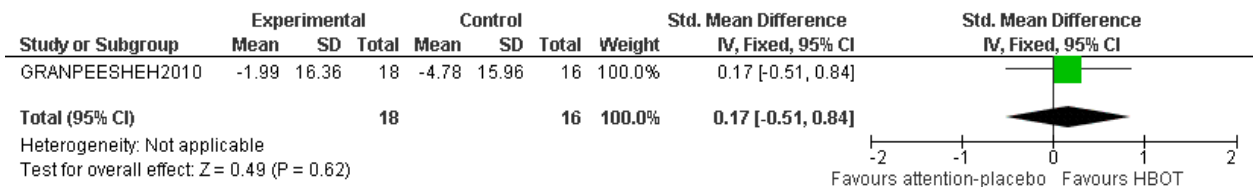
**Positive treatment response (improvement in ADOS diagnostic classification based on Socialization domain)**



**Social impairment (SRS change score)**

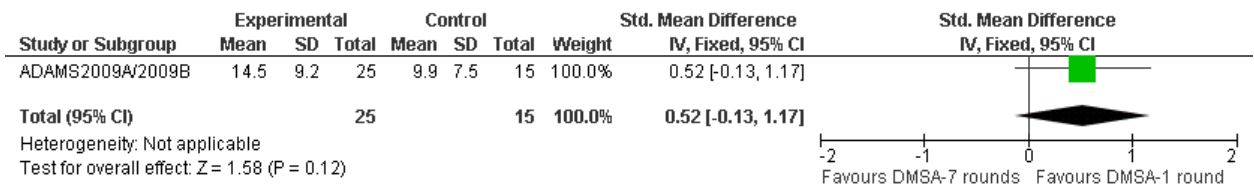


**Appropriate vocalization (behavioural observation change score)**

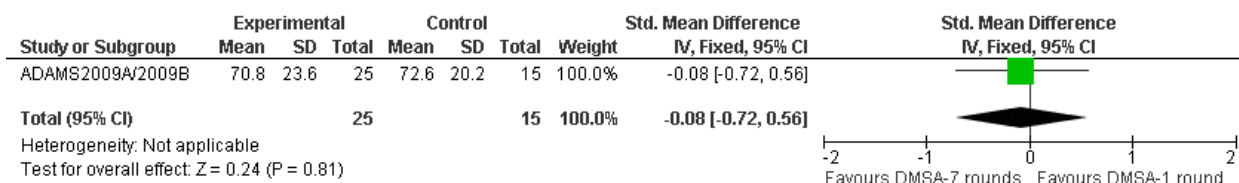


*Long-term chelation (7-rounds of DMSA therapy) versus short-term chelation (1-round of DMSA therapy and 6-rounds of placebo) for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome*

**Social Pragmatic Problems (PDDBI)**



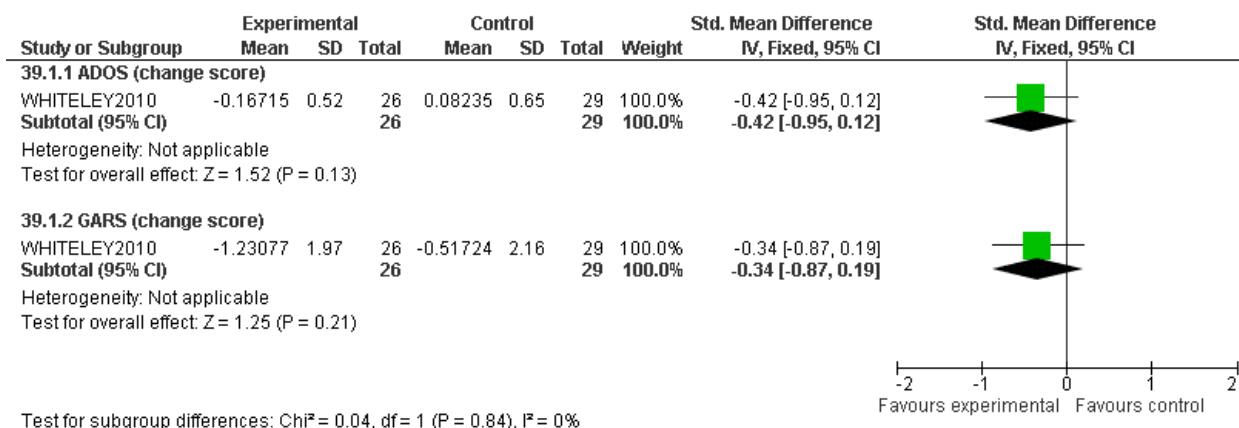
### Social Approach Behaviours (PDDBI)



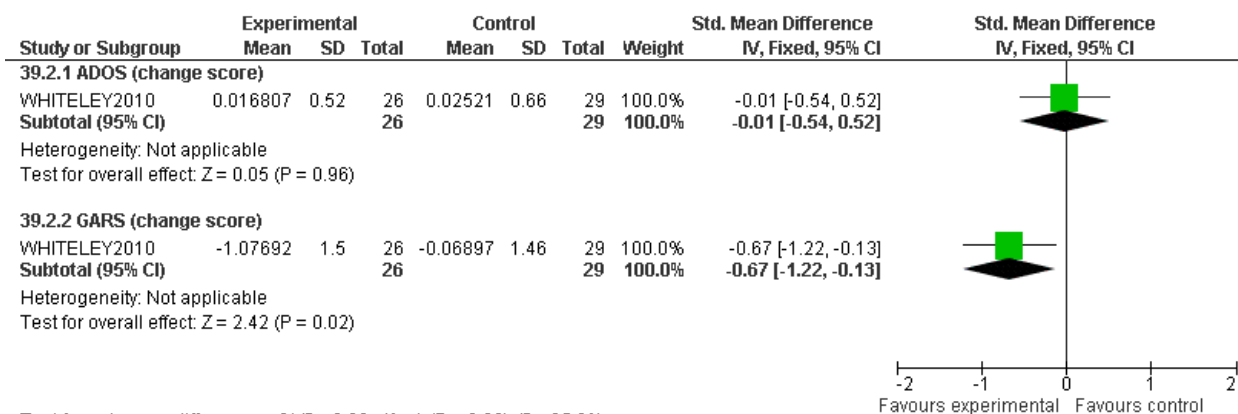
## 1.8.4 Nutritional interventions for the core autism feature of impaired reciprocal social communication and interaction as a direct or indirect outcome

*Gluten-free and casein-free diet versus treatment-as-usual for the core autism feature of impaired reciprocal social communication and interaction as a direct or indirect outcome*

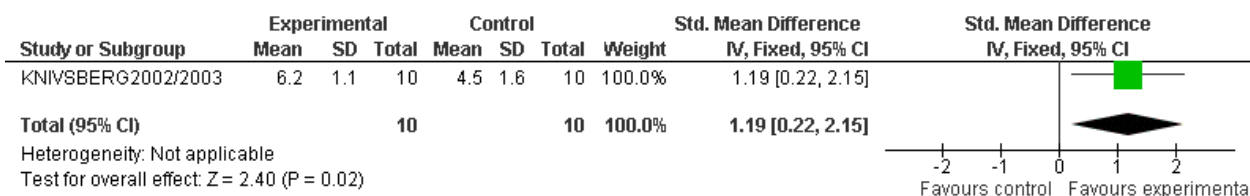
### Communication (direct outcome)



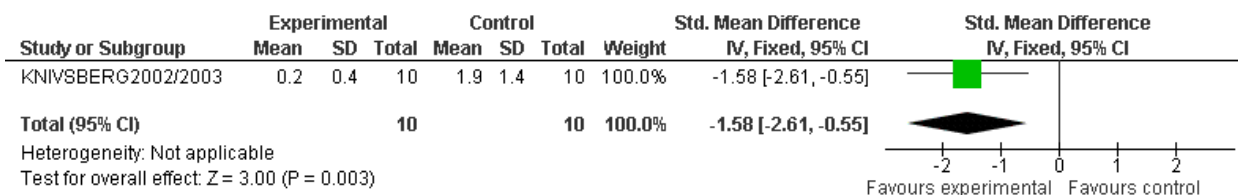
### Social Interaction (direct outcome)



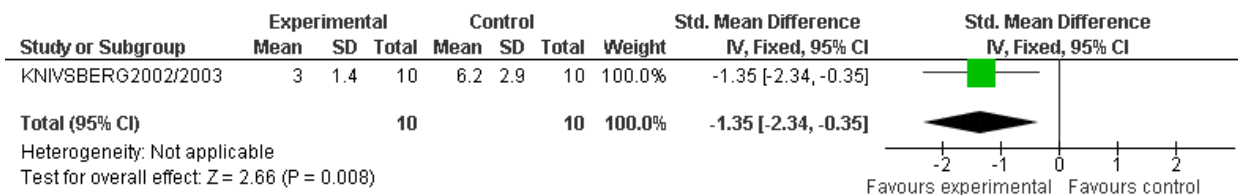
### Communication and interaction (DIPAB; indirect outcome)



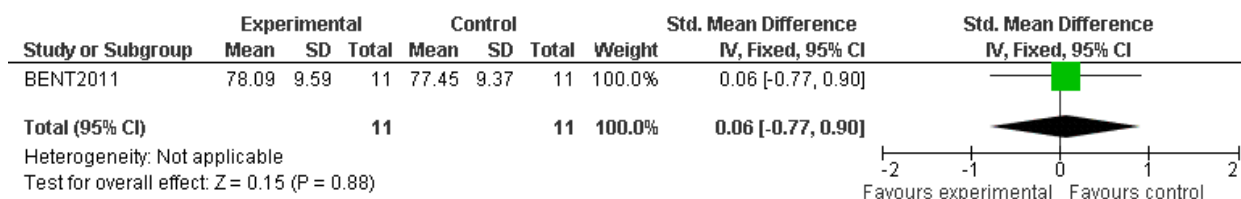
### Resistance to communication and interaction (DIPAB; indirect outcome)



### Social isolation (DIPAB; indirect outcome)

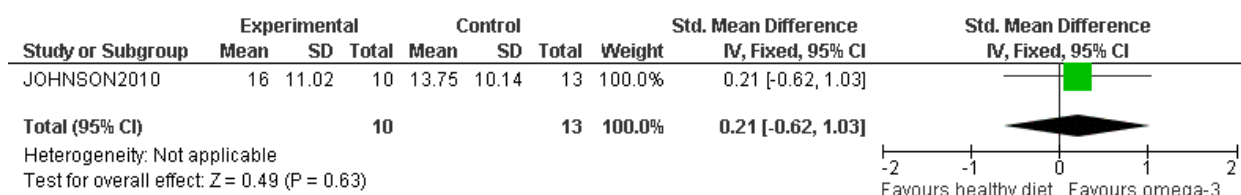


### *Omega-3 fatty acids versus placebo for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome*

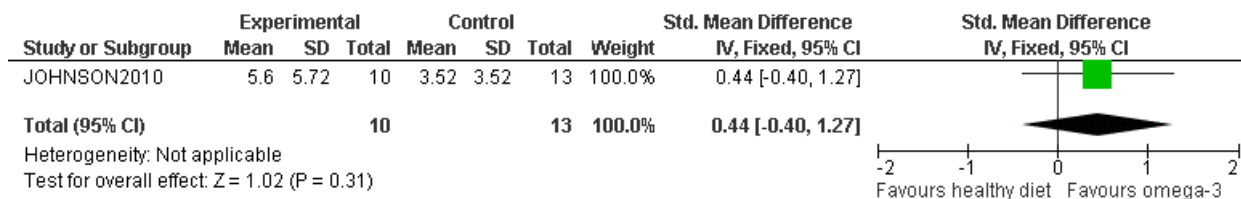


*Omega-3 fatty acids versus healthy diet control for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome*

**Frequency of positive vocalizations (behavioural observation)**

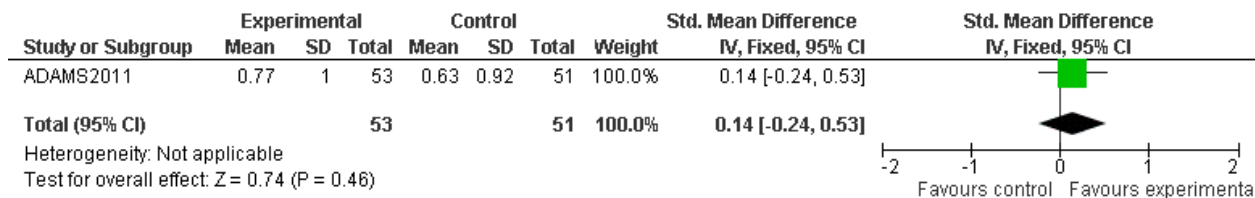


**Frequency of social initiations (behavioural observation)**



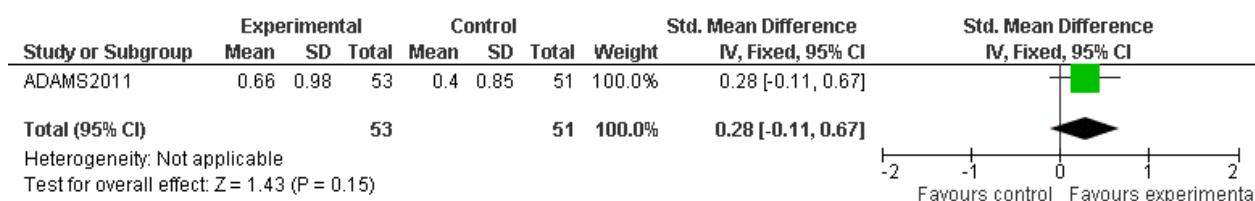
*Multivitamin/mineral supplement versus placebo for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome*

**Sociability improvement (PGI-R)**



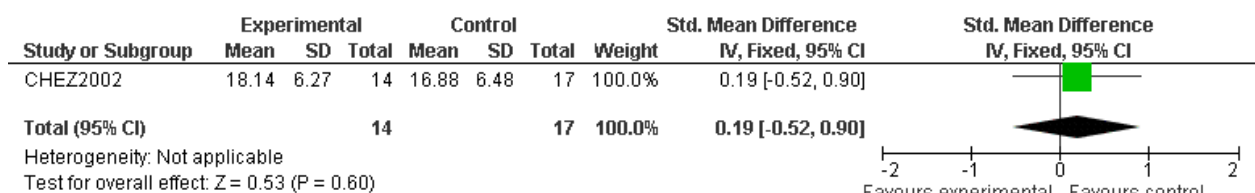
**Eye contact improvement (PGI-R)**



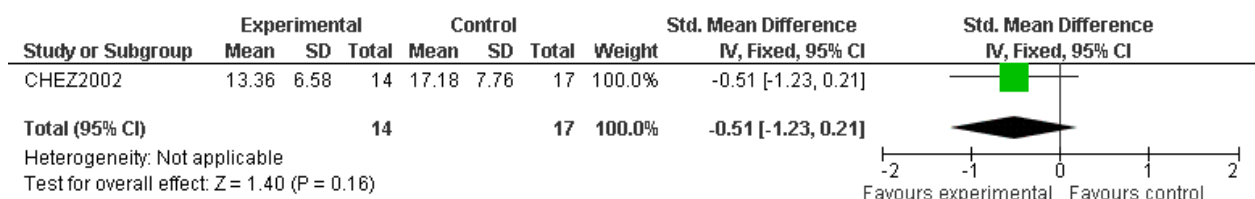


*L-carnosine supplement versus placebo for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome*

**Communication (GARS)**



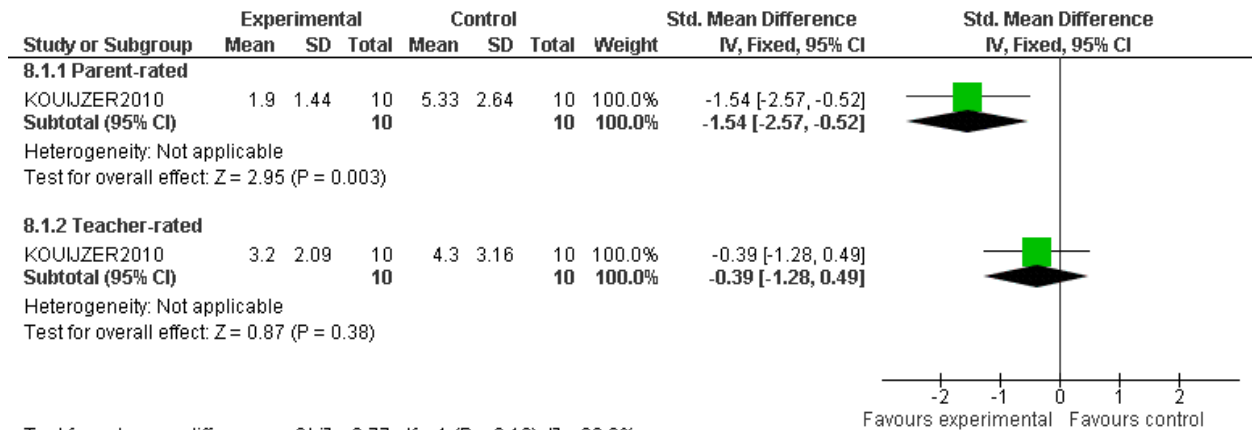
**Social interaction (GARS)**



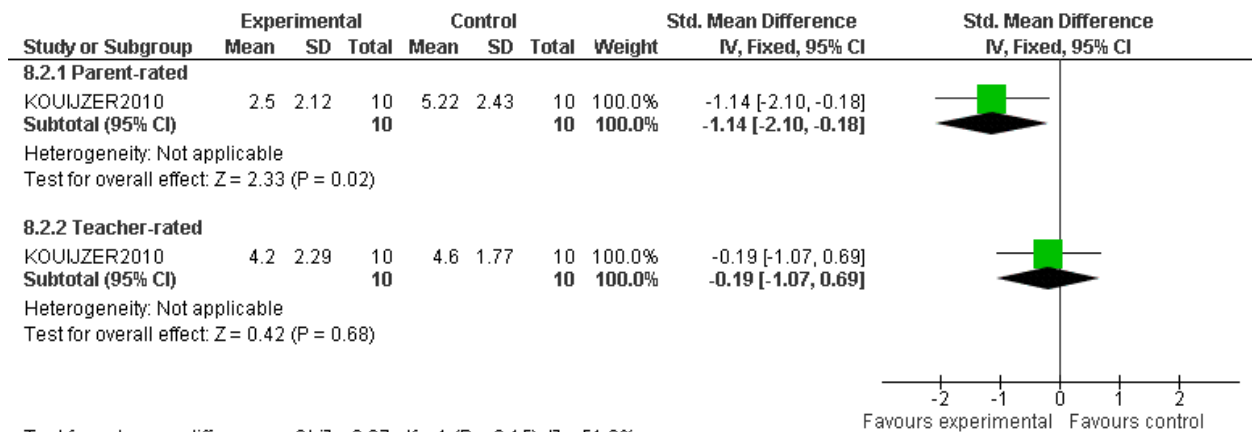
**1.8.5 Sensory interventions for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome**

*Neurofeedback versus treatment-as-usual for the core autism feature of impaired reciprocal social communication and interaction as an indirect outcome*

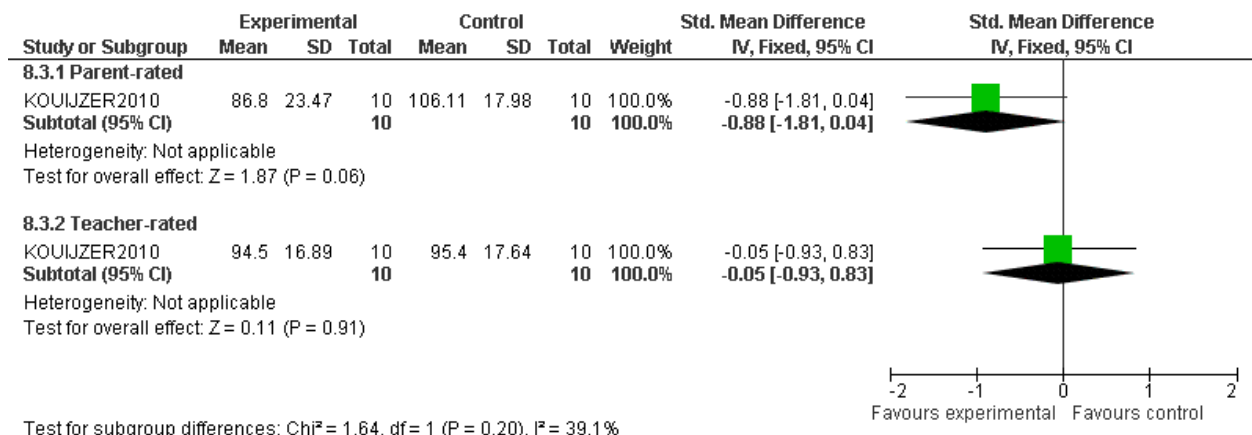
**Reciprocal social interaction (SCQ)**



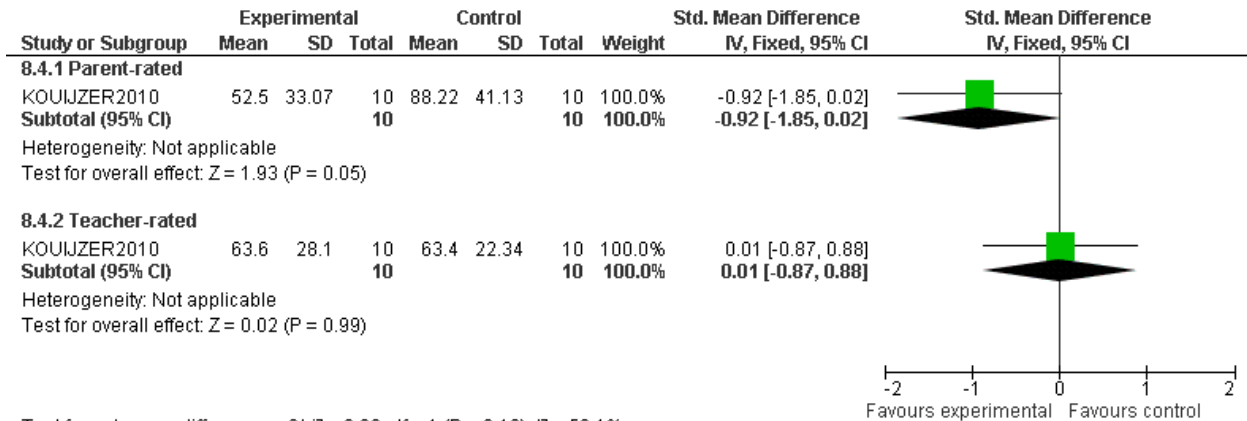
### Communication (SCQ)



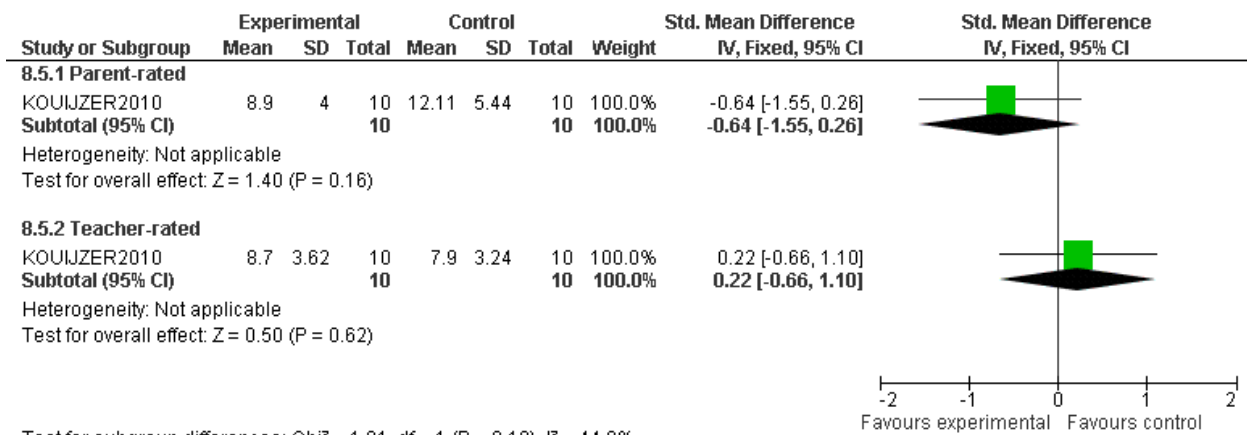
### Communication (CCC-2)



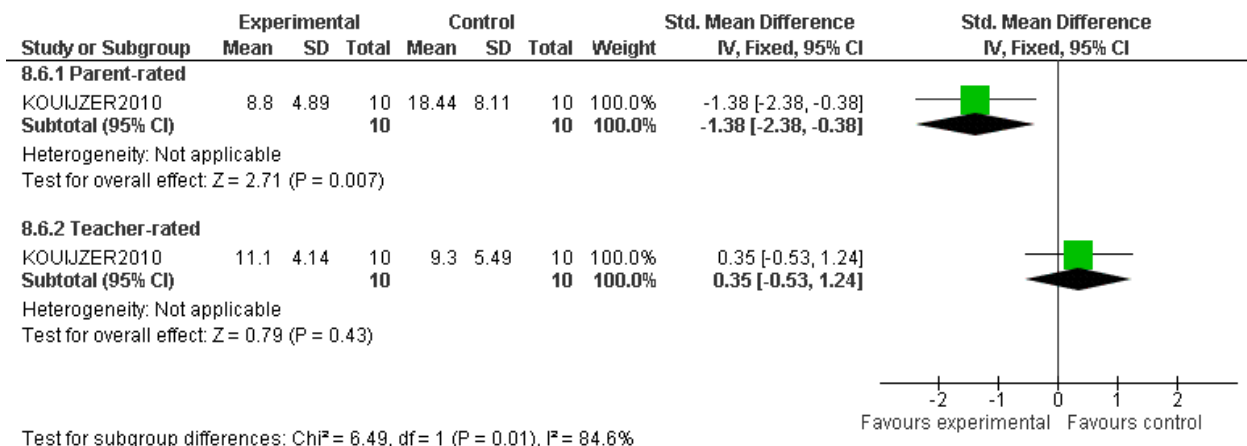
### Social impairment (SRS)



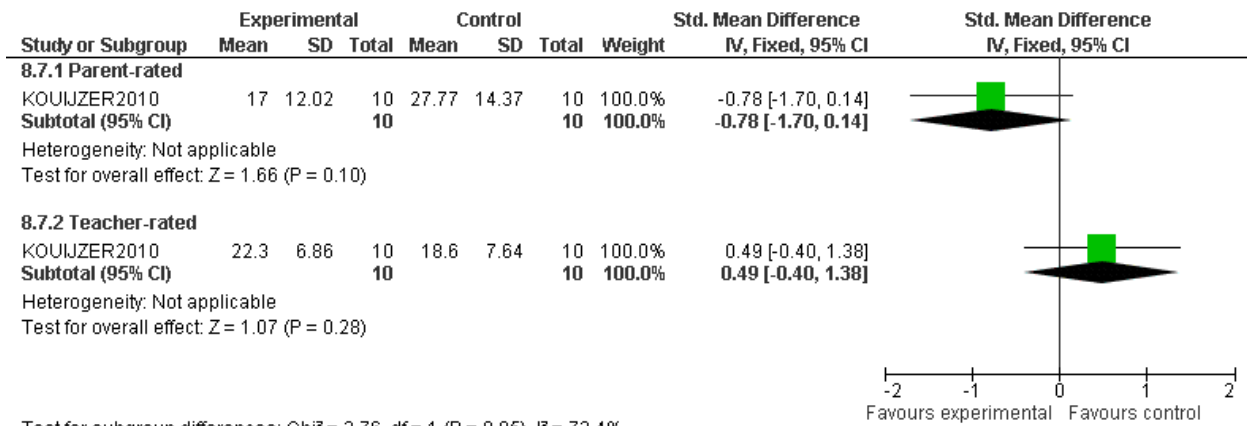
### Social Awareness (SRS)



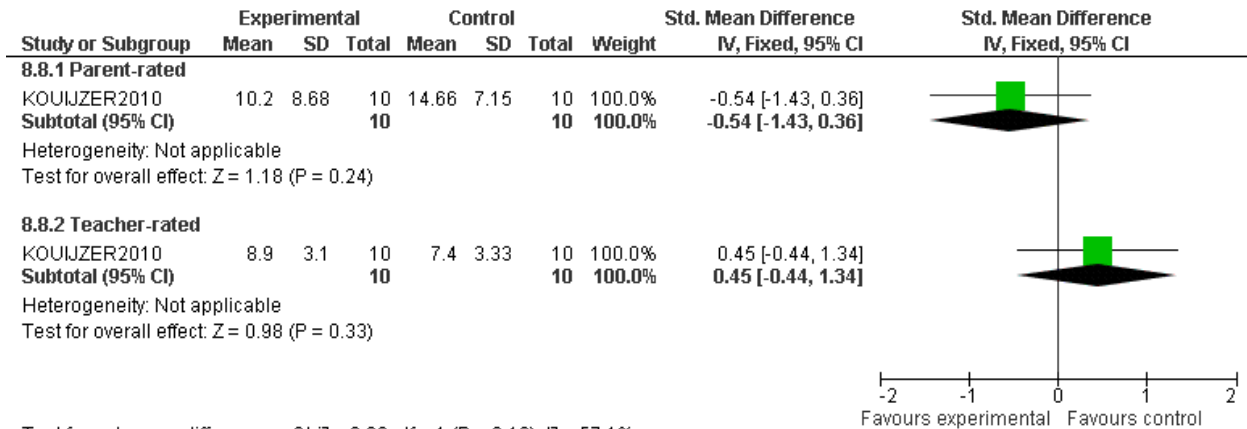
### Social Cognition (SRS)



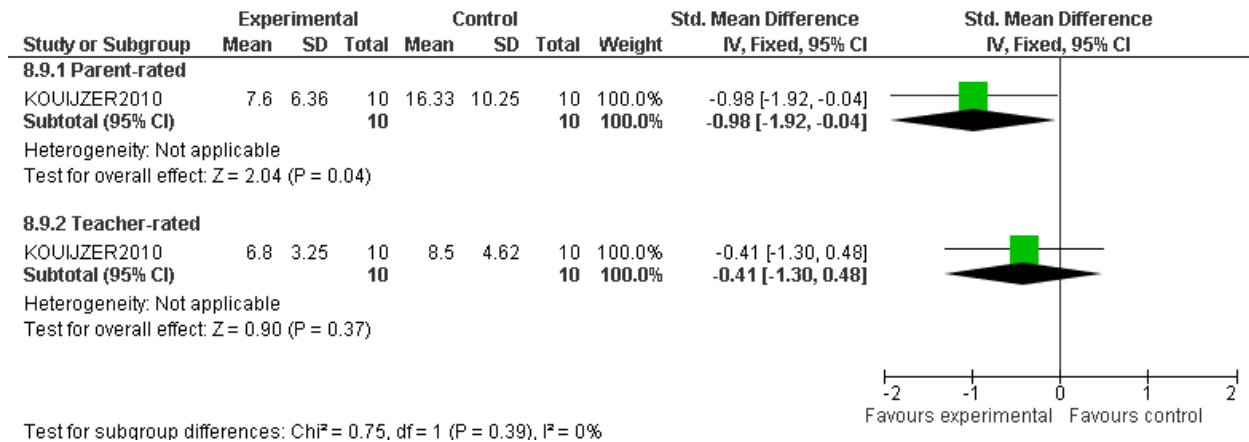
### Social Communication (SRS)



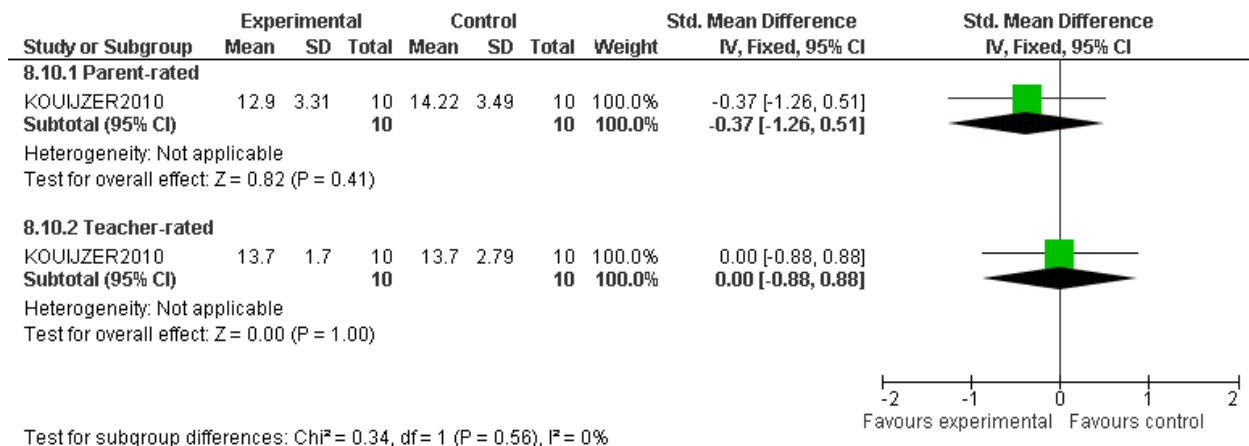
### Social Motivation (SRS)



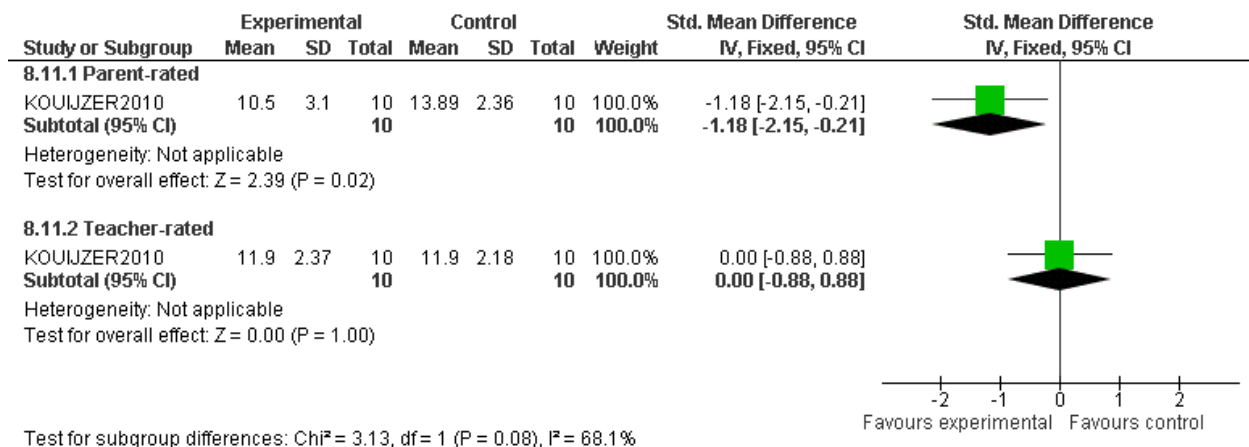
### Autistic Mannerisms (SRS)



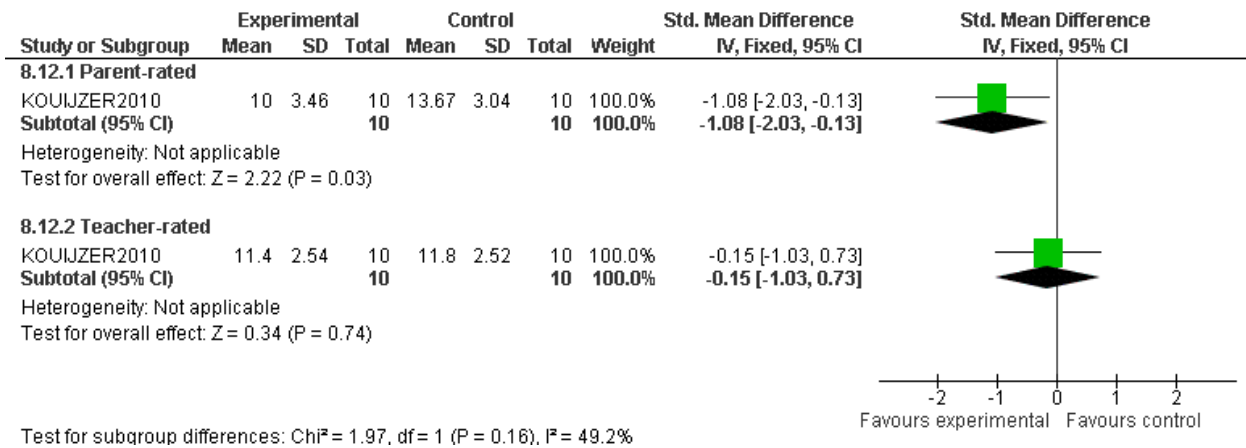
### Social relations (CCC-2)



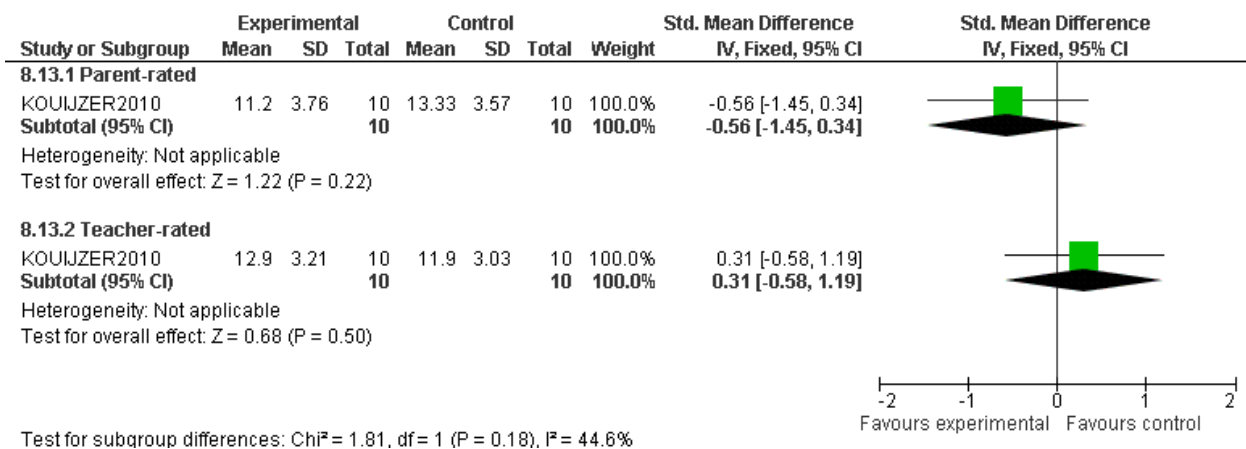
### Interests (CCC-2)



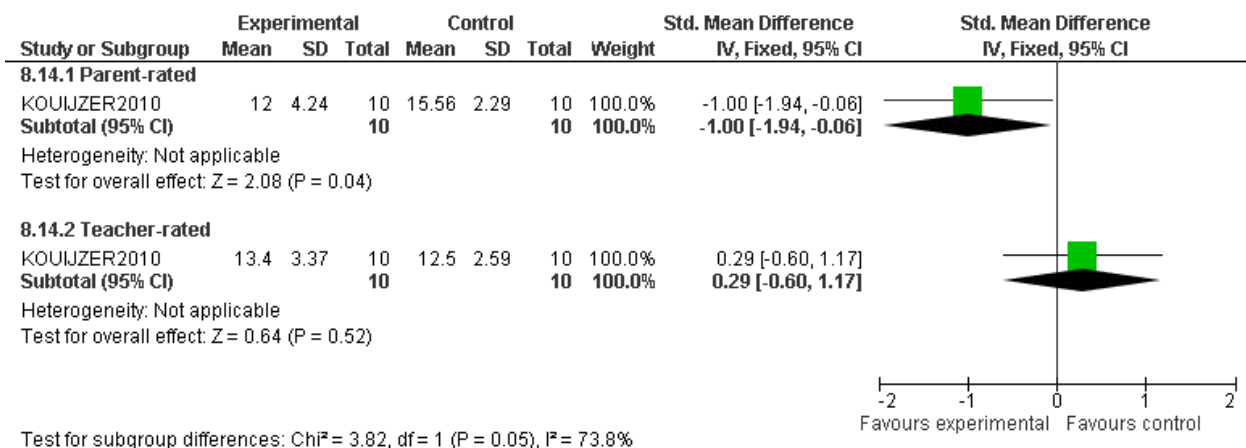
### Inappropriate initialization (CCC-2)



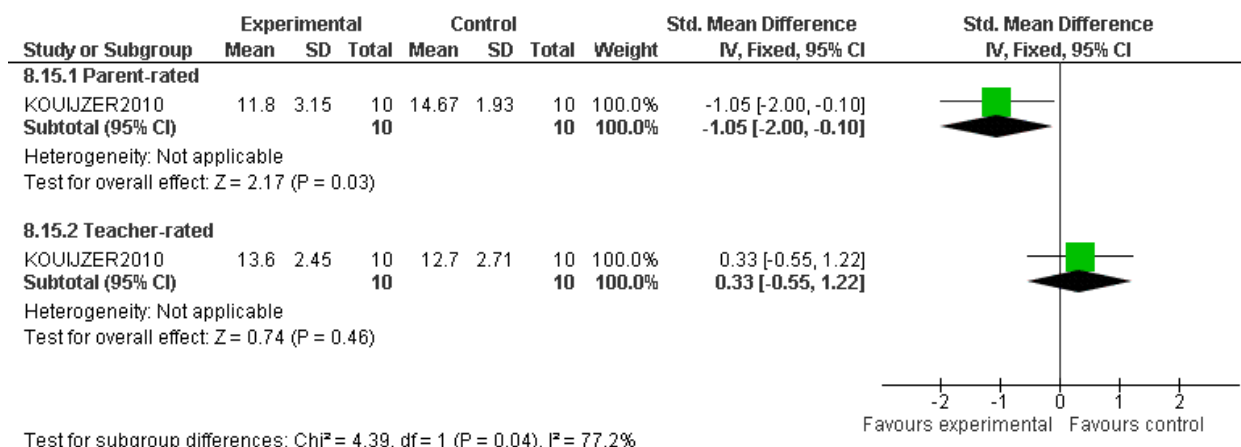
### Stereotyped conversation (CCC-2)



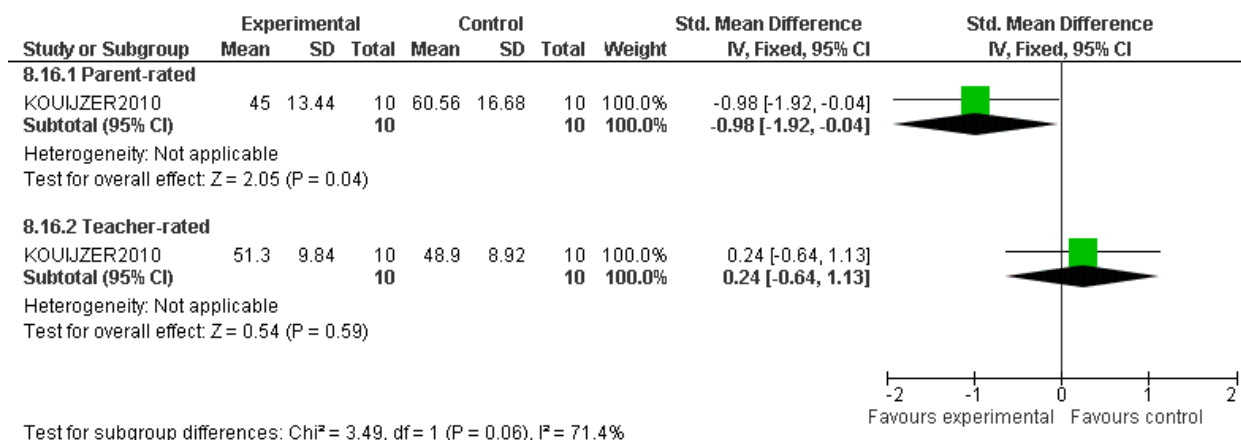
### Context use (CCC-2)



## Non-verbal communication (CCC-2)



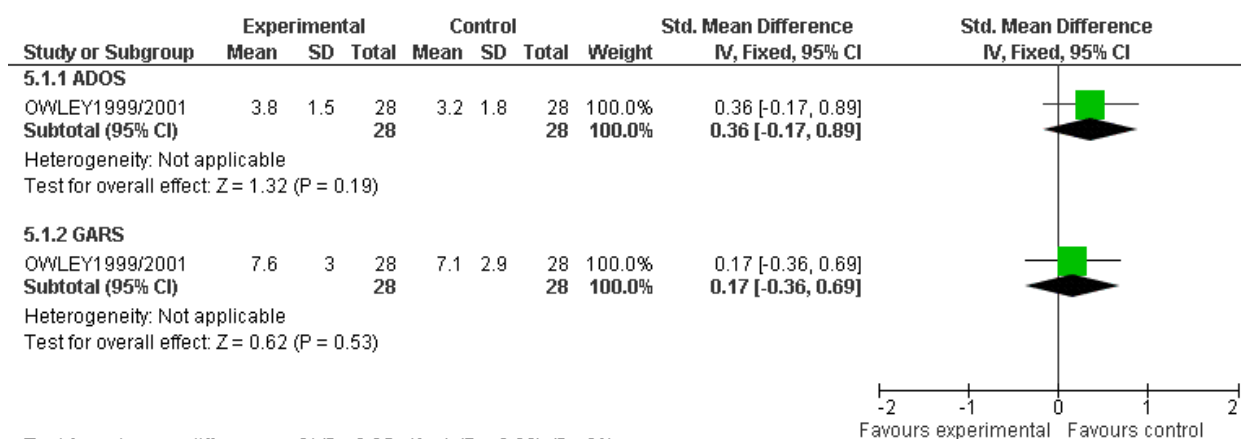
## Pragmatics (CCC-2)



# 1.9 BIOMEDICAL INTERVENTIONS AIMED AT THE CORE AUTISM FEATURE OF RESTRICTED INTERESTS AND RIGID AND REPETITIVE BEHAVIOURS

## 1.9.1 Hormones for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome

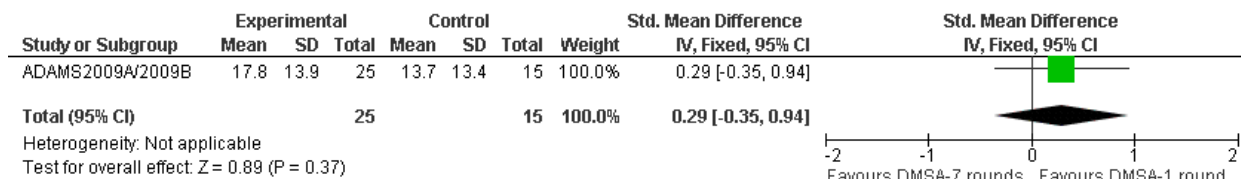
*Secretin versus placebo for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome*



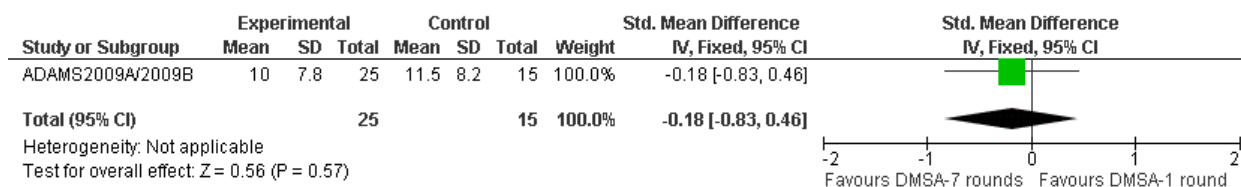
## 1.9.2 Medical procedures for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome

*Long-term chelation (7-rounds of DMSA therapy) versus short-term chelation (1-round of DMSA therapy and 6-rounds of placebo) for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome*

### Sensory/Perceptual Approach Behaviours (PDDBI)



### Ritualisms/Resistance to Change (PDDBI)

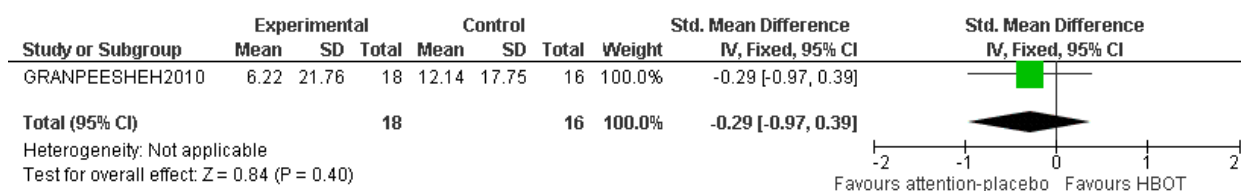


*HBOT versus attention-placebo for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome*

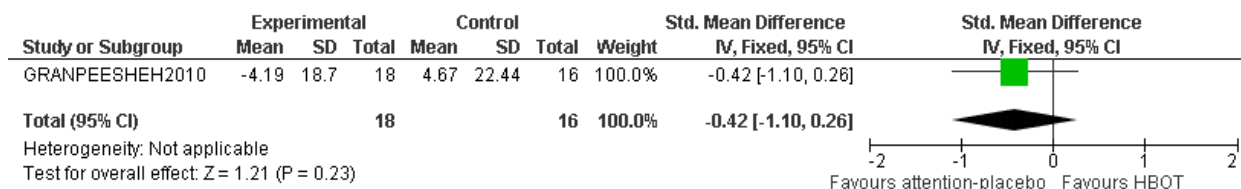
### Vocal stereotypy (behavioural observation; change score)

Autism: the management and support of children and young people on the autism spectrum (March 2013)



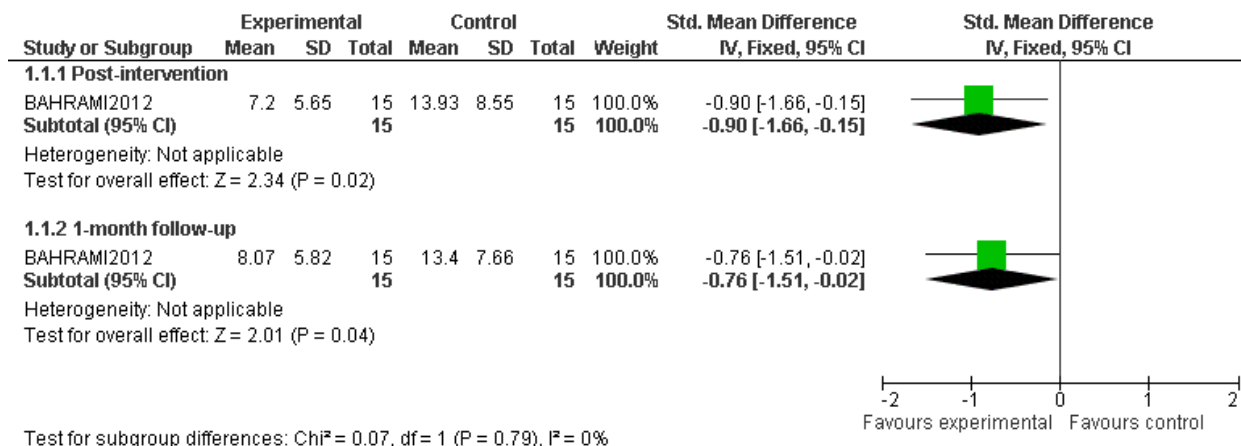


### Physical stereotypy (behavioural observation; change score)



## 1.9.3 Motor intervention for the core autism feature of restricted interests and rigid and repetitive behaviours as a direct outcome

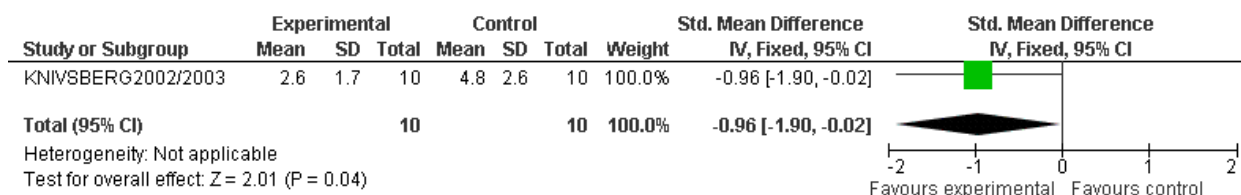
*Kata exercise training versus treatment-as-usual for the core autism feature of restricted interests and rigid and repetitive behaviours as a direct outcome*



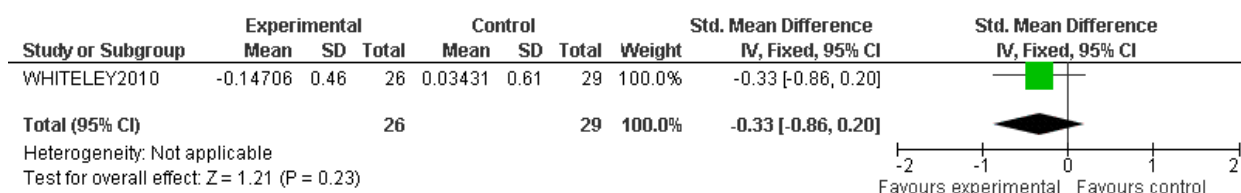
## 1.9.4 Nutritional interventions for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome

*Gluten-free and casein-free diet versus treatment-as-usual for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome*

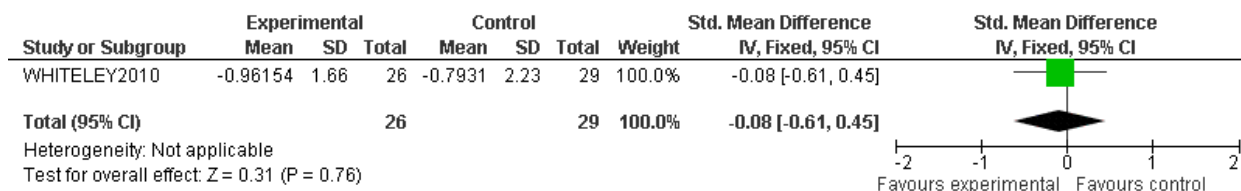
### Unusual or bizarre behaviour (DIPAB)



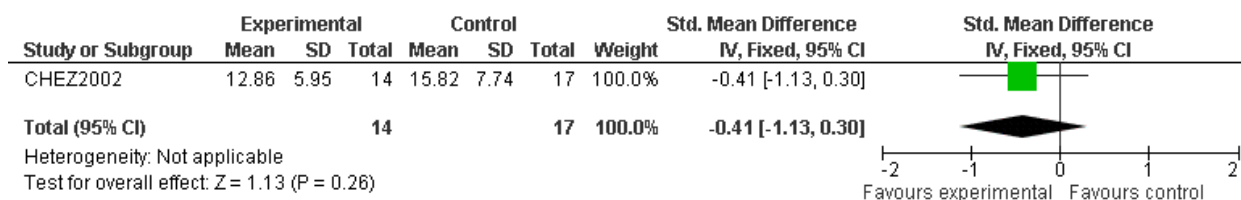
### Repetitive Behaviours (change score; ADOS)



### Stereotyped behaviour (change score; GARS)

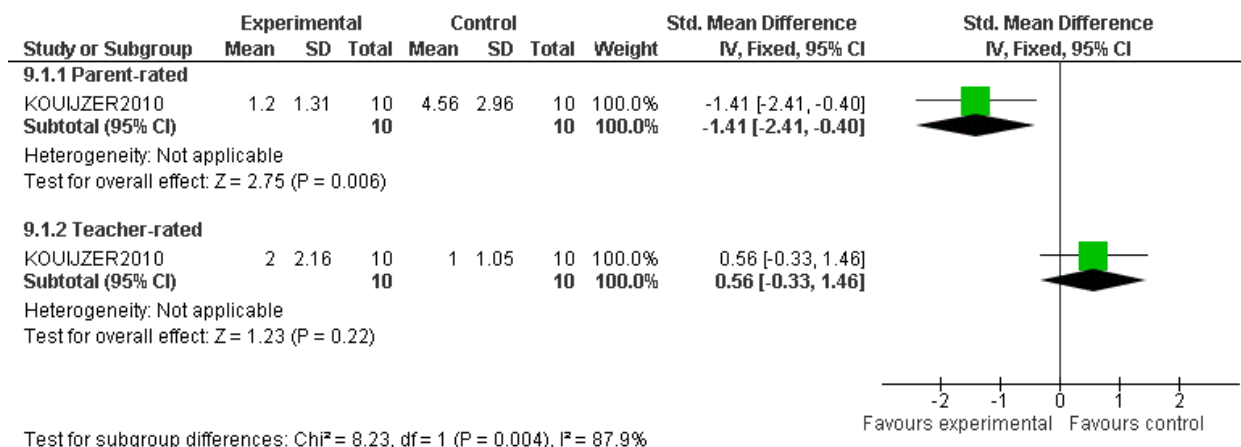


### *L-carnosine supplement versus placebo for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome*



## 1.9.5 Sensory intervention for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome

*Neurofeedback versus treatment-as-usual for the core autism feature of restricted interests and rigid and repetitive behaviours as an indirect outcome*

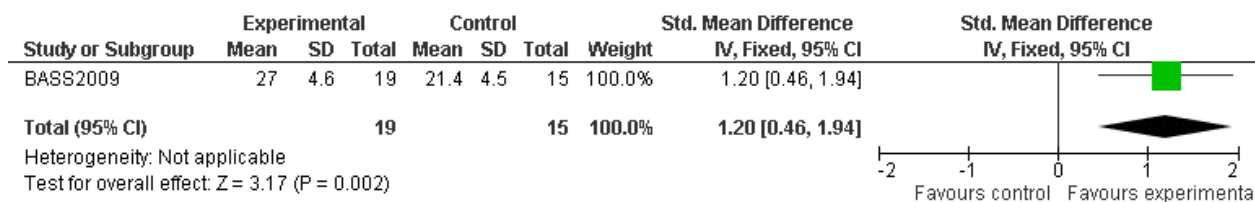


## 1.10 PSYCHOSOCIAL INTERVENTIONS AIMED AT BEHAVIOUR THAT CHALLENGES

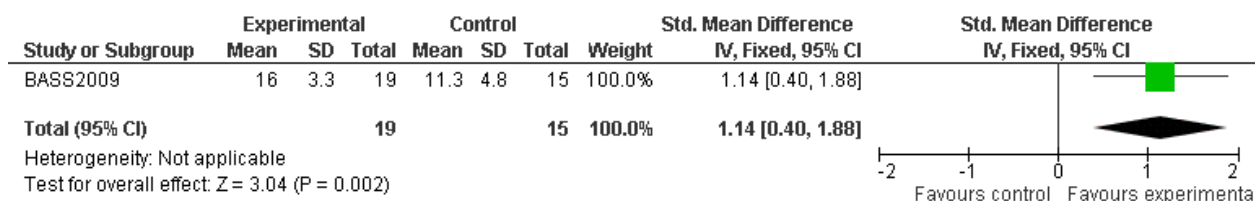
### 1.10.1 Animal-based intervention for behaviour that challenges as an indirect outcome

*Horseback riding versus waitlist control for behaviour that challenges as an indirect outcome*

#### Inattention/distractability (Sensory Profile)

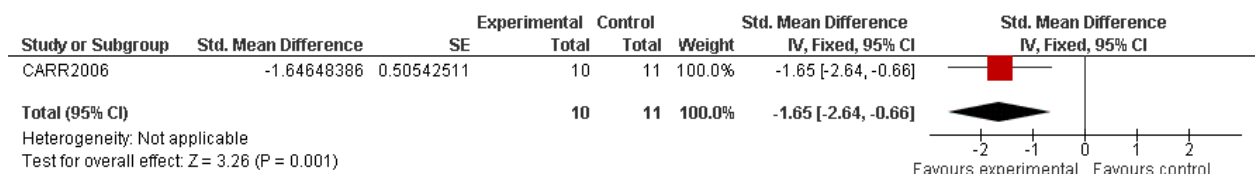


#### Sedentary (Sensory Profile)

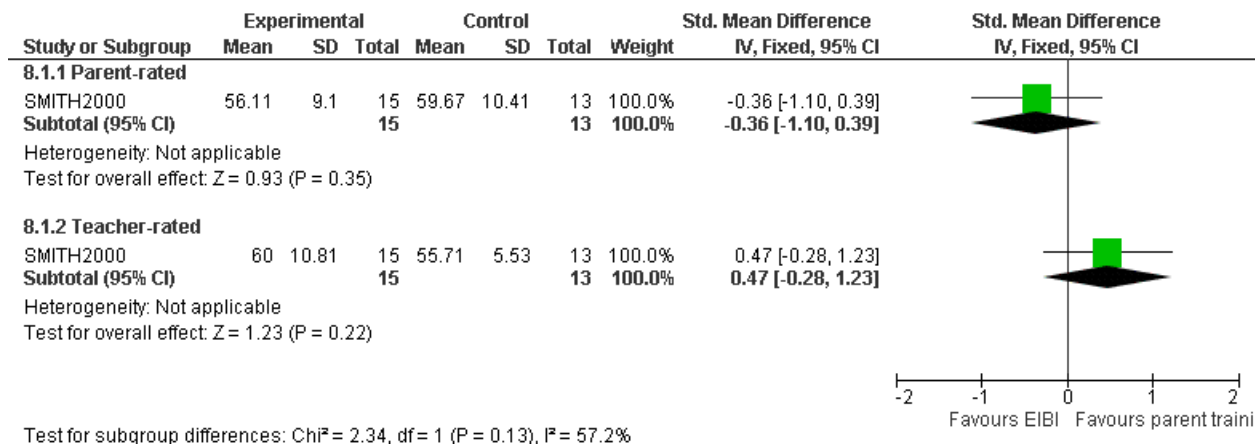


### 1.10.2 Behavioural interventions for behaviour that challenges as a direct or indirect outcome

#### *Behavioural and medical intervention versus medical intervention only for behaviour that challenges as a direct outcome*



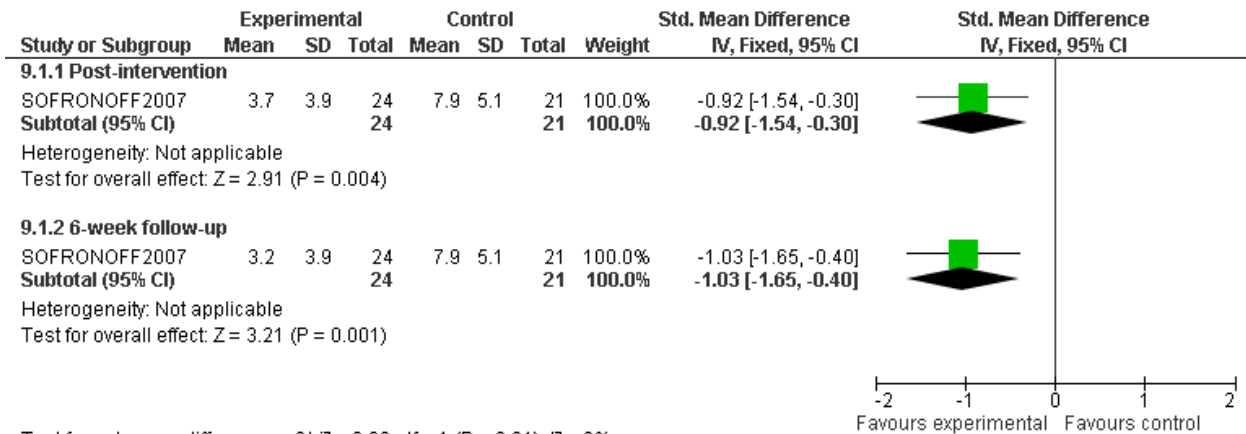
#### *EIBI versus parent training for behaviour that challenges as an indirect outcome*



### 1.10.3 Cognitive-behavioural interventions for behaviour that challenges as a direct or indirect outcome

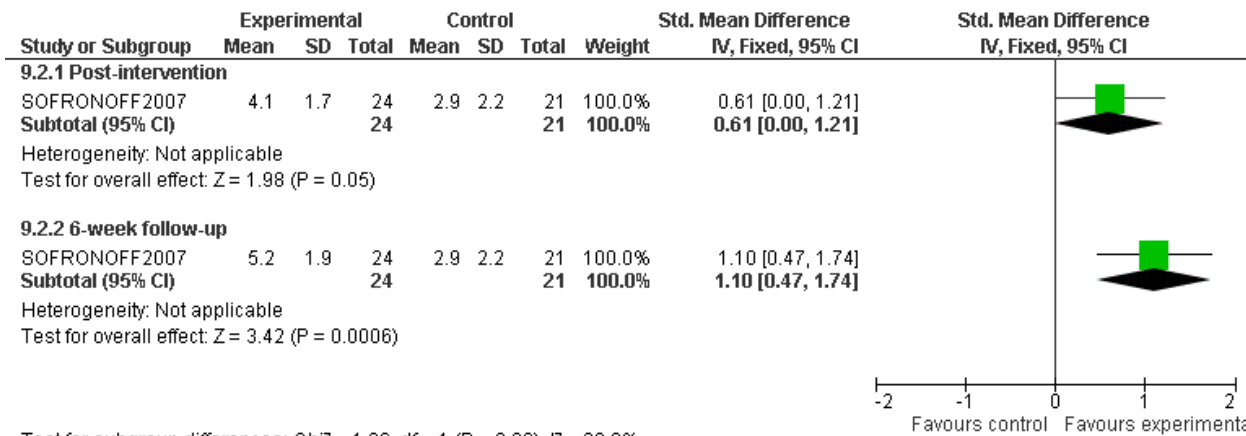
#### *CBT versus waitlist control for behaviour that challenges as a direct outcome*

##### Parent-reported instances of child anger



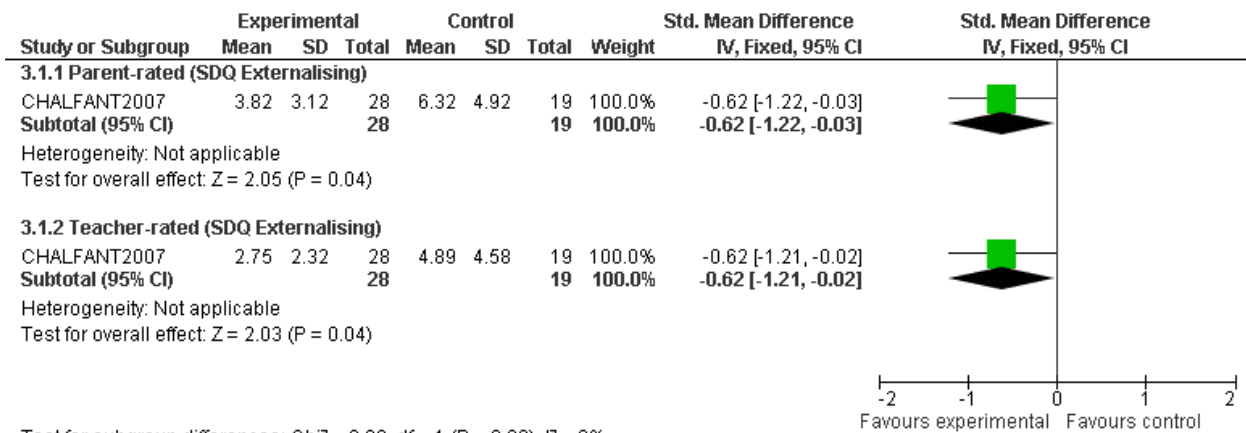
Test for subgroup differences: Chi<sup>2</sup> = 0.06, df = 1 (P = 0.81), I<sup>2</sup> = 0%

### Parent confidence in child managing own anger



Test for subgroup differences: Chi<sup>2</sup> = 1.26, df = 1 (P = 0.26), I<sup>2</sup> = 20.8%

### *CBT versus waitlist control for behaviour that challenges as an indirect outcome*

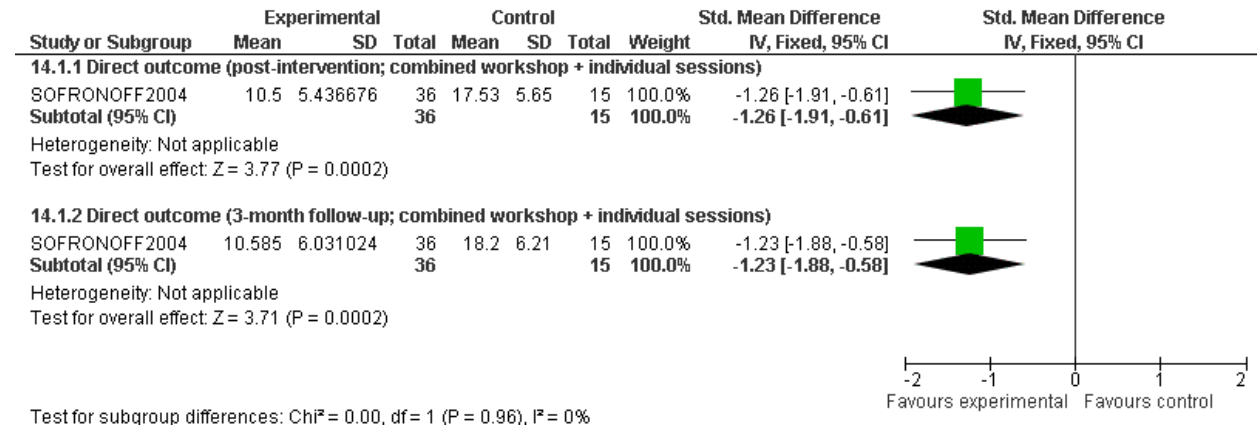


Test for subgroup differences: Chi<sup>2</sup> = 0.00, df = 1 (P = 0.99), I<sup>2</sup> = 0%

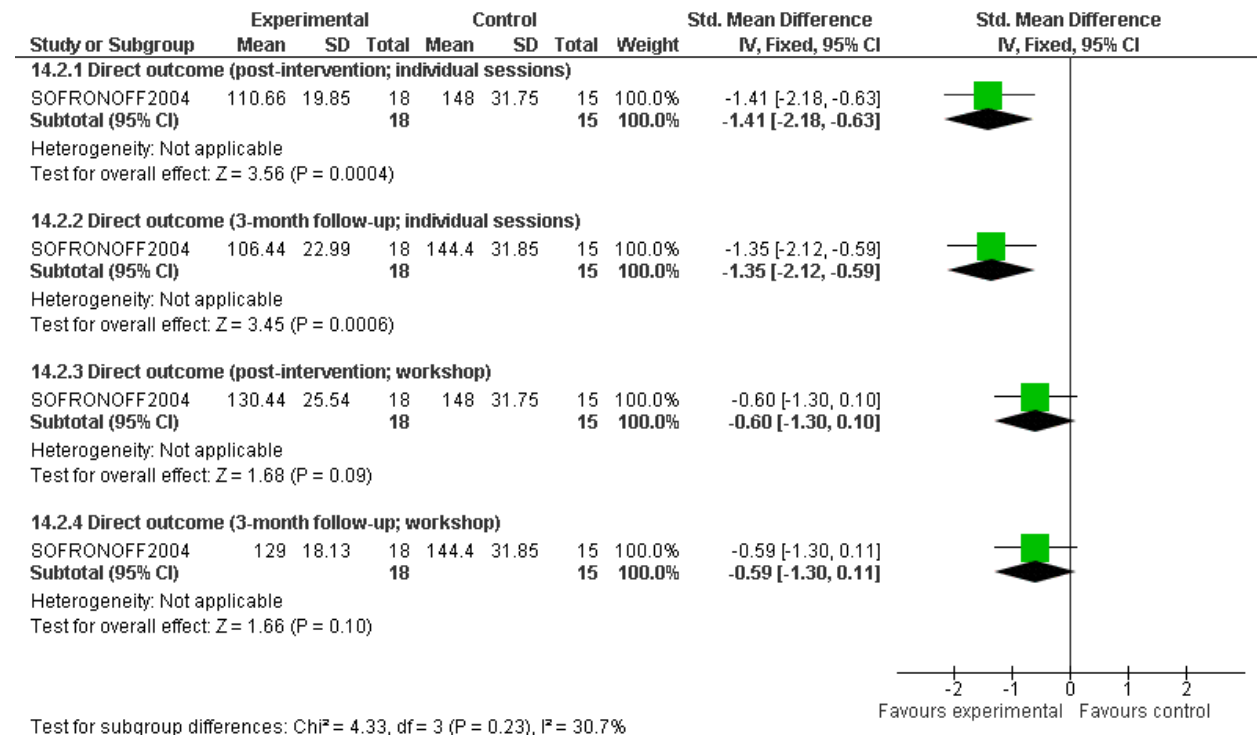
## 1.10.4 Parent training for behaviour that challenges as a direct or indirect outcome

### *Parent training versus treatment-as-usual for behaviour that challenges as a direct or indirect outcome*

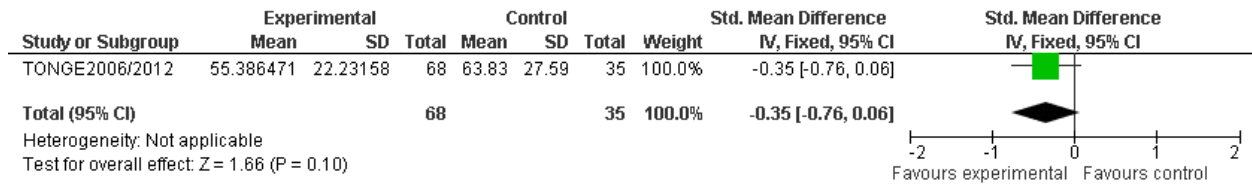
#### Frequency of problem behaviours



#### Intensity of problem behaviours

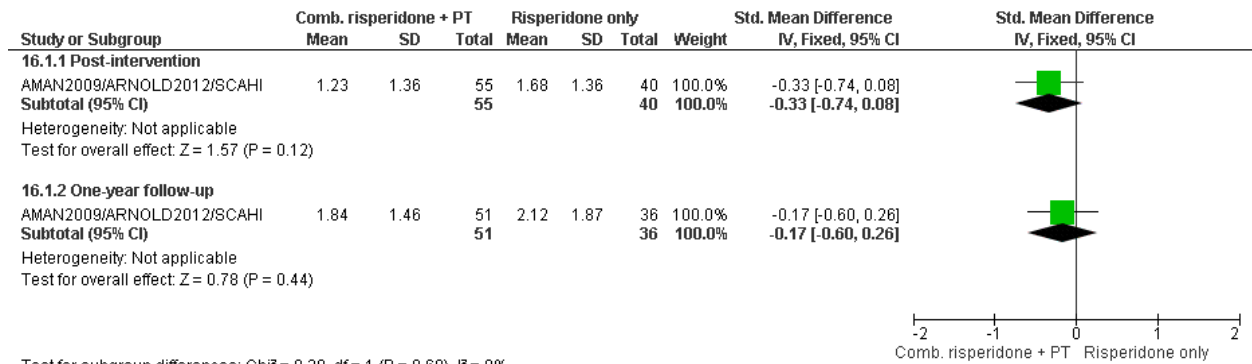


#### Problem behaviour (indirect outcome; DBC-TBPS; 6-month follow-up; PEC+PEBM combined)

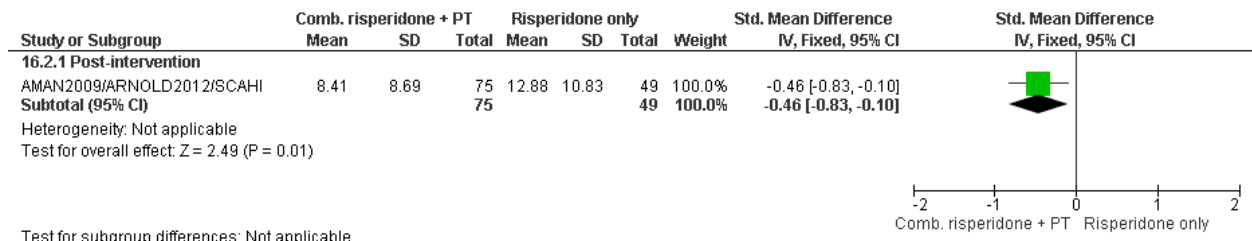


*Combined parent training and antipsychotic versus antipsychotic-only for behaviour that challenges as a direct outcome*

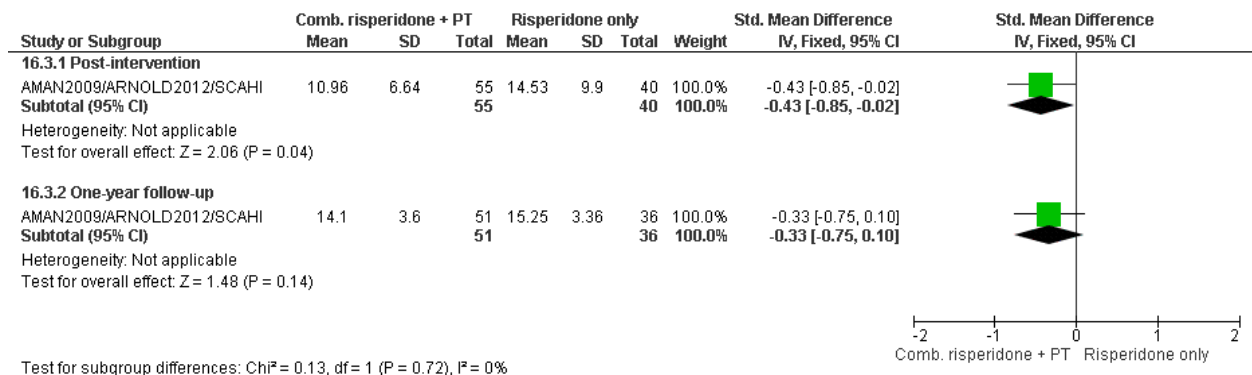
**Noncompliant behaviour in everyday circumstances (HSQ)**



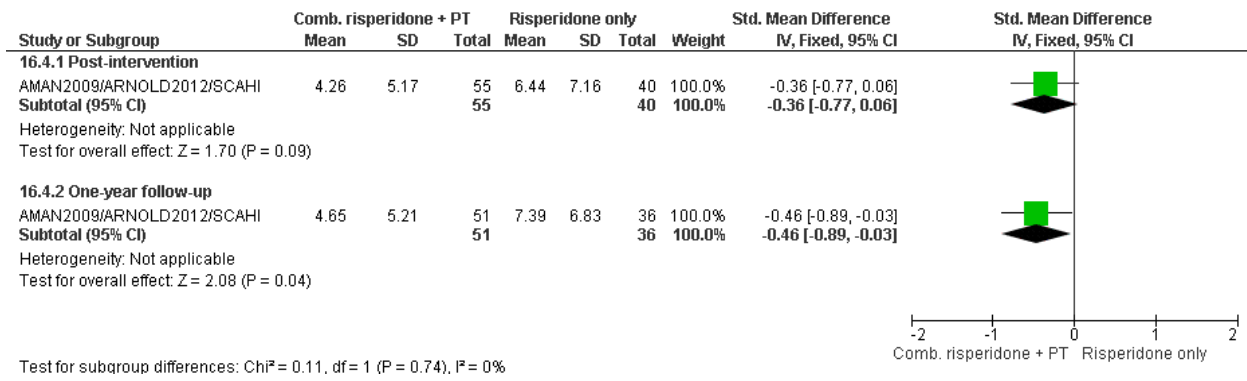
**Noncompliant behaviour in everyday circumstances (Noncompliance index - Daily Living Skills [VABS])**



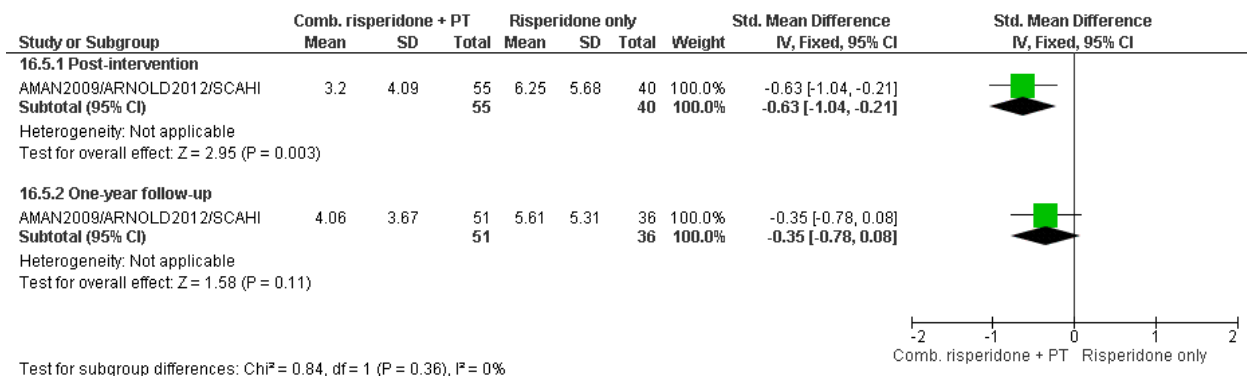
**Irritability (ABC)**



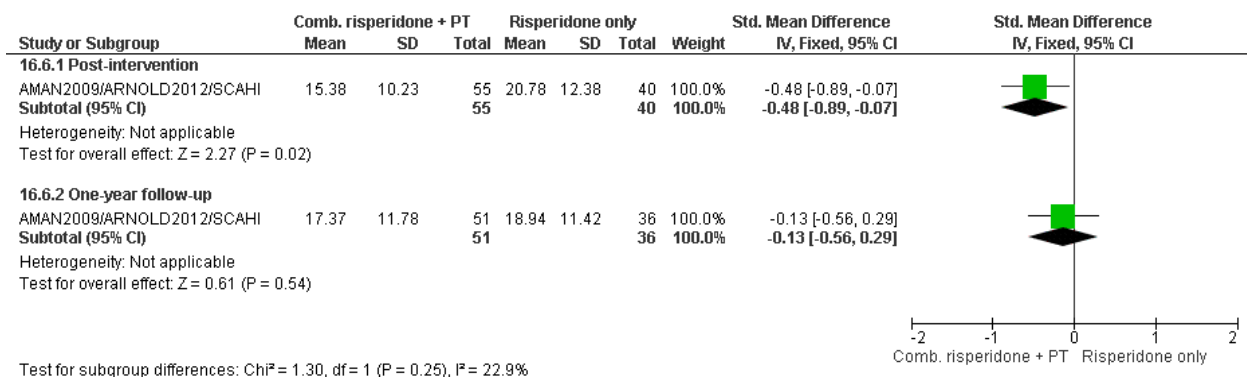
### Lethargy/Social withdrawal (ABC)



### Stereotypic behaviour (ABC)

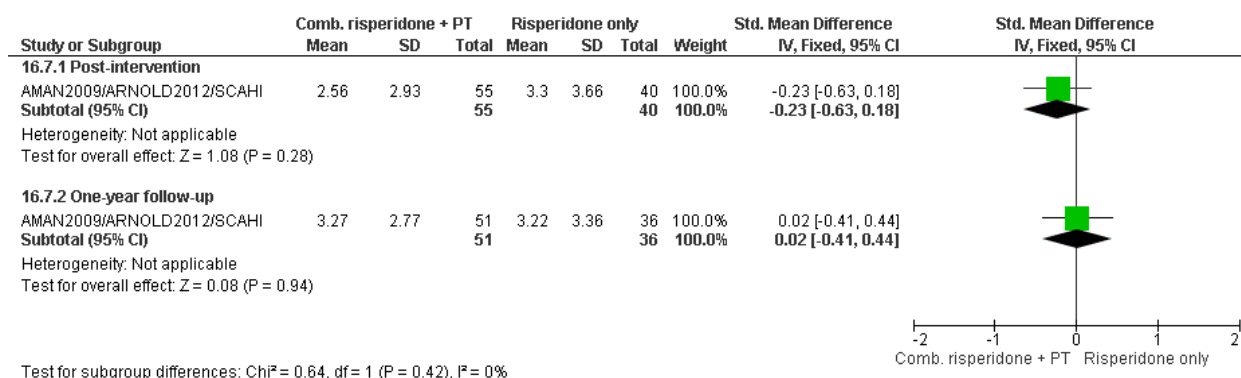


### Hyperactivity/Noncompliance (ABC)



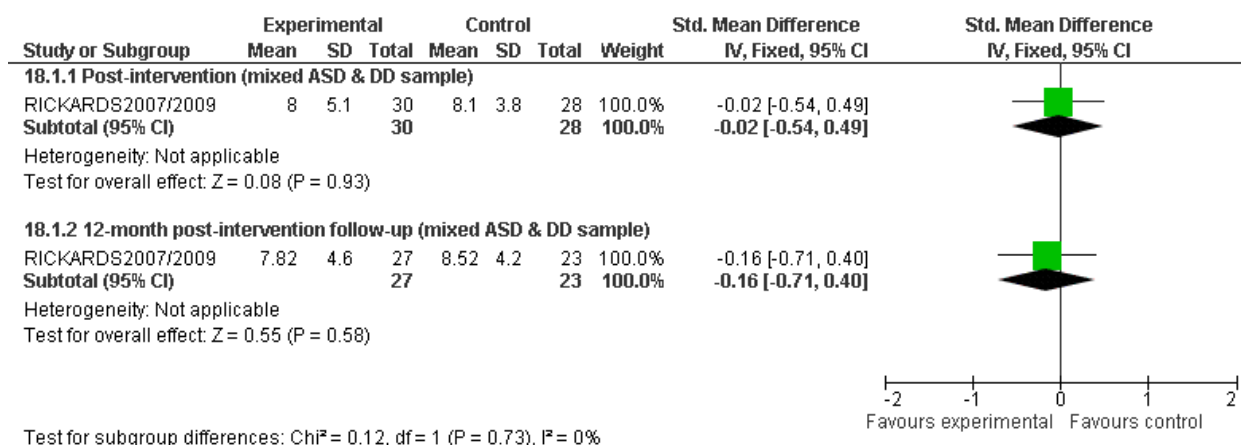
### Inappropriate speech (ABC)



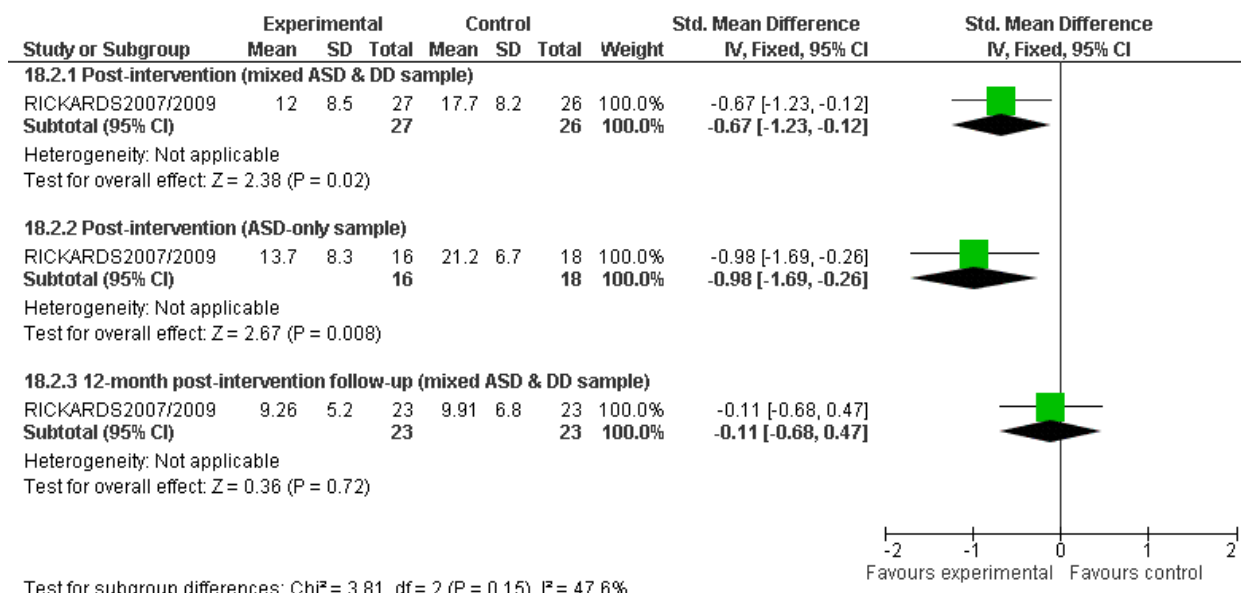


*Combined parent training and early intervention centre programme versus early intervention centre programme only for behaviour that challenges as an indirect outcome*

**Parent-reported behaviour that challenges (BSQ)**



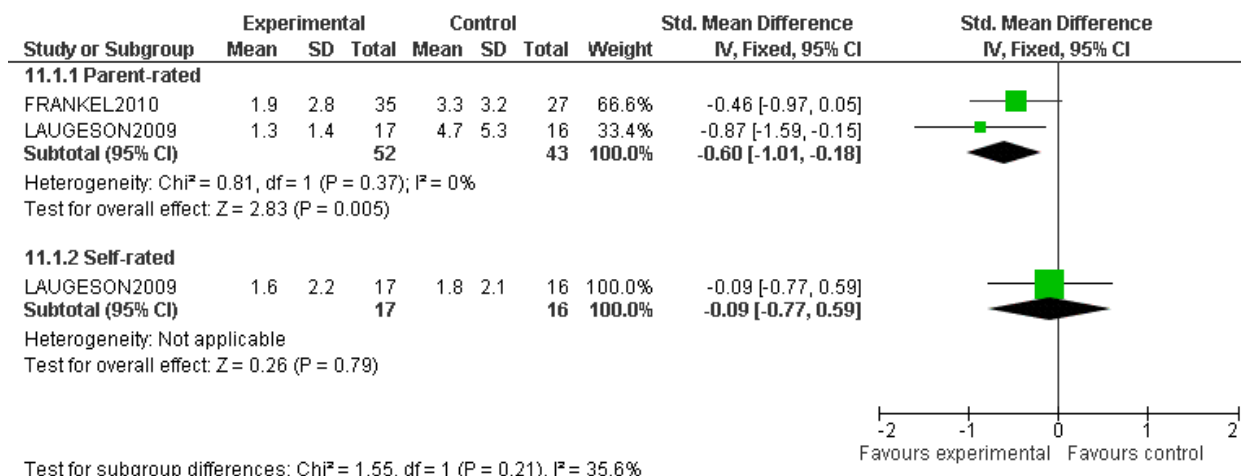
**Teacher-rated behaviour that challenges (PBCL)**



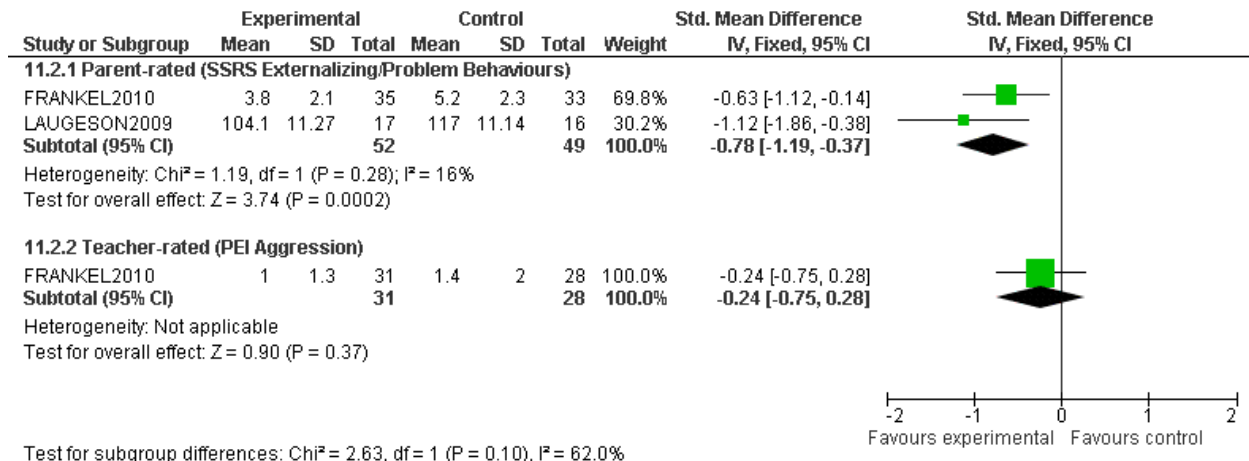
### 1.10.5 Social-communication interventions for behaviour that challenges as an indirect outcome

#### *Social skills group versus treatment-as-usual for behaviour that challenges as an indirect outcome*

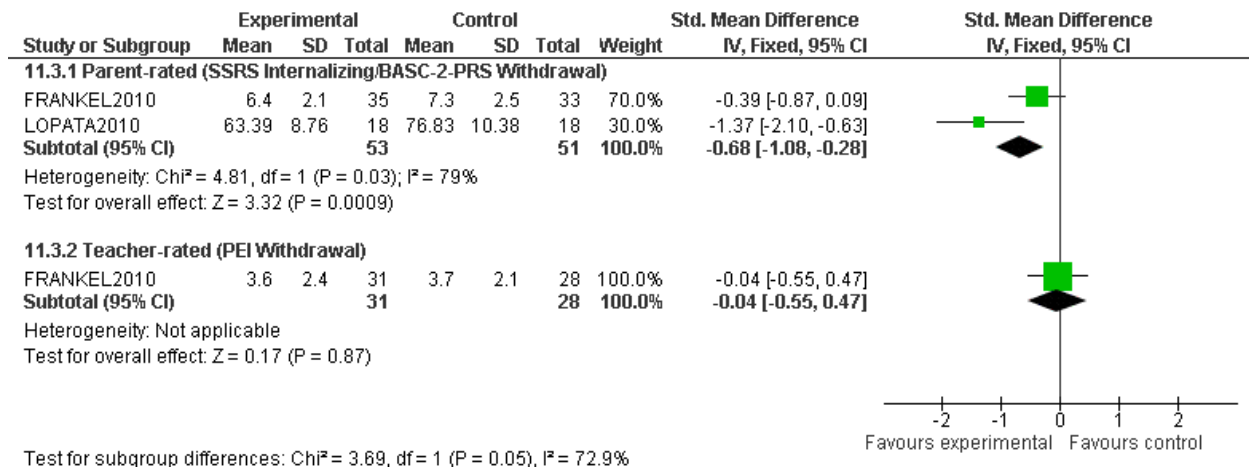
##### Conflict (QPQ Conflict)



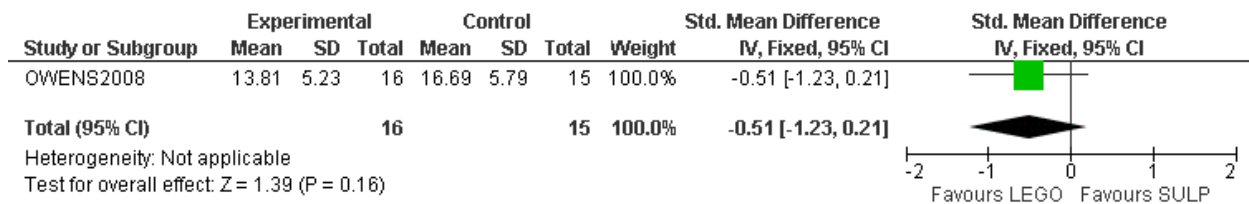
##### Intrusive/aggressive behaviour



**Social withdrawal**



**LEGO therapy versus SULP for behaviour that challenges as an indirect outcome**

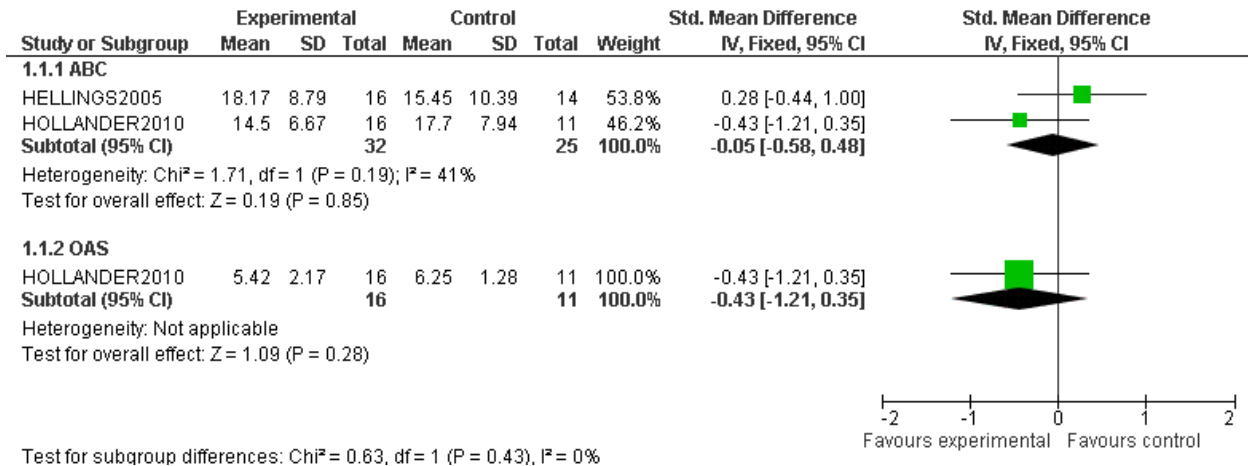


## 1.11 PHARMACOLOGICAL INTERVENTIONS AIMED AT BEHAVIOUR THAT CHALLENGES

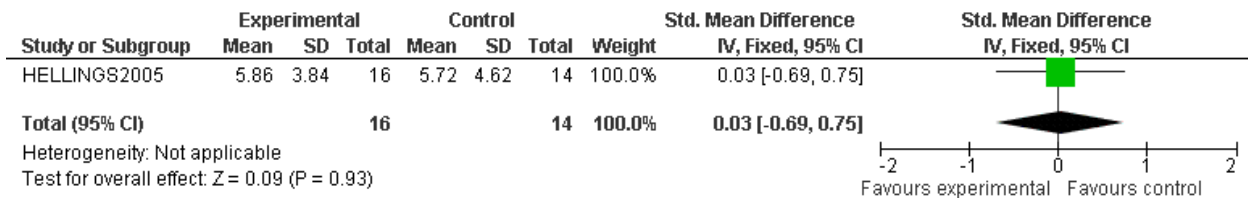
### 1.11.1 Anticonvulsants for behaviour that challenges as a direct outcome

#### *Divalproex versus placebo for behaviour that challenges as a direct outcome*

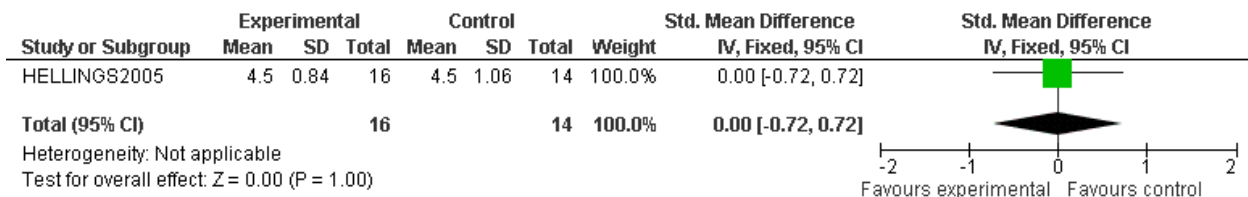
##### Irritability



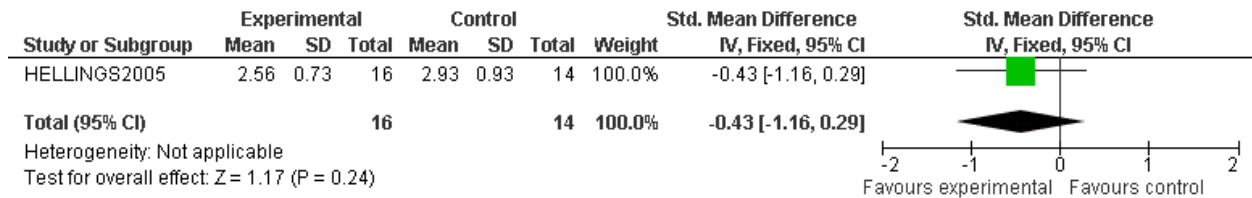
##### Aggression (OAS)



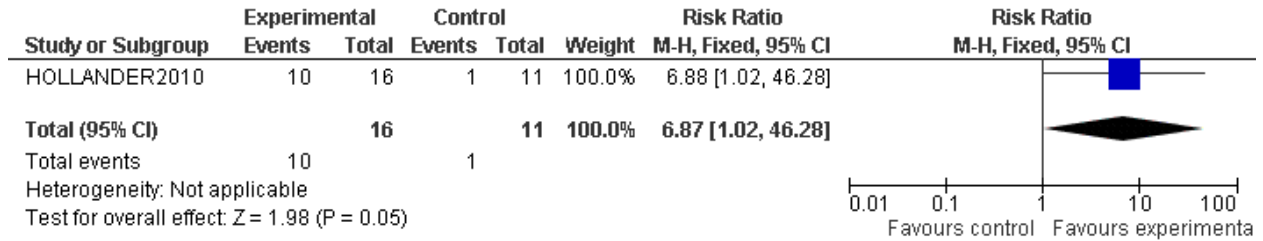
##### Global severity (CGI-S)



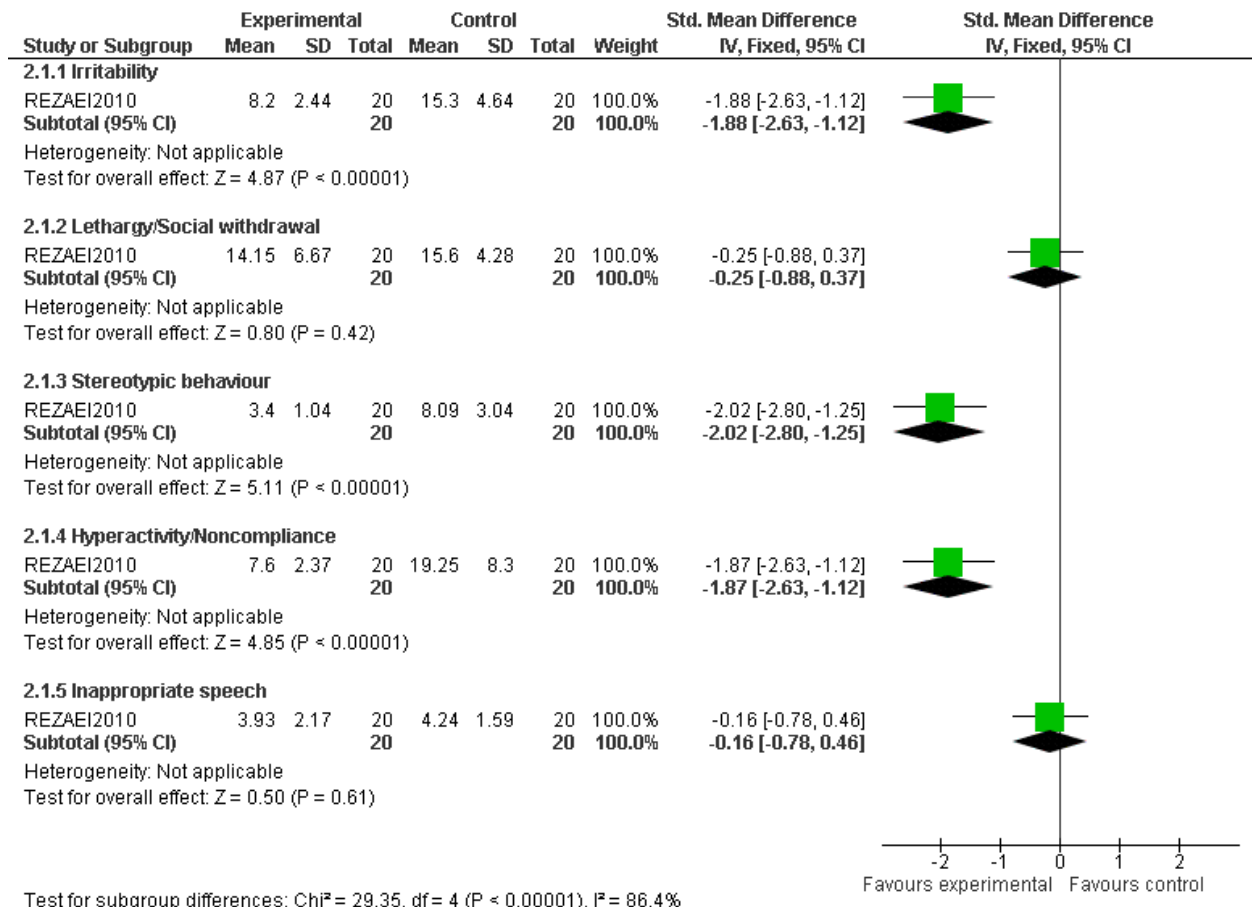
##### Global improvement (CGI-I)



**Global improvement ('much improved/very improved' on CGI-improvement)**

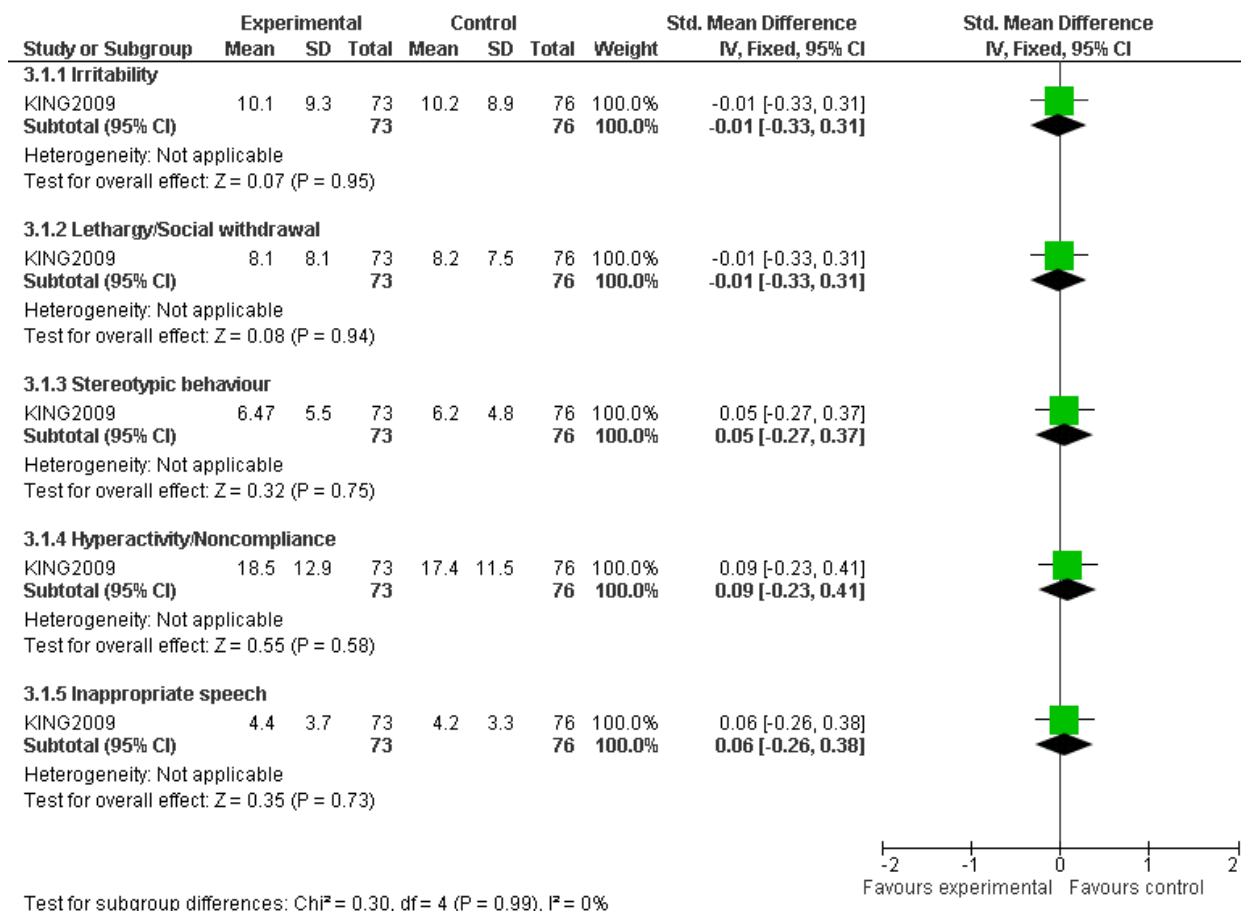


*Topiramate and risperidone versus placebo and risperidone for behaviour that challenges as a direct outcome*



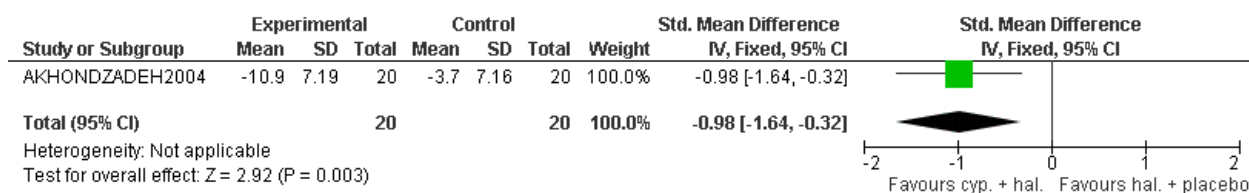
### 1.11.2 Antidepressants for behaviour that challenges as an indirect outcome

#### *Citalopram versus placebo for behaviour that challenges as an indirect outcome*



### 1.11.3 Antihistamines for behaviour that challenges as a direct outcome

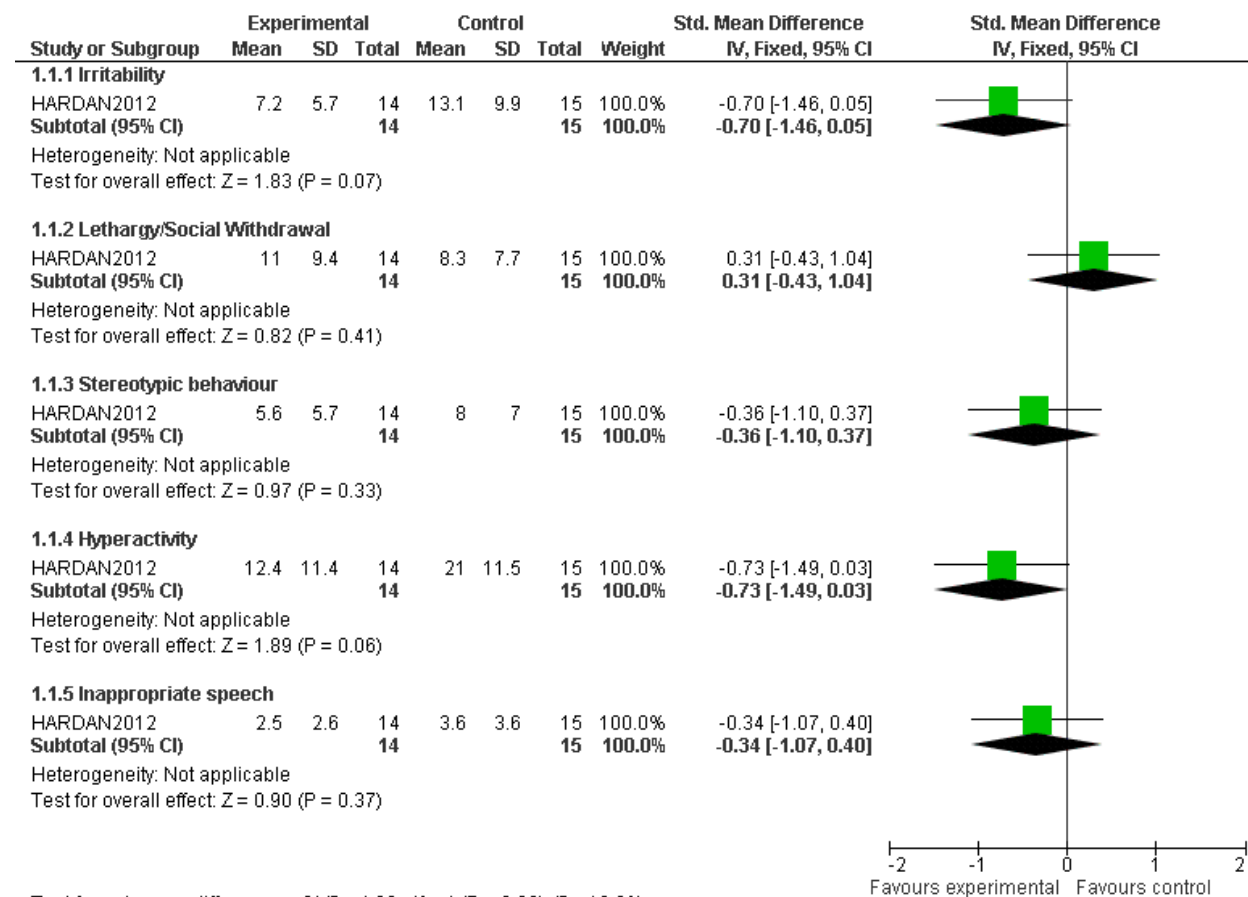
#### *Cyproheptadine and haloperidol versus placebo and haloperidol for behaviour that challenges as a direct outcome*



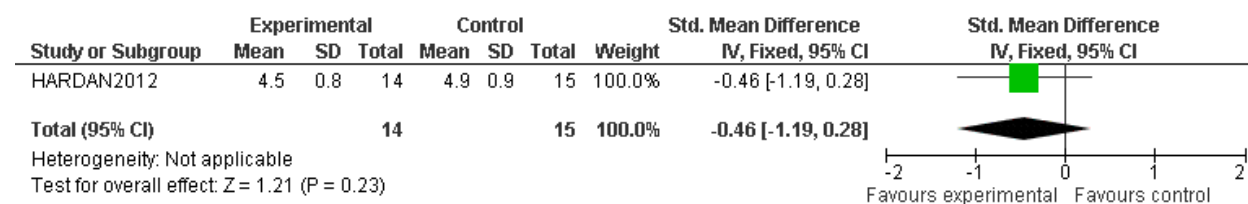
### 1.11.4 Antioxidants for behaviour that challenges as a direct outcome

#### *N-acetylcysteine versus placebo for behaviour that challenges as a direct outcome*

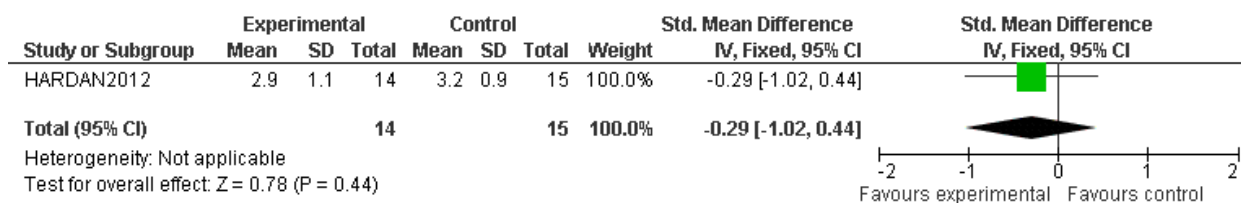
##### Behaviour that challenges (ABC)



##### Global severity (CGI-S)



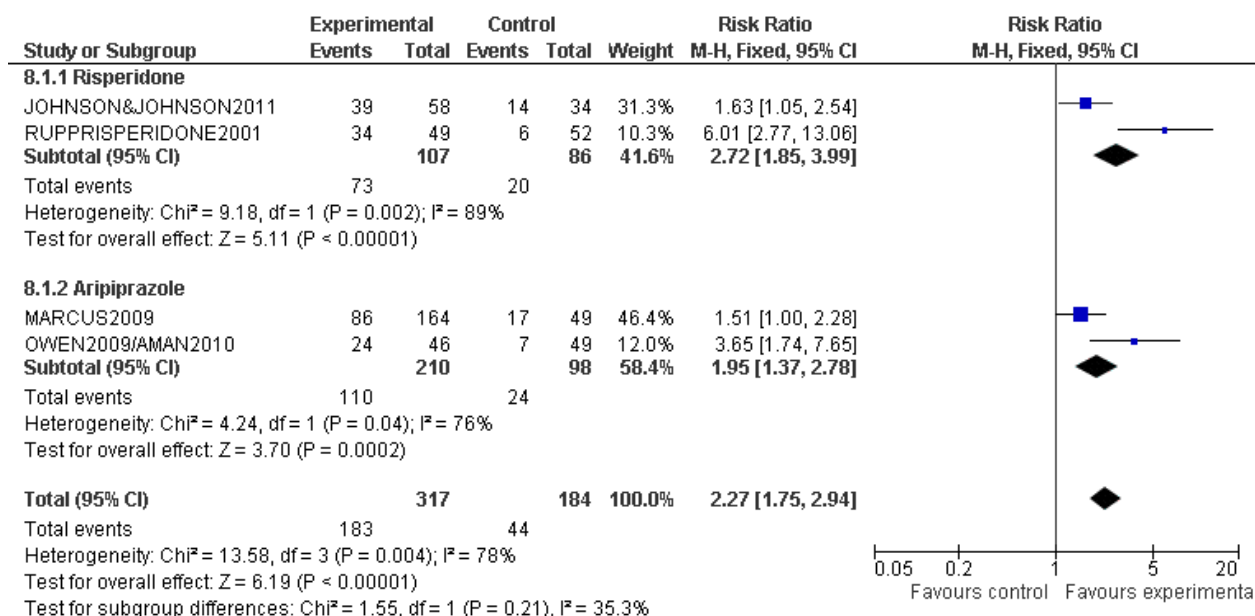
##### Global improvement (CGI-I)



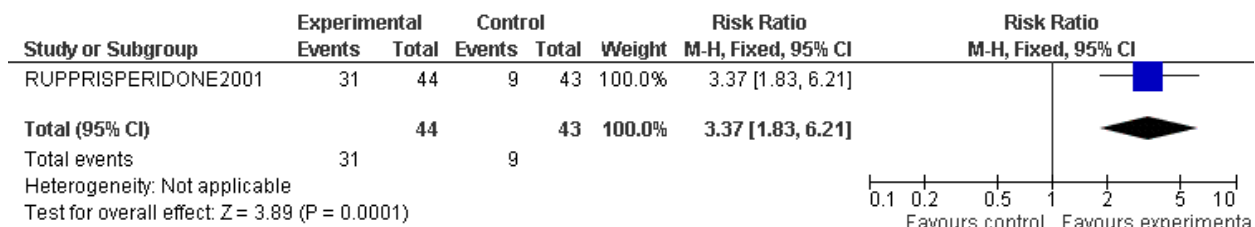
### 1.11.5 Antipsychotics for behaviour that challenges as a direct or indirect outcome

#### *Antipsychotic (risperidone or aripiprazole) versus placebo for behaviour that challenges as a direct outcome*

#### Positive treatment response (clinician-rated: >25% improvement on ABC-Irritability with or without 'much improved/very improved' on CGI-improvement)

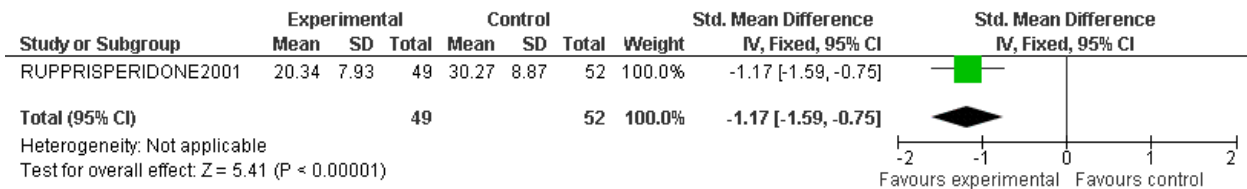


#### Positive treatment response (parent-defined target symptoms)

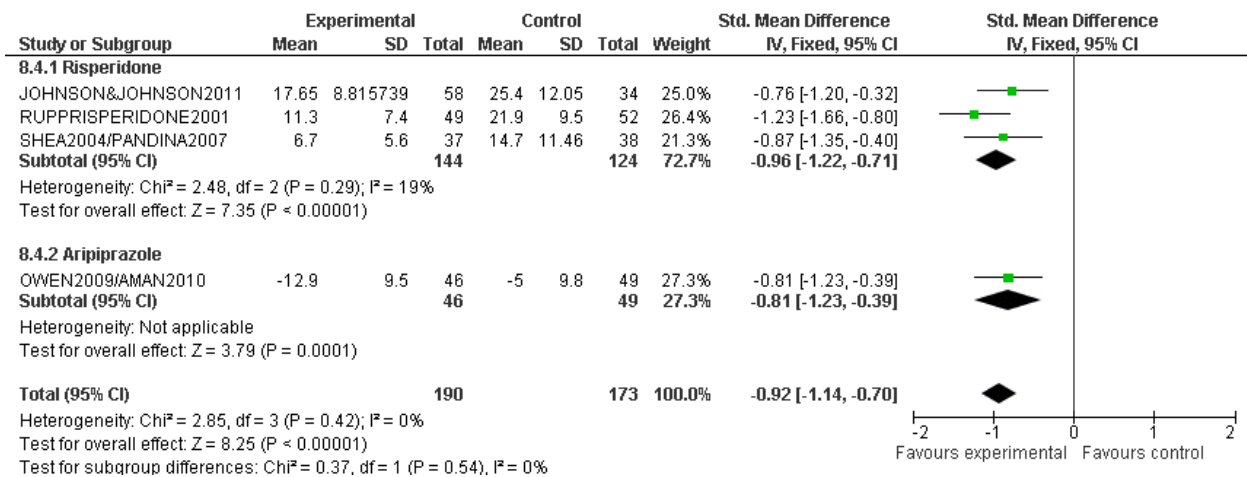




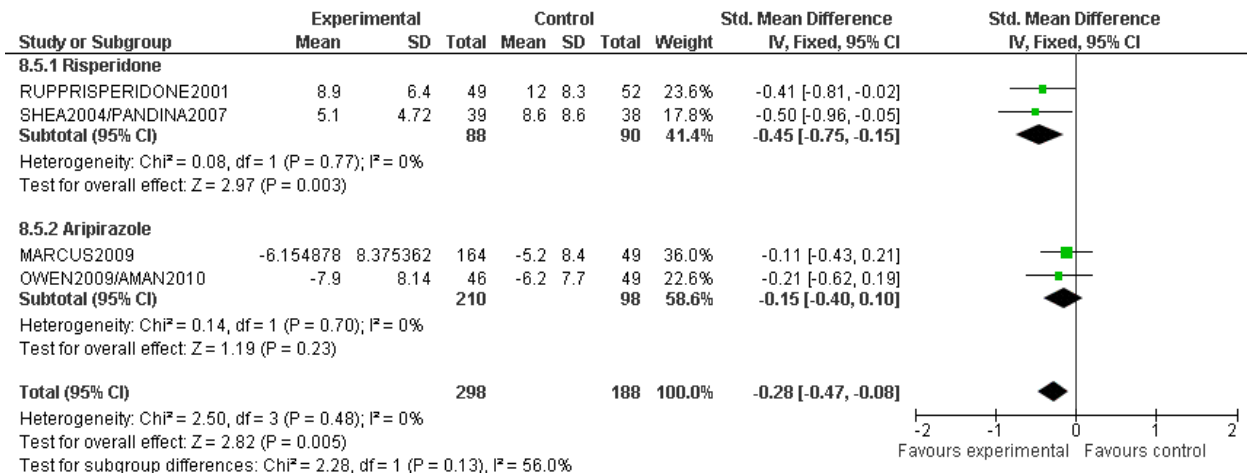
## Maladaptive behaviour (VABS)



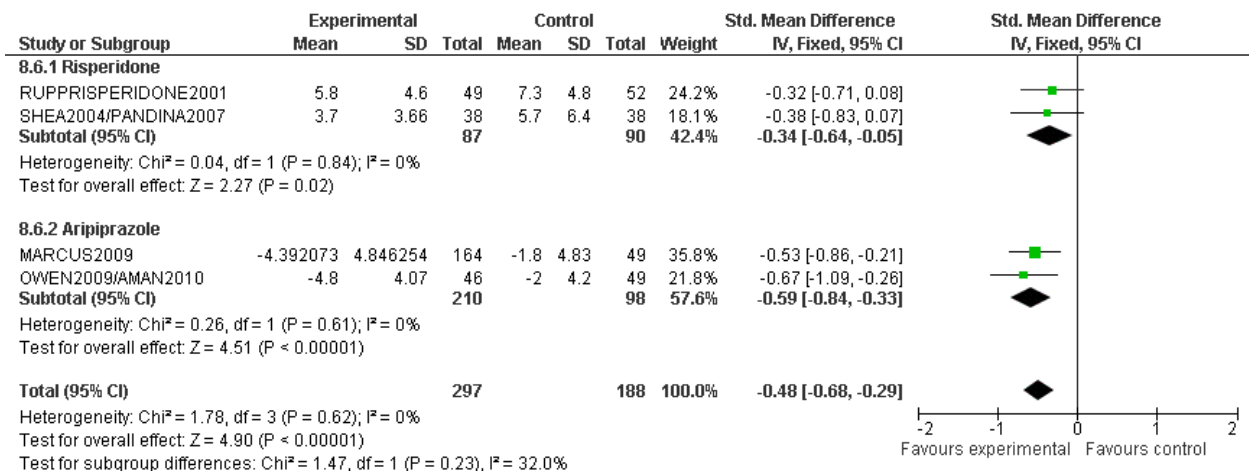
## Irritability (ABC)



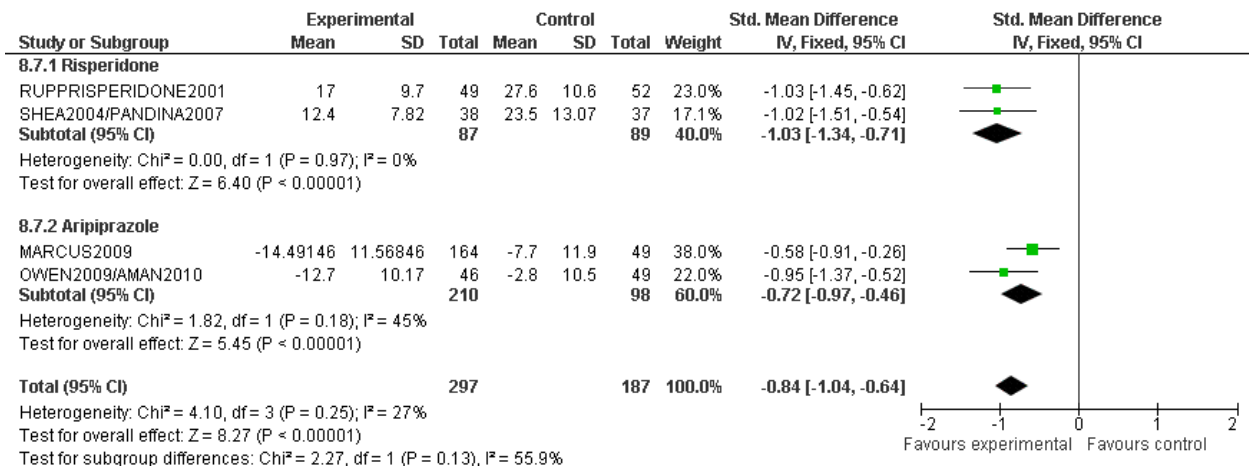
## Lethargy/Social withdrawal (ABC)



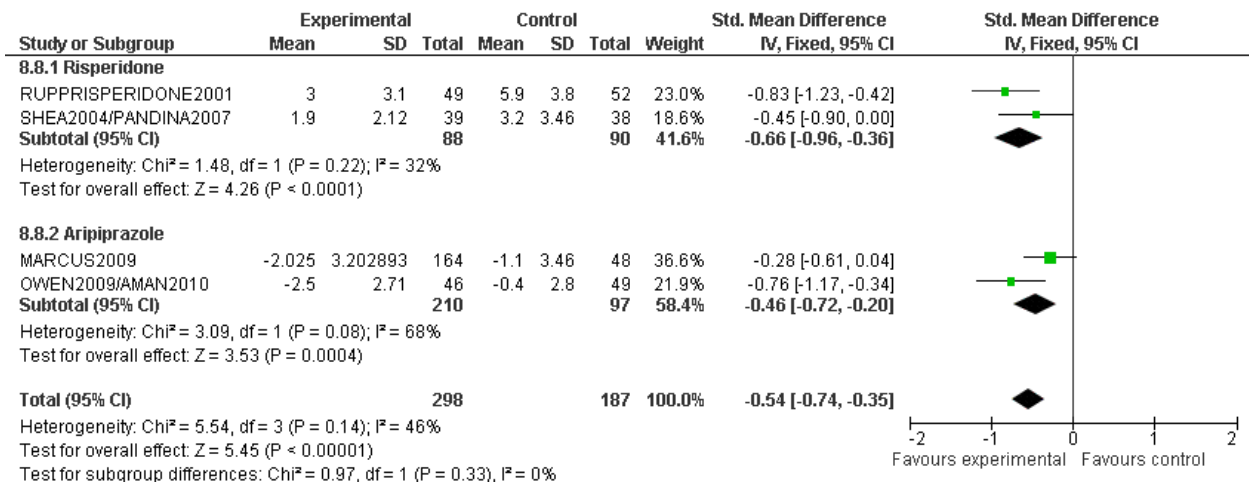
## Stereotypic behaviour (ABC)



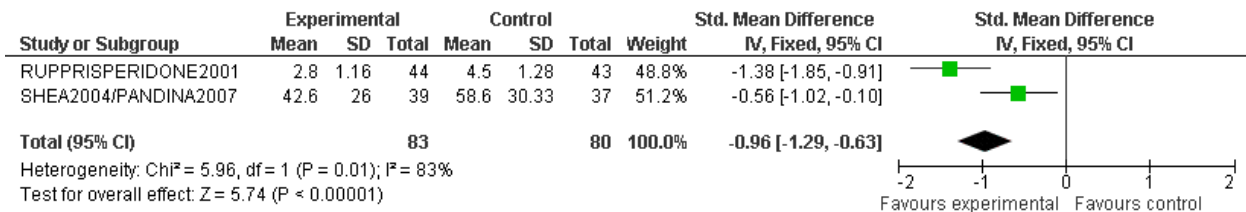
### Hyperactivity (ABC)



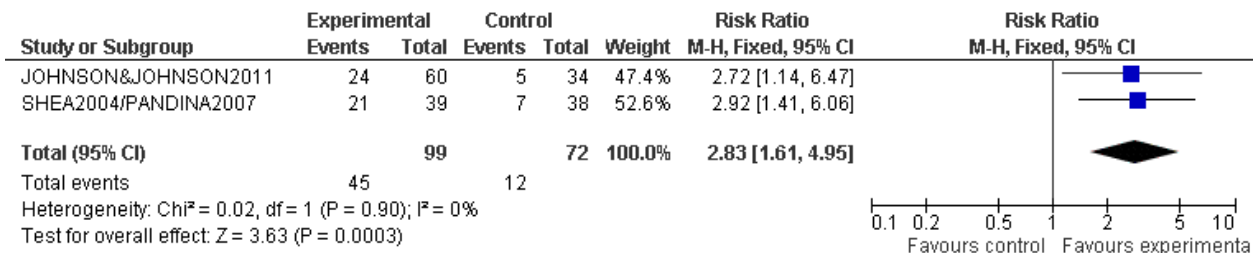
### Inappropriate speech (ABC)



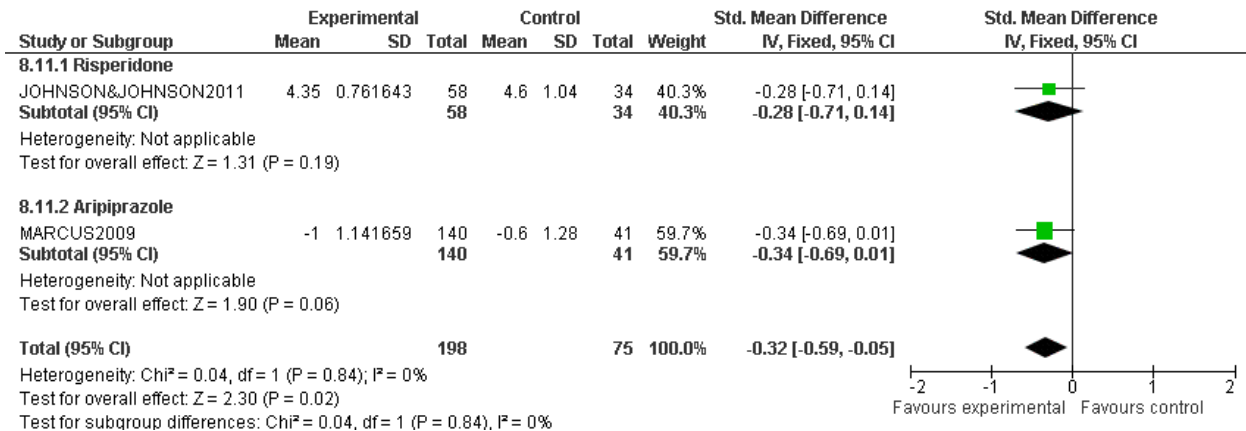
Parent-defined target symptoms



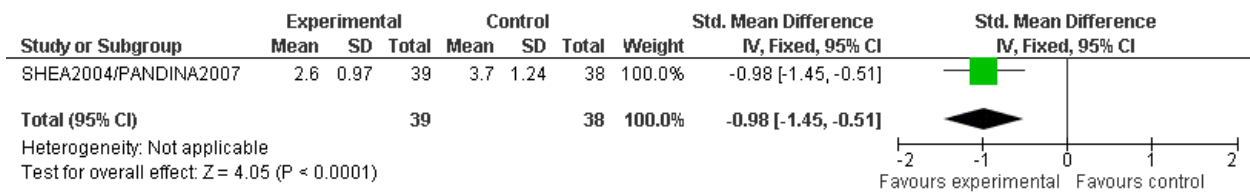
Global state: Positive treatment response (CGI)



Global severity (CGI-S)

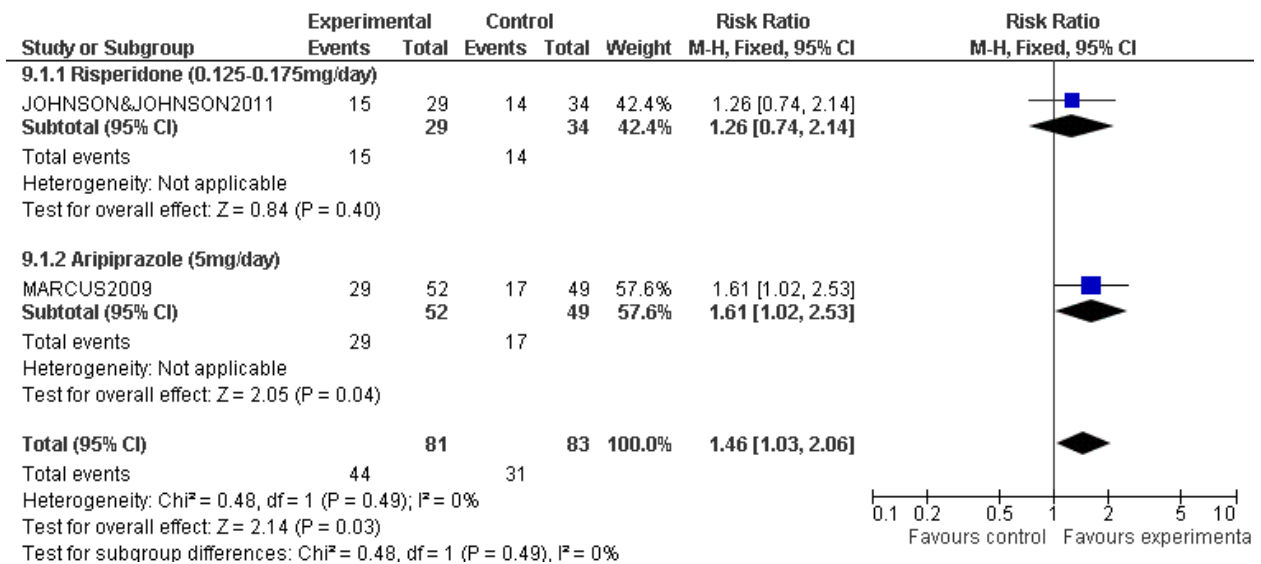


Global improvement (CGI-I)

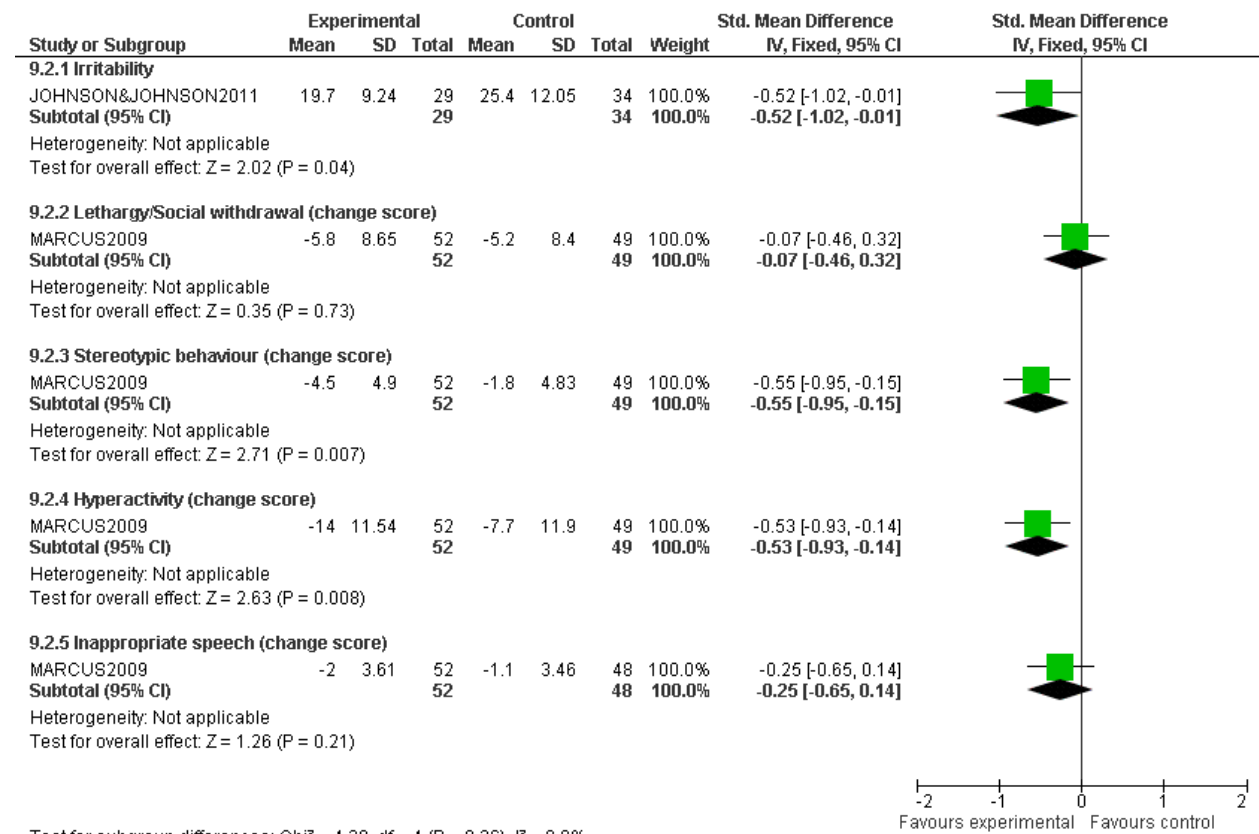


*Low dose antipsychotic (risperidone or aripiprazole) versus placebo for behaviour that challenges as a direct outcome*

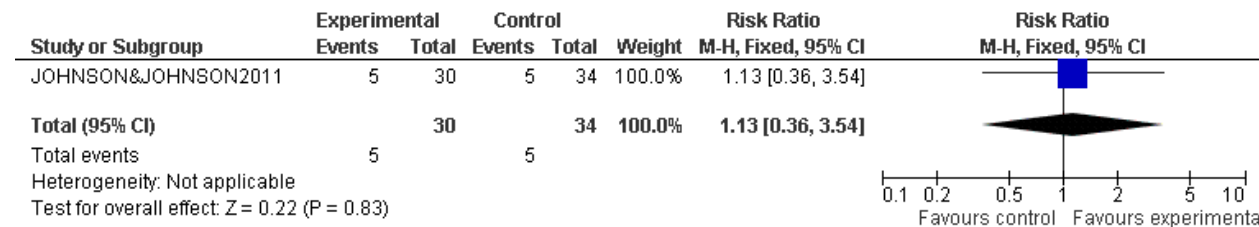
**Positive treatment response (clinician-rated: >25% improvement on ABC-Irritability with or without 'much improved/very improved' on CGI-improvement)**



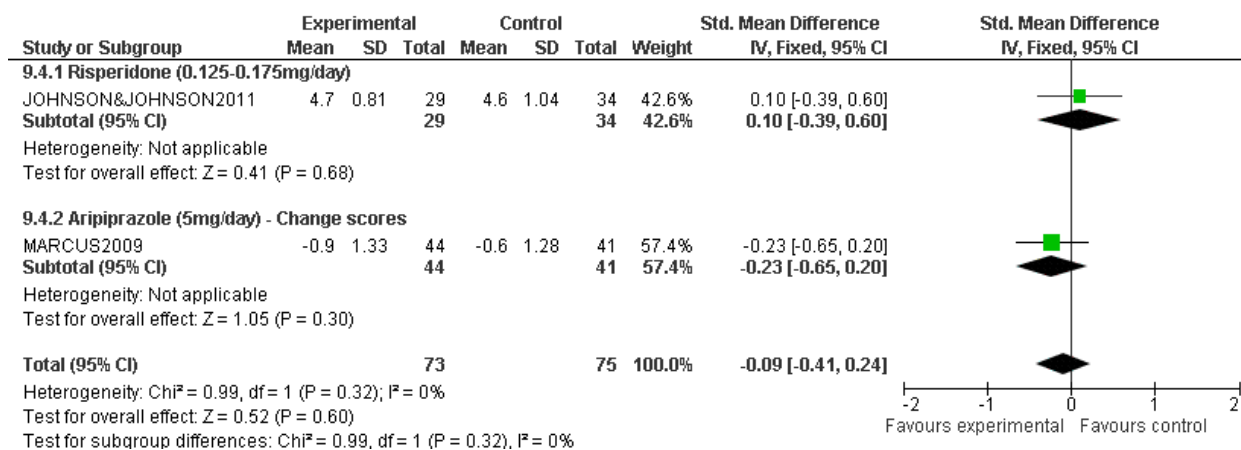
**Behaviour that challenges (ABC)**



**Global state: Positive treatment response (CGI)**

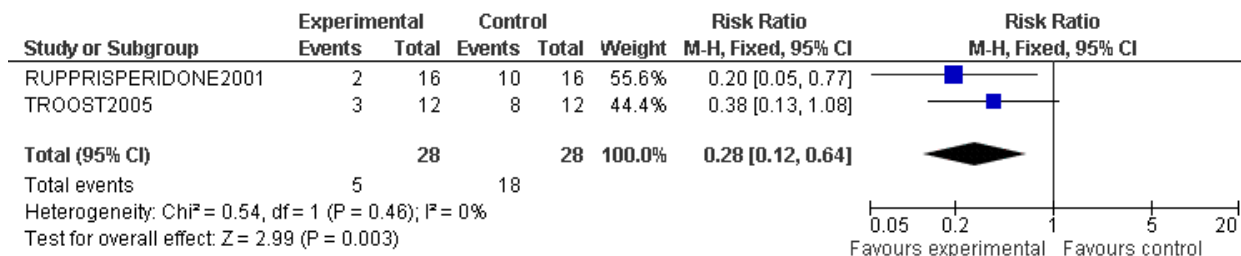


**Global severity (CGI-S)**

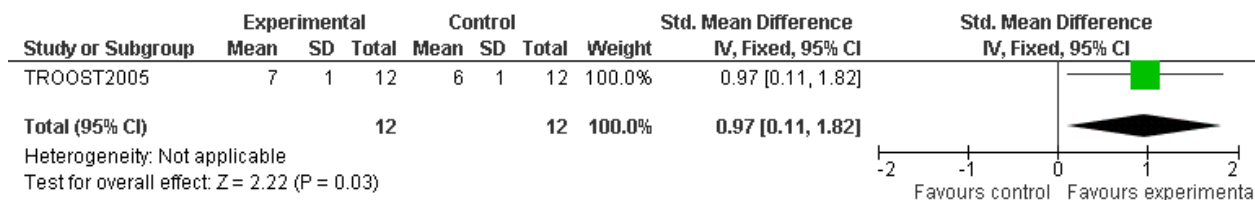


*Continued risperidone versus switch to placebo for behaviour that challenges as a direct outcome*

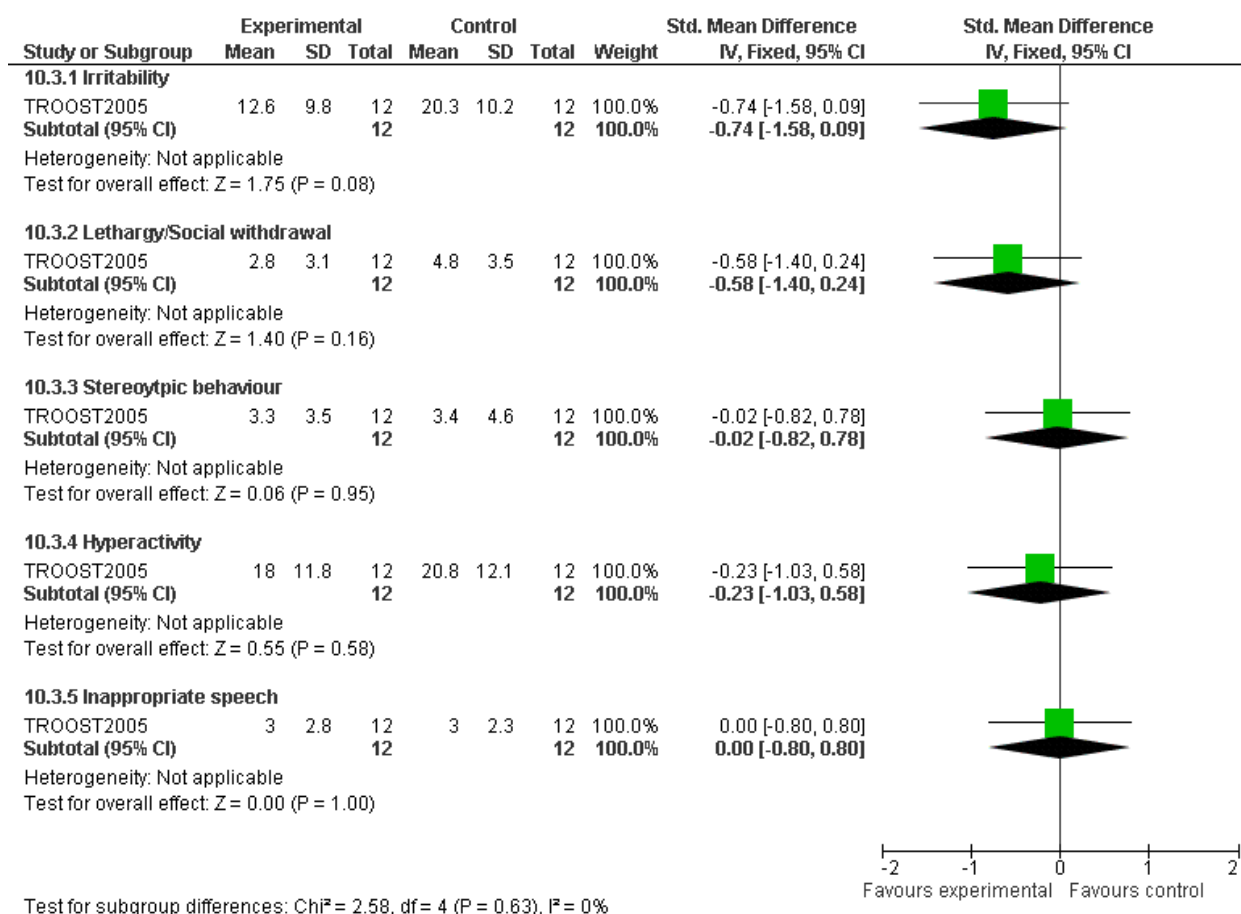
**Relapse rate after discontinuation**



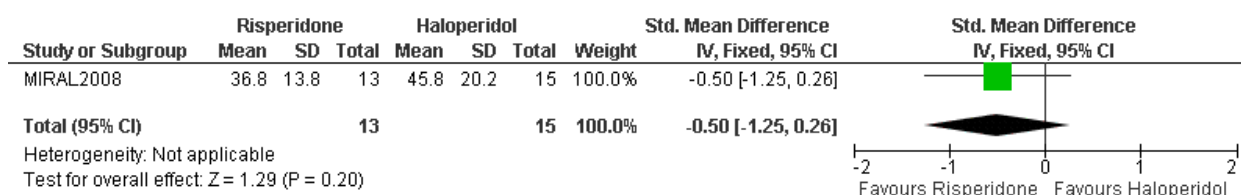
**Time to relapse after discontinuation (in weeks)**



**Behaviour that challenges (ABC)**



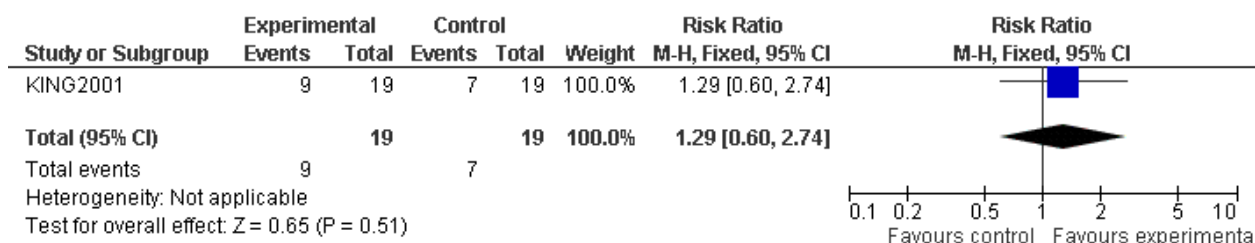
**Risperidone versus haloperidol for behaviour that challenges as an indirect outcome**



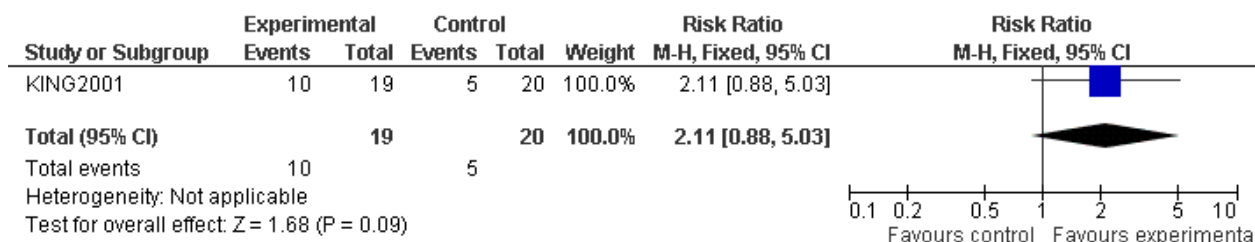
**1.11.6 Antivirals for behaviour that challenges as a direct outcome**

**Amantadine hydrochloride versus placebo for behaviour that challenges as a direct outcome**

**Positive parent-rated treatment response (>25% improvement on ABC-Irritability and/or hyperactivity)**

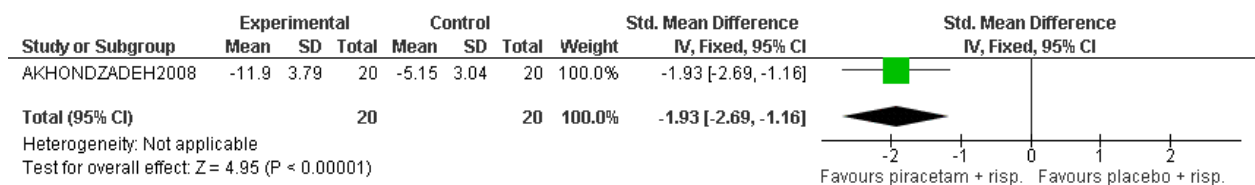


### Positive investigator-rated treatment response ('much improved/very improved' on CGI-improvement)



### 1.11.7 Cognitive enhancers for behaviour that challenges as a direct outcome

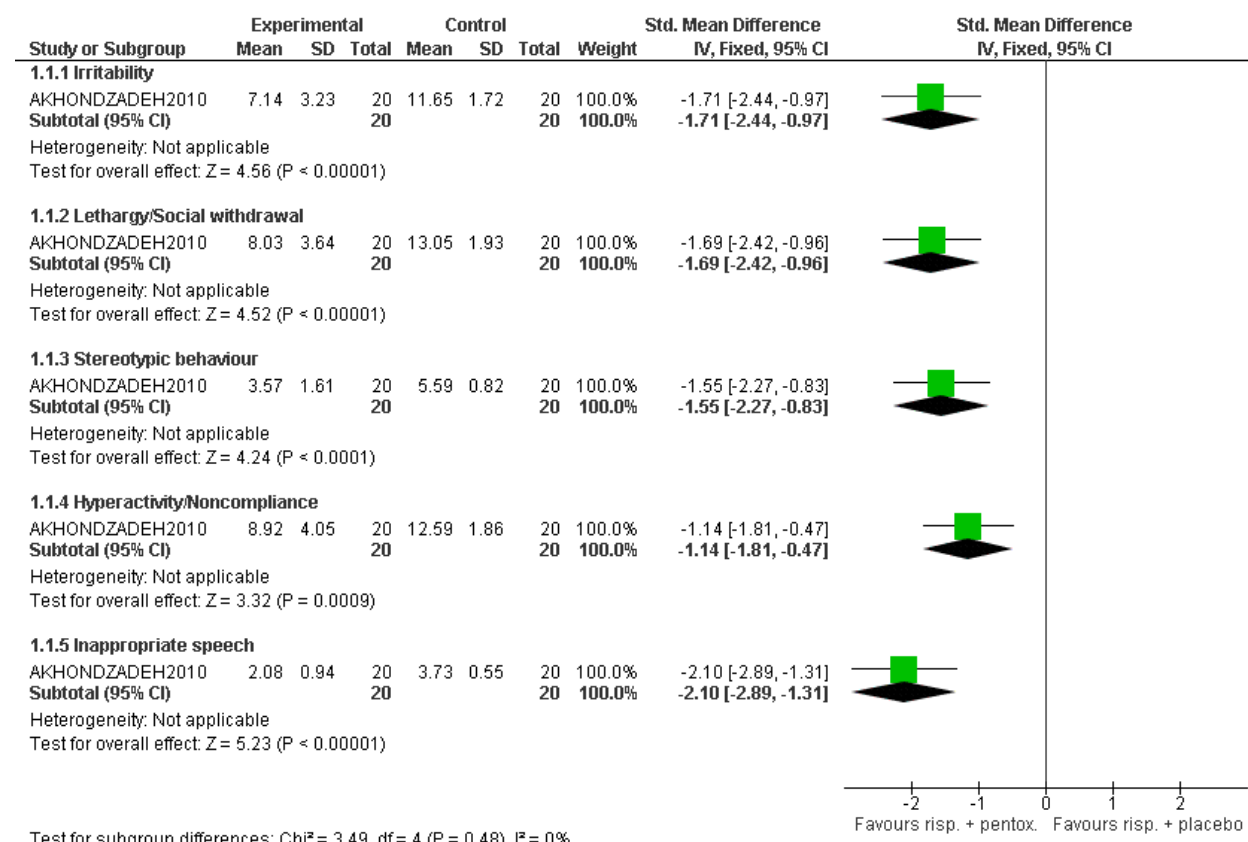
#### *Piracetam and risperidone versus placebo and risperidone for behaviour that challenges as a direct outcome*



### 1.11.8 Methylxanthines for behaviour that challenges as a direct outcome

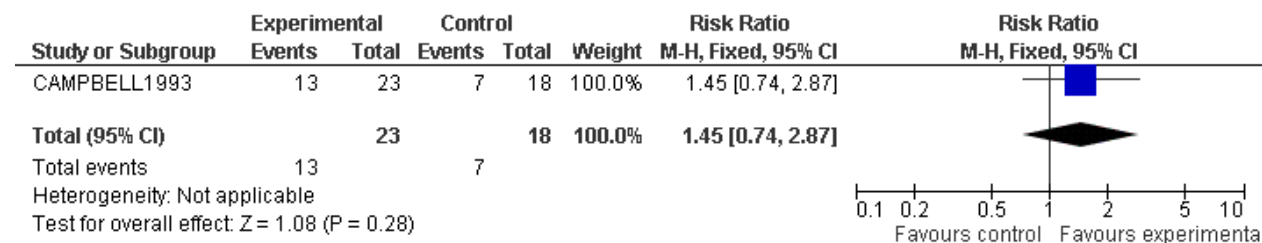
#### *Pentoxifylline and risperidone versus placebo and risperidone for behaviour that challenges as a direct outcome*





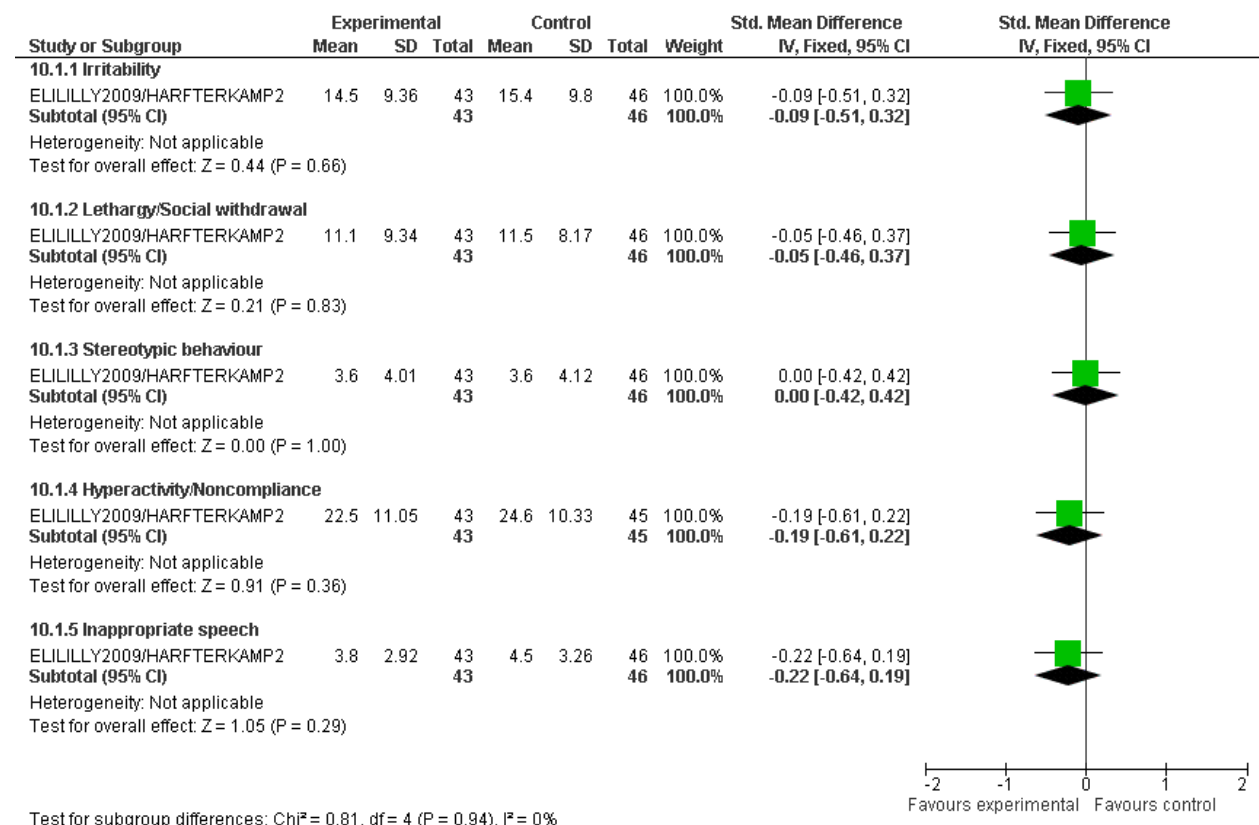
### 1.11.9 Opioid antagonists for behaviour that challenges as a direct outcome

#### *Naltrexone versus placebo for behaviour that challenges as a direct outcome*



### 1.11.10 Selective noradrenaline reuptake inhibitors (SNRIs) for behaviour that challenges as an indirect outcome

#### *Atomoxetine versus placebo for behaviour that challenges as an indirect outcome*

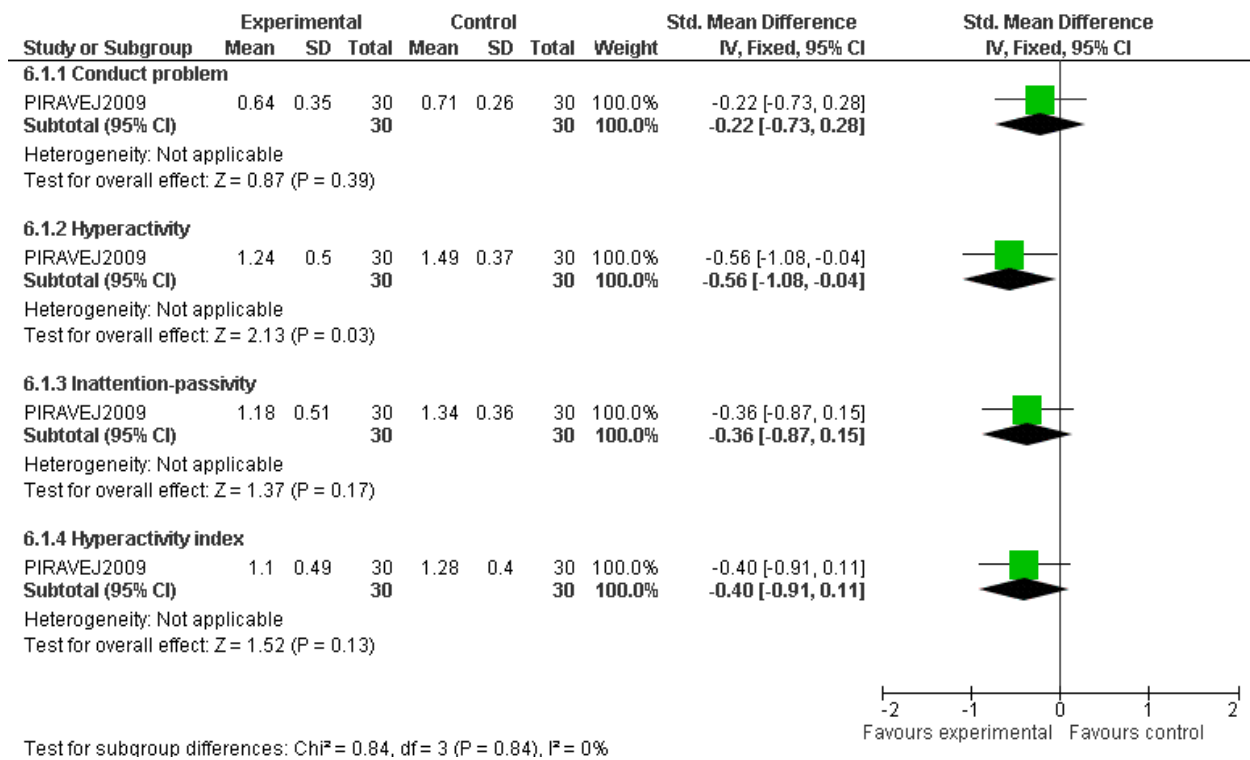


## 1.12 BIOMEDICAL INTERVENTIONS AIMED AT BEHAVIOUR THAT CHALLENGES

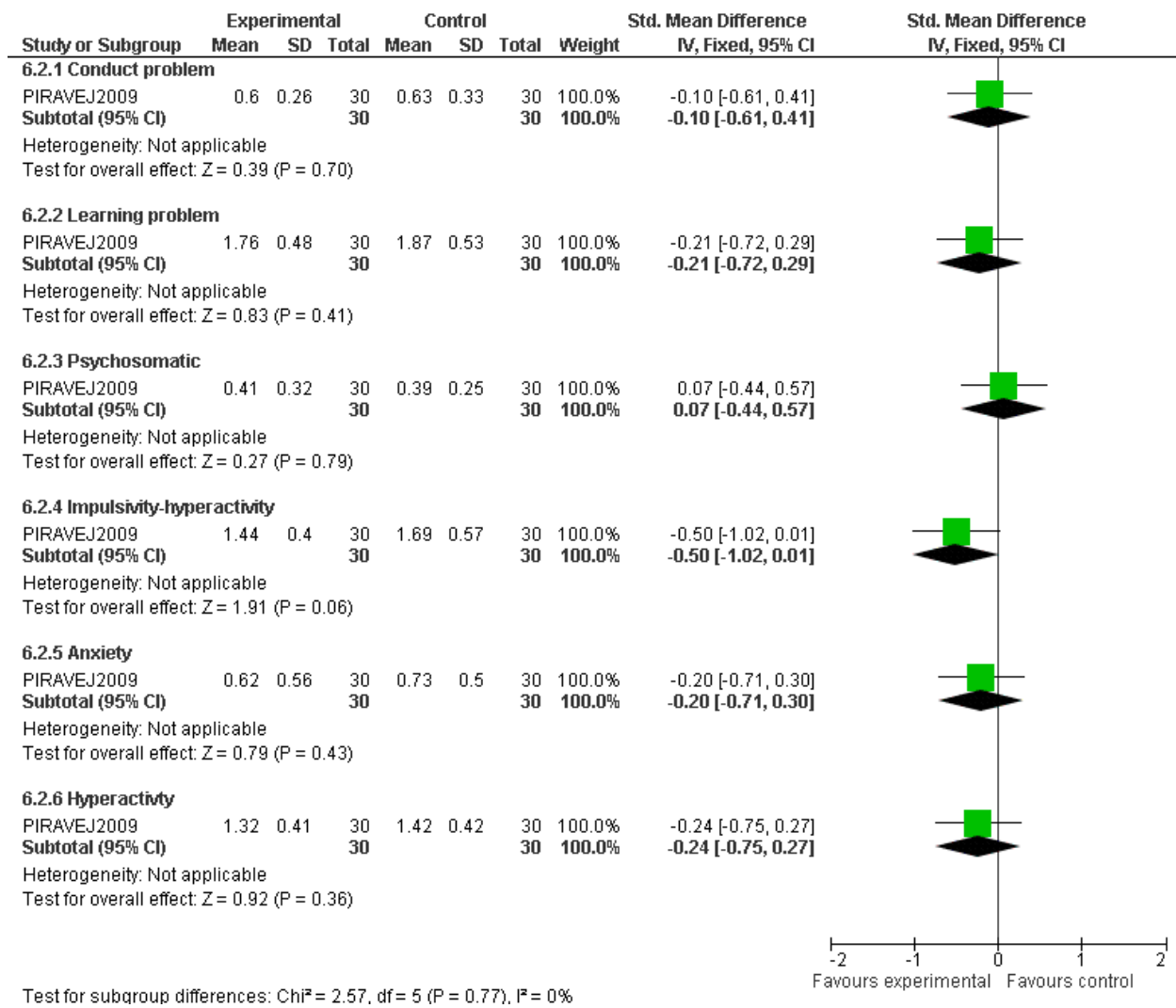
### 1.12.1 Complementary therapies for behaviour that challenges as a direct or indirect outcome

*Thai massage and sensory integration therapy versus sensory integration therapy only for behaviour that challenges as a direct outcome*

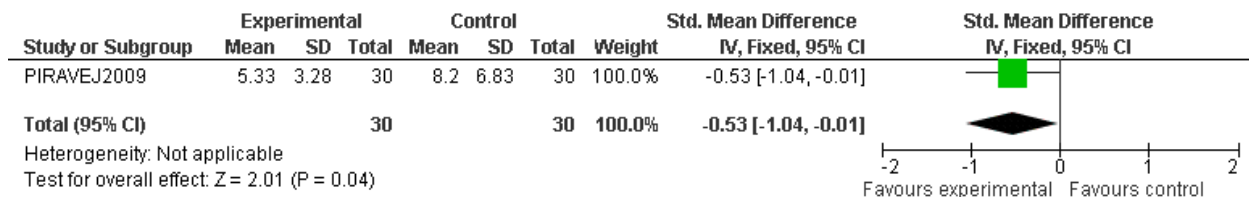
Teacher-rated behaviour that challenges (CTRS)



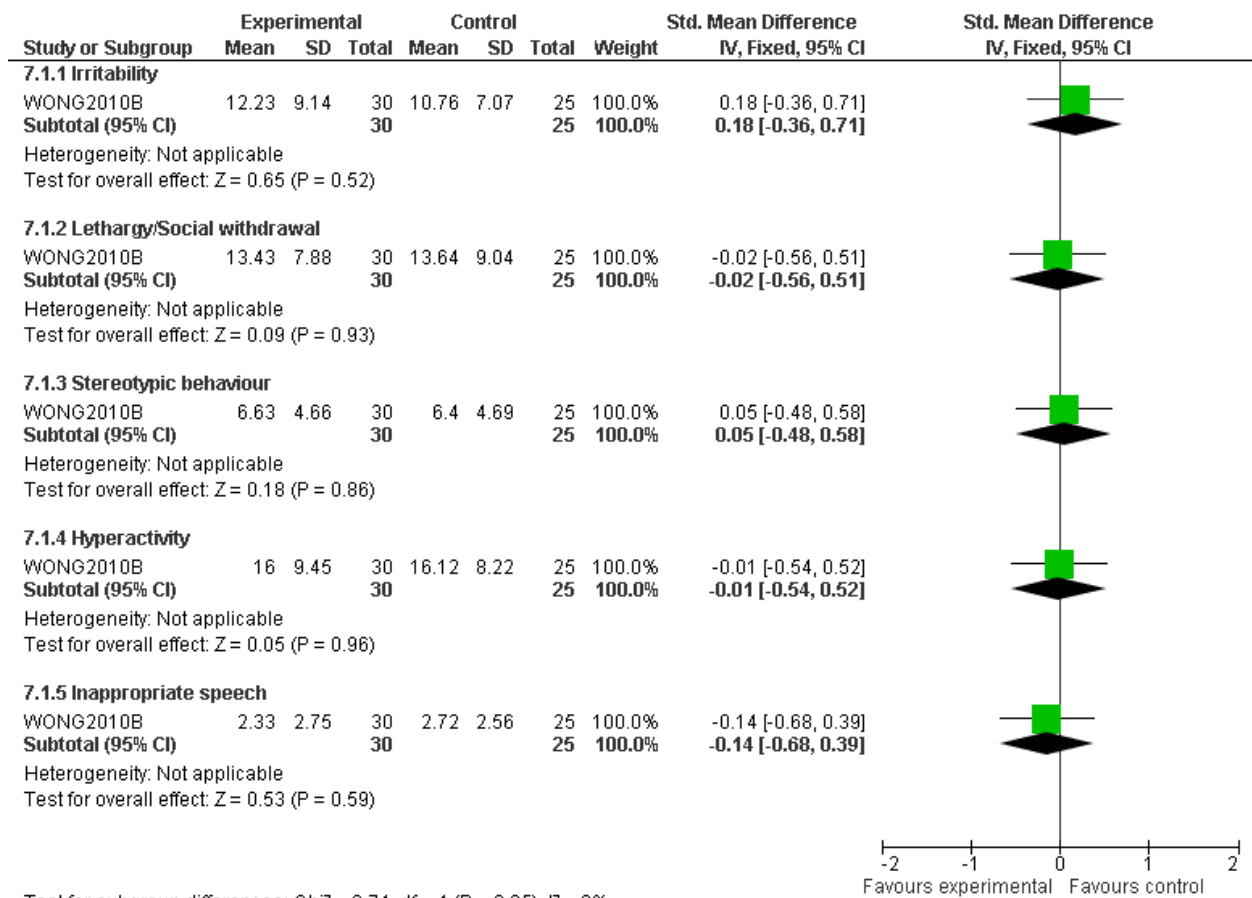
**Parent-rated behaviour that challenges (CPRS)**



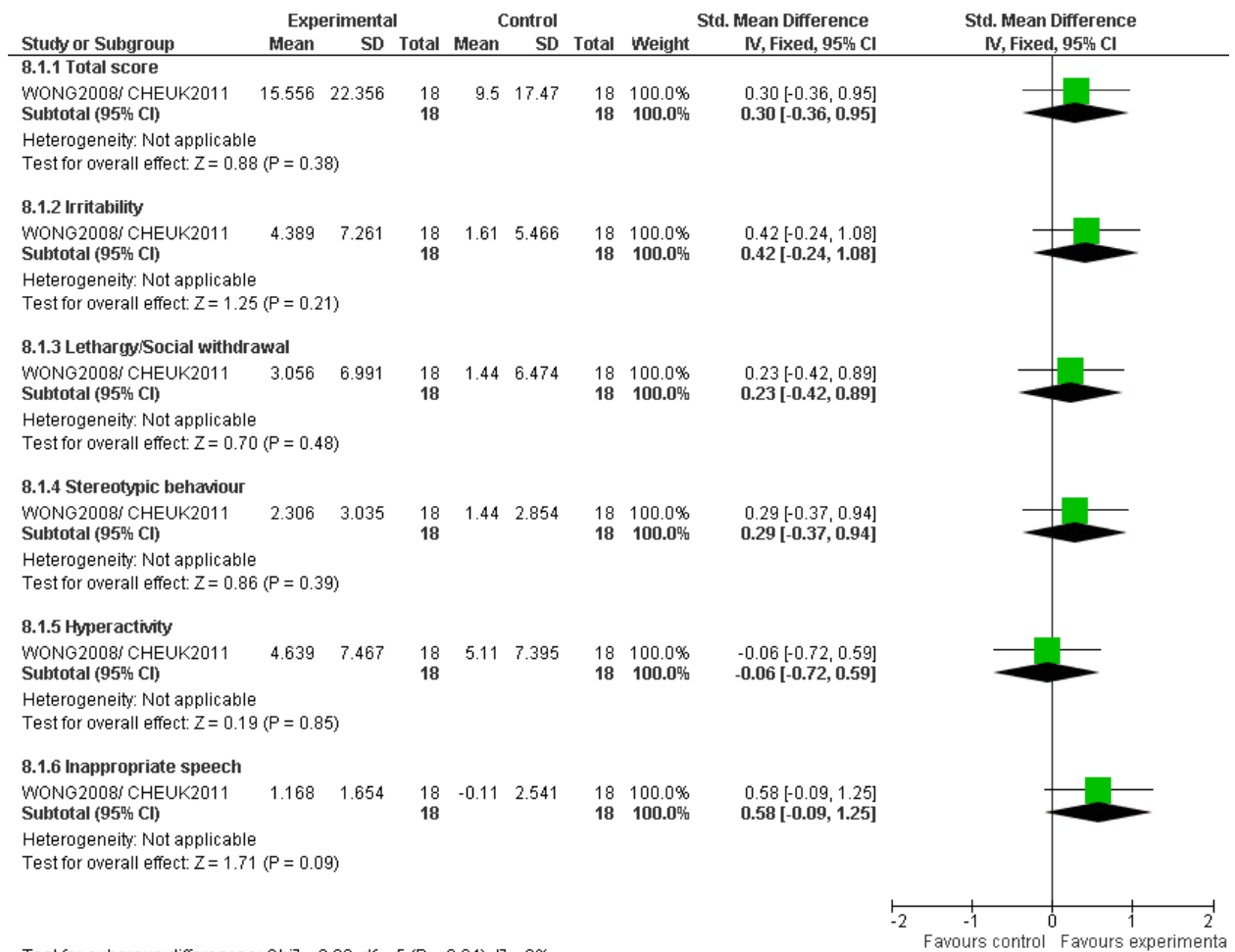
**Parent-rated sleep-related problems (sleep diary)**



*Electro-acupuncture versus sham electro-acupuncture for behaviour that challenges as an indirect outcome*



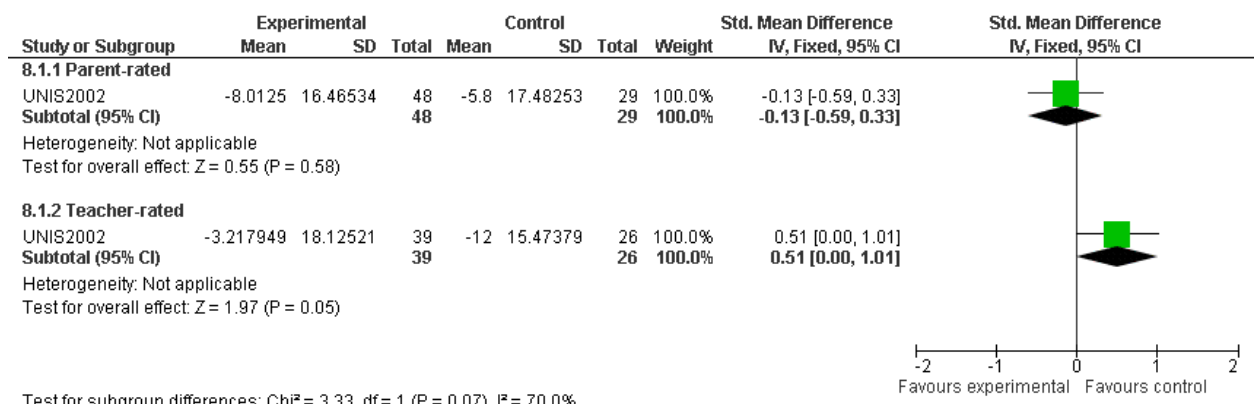
*Electro-acupuncture and conventional educational programme versus conventional educational programme only for behaviour that challenges as an indirect outcome*



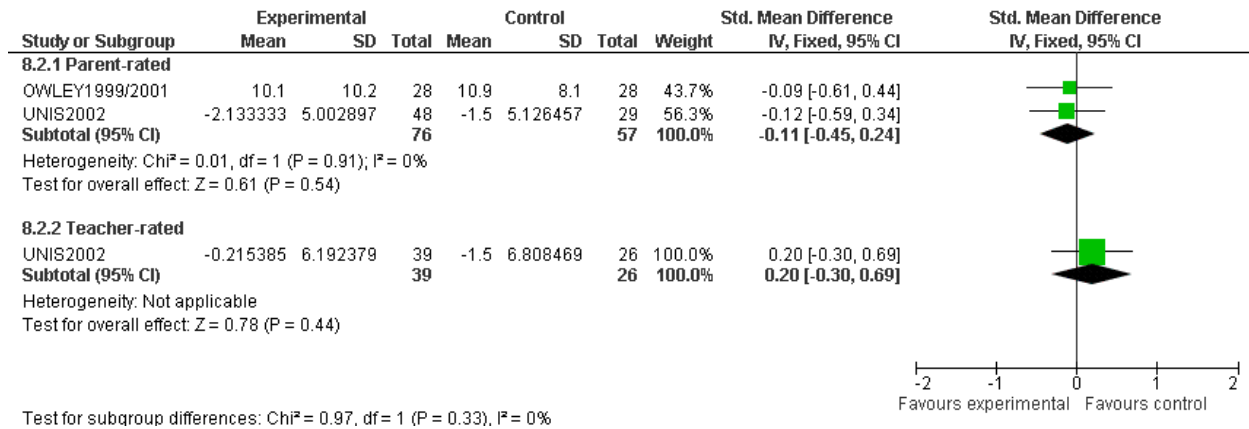
### 1.12.2 Hormones for behaviour that challenges as an indirect outcome

#### *Secretin versus placebo for behaviour that challenges as an indirect outcome*

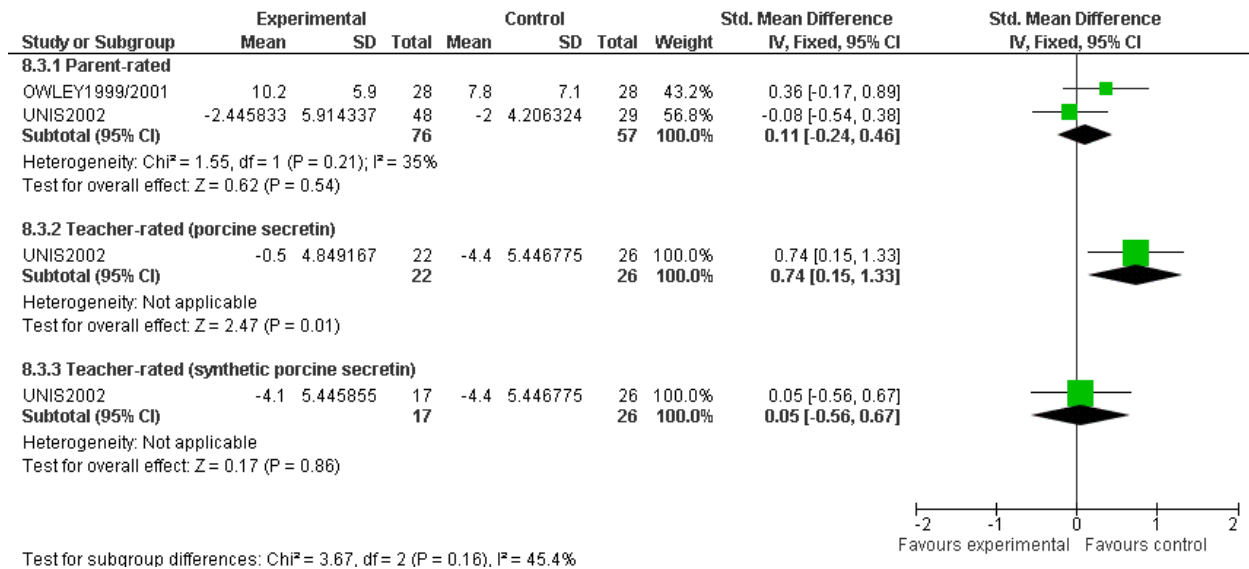
#### Behaviour that challenges (ABC total change score; porcine+synthetic groups combined)



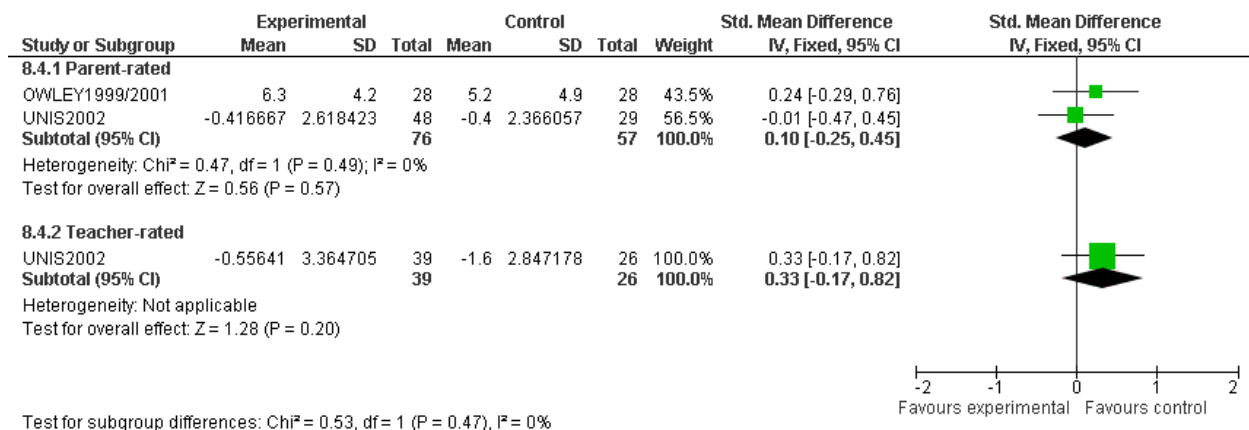
### Irritability (ABC; endpoint and change scores)



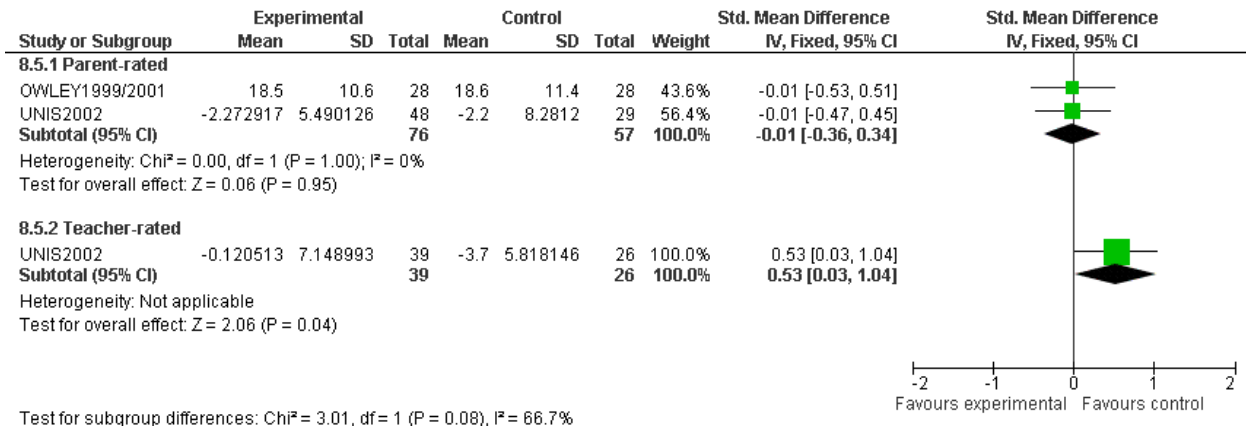
### Lethargy (ABC; endpoint and change scores)



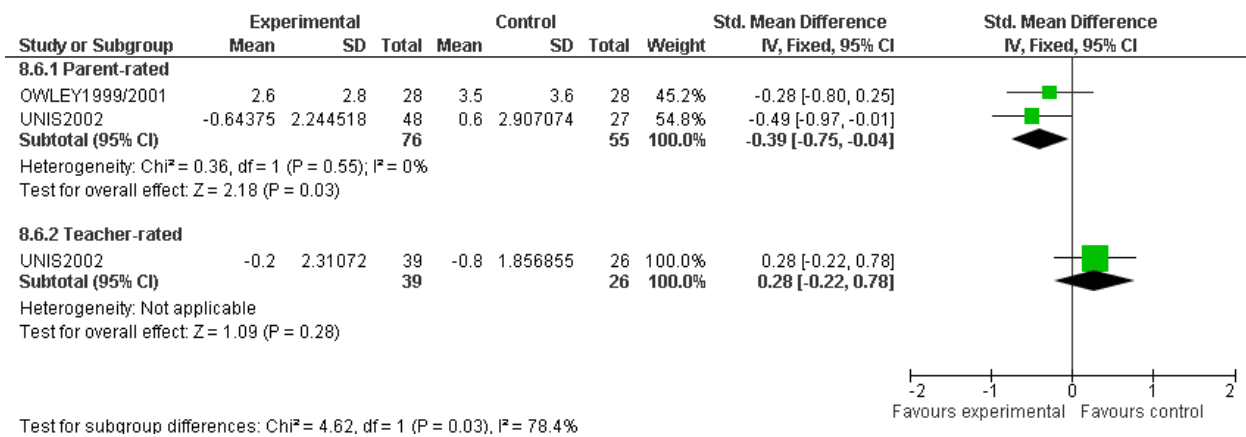
### Stereotyped behaviour (ABC; endpoint and change scores)



### Hyperactivity (ABC; endpoint and change scores)



### Inappropriate speech (ABC; endpoint and change scores)

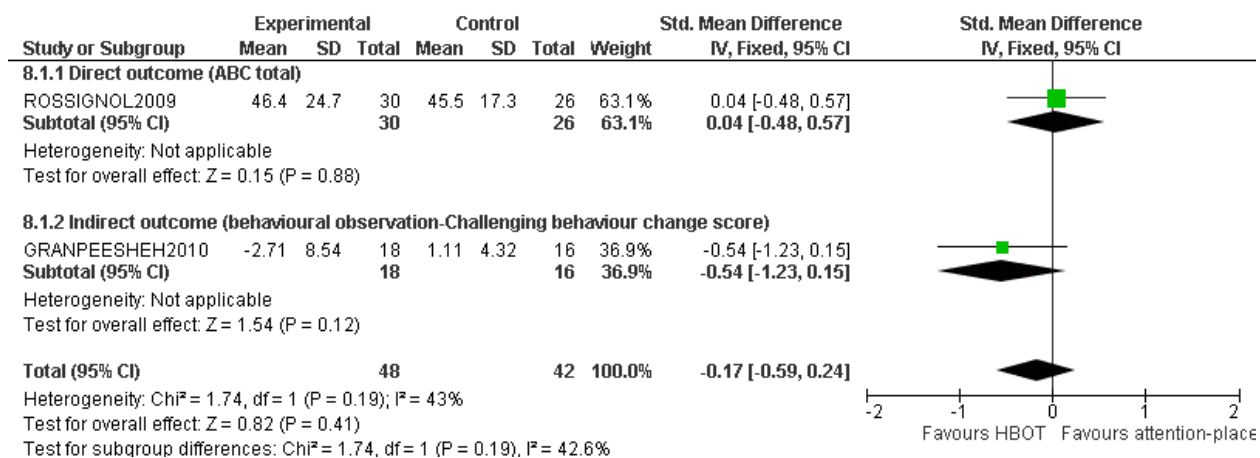


## 1.12.3 Medical procedures for behaviour that challenges as a direct or indirect outcome

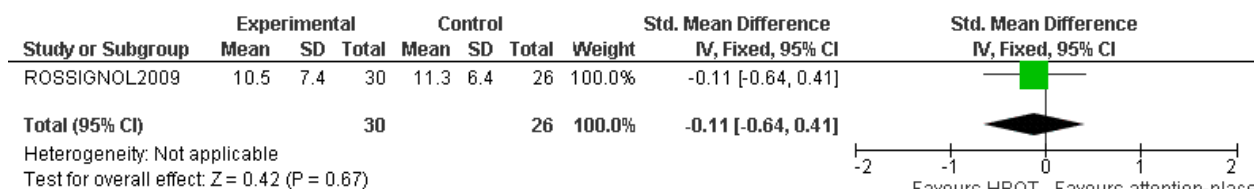
### *HBOT versus attention-placebo for behaviour that challenges as a direct or indirect outcome*

#### Behaviour that challenges

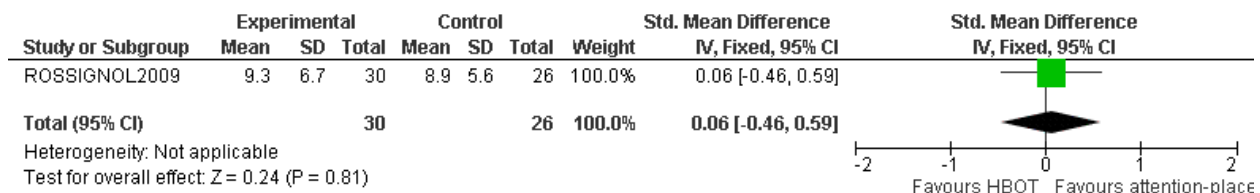




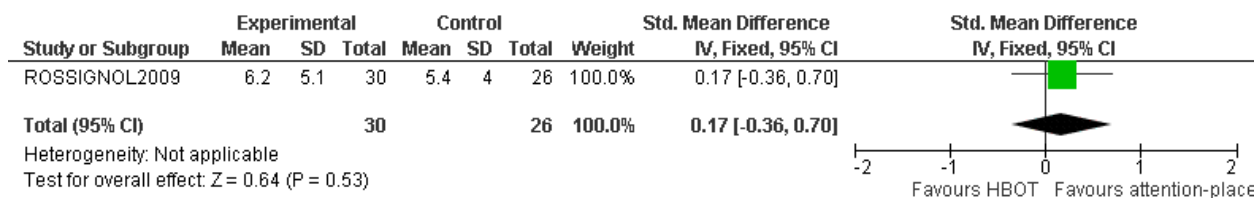
### Irritability (ABC; direct outcome)



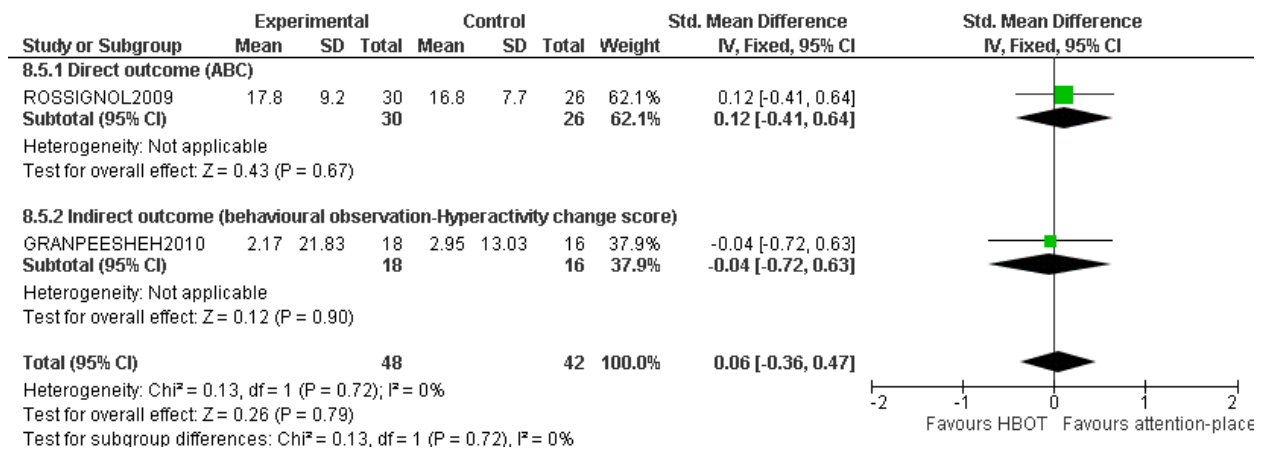
### Lethargy/Social withdrawal (ABC; direct outcome)



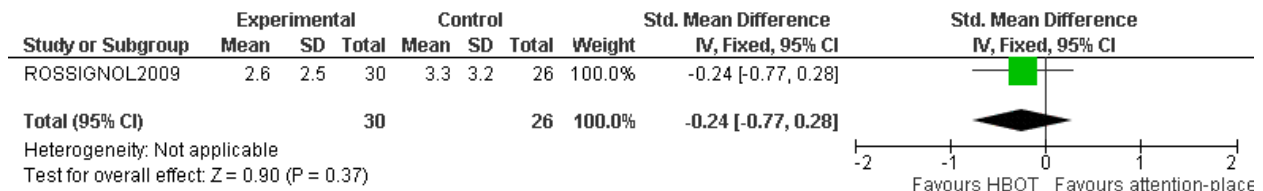
### Stereotypy (ABC; direct outcome)



### Hyperactivity

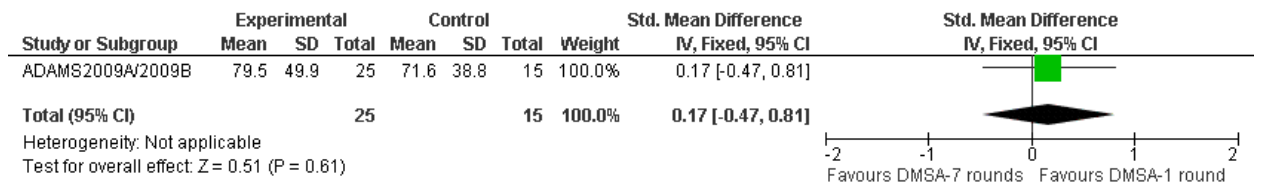


**Inappropriate speech (ABC; direct outcome)**

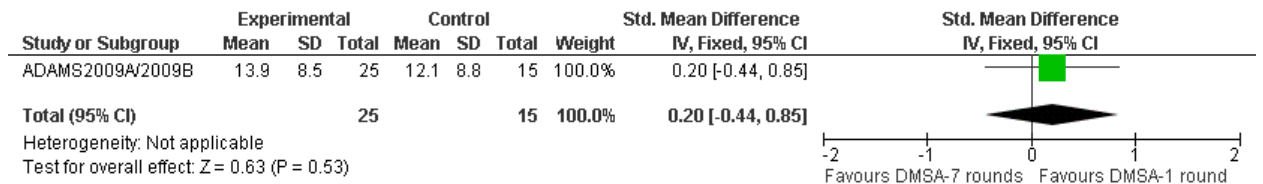


*Long-term chelation (7-rounds of DMSA therapy) versus short-term chelation (1-round of DMSA therapy and 6-rounds of placebo) for behaviour that challenges as an indirect outcome*

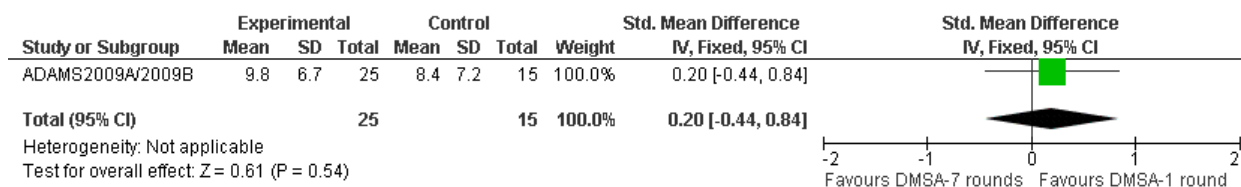
**Maladaptive Behaviours Composite (PDDBI)**



**Arousal Regulation Problems (PDDBI)**



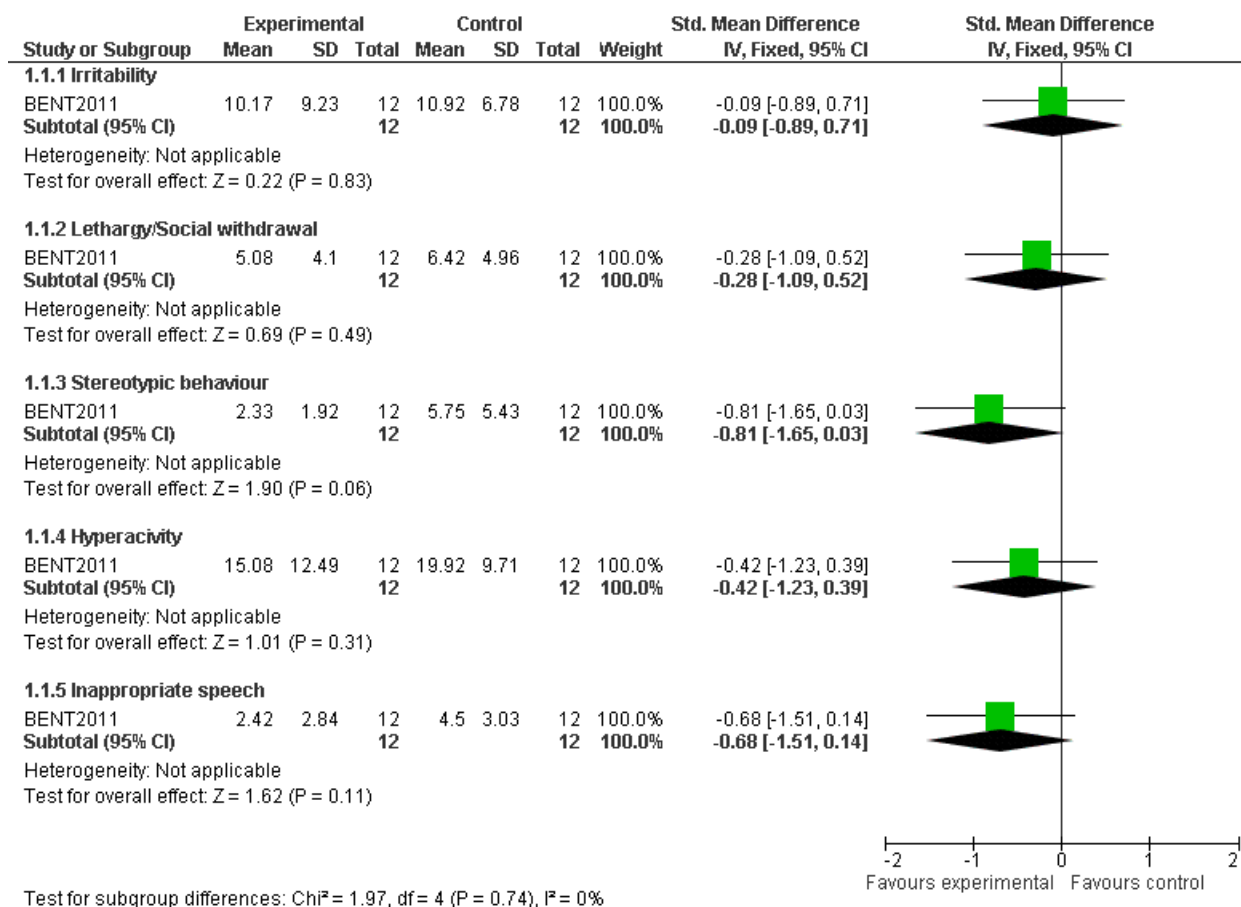
**Aggressiveness (PDDBI)**



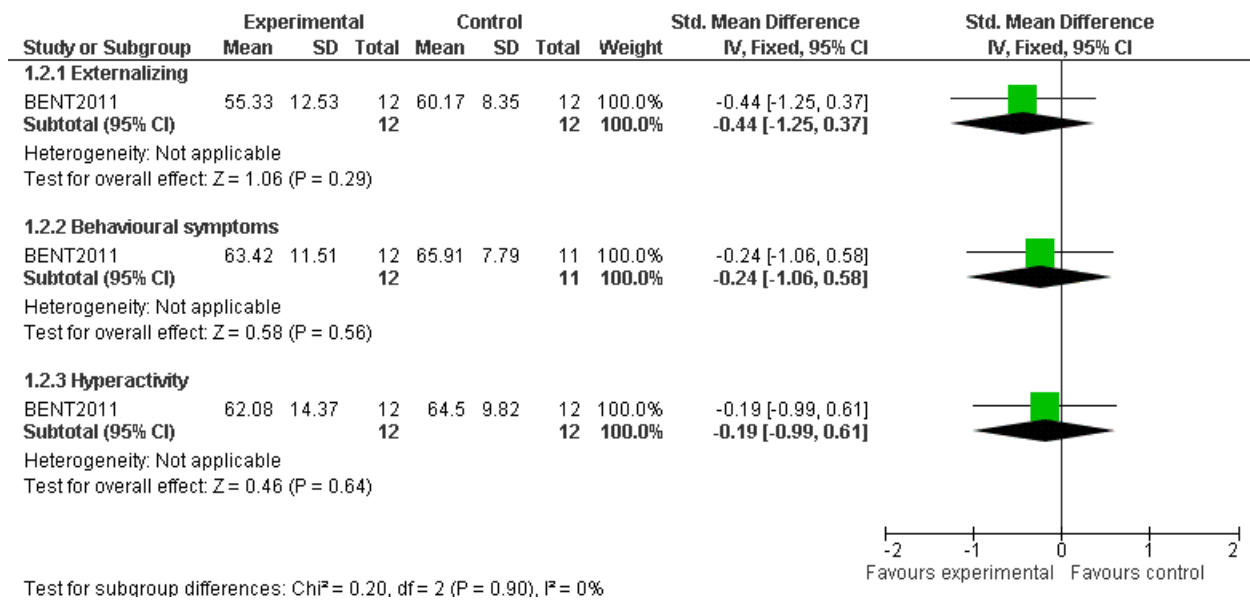
### 1.12.4 Nutritional interventions for behaviour that challenges as a direct or indirect outcome

#### *Omega-3 fatty acids versus placebo for behaviour that challenges as a direct outcome*

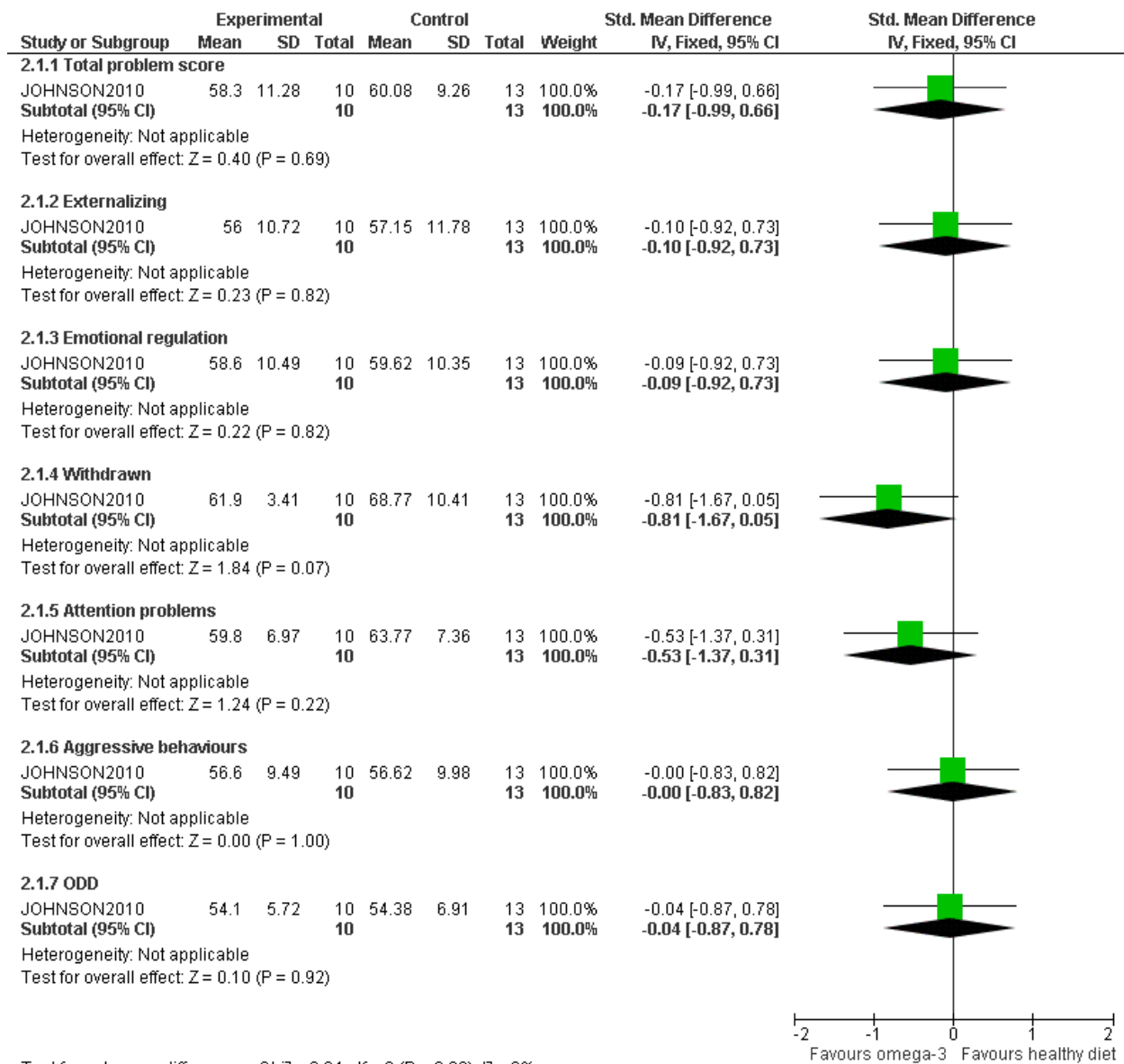
##### Behaviour that challenges (ABC)



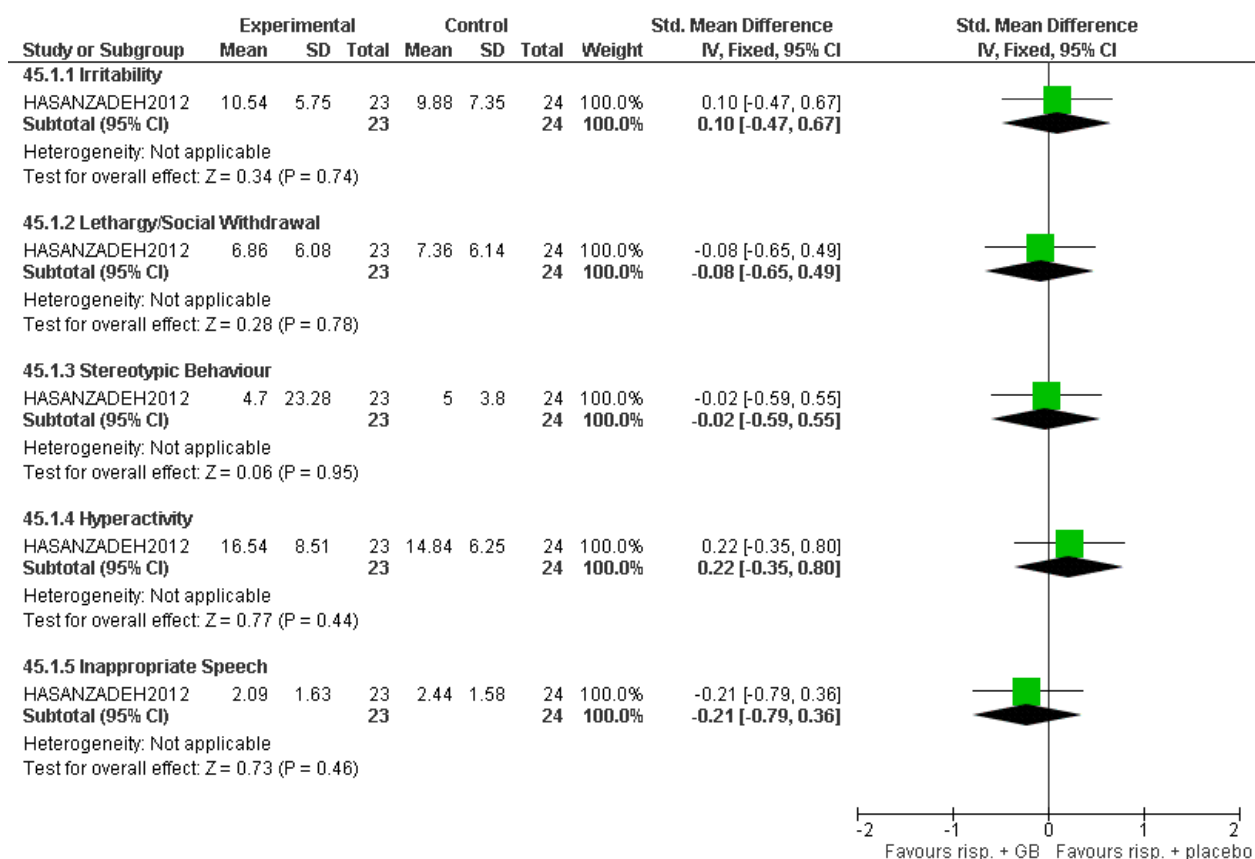
##### Behaviour that challenges (BASC)



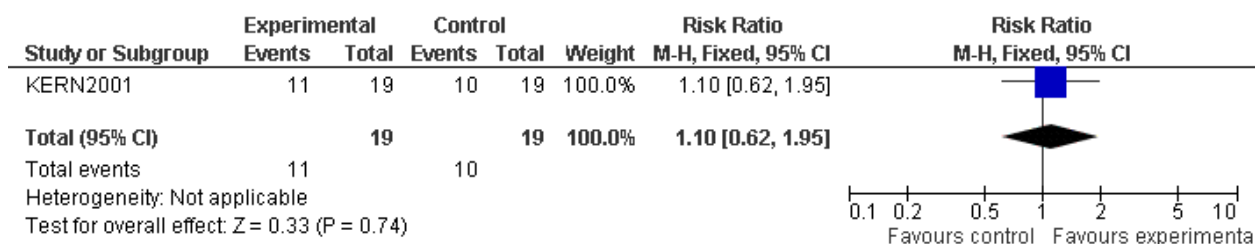
*Omega-3 fatty acids versus healthy diet control for behaviour that challenges as a direct outcome*



*Ginkgo biloba and risperidone versus placebo and risperidone for behaviour that challenges as a direct outcome*

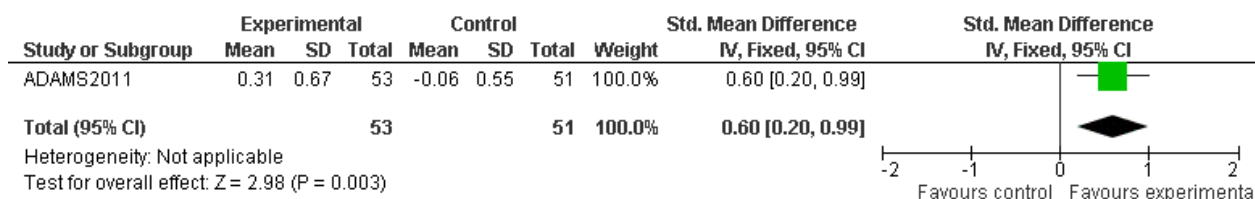


*Dimethylglycine supplement versus placebo for behaviour that challenges as a direct outcome*

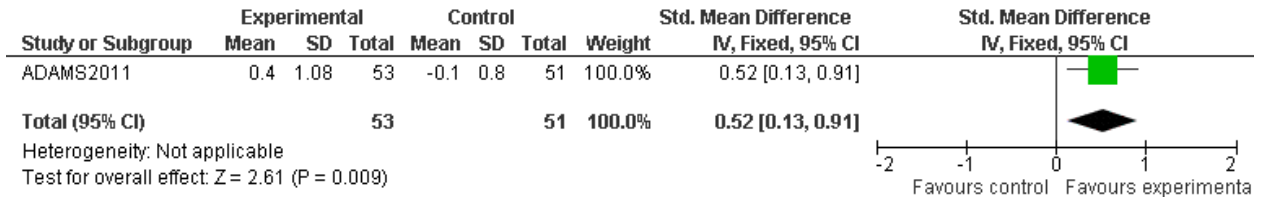


*Multivitamin/mineral supplement versus placebo for behaviour that challenges as an indirect outcome*

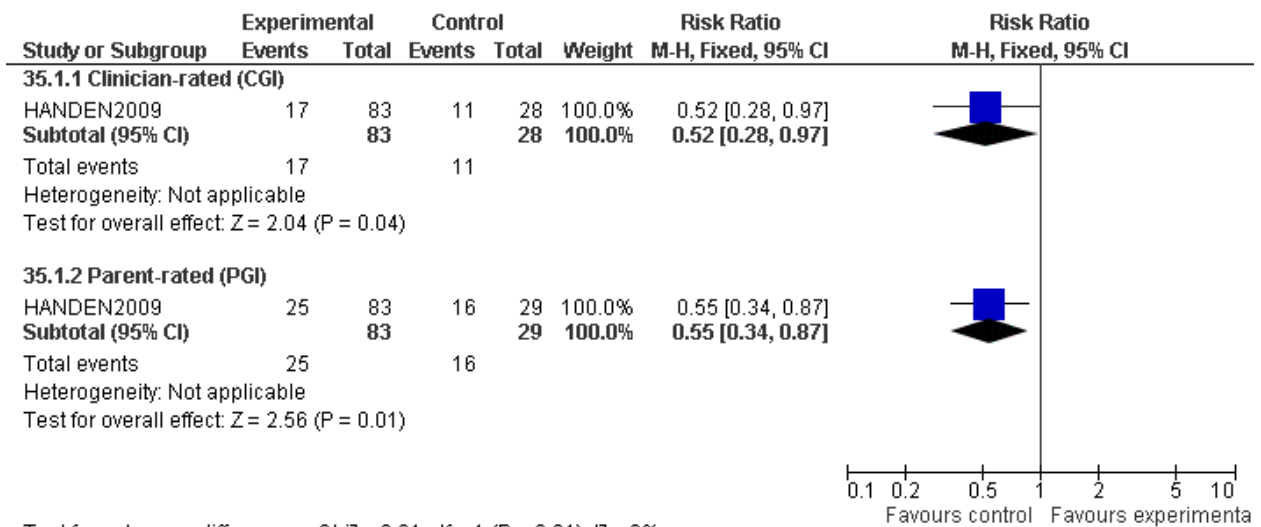
**Hyperactivity improvement (PGI-R)**



### Tantrumming improvement (PGI-R)



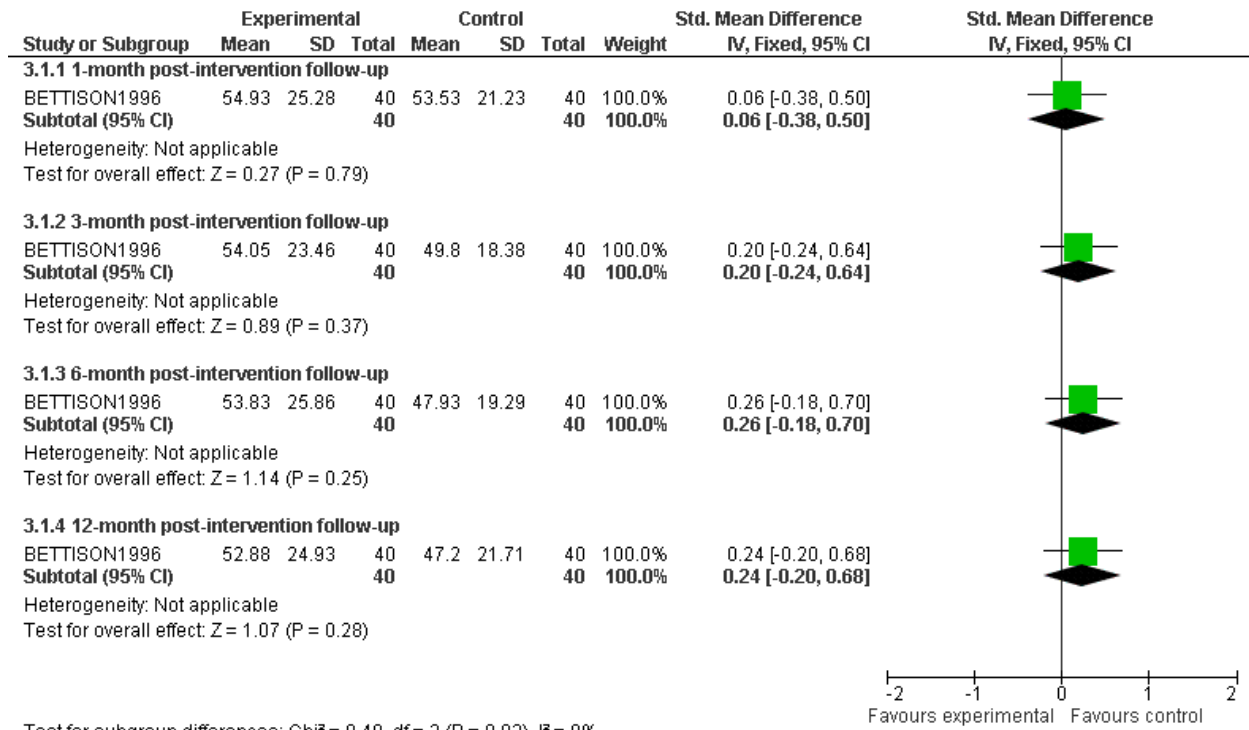
### *Immunoglobulin (dosages combined) versus placebo for behaviour that challenges as an indirect outcome*



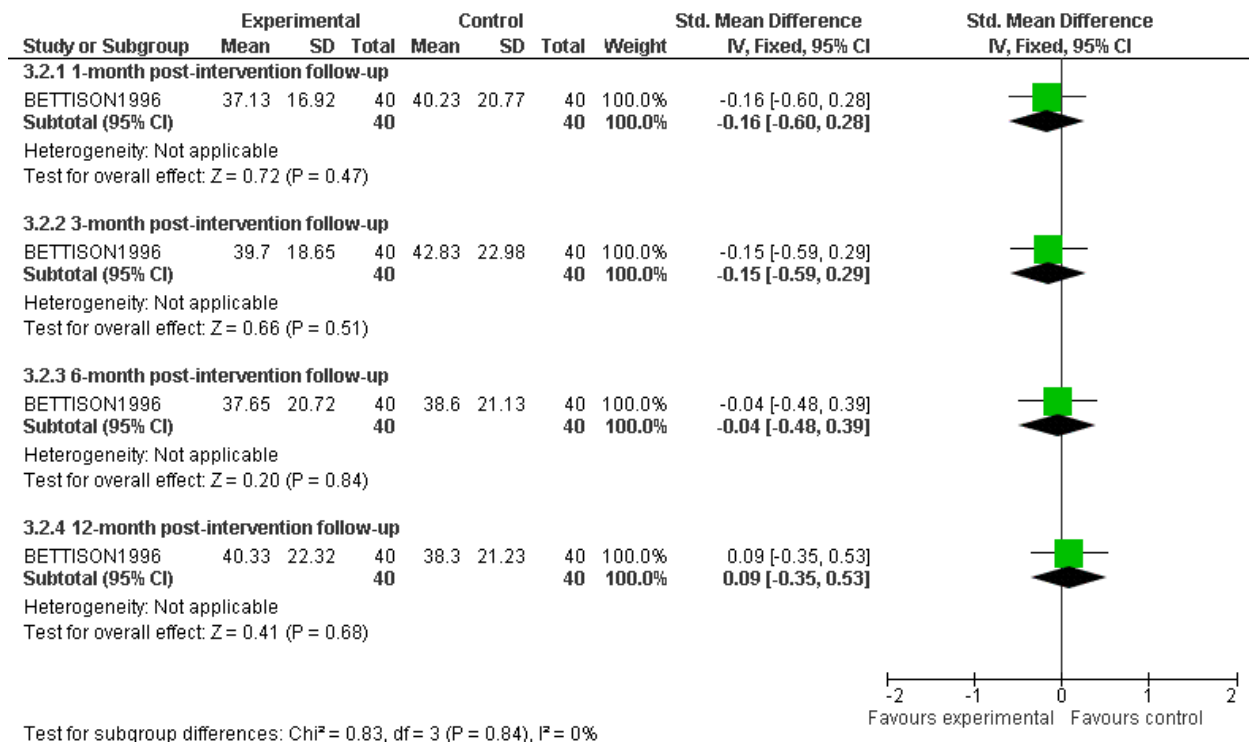
### 1.12.5 Sensory interventions for behaviour that challenges as an indirect outcome

#### *Auditory integration training versus attention-placebo (structured listening) for behaviour that challenges as an indirect outcome*

#### Parent-rated behaviour that challenges (DBC)



### Teacher-rated behaviour that challenges (DBC)

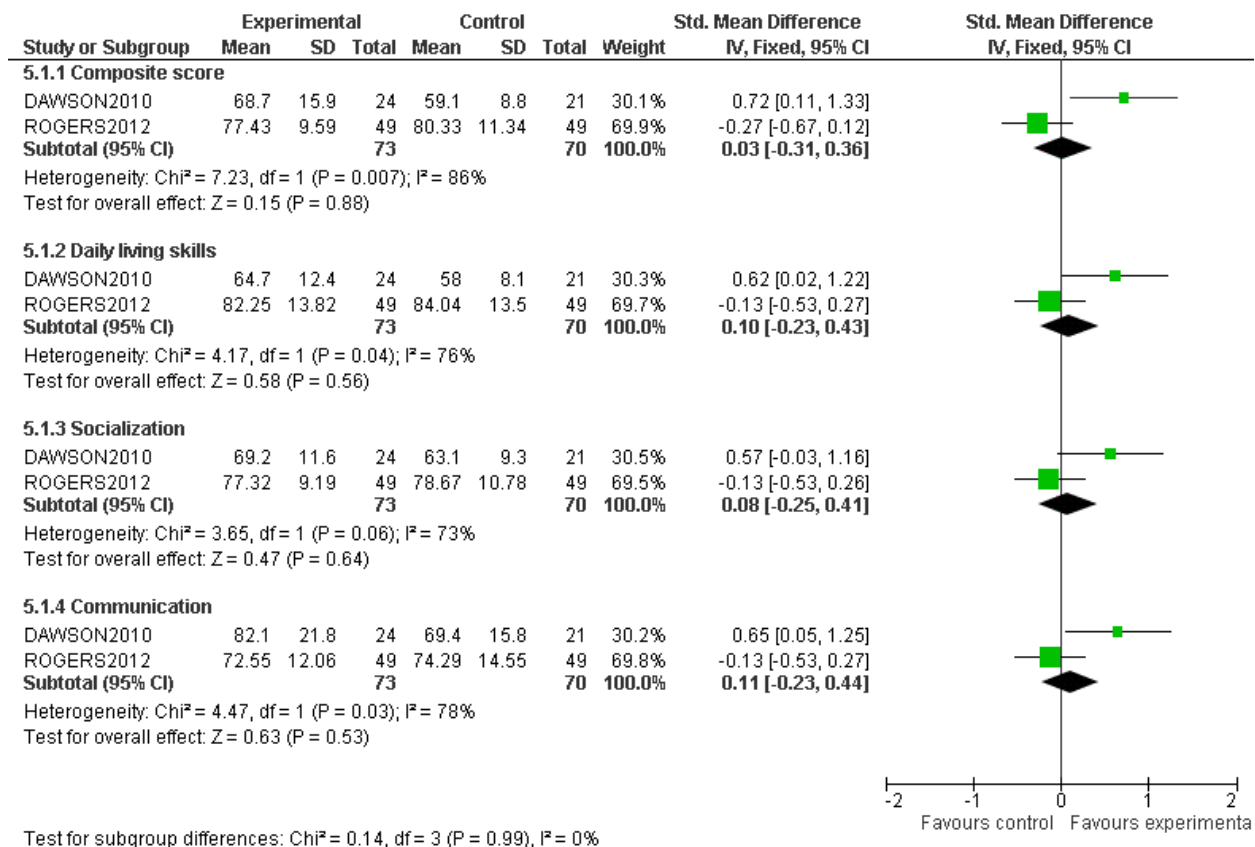




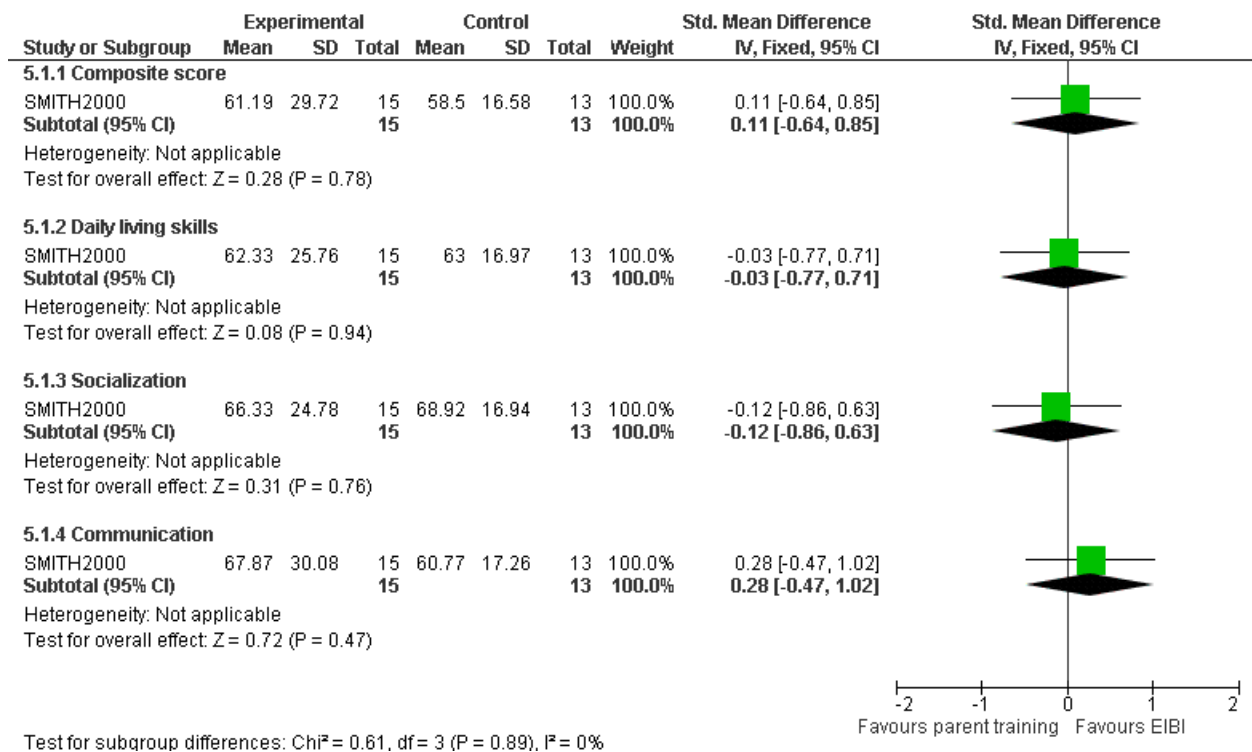
## 1.13 PSYCHOSOCIAL INTERVENTIONS AIMED AT ADAPTIVE BEHAVIOUR

### 1.13.1 Behavioural interventions for adaptive behaviour as a direct or indirect outcome

*EIBI or EBI (ESDM or P-ESDM) versus treatment-as-usual for adaptive behaviour as a direct or indirect outcome*

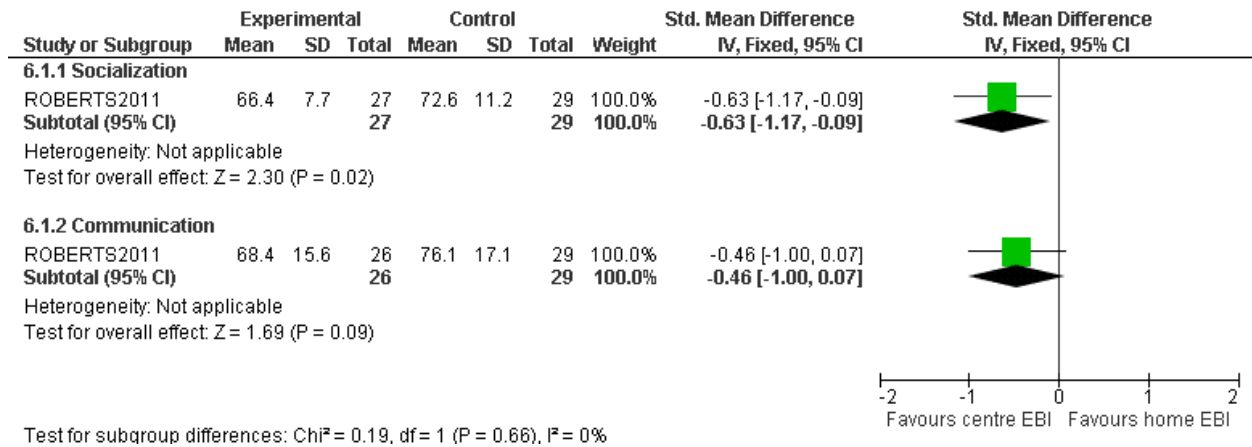


*EIBI versus parent training for adaptive behaviour as a direct outcome*

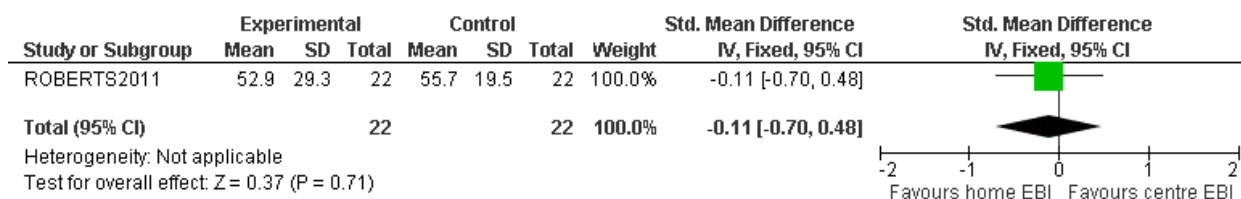


*Home-based EBI versus centre-based EBI for adaptive behaviour as a direct outcome*

**Adaptive behaviour (VABS)**

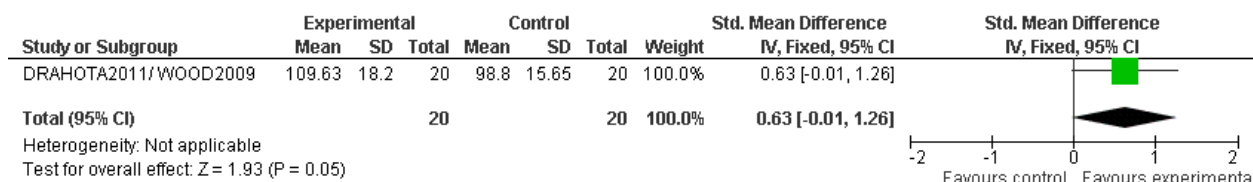


**Adaptive functioning and psychopathology (DBC total)**



### 1.13.2 Cognitive-behavioural interventions for adaptive behaviour as an indirect outcome

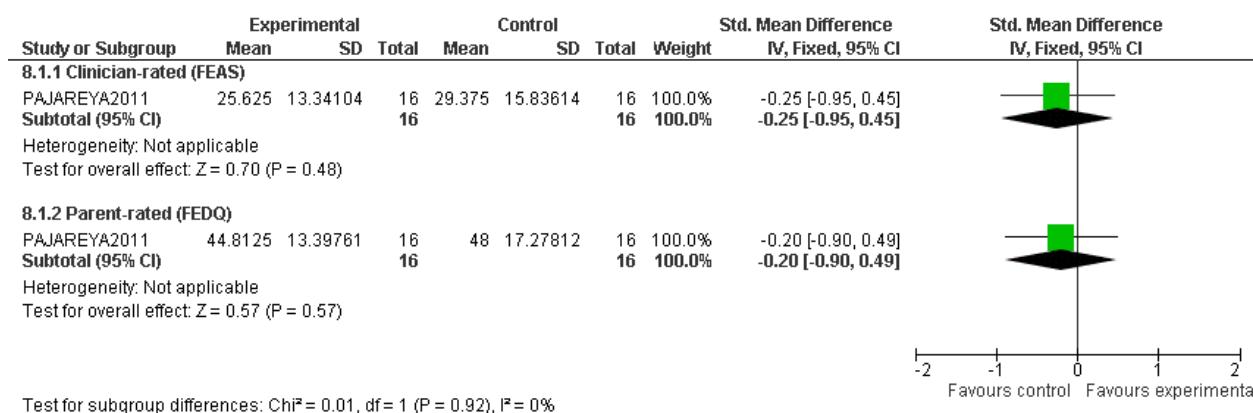
#### *CBT versus waitlist for adaptive behaviour as an indirect outcome*



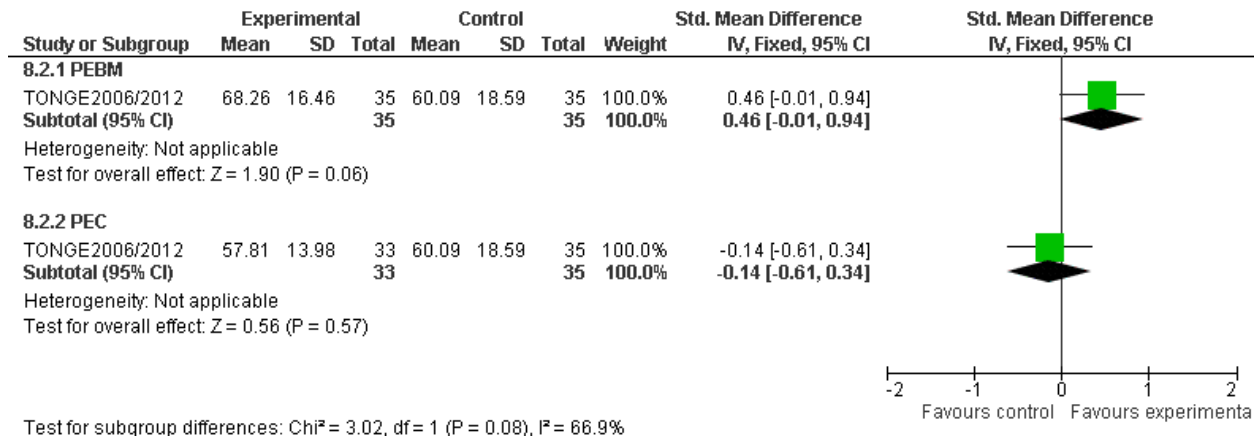
### 1.13.3 Parent training for adaptive behaviour as a direct or indirect outcome

#### *Parent training versus treatment-as-usual for adaptive behaviour as a direct or indirect outcome*

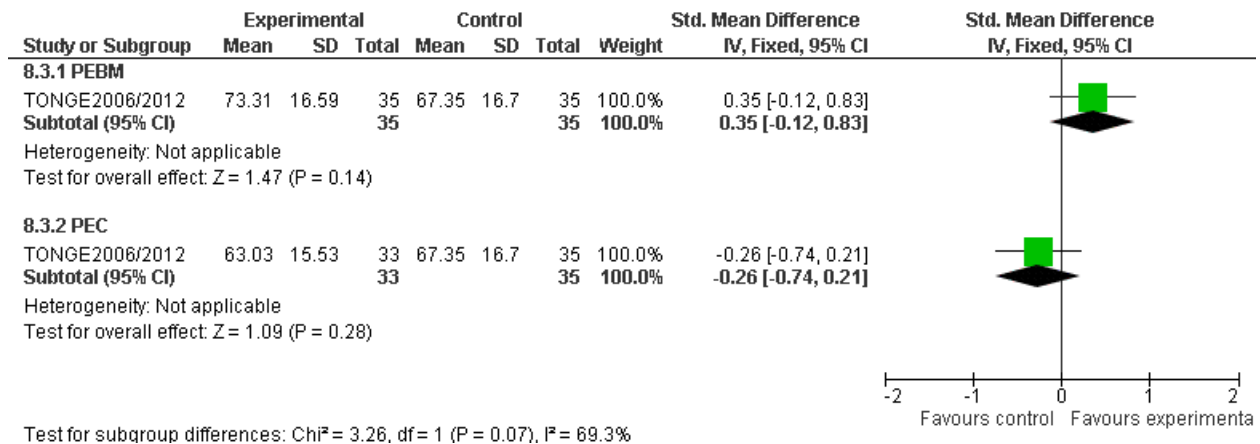
#### Functional emotional development (direct outcome)



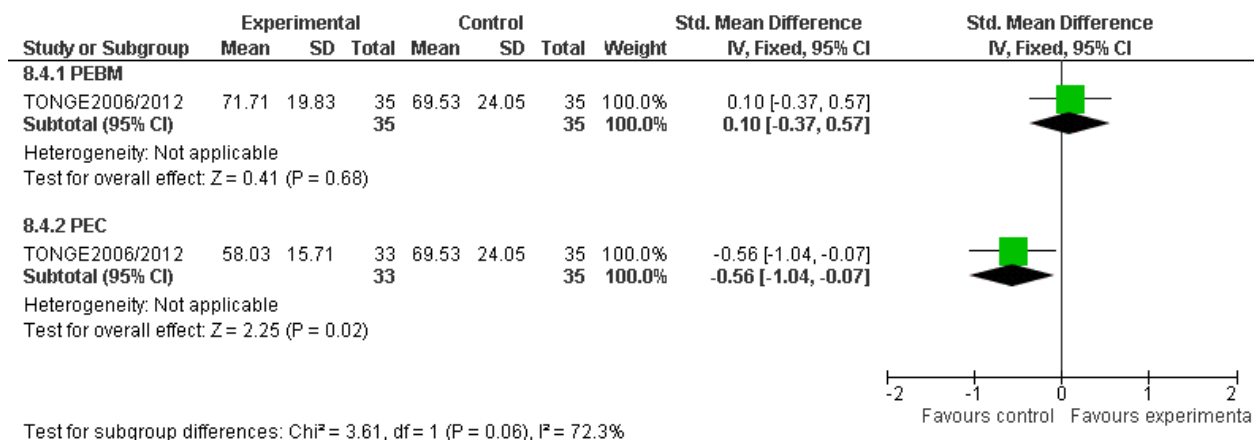
#### Daily living skills (VABS; 6-month follow-up; indirect outcome)



**Socialization (VABS; 6-month follow-up; indirect outcome)**

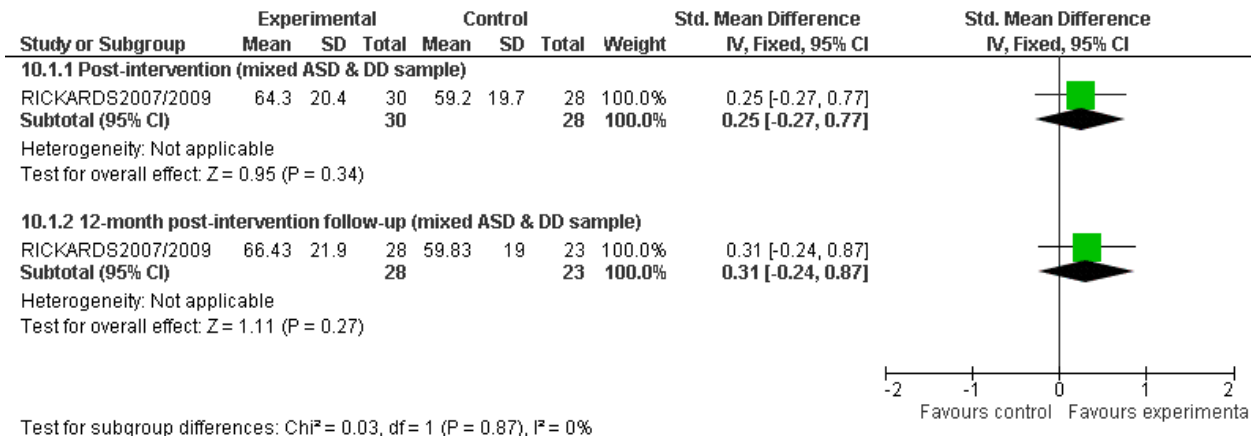


**Communication (VABS; 6-month follow-up; indirect outcome)**

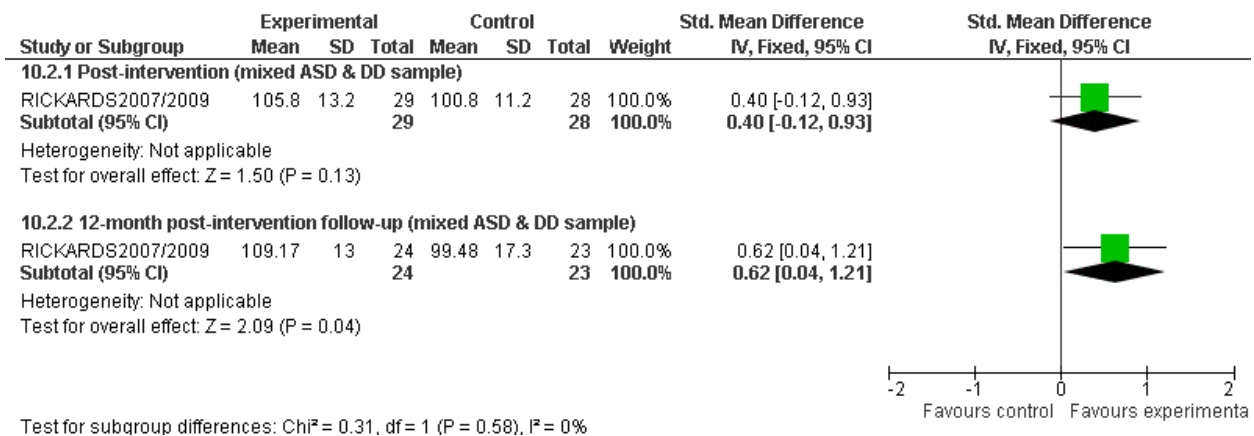


*Combined parent training and early intervention centre programme versus early intervention centre programme only for adaptive behaviour as a direct outcome*

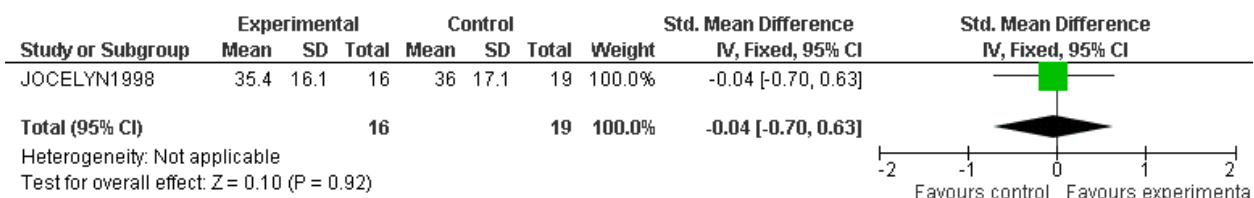
**Parent-reported adaptive behaviour (VABS)**



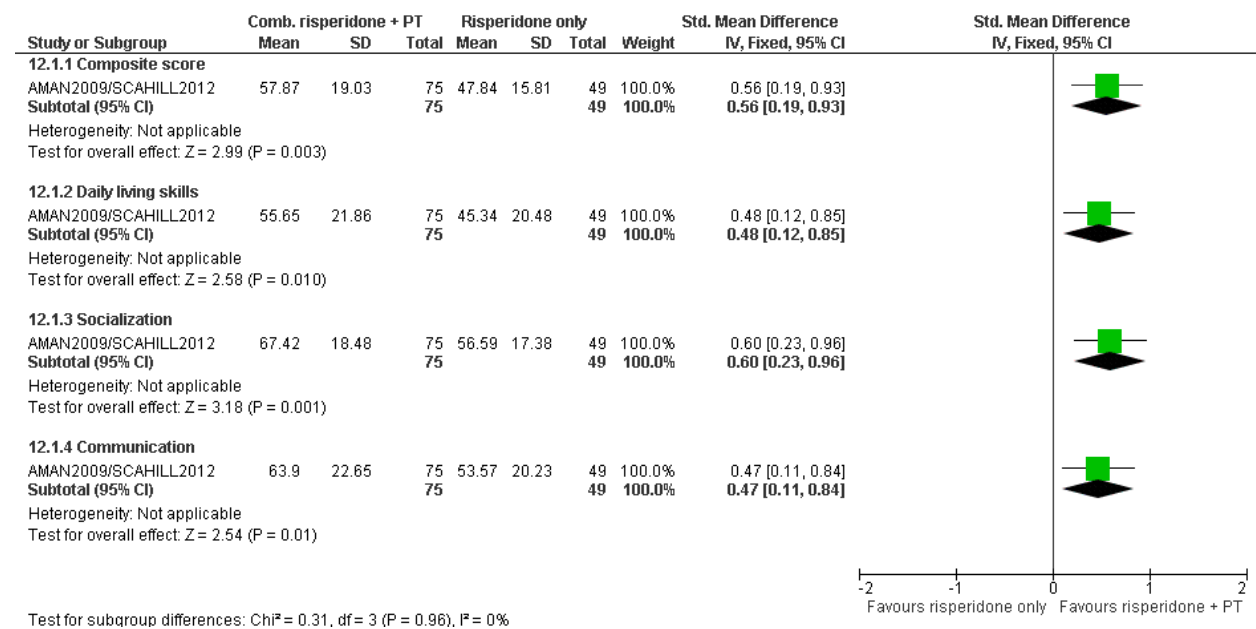
**Clinician-rated adaptive behaviour (Bayley BRS)**



*Parent and day-care staff training versus standard day-care for adaptive behaviour as an indirect outcome*

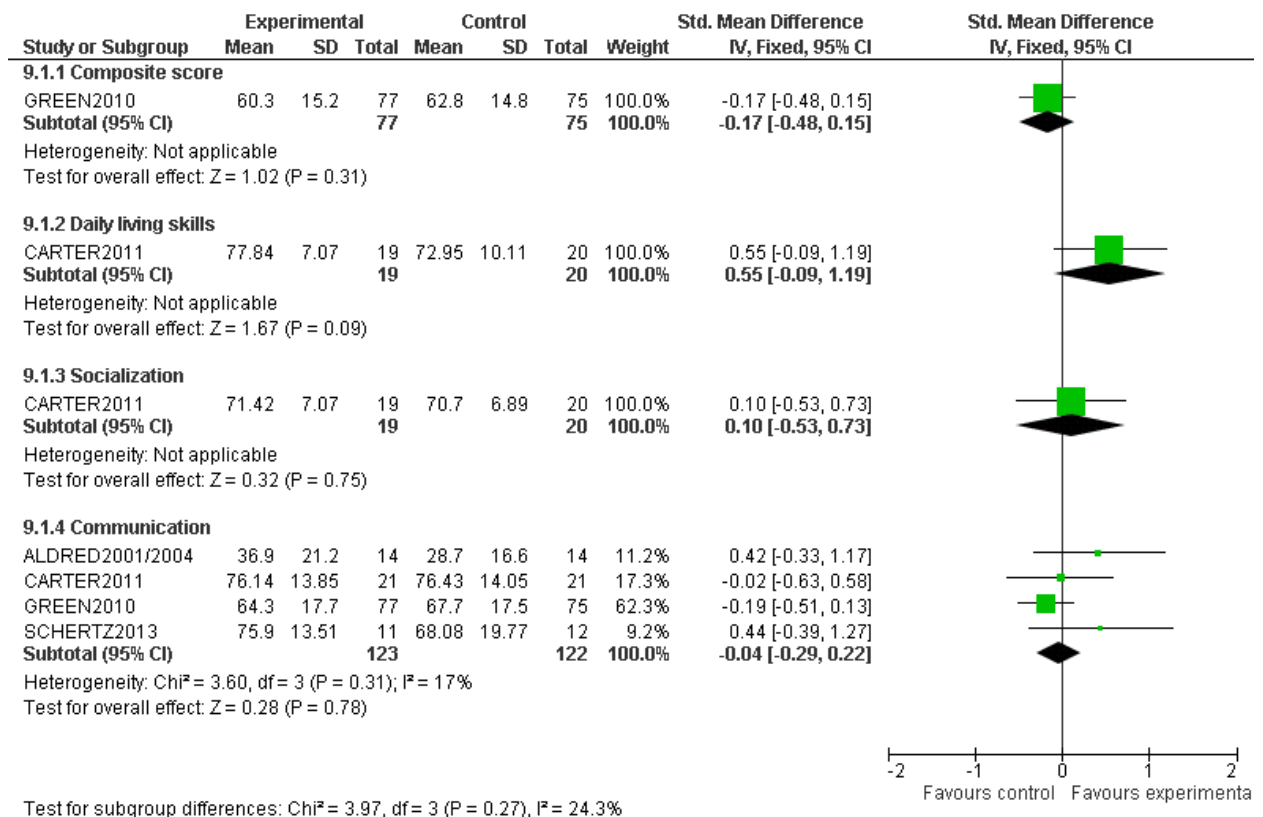


*Combined parent training and antipsychotic versus antipsychotic-only for adaptive behaviour as an indirect outcome*

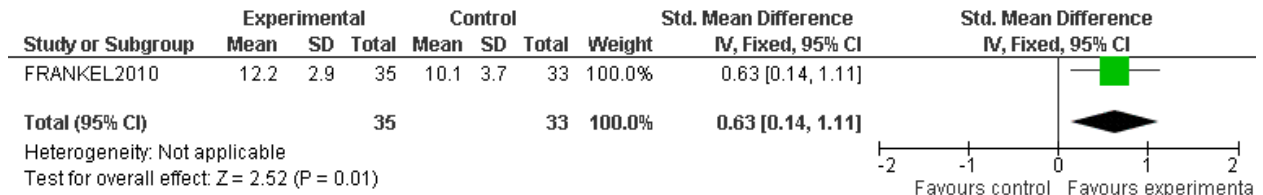


### 1.13.4 Social-communication interventions for adaptive behaviour as an indirect outcome

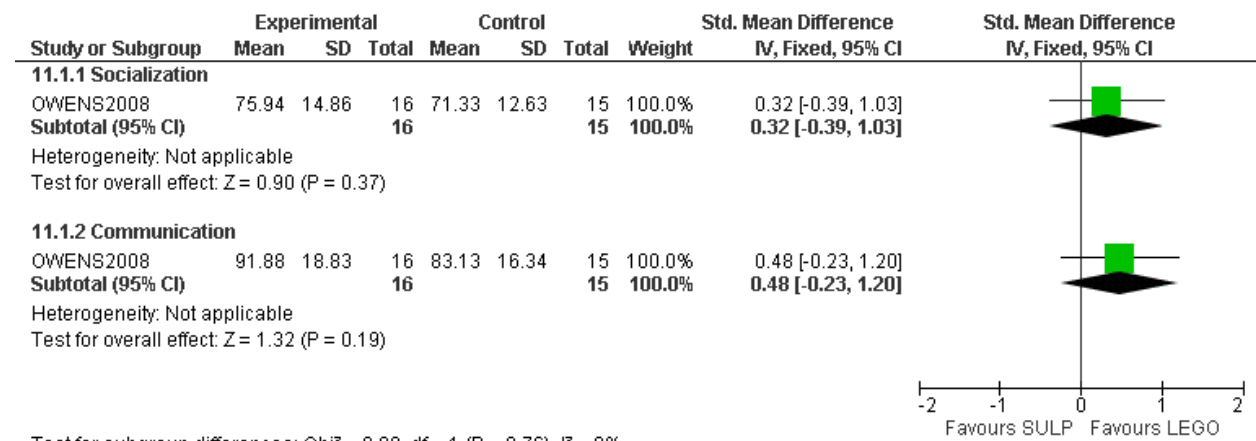
*Caregiver-mediated social communication intervention versus treatment-as-usual for adaptive behaviour as an indirect outcome*



**Social skills group versus treatment-as-usual for adaptive behaviour as an indirect outcome**



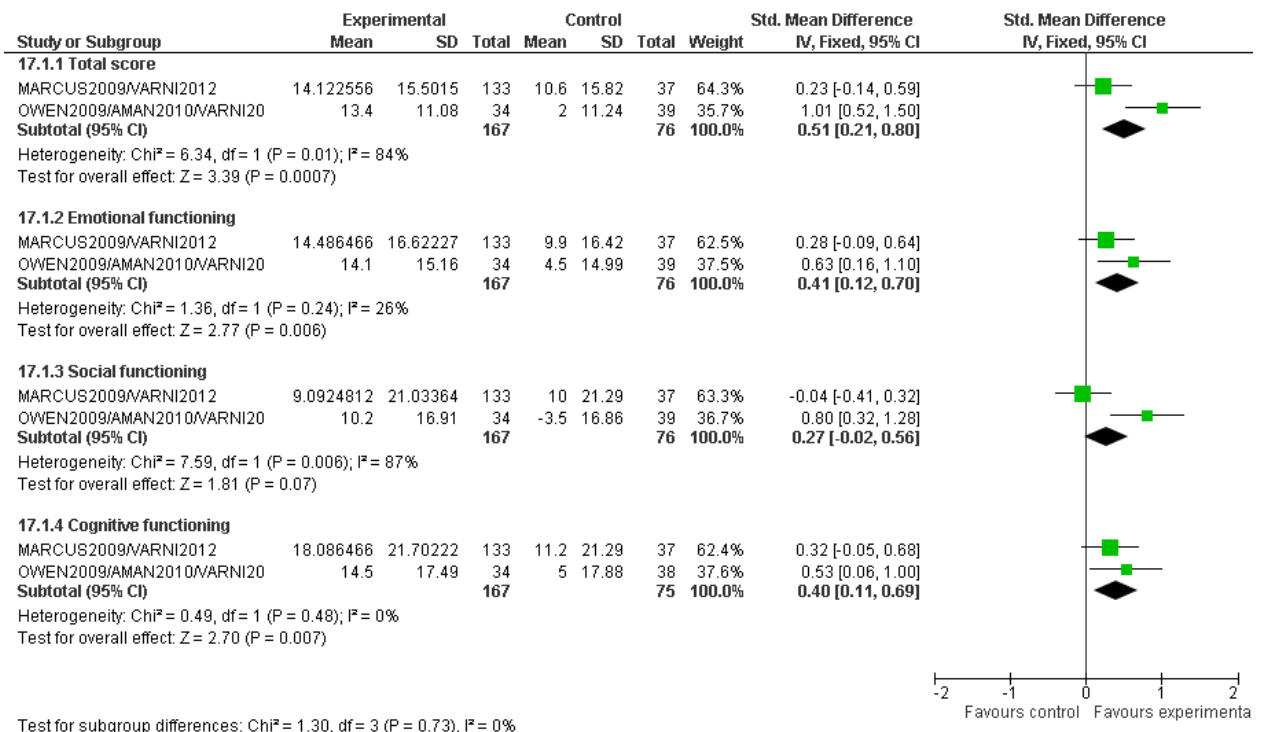
**LEGO® therapy versus SLP for adaptive behaviour as an indirect outcome**



## 1.14 PHARMACOLOGICAL INTERVENTIONS AIMED AT ADAPTIVE BEHAVIOUR

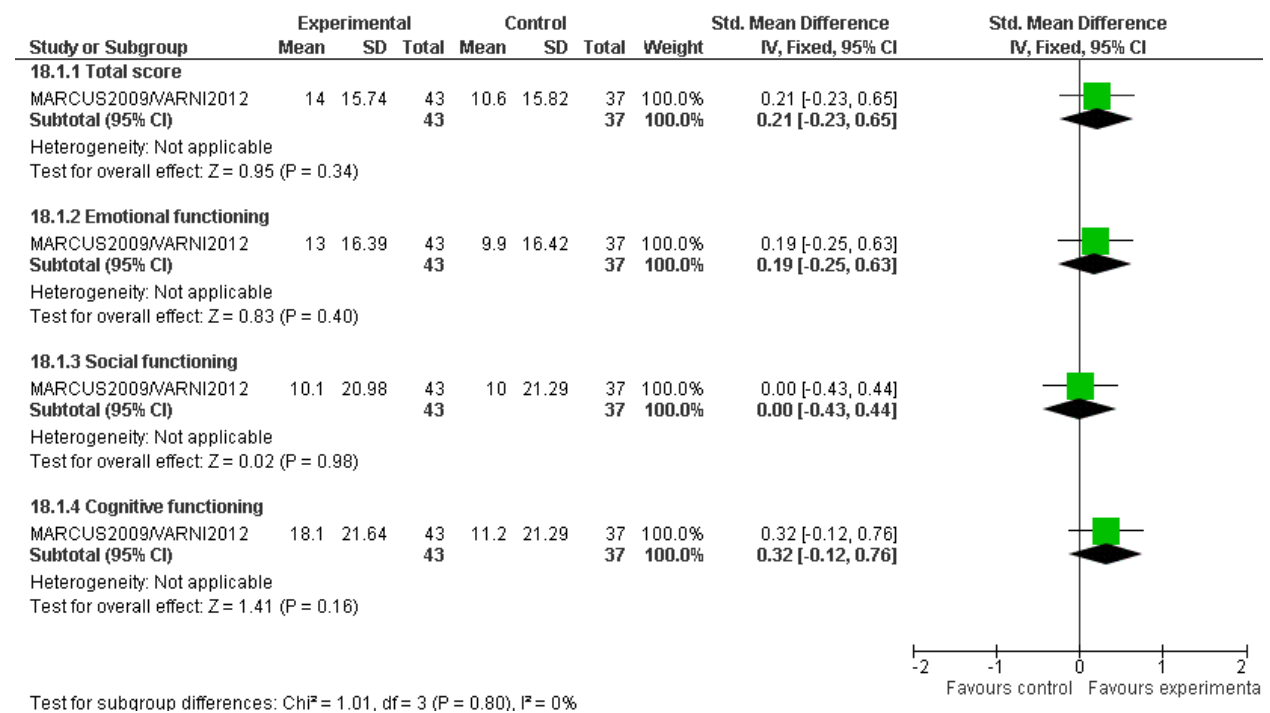
### 1.14.1 Antipsychotics for adaptive behaviour as an indirect outcome

#### *Aripiprazole versus placebo for adaptive behaviour as an indirect outcome*



#### *Low dose aripiprazole versus placebo for adaptive behaviour as an indirect outcome*



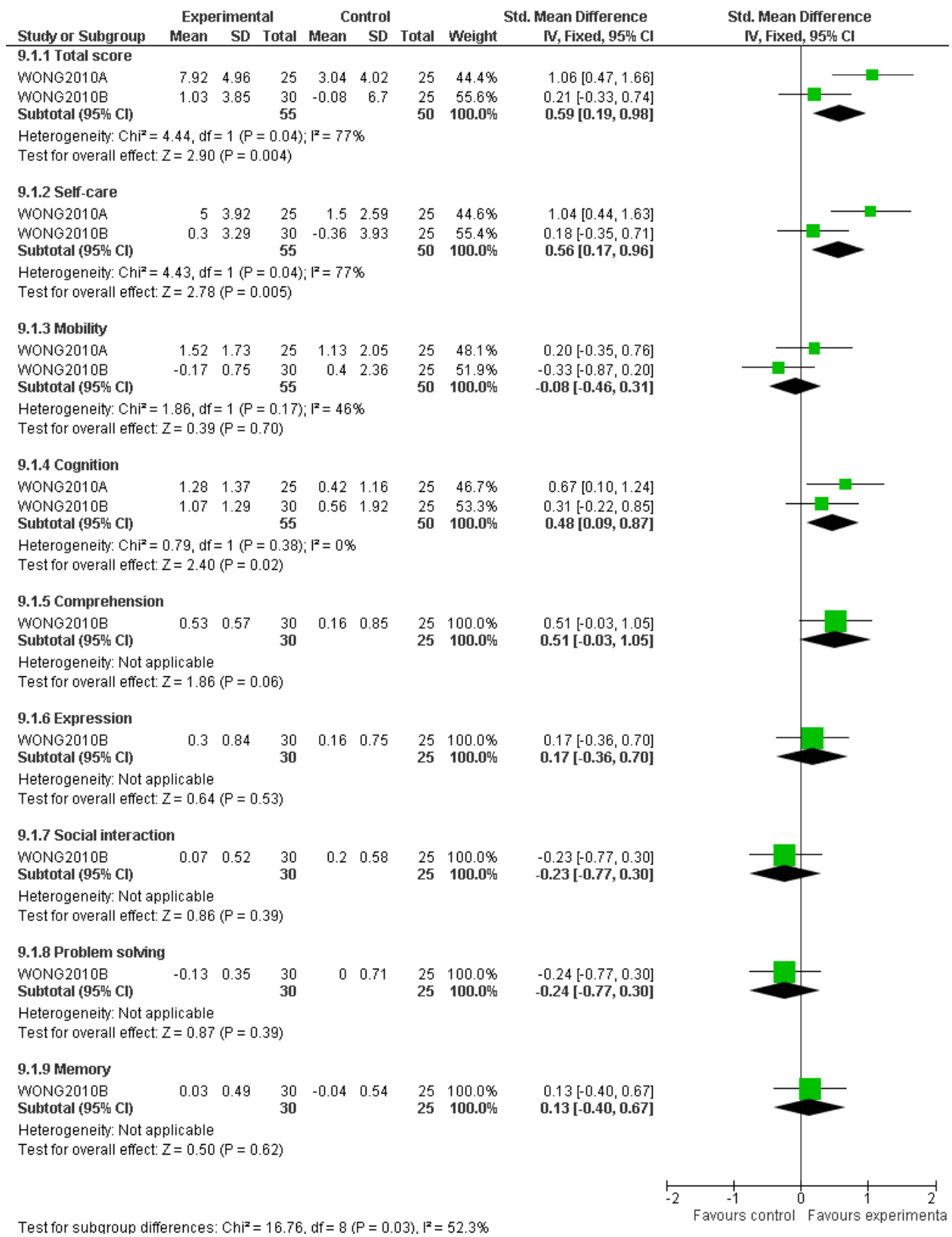


## 1.15 BIOMEDICAL INTERVENTIONS AIMED AT ADAPTIVE BEHAVIOUR

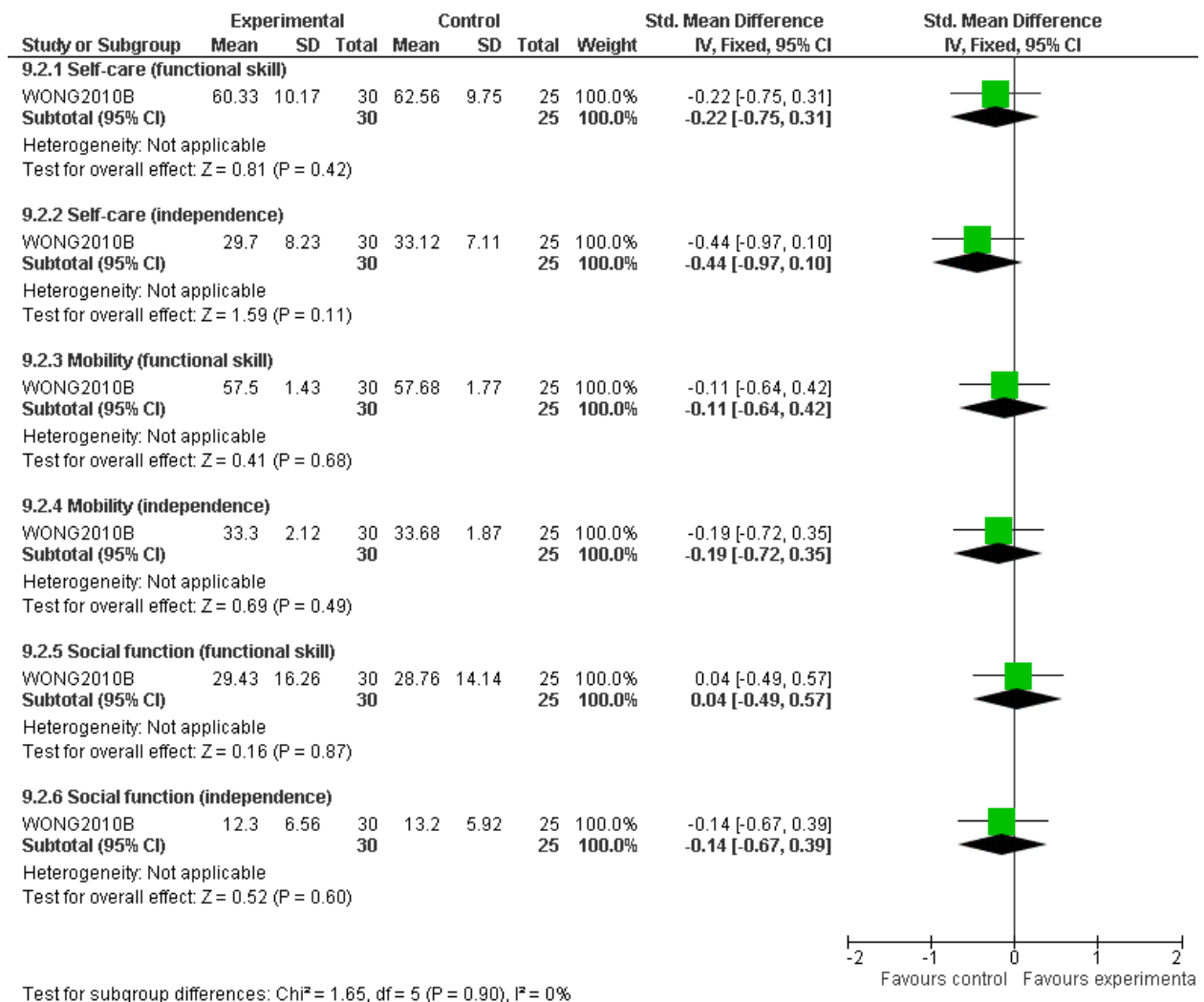
### 1.15.1 Complementary therapies for adaptive behaviour as an indirect outcome

*Acupuncture/electro-acupuncture versus sham acupuncture/electro-acupuncture for adaptive behaviour as an indirect outcome*

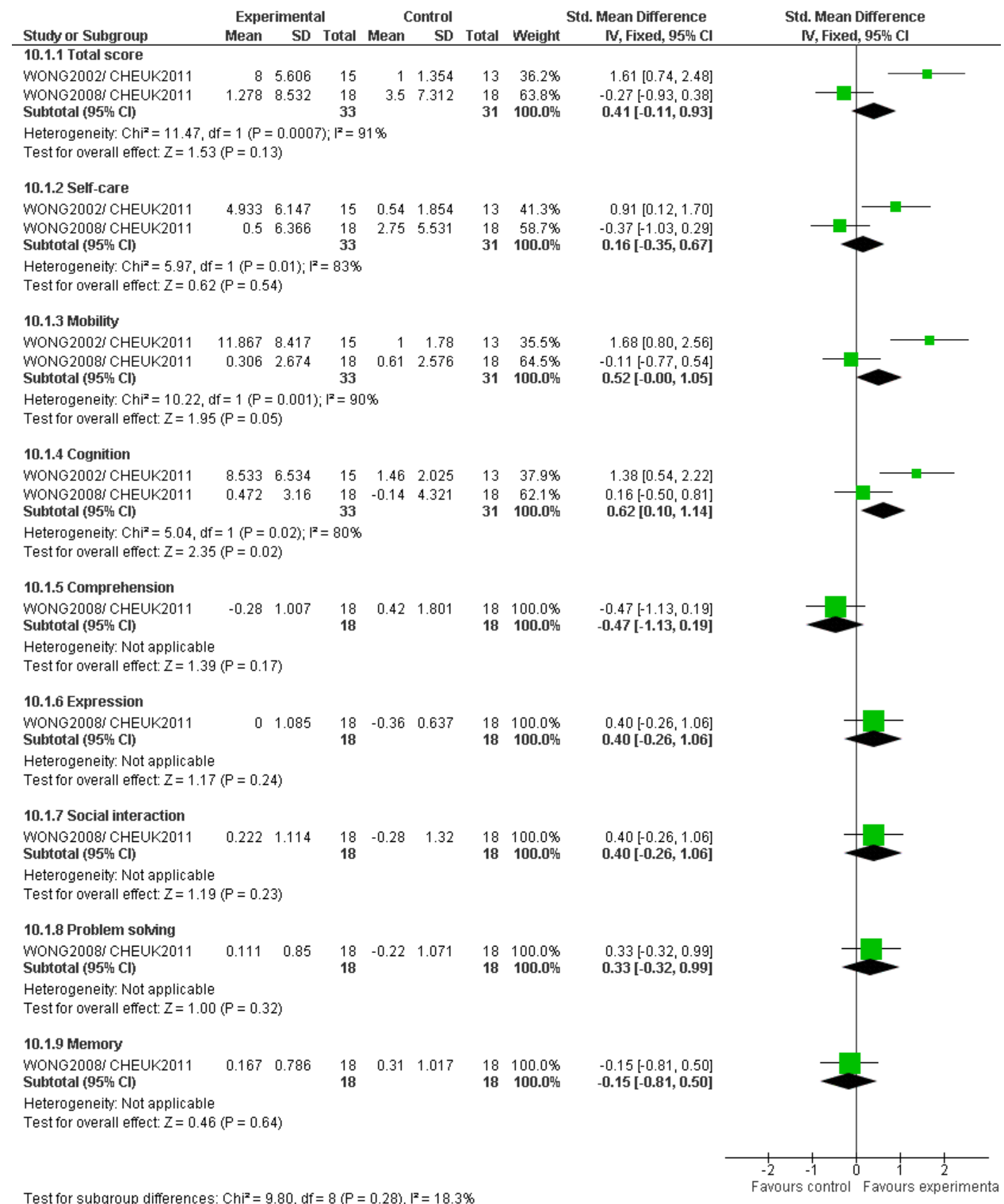
Adaptive behaviour (WeeFIM; change scores)



### Adaptive behaviour (PEDI)

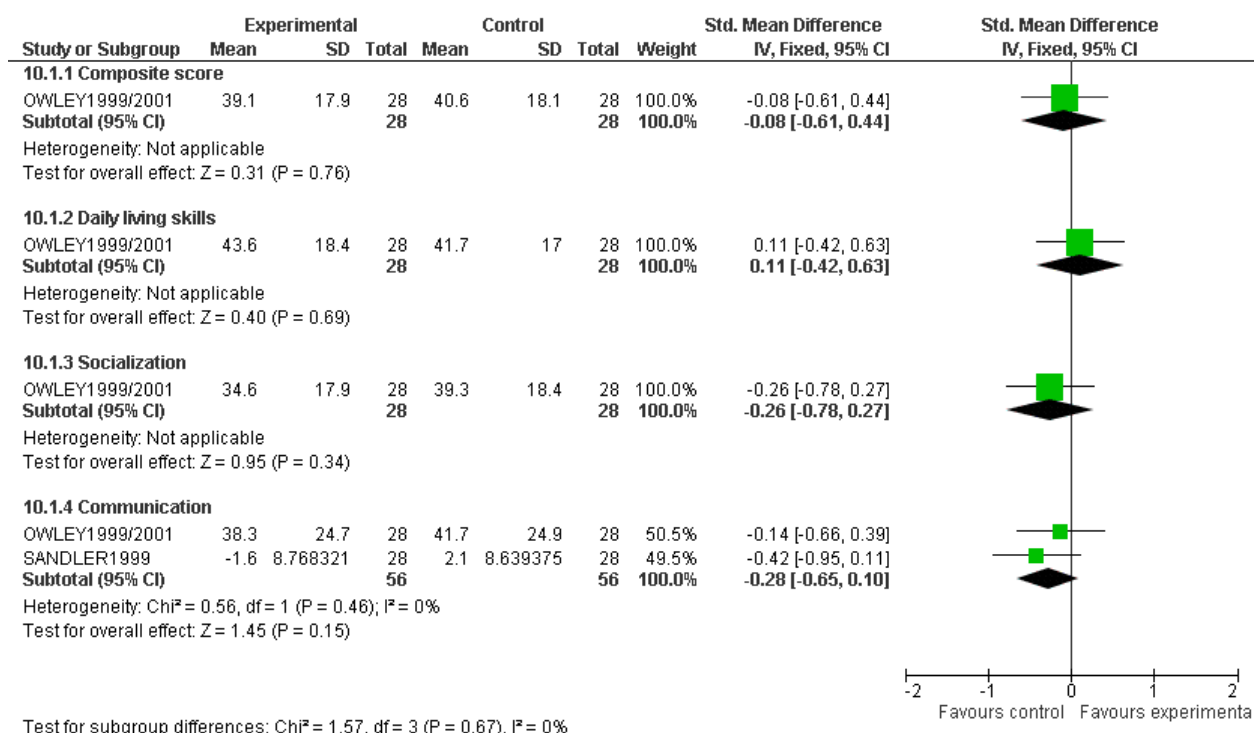


*Acupuncture/electro-acupuncture and conventional educational programme versus conventional educational programme only for adaptive behaviour as an indirect outcome*



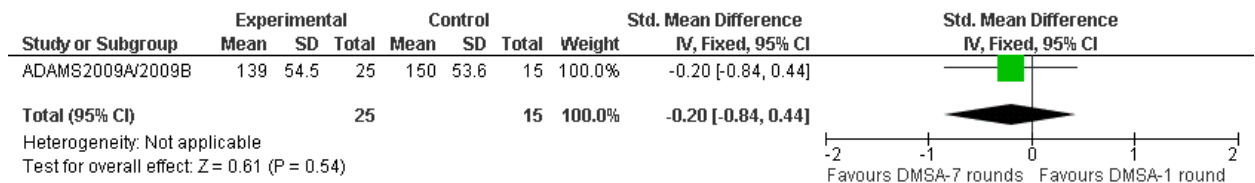
## 1.15.2 Hormones for adaptive behaviour as an indirect outcome

### *Secretin versus placebo for adaptive behaviour as an indirect outcome*



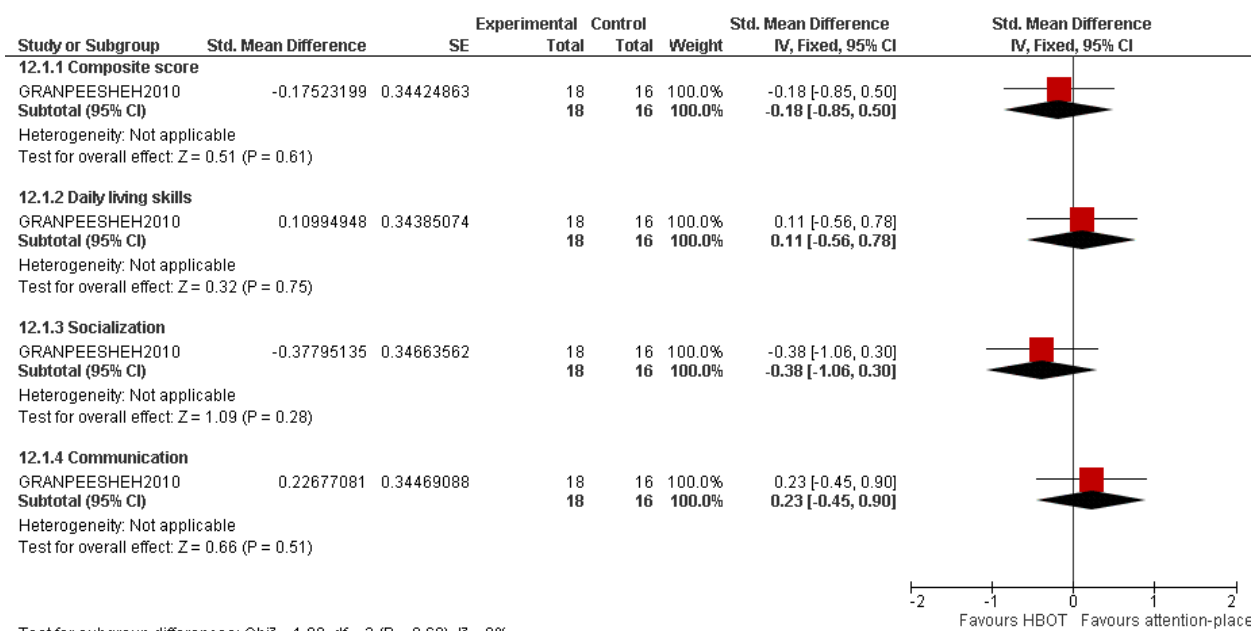
### 1.15.3 Medical procedures for adaptive behaviour as an indirect outcome

*Long-term chelation (7-rounds of DMSA therapy) versus short-term chelation (1-round of DMSA therapy and 6-rounds of placebo) for adaptive behaviour as an indirect outcome*

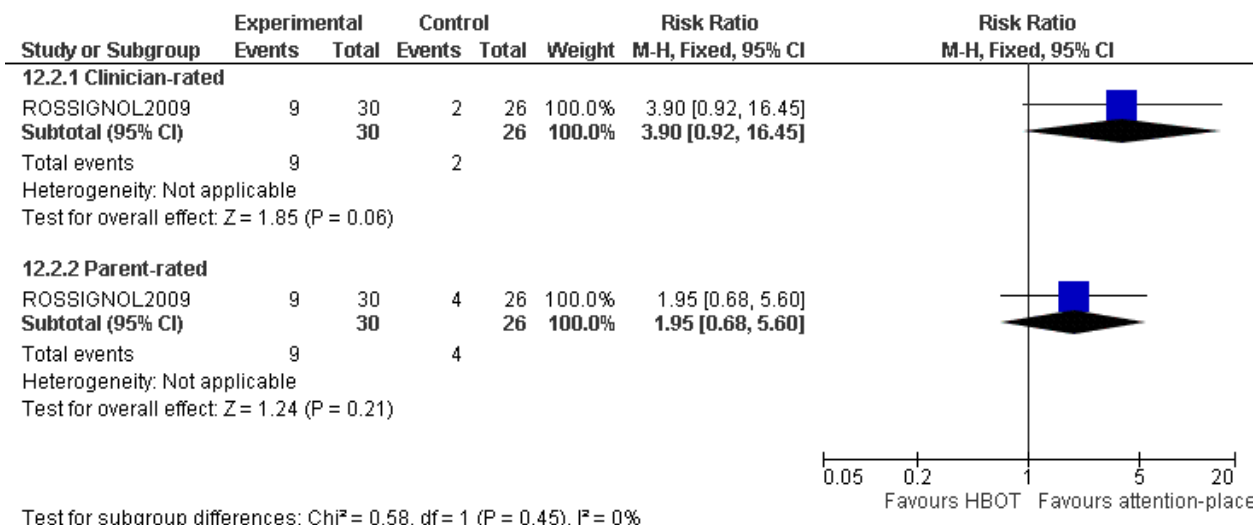


*HBOT versus attention-placebo for adaptive behaviour as an indirect outcome*

Adaptive behaviours (VABS; change scores)

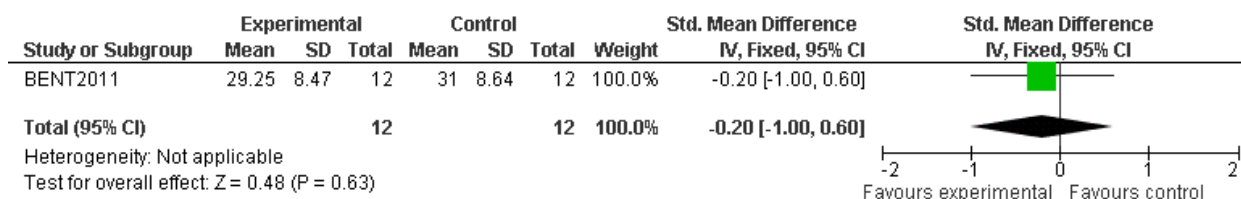


### Positive treatment response ('much improved/very improved' on CGI/PGI-improvement for overall functioning)

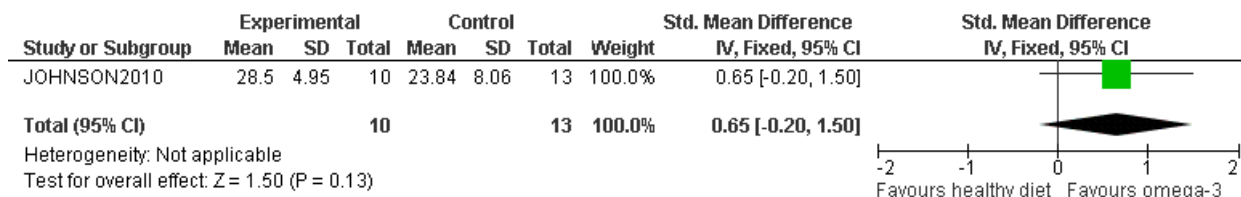


## 1.15.4 Nutritional interventions for adaptive behaviour as an indirect outcome

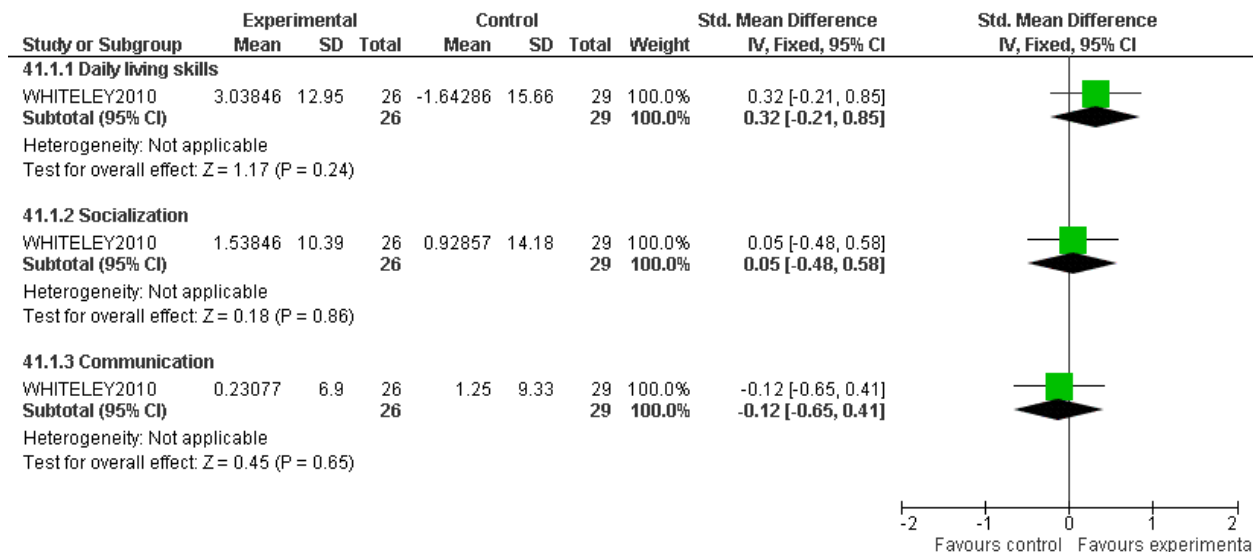
### *Omega-3 fatty acids versus placebo for adaptive behaviour as an indirect outcome*



*Omega-3 fatty acids versus healthy diet control for adaptive behaviour as an indirect outcome*



*Gluten-free and casein-free diet versus treatment-as-usual for adaptive behaviour as an indirect outcome*

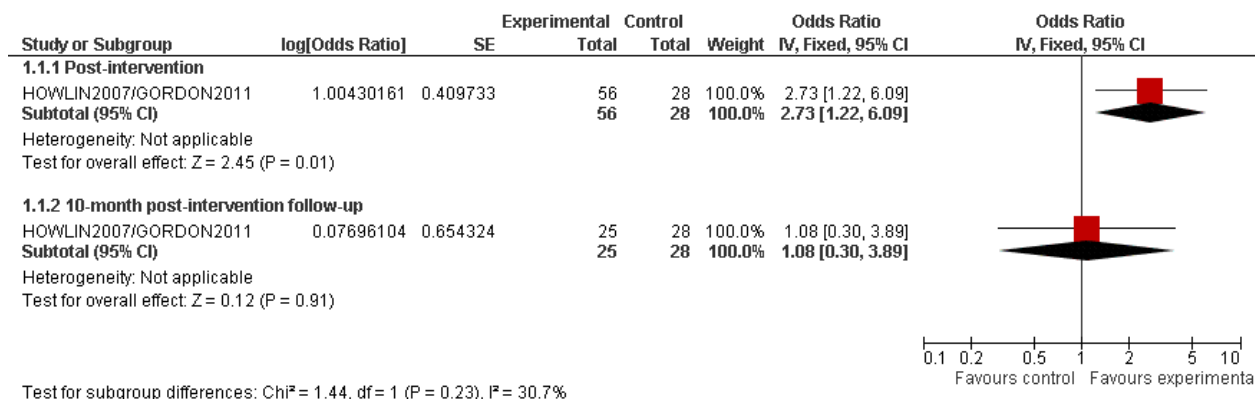


## 1.16 PSYCHOSOCIAL INTERVENTIONS AIMED AT SPEECH AND LANGUAGE

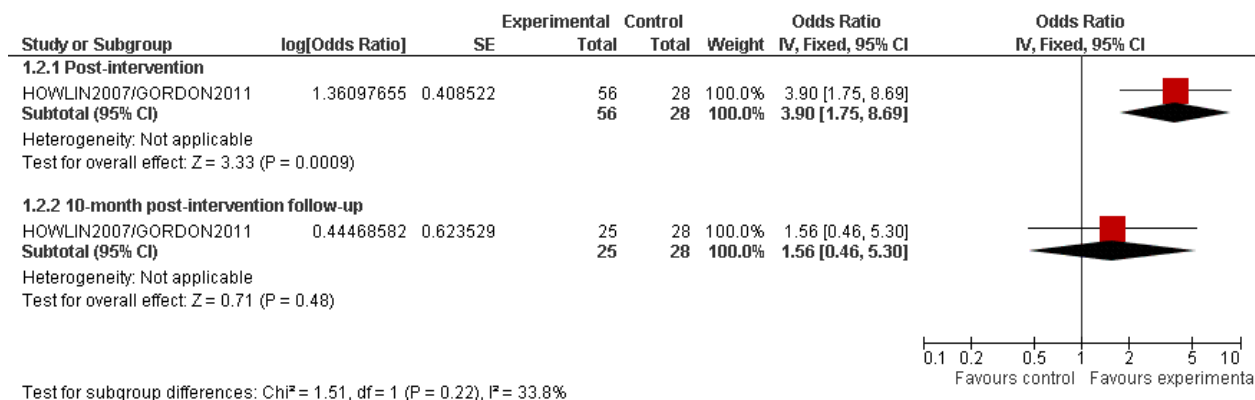
### 1.16.1 AAC interventions for speech and language as a direct outcome

*PECS training for teachers versus treatment-as-usual for speech and language as a direct outcome*

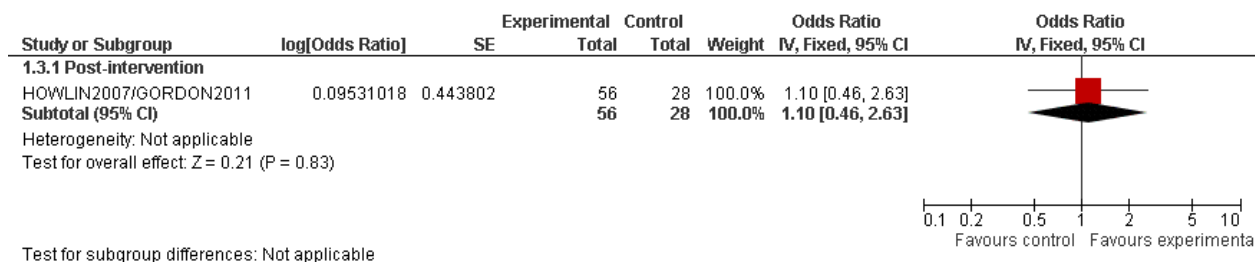
### Spontaneous child communicative initiations (odds of being in a higher initiation category)



### PECS use (odds of being in a higher category for rate of PECS use)

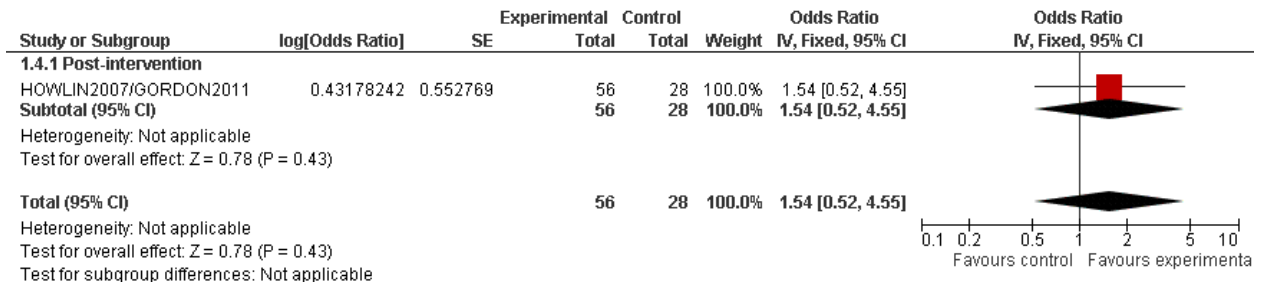


### Speech/vocalisation use (odds of being in a higher category for rate of speech/vocalisation use)

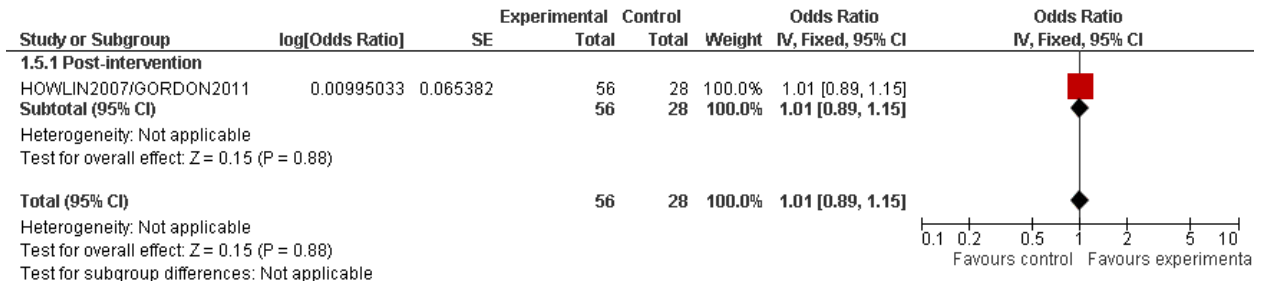


### Receptive language (odds of being in a higher category on BPVS)



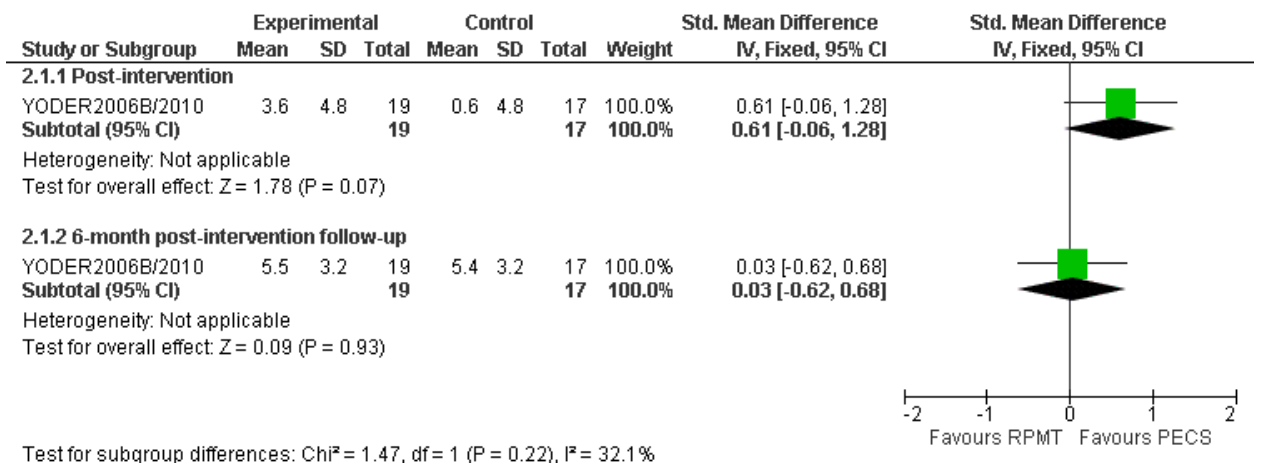


### Expressive language (odds of being in a higher category on EOWPVT)

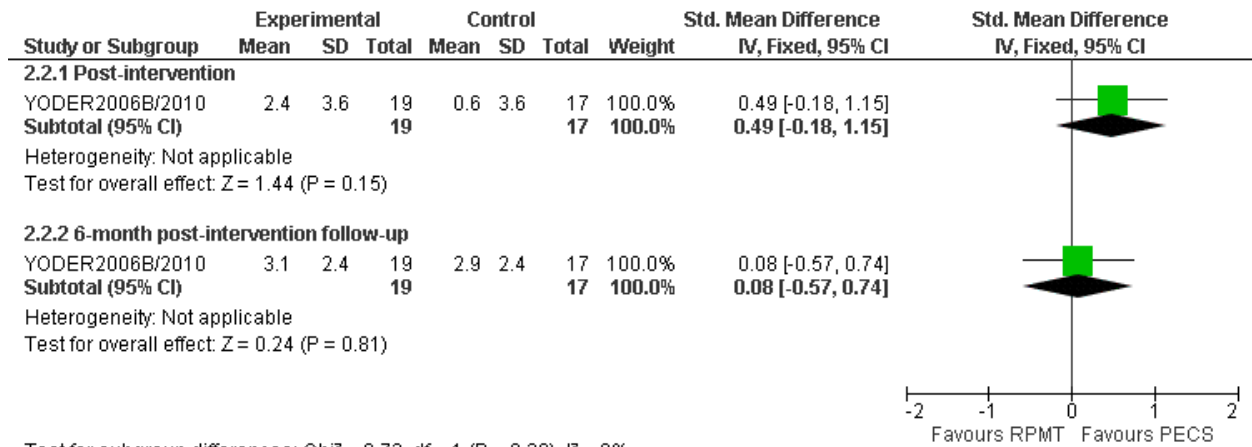


### PECS versus RPMT for speech and language as a direct outcome

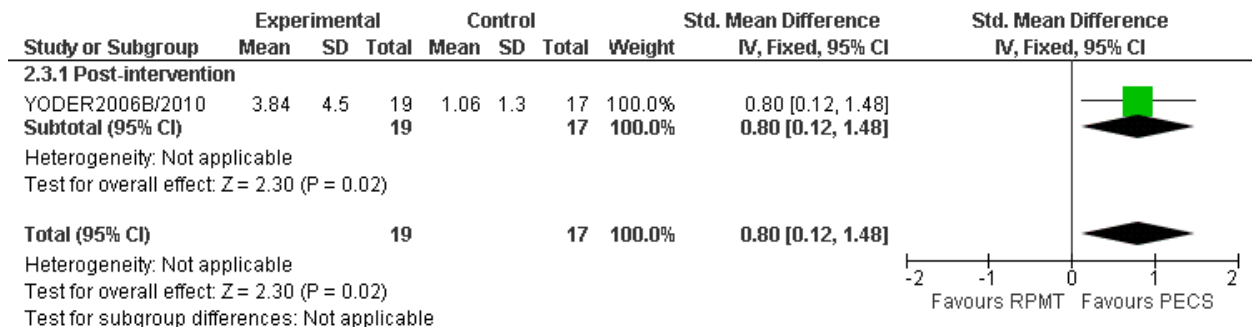
#### Frequency of nonimitative spoken acts



#### Number of different nonimitative words



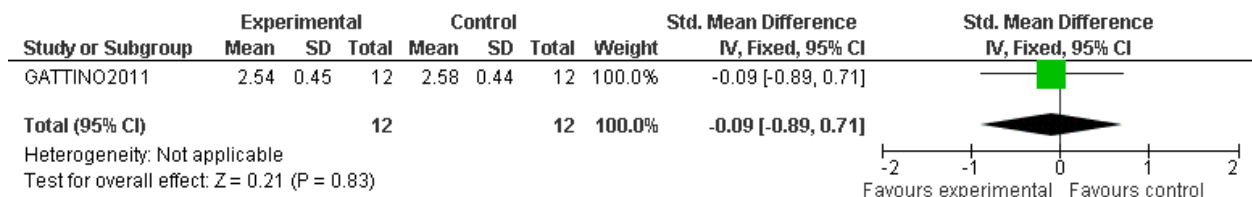
### Number of picture exchanges (EScs-Abridged)



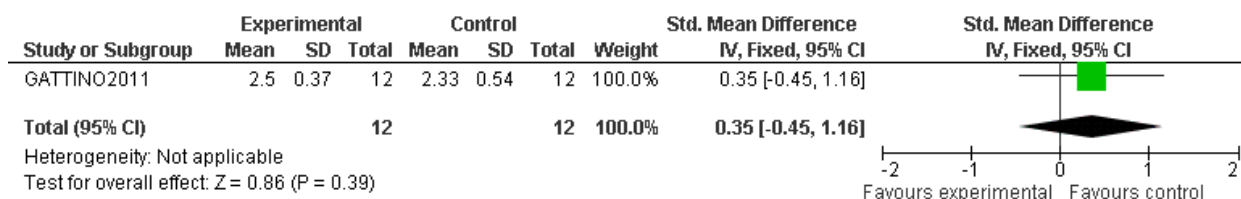
## 1.16.2 Arts-based interventions for speech and language as a direct outcome

### *Music therapy versus treatment-as-usual for speech and language as a direct outcome*

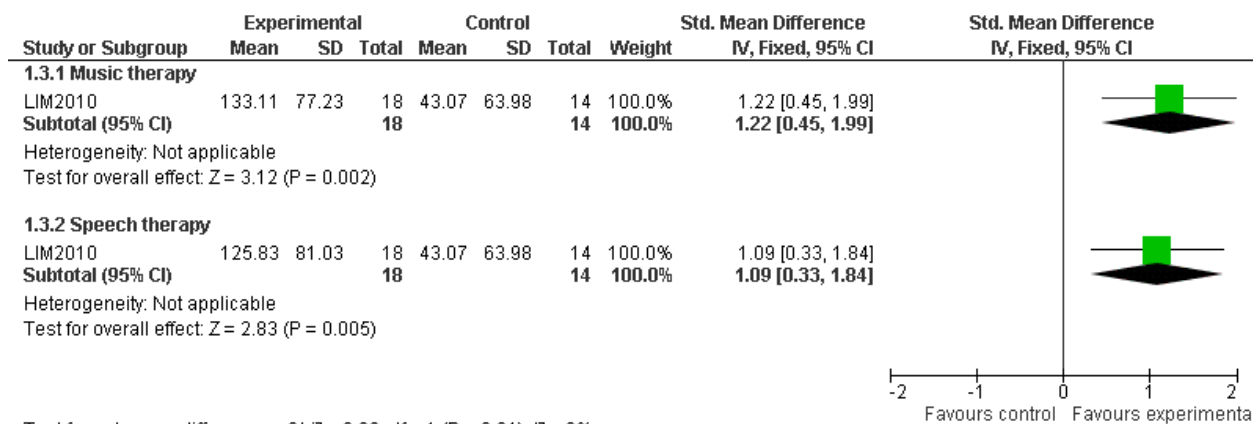
#### Verbal communication (CARS-BR)



#### Non-verbal communication (CARS-BR)



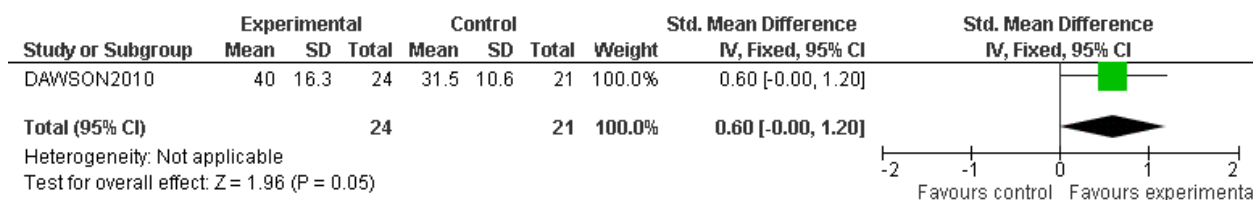
### Expressive language (study-specific VPES)



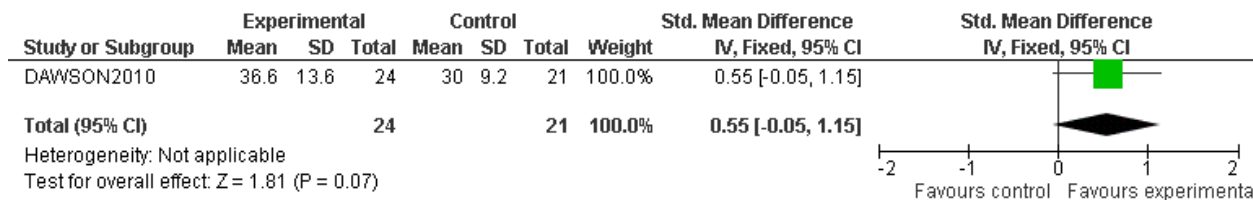
### 1.16.3 Behavioural interventions for speech and language as an indirect outcome

#### *EIBI (ESDM) versus treatment-as-usual for speech and language as an indirect outcome*

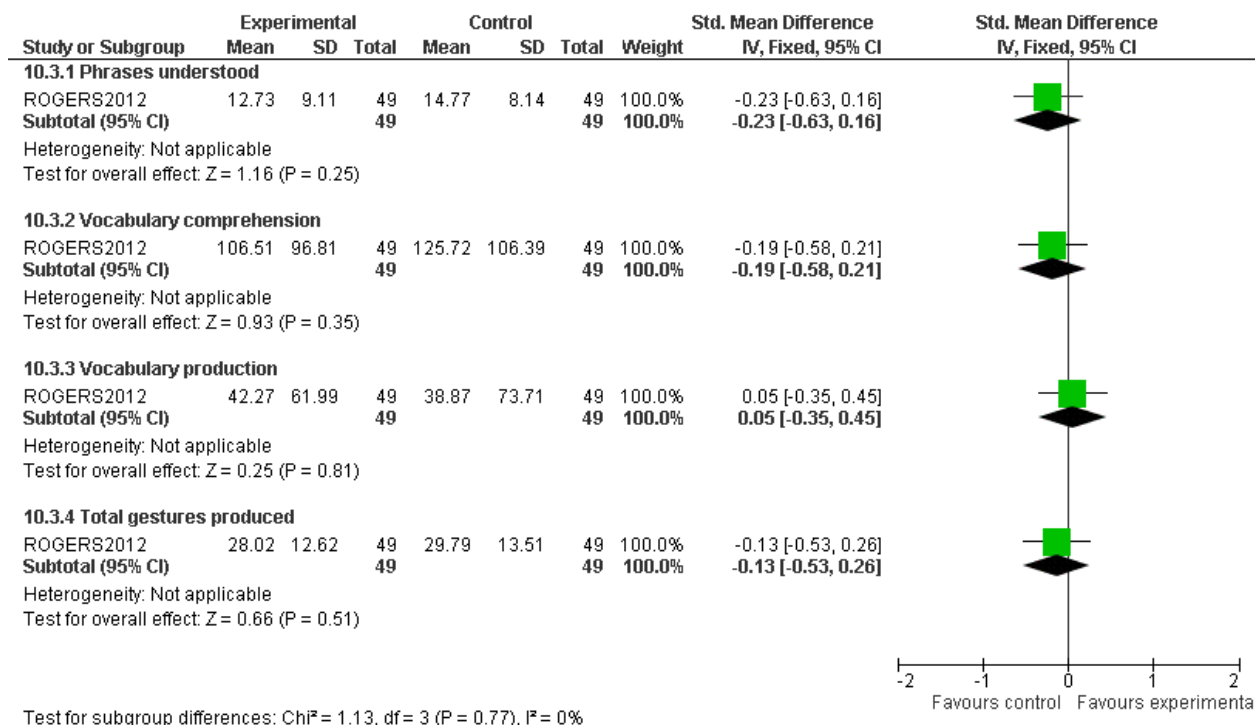
### Receptive language (MSEL)



### Expressive language (MSEL)

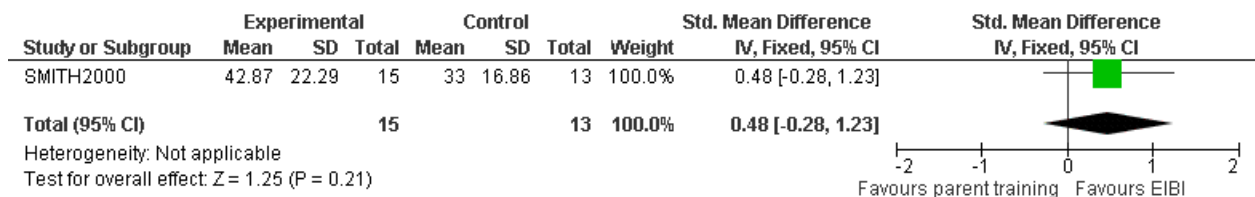


*EBI (P-ESDM) versus treatment-as-usual for speech and language as an indirect outcome*

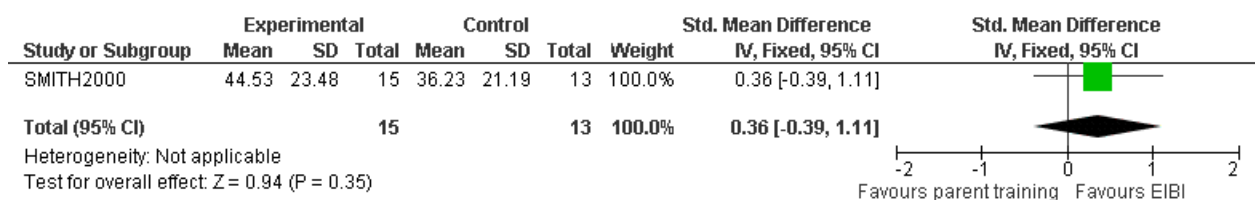


*EIBI versus parent training for speech and language as an indirect outcome*

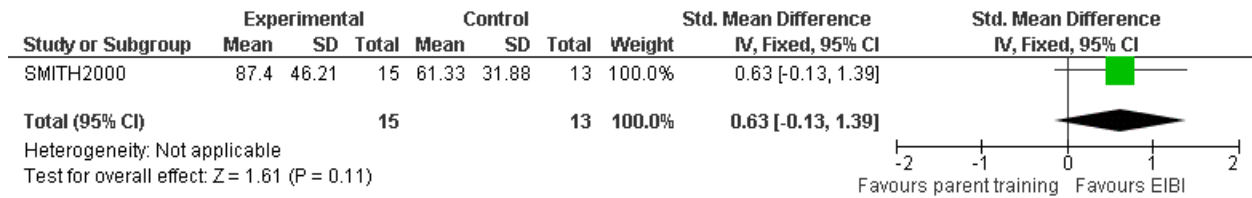
**Receptive language (Reynell Developmental Language Scale-Comprehension)**



**Expressive language (Reynell Developmental Language Scale-Expressive)**

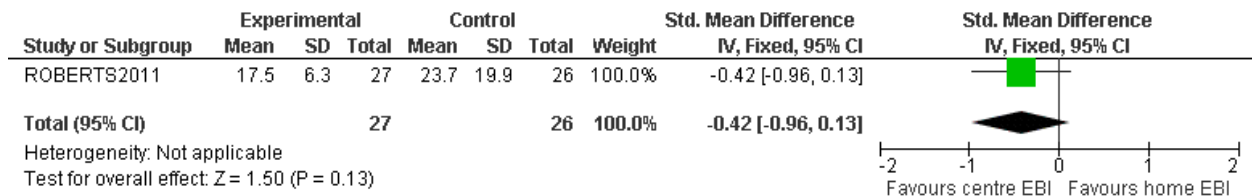


**Receptive + Expressive language (Reynell Developmental Language Scale-Comprehension+Expression)**

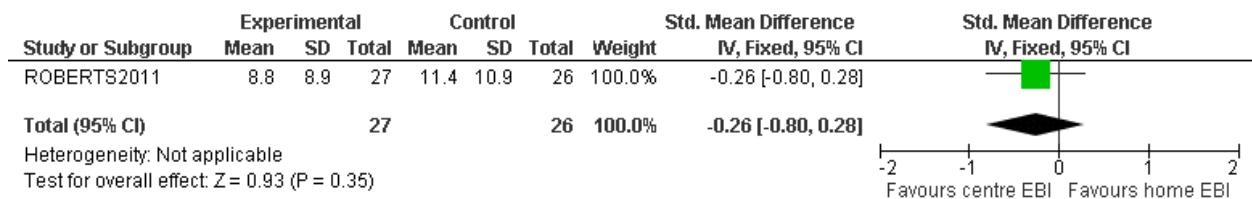


*Home-based EBI versus centre-based EBI for speech and language as an indirect outcome*

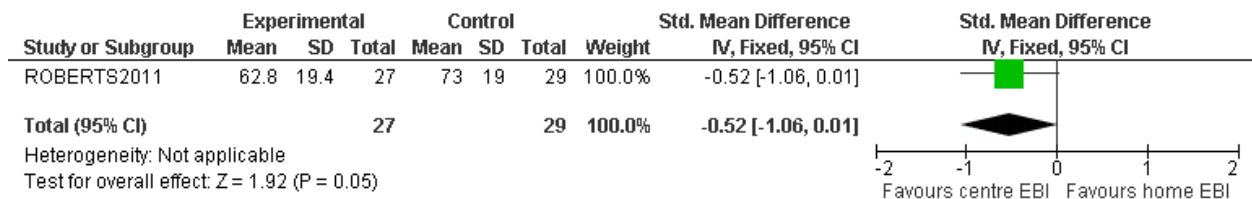
**Receptive language (Reynell Developmental Language Scale-Comprehension)**



**Expressive language (Reynell Developmental Language Scale-Expressive)**



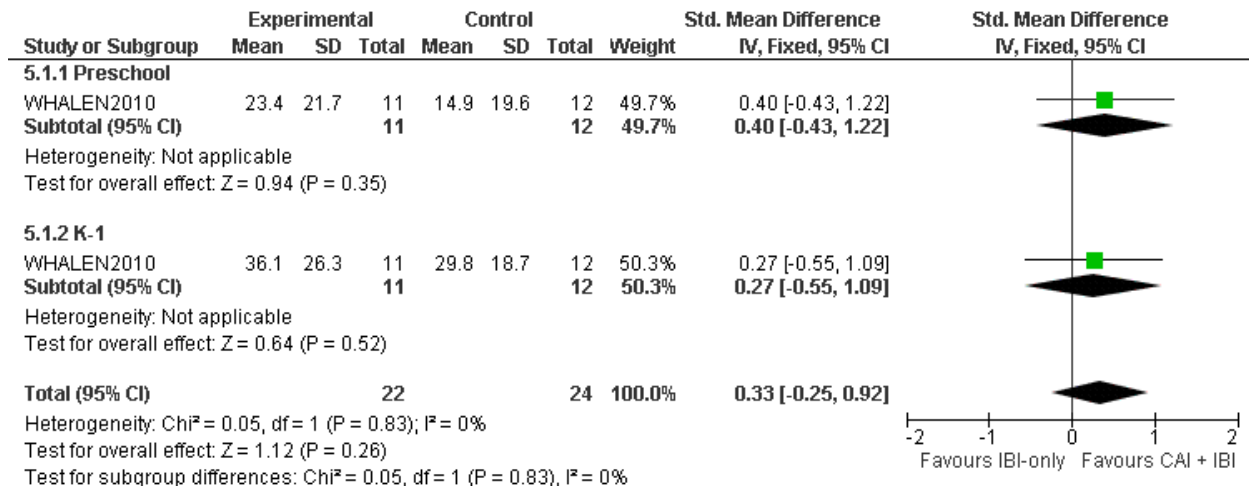
**Everyday language functioning (Pragmatics Profile)**



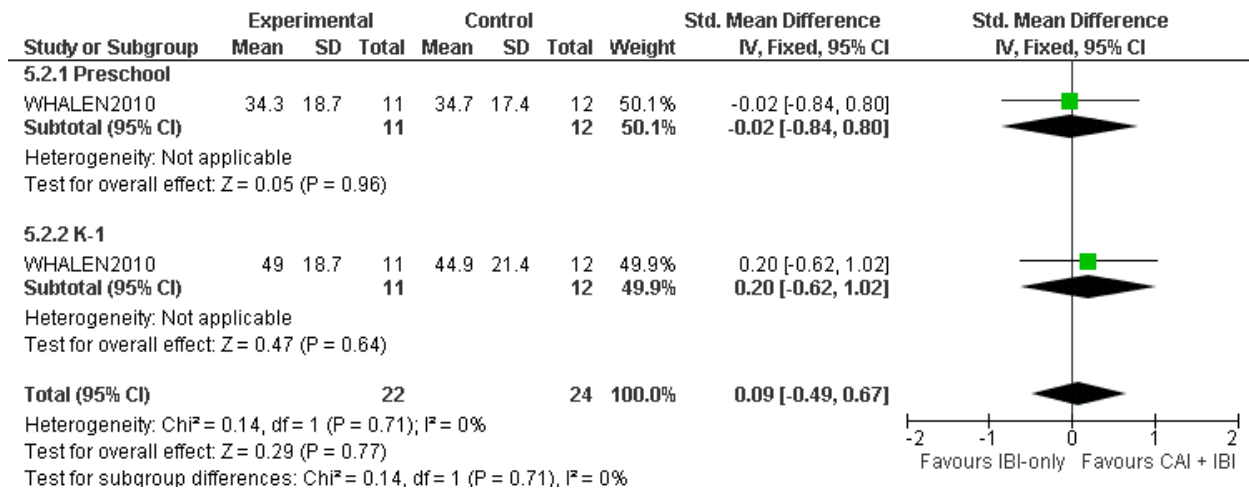
**1.16.4 Educational interventions for speech and language as a direct or indirect outcome**

*Combined TeachTown and IBI versus IBI-only for speech and language as a direct outcome*

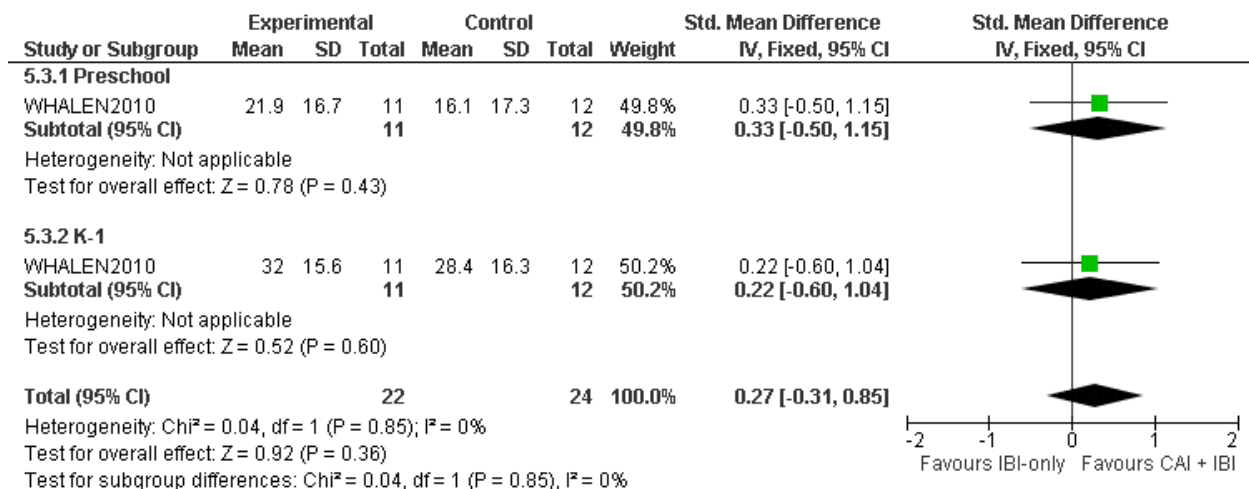
**Receptive language (PPVT-III)**



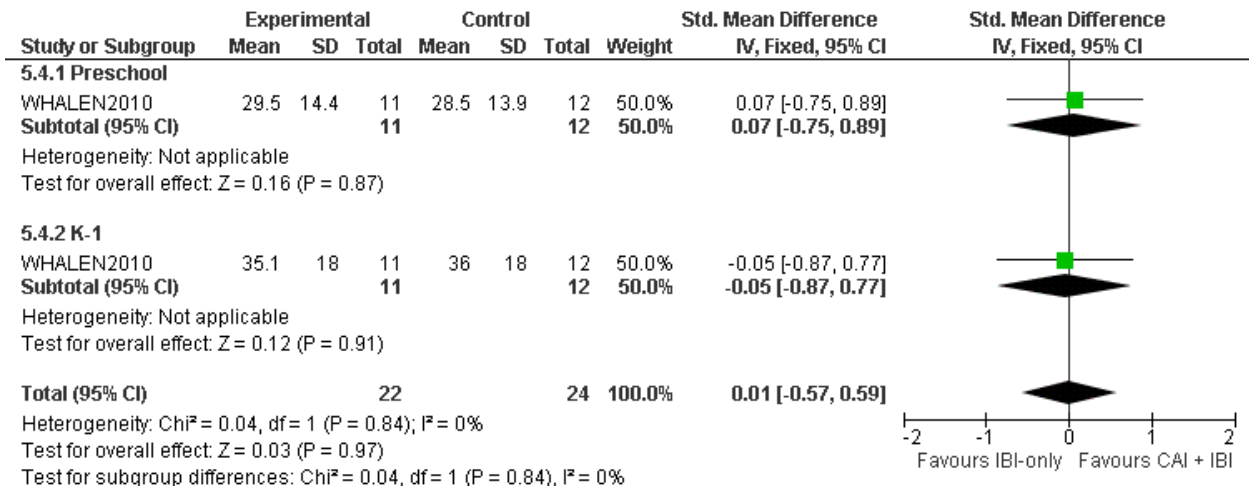
### Receptive language (Brigance Inventory of Child Development)



### Expressive language (EVT)

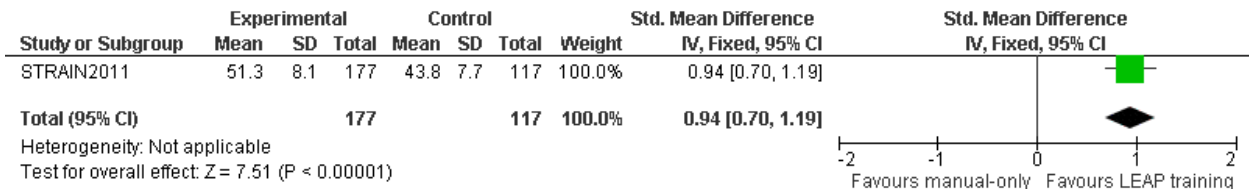


### Expressive language (Brigance Inventory of Child Development)

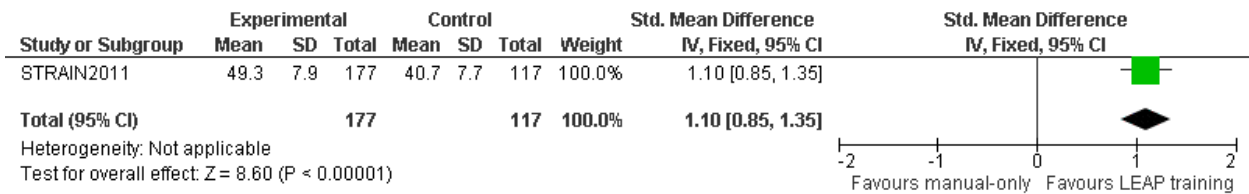


### LEAP training versus manual-only control for speech and language as an indirect outcome

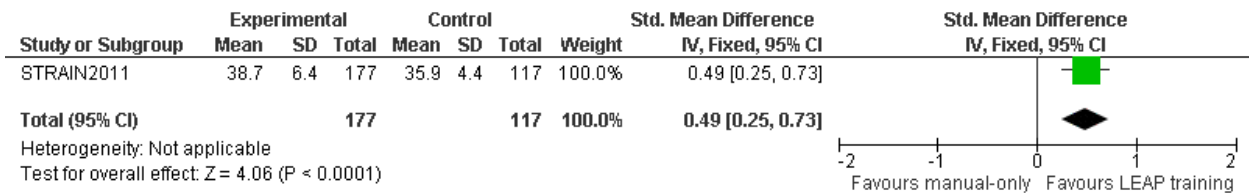
#### Total language score (PLS-4)



#### Receptive language (MSEL; language age in months)



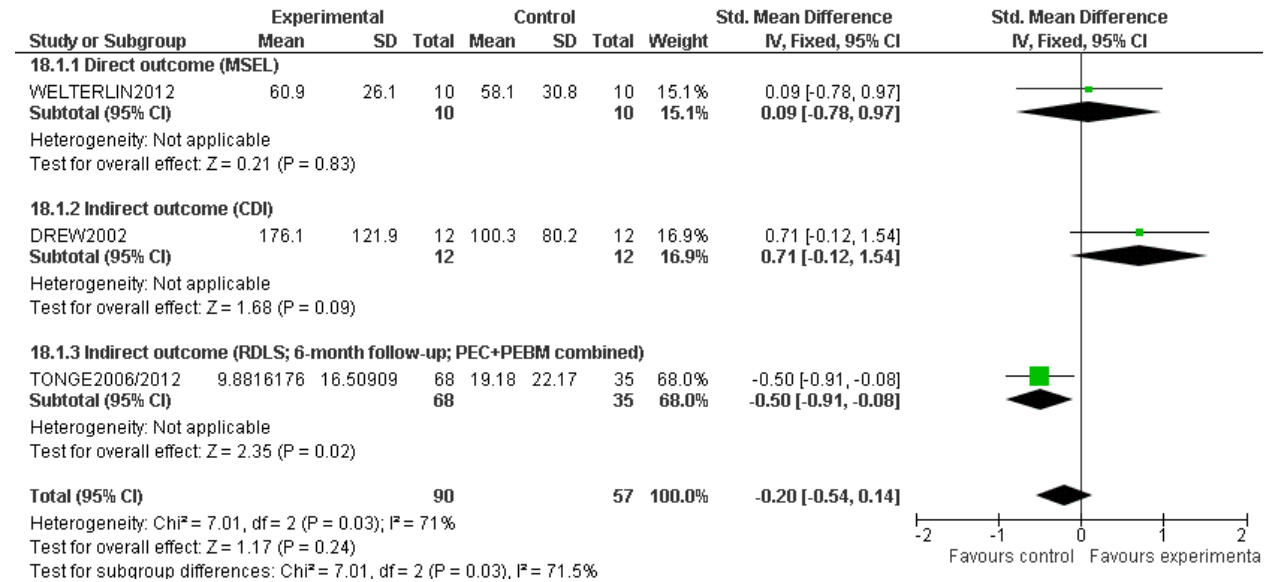
#### Expressive language (MSEL; language age in months)



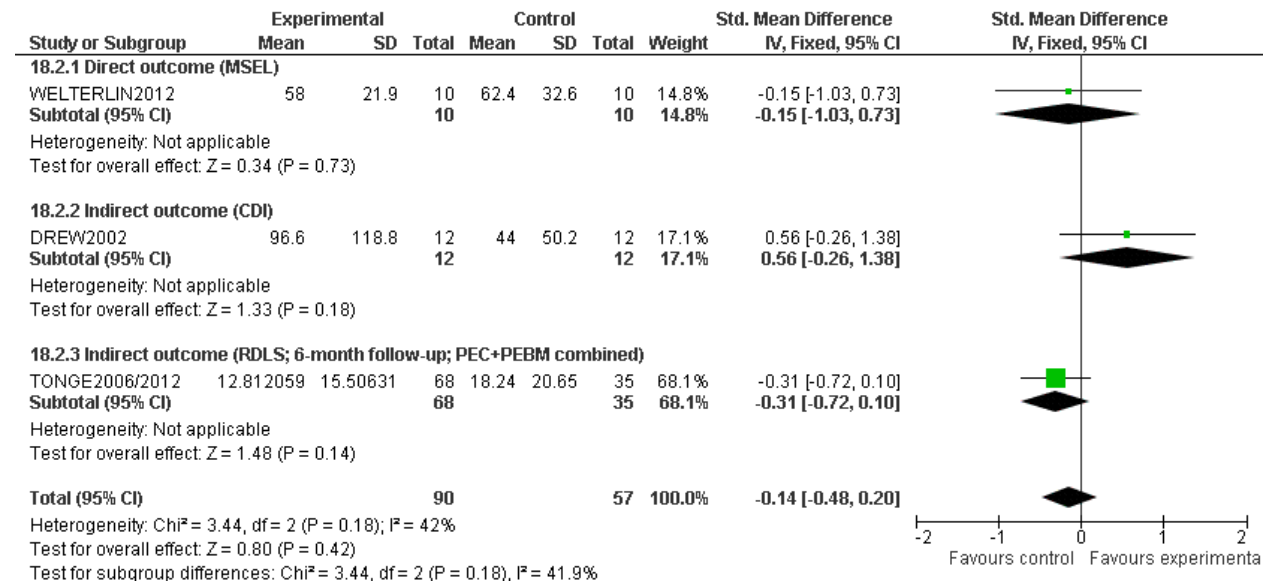
## 1.16.5 Parent training for speech and language as a direct or indirect outcome

### *Parent training versus treatment-as-usual for speech and language as a direct or indirect outcome*

#### Receptive language

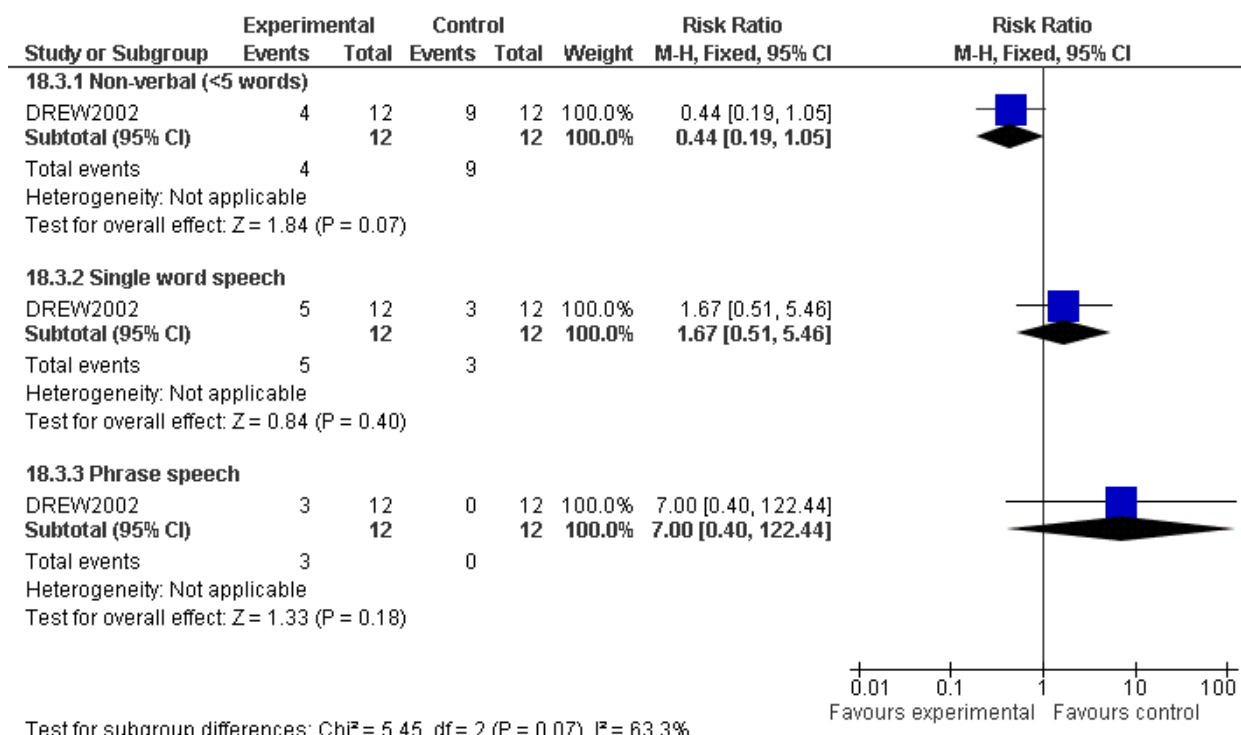


#### Expressive language

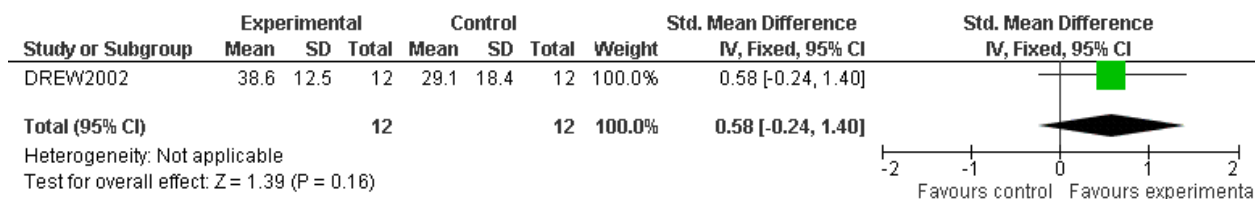


#### Overall language rating (ADI-R; indirect outcome)

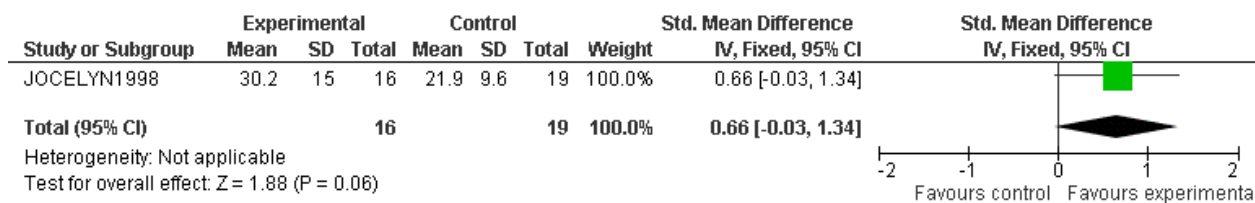




**Total gestures produced (CDI; indirect outcome)**



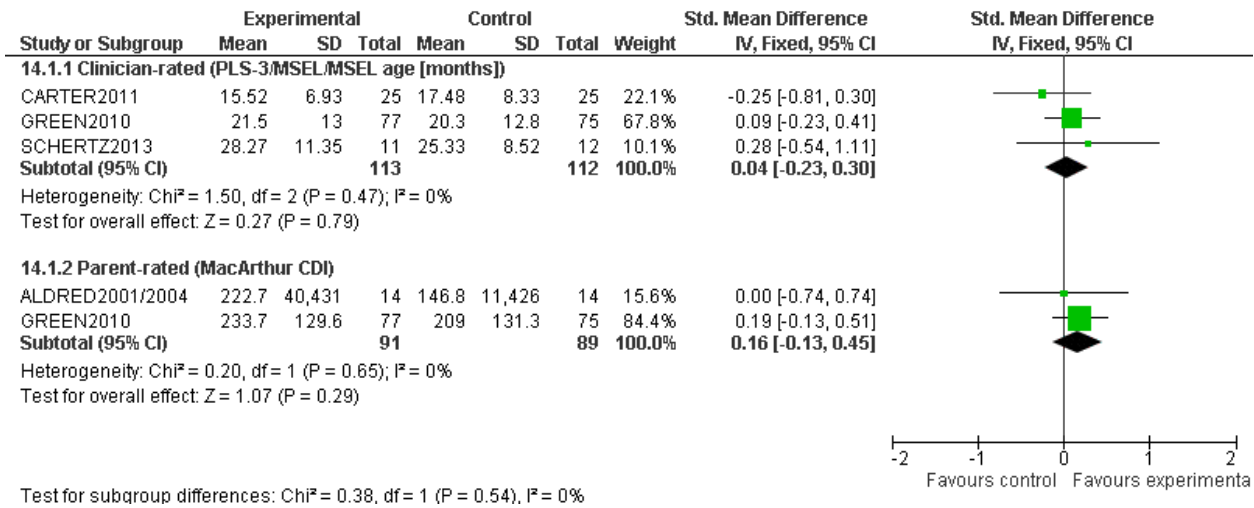
**Parent and day-care staff training versus standard day-care for speech and language as an indirect outcome**



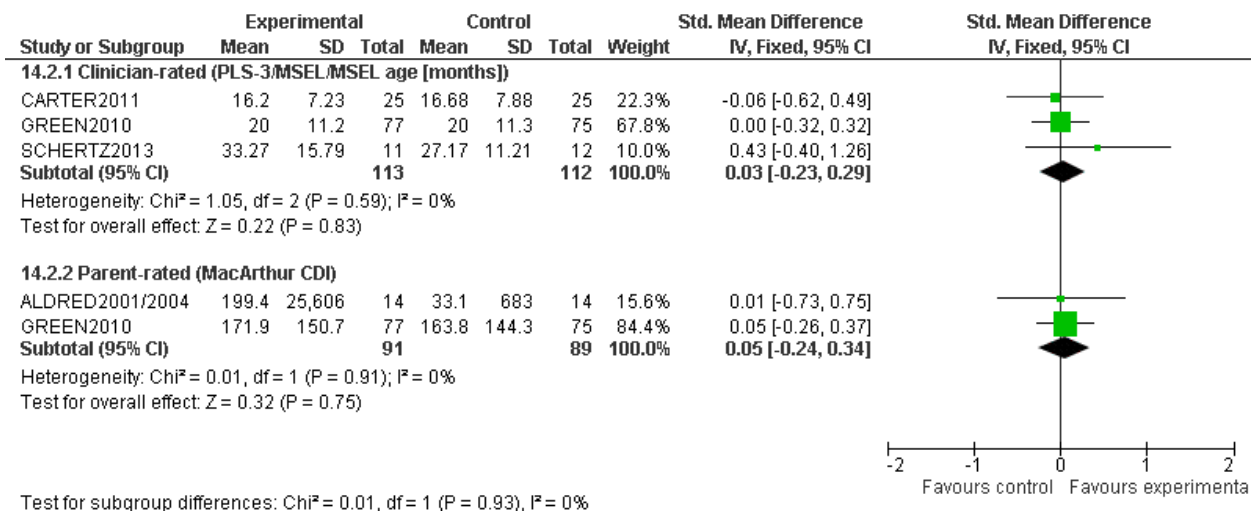
**1.16.6 Social-communication interventions for speech and language as an indirect outcome**

**Caregiver-mediated social communication intervention versus treatment-as-usual for speech and language as an indirect outcome**

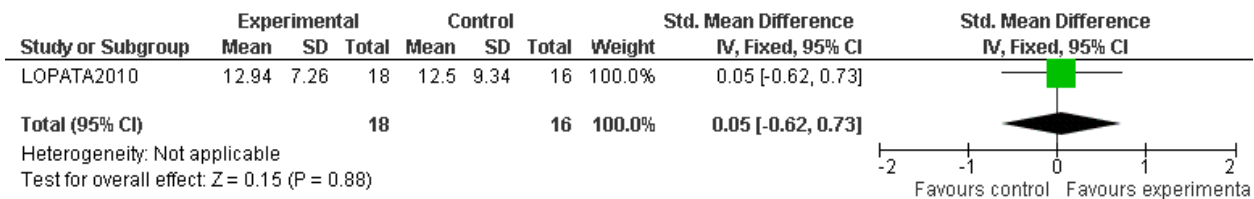
## Receptive language



## Expressive language

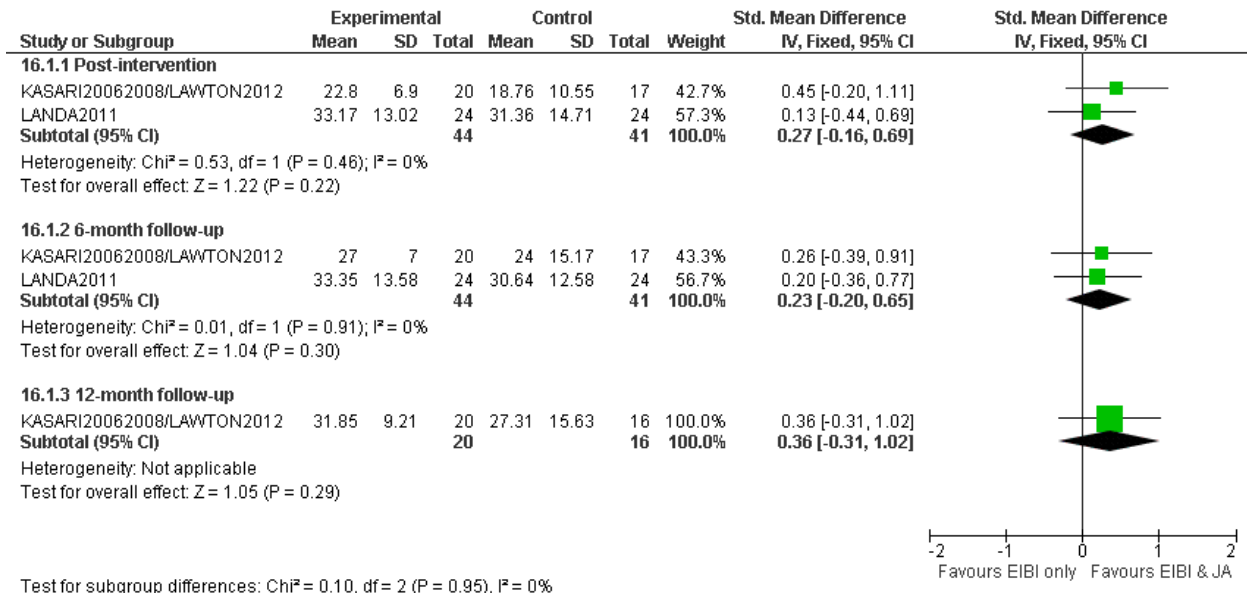


## Social skills group versus treatment-as-usual for speech and language as an indirect outcome

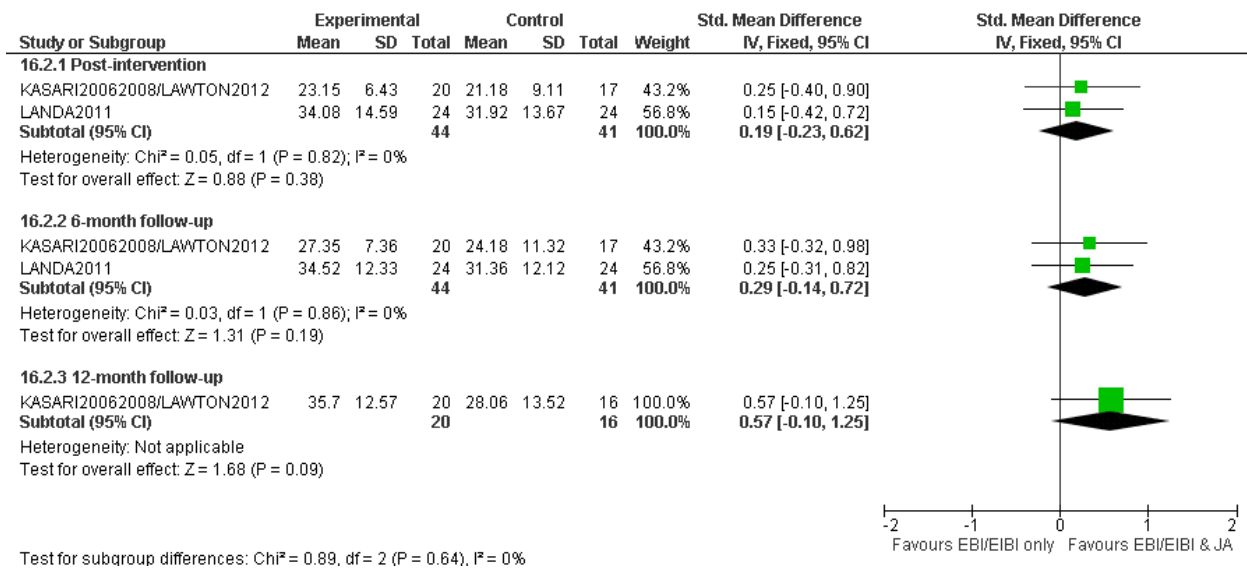


*Joint attention training and EBI/EIBI versus EBI/EIBI only for speech and language as an indirect outcome*

**Receptive language (Reynell or MSEL)**



**Expressive language (Reynell or MSEL)**

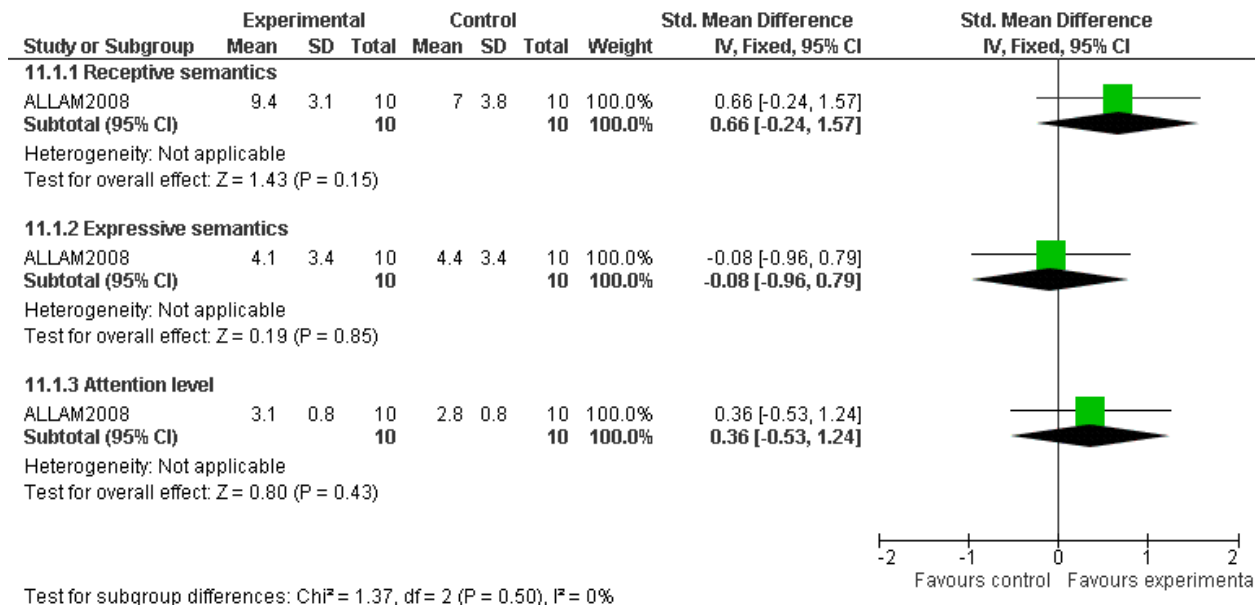


## 1.17 BIOMEDICAL INTERVENTIONS AIMED AT SPEECH AND LANGUAGE

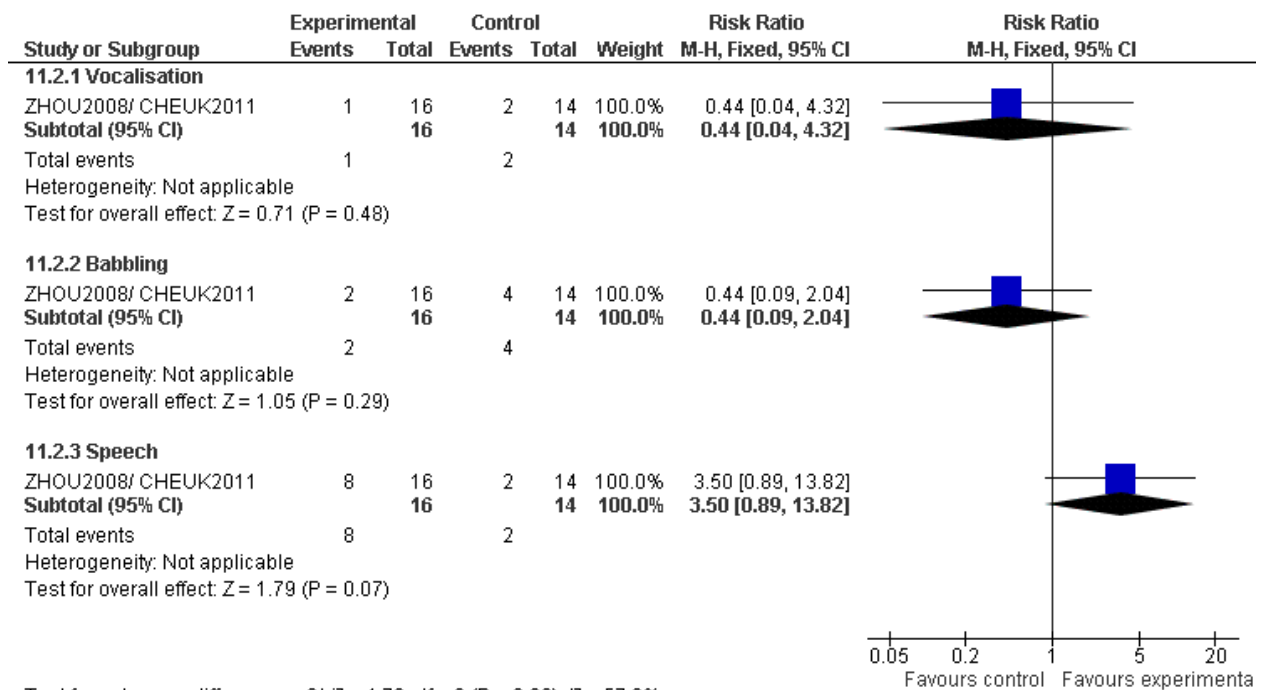
### 1.17.1 Complementary therapies for speech and language as a direct or indirect outcome

*Acupuncture/acupressure and language therapy versus language therapy only for speech and language as a direct outcome*

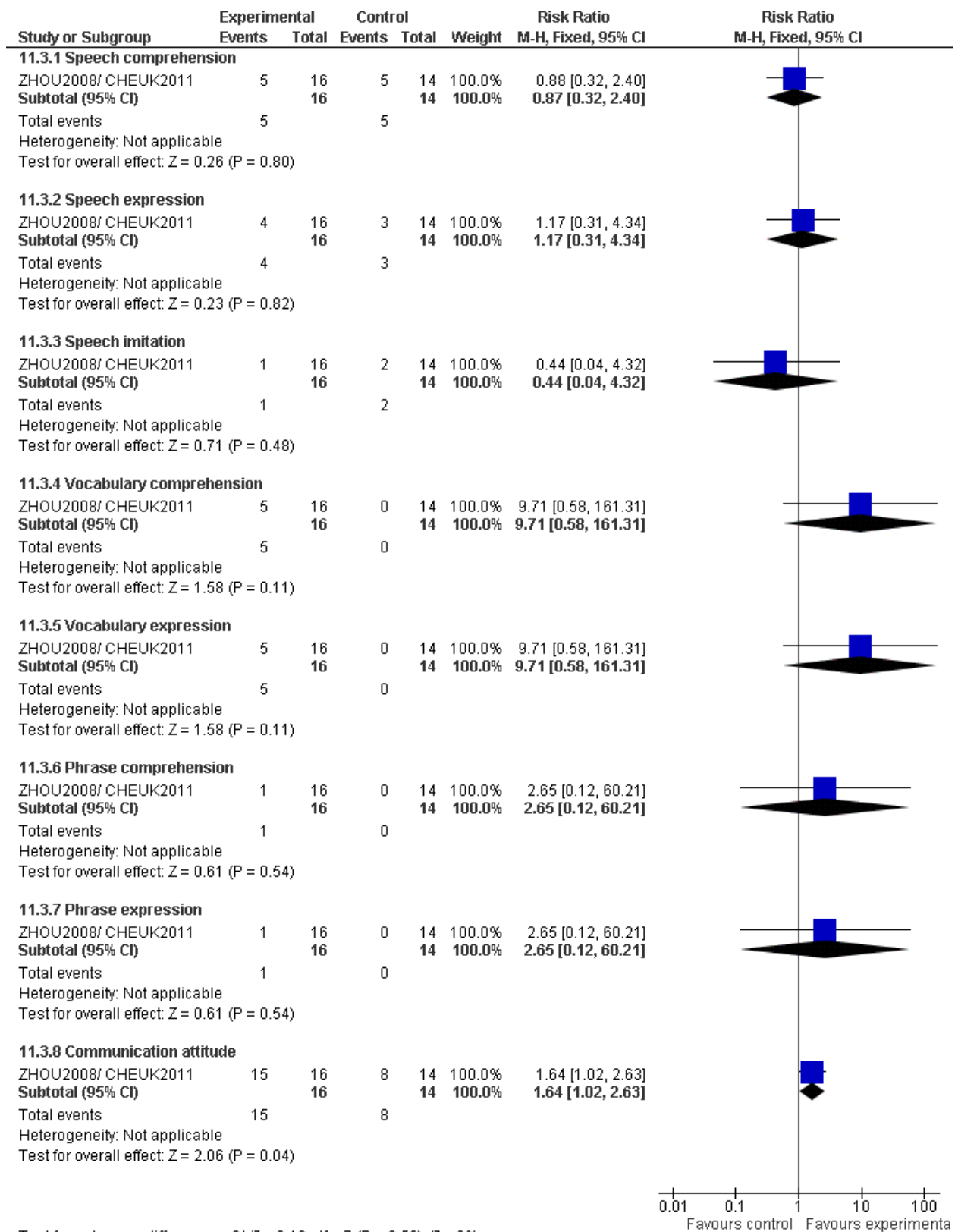
#### Language and attention (Arabic Language Test)



#### Positive treatment response (improvement in basic developmental assessment)

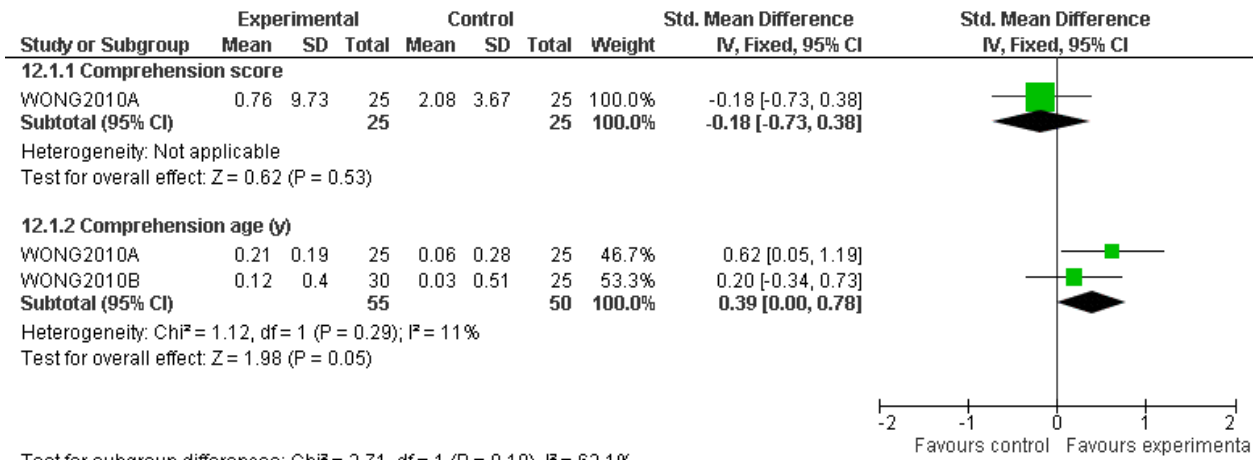


**Positive treatment response (number of participants improved on CRRC significance relations scale)**

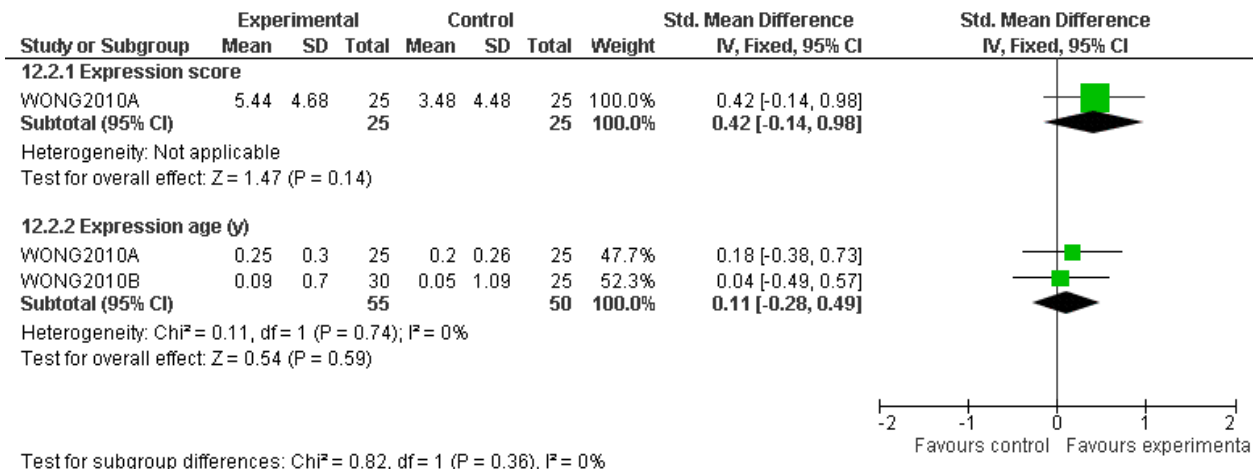


*Acupuncture/electro-acupuncture versus sham acupuncture/electro-acupuncture for speech and language as an indirect outcome*

**Receptive language (RDLS; change score)**



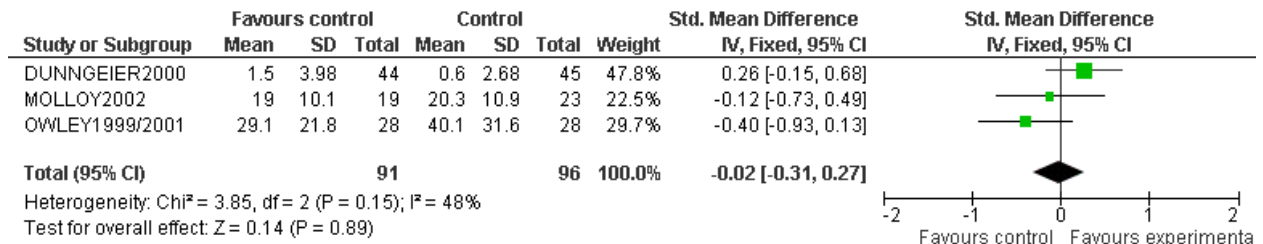
**Expressive language (RDLS; change score)**



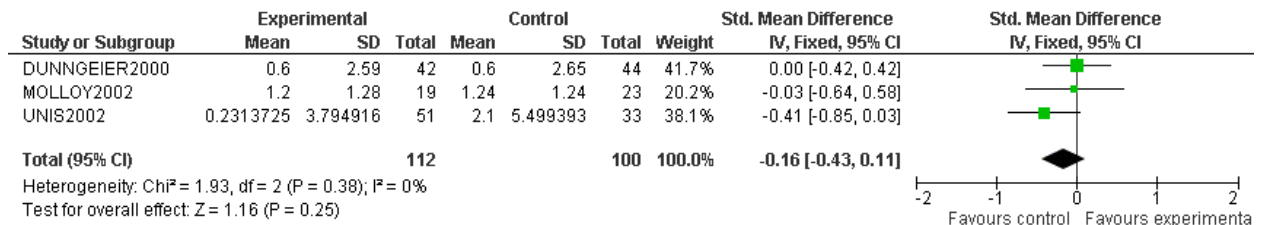
**1.17.2 Hormones for speech and language as an indirect outcome**

*Secretin versus placebo for speech and language as an indirect outcome*

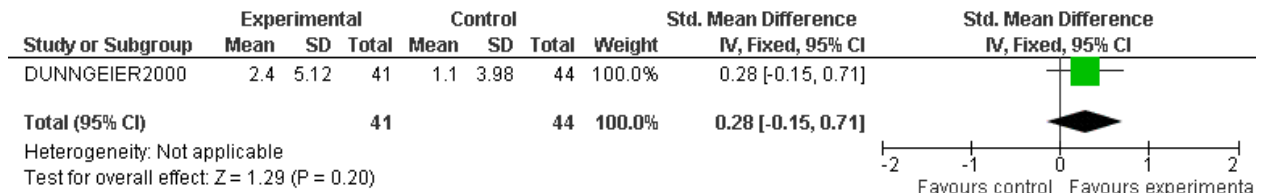
**Receptive Language (PLS-3/MSEL/PPVT-III or MSEL)**



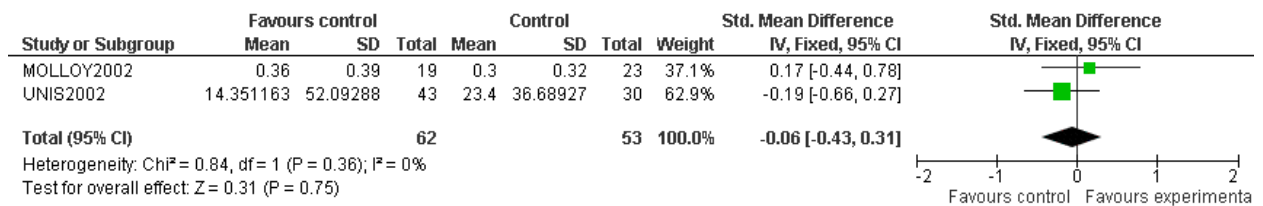
### Expressive language (PLS-3 change score/MLU behavioural observation/EOWPVT-R change score)



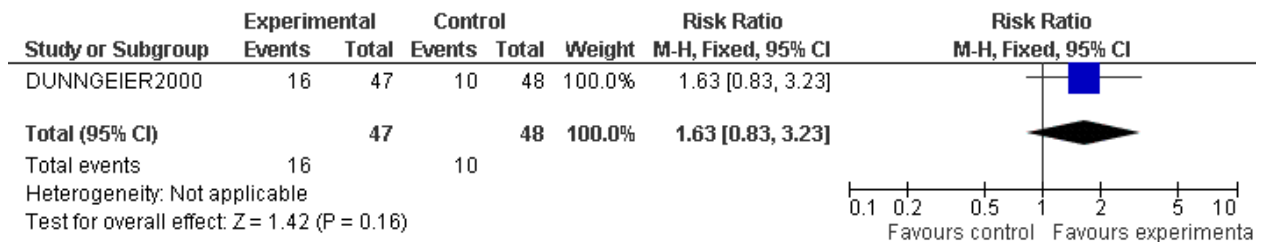
### Receptive and expressive language (PLS-3 total; change score)



### Vocabulary (type-token ratio behavioural observation or CDI vocabulary)



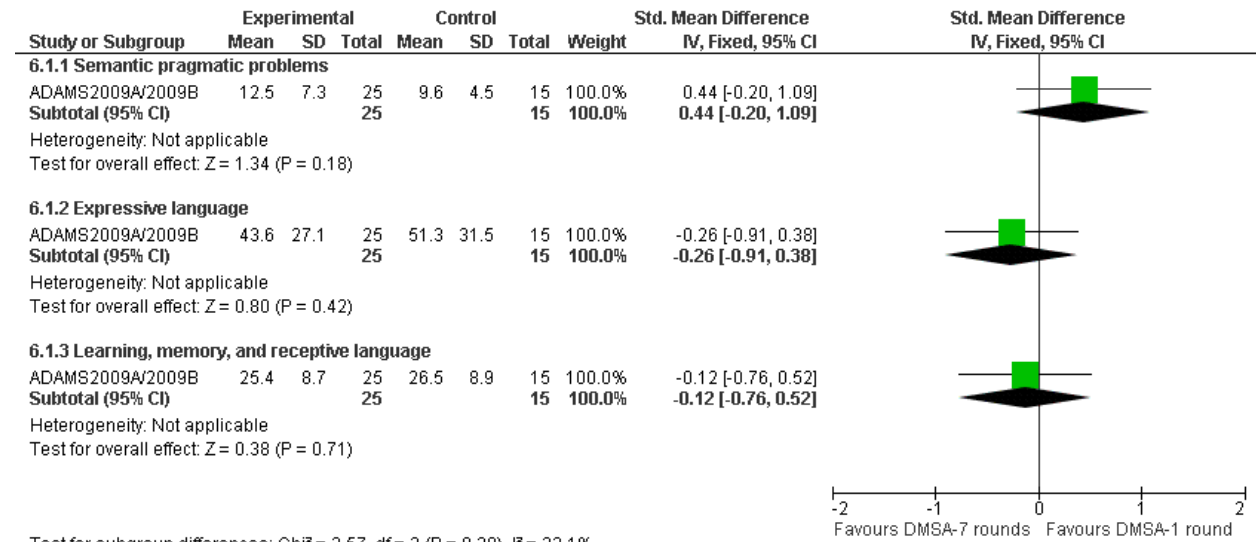
### Positive treatment response (>=4 points improvement on PLS-3)



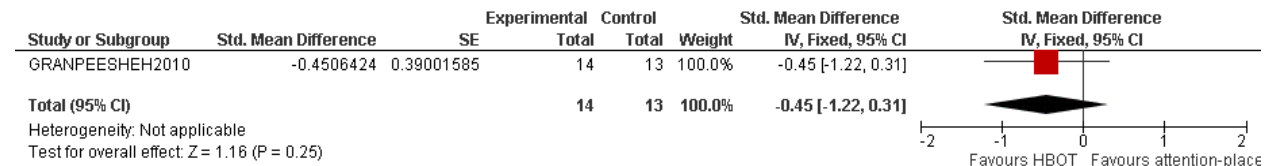


### 1.17.3 Medical procedures for speech and language as an indirect outcome

#### *Long-term chelation (7-rounds of DMSA therapy) versus short-term chelation (1-round of DMSA therapy and 6-rounds of placebo) for speech and language as an indirect outcome*



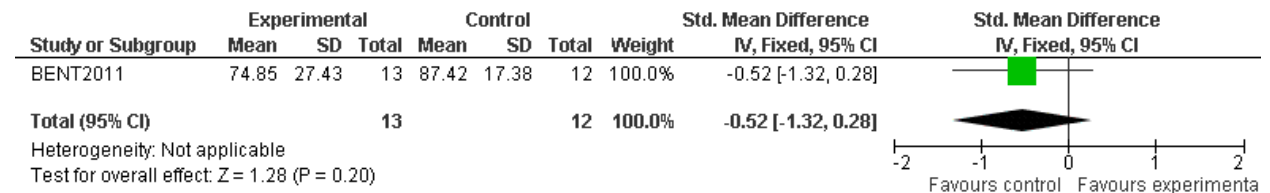
#### *HBOT versus attention-placebo for speech and language as an indirect outcome*



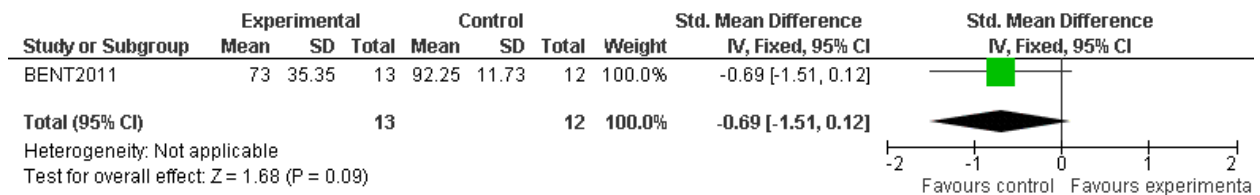
### 1.17.4 Nutritional interventions for speech and language as an indirect outcome

#### *Omega-3 fatty acids versus placebo for speech and language as an indirect outcome*

##### Receptive language (PPVT)

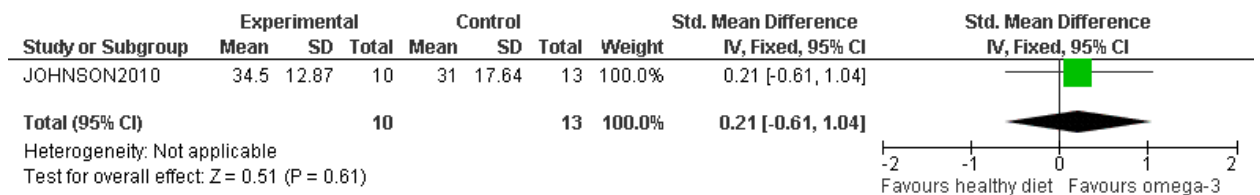


### Expressive language (EVT)

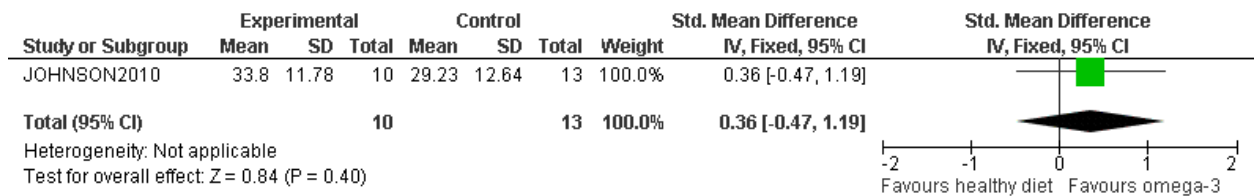


### *Omega-3 fatty acids versus healthy diet control for speech and language as an indirect outcome*

#### Receptive language (MSEL)

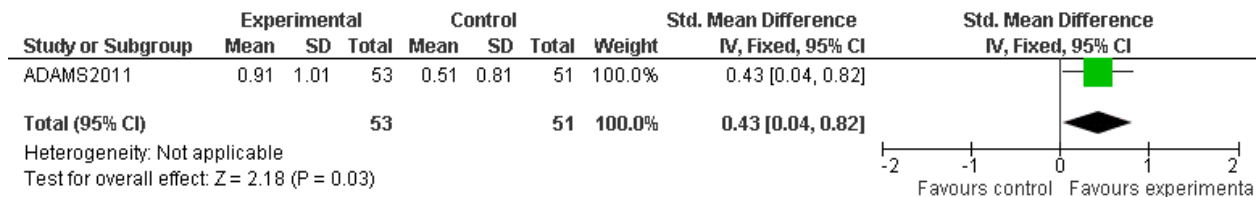


#### Expressive language (MSEL)



### *Multivitamin/ mineral supplement versus placebo for speech and language as an indirect outcome*

#### Receptive language improvement (PGI-R)



#### Expressive language improvement (PGI-R)

Study or Subgroup	Experimental			Control			Weight	Std. Mean Difference IV, Fixed, 95% CI	Std. Mean Difference IV, Fixed, 95% CI
	Mean	SD	Total	Mean	SD	Total			
ADAMS2011	1.09	1.11	53	0.71	0.92	51	100.0%	0.37 [-0.02, 0.76]	
<b>Total (95% CI)</b>			<b>53</b>			<b>51</b>	<b>100.0%</b>	<b>0.37 [-0.02, 0.76]</b>	

Heterogeneity: Not applicable  
Test for overall effect: Z = 1.87 (P = 0.06)

*L-carnosine supplement versus placebo for speech and language as an indirect outcome*

**Receptive language (ROWPVT)**

Study or Subgroup	Experimental			Control			Weight	Std. Mean Difference IV, Fixed, 95% CI	Std. Mean Difference IV, Fixed, 95% CI
	Mean	SD	Total	Mean	SD	Total			
<b>28.1.1 Raw score</b>									
CHEZ2002	44.64	26.56	14	37.11	30.89	17	100.0%	0.25 [-0.46, 0.96]	
<b>Subtotal (95% CI)</b>			<b>14</b>			<b>17</b>	<b>100.0%</b>	<b>0.25 [-0.46, 0.96]</b>	
Heterogeneity: Not applicable Test for overall effect: Z = 0.70 (P = 0.49)									
<b>28.1.2 Age adjusted score</b>									
CHEZ2002	47.86	28.37	14	41.65	30.46	17	100.0%	0.20 [-0.50, 0.91]	
<b>Subtotal (95% CI)</b>			<b>14</b>			<b>17</b>	<b>100.0%</b>	<b>0.20 [-0.50, 0.91]</b>	
Heterogeneity: Not applicable Test for overall effect: Z = 0.57 (P = 0.57)									

Test for subgroup differences: Chi<sup>2</sup> = 0.01, df = 1 (P = 0.93), I<sup>2</sup> = 0%

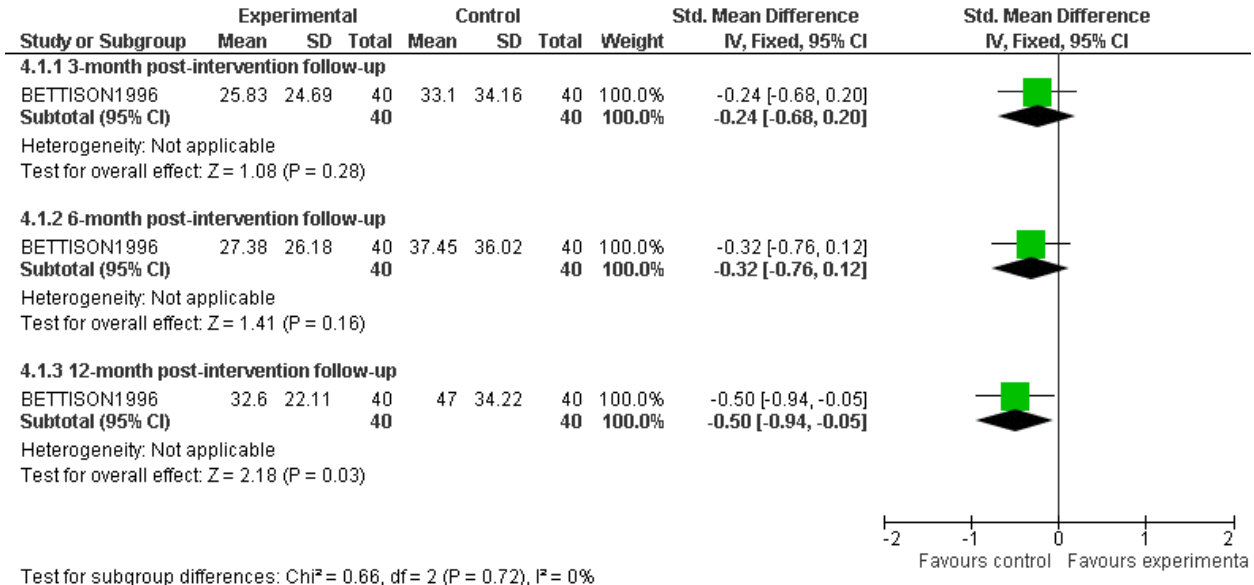
**Expressive language (EOWPVT)**

Study or Subgroup	Experimental			Control			Weight	Std. Mean Difference IV, Fixed, 95% CI	Std. Mean Difference IV, Fixed, 95% CI
	Mean	SD	Total	Mean	SD	Total			
<b>28.2.1 Raw score</b>									
CHEZ2002	37.28	25.66	14	31.65	29.19	17	100.0%	0.20 [-0.51, 0.91]	
<b>Subtotal (95% CI)</b>			<b>14</b>			<b>17</b>	<b>100.0%</b>	<b>0.20 [-0.51, 0.91]</b>	
Heterogeneity: Not applicable Test for overall effect: Z = 0.55 (P = 0.58)									
<b>28.2.2 Age adjusted score</b>									
CHEZ2002	43.78	28.22	14	37.12	33.38	17	100.0%	0.21 [-0.50, 0.92]	
<b>Subtotal (95% CI)</b>			<b>14</b>			<b>17</b>	<b>100.0%</b>	<b>0.21 [-0.50, 0.92]</b>	
Heterogeneity: Not applicable Test for overall effect: Z = 0.57 (P = 0.57)									

Test for subgroup differences: Chi<sup>2</sup> = 0.00, df = 1 (P = 0.98), I<sup>2</sup> = 0%

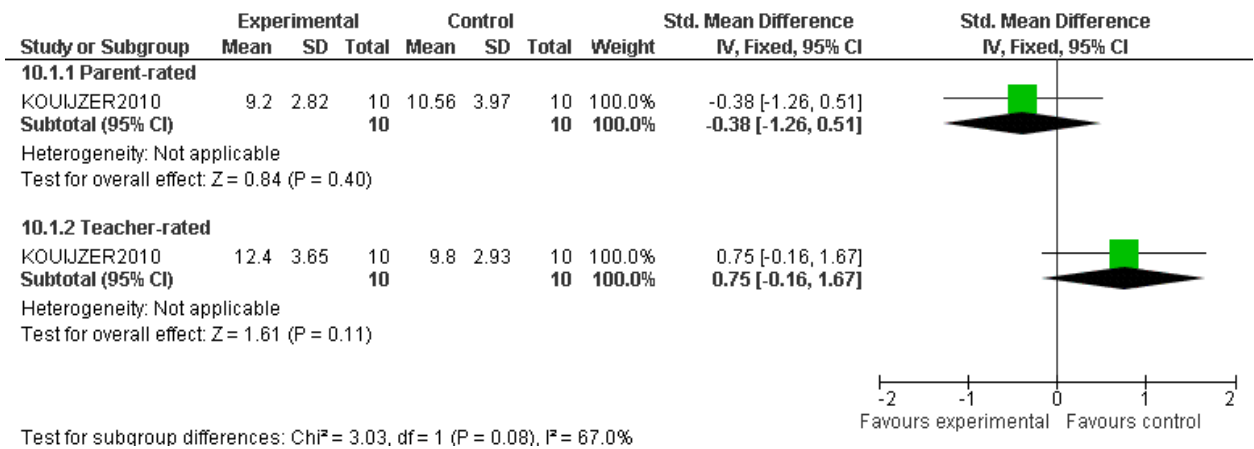
### 1.17.5 Sensory interventions for speech and language as an indirect outcome

#### *Auditory integration training versus attention-placebo (structured listening) for speech and language as an indirect outcome*

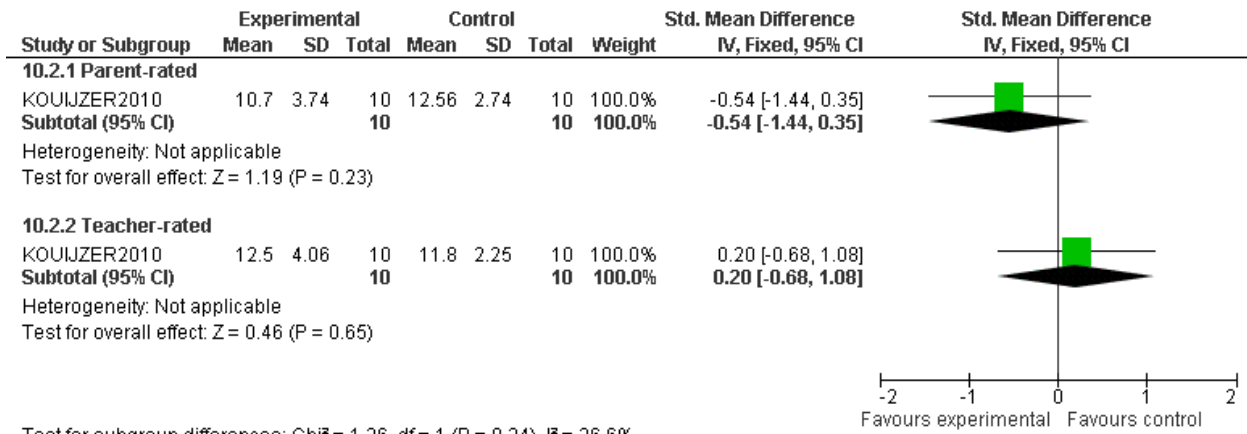


#### *Neurofeedback versus treatment-as-usual for speech and language as an indirect outcome*

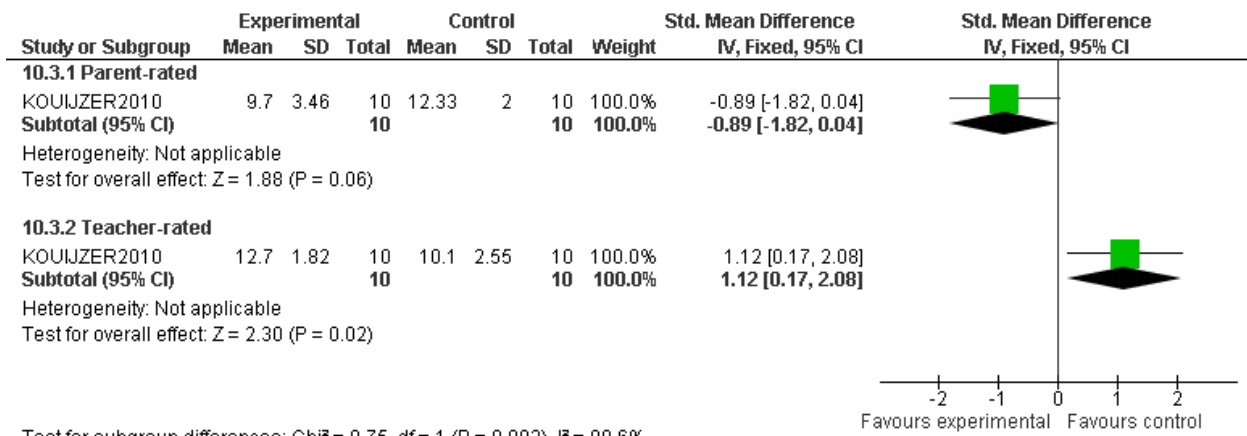
##### Speech production (CCC-2)



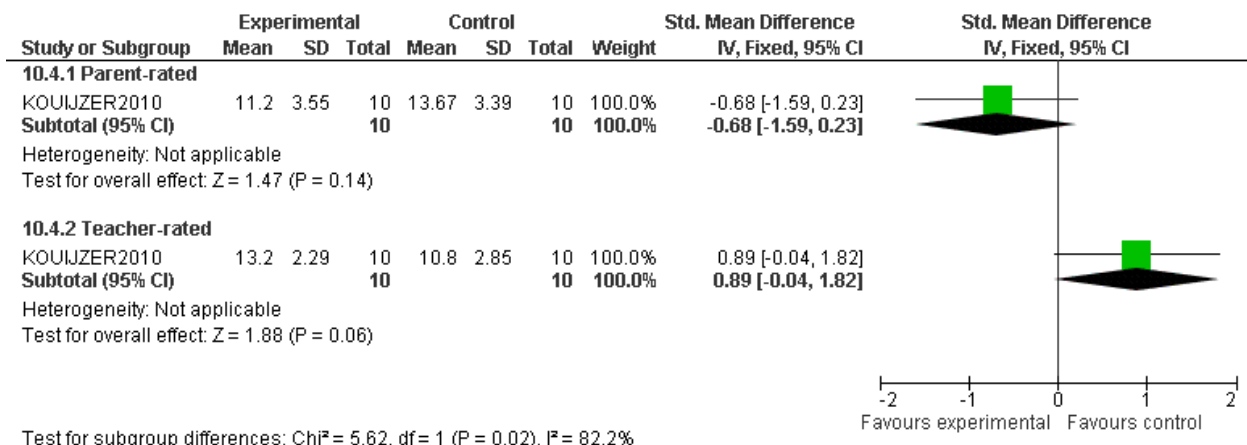
##### Syntax (CCC-2)



### Semantics (CCC-2)



### Coherence (CCC-2)

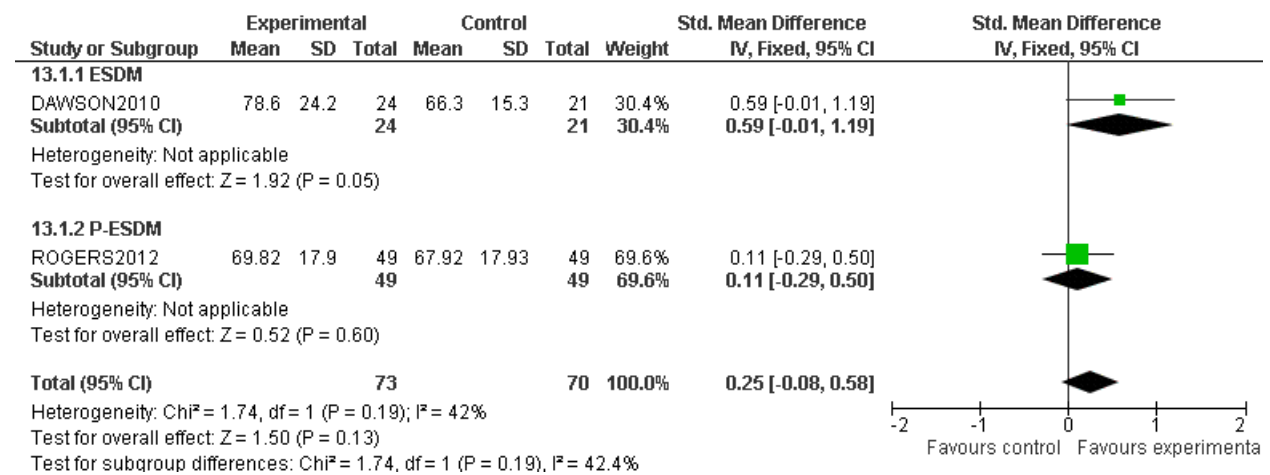


## 1.18 PSYCHOSOCIAL INTERVENTIONS AIMED AT IQ AND ACADEMIC SKILLS

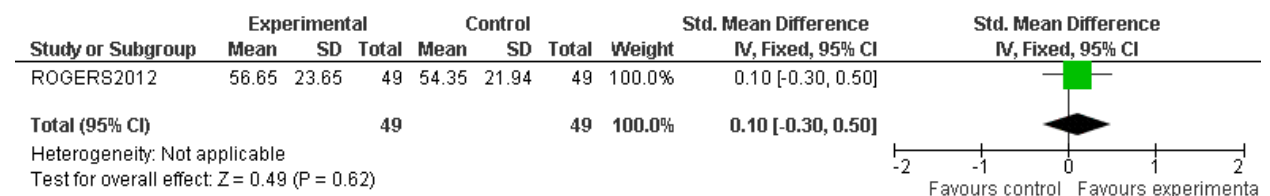
### 1.18.1 Behavioural interventions for IQ and/or academic skills as a direct or indirect outcome

*EIBI or EBI (ESDM or P-ESDM) versus treatment-as-usual for IQ as a direct or indirect outcome*

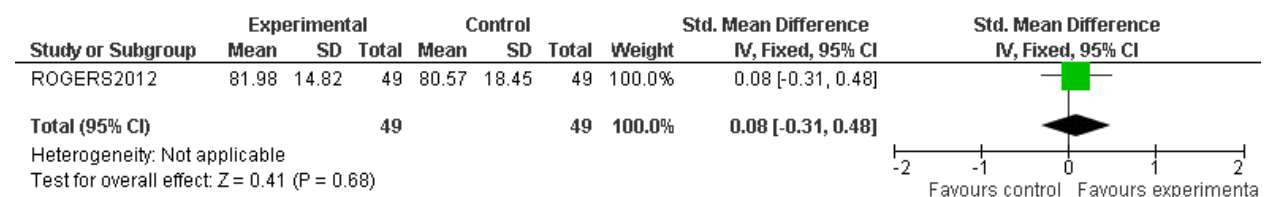
#### IQ (MSEL - Early-learning composite score; Developmental quotient)



#### Verbal developmental quotient (MSEL)

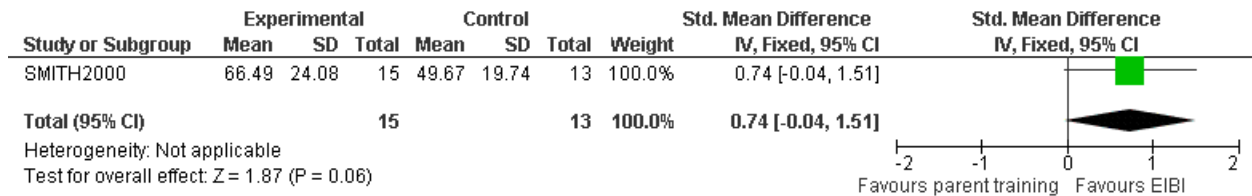


#### Non-verbal developmental quotient (MSEL)

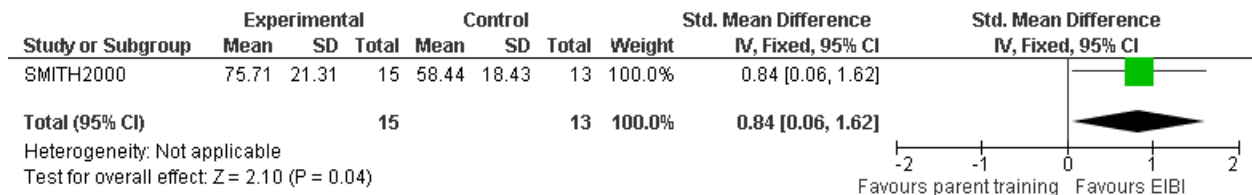


*EIBI versus parent training for IQ and academic skills as an indirect outcome*

**IQ (Bayley Scales of Infant Development - Mental Development Index)**

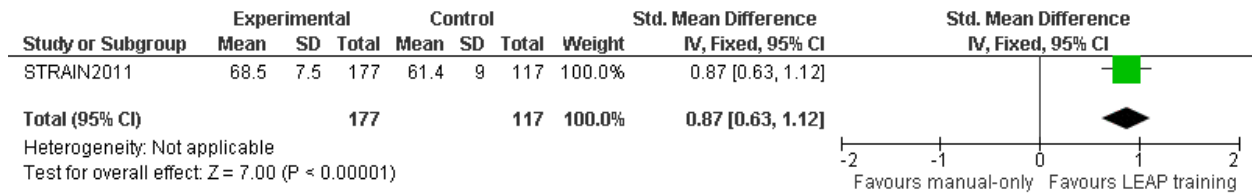


**Academic skills (WIAT total score)**



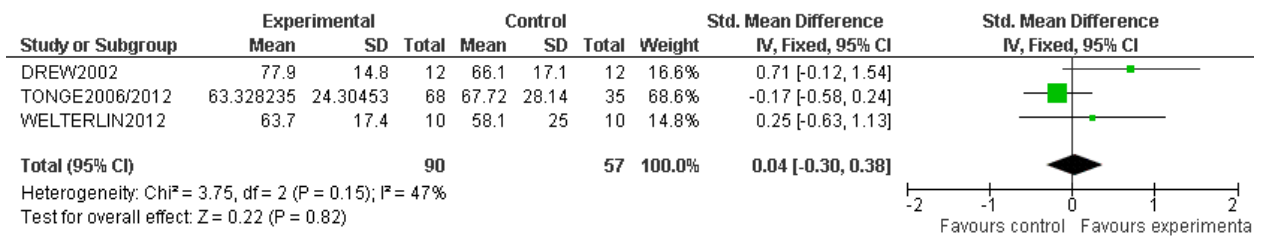
**1.18.2 Educational interventions for IQ as an indirect outcome**

*LEAP training versus manual-only control for IQ as an indirect outcome*

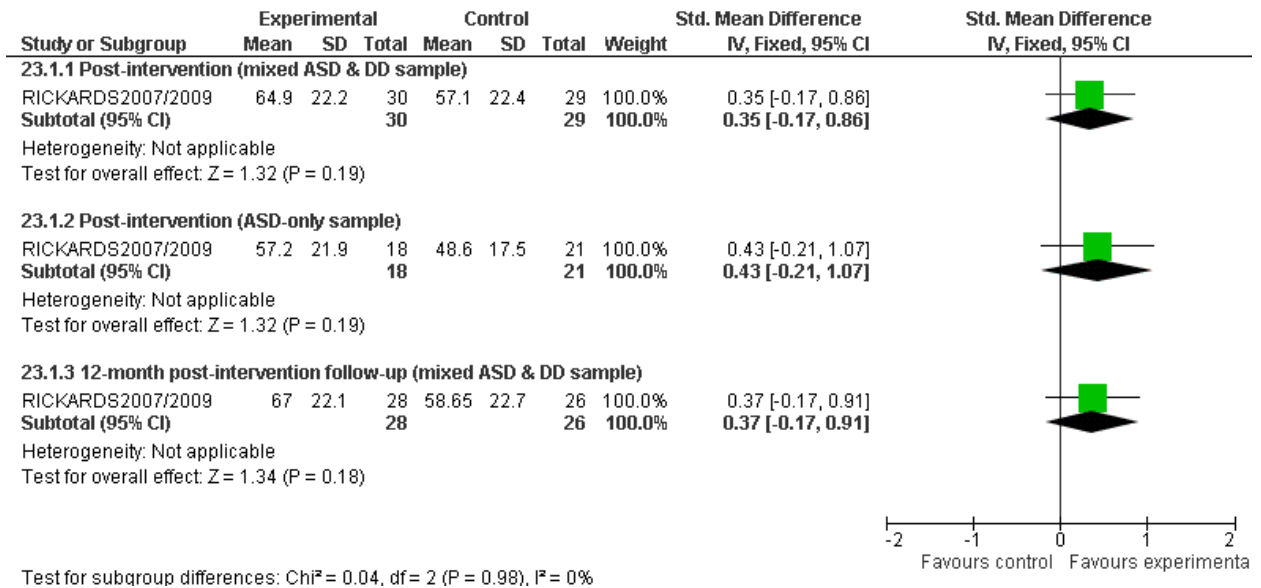


**1.18.3 Parent training for IQ as an indirect outcome**

*Parent training versus treatment-as-usual for IQ as an indirect outcome*

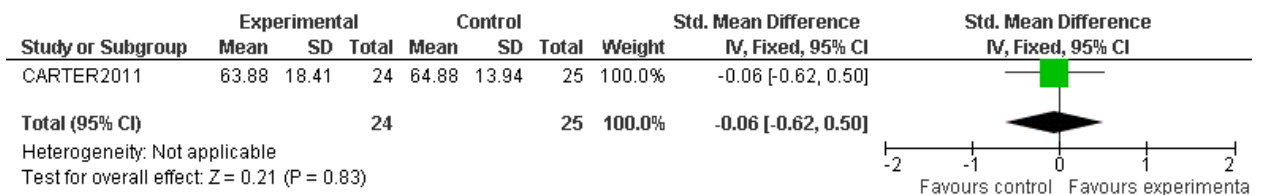


*Combined parent training and early intervention centre programme versus early intervention centre programme only for IQ as an indirect outcome*



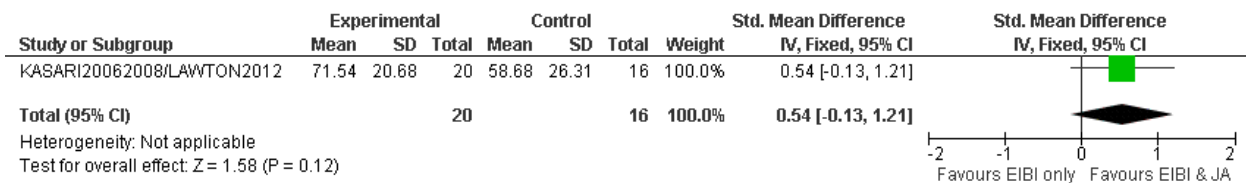
**1.18.4 Social-communication interventions for IQ as an indirect outcome**

*Caregiver-mediated social communication intervention versus treatment-as-usual for IQ as an indirect outcome*



*Joint attention training and EIBI versus EIBI only for IQ as an indirect outcome*

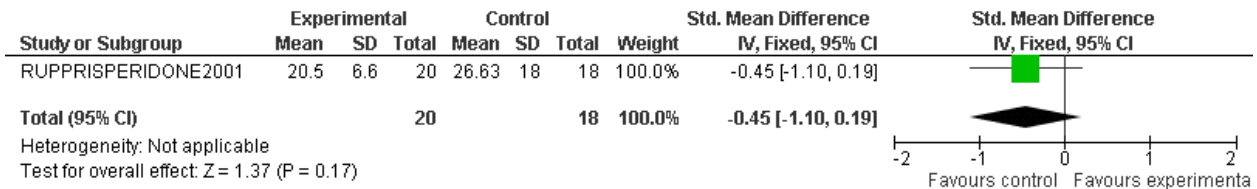




## 1.19 PHARMACOLOGICAL INTERVENTIONS AIMED AT ACADEMIC SKILLS

### 1.19.1 Antipsychotics for academic skills as an indirect outcome

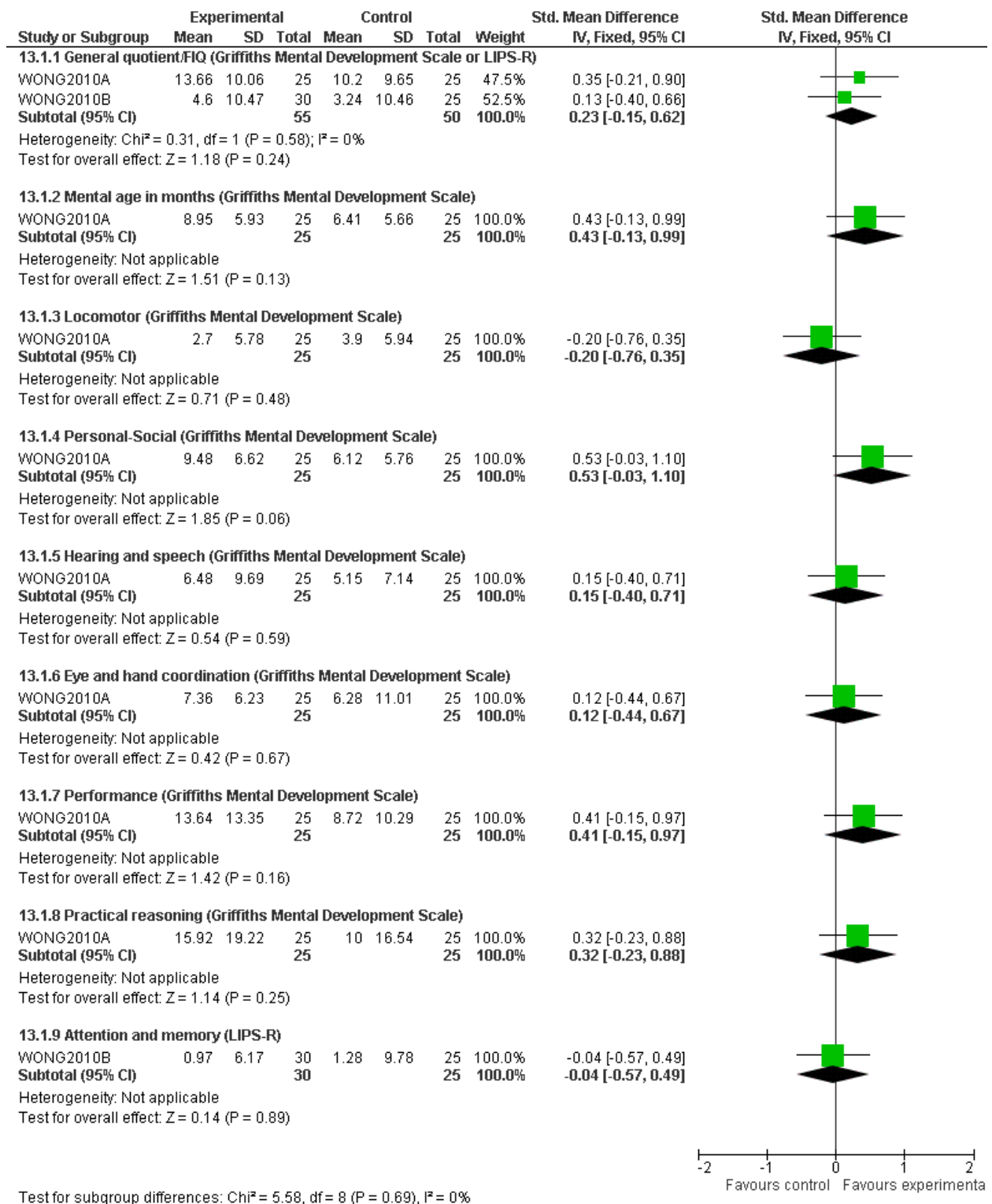
#### *Risperidone versus placebo for academic skills as an indirect outcome*



## 1.20 BIOMEDICAL INTERVENTIONS AIMED AT IQ

### 1.20.1 Complementary therapies for IQ as a direct outcome

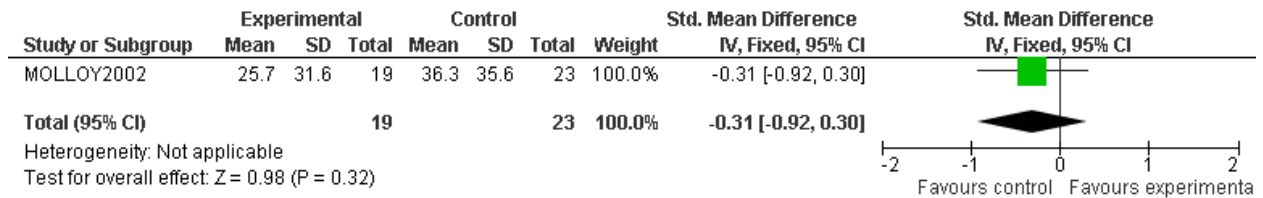
#### *Acupuncture/electro-acupuncture versus sham acupuncture/electro-acupuncture for IQ as a direct outcome*



## 1.20.2 Hormones for IQ as an indirect outcome

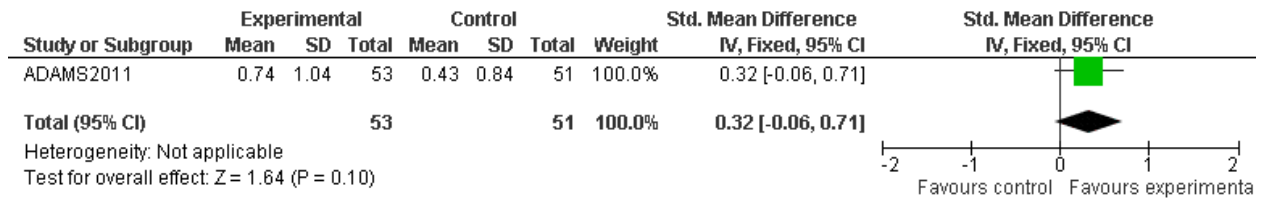
### Secretin versus placebo for IQ as an indirect outcome

Autism: the management and support of children and young people on the autism spectrum (March 2013)



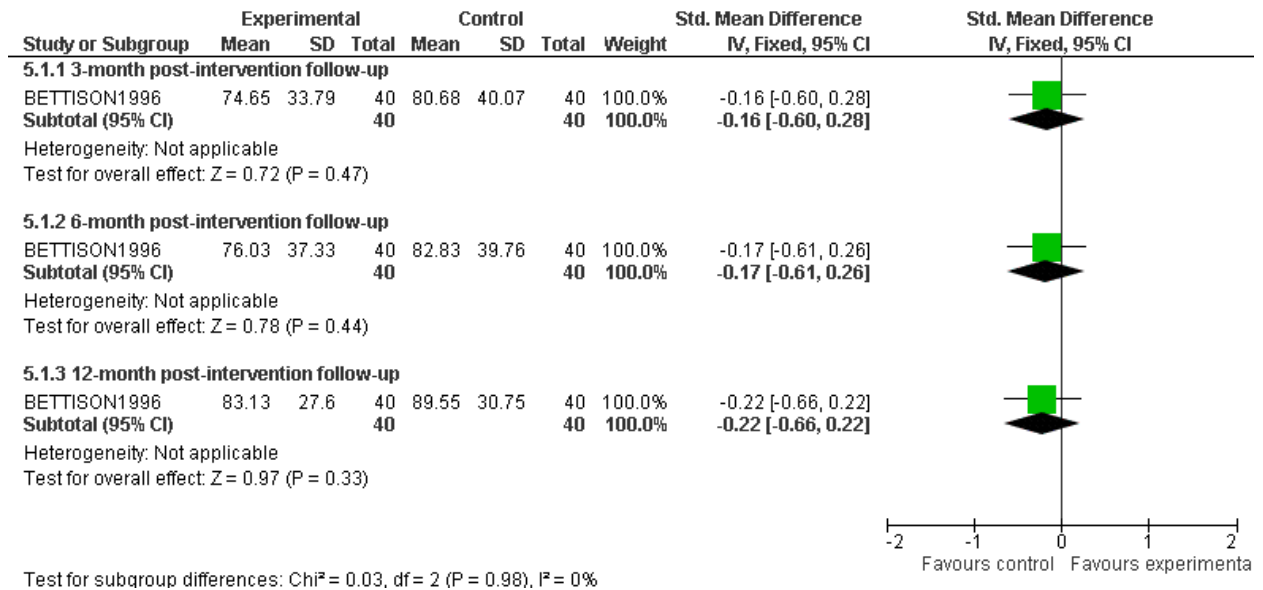
### 1.20.3 Nutritional intervention for IQ as an indirect outcome

#### *Multivitamin/ mineral supplement versus placebo for IQ as an indirect outcome*



### 1.20.4 Sensory intervention for IQ as an indirect outcome

#### *Auditory integration training versus attention-placebo (structured listening) for IQ as an indirect outcome*

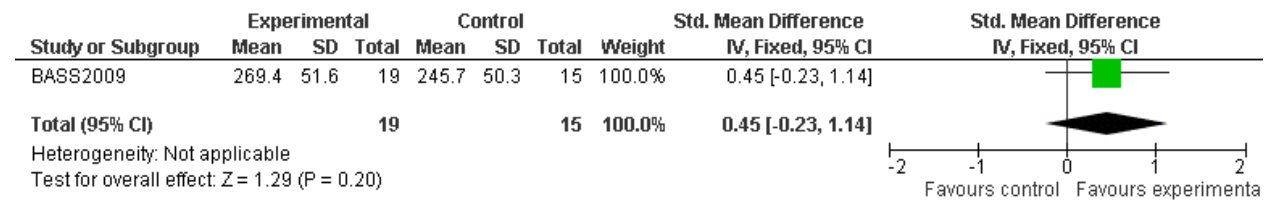


## 1.21 PSYCHOSOCIAL INTERVENTIONS AIMED AT SENSORY SENSITIVITIES

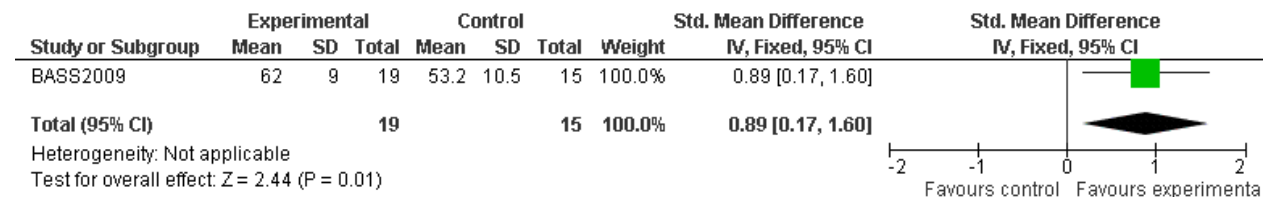
### 1.21.1 Animal-based interventions for sensory sensitivities as an indirect outcome

*Horseback riding versus waitlist control for sensory sensitivities as an indirect outcome*

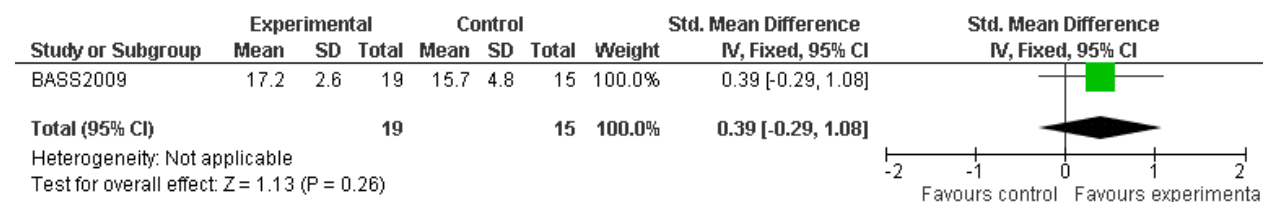
#### Sensory problems (Sensory Profile Total)



#### Sensory seeking (Sensory Profile)

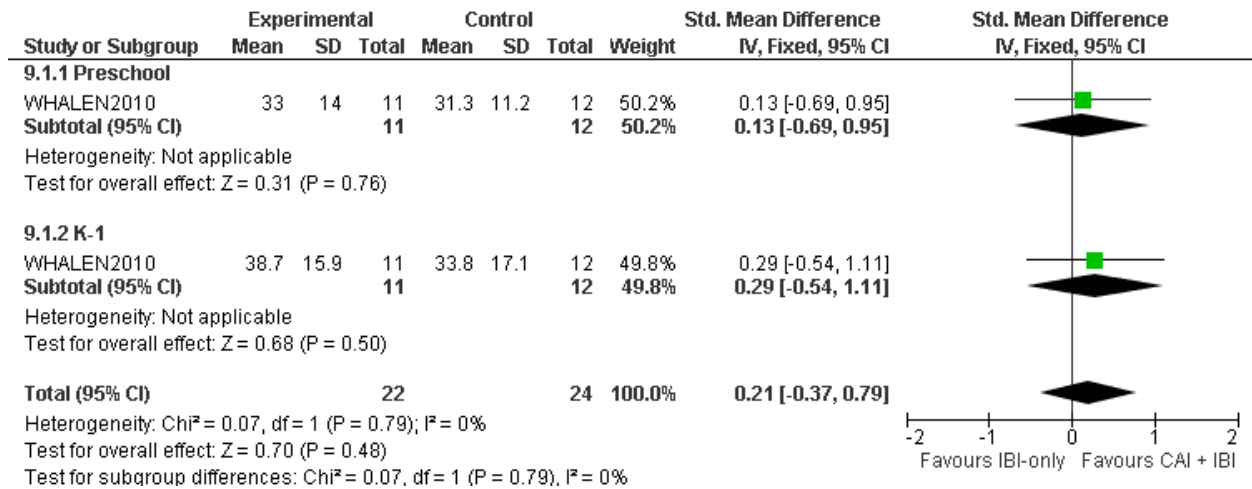


#### Sensory sensitivity (Sensory Profile)



### 1.21.2 Educational interventions for sensory sensitivities as an indirect outcome

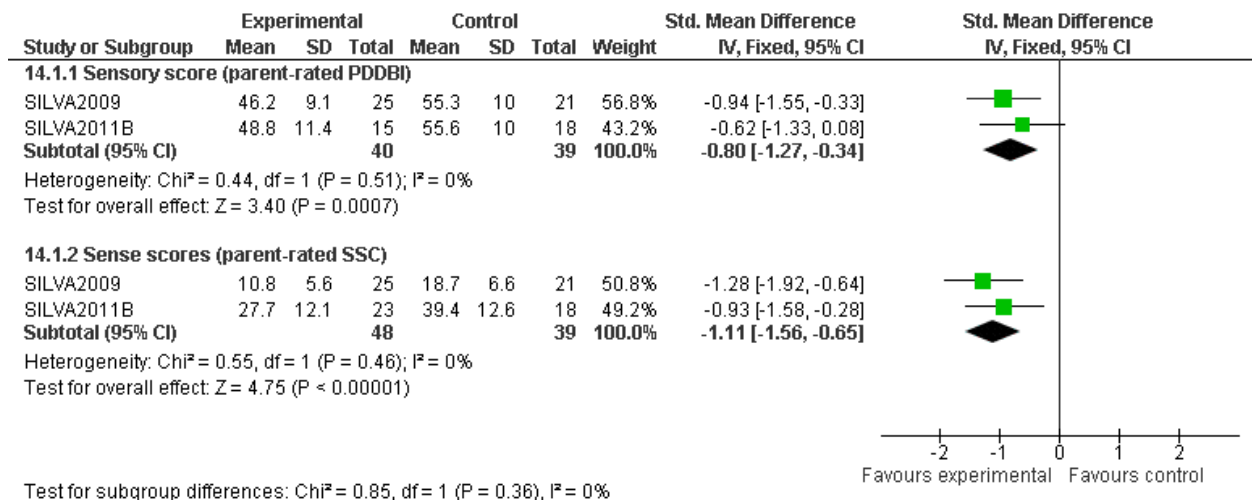
*Combined TeachTown and IBI versus IBI-only for sensory sensitivities as an indirect outcome*



## 1.22 BIOMEDICAL INTERVENTIONS AIMED AT SENSORY SENSITIVITIES

### 1.22.1 Complementary therapies for sensory sensitivities as a direct outcome

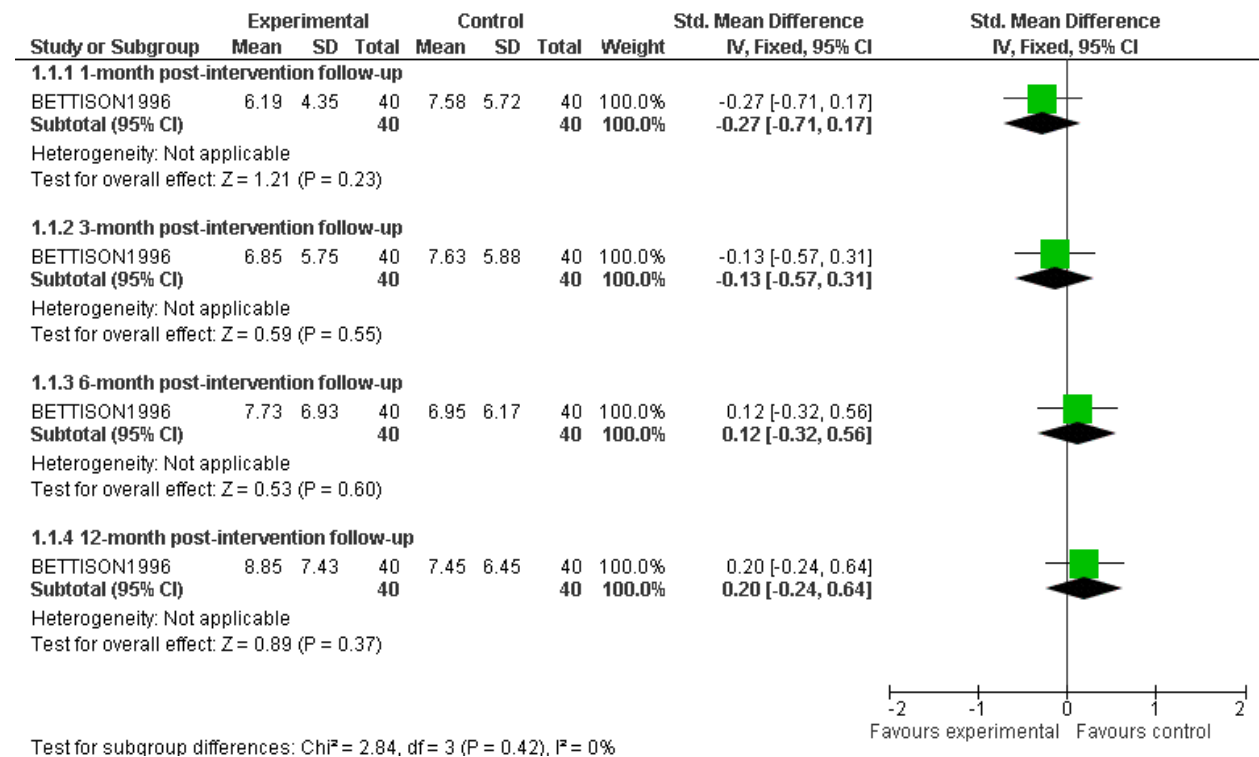
*Qigong massage training versus waitlist for sensory sensitivities as a direct outcome*



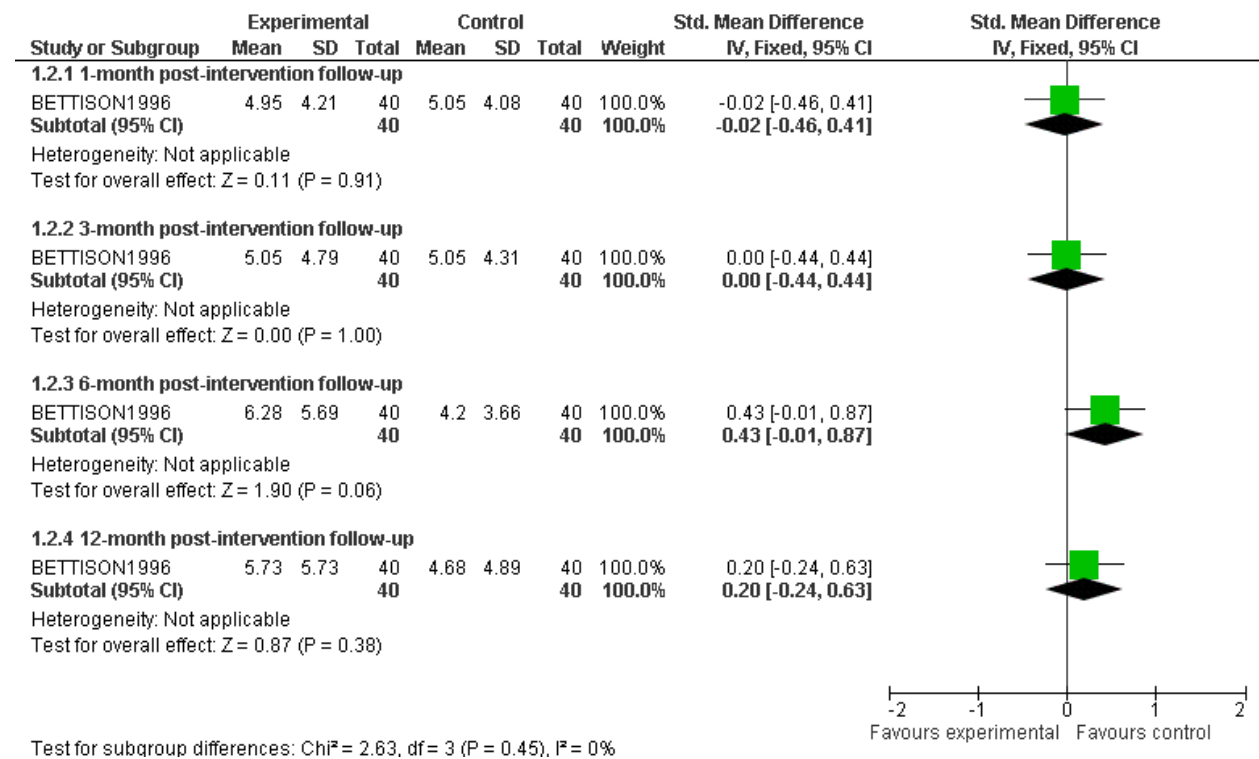
### 1.22.2 Sensory interventions for sensory sensitivities as a direct outcome

*Auditory integration training versus attention-placebo (structured listening) for sensory sensitivities as a direct outcome*

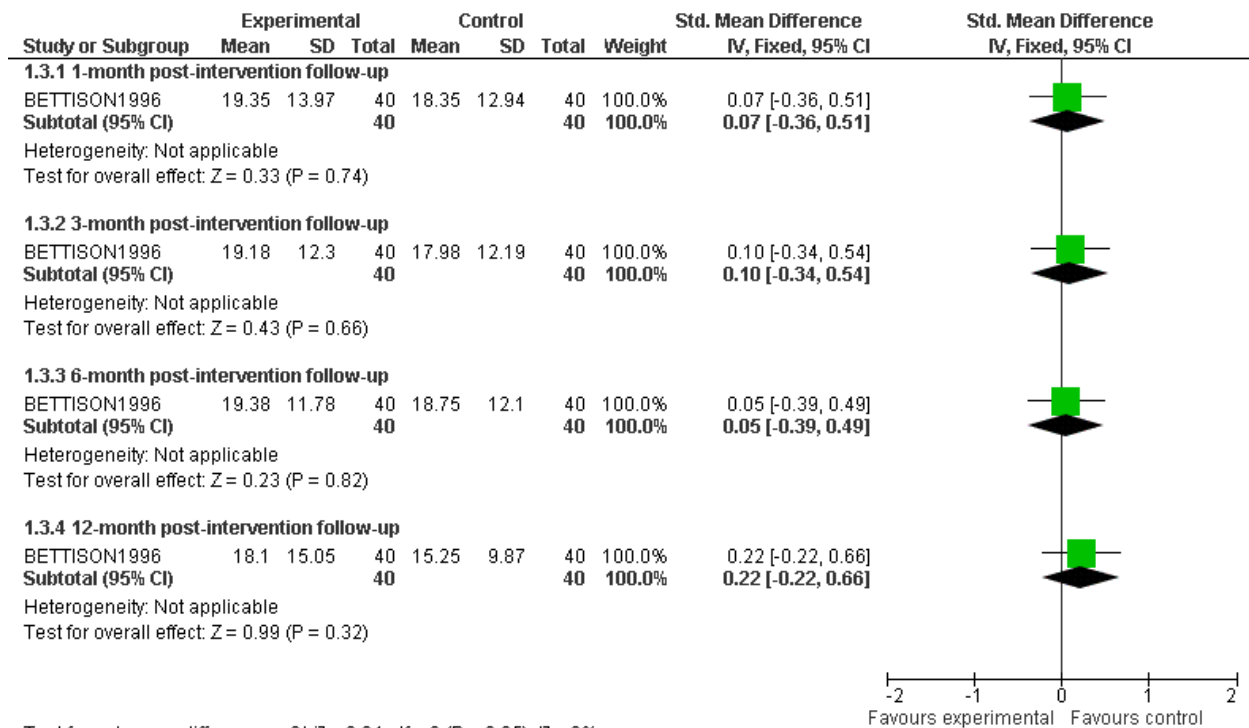
### Sound sensitivity (SSQ)



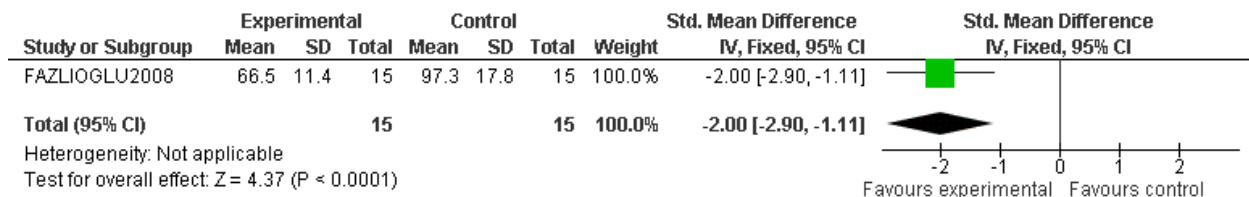
### Sound distress (SSQ)



## Sensory self-stimulation (SP)



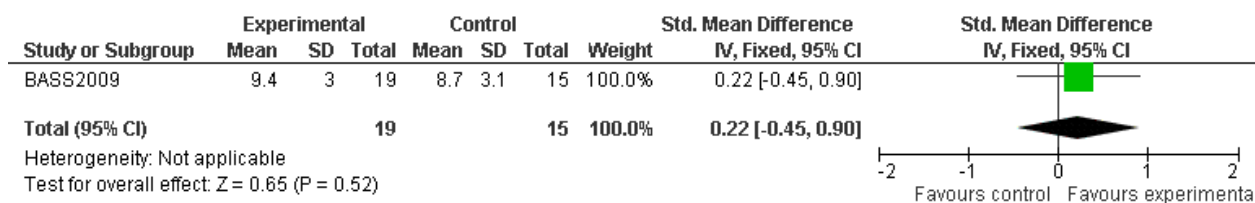
## Sensory integration therapy versus treatment-as-usual for sensory sensitivities as a direct outcome



## 1.23 PSYCHOSOCIAL INTERVENTIONS AIMED AT MOTOR SKILLS

### 1.23.1 Animal-based interventions for motor skills as an indirect outcome

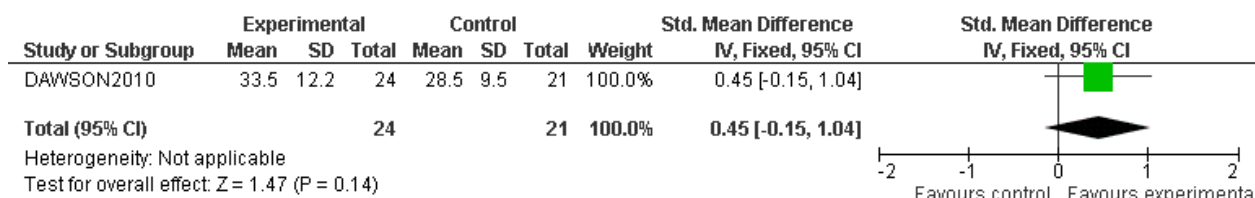
#### Horseback riding versus waitlist control for motor skills as an indirect outcome



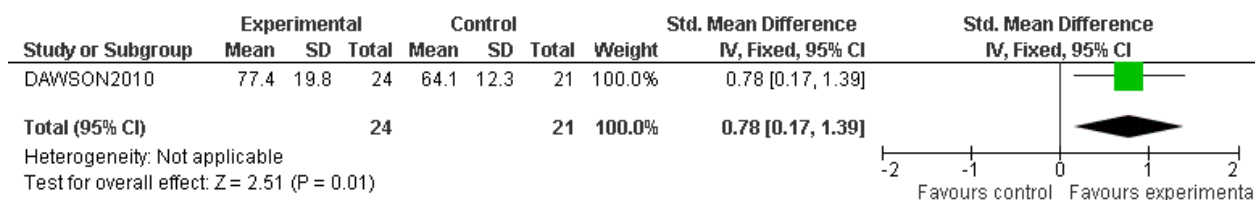
### 1.23.2 Behavioural interventions for motor skills as an indirect outcome

#### *EIBI (ESDM) versus treatment-as-usual for motor skills as an indirect outcome*

##### Fine motor skills (MSEL)

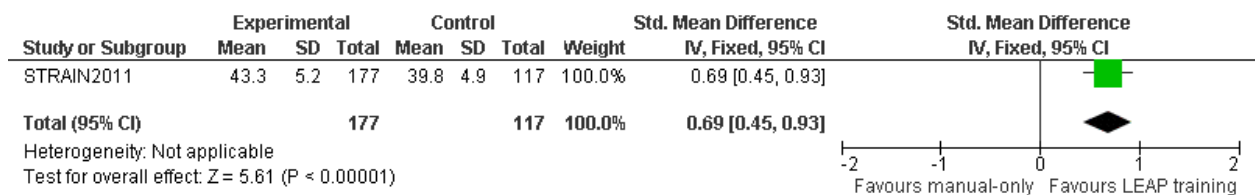


##### Motor skills (VABS)



### 1.23.3 Educational interventions for motor skills as an indirect outcome

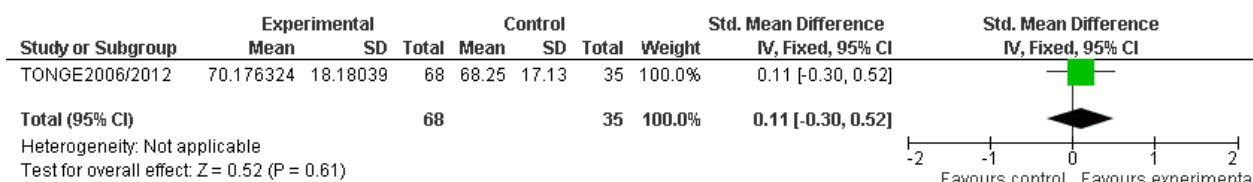
#### *LEAP training versus manual-only control for motor skills as an indirect outcome*





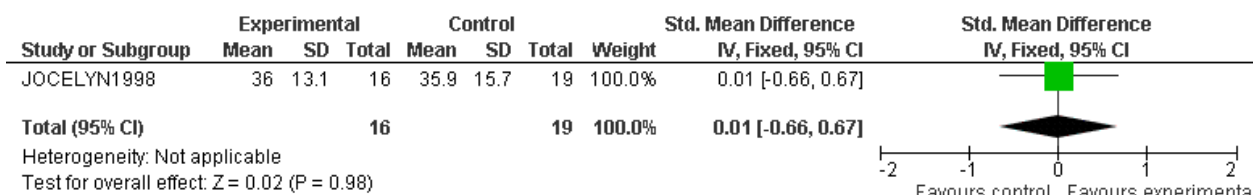
### 1.23.4 Parent training for motor skills as an indirect outcome

#### *Parent training versus treatment-as-usual for motor skills as an indirect outcome*

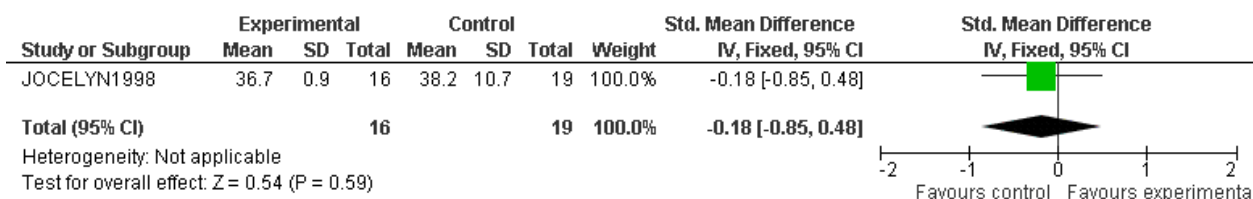


#### *Parent and day-care staff training versus standard day-care for motor skills as an indirect outcome*

##### Perceptual/Fine Motor Skills (EIDP/PSDP developmental age)



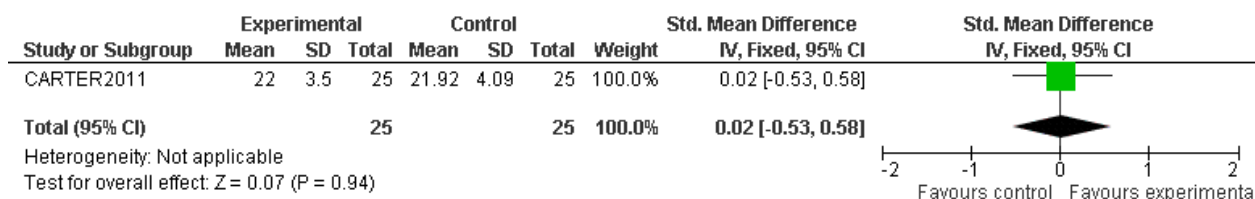
##### Gross Motor Skills (EIDP/PSDP developmental age)



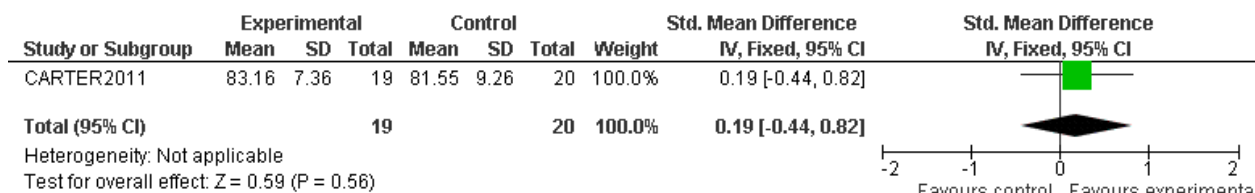
### 1.23.5 Social-communication interventions for motor skills as an indirect outcome

#### *Caregiver-mediated social-communication intervention versus treatment-as-usual for motor skills as an indirect outcome*

##### Fine motor skills (MSEL age [months])



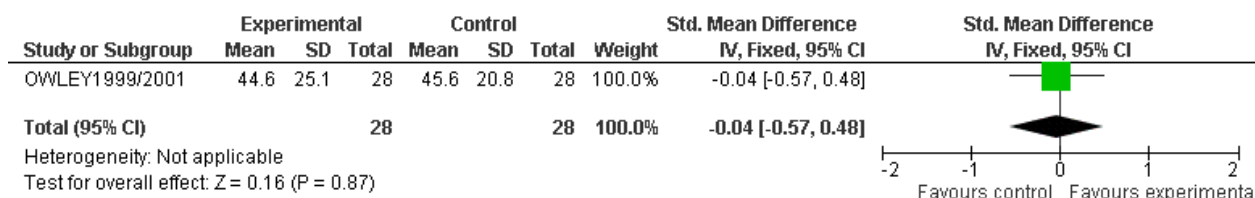
### Motor skills (VABS)



## 1.24 BIOMEDICAL INTERVENTIONS AIMED AT MOTOR SKILLS

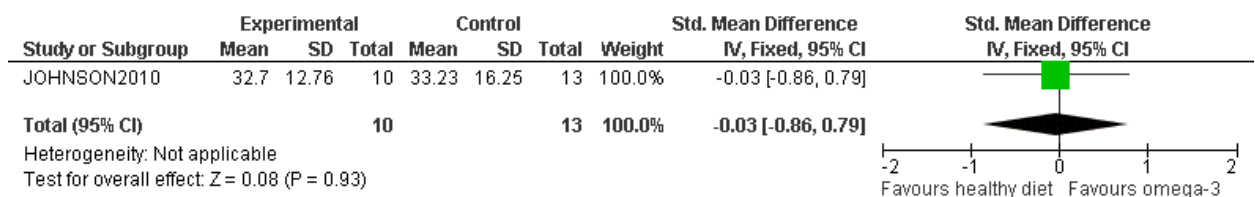
### 1.24.1 Hormones for motor skills as an indirect outcome

#### *Secretin versus placebo for motor skills as an indirect outcome*

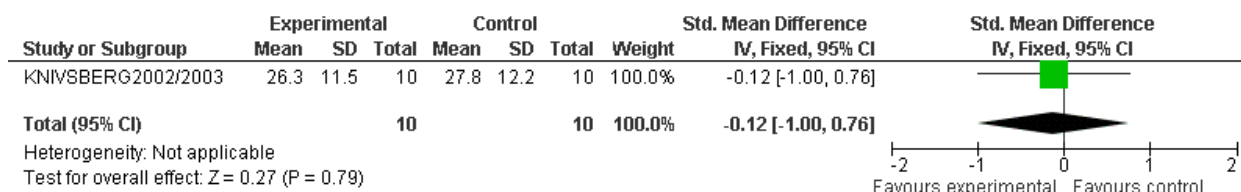


### 1.24.2 Nutritional interventions for motor skills as an indirect outcome

#### *Omega-3 fatty acids versus healthy diet control for motor skills as an indirect outcome*



#### *Gluten-free and casein-free diet versus treatment-as-usual for motor skills as an indirect outcome*

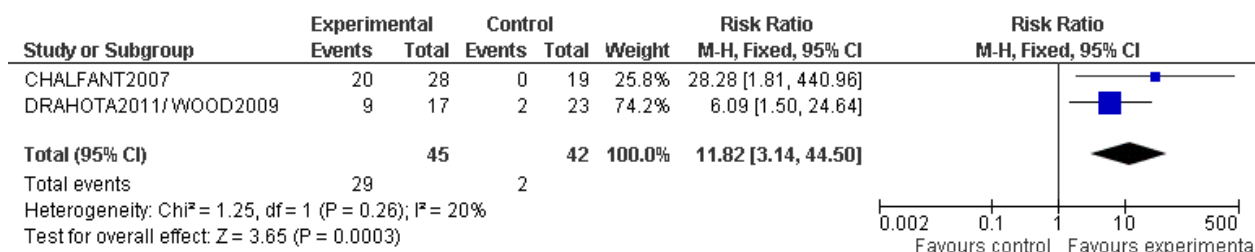


## 1.25 PSYCHOSOCIAL INTERVENTIONS AIMED AT COEXISTING MENTAL HEALTH PROBLEMS

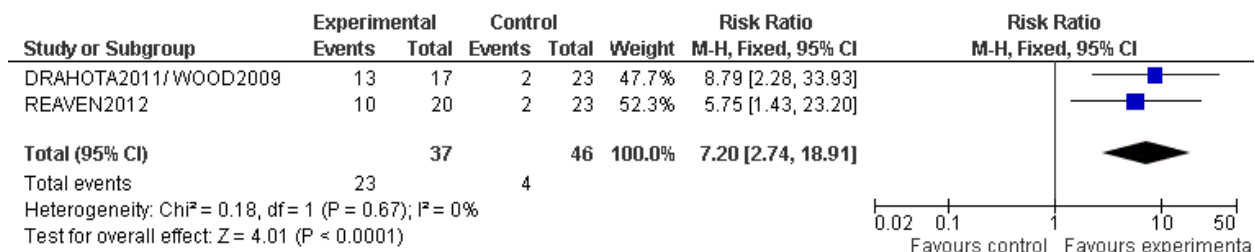
### 1.25.1 Cognitive-behavioural interventions for anxiety as a direct outcome

#### *CBT versus treatment-as-usual for anxiety as a direct outcome*

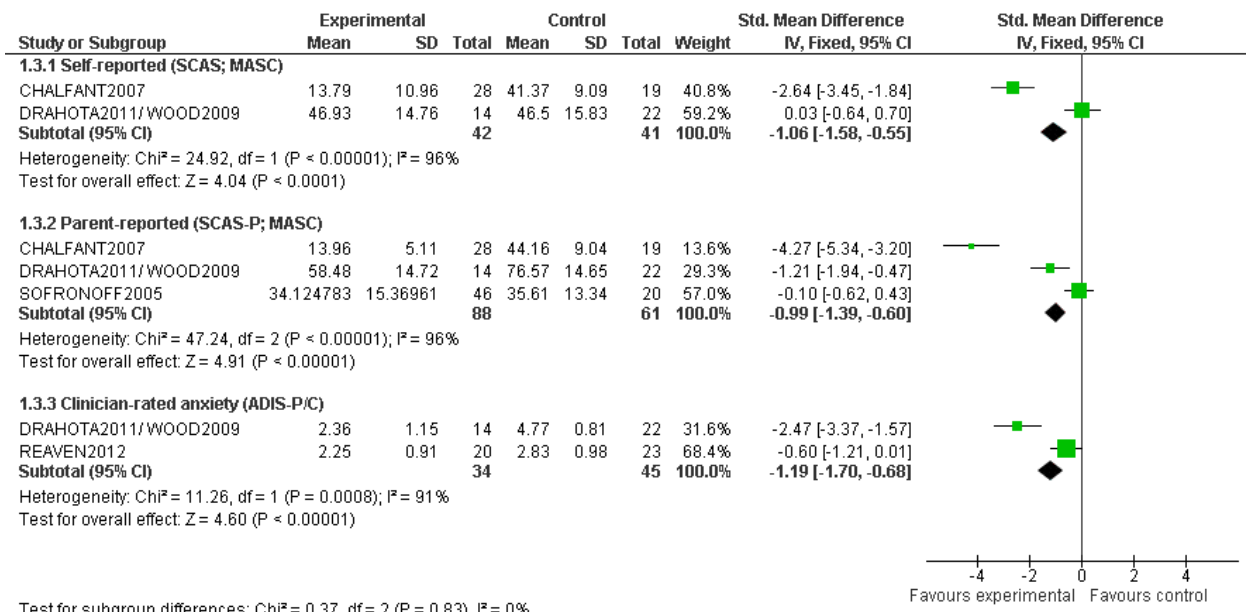
##### No longer meet anxiety disorder diagnosis



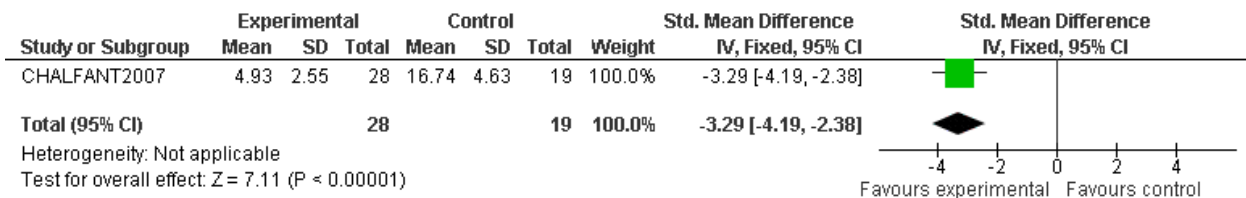
##### Improvement in anxiety symptoms (CGI- Improvement)



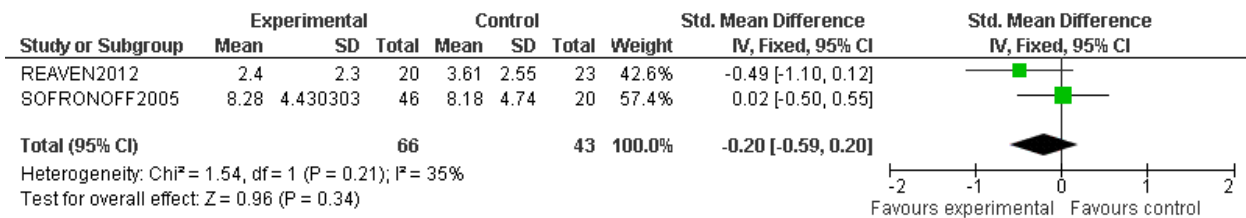
## Anxiety



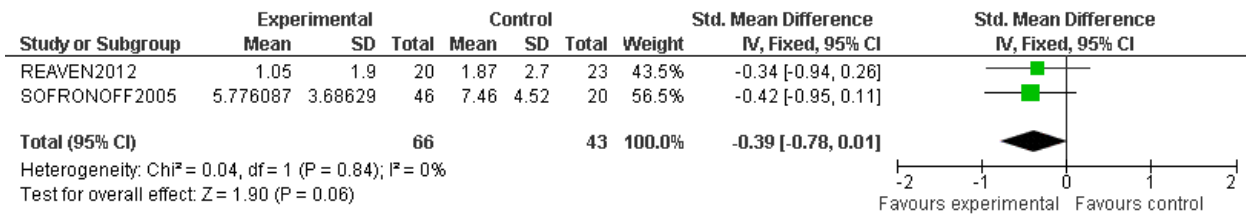
### Chronic anxiety (RCMAS)



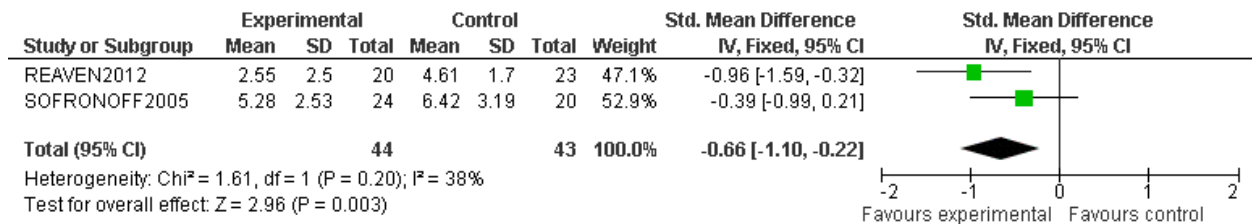
### Social anxiety (ADIS-P or SCAS-P; post-treatment)



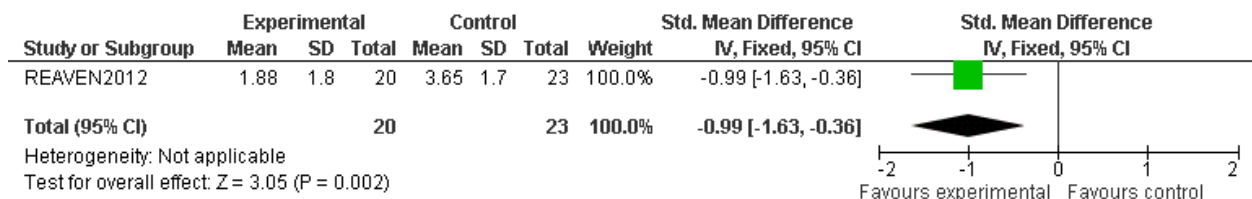
### Separation anxiety (ADIS-P or SCAS-P; post-treatment)



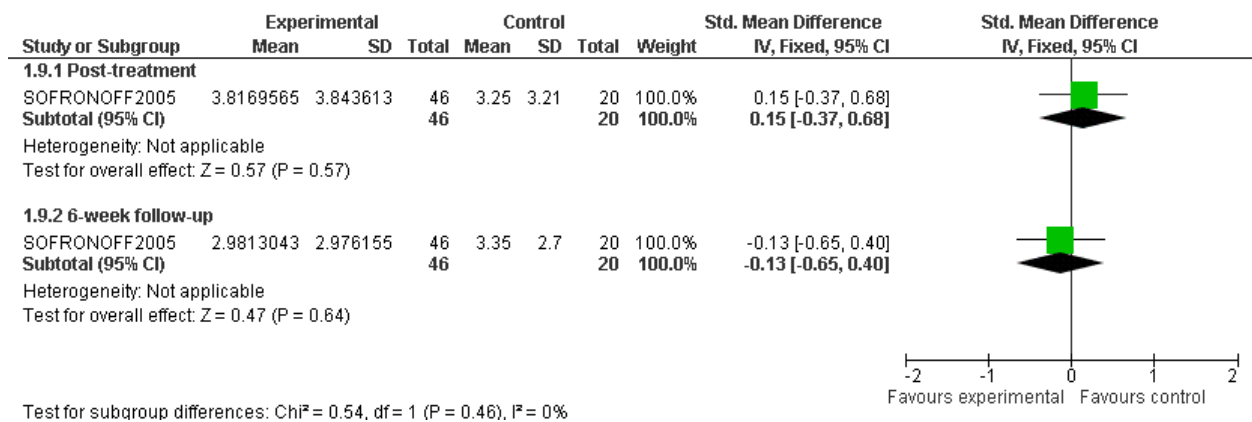
**Generalized Anxiety Disorder (ADIS-P or SCAS-P; post-treatment)**



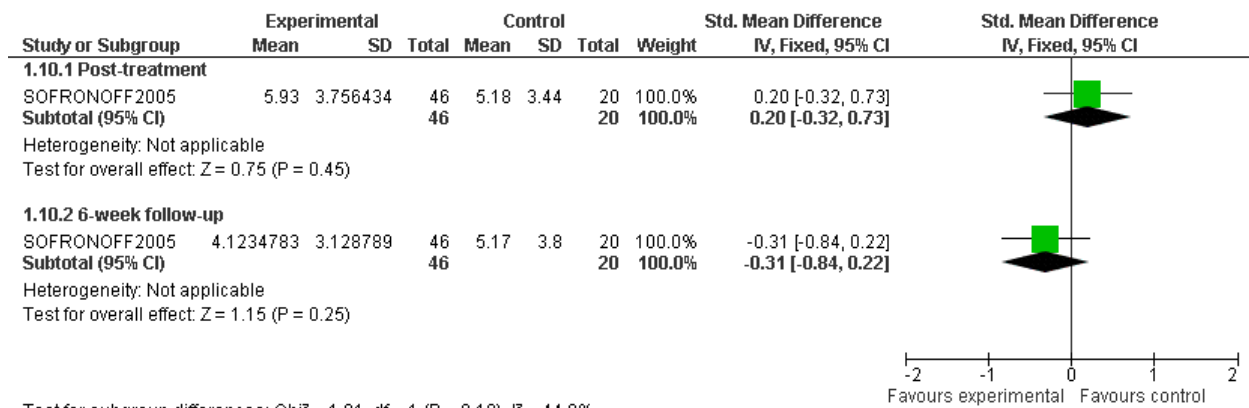
**Anxiety relating to a specific phobia (ADIS-P)**



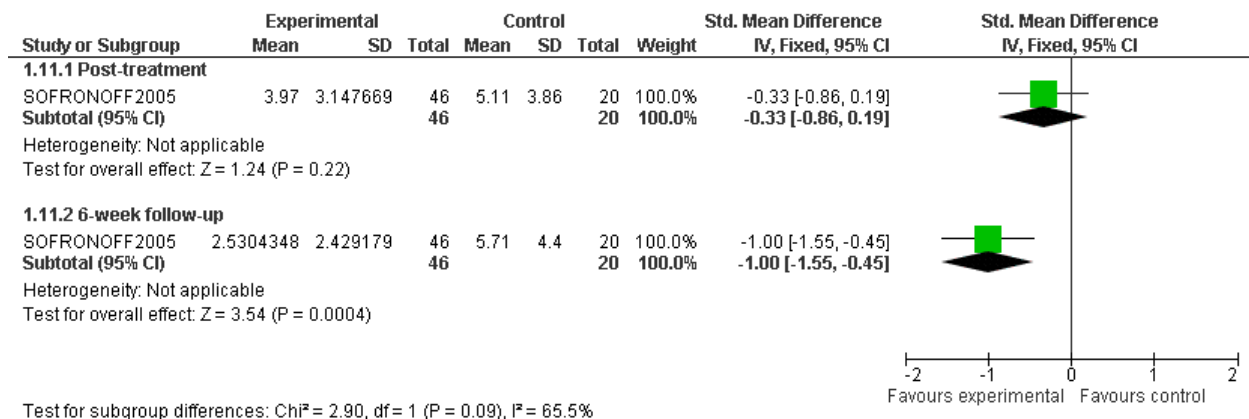
**Panic (SCAS-P; child-only and child and parent combined)**



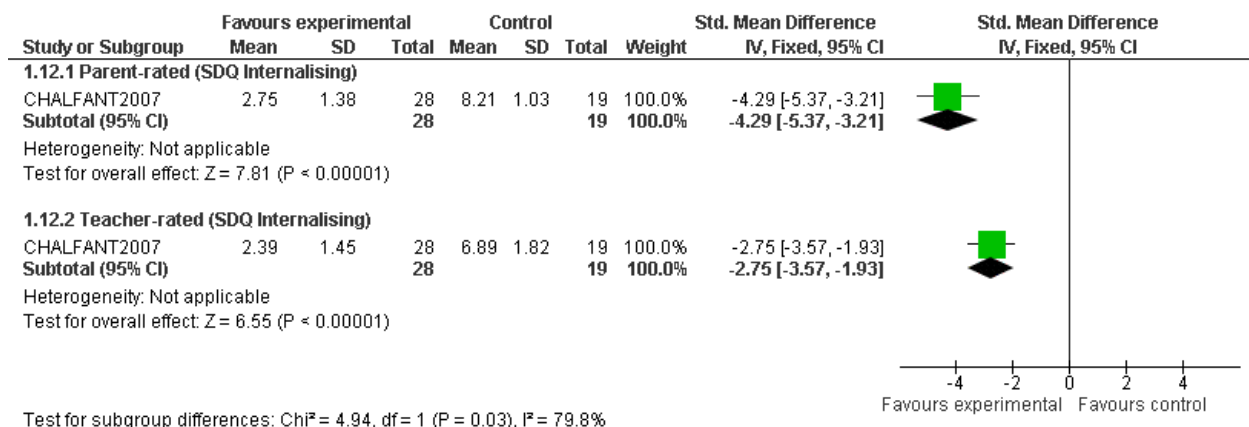
**Fear of personal injury (SCAS-P; child-only and child and parent combined)**



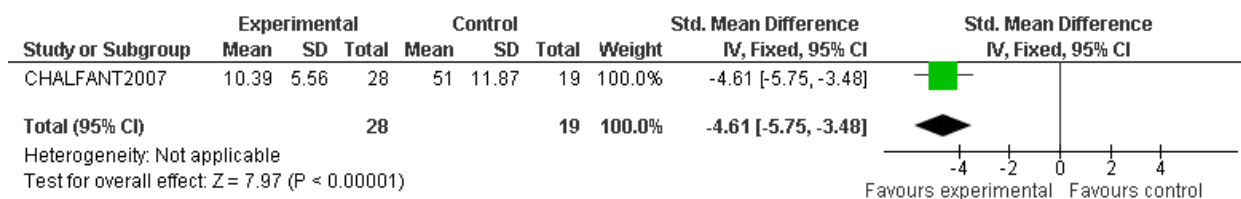
### OCD (SCAS-P; child-only and child and parent combined)



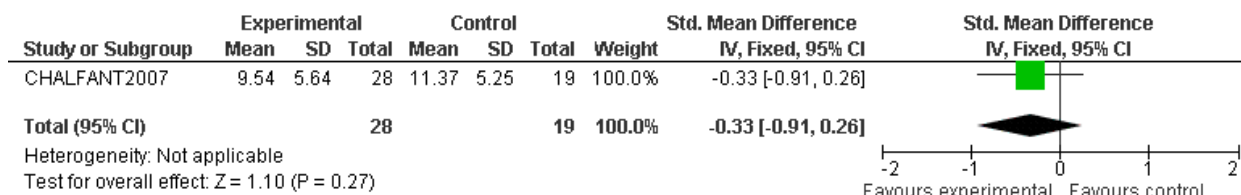
### Emotional symptoms



### Self-directed negative thoughts (CATS: internalising)



### Outward-directed negative thoughts (CATS: Hostile Intent)

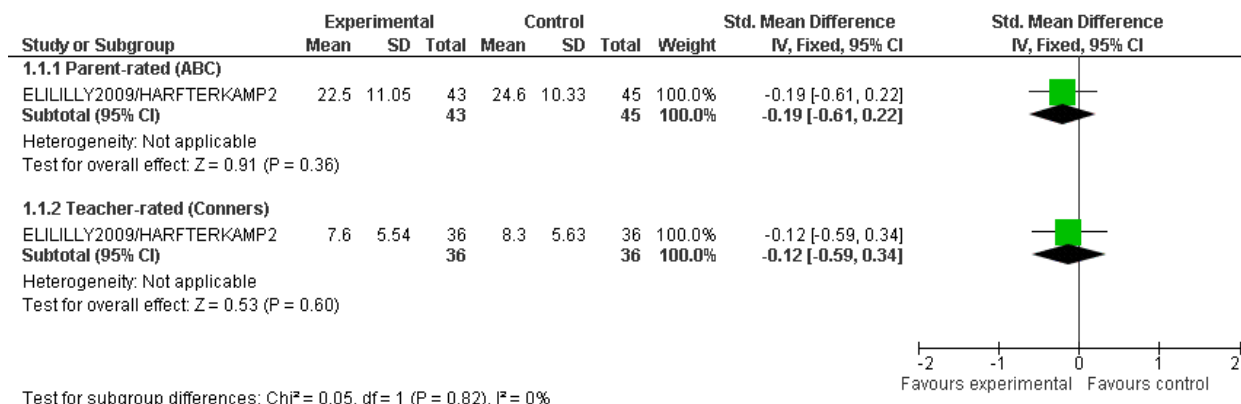


## 1.26 PHARMACOLOGICAL INTERVENTIONS AIMED AT COEXISTING MENTAL HEALTH PROBLEMS

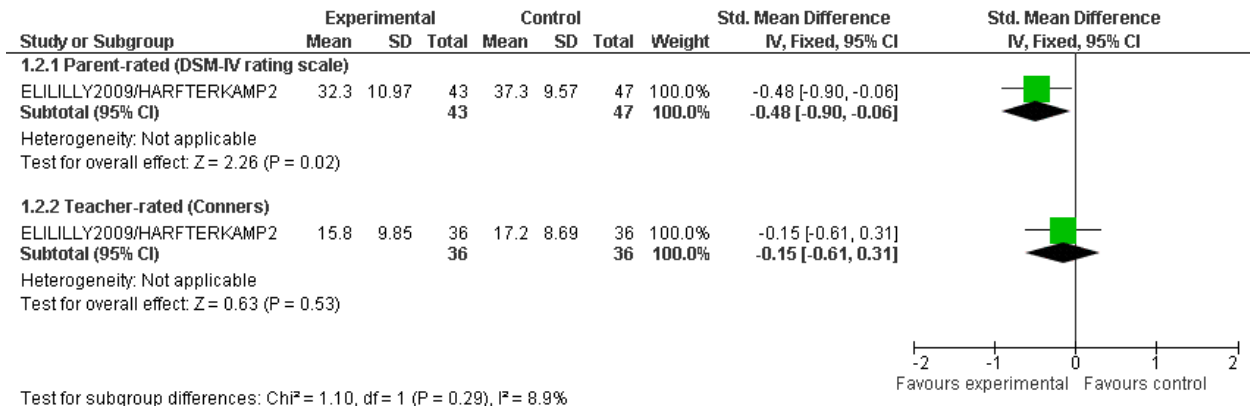
### 1.26.1 SNRIs for ADHD as a direct outcome

#### *Atomoxetine versus placebo for ADHD as a direct outcome*

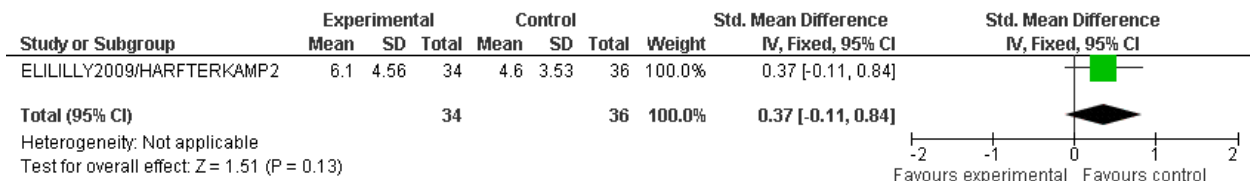
#### Hyperactivity



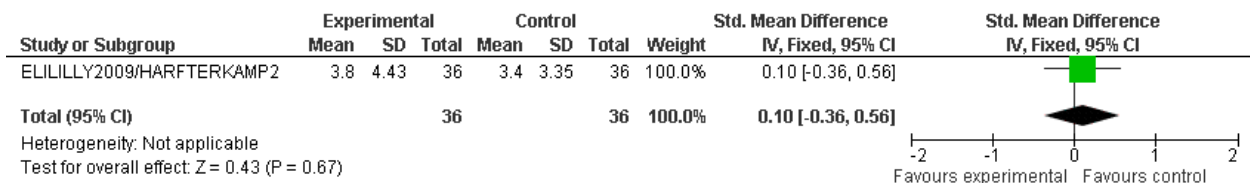
#### ADHD symptoms



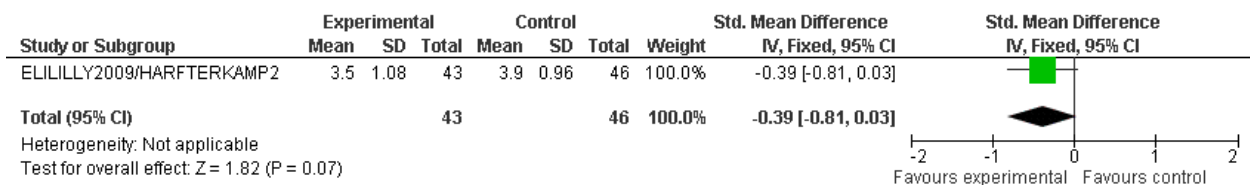
### Inattention (Conners)



### Oppositional (Conners)



### Improvement in ADHD symptoms (CGI-ADHD-I)

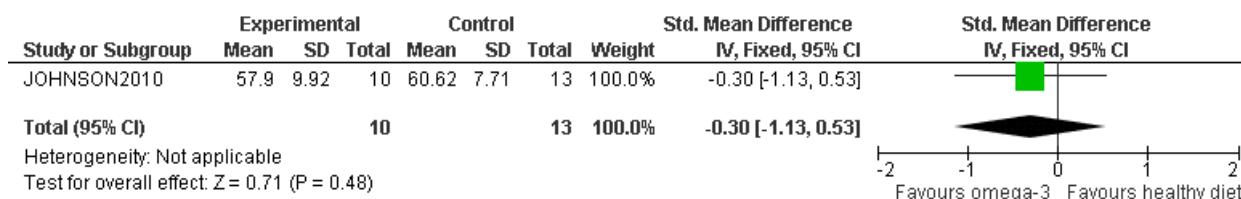


## 1.2.7 BIOMEDICAL INTERVENTIONS AIMED AT COEXISTING MENTAL HEALTH PROBLEMS

### 1.2.7.1 Nutritional interventions for ADHD as an indirect outcome

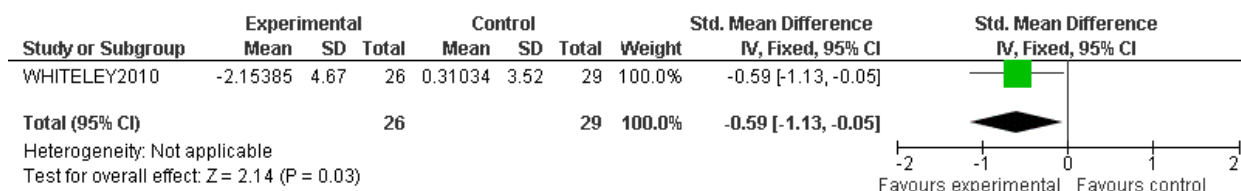
#### *Omega-3 fatty acids versus healthy diet control for ADHD as an indirect outcome*



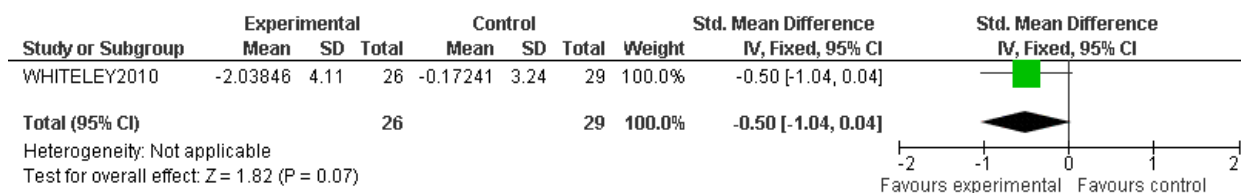


*Gluten-free and casein-free diet versus treatment-as-usual for ADHD as an indirect outcome*

**Inattention (change score; ADHD-IV)**

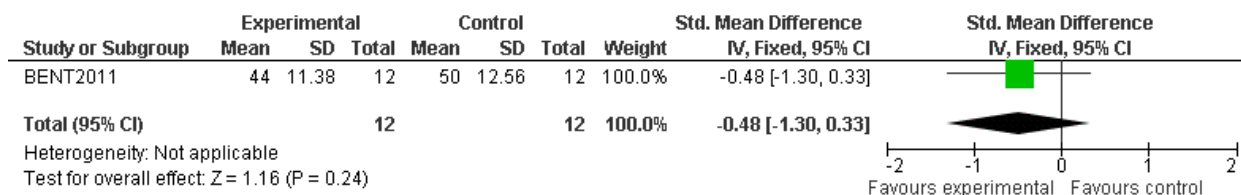


**Hyperactivity (change score; ADHD-IV)**

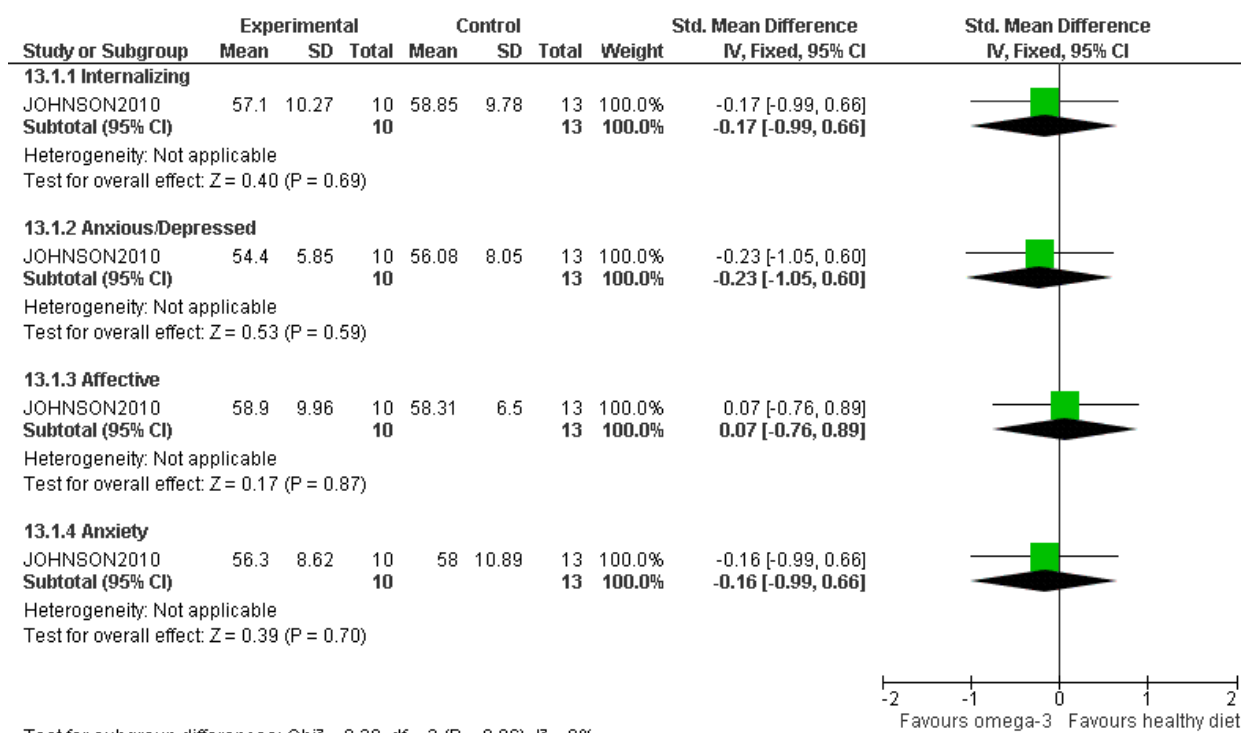


**1.27.2 Nutritional interventions for anxiety as an indirect outcome**

*Omega-3 fatty acids versus placebo for anxiety as an indirect outcome*

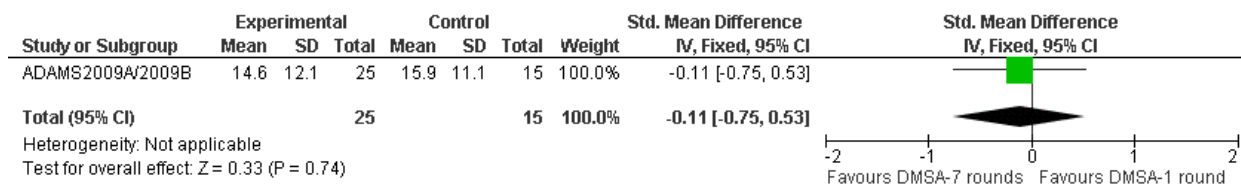


*Omega-3 fatty acids versus healthy diet control for anxiety as an indirect outcome*



### 1.27.3 Medical procedures for anxiety as an indirect outcome

*Long-term chelation (7-rounds of DMSA therapy) versus short-term chelation (1-round of DMSA therapy and 6-rounds of placebo) for anxiety as an indirect outcome*

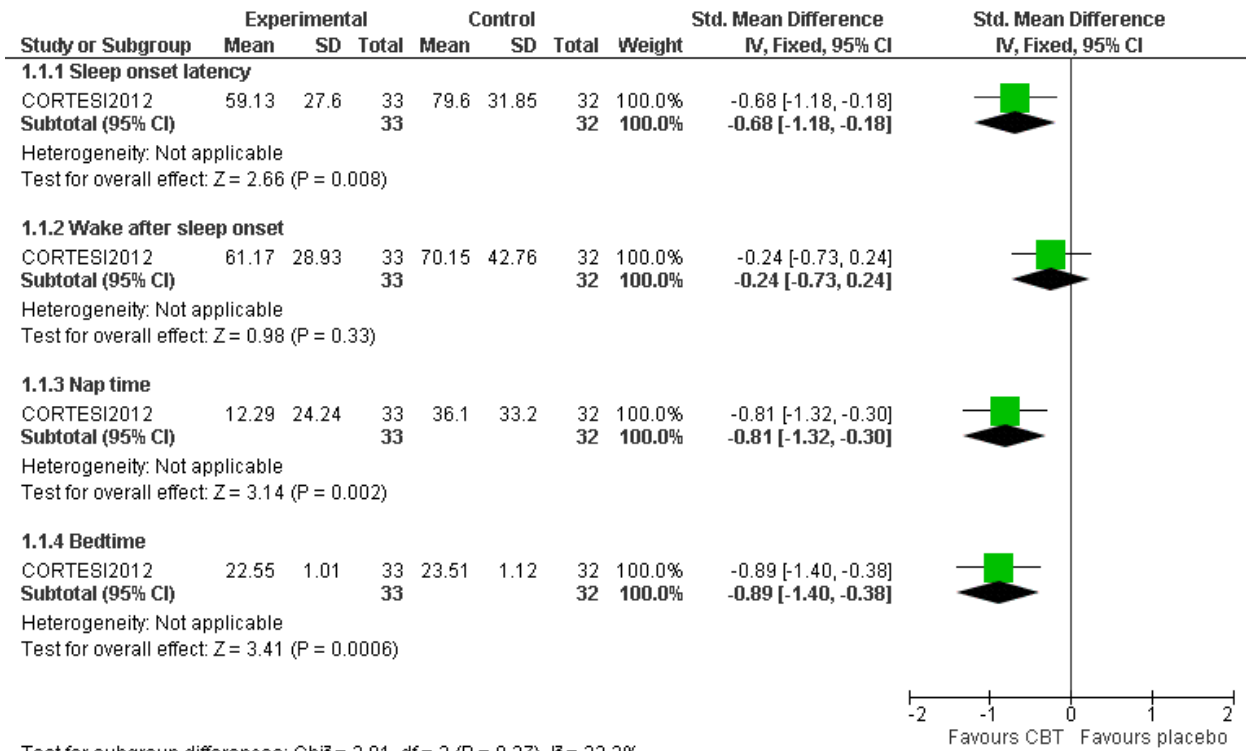


## 1.28 PSYCHOSOCIAL AND PHARMACOLOGICAL INTERVENTIONS AIMED AT COEXISTING MEDICAL OR FUNCTIONAL PROBLEMS

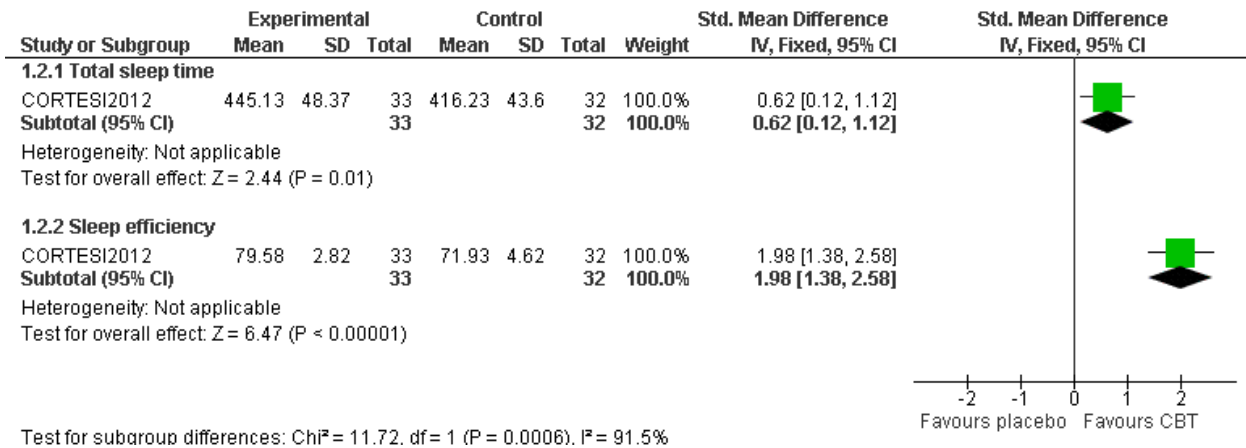
### 1.28.1 Cognitive-behavioural interventions for sleep problems as a direct outcome

*CBT versus placebo for sleep problems as a direct outcome*

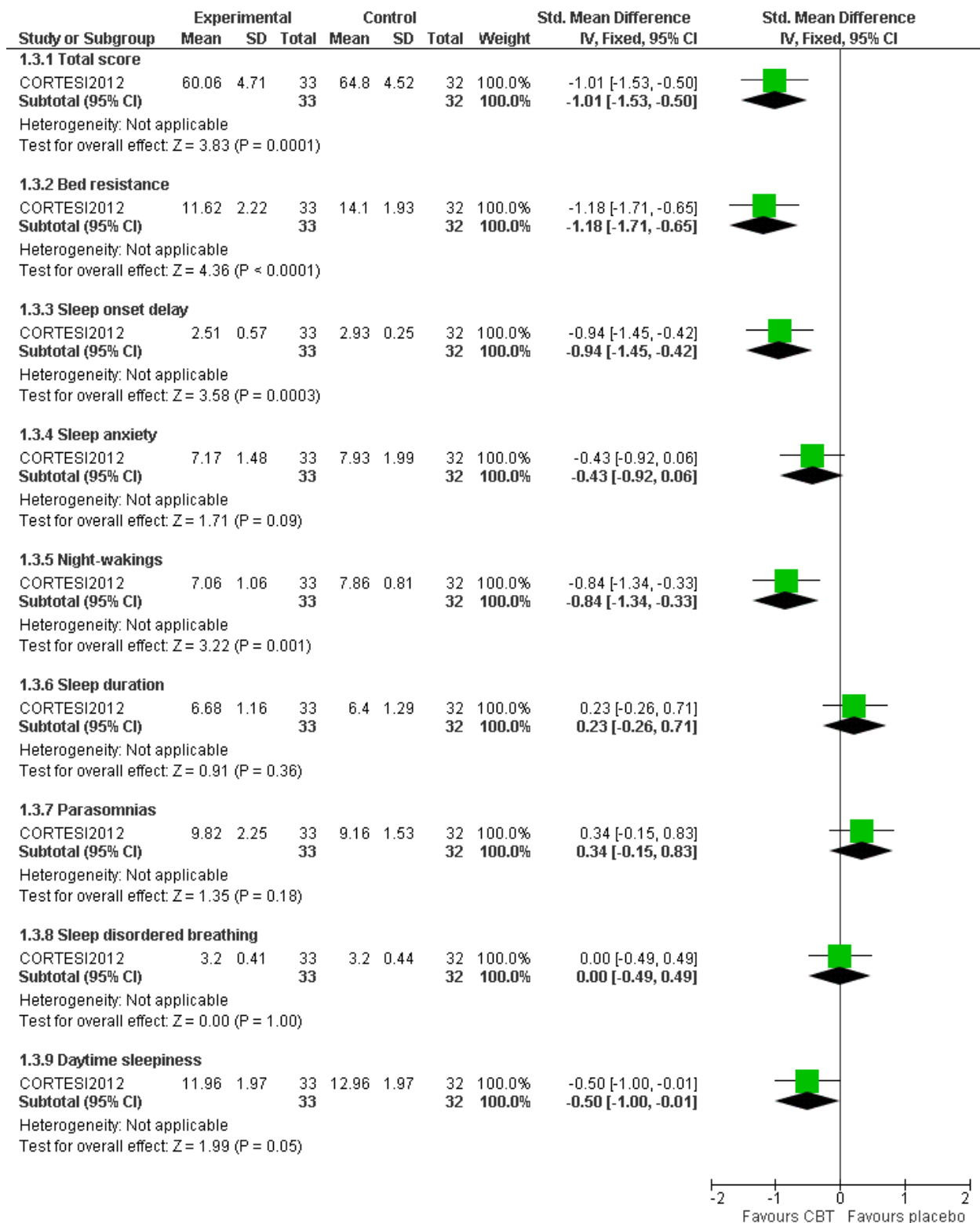
**Sleep problems (actigraph)**



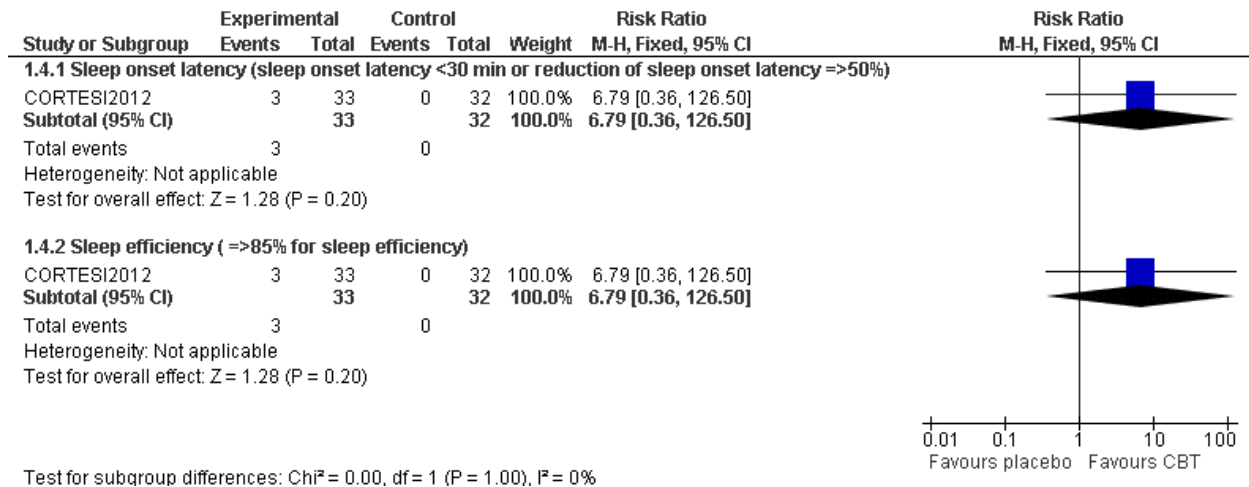
**Positive sleep behaviour (actigraph)**



**Sleep problems (Childrens Sleep Habits Questionnaire)**



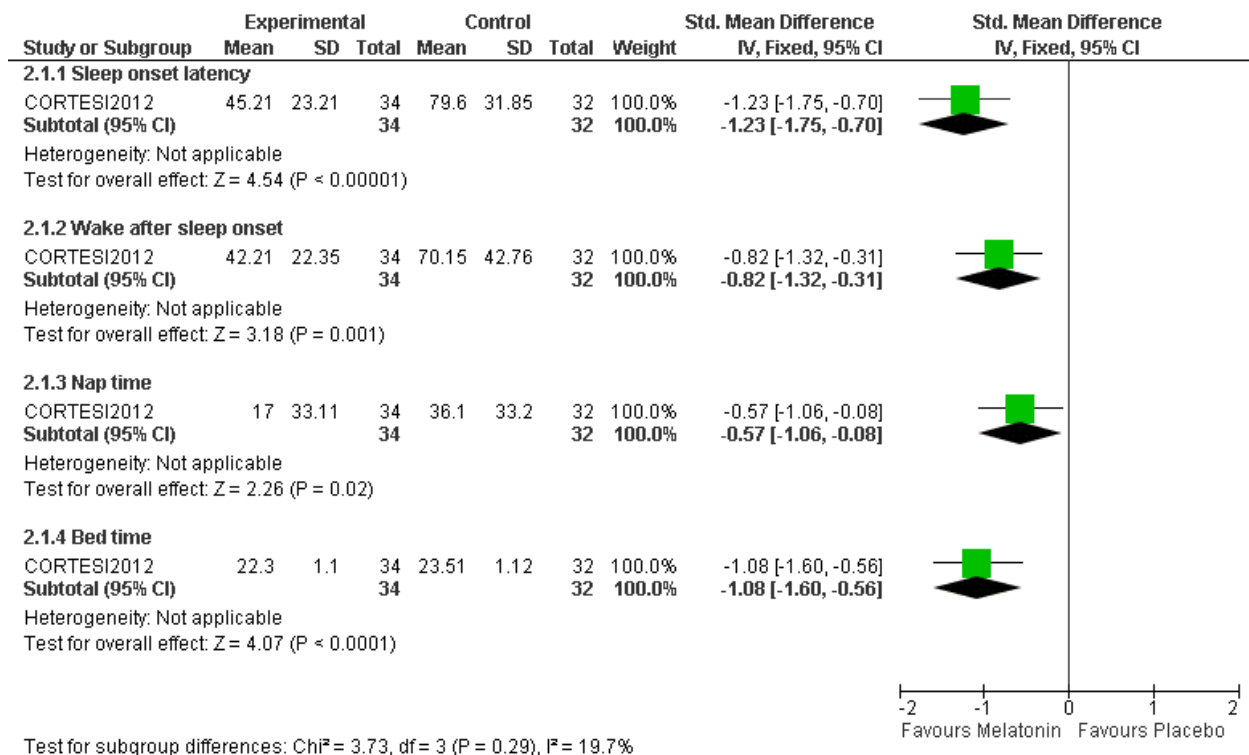
**Positive treatment response**



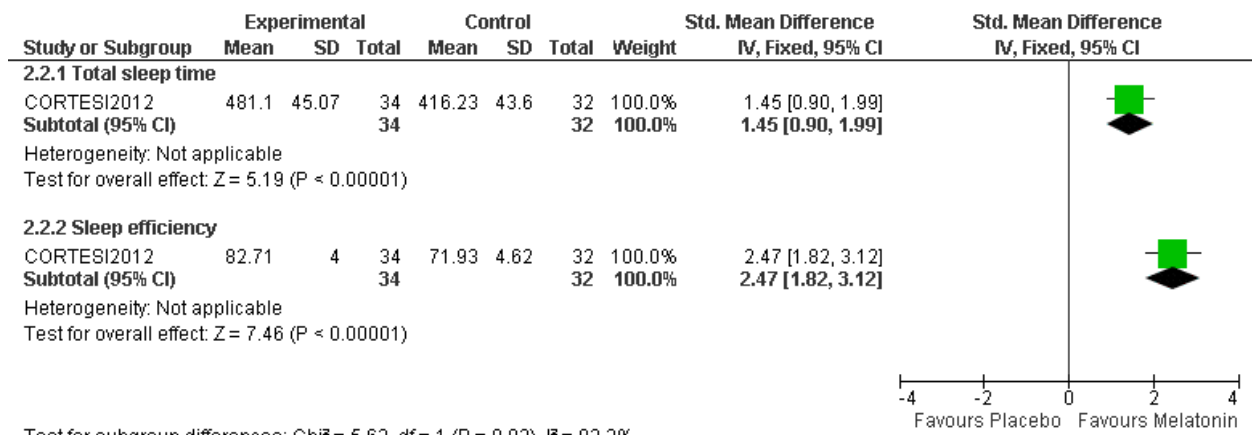
## 1.28.2 Melatonin for sleep problems as a direct outcome

### *Melatonin versus placebo for sleep problems as a direct outcome*

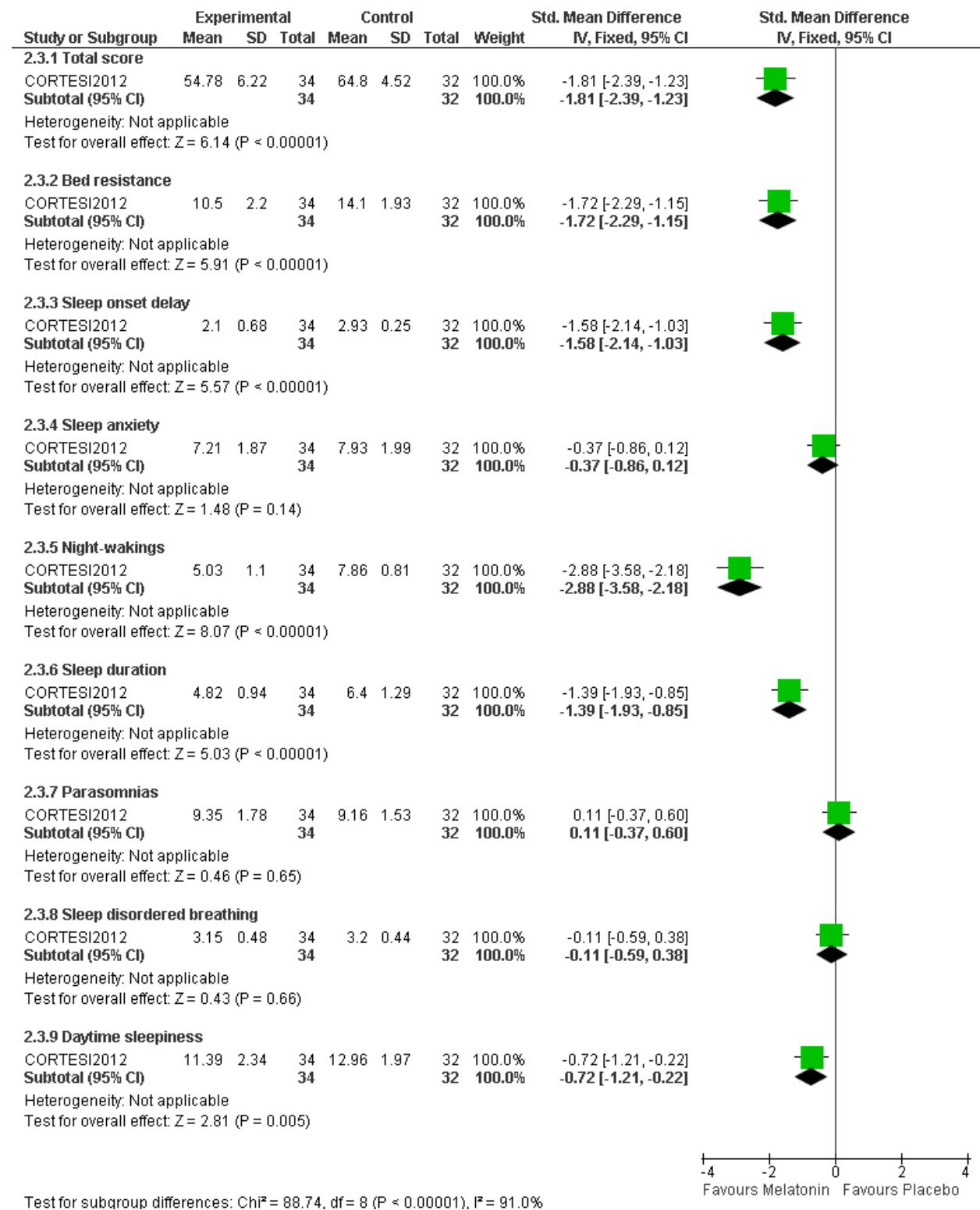
#### Sleep problems (actigraph)



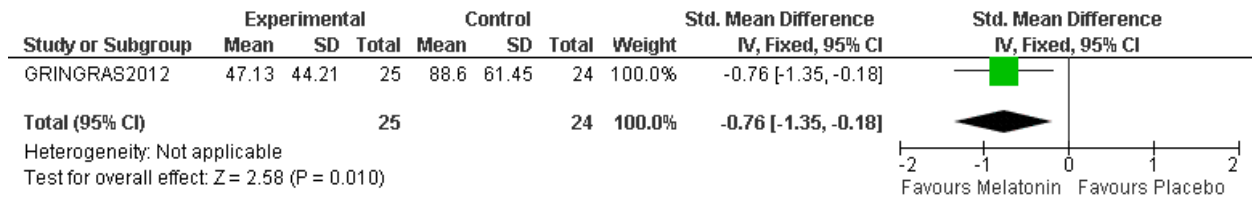
#### Positive sleep behaviour (actigraph)



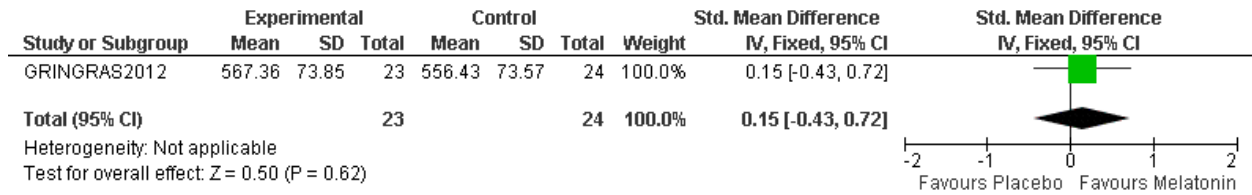
### Sleep problems (Children's Sleep Habits Questionnaire)



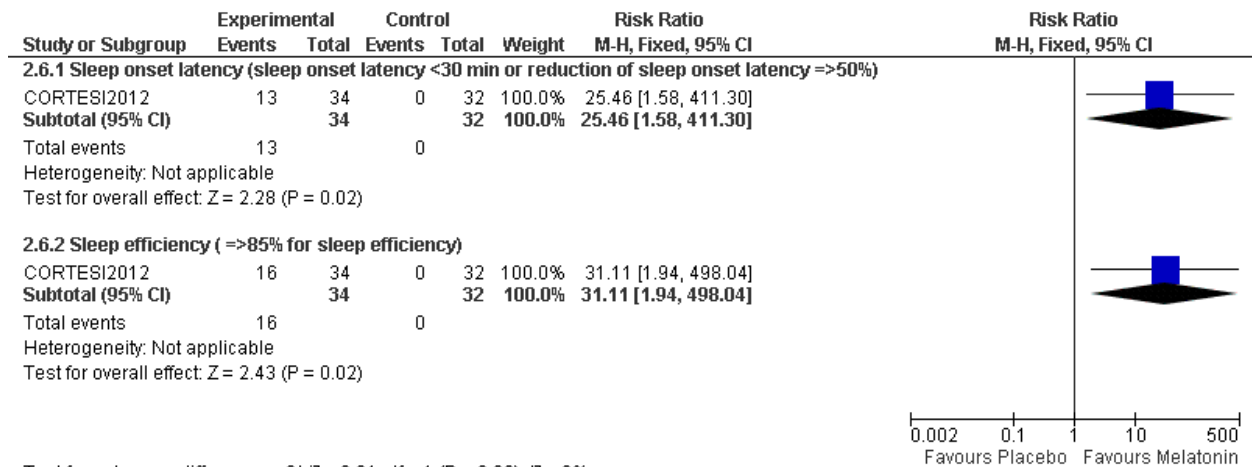
**Sleep onset latency (sleep diary)**



### Total sleep time (sleep diary)



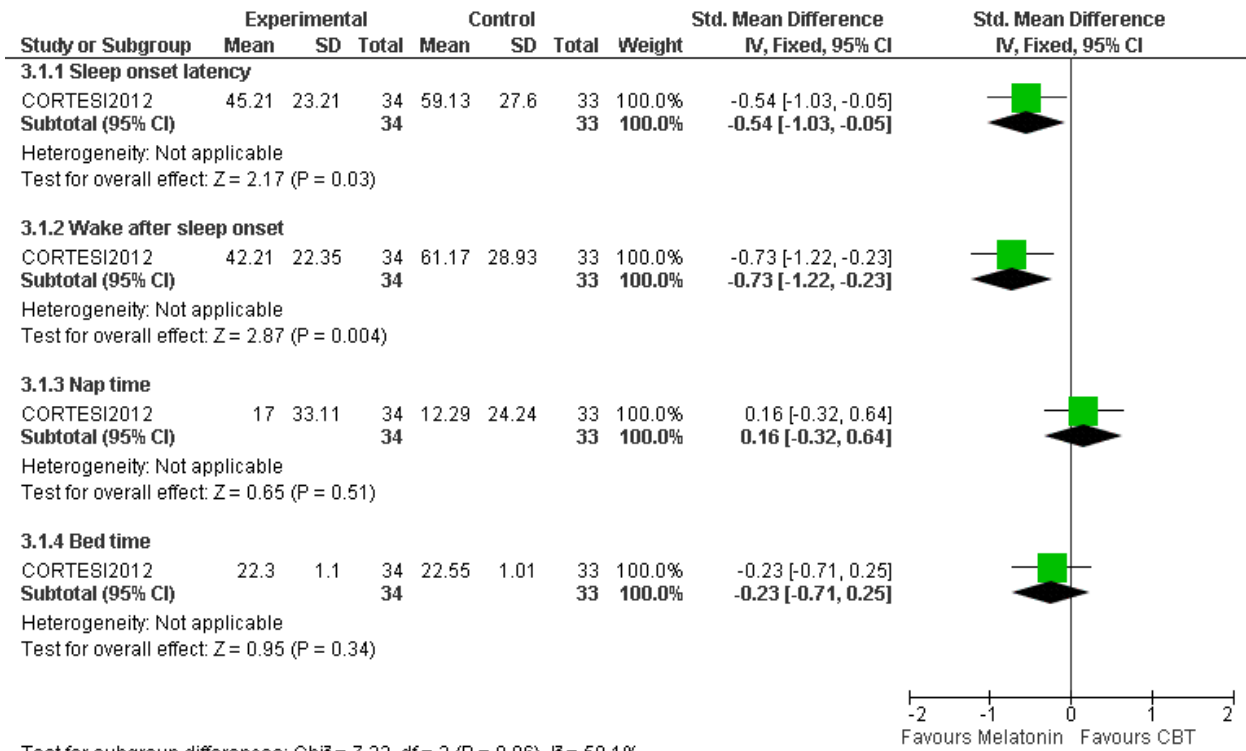
### Positive treatment response



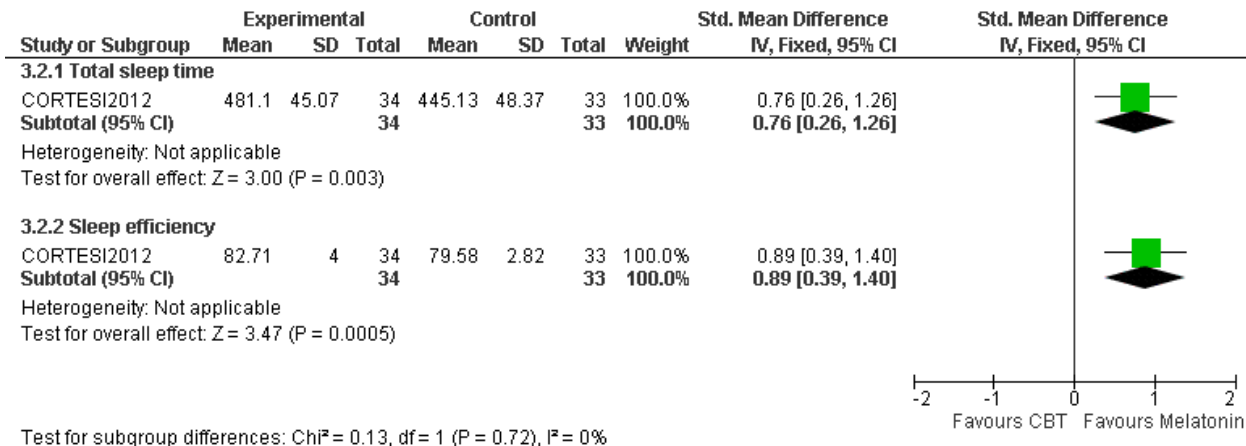
## Melatonin versus CBT for sleep problems as a direct outcome

### Sleep problems (actigraph)

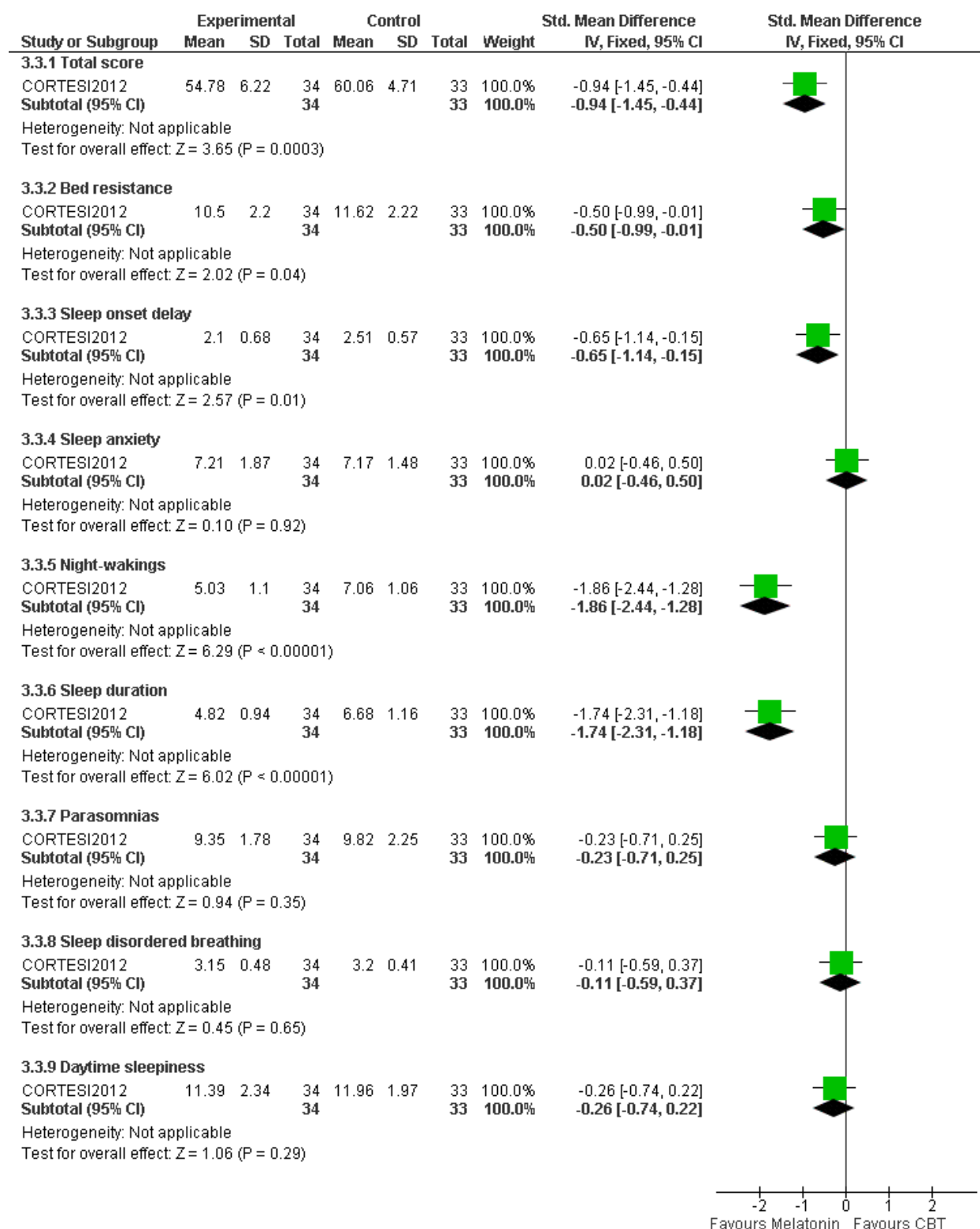




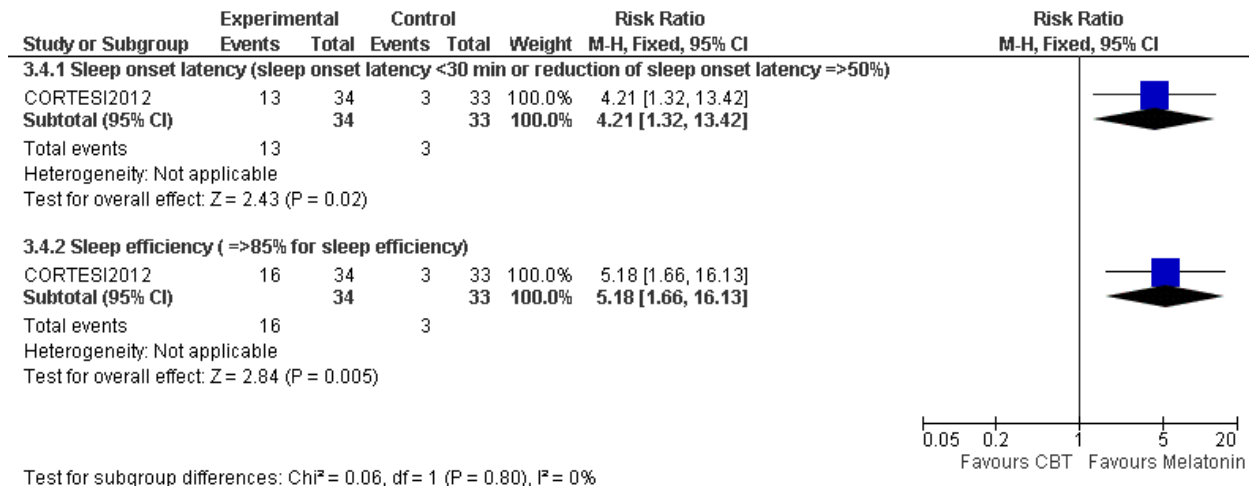
### Positive sleep behaviour (actigraph)



### Sleep problems (Children's sleep habits questionnaire)



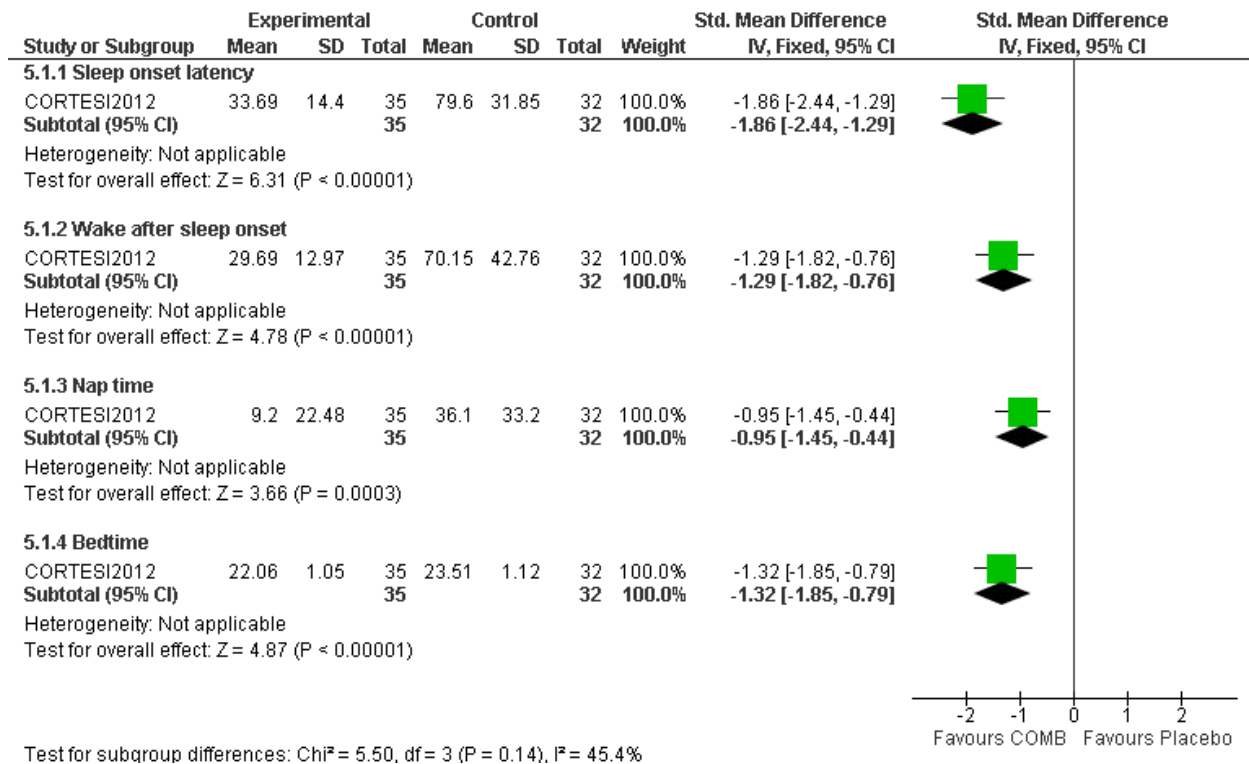
## Positive treatment response



### 1.28.3 Combined cognitive-behavioural intervention and melatonin for sleep problems as a direct outcome

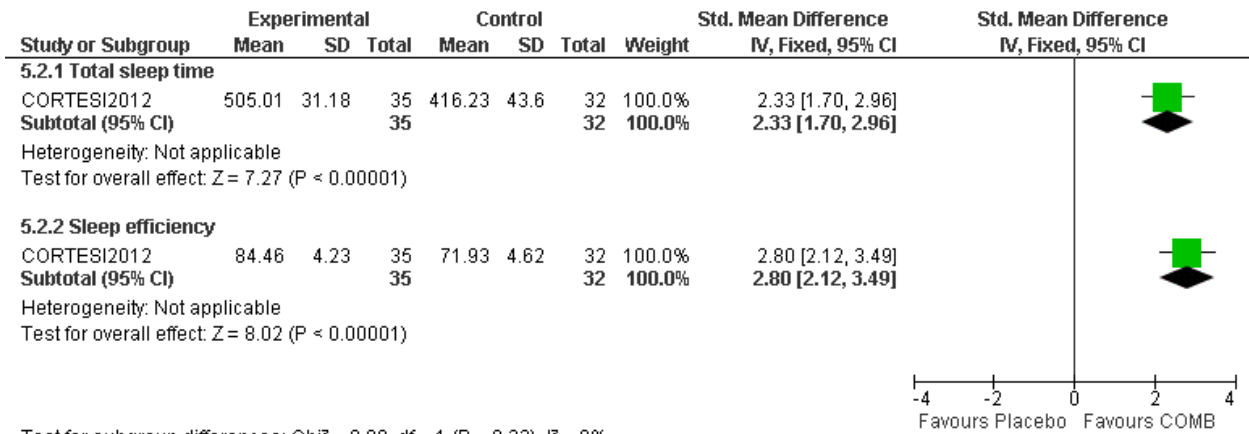
#### COMB versus placebo for sleep problems as a direct outcome

##### Sleep problems (actigraph)

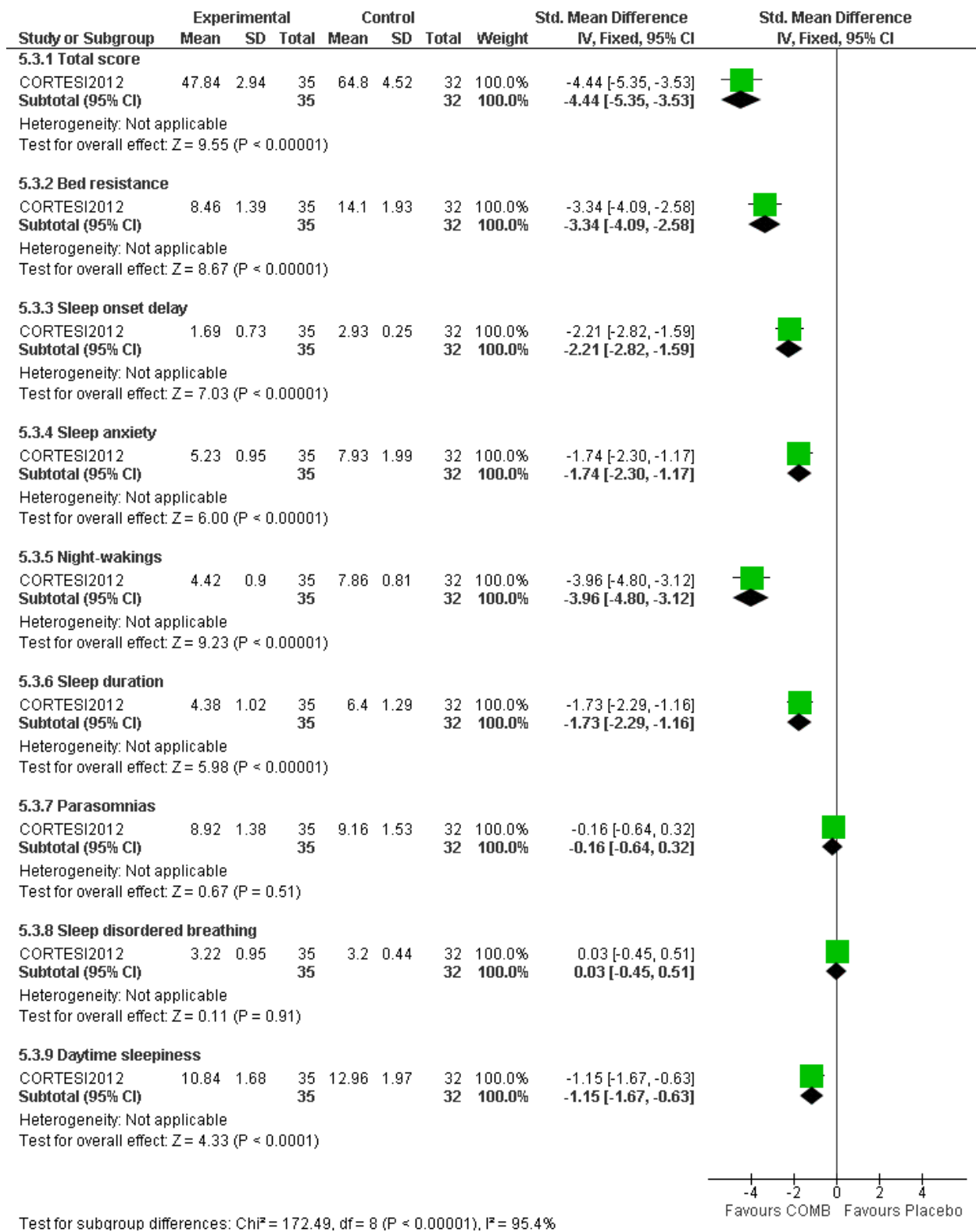


##### Positive sleep behaviour (actigraph)

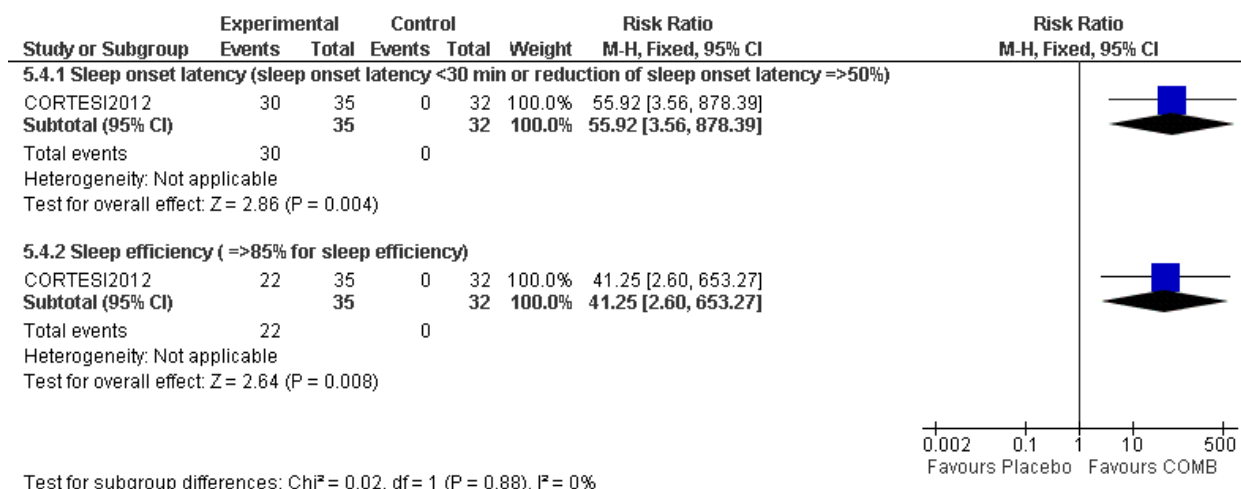
Autism: the management and support of children and young people on the autism spectrum (March 2013)



**Sleep problems (Children's sleep habits questionnaire)**

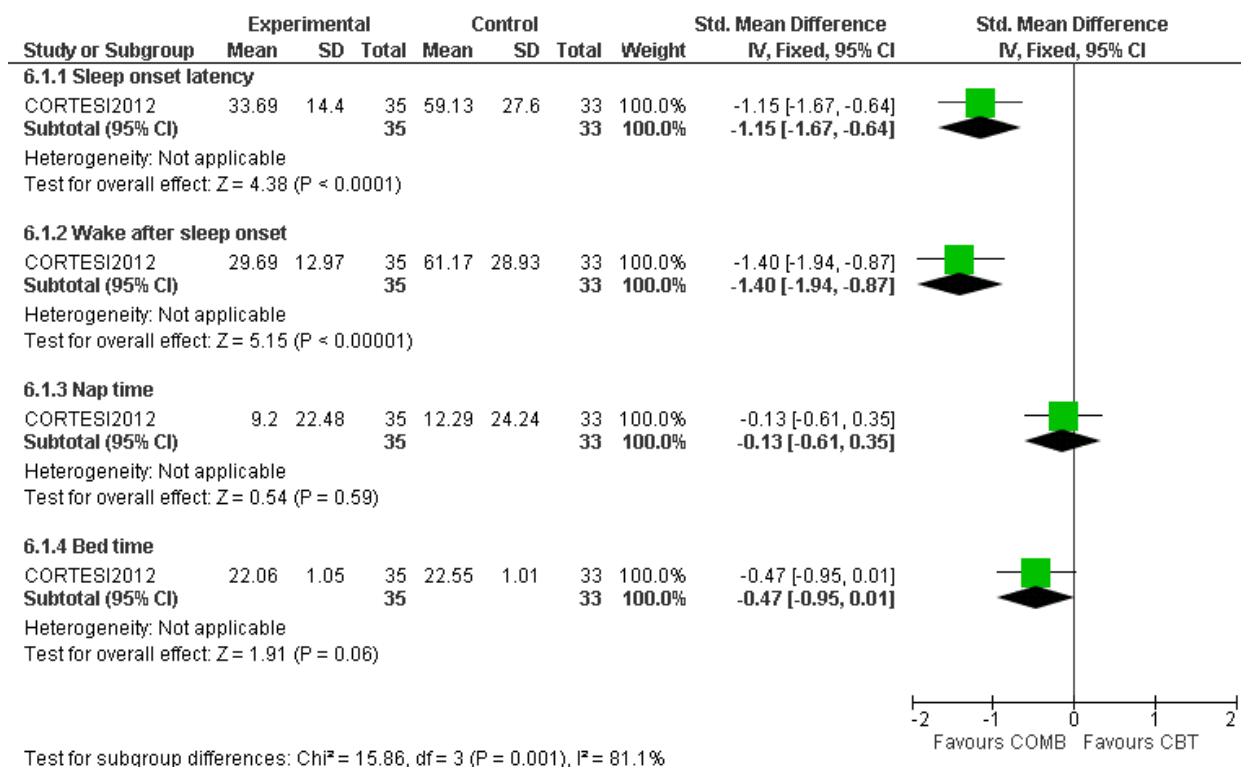


**Positive treatment response**

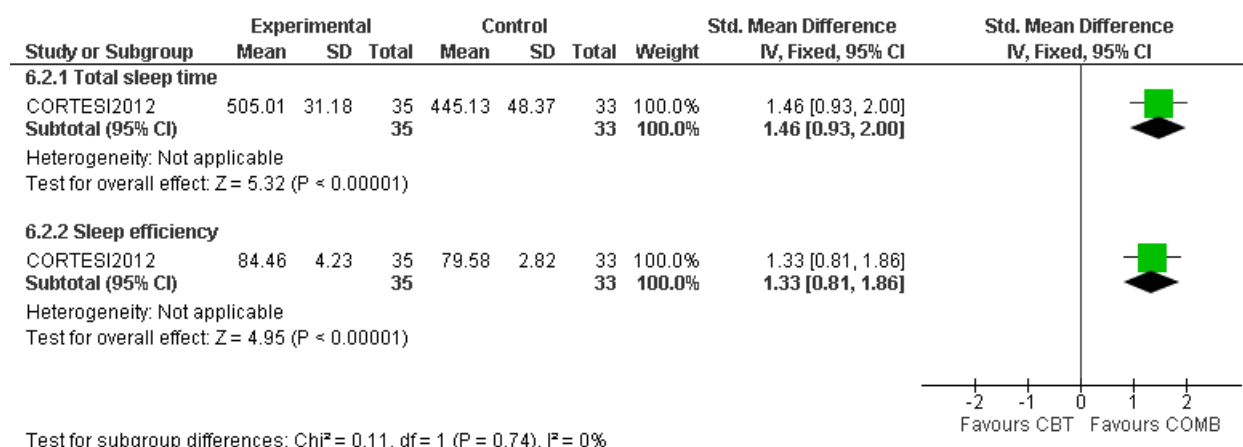


### COMB versus CBT-only for sleep problems as a direct outcome

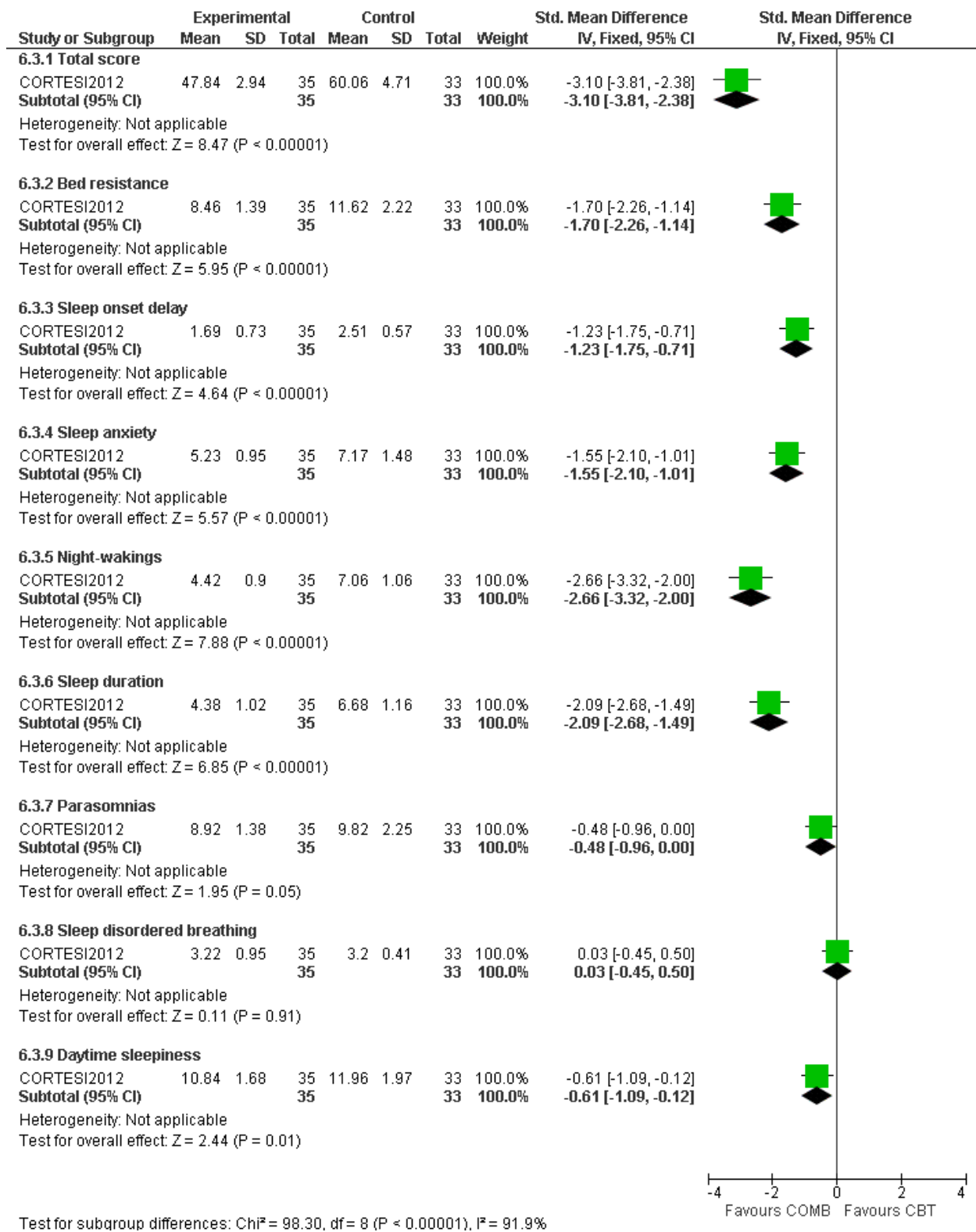
#### Sleep problems (actigraph)



#### Positive sleep behaviour (actigraph)

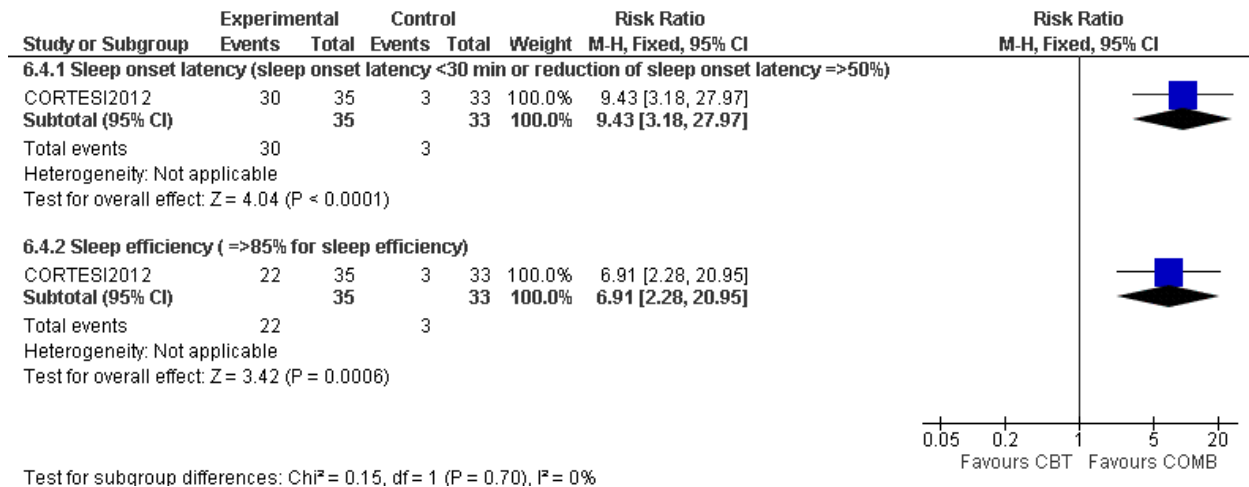


### Sleep problems (Children's sleep habits questionnaire)



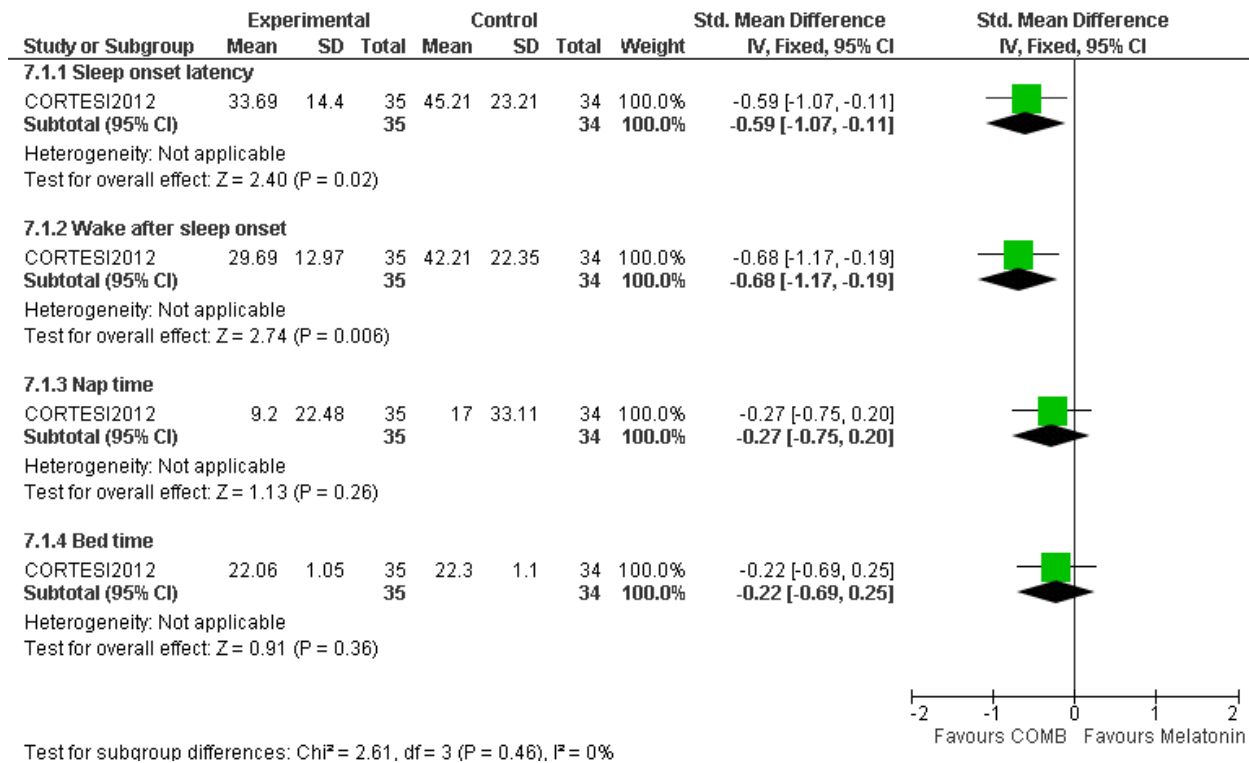
**Positive treatment response**



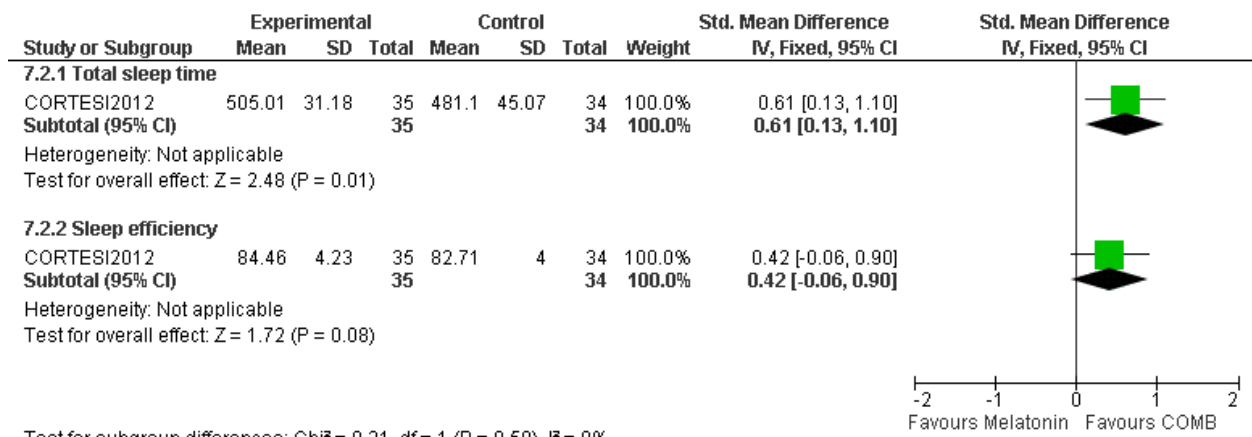


*COMB versus melatonin-only for sleep problems as a direct outcome*

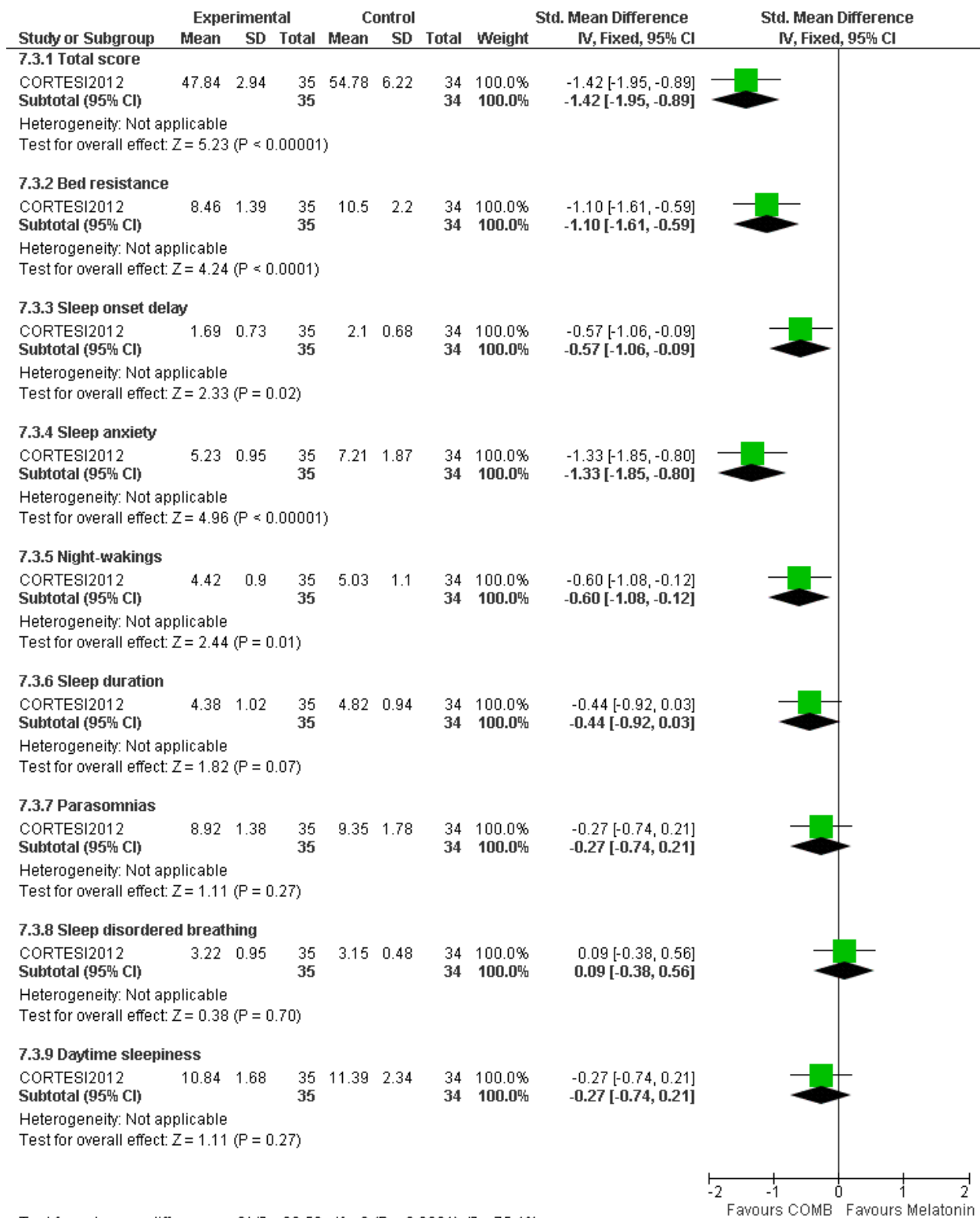
**Sleep problems (actigraph)**



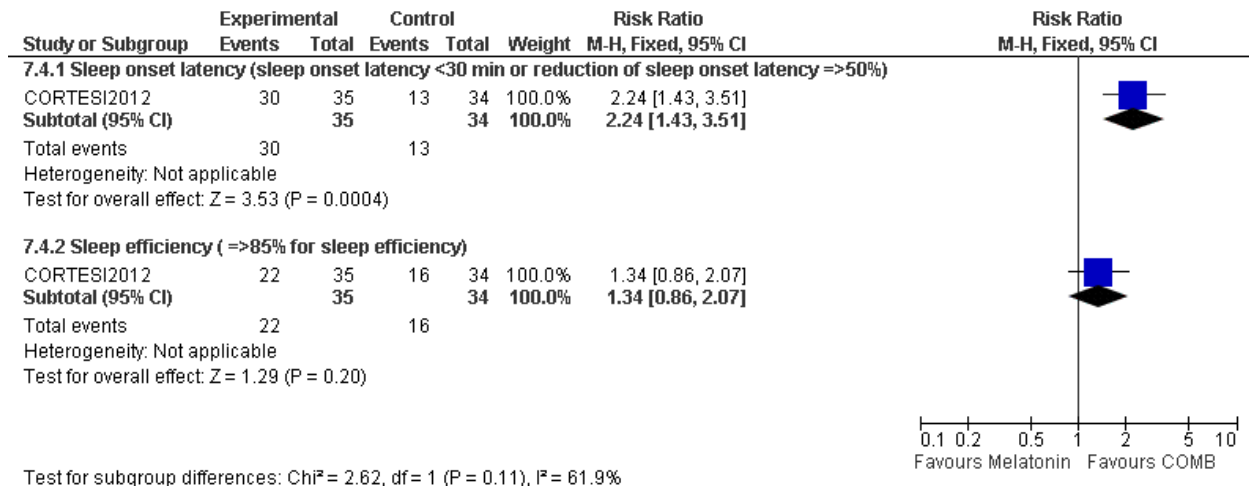
**Positive sleep behaviour (actigraph)**



**Sleep problems (Children's sleep habits questionnaire)**



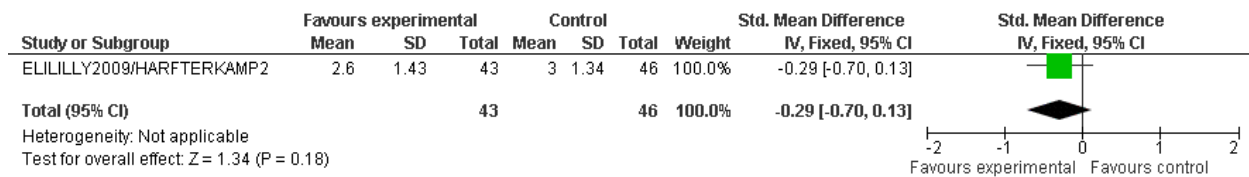
**Positive treatment response**



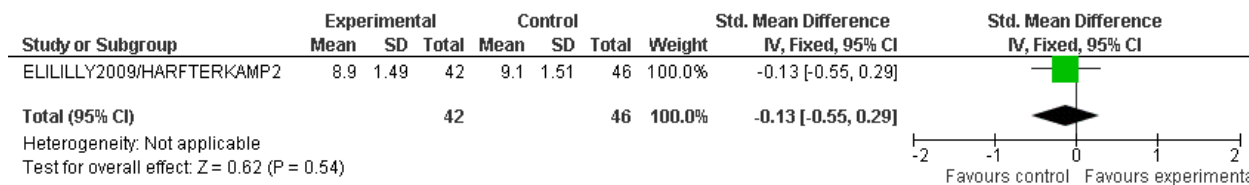
### 1.28.4 SNRIs for sleep problems as an indirect outcome

#### *Atomoxetine versus placebo for sleep problems as an indirect outcome*

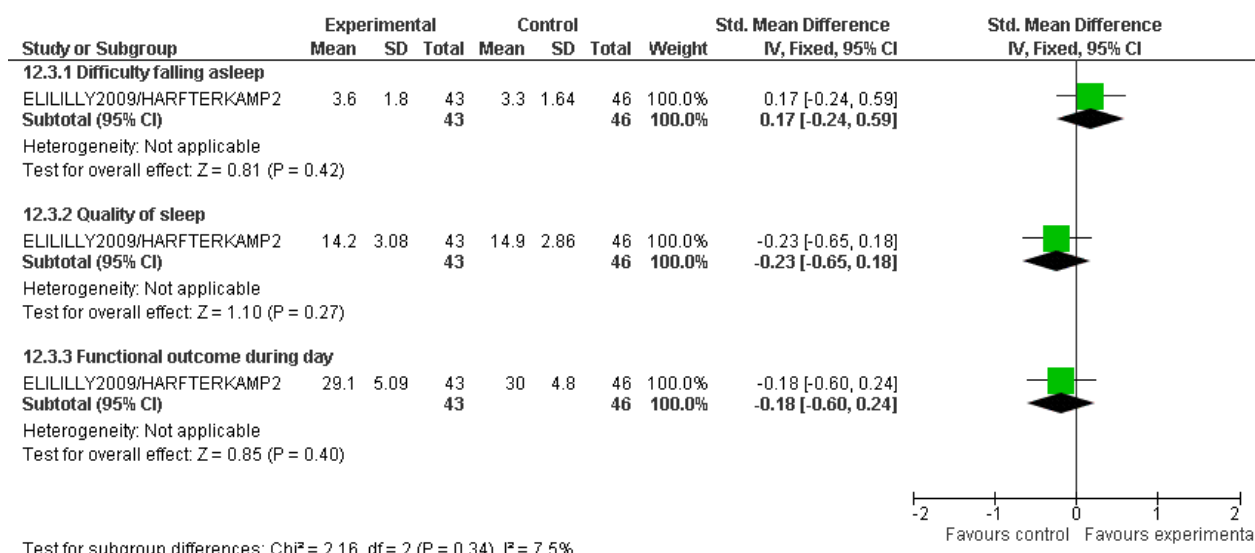
##### Time to fall asleep



##### Total hours of sleep



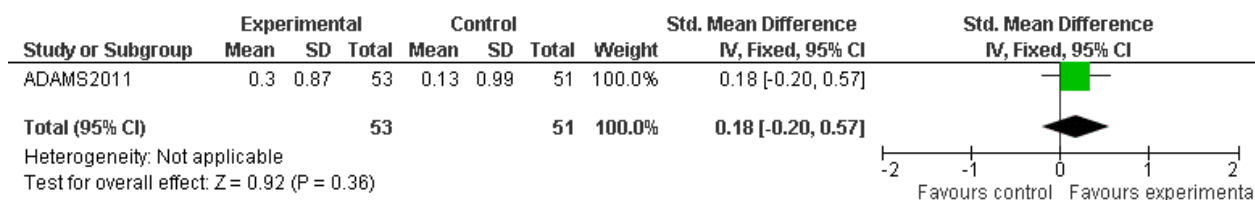
##### Sleep problems



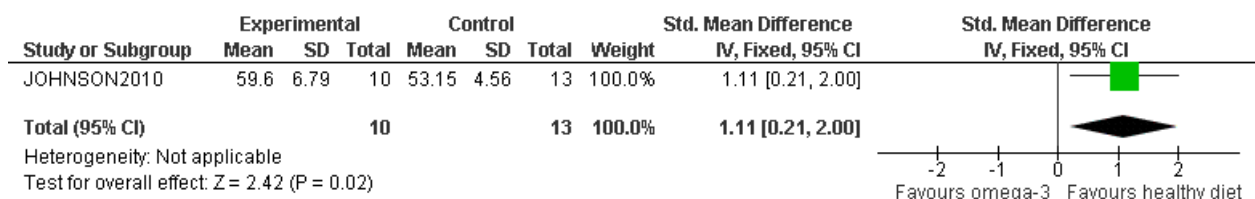
## 1.29 BIOMEDICAL INTERVENTIONS AIMED AT COEXISTING MEDICAL OR FUNCTIONAL PROBLEMS

### 1.29.1 Nutritional interventions for sleep problems as an indirect outcome

*Multivitamin/mineral supplement versus placebo for sleep problems as an indirect outcome*

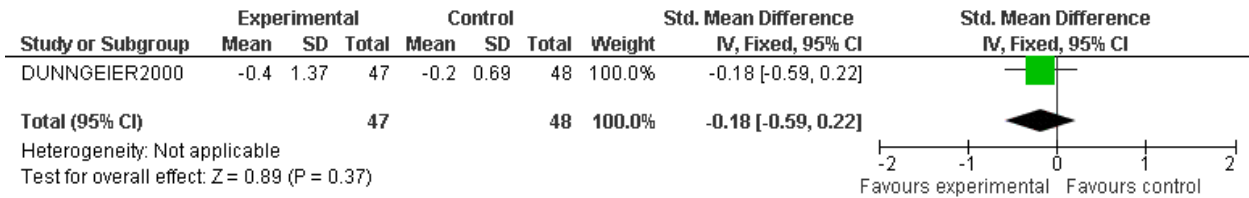


*Omega-3 fatty acids versus healthy diet control for sleep problems as an indirect outcome*



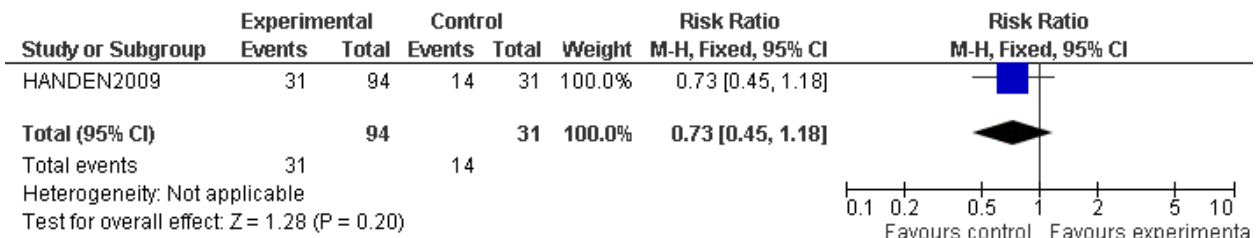
### 1.29.2 Hormones for gastrointestinal symptoms as an indirect outcome

#### *Secretin versus placebo for gastrointestinal symptoms as an indirect outcome*

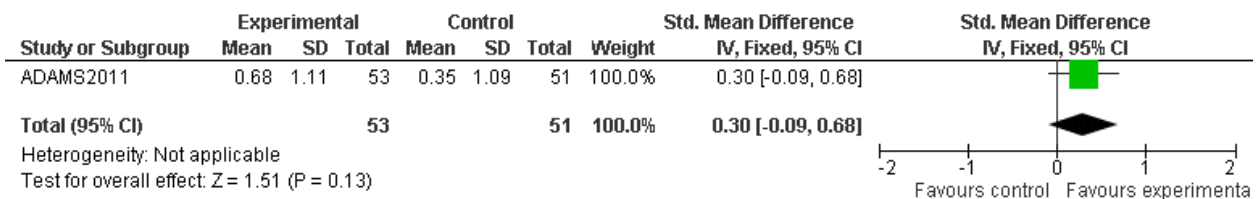


### 1.29.3 Nutritional interventions for gastrointestinal symptoms as a direct or indirect outcome

#### *Immunoglobulin versus placebo for gastrointestinal symptoms as a direct outcome*



#### *Multivitamin/ mineral supplement versus placebo for gastrointestinal symptoms as an indirect outcome*

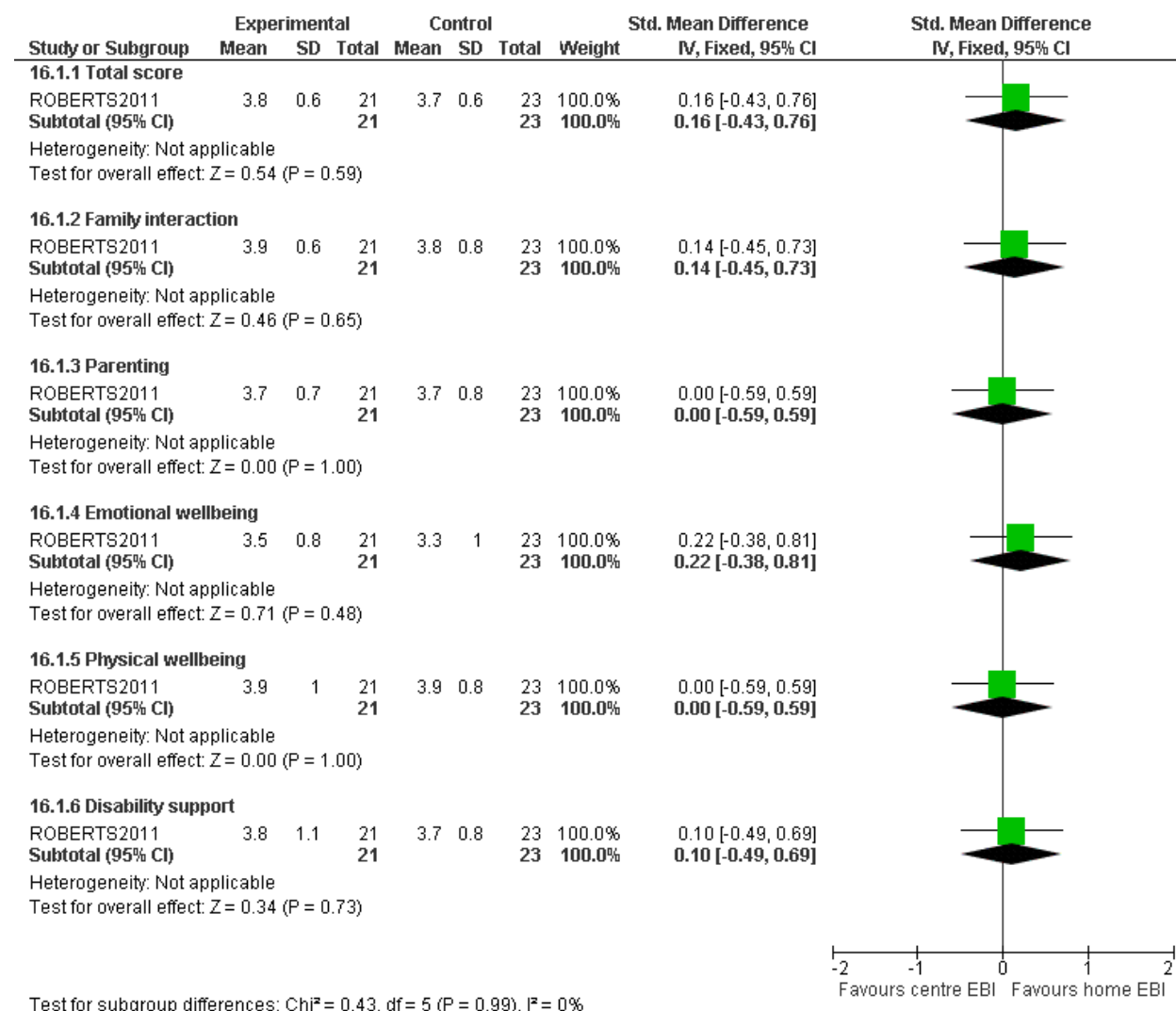


## 1.30 PSYCHOSOCIAL INTERVENTIONS AIMED AT IMPROVING THE IMPACT OF AUTISM ON THE FAMILY

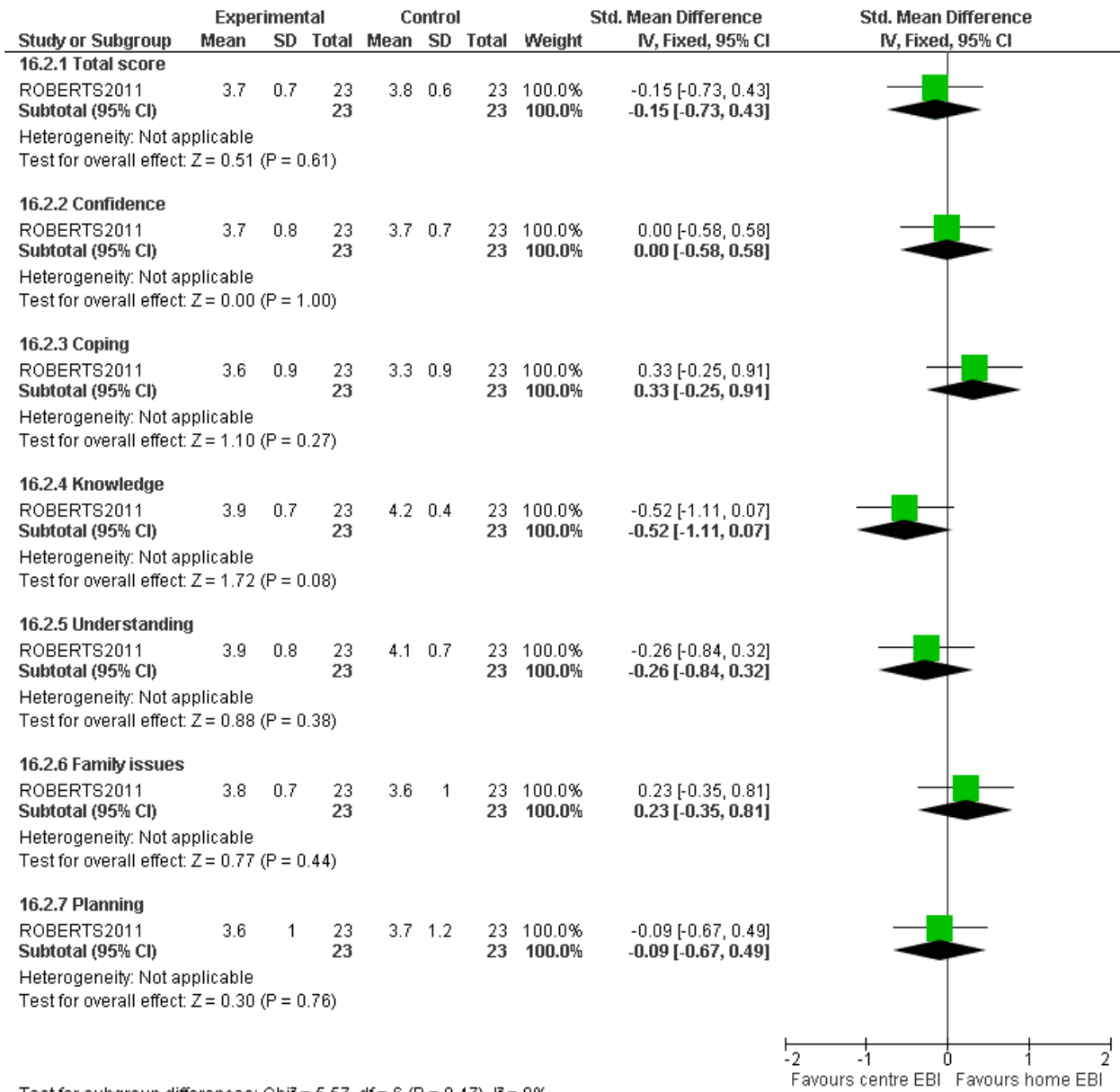
### 1.30.1 Behavioural interventions for improving the impact of autism on the family as an indirect outcome

*Home-based EBI versus centre-based EBI for improving the impact of autism on the family as an indirect outcome*

#### Family quality of life (Beach Family Quality of Life Questionnaire)

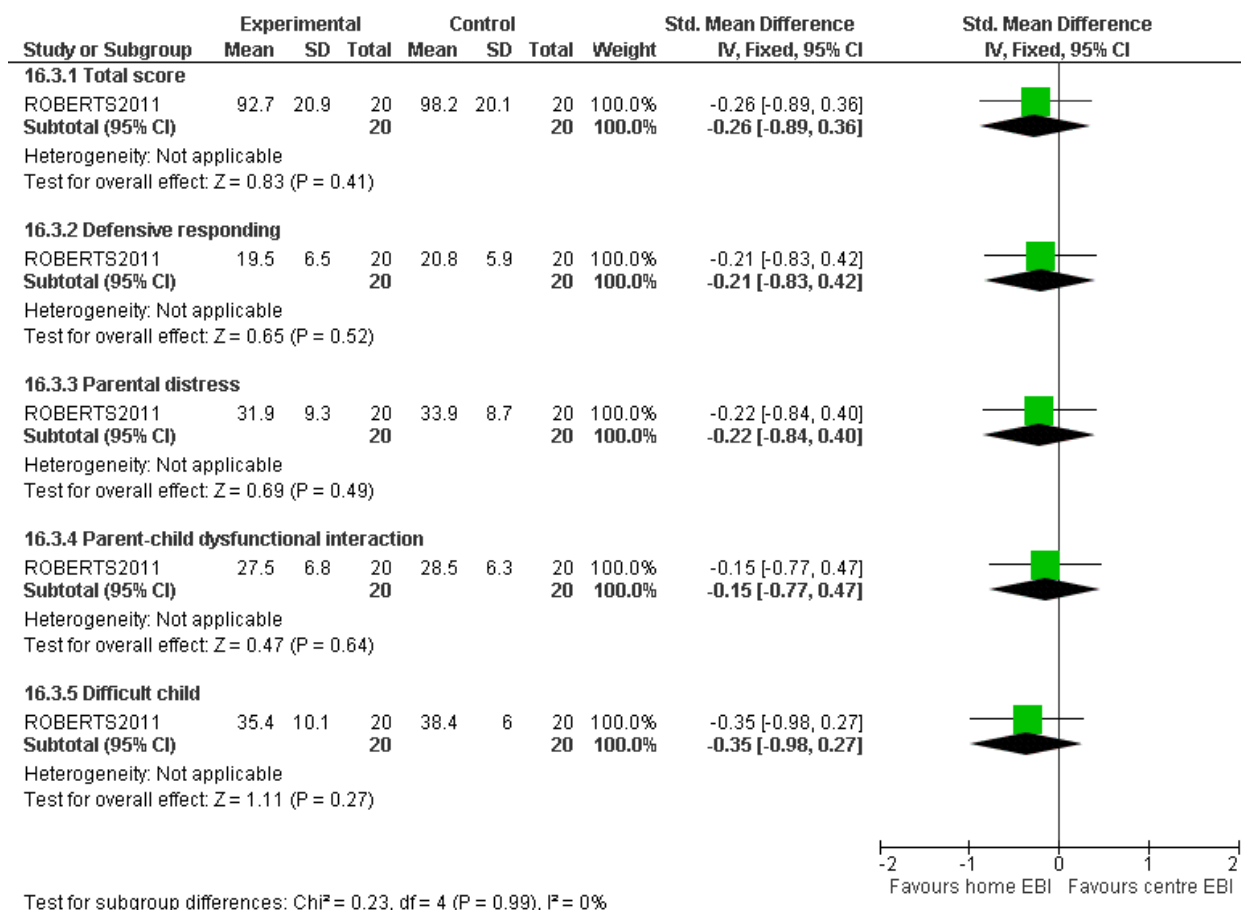


#### Parental coping skills (study-specific questionnaire)



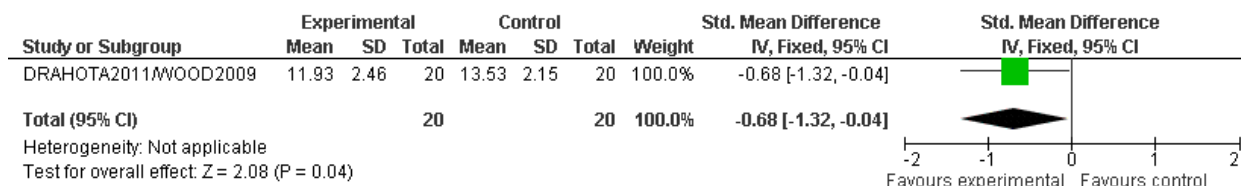
**Parental stress (PSI)**





### 1.30.2 Cognitive-behavioural interventions for improving the impact of autism on the family as an indirect outcome

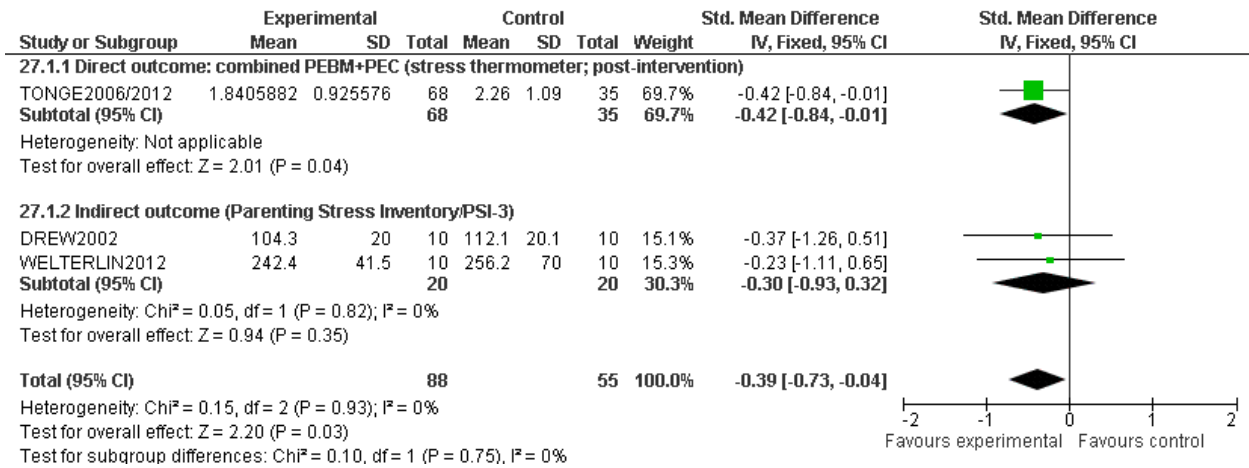
*CBT versus waitlist for improving the impact of autism on the family as an indirect outcome*



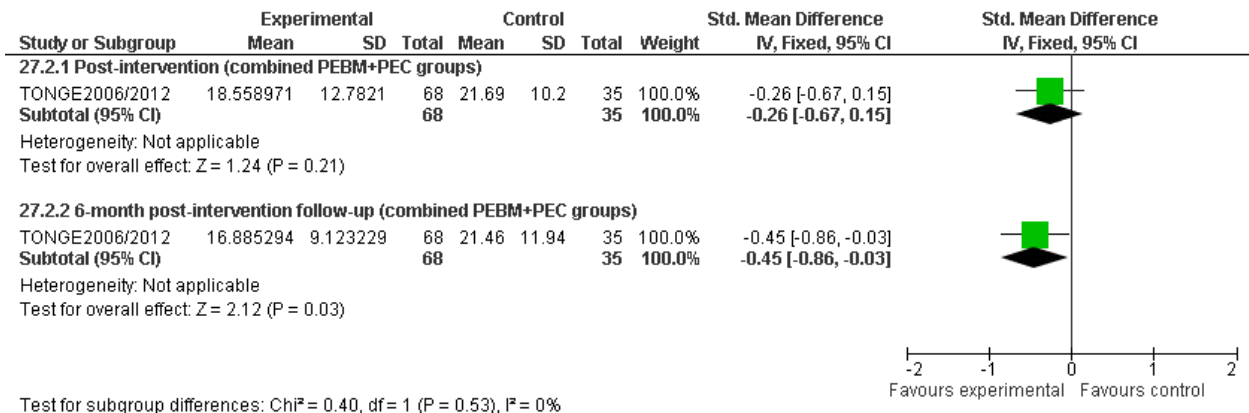
### 1.30.3 Parent training for improving the impact of autism on the family as a direct or indirect outcome

*Parent training versus treatment as usual for improving the impact of autism on the family as a direct or indirect outcome*

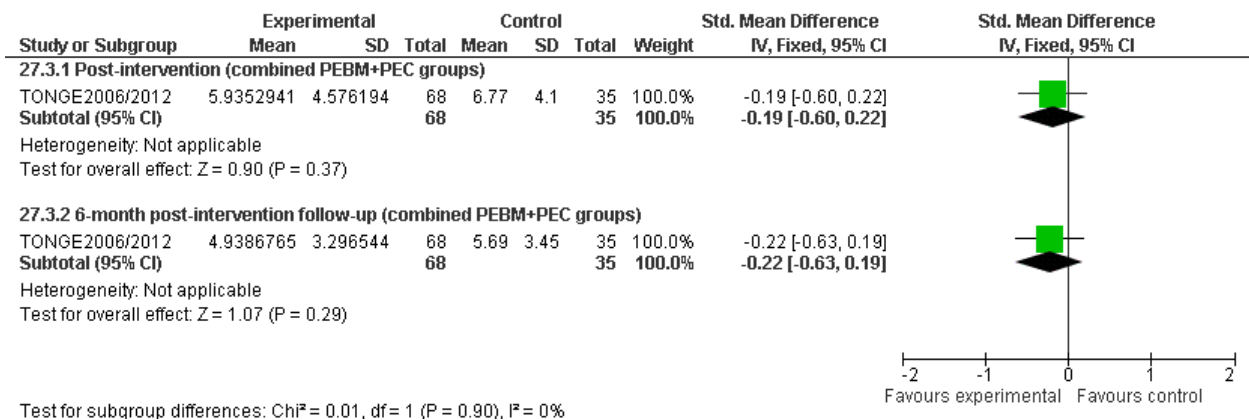
#### Parental stress



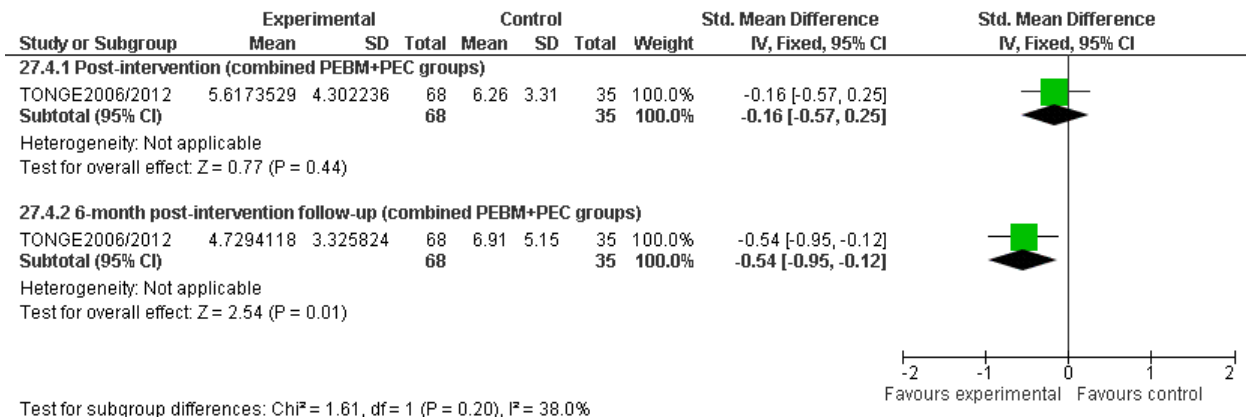
### Parental mental health (GHQ-28)



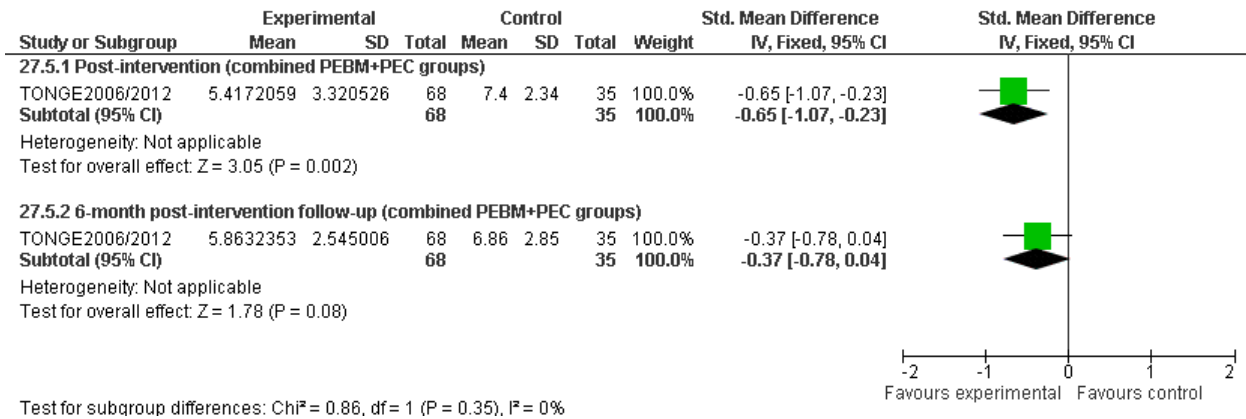
### Parental somatic symptoms (GHQ-28)



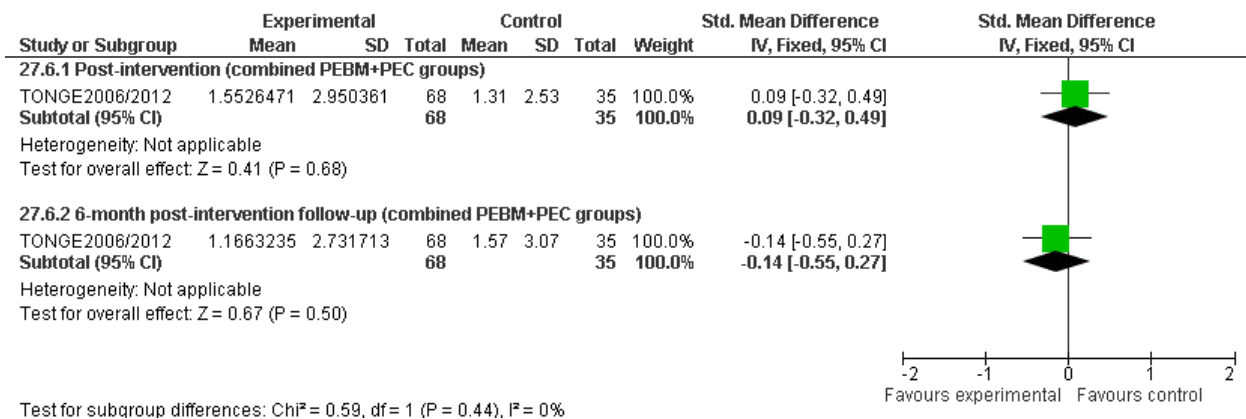
### Parental anxiety and insomnia (GHQ-28)



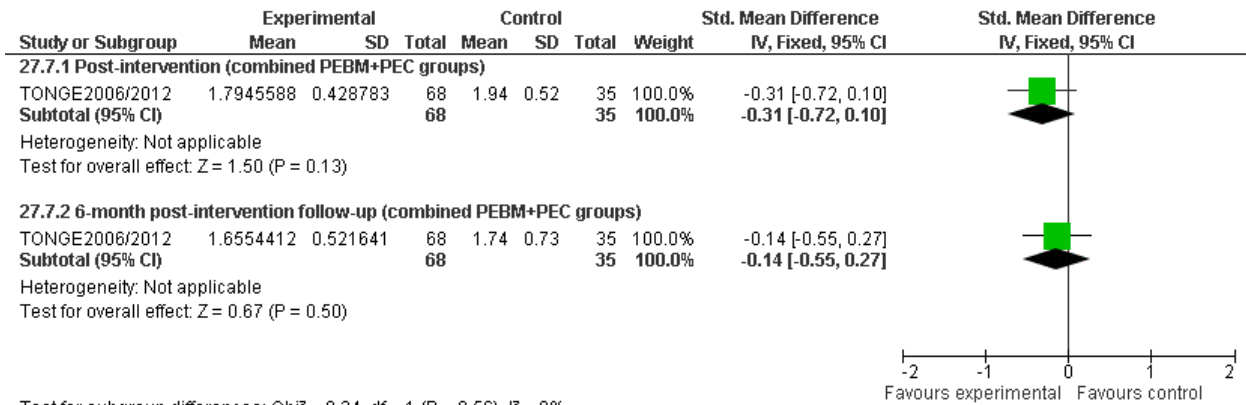
### Parental social dysfunction (GHQ-28)



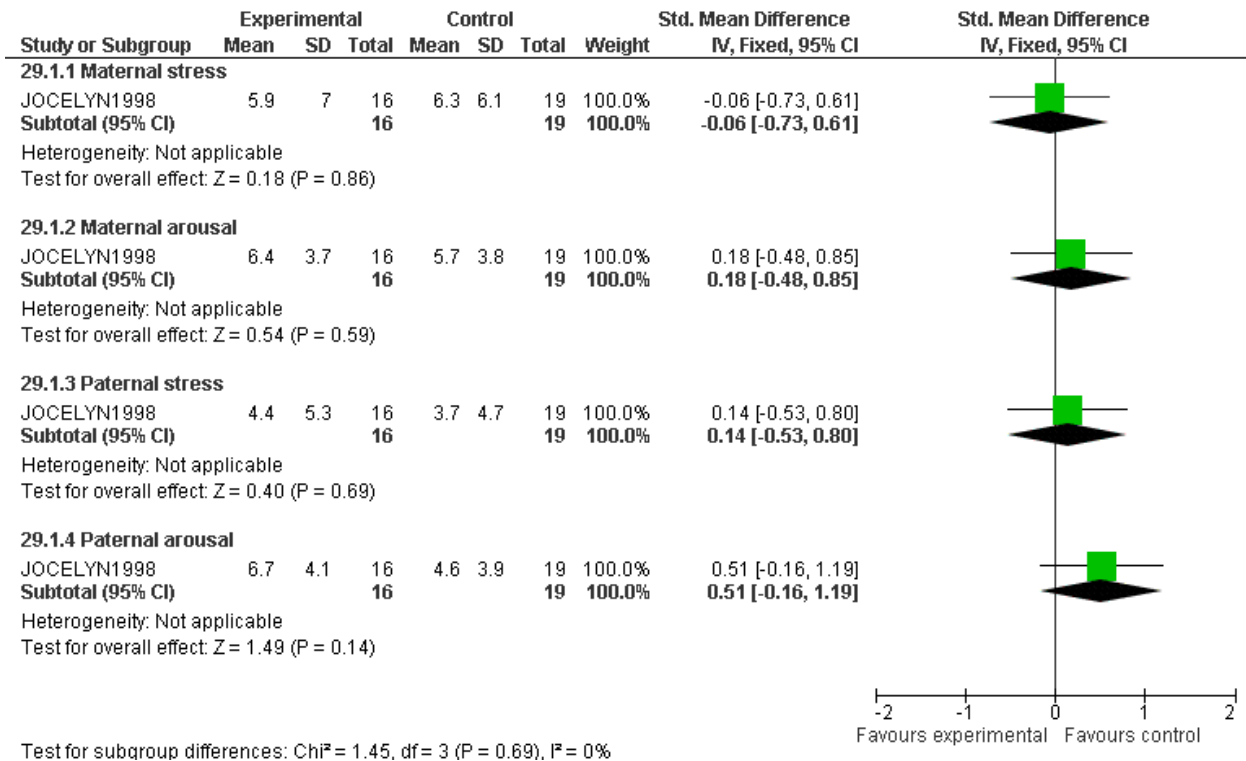
### Parental severe depression (GHQ-28)



### General family function (FAD)



*Parent and day-care staff training versus standard day-care for improving the impact of autism on the family as an indirect outcome*

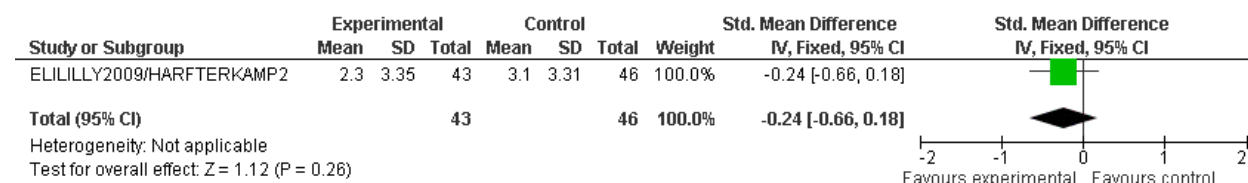


## 1.31 PHARMACOLOGICAL INTERVENTIONS AIMED AT IMPROVING THE IMPACT OF AUTISM ON THE FAMILY

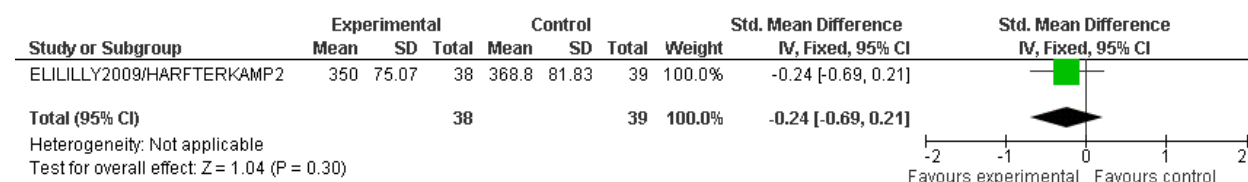
### 1.31.1 SNRIs for improving the impact of autism on the family as an indirect outcome

*Atomoxetine versus placebo for improving the impact of autism on the family as an indirect outcome*

#### Parental mental health (GHQ)



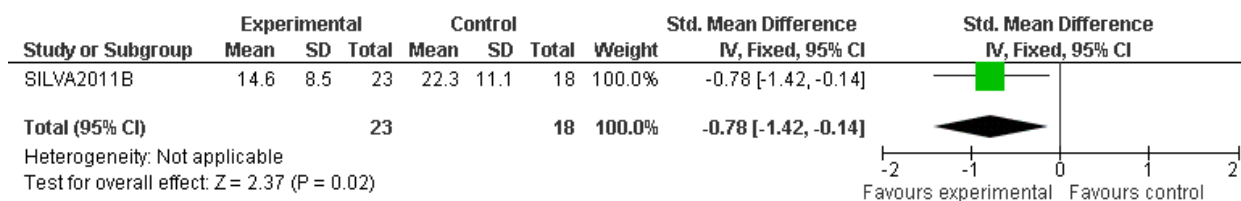
#### Parental stress (NOSI)



## 1.32 BIOMEDICAL INTERVENTIONS AIMED AT IMPROVING THE IMPACT OF AUTISM ON THE FAMILY

### 1.32.1 Complementary therapies for improving the impact of autism on the family as an indirect outcome

*Qigong massage training versus waitlist for improving the impact of autism on the family as an indirect outcome*

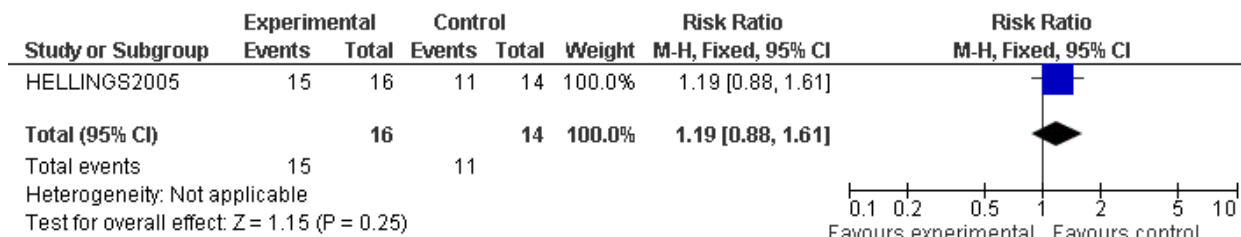


## 1.33 ADVERSE EVENTS ASSOCIATED WITH PHARMACOLOGICAL INTERVENTIONS

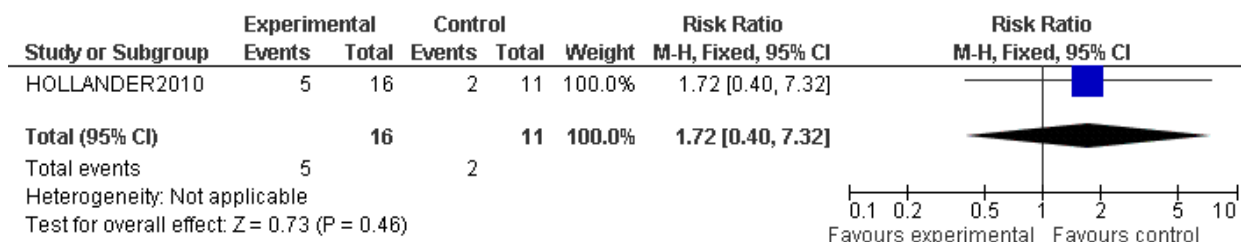
### 1.33.1 Adverse events associated with anticonvulsants

*Adverse events associated with divalproex versus placebo*

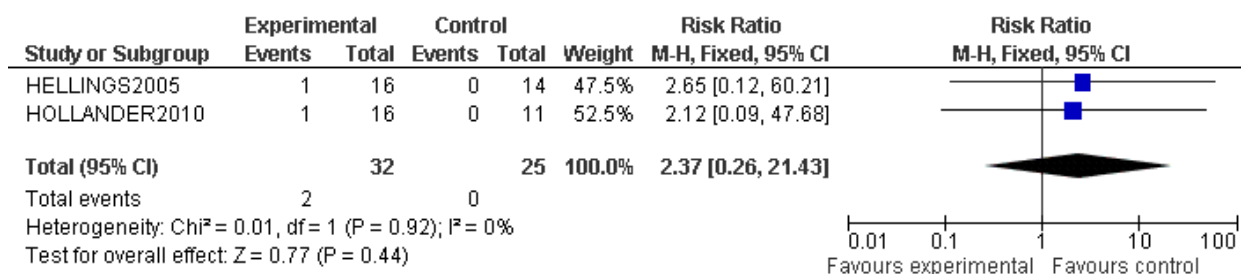
#### Any adverse event



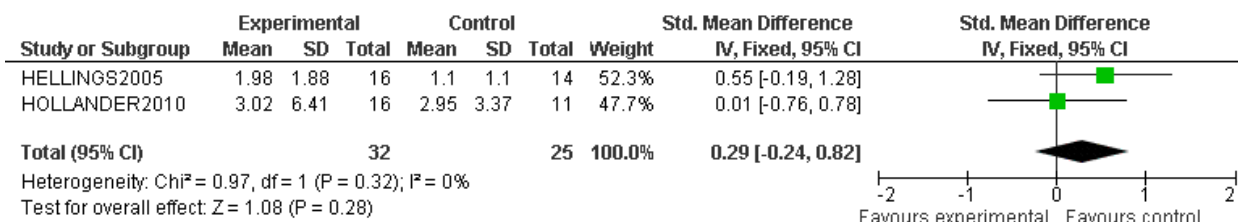
#### More than one adverse event



#### Discontinuation due to adverse event



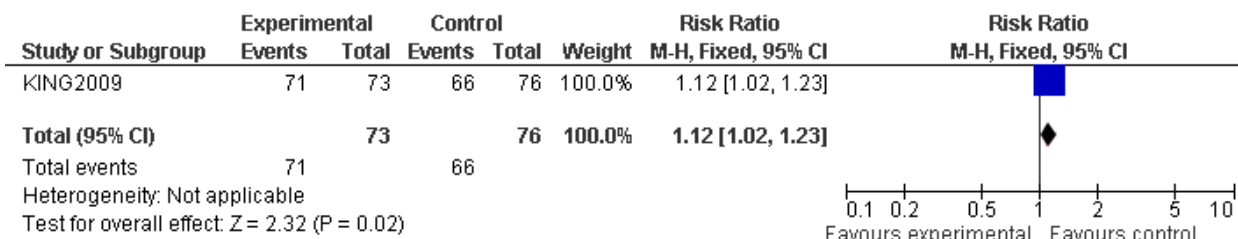
## Weight gain (in kg or lb)



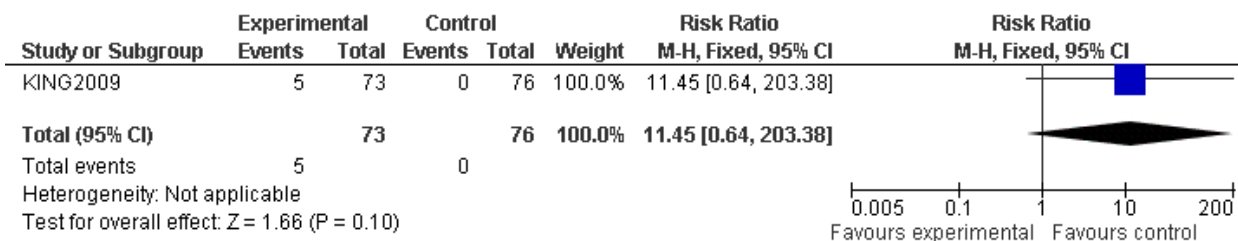
## 1.33.2 Adverse events associated with antidepressants

### *Adverse events associated with citalopram versus placebo*

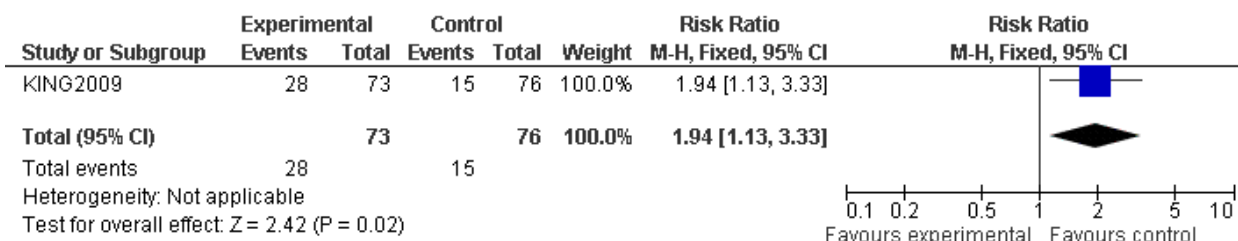
#### Any adverse event



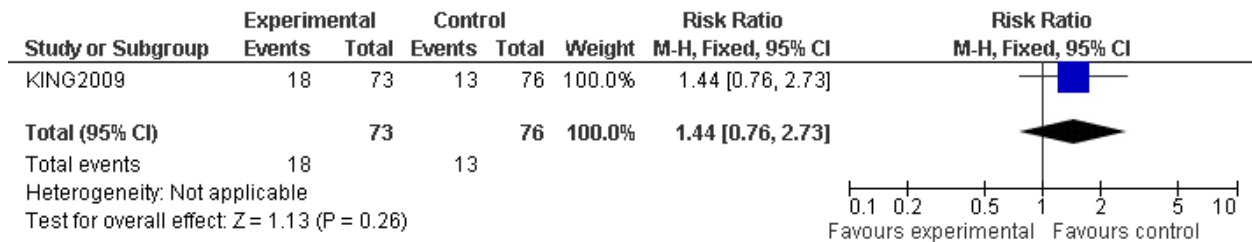
#### Nightmares



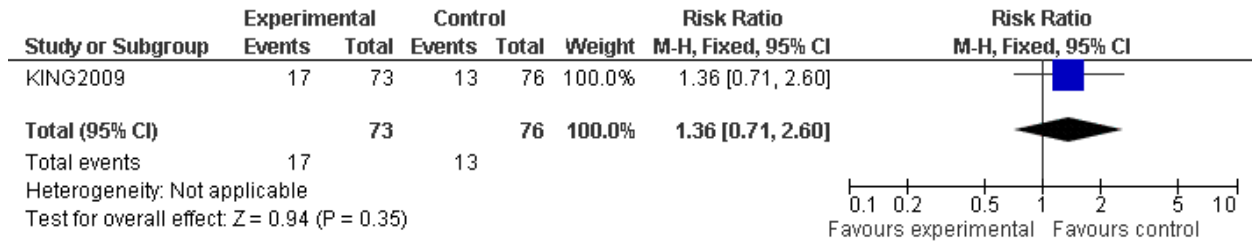
#### Increased energy level



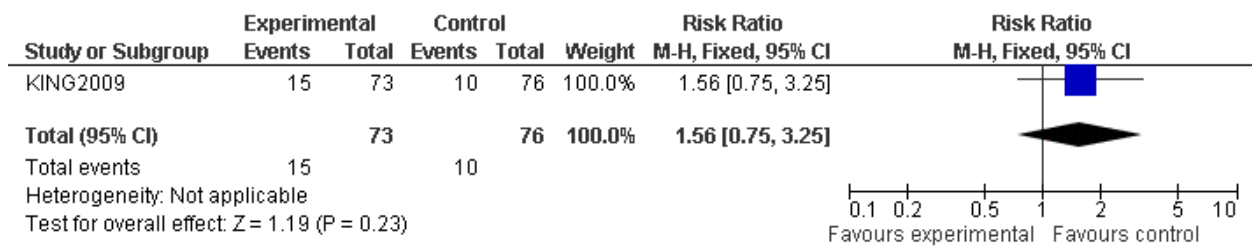
#### Anger or irritability



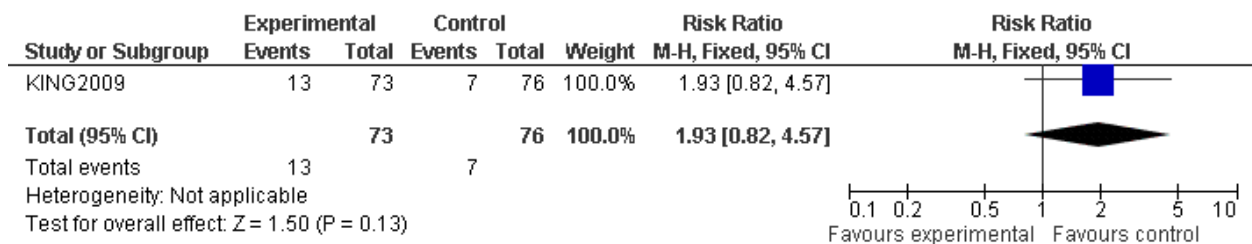
### Aggression or hostility



### Headache or migraine

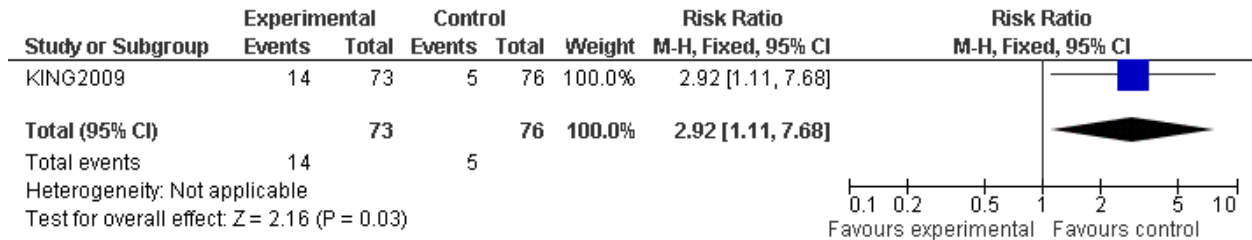


### Restlessness or difficulty settling down

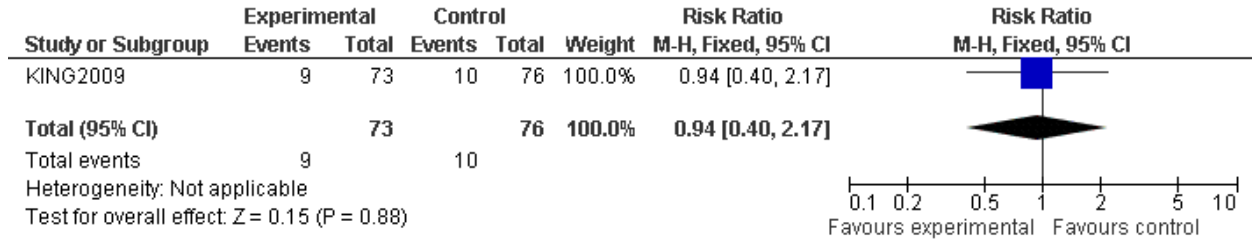


### Disinhibited, impulsive, or intrusive behaviour

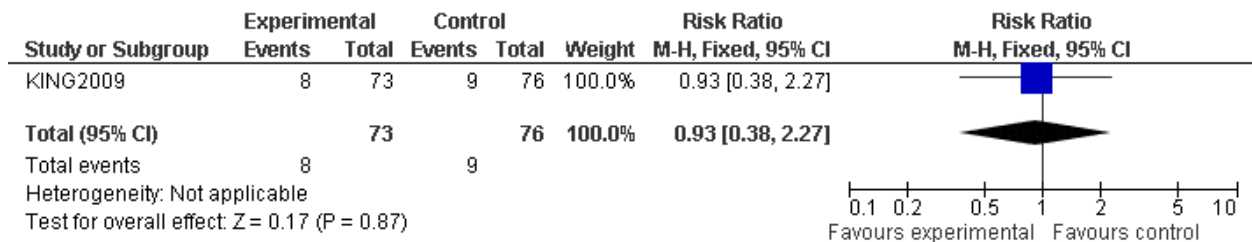




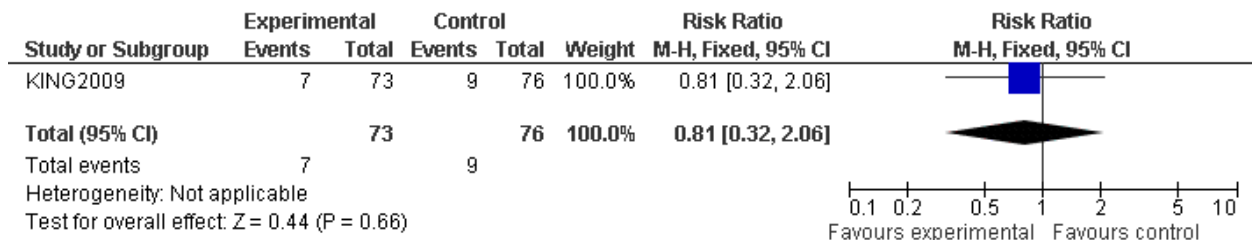
### Silliness



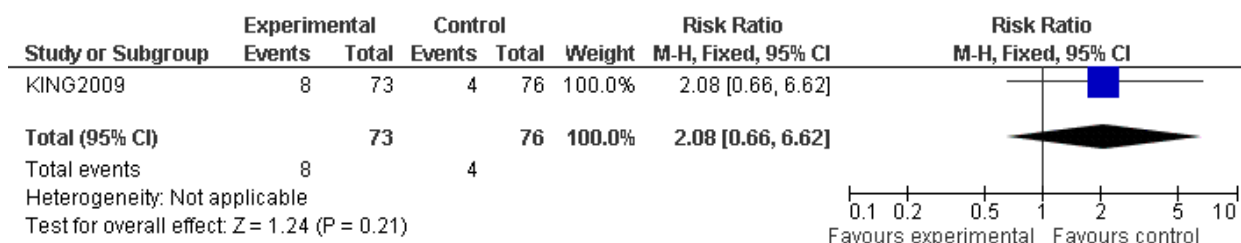
### Anxiety



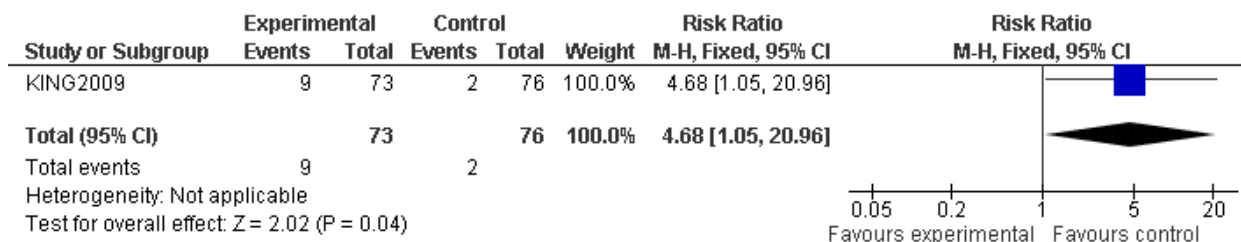
### Mood lability



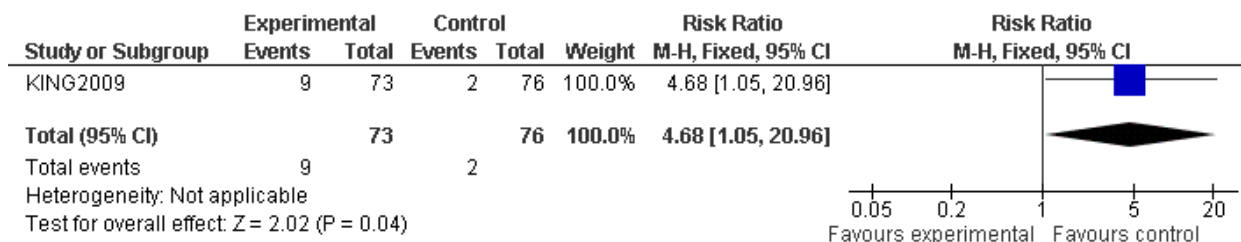
### Increased speech



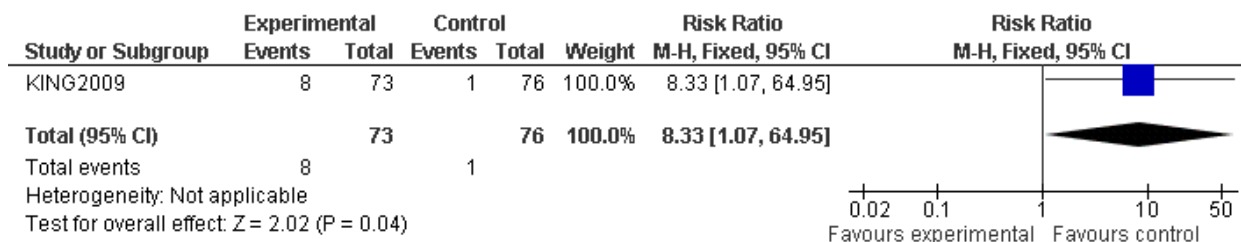
### Decreased attention and concentration



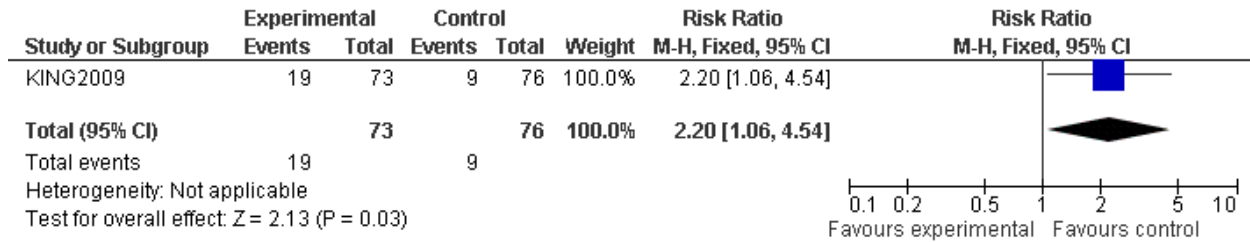
### Hyperactivity



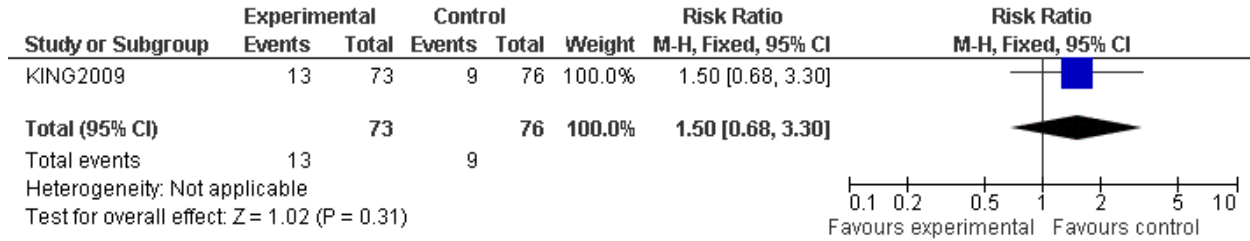
### Stereotypy



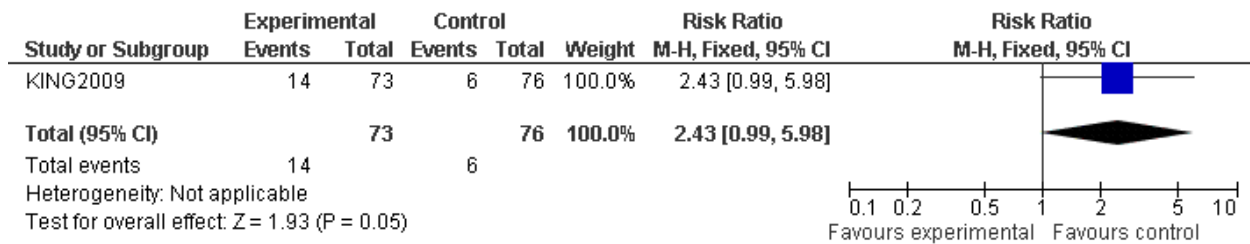
### Diarrhoea or loose stools



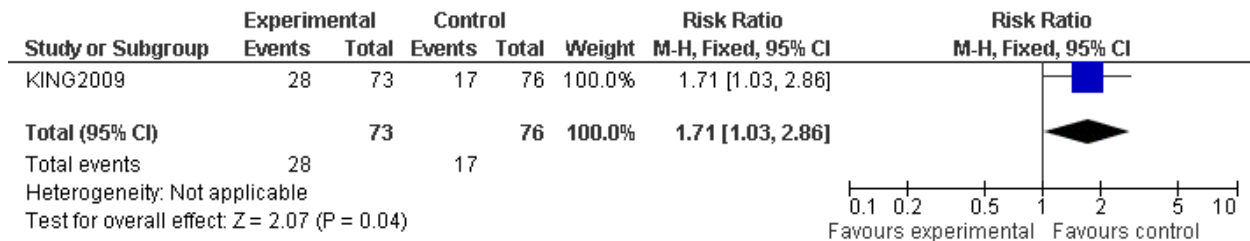
### Abdominal discomfort



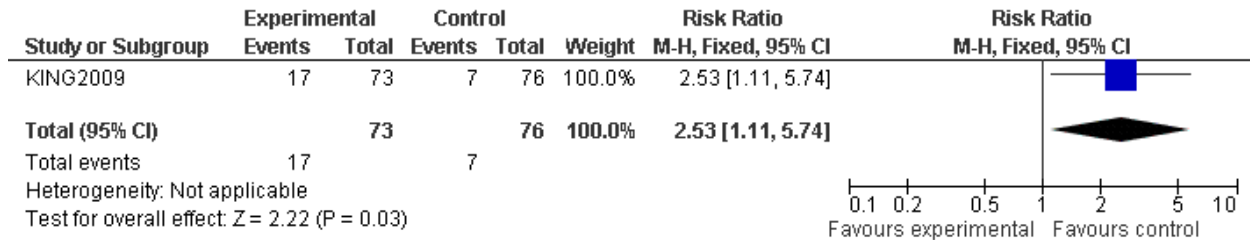
### Vomiting or nausea



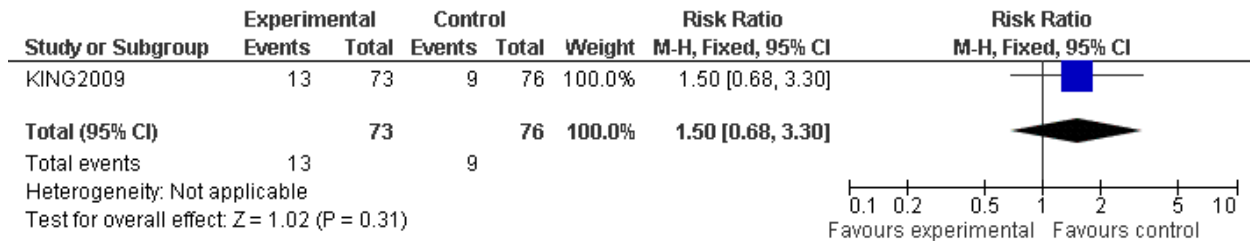
### Any insomnia



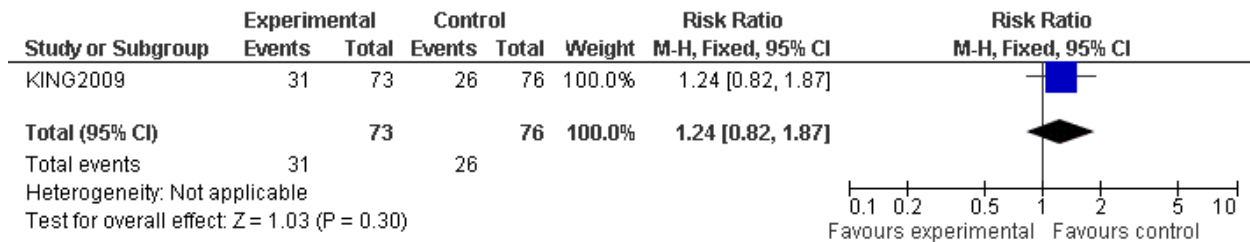
### Initial insomnia or difficulty falling asleep



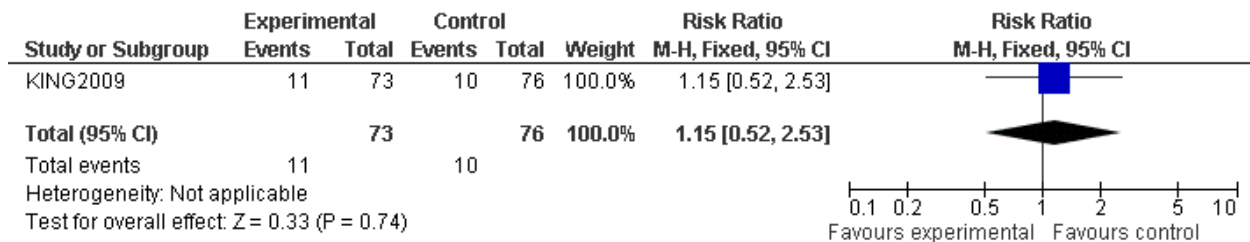
### Midcycle or other insomnia



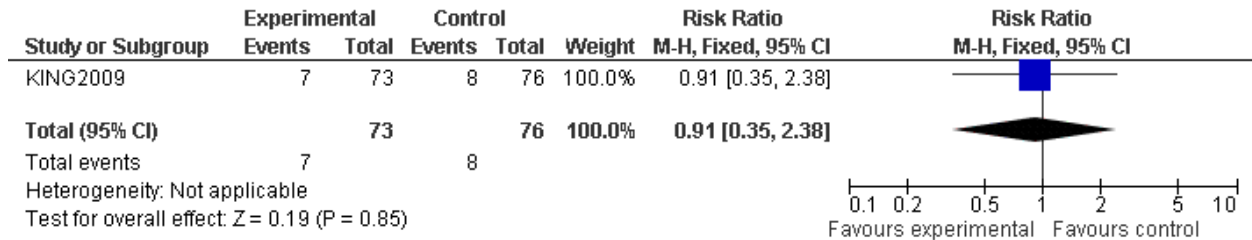
### Cold, flu or other systemic infection



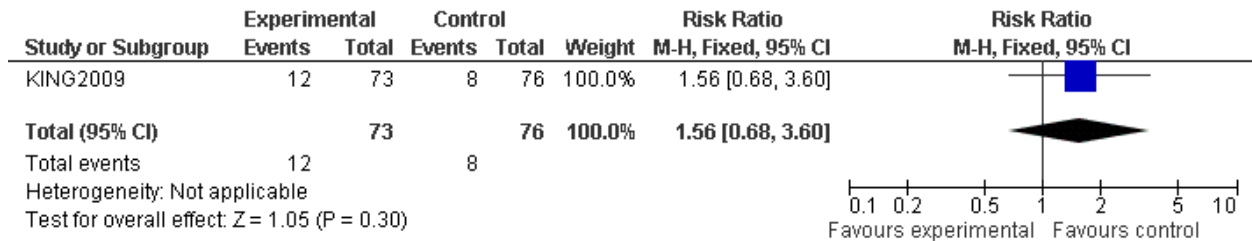
### Decreased appetite



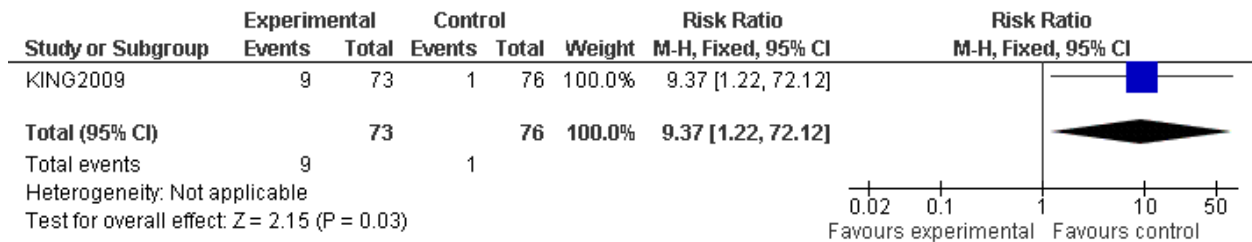
### Increased appetite



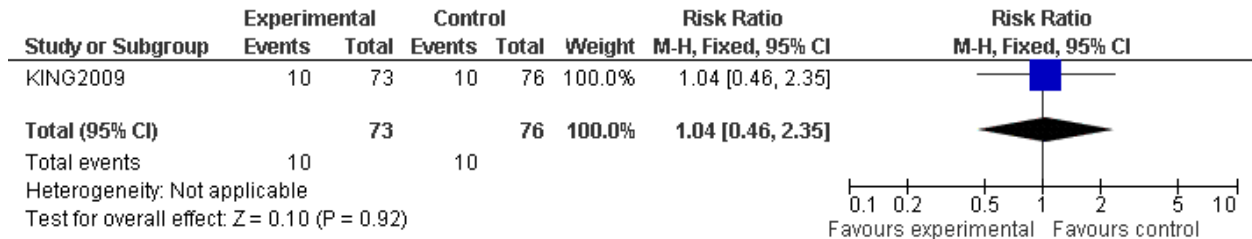
### Rash



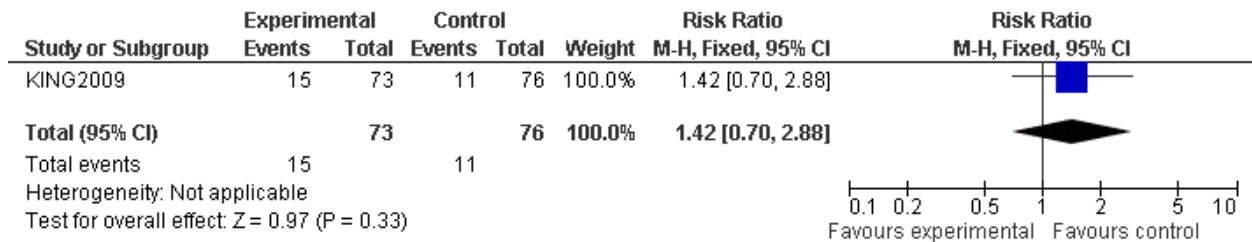
### Other skin or subcutaneous tissue disorder



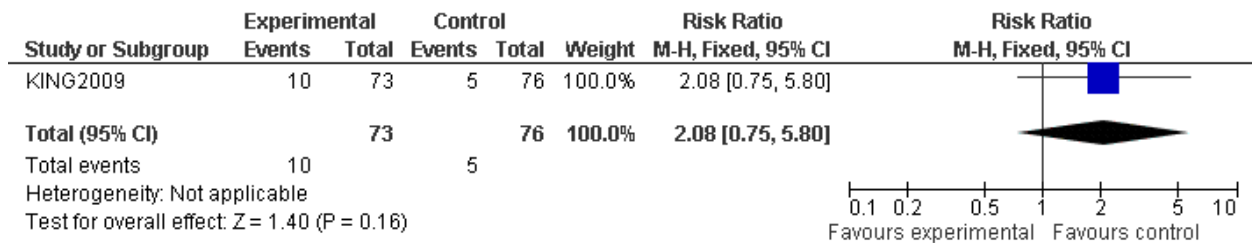
### Fatigue



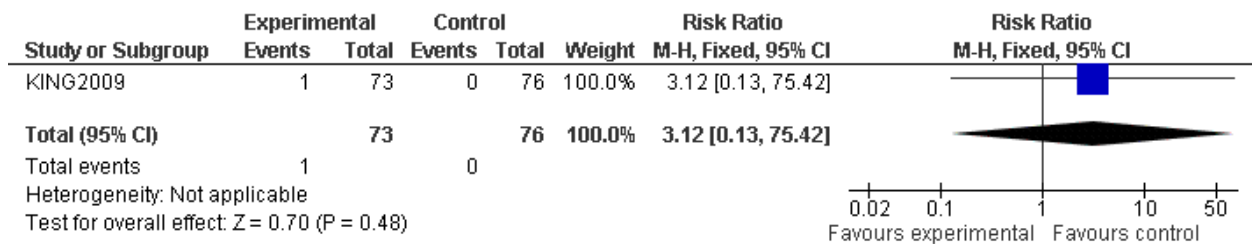
### Allergies



### Cough



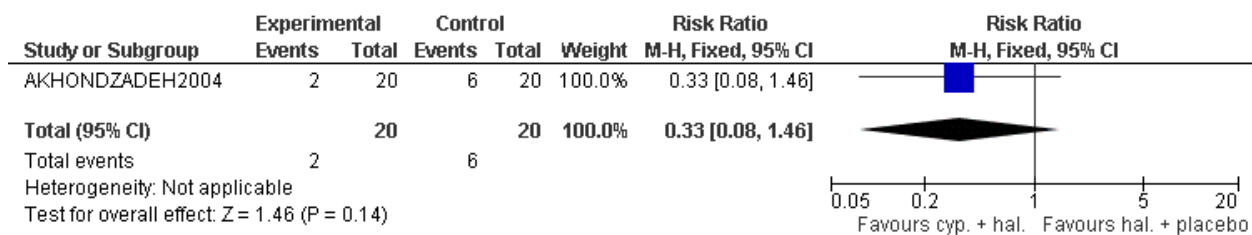
### Any serious adverse event



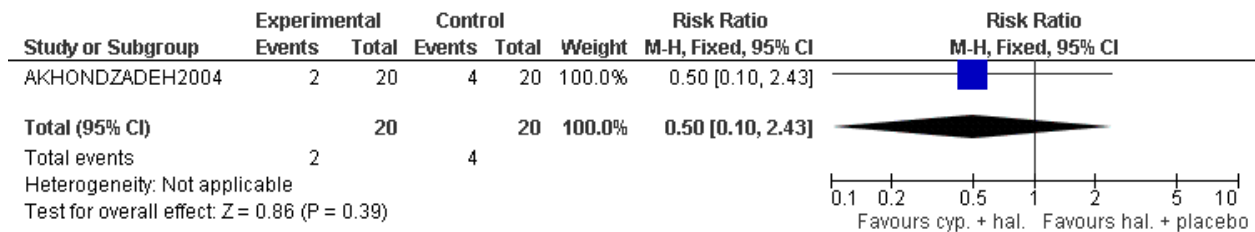
### 1.33.3 Adverse events associated with antihistamines

*Adverse events associated with cyproheptadine and haloperidol versus placebo and haloperidol*

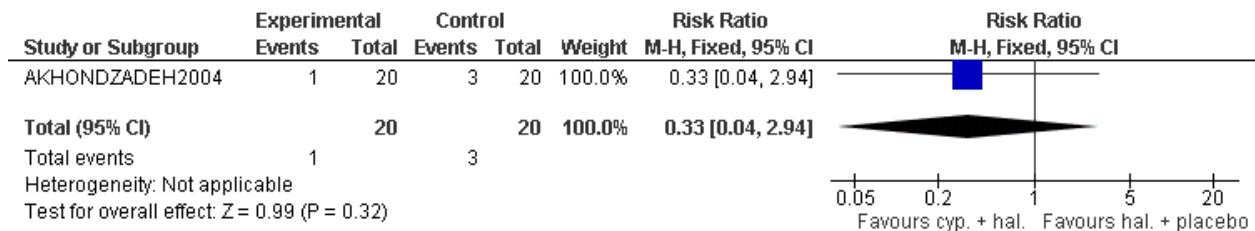
#### Extrapyramidal symptoms



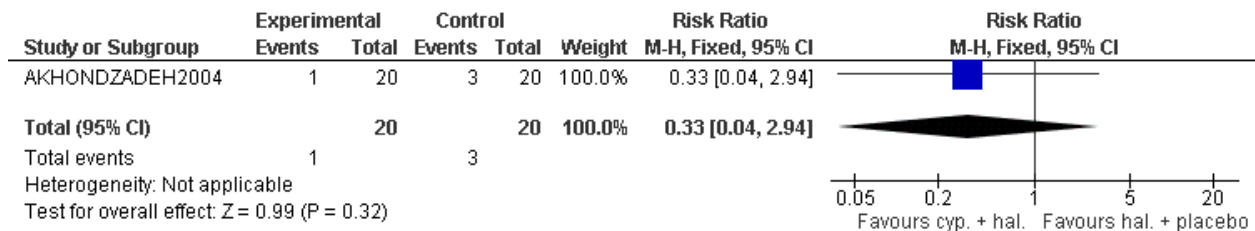
### Trouble swallowing



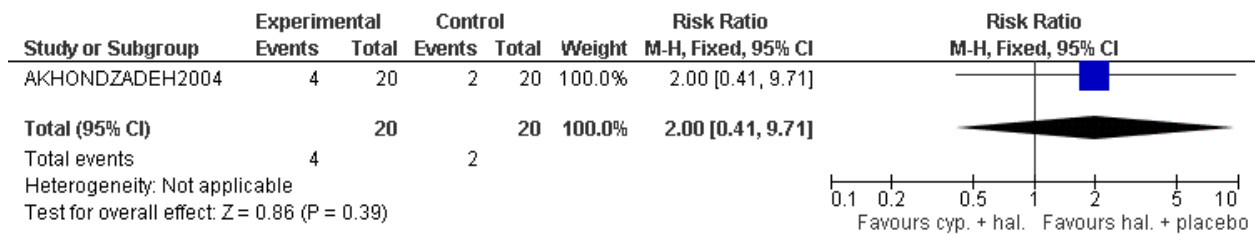
### Stiffness



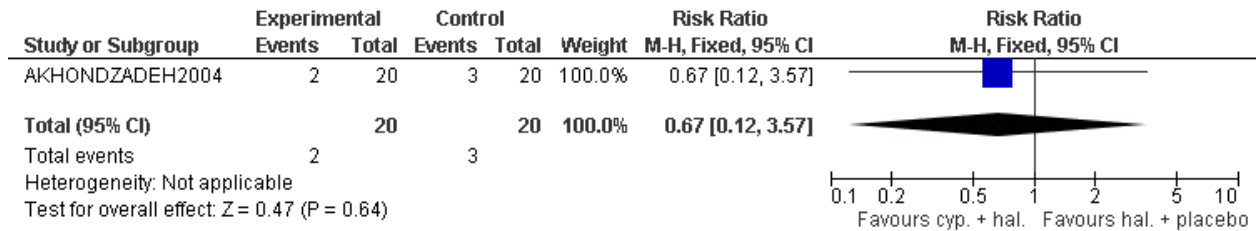
### Slow movement



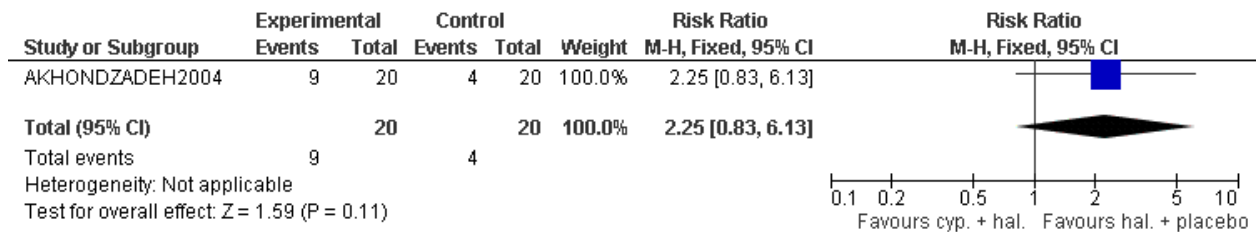
### Constipation



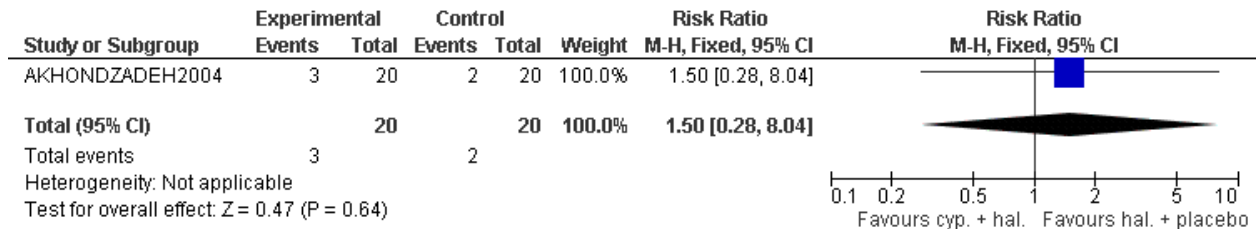
## Diarrhoea



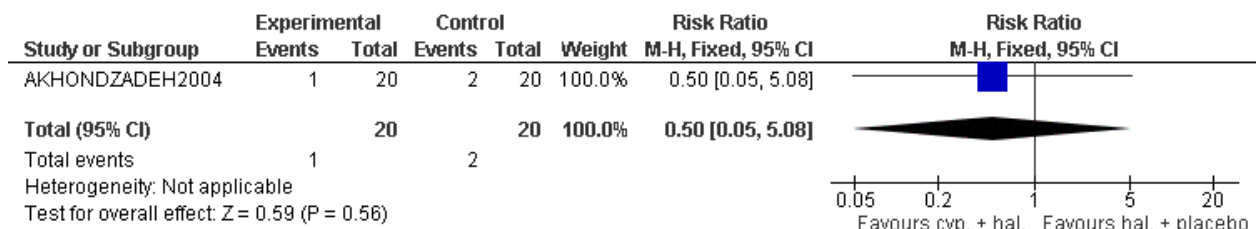
## Increased appetite



## Morning drowsiness

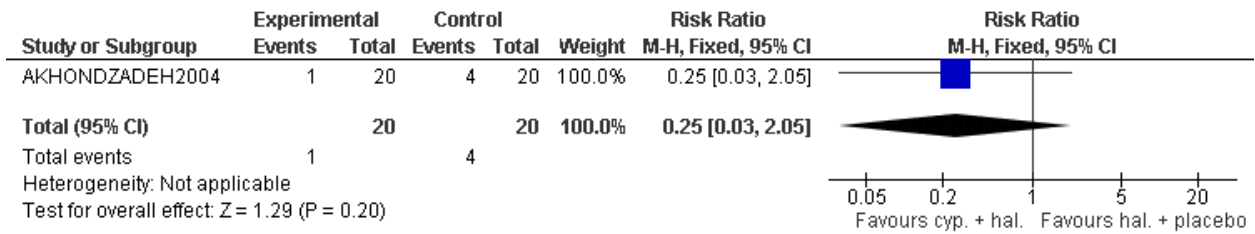


## Day time drowsiness

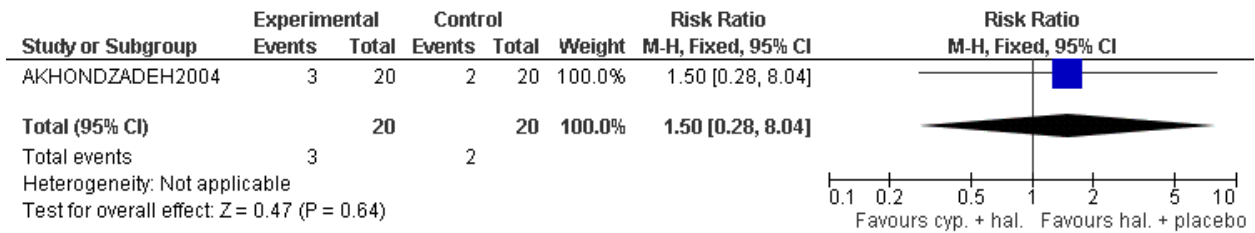


## Restlessness





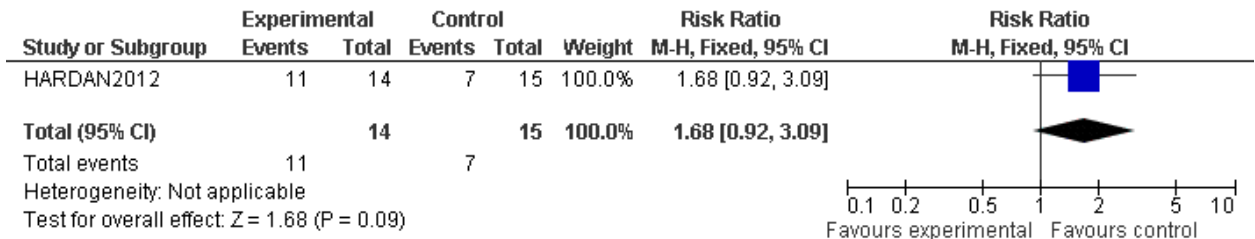
## Fatigue



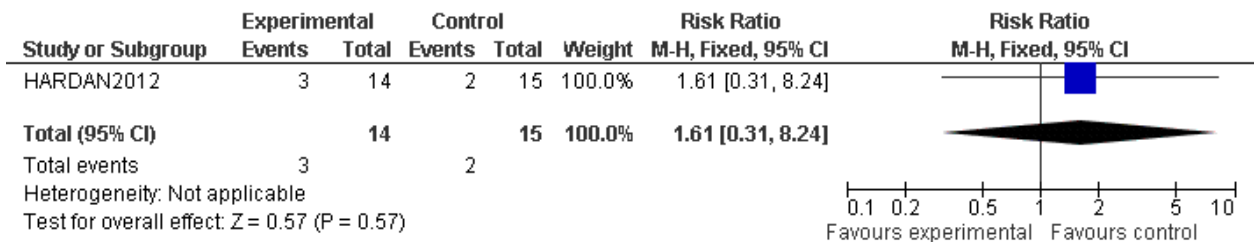
## 1.33.4 Adverse events associated with antioxidants

### *Adverse events associated with N-acetylcysteine versus placebo*

#### Any gastrointestinal side effect

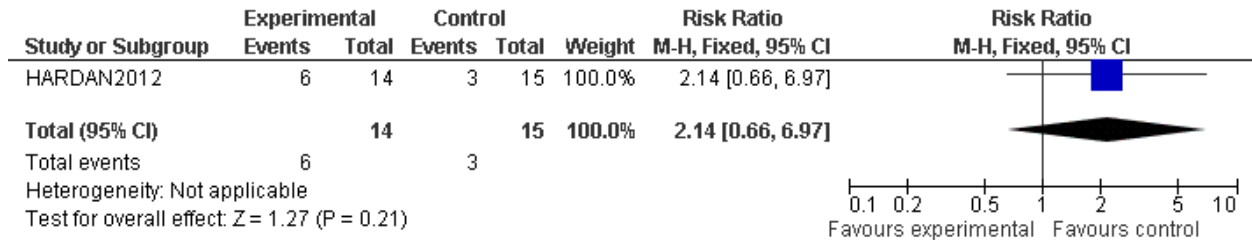


## Constipation

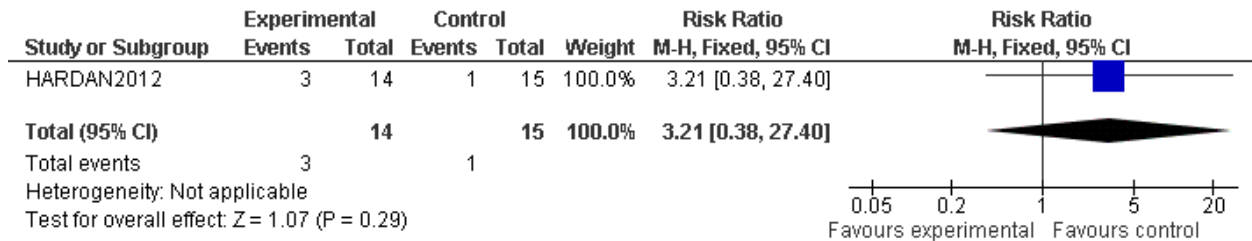


## Nausea

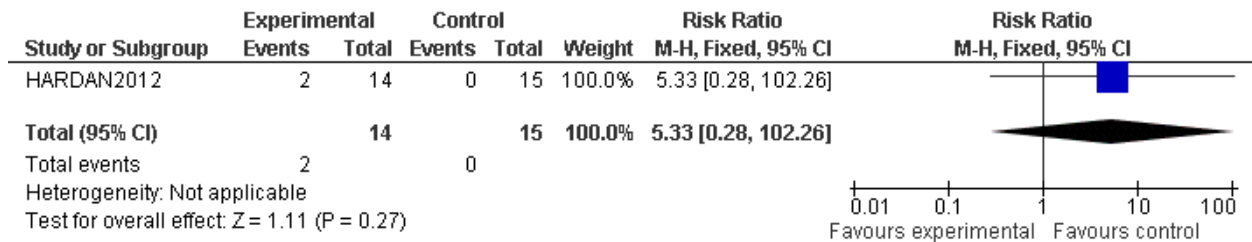
Autism: the management and support of children and young people on the autism spectrum (March 2013)



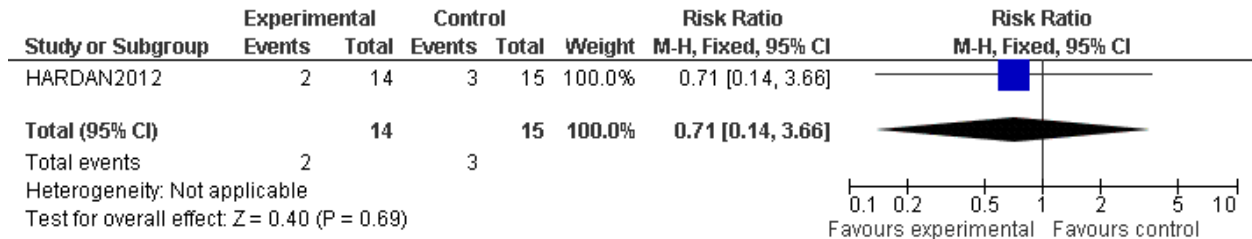
### Diarrhoea



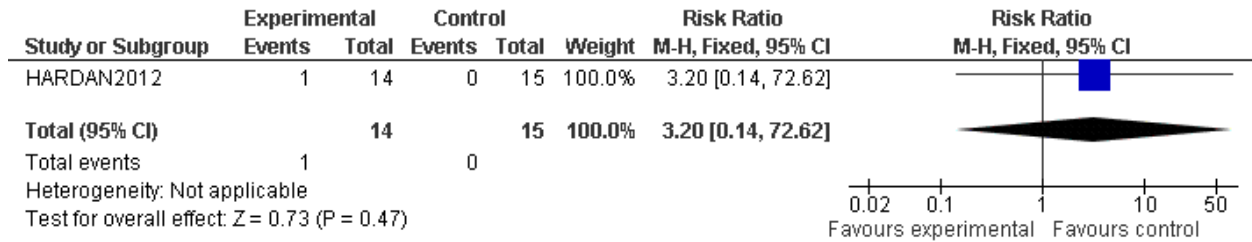
### Increased appetite



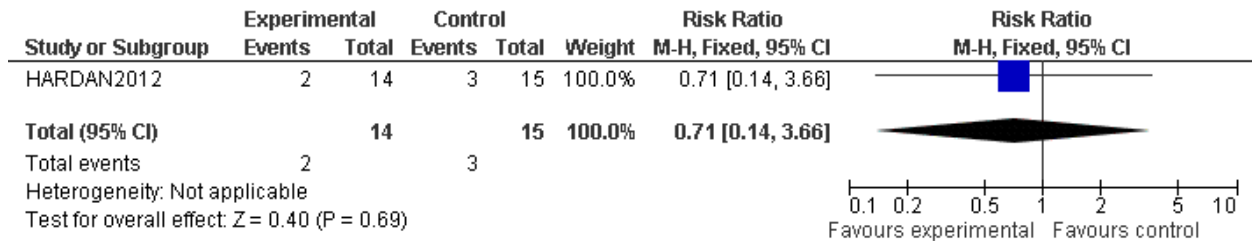
### Loss of appetite



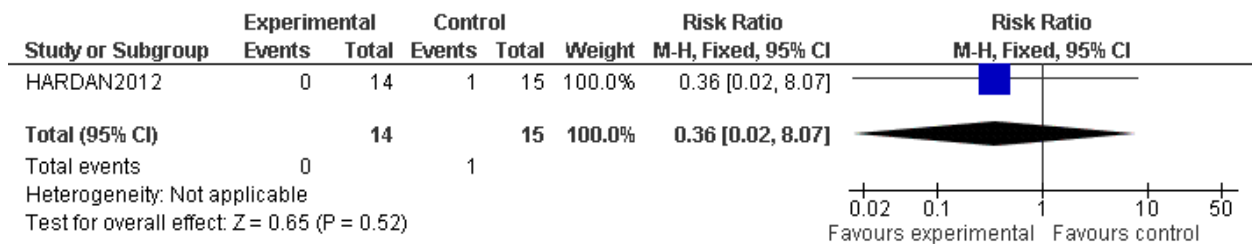
### Akathisia



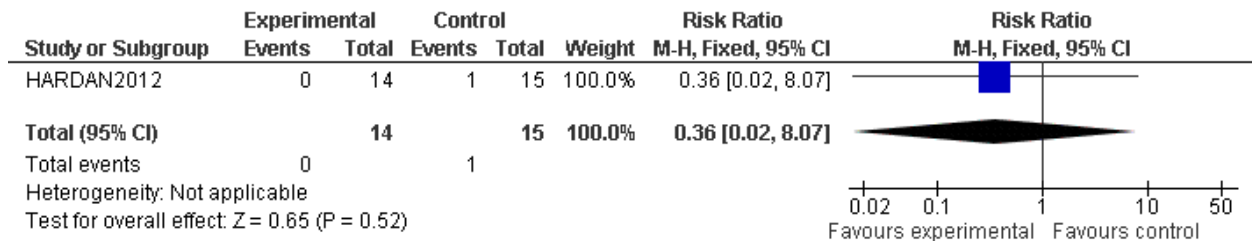
### Increased motor activity



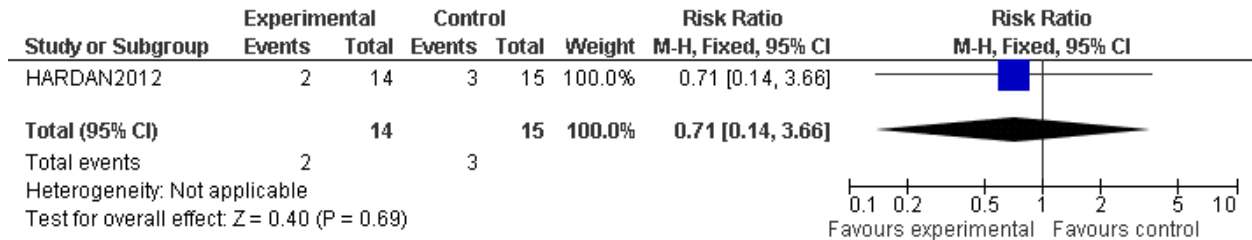
### Tremor



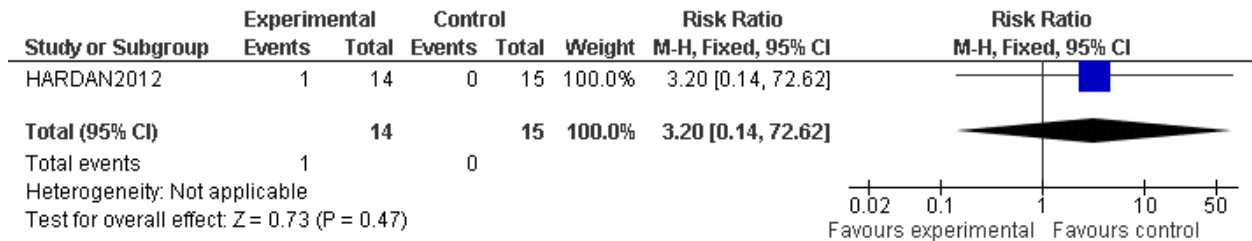
### Dizziness



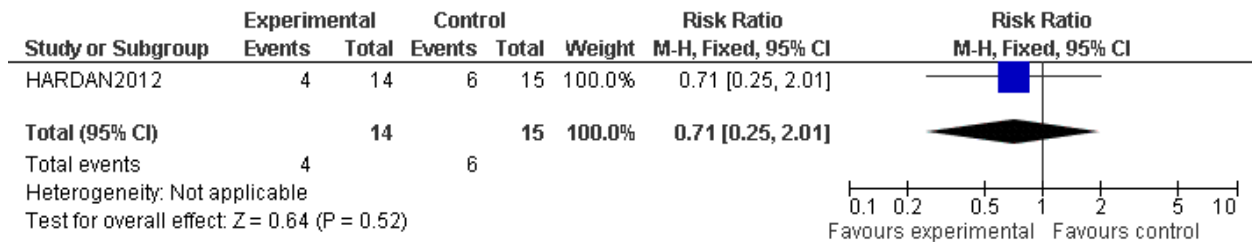
### Excitement/agitation



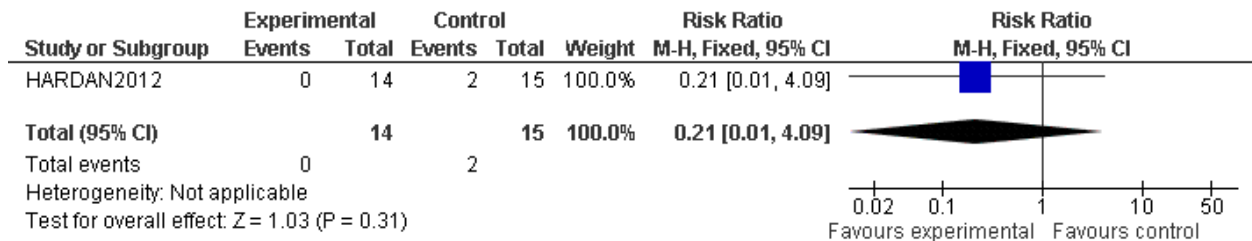
### Depressed affect



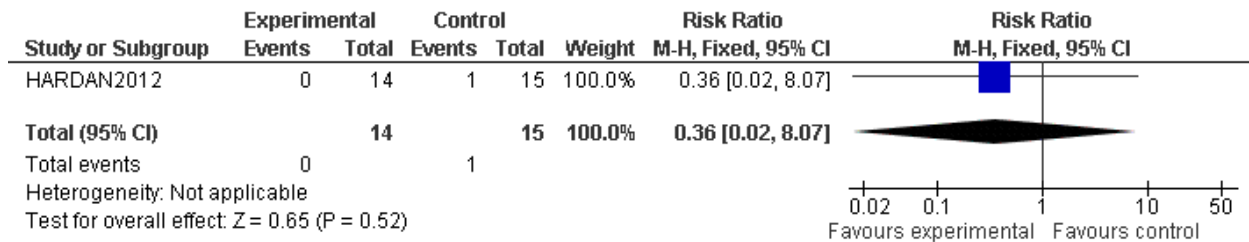
### Nasal congestion



### Increased salivation



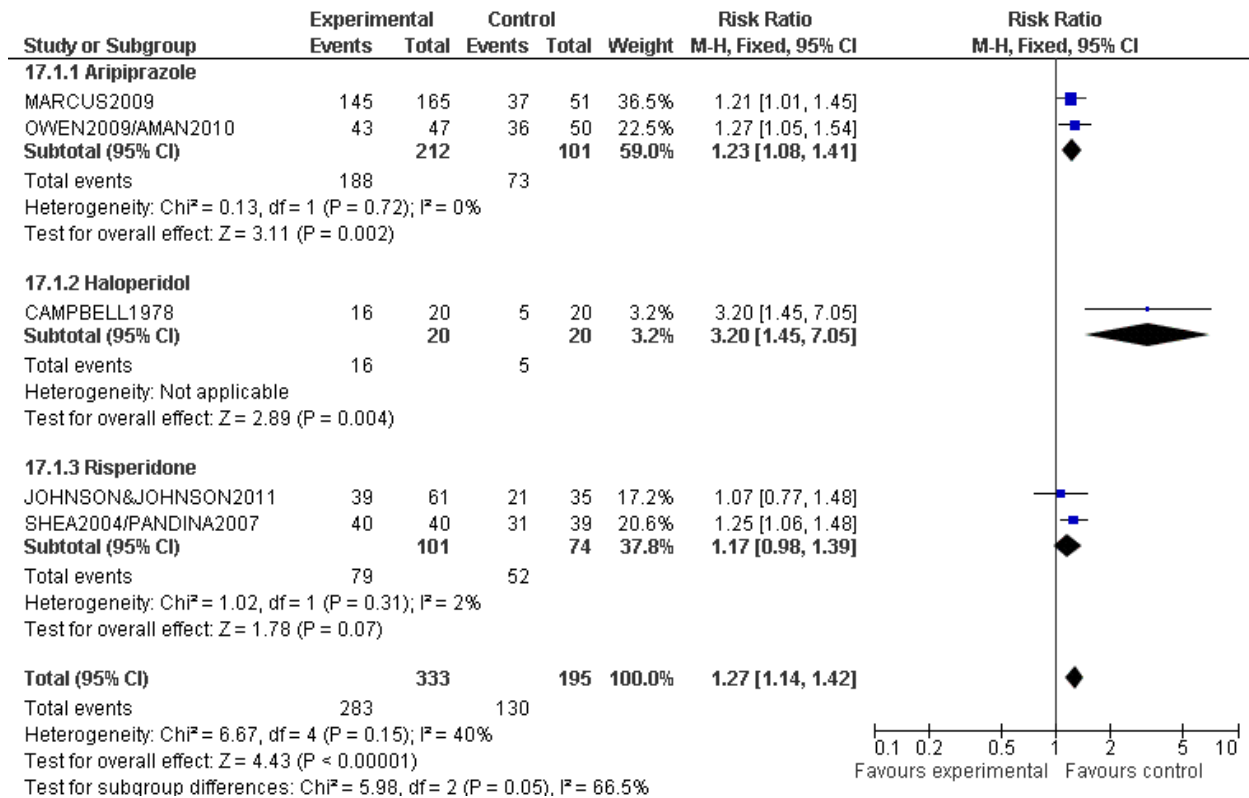
### Sweating



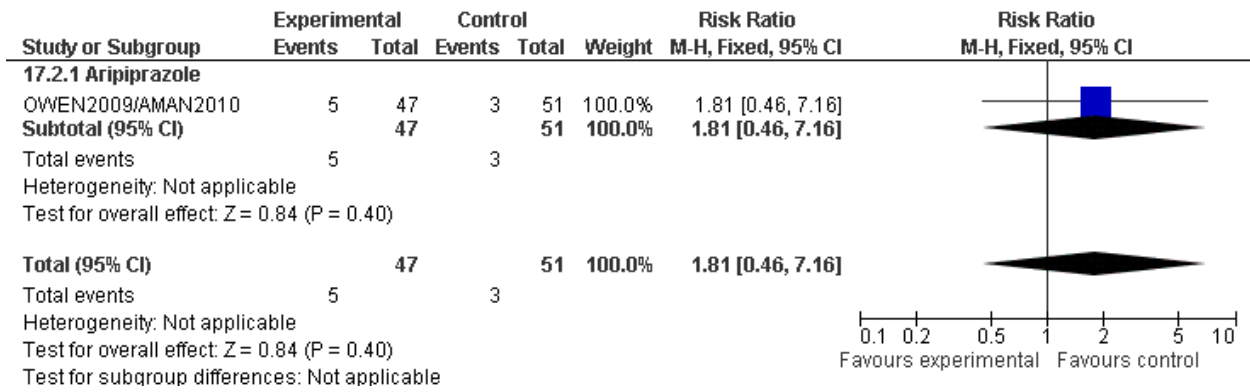
### 1.33.5 Adverse events associated with antipsychotics

#### *Adverse events associated with antipsychotics versus placebo*

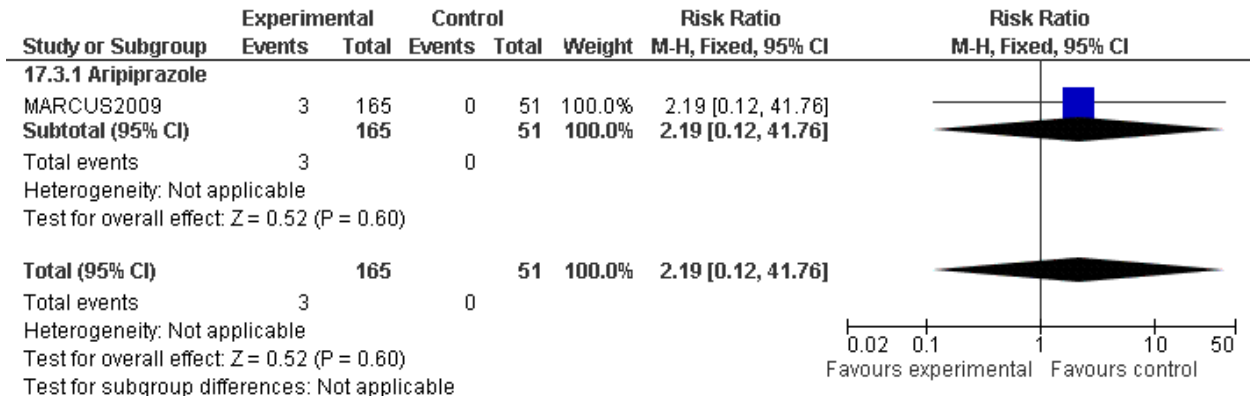
##### Any side effect



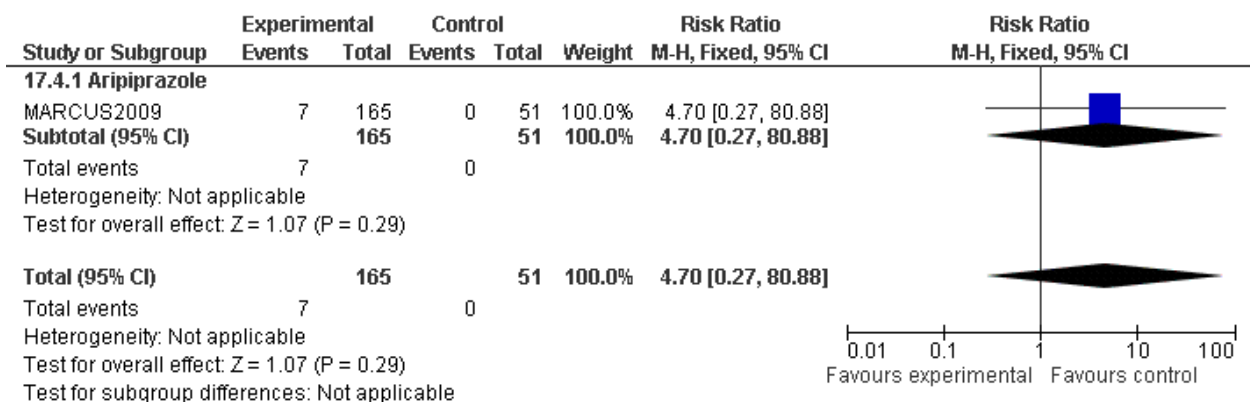
#### Discontinuation due to adverse events



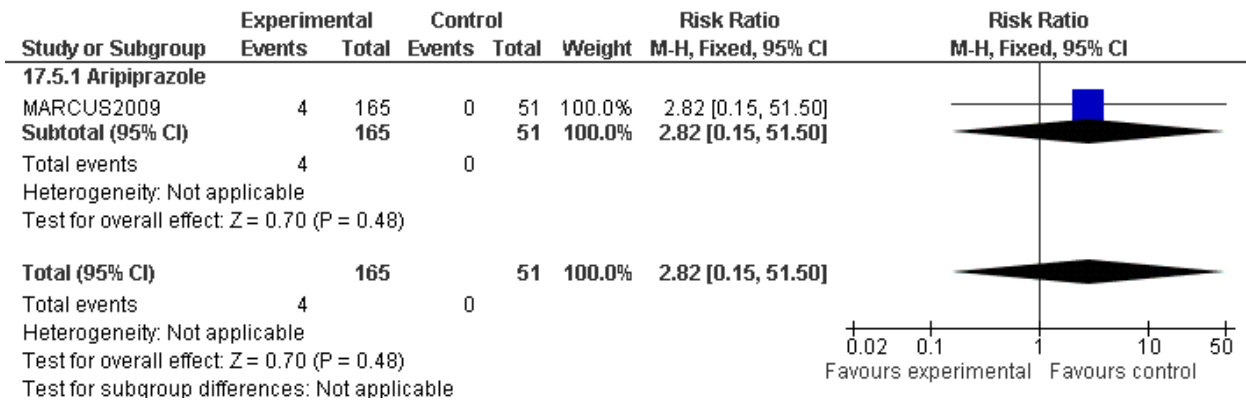
### Discontinuation due to drooling



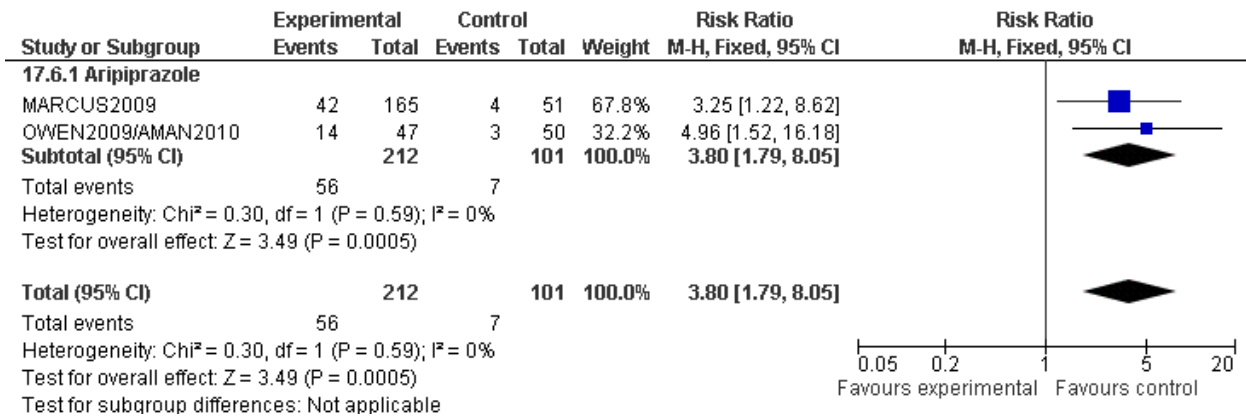
### Discontinuation due to sedation



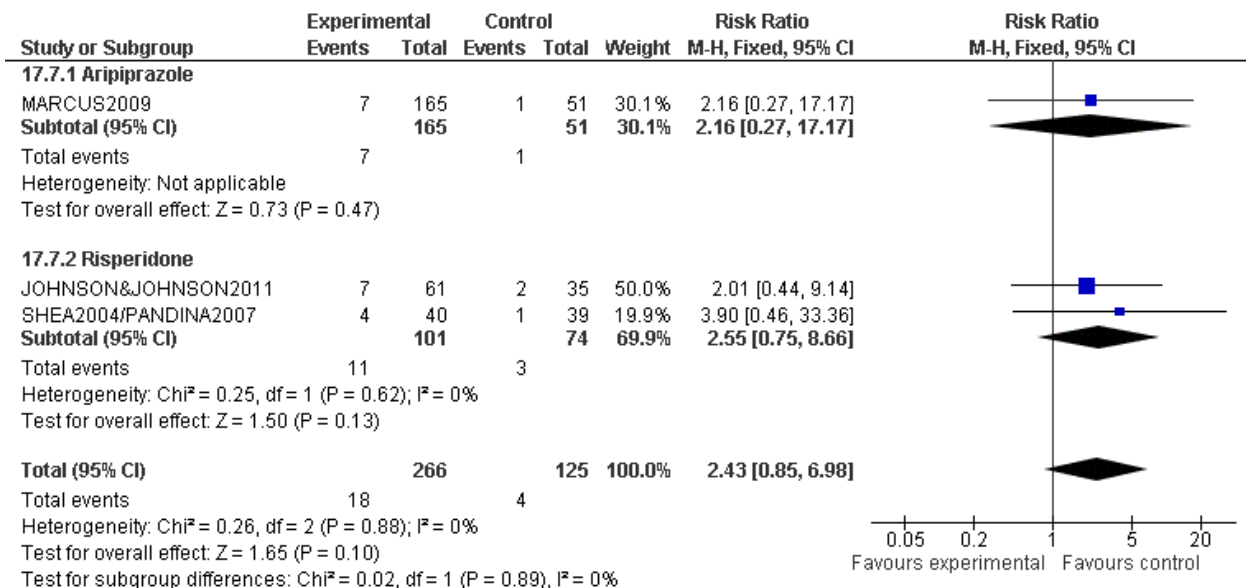
### Discontinuation due to tremor



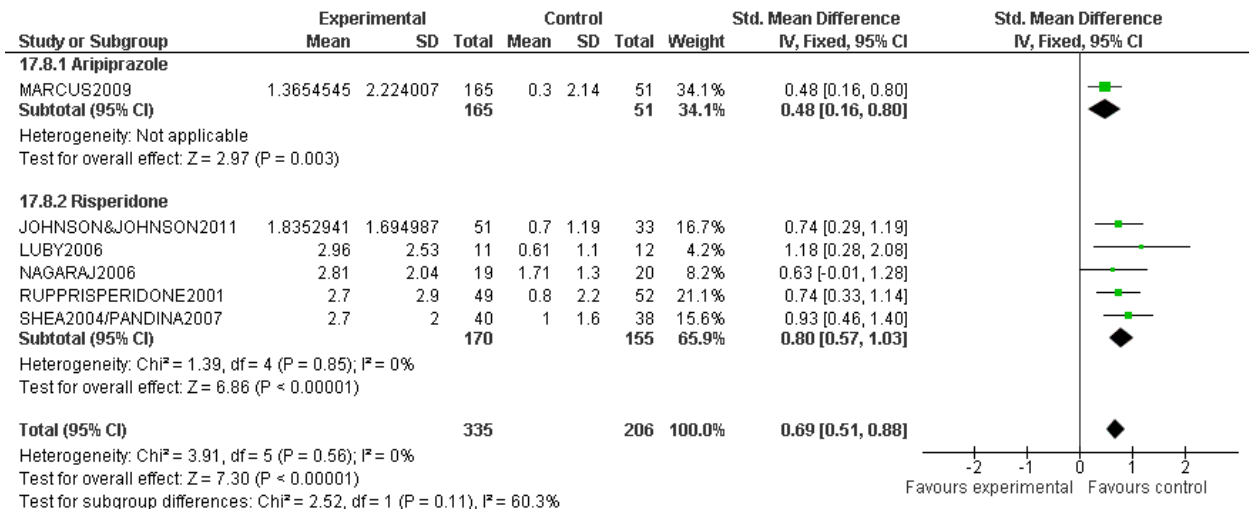
**Clinically relevant ( $\geq 7\%$ ) weight gain**



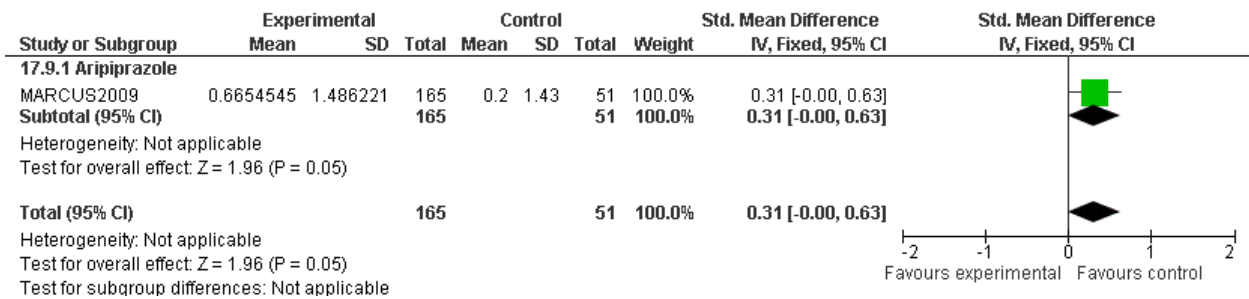
**Weight gain**



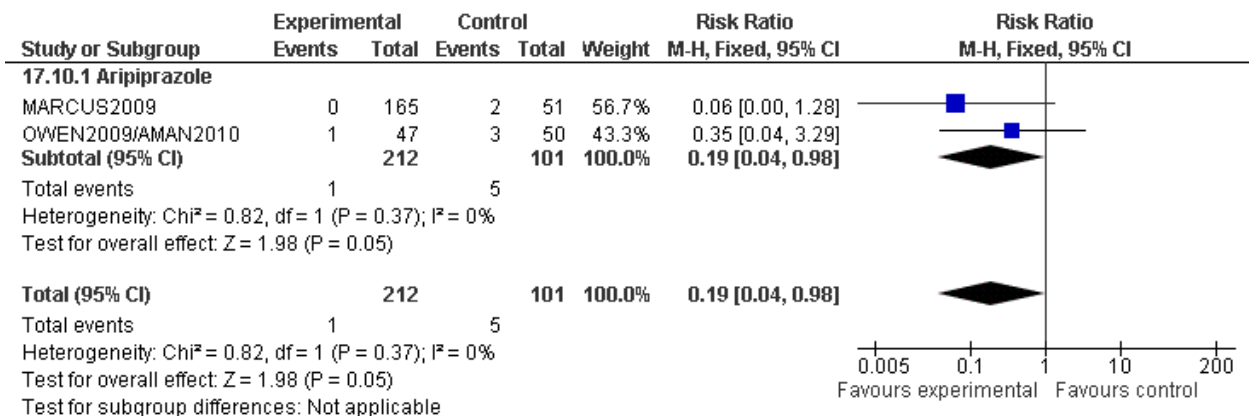
### Weight gain (in kg)



### BMI change (kg/m-squared)

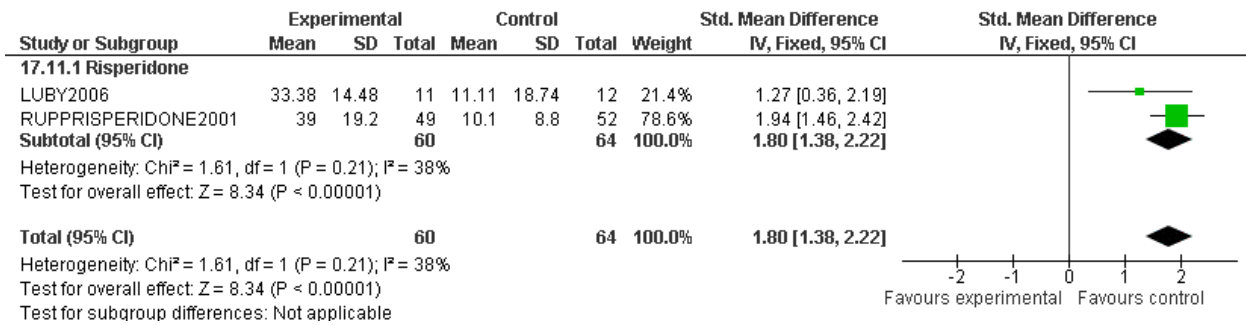


### Clinically relevant prolactin elevation (above upper limit of normal for age & gender)

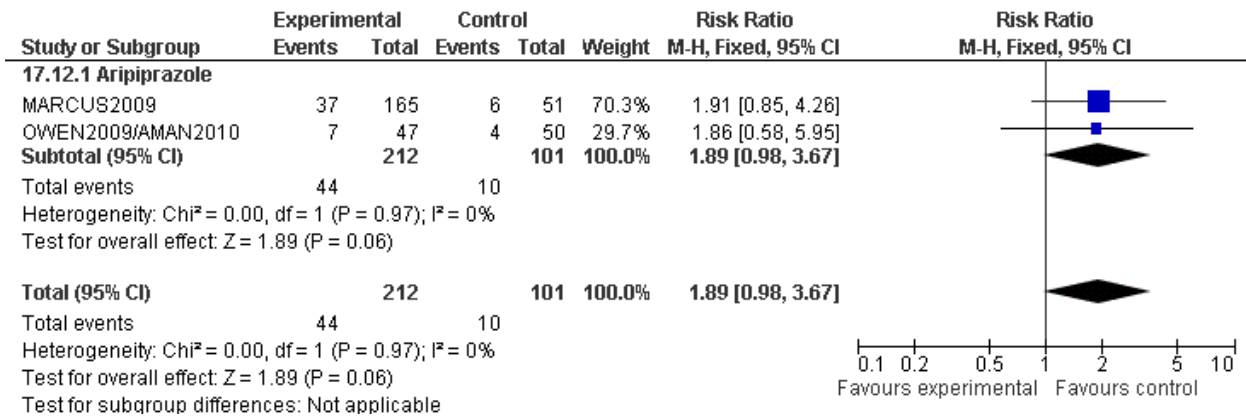




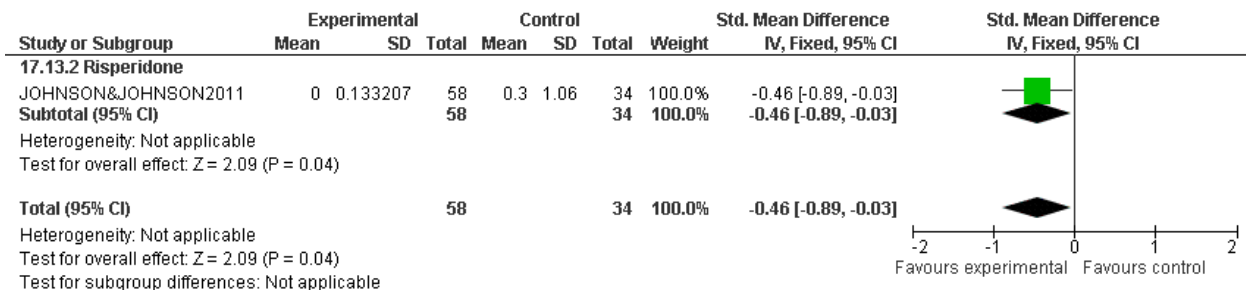
### Prolactin concentration (ng/ml)



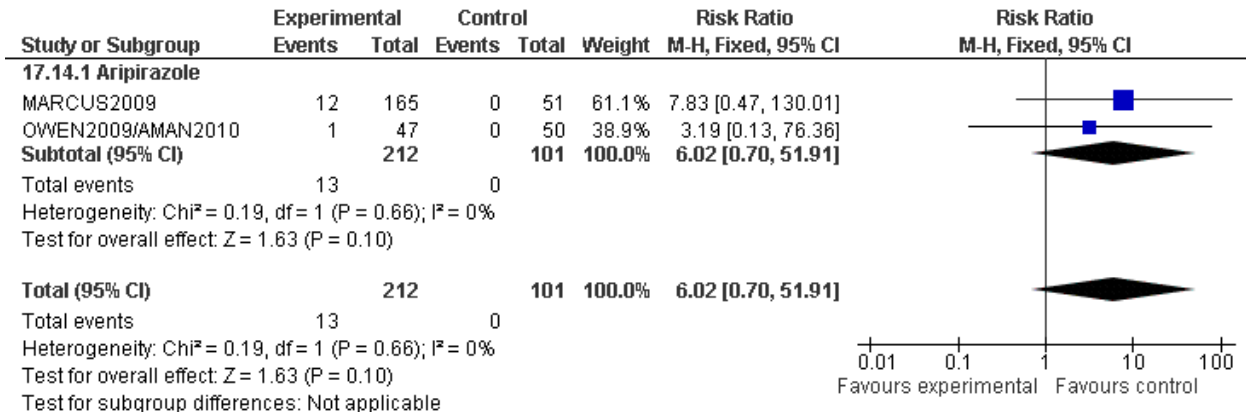
### Any treatment-emergent extrapyramidal symptom



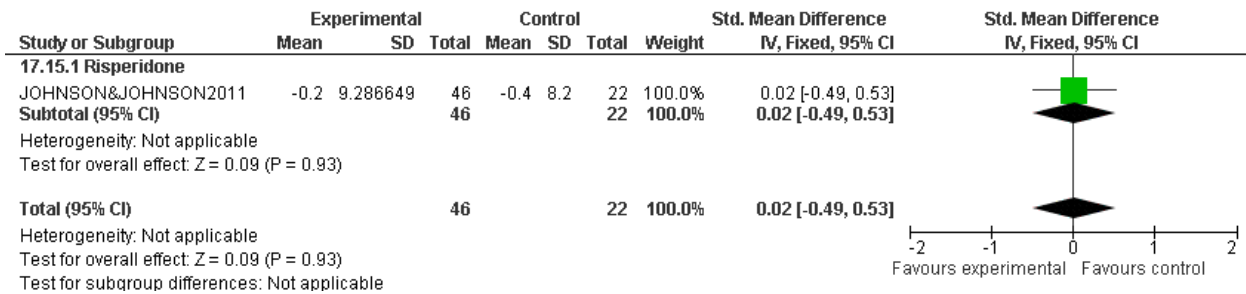
### Extrapyramidal symptoms



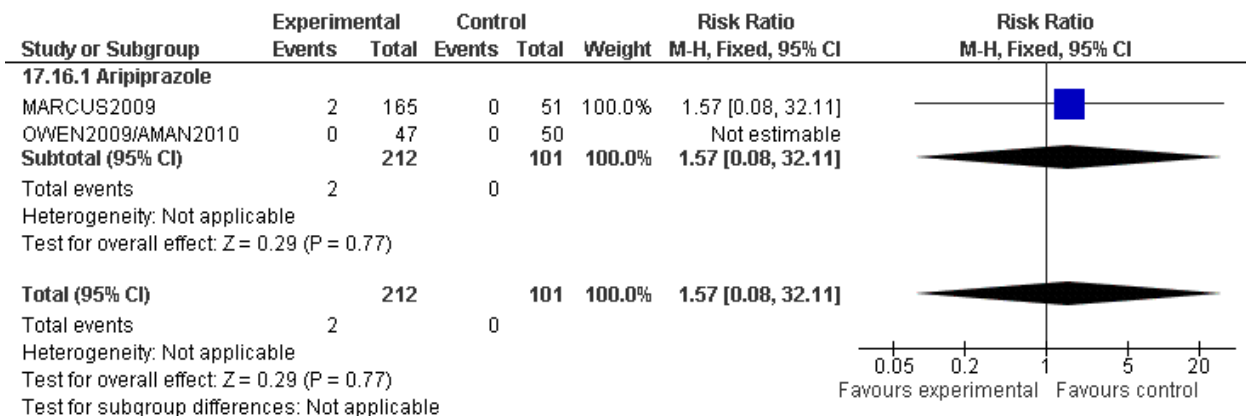
### Extrapyramidal disorder



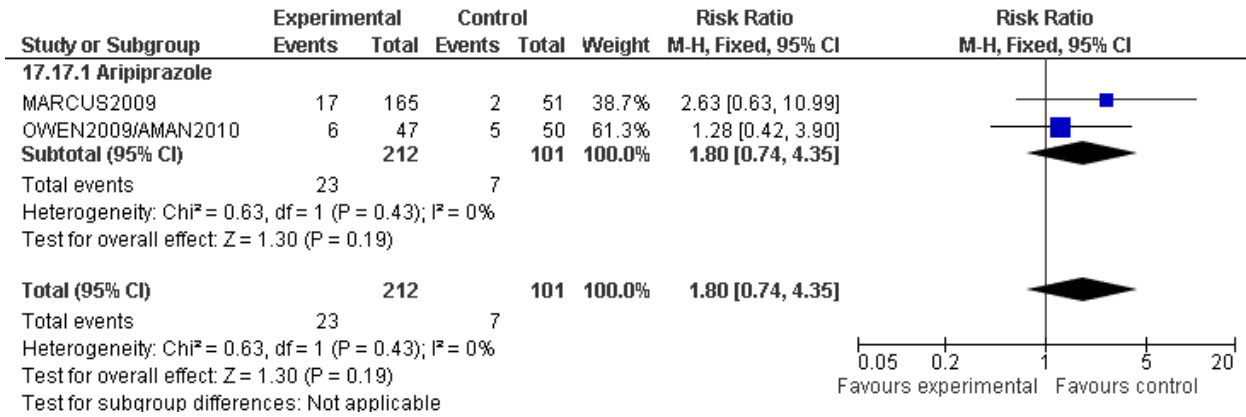
### Fasting glucose (mg/dL) change score



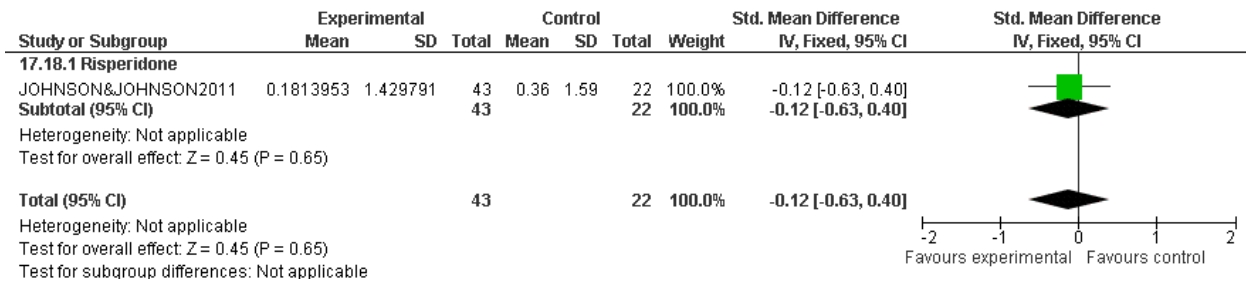
### Fasting glucose (=>115 mg/dL)



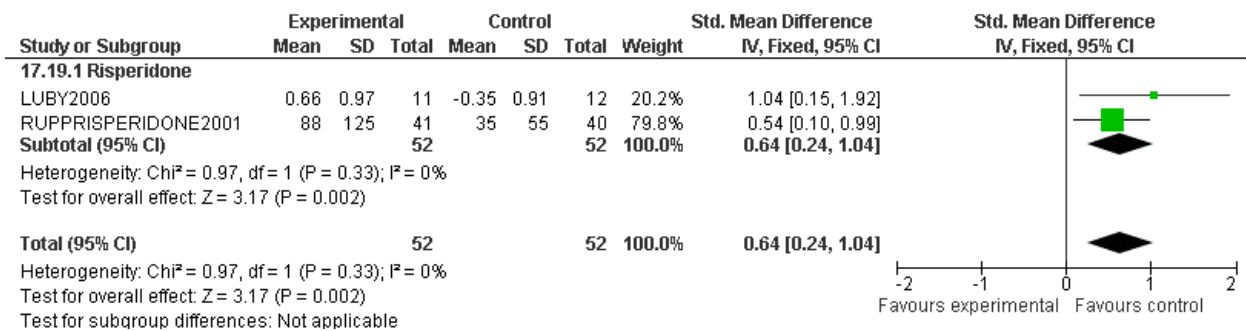
### Fasting triglycerides (=>120 mg/dL for females or 160 mg/dL for males)



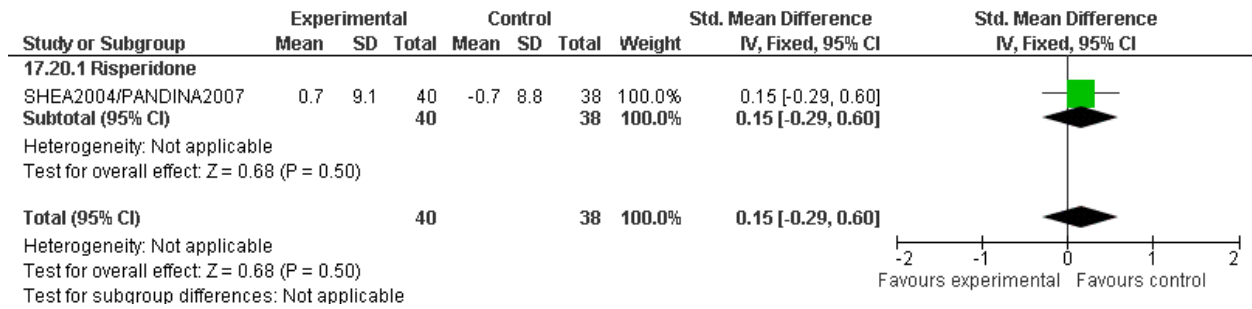
### Insulin resistance (HOMA-IR) change score



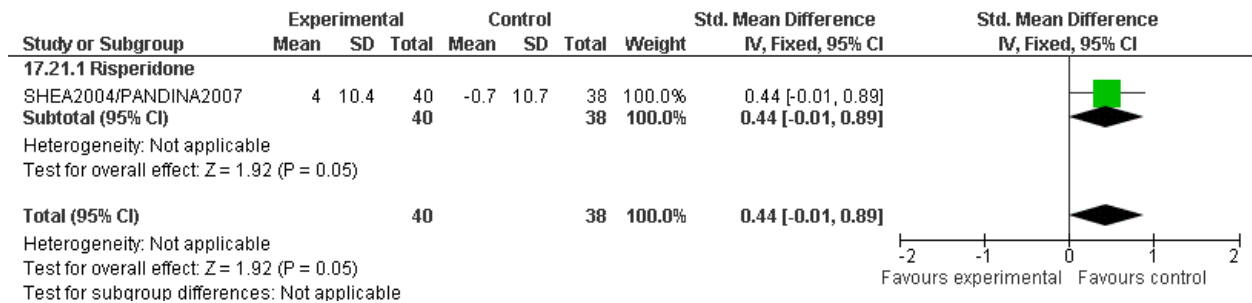
### Leptin (mg/L) change score



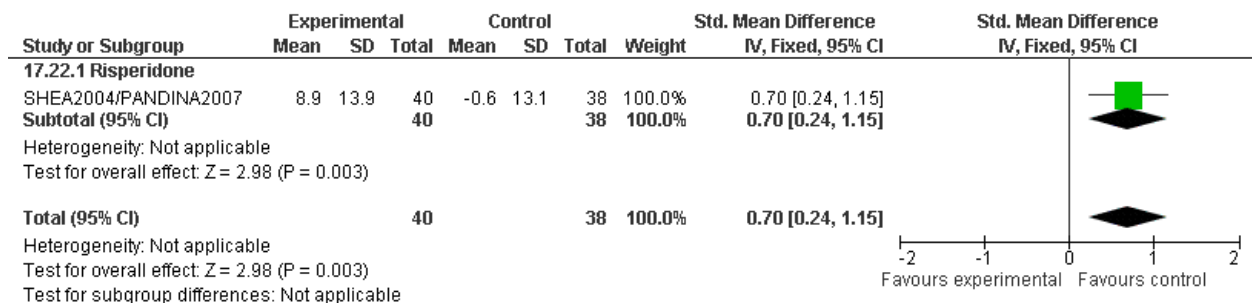
### Diastolic blood pressure (mm Hg) change scores



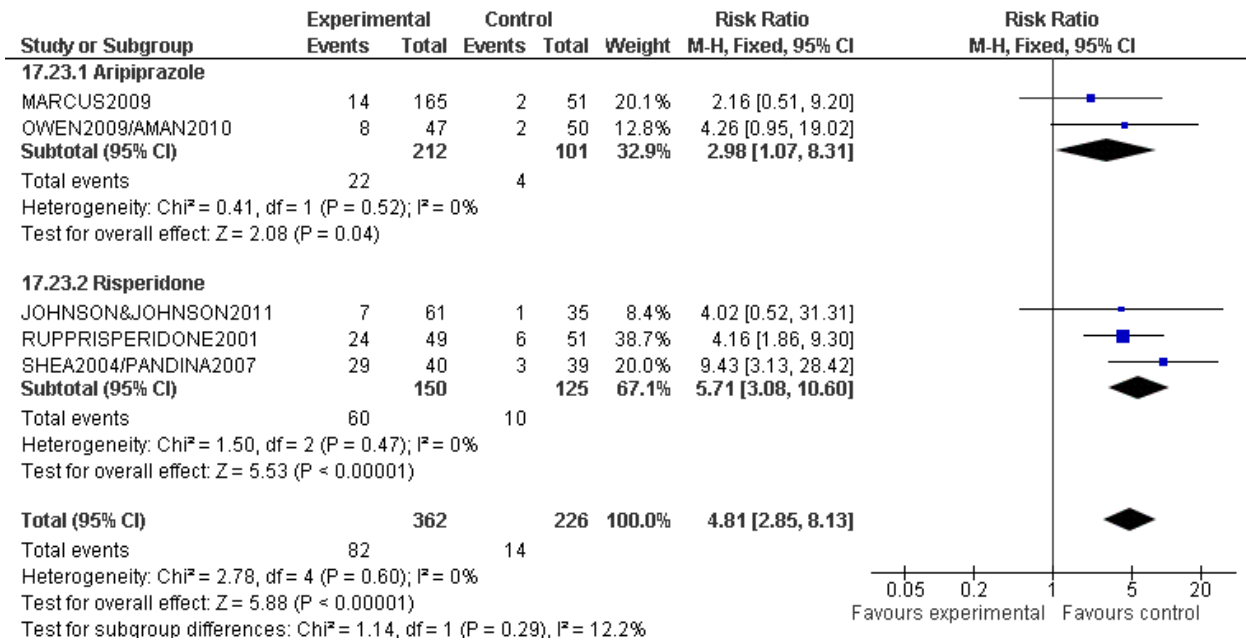
### Systolic blood pressure (mm Hg) change scores



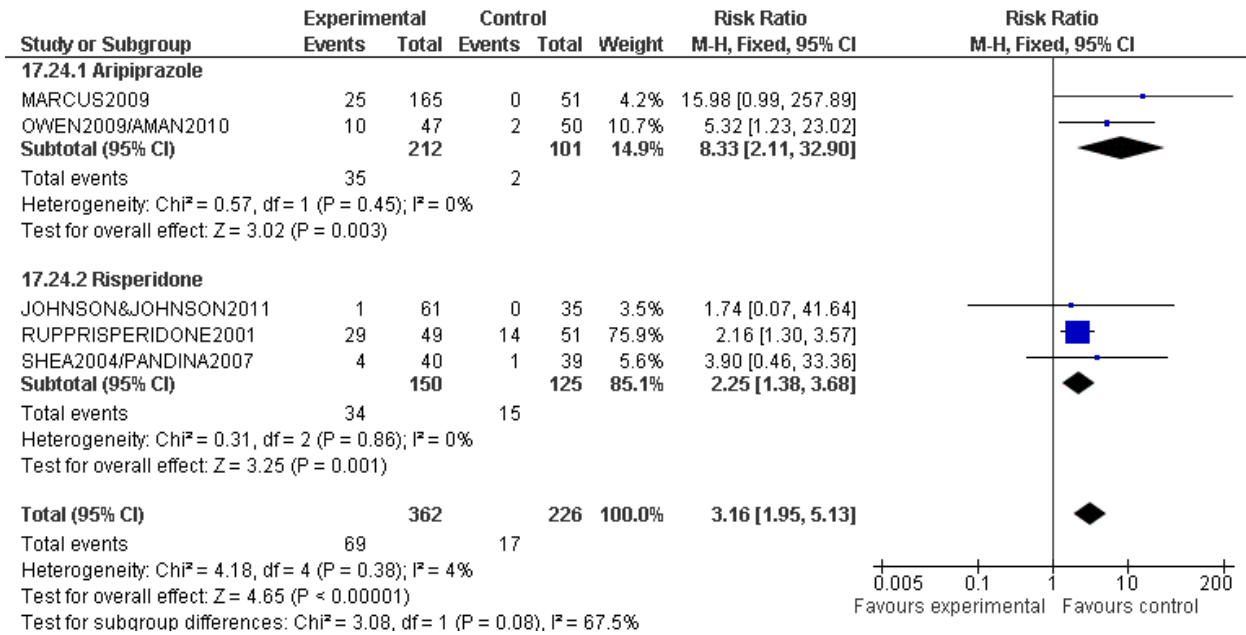
### Pulse (bpm) change score



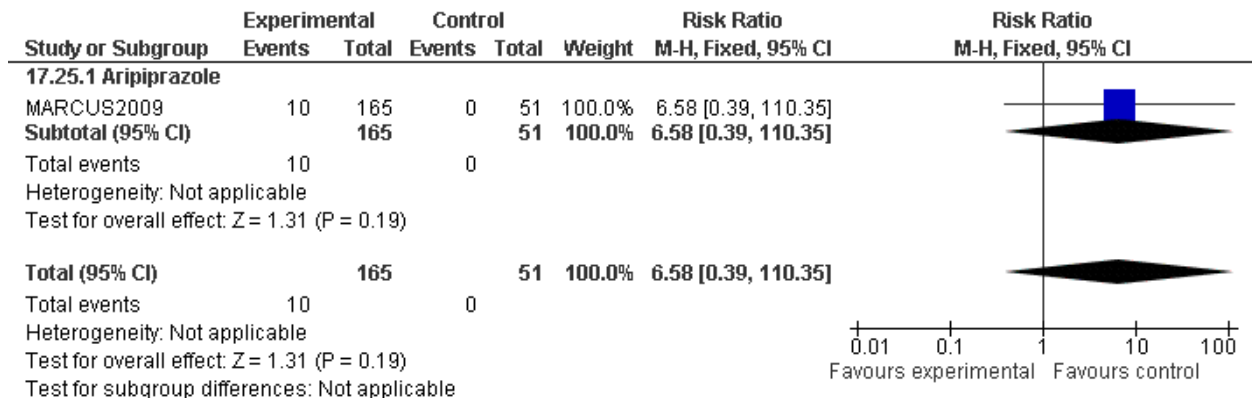
### Somnolence/Drowsiness



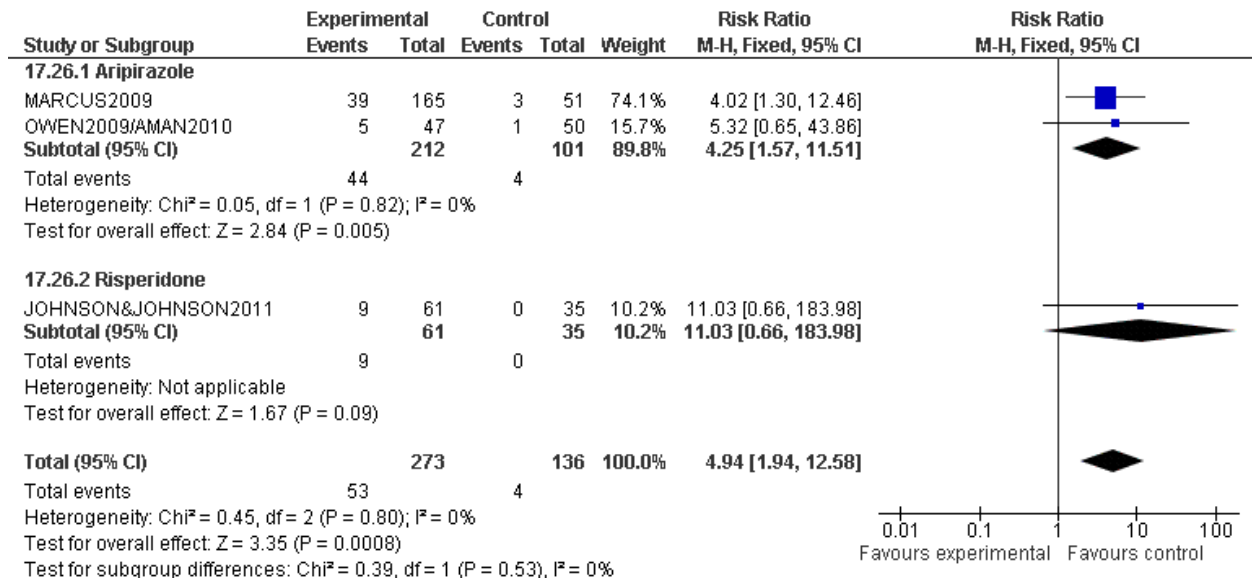
## Fatigue



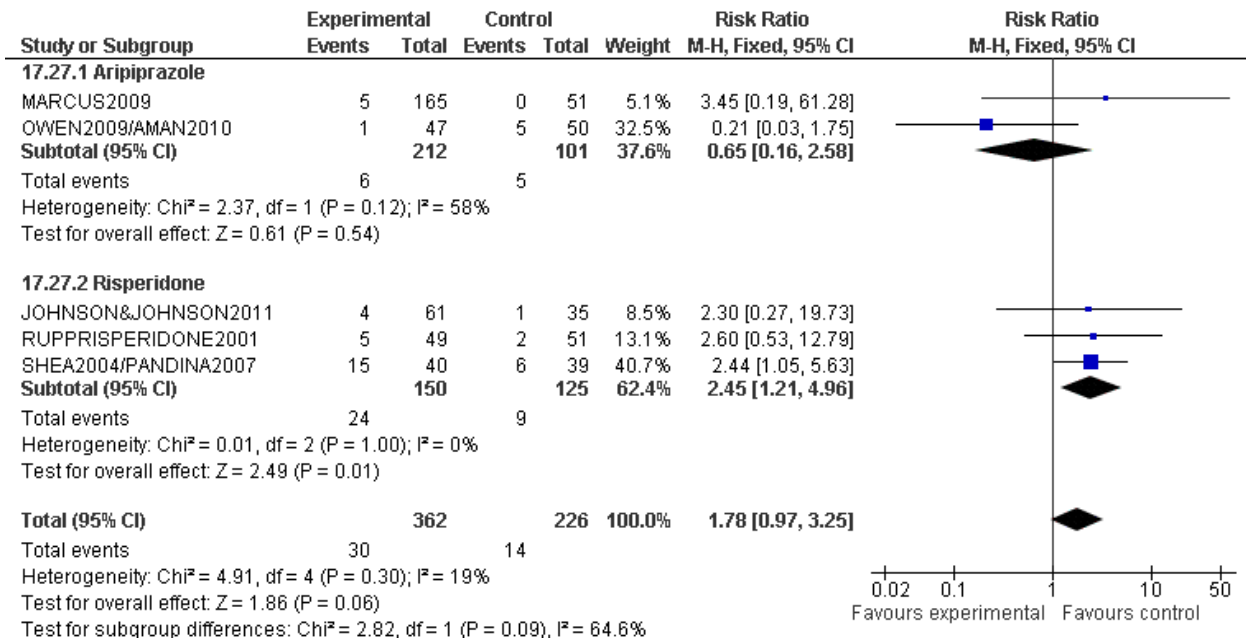
## Lethargy



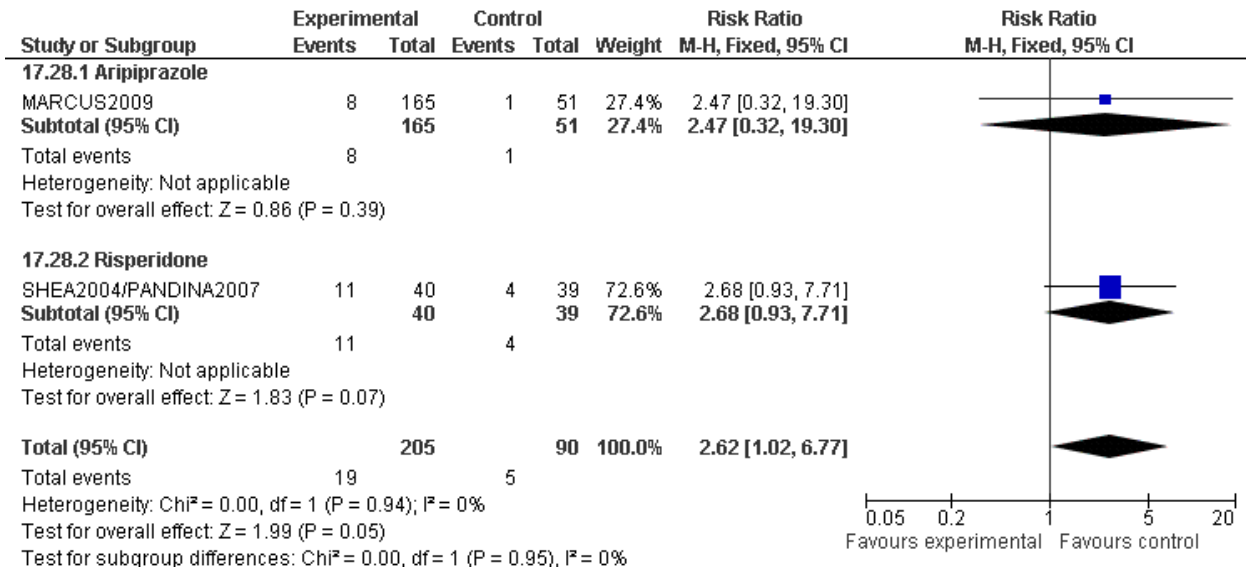
## Sedation



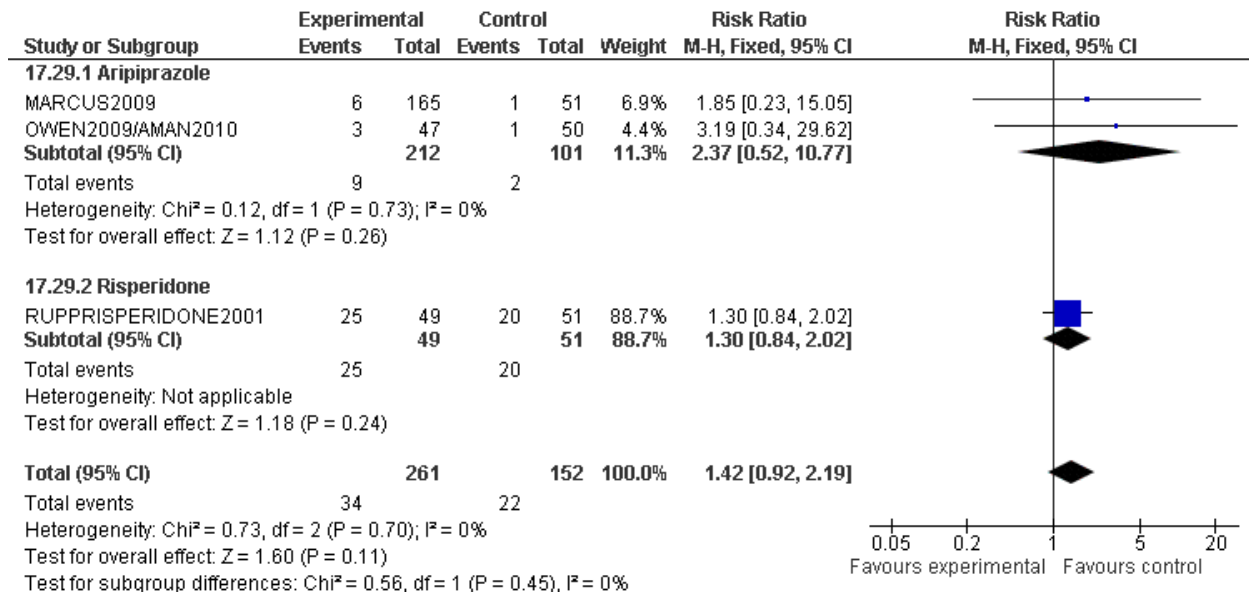
## Upper respiratory tract infection



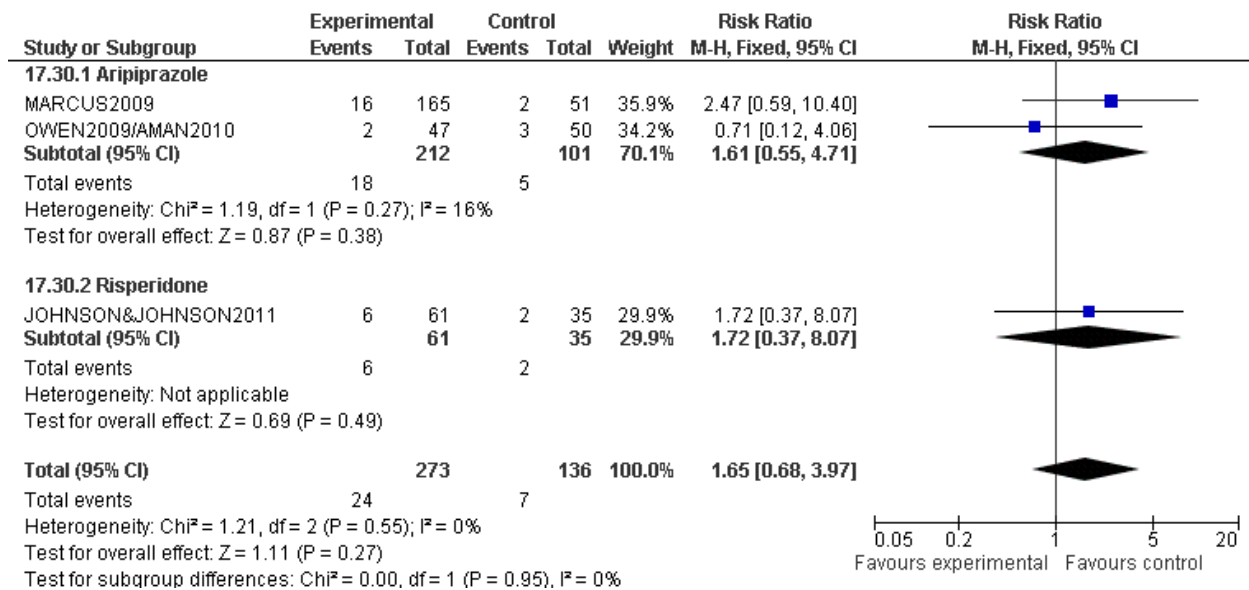
### Rhinitis/rhinorrhea



### Nasal congestion

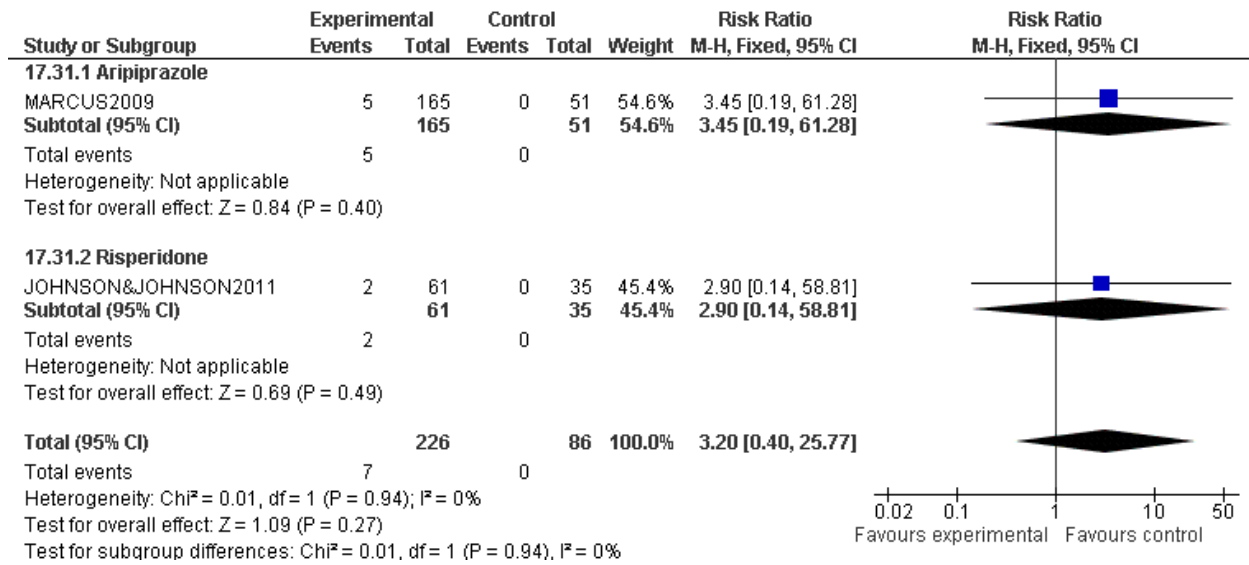


## Nasopharyngitis

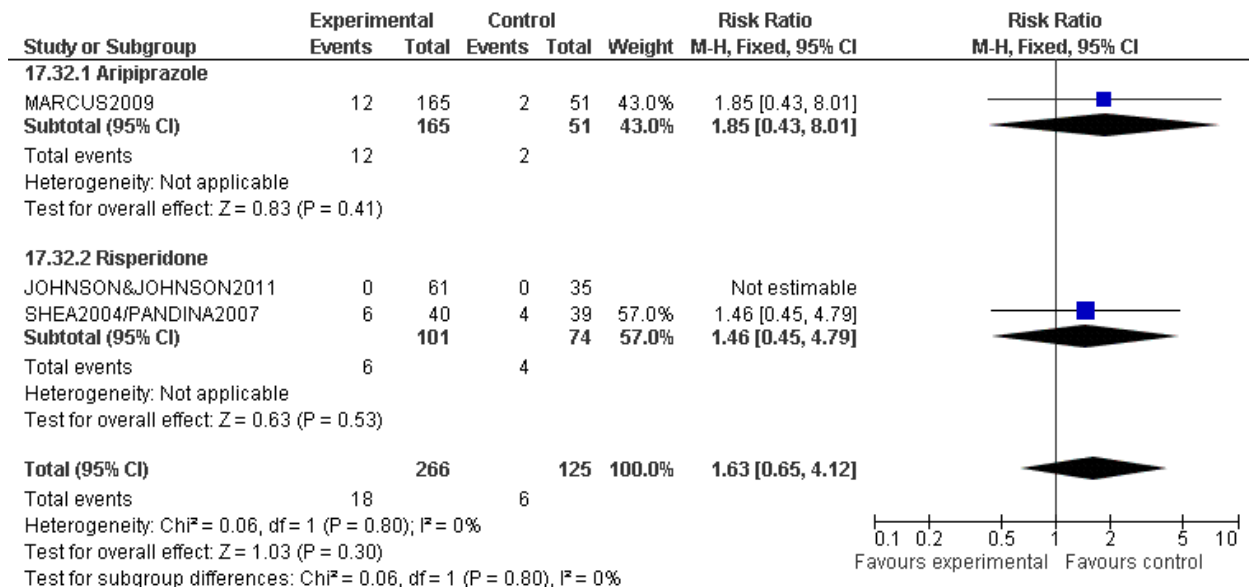


## Nose bleed

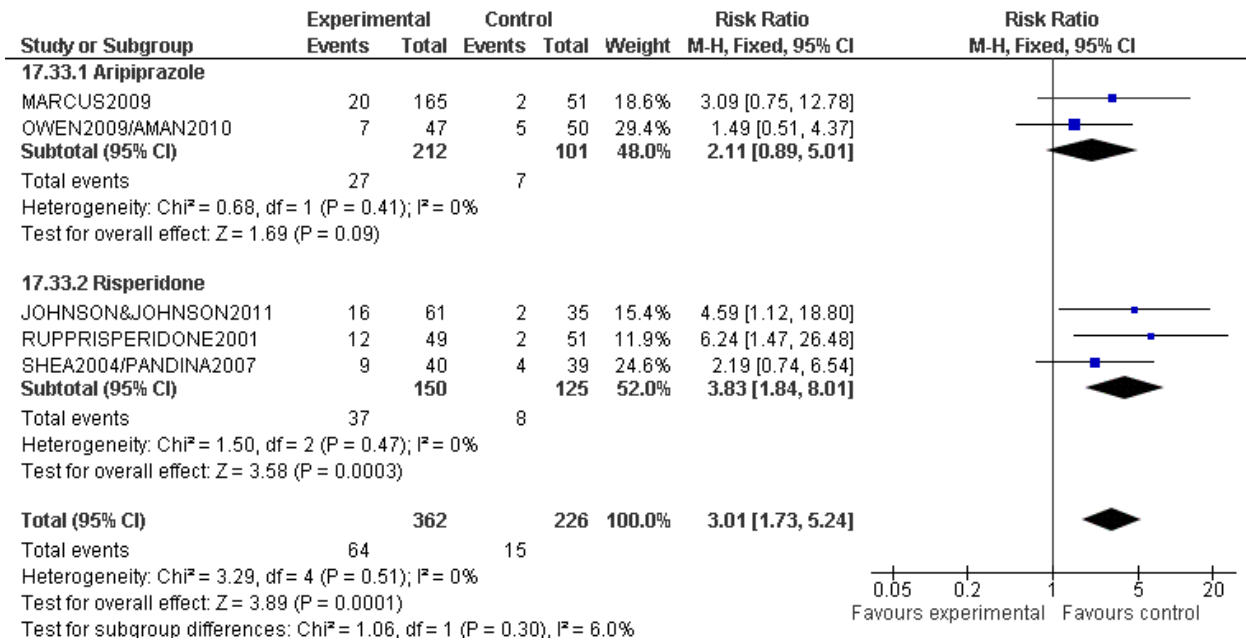




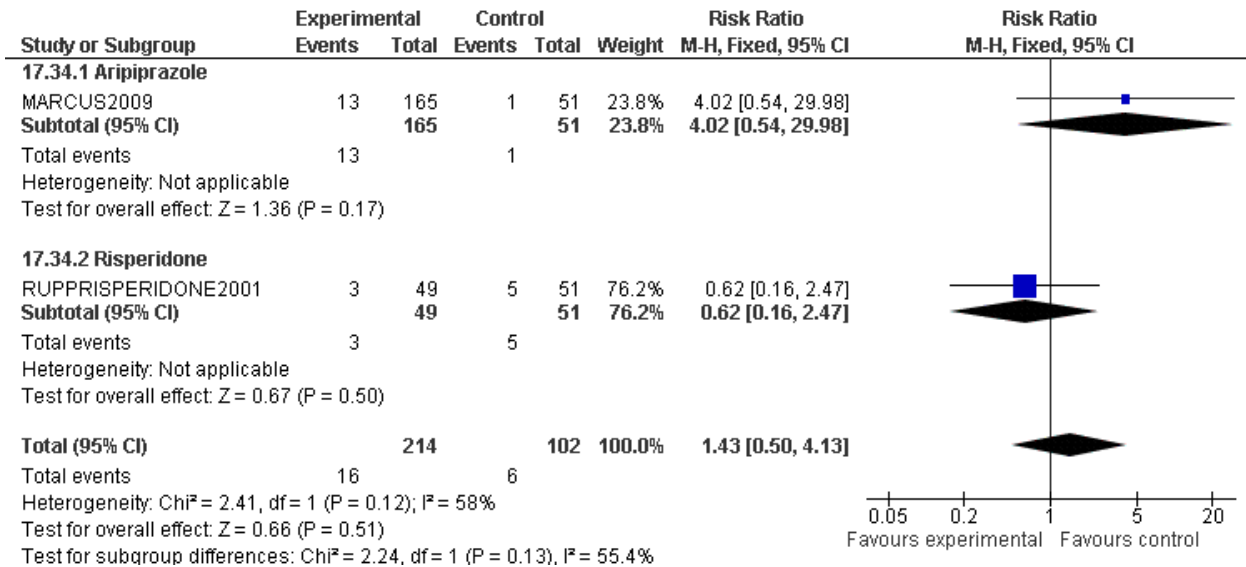
## Coughing



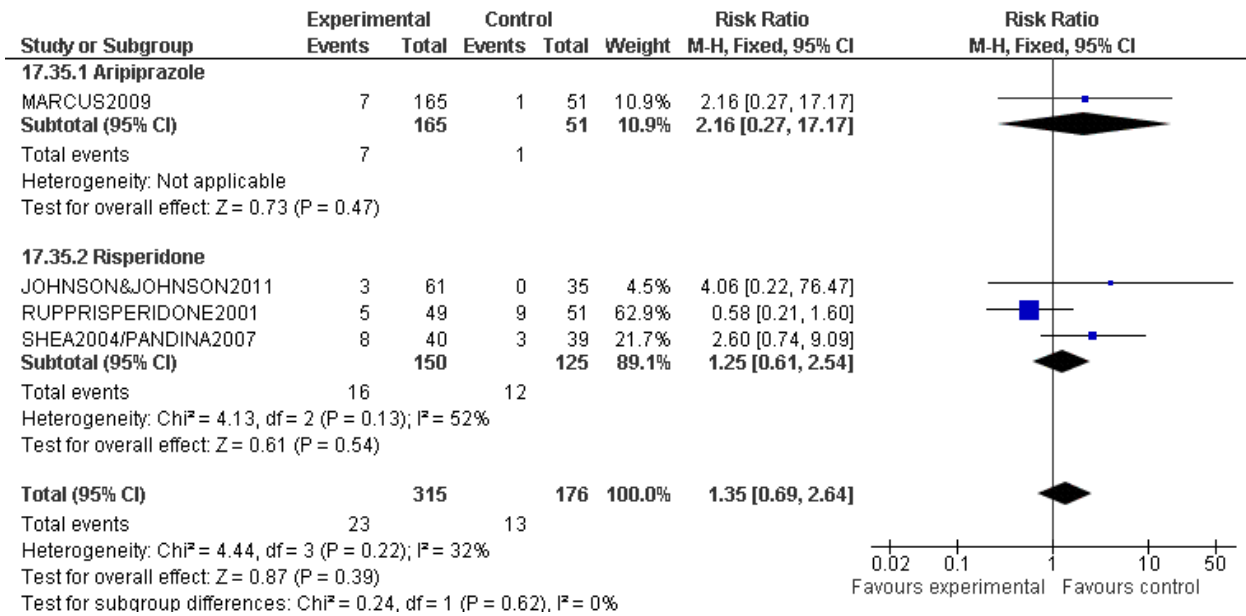
## Increased appetite



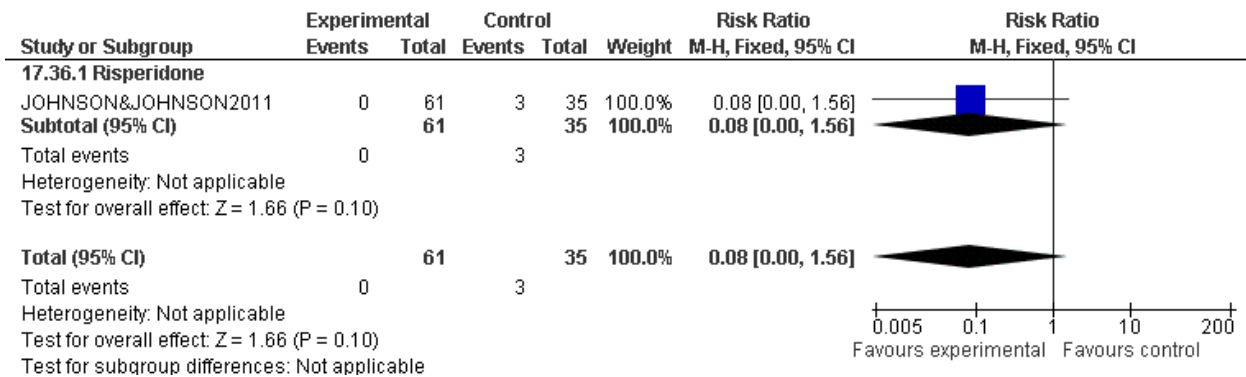
### Decreased appetite



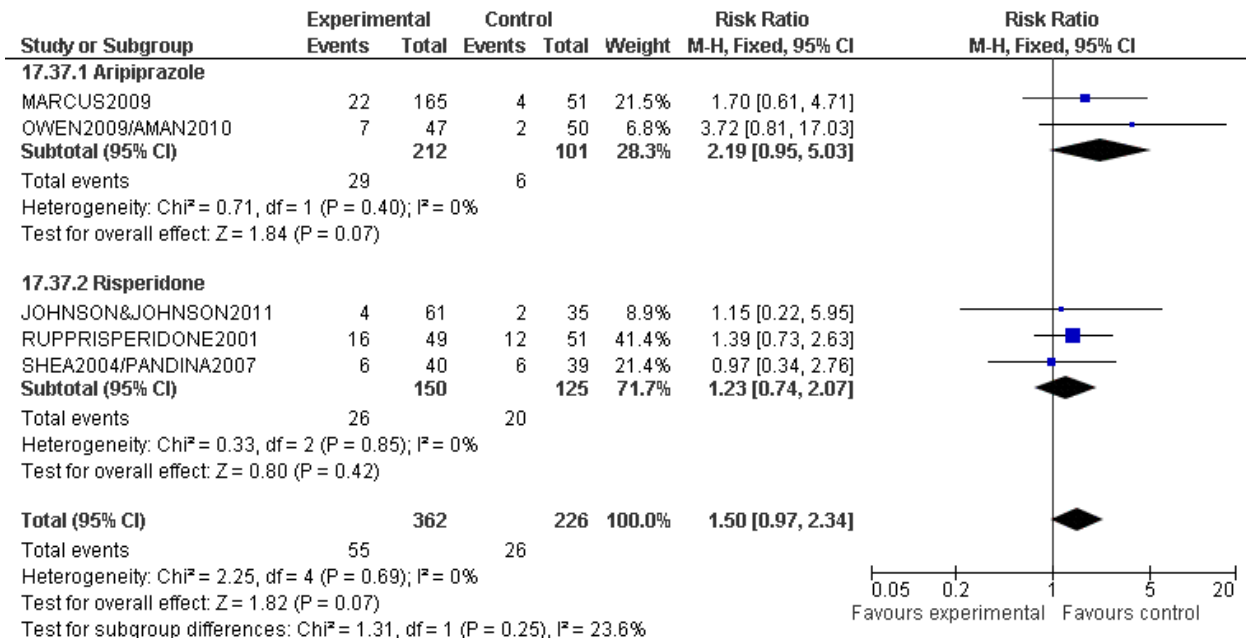
### Abdominal pain/Stomachache



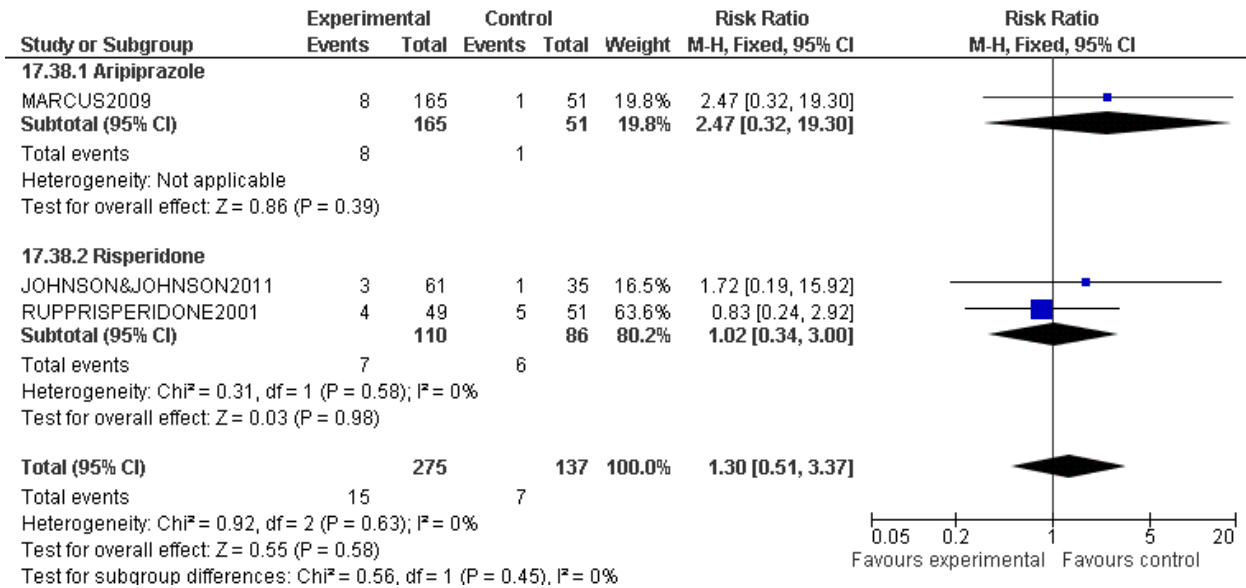
### Abdominal discomfort



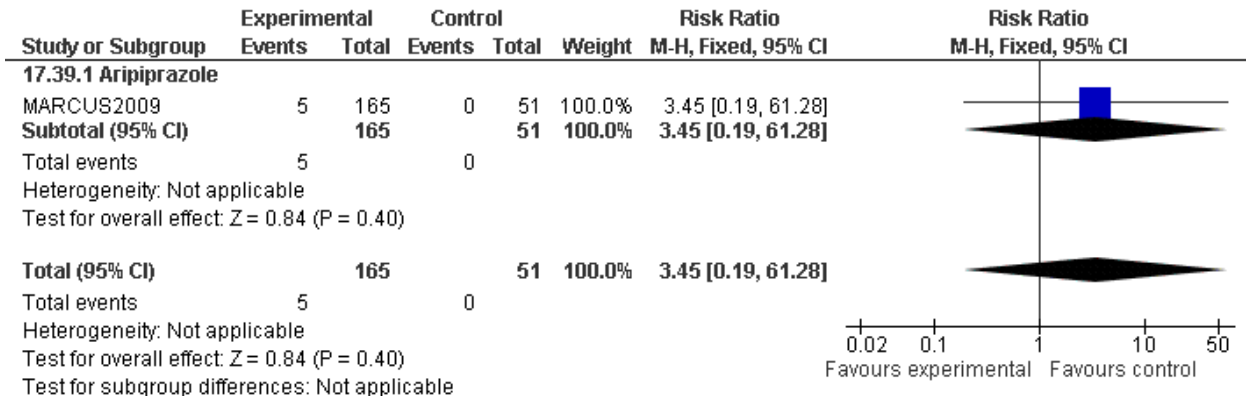
### Vomiting



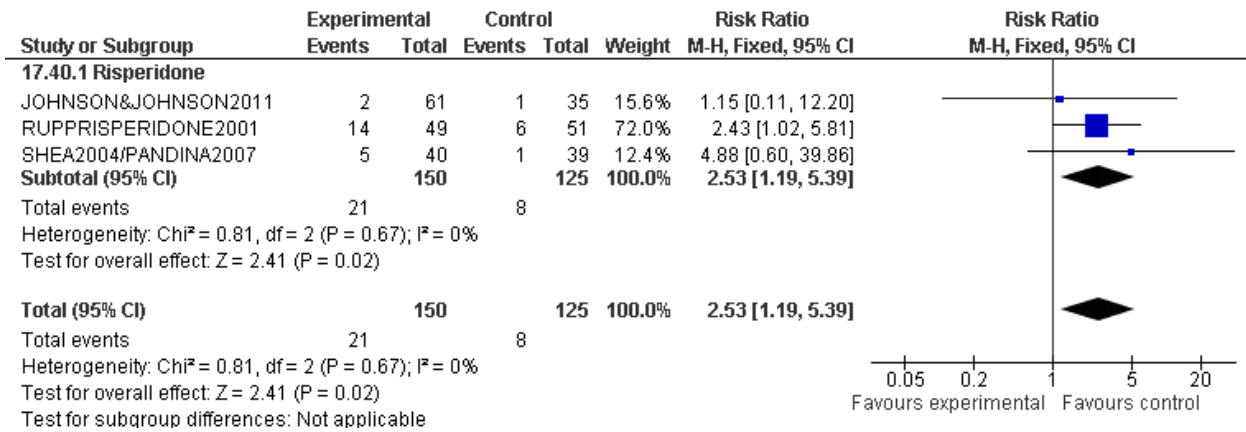
## Nausea



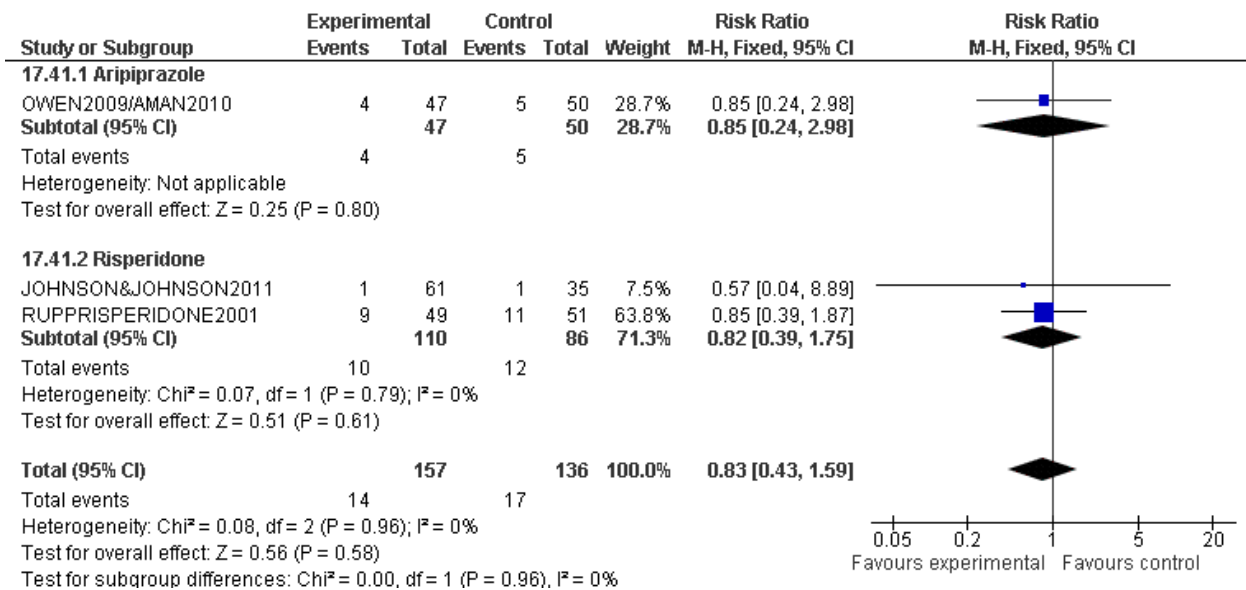
## Gastroenteritis viral



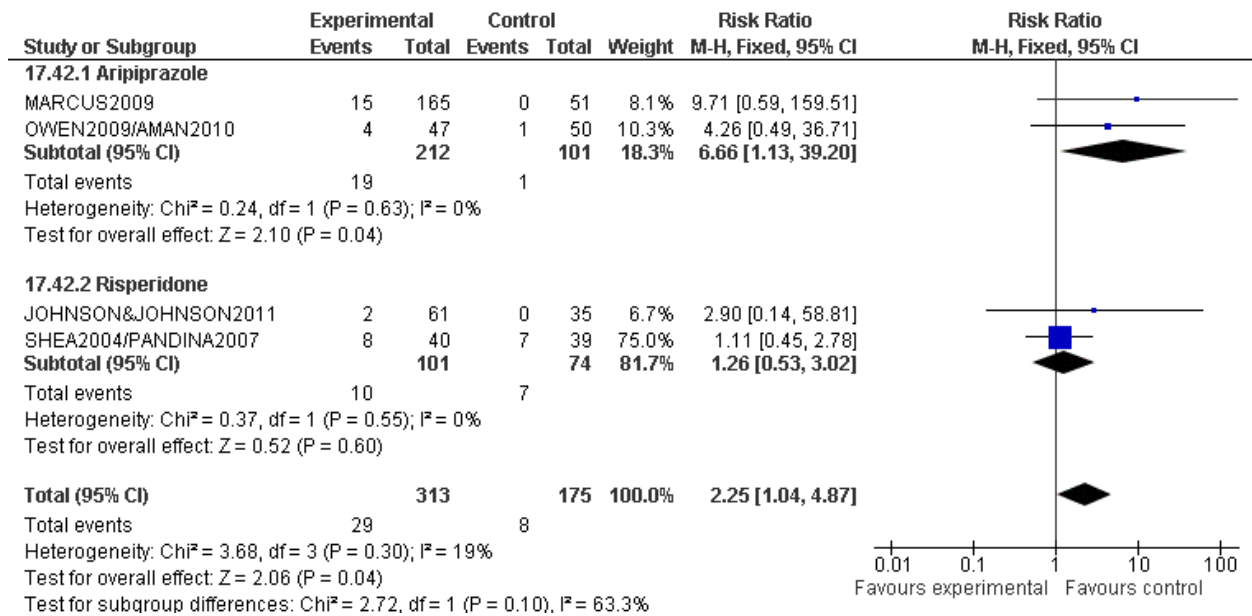
### Constipation



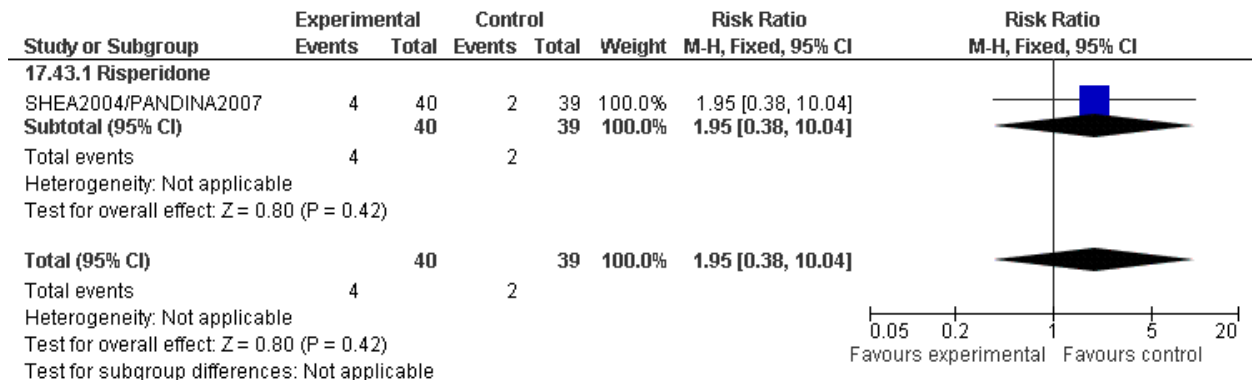
### Diarrhoea



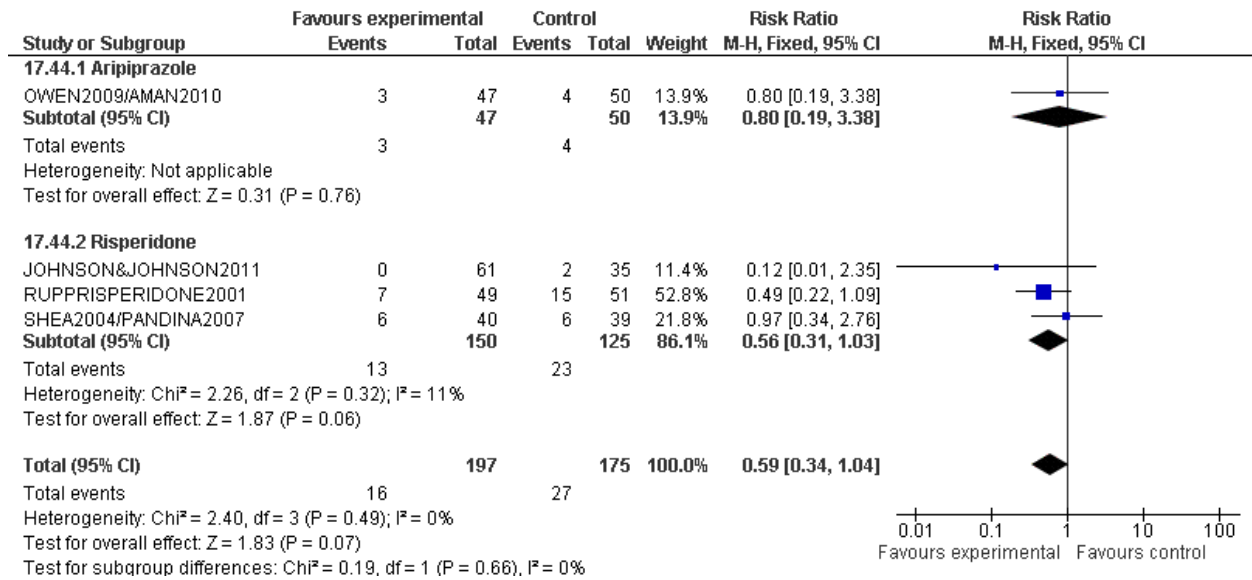
**Fever**



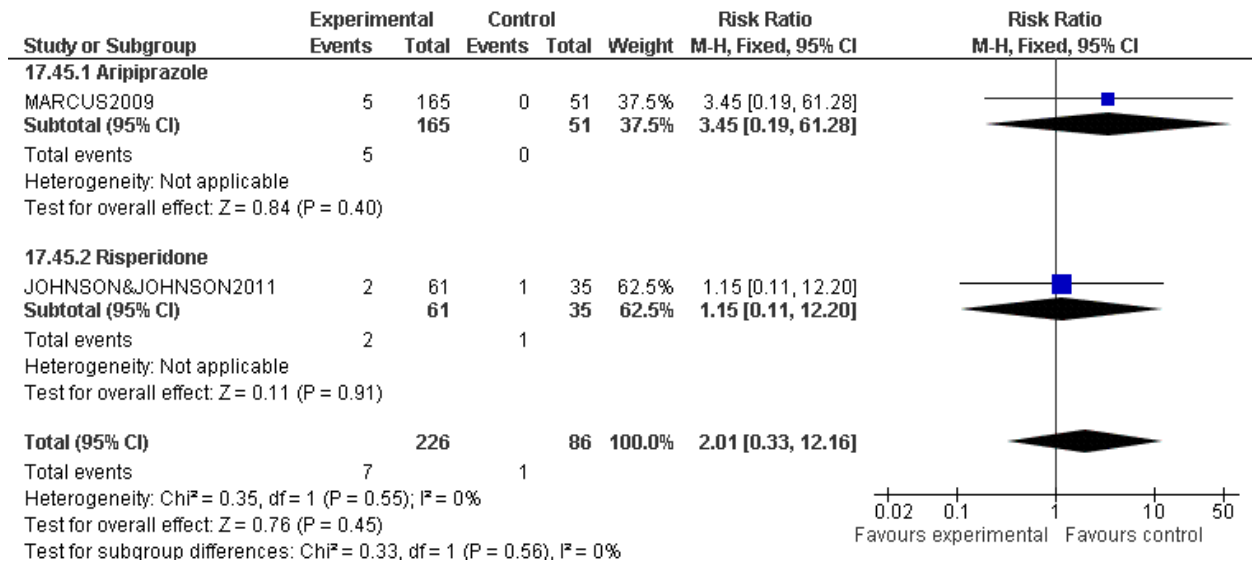
**Influenza-like symptoms**



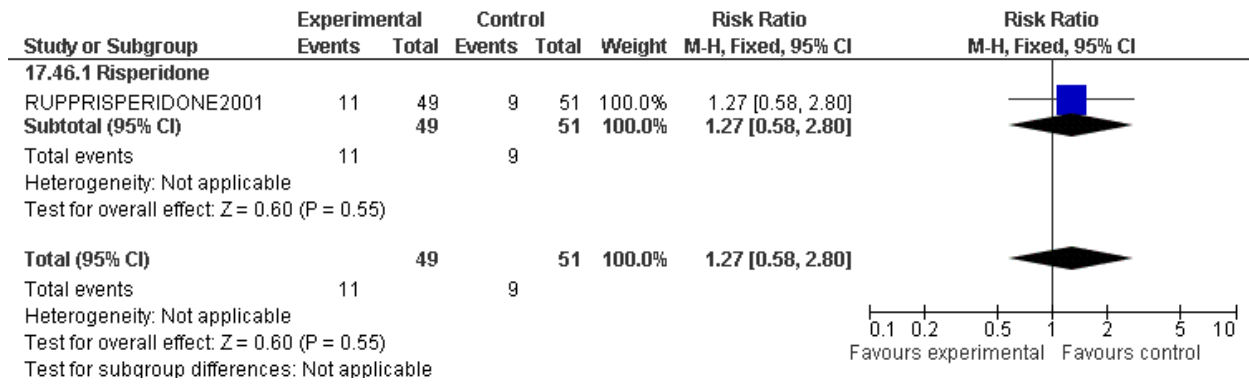
**Insomnia**



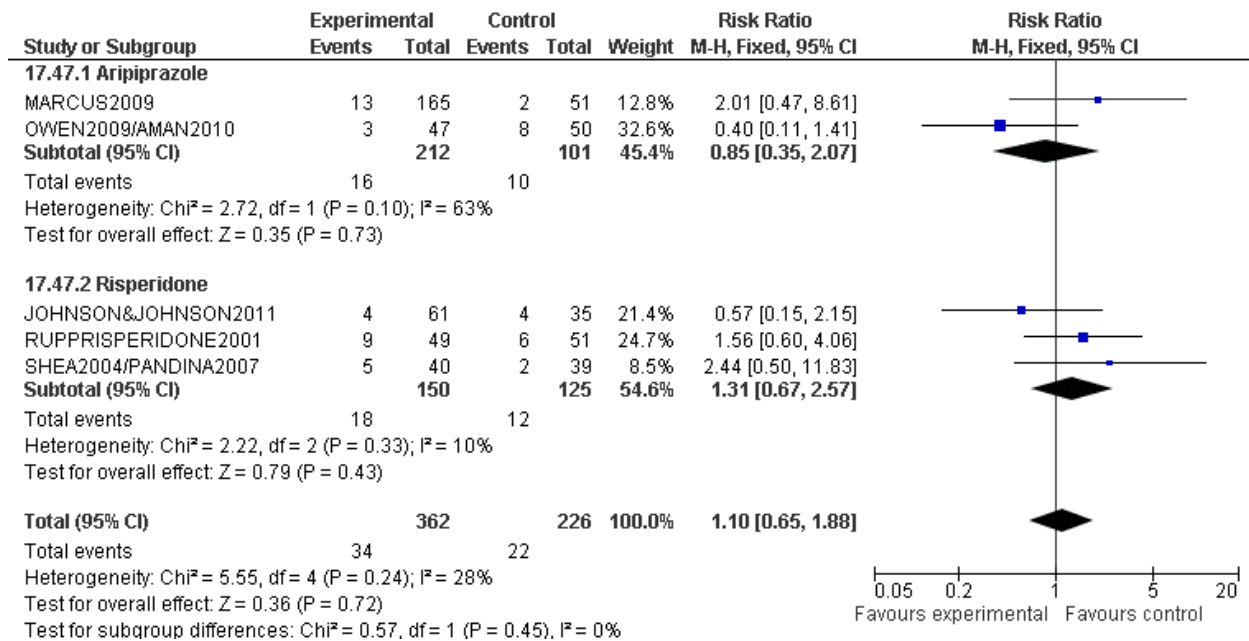
## Hypersomnia



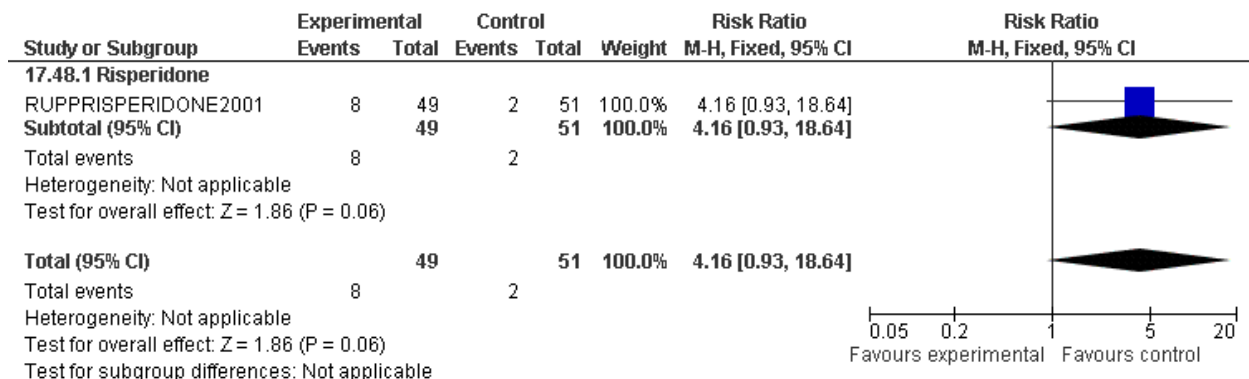
## Sleep problems



## Headache

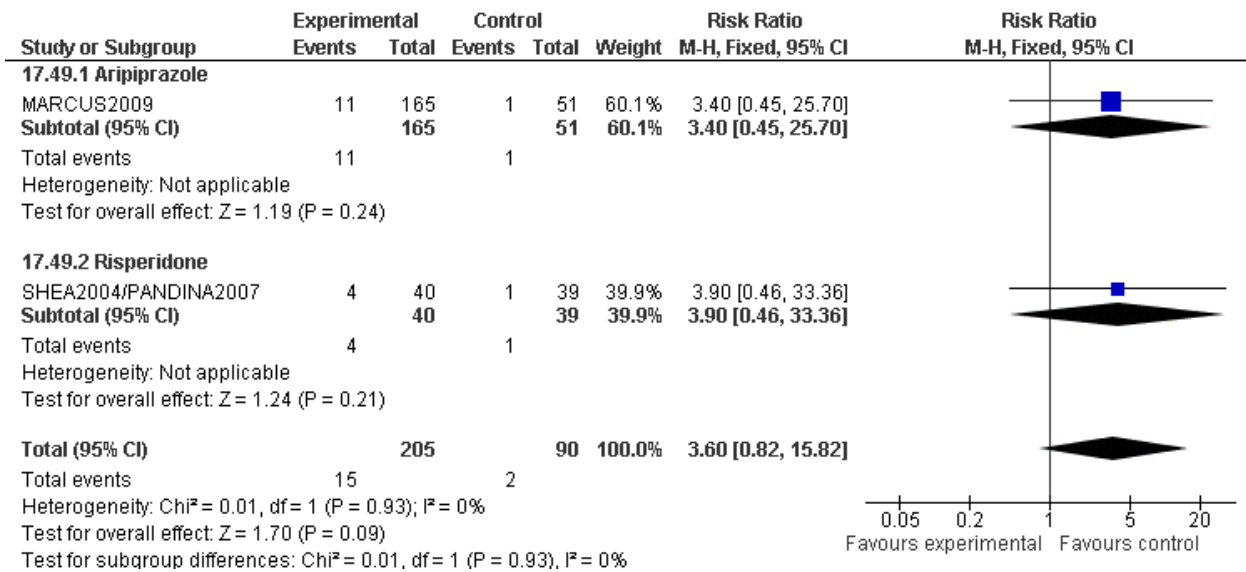


## Dizziness

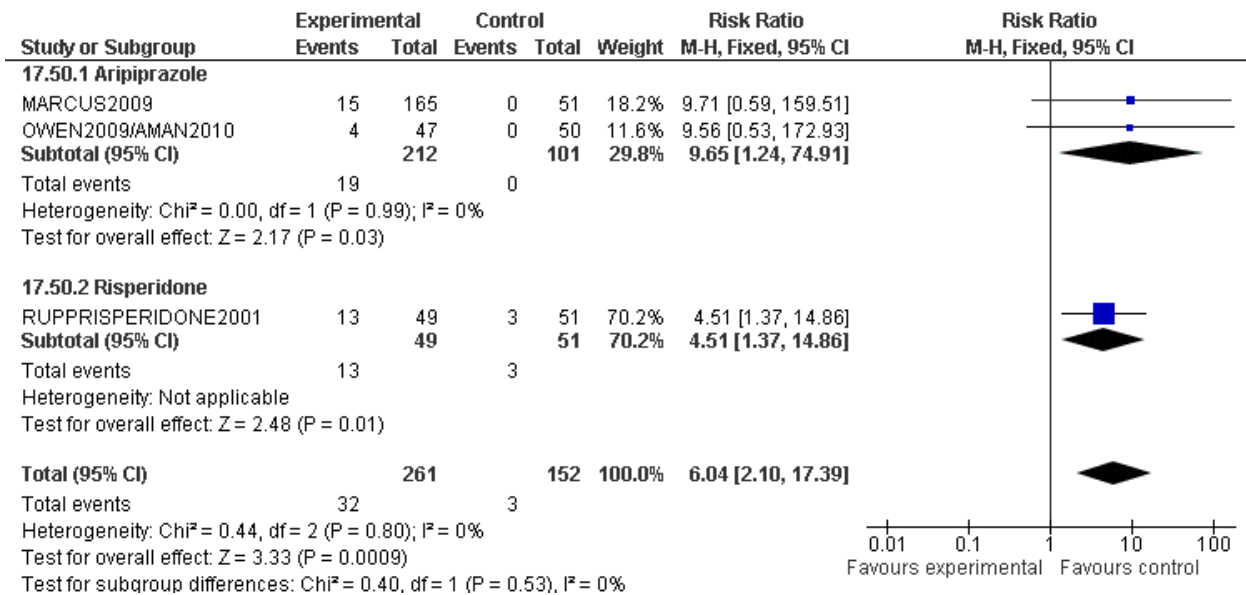




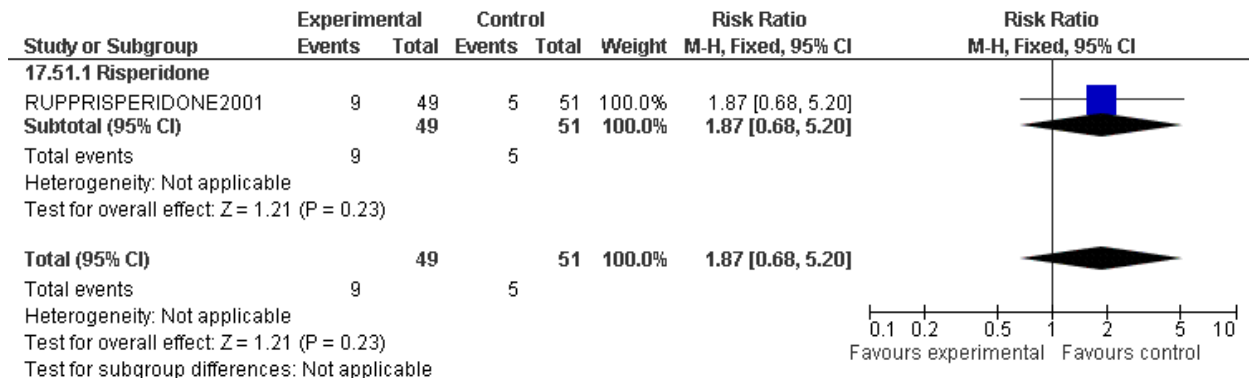
### Increased salivation



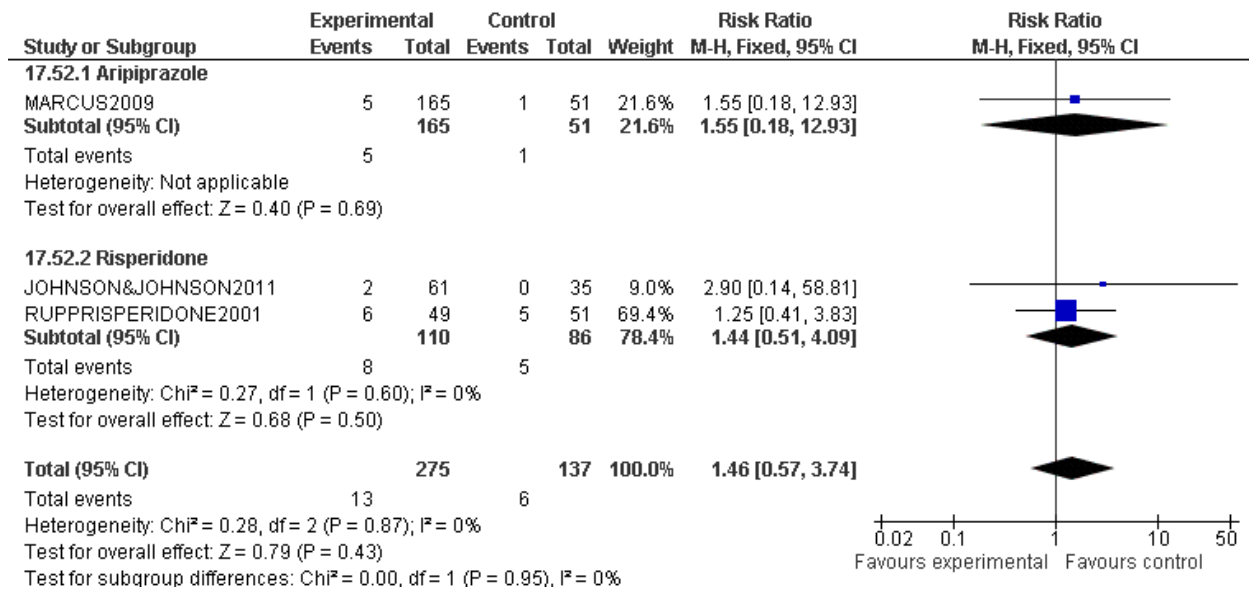
### Drooling



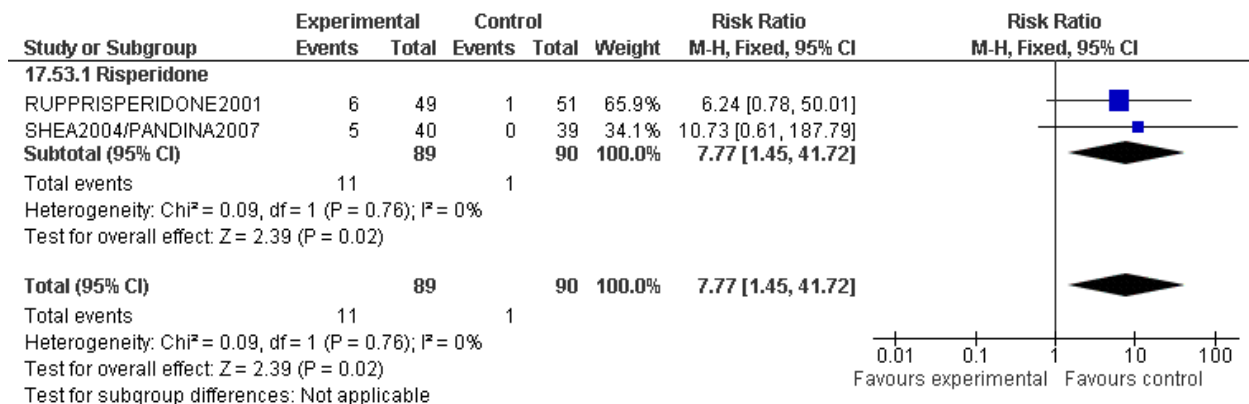
### Dry mouth



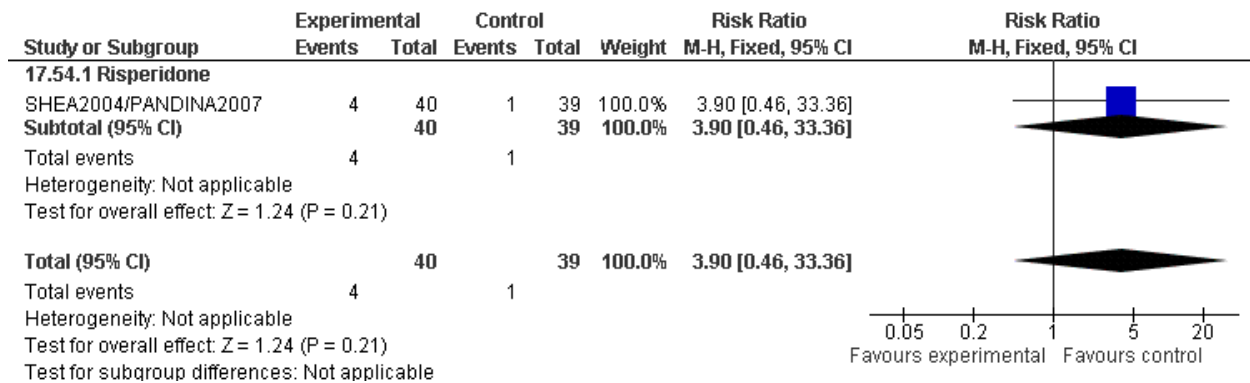
### Increased thirst



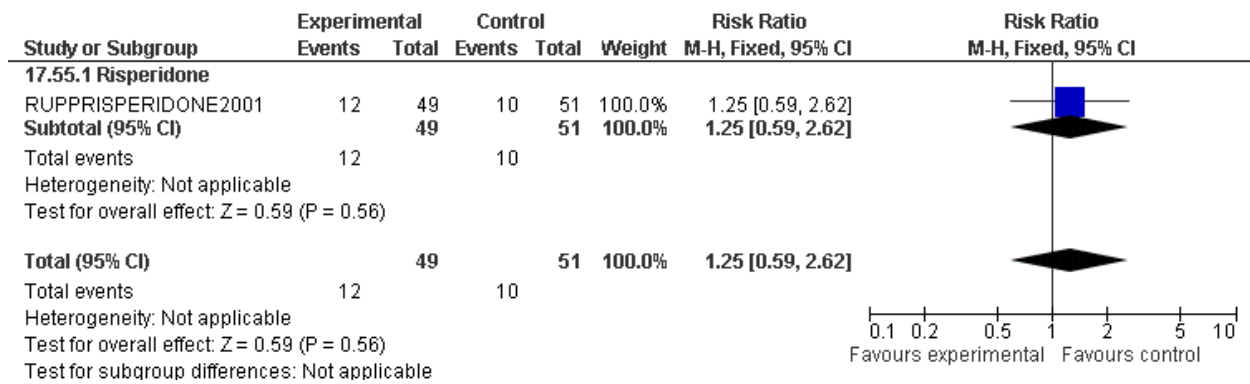
### Tachycardia



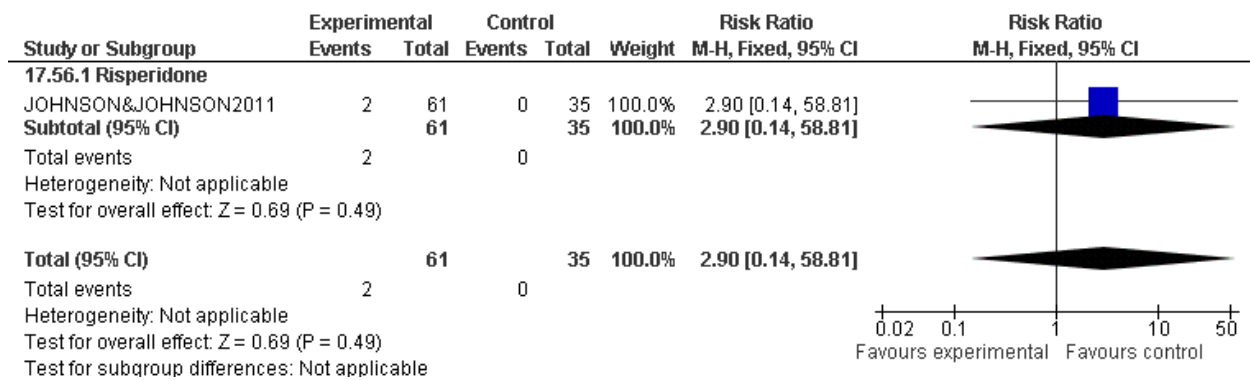
## Anorexia



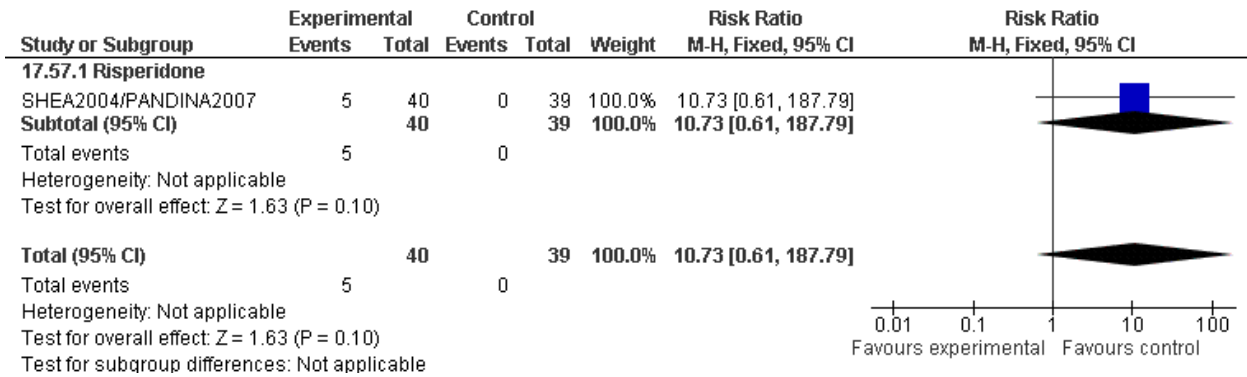
## Anxiety



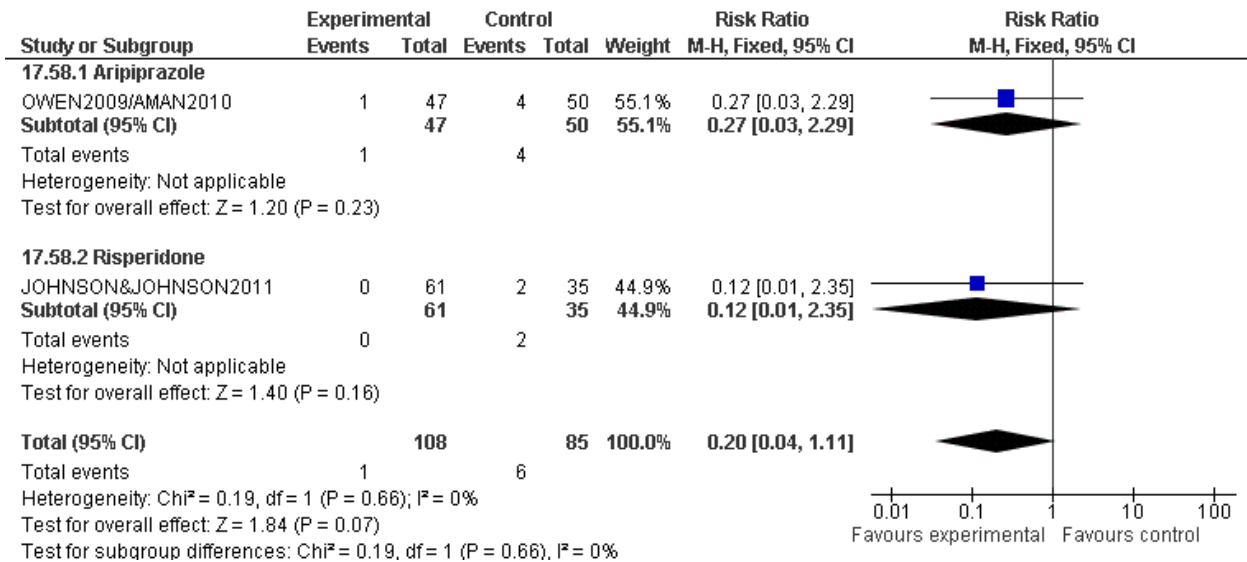
## Depression



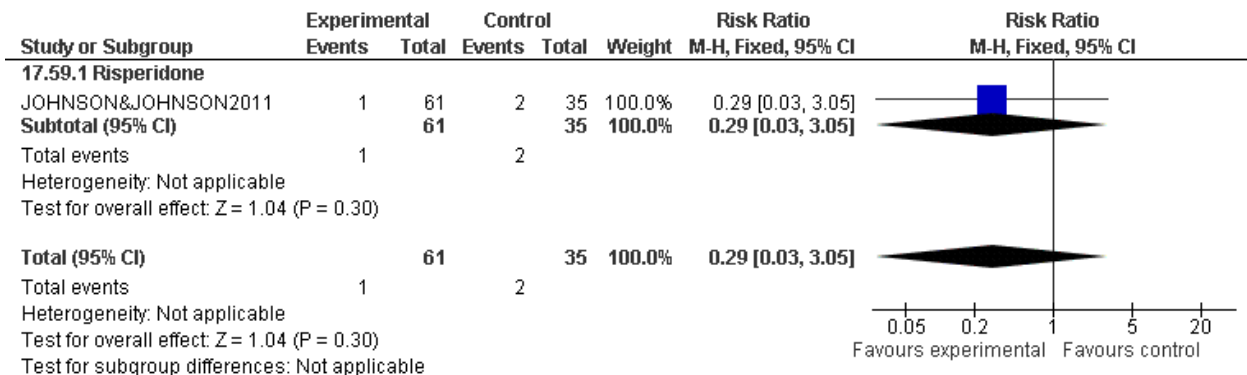
## Apathy



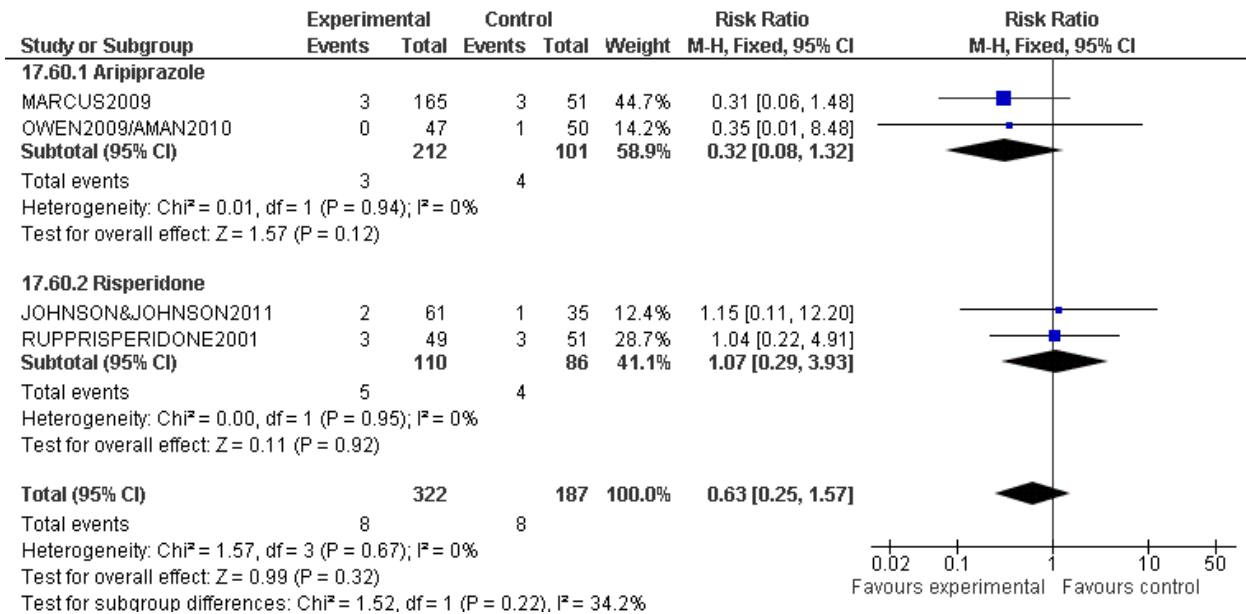
## Aggression



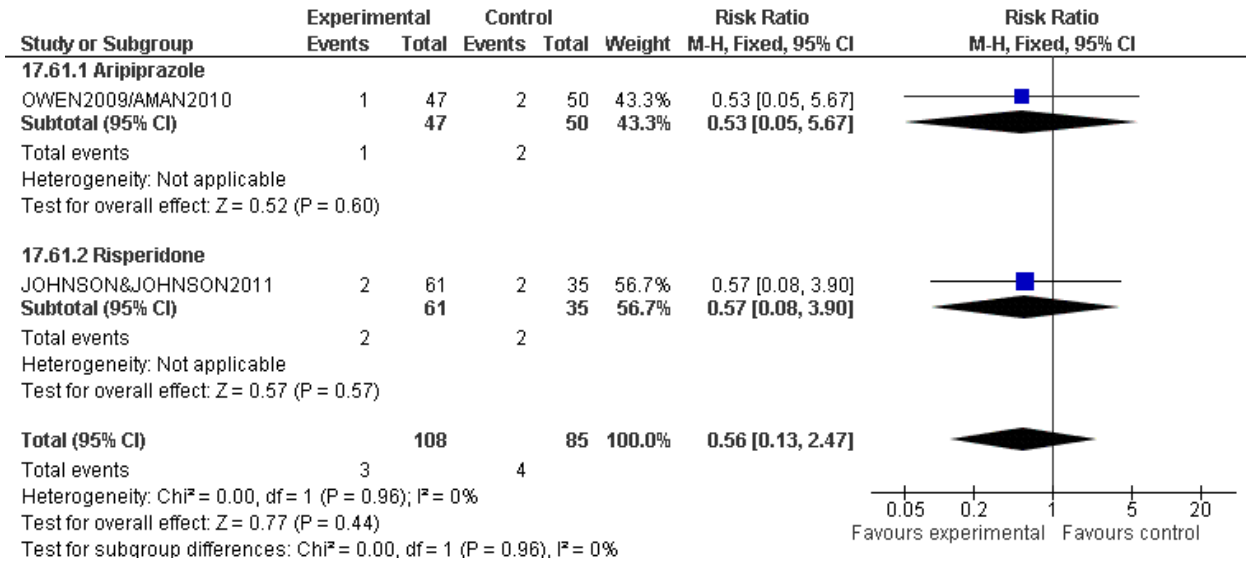
## Agitation



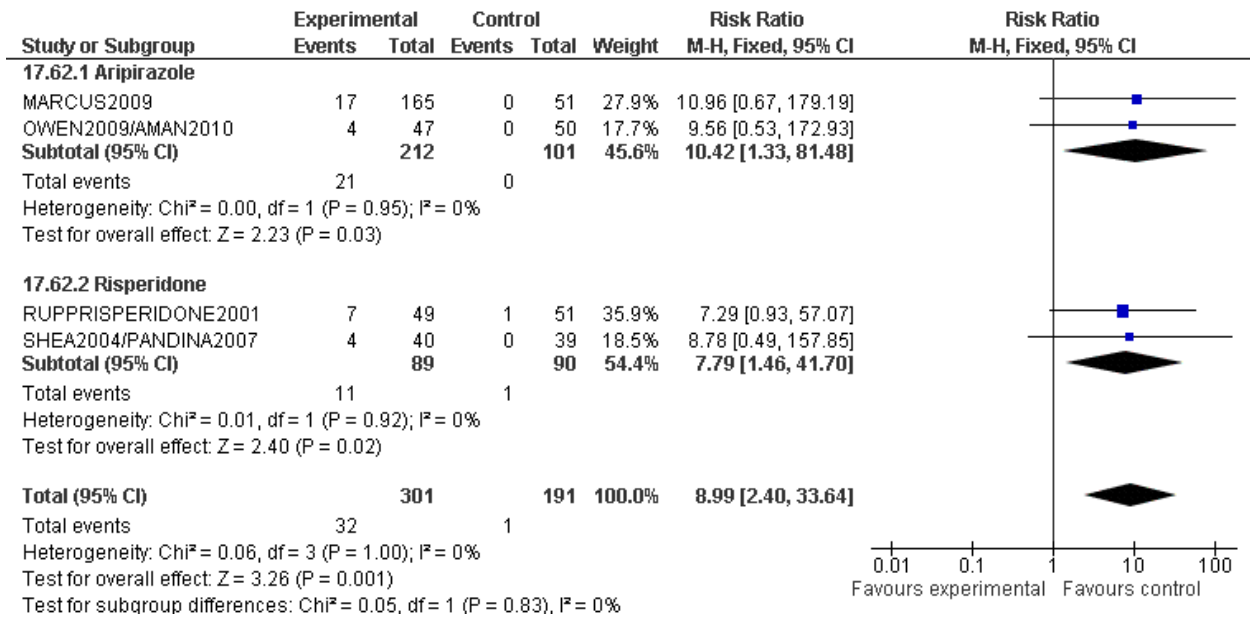
## Restlessness



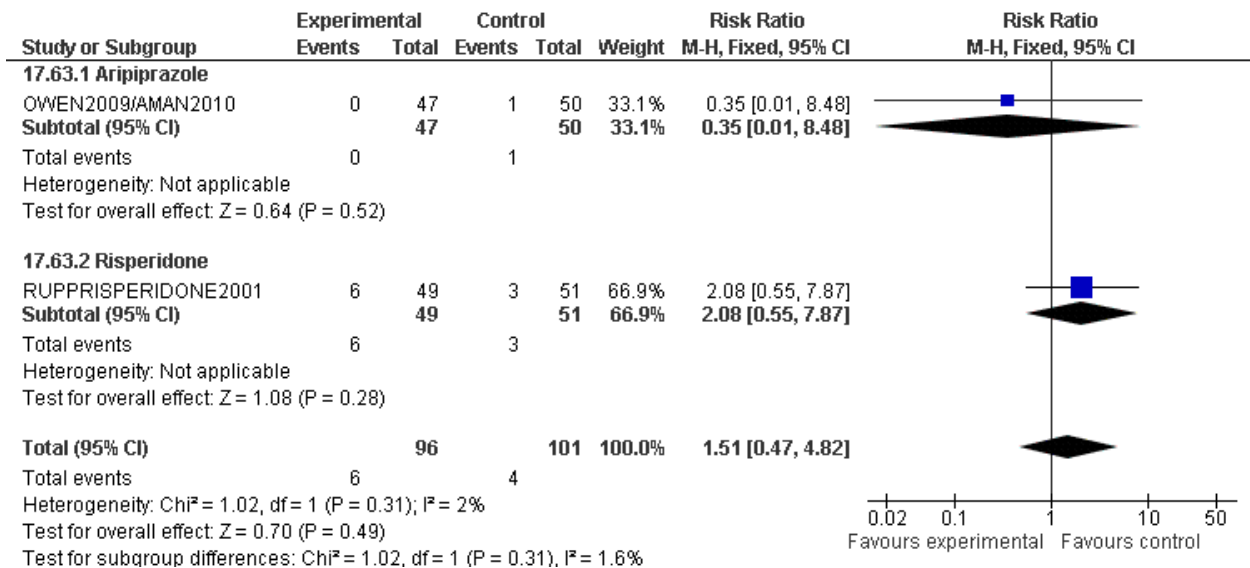
## Psychomotor hyperactivity



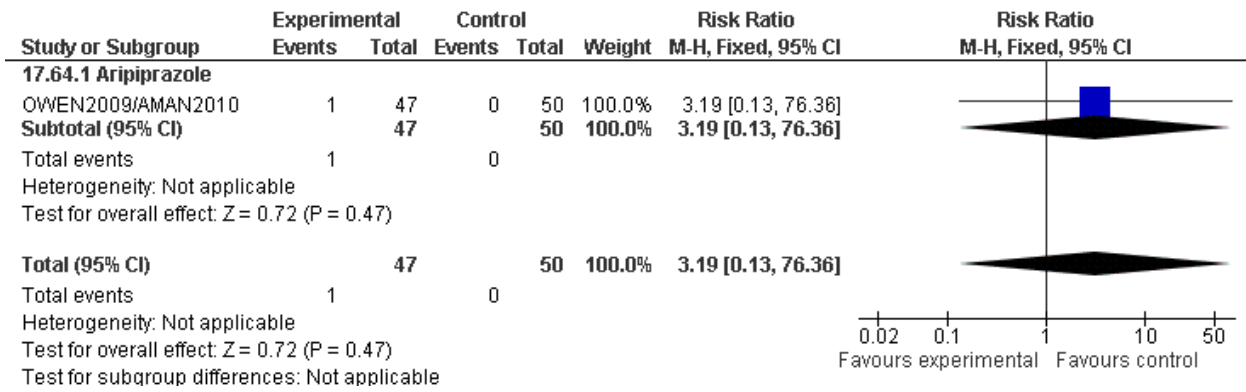
## Tremor



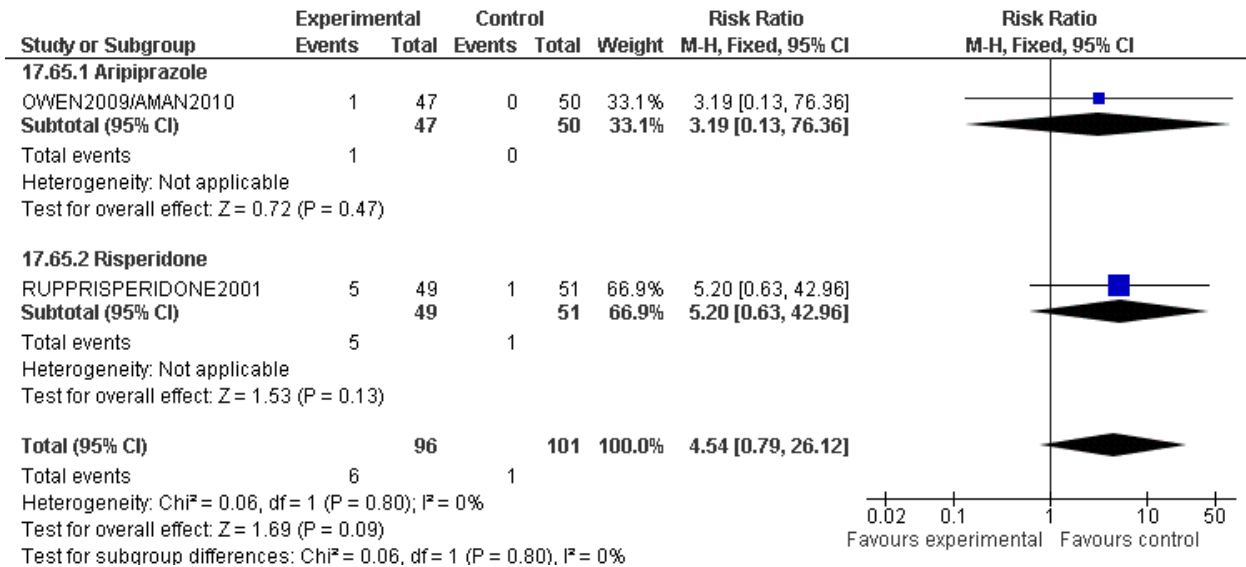
### Dyskinesia/Hyperkinesia



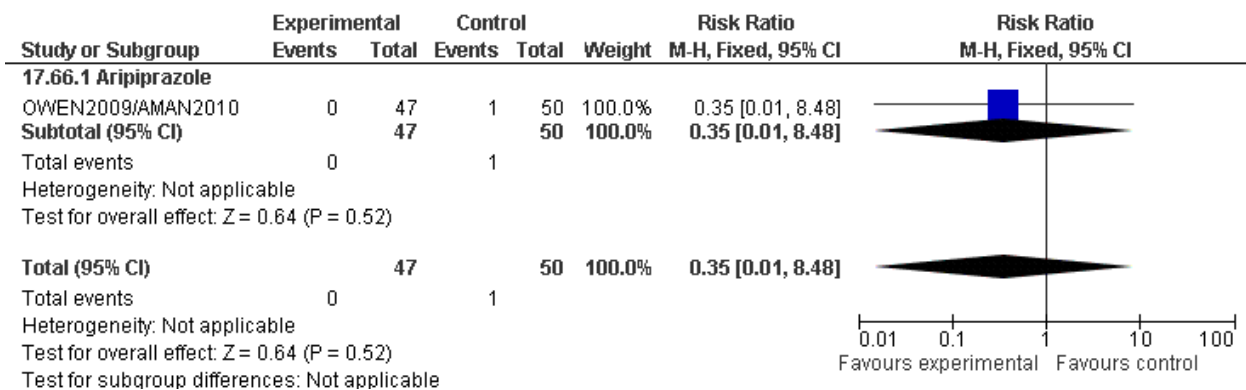
### Hypokinesia



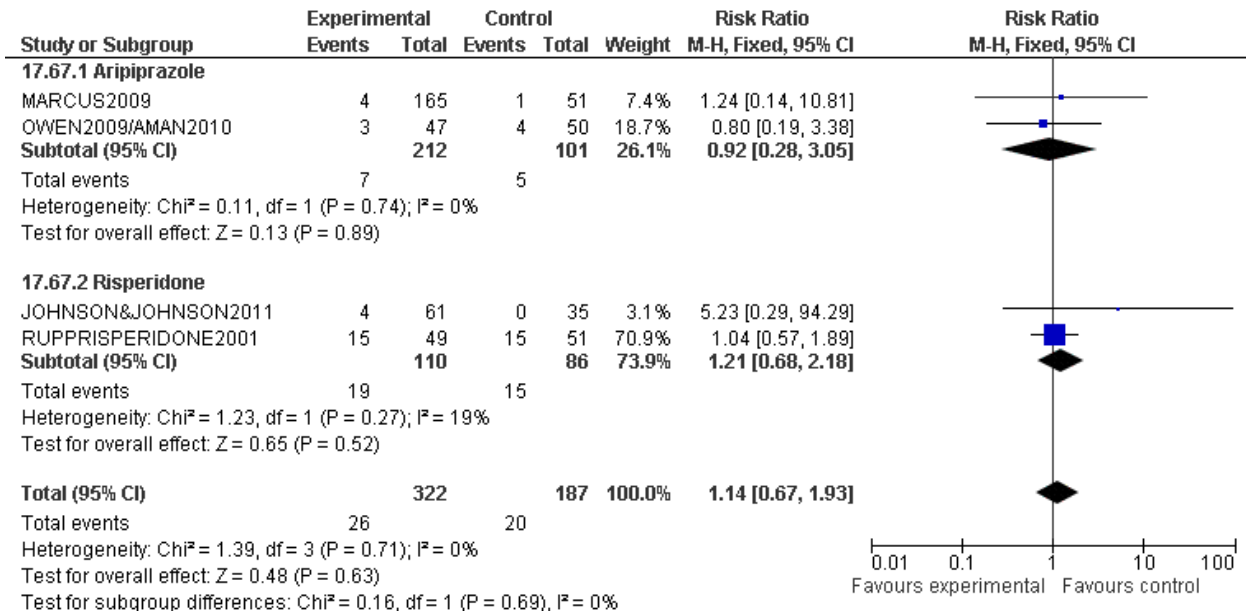
### Muscle rigidity



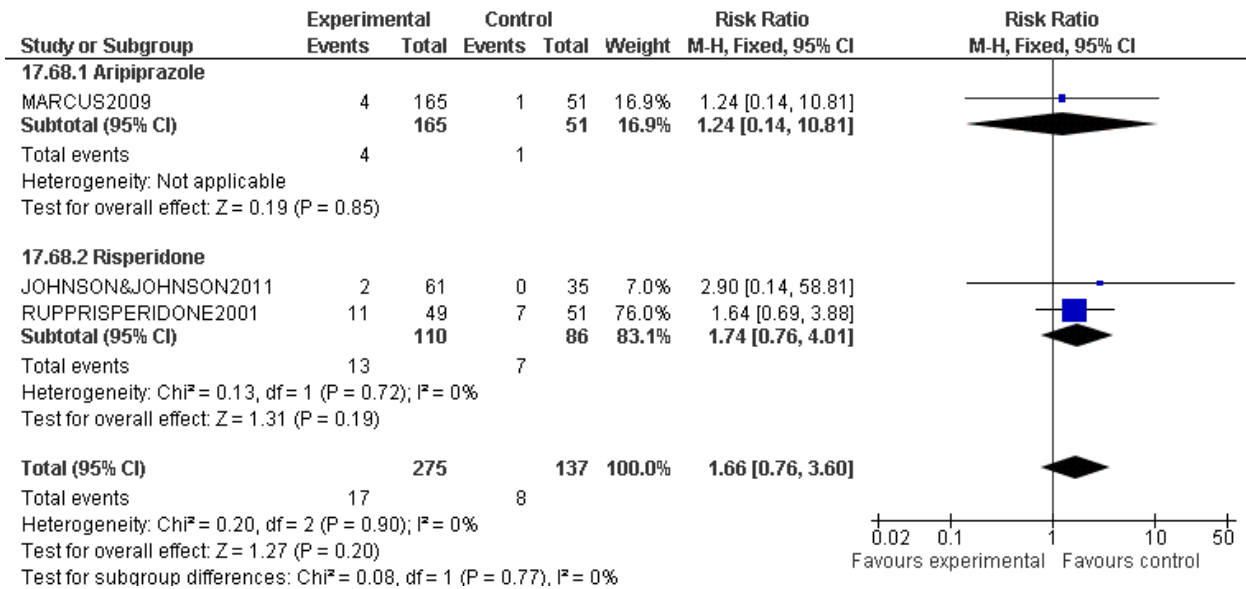
### Muscle spasms



**Enuresis**

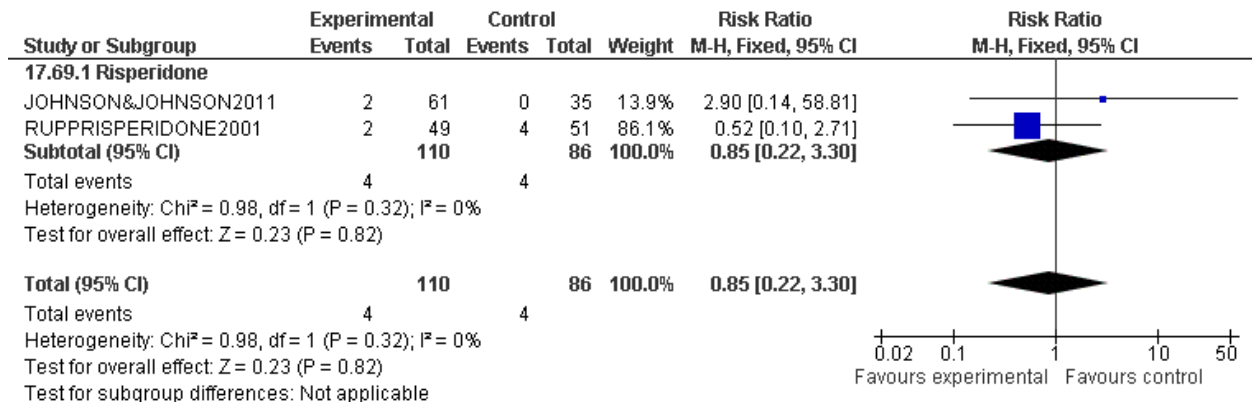


**Skin irritation/Rash**

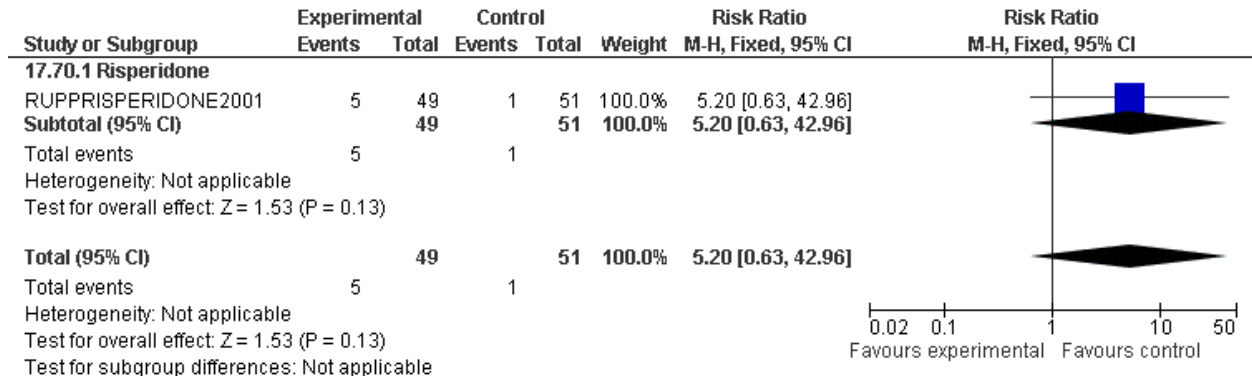


**Earache/Ear infection**



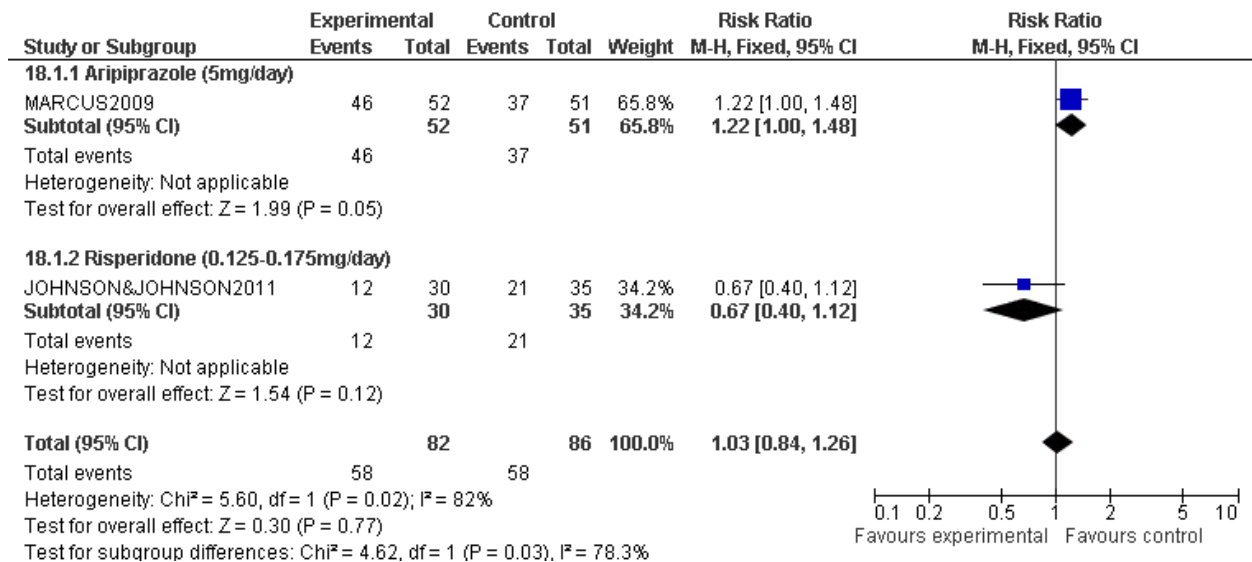


Sore throat

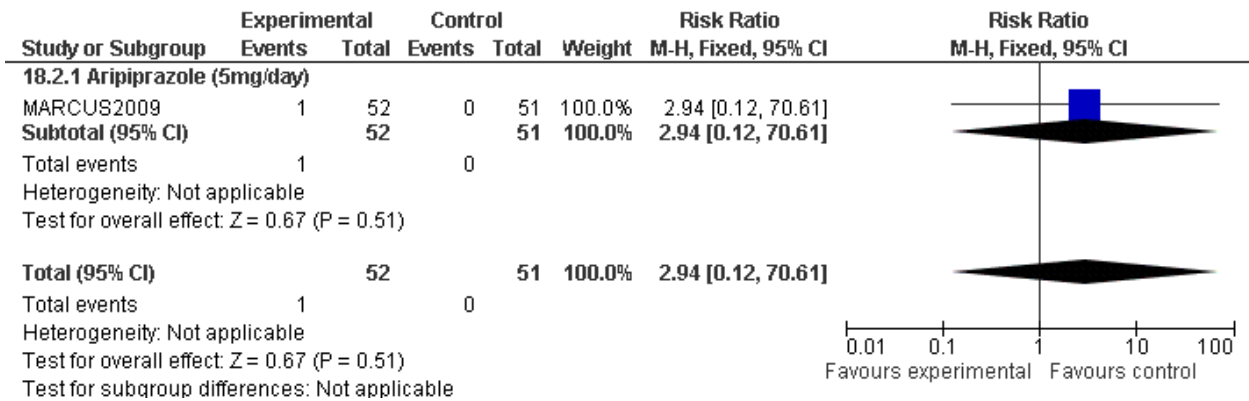


*Adverse events associated with low dose antipsychotics versus placebo*

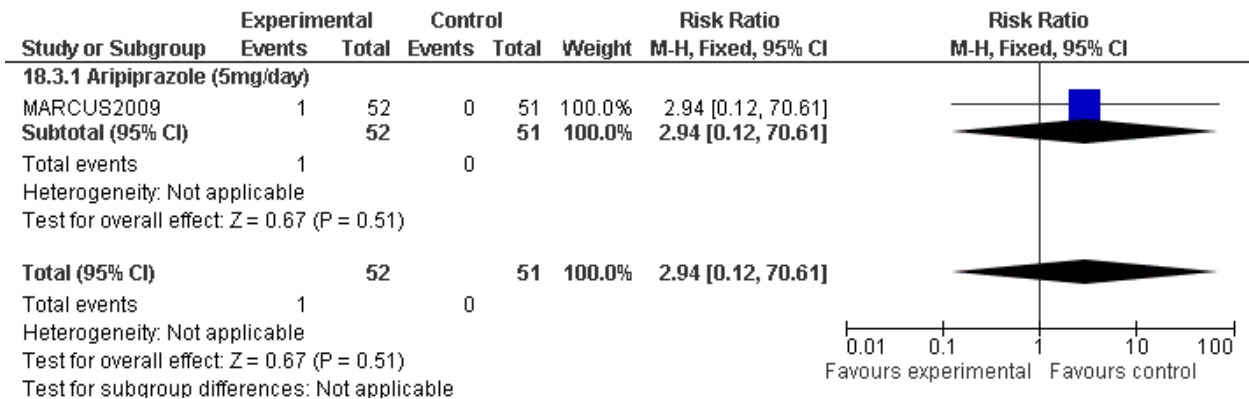
Any side effect



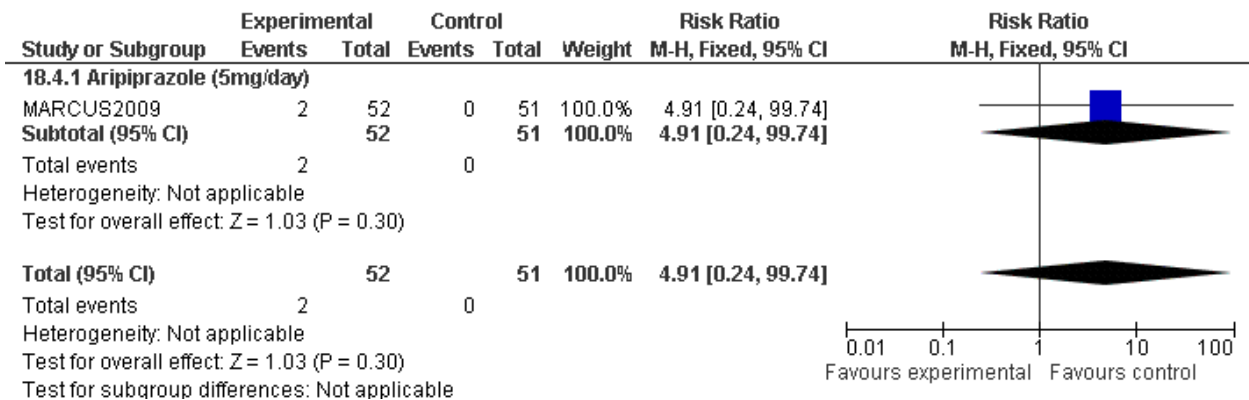
### Discontinuation due to sedation



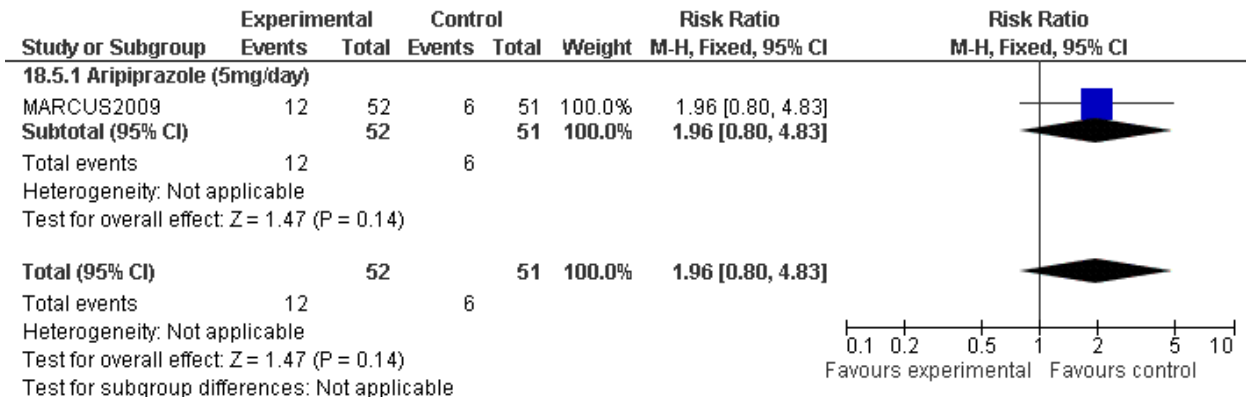
### Discontinuation due to drooling



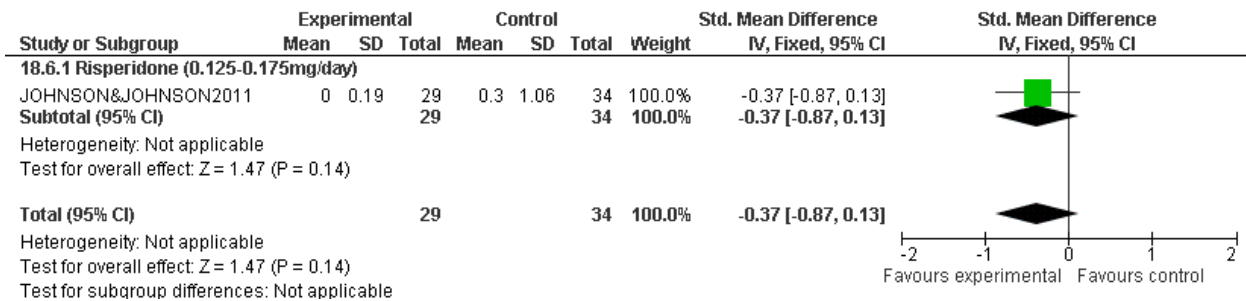
### Discontinuation due to tremor



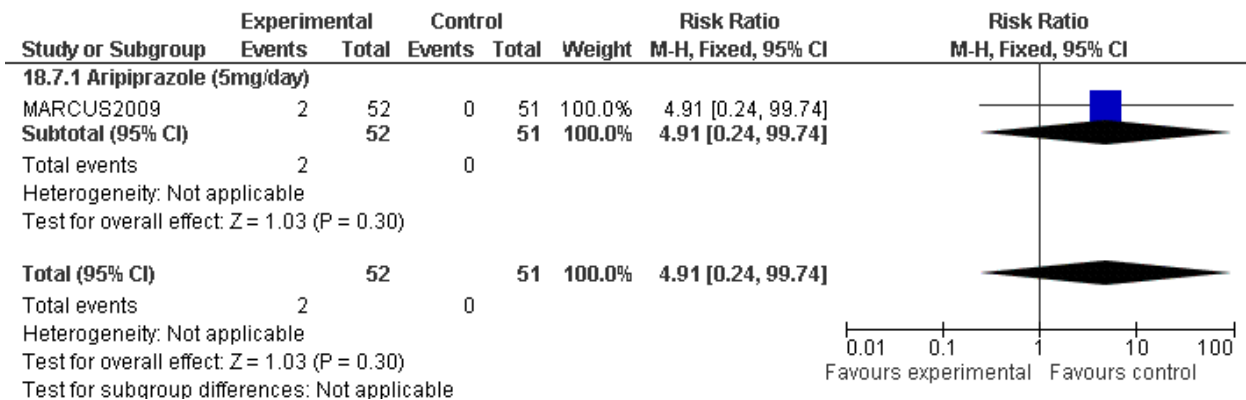
### Any treatment-emergent extrapyramidal symptoms



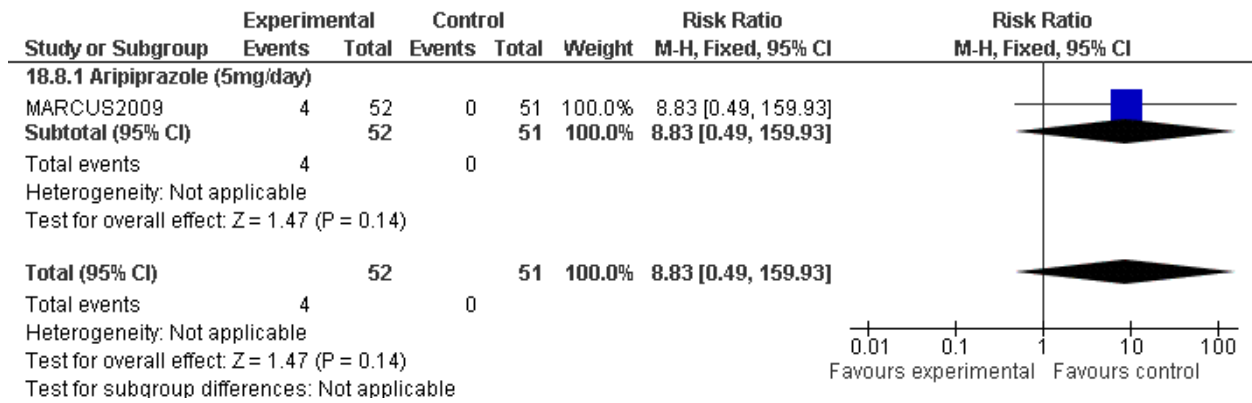
### Extrapyramidal symptoms



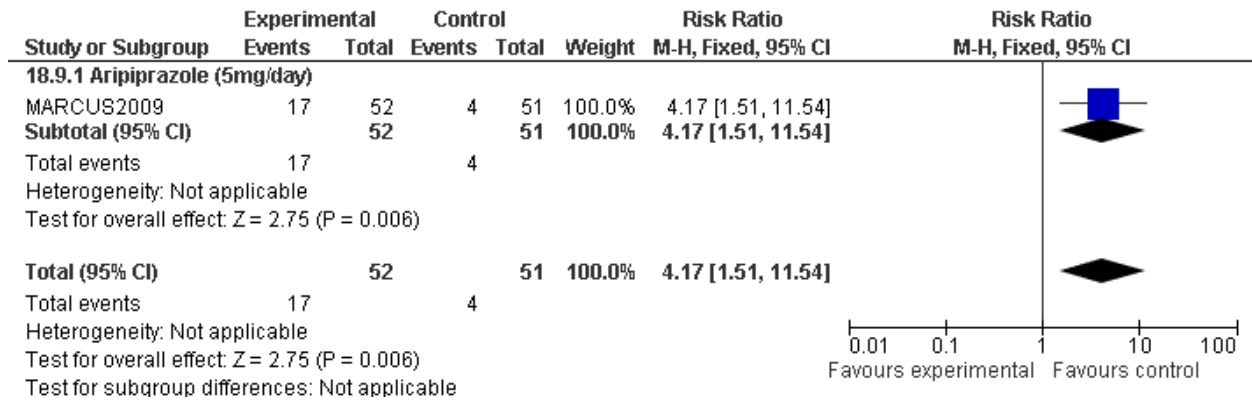
### Extrapyramidal disorder



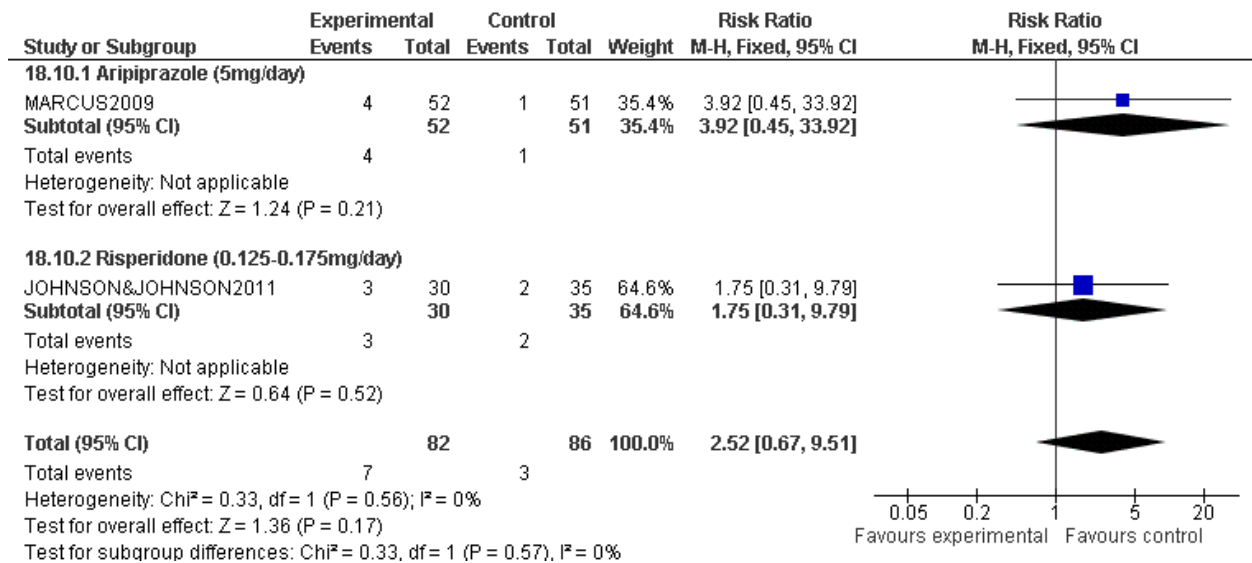
### Tremor



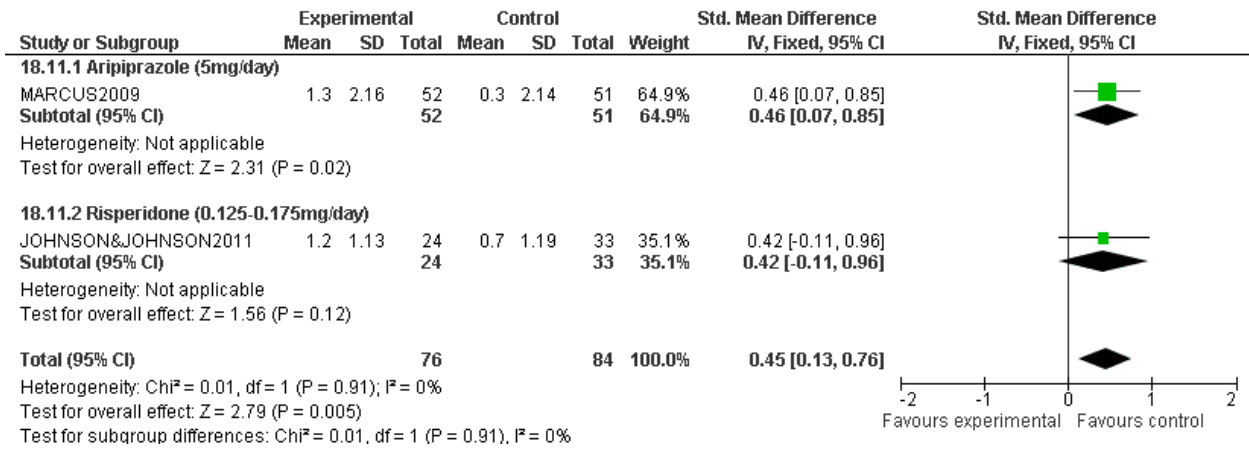
**Clinically relevant (>=7%) weight gain**



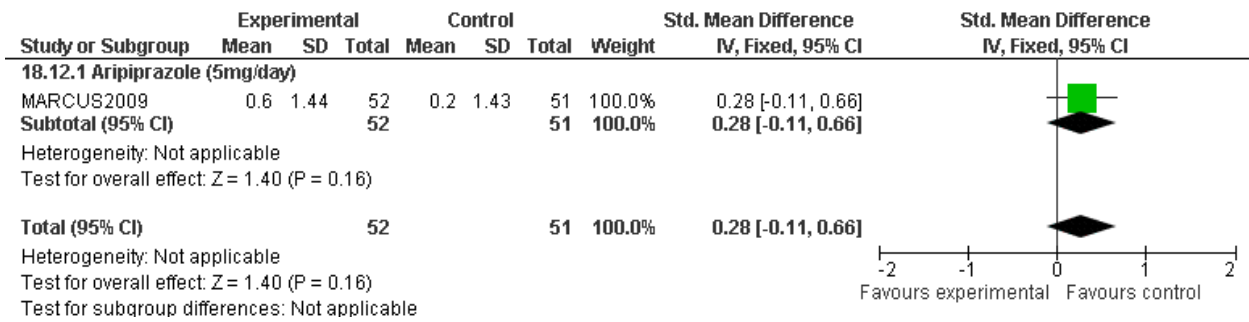
**Weight gain**



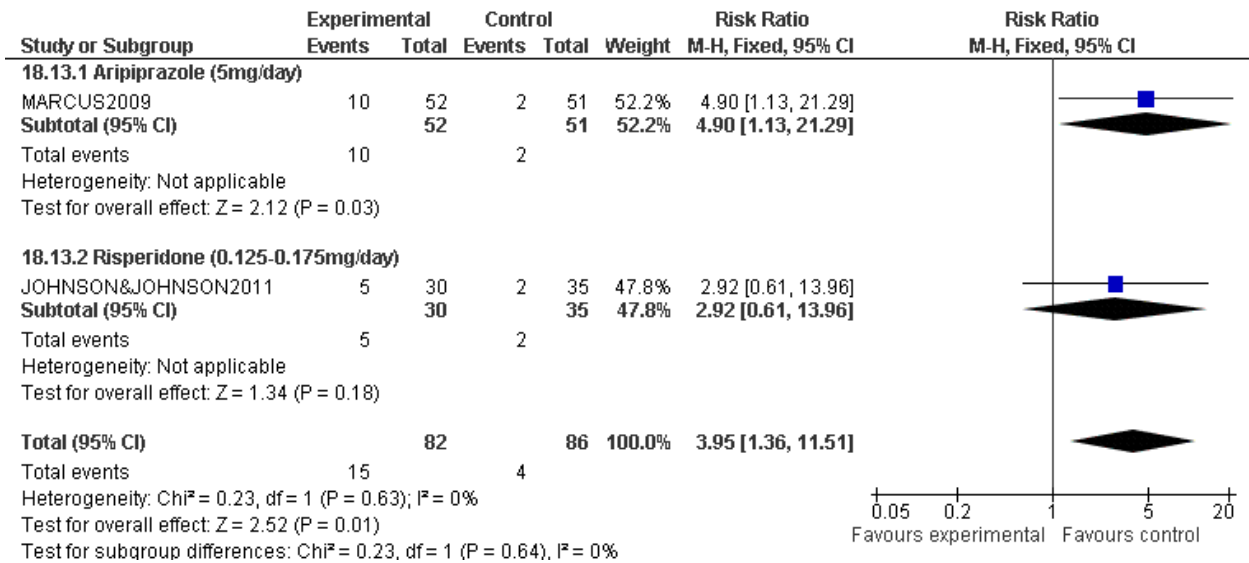
### Weight gain (in kg)



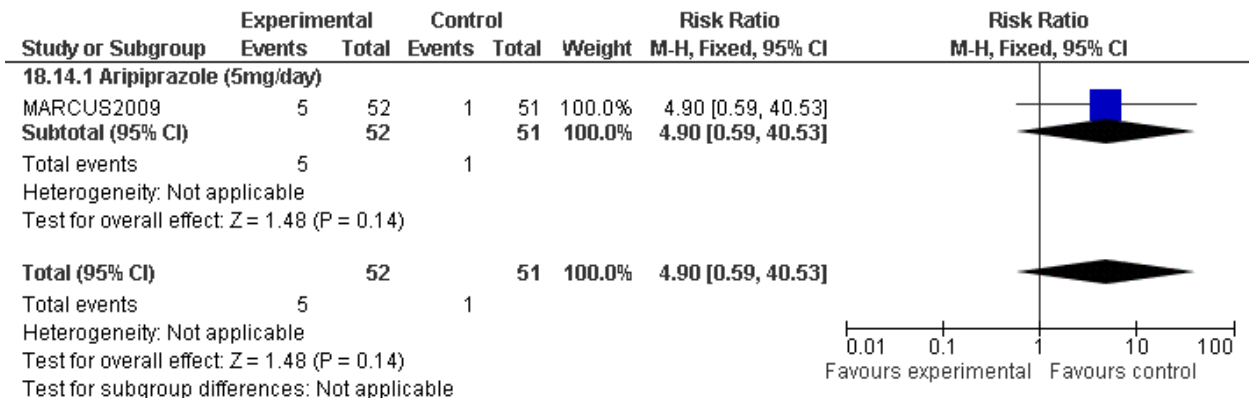
### BMI change (kg/m-squared)



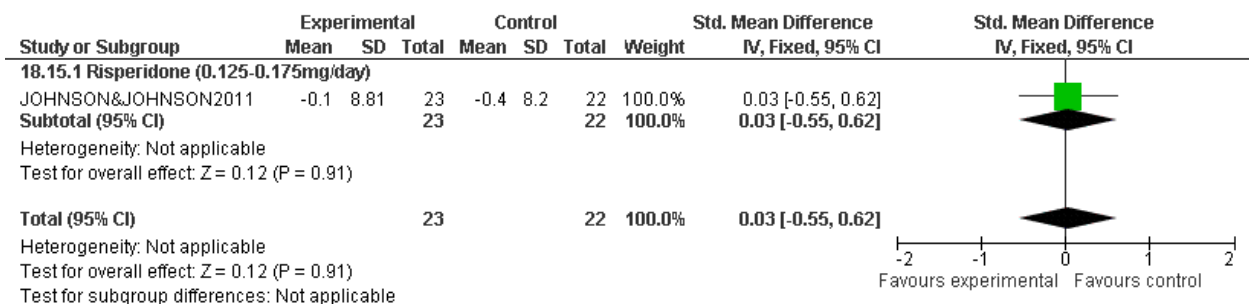
### Increased appetite



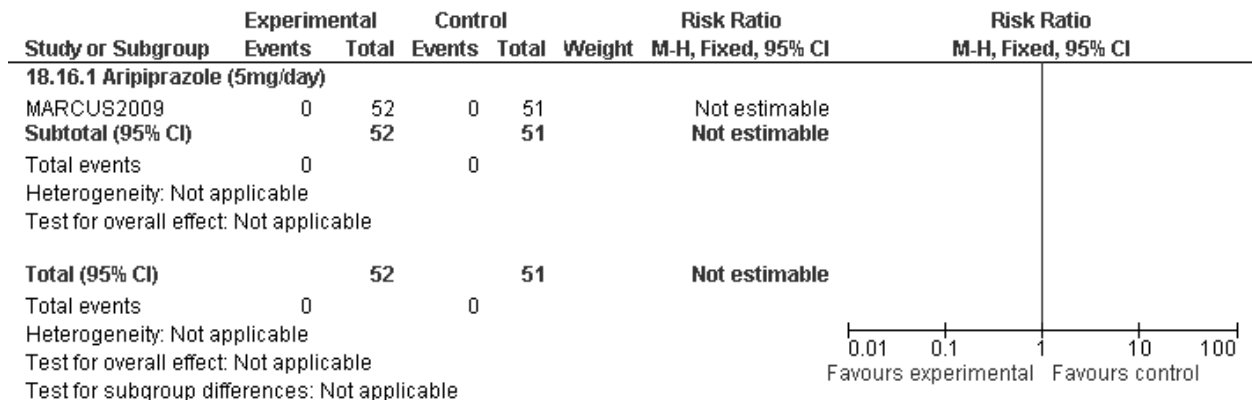
### Decreased appetite



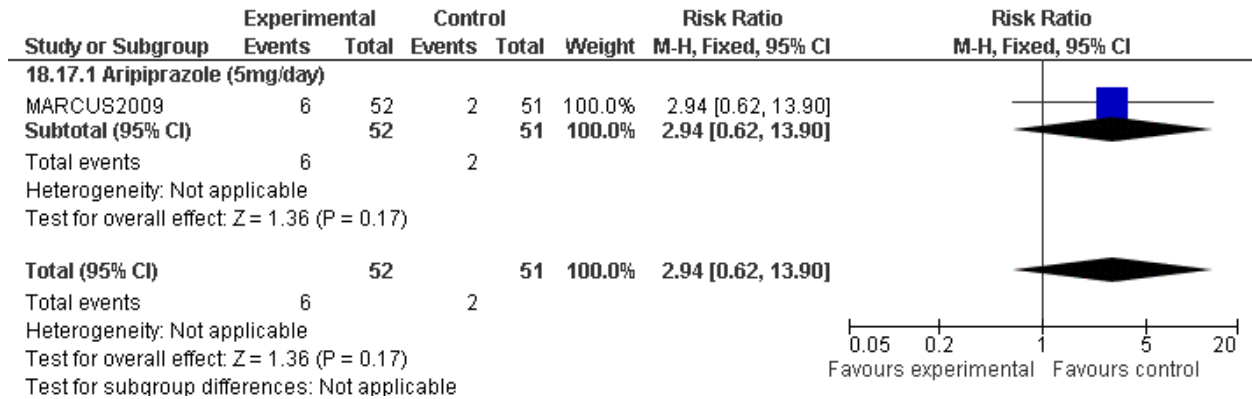
### Fasting Glucose (mg/dL) (Change Score)



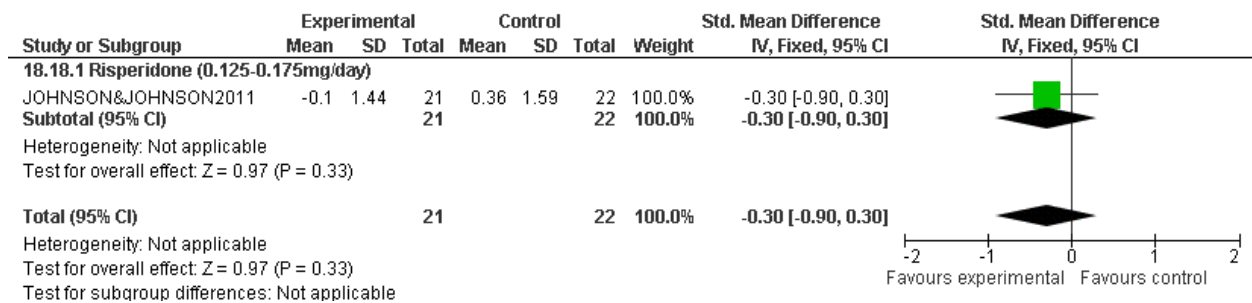
### Fasting glucose (=>115 mg/dL)



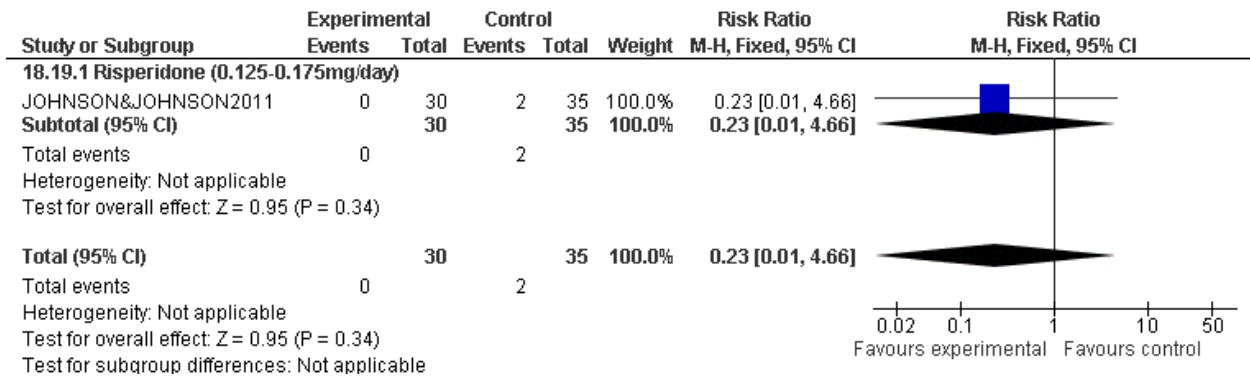
**Fasting triglycerides (=>120 mg/dL for females or 160 mg/dL for males)**



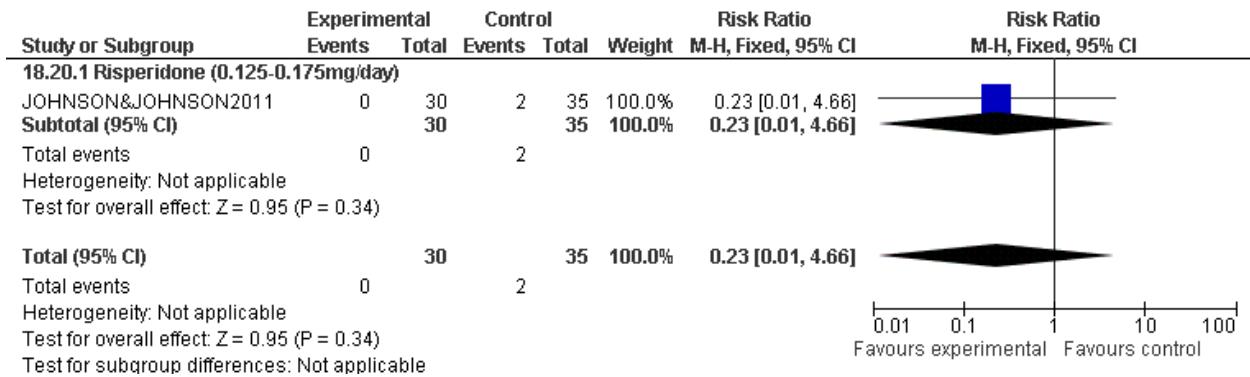
**Insulin Resistance (HOMA-IR) (Change Score)**



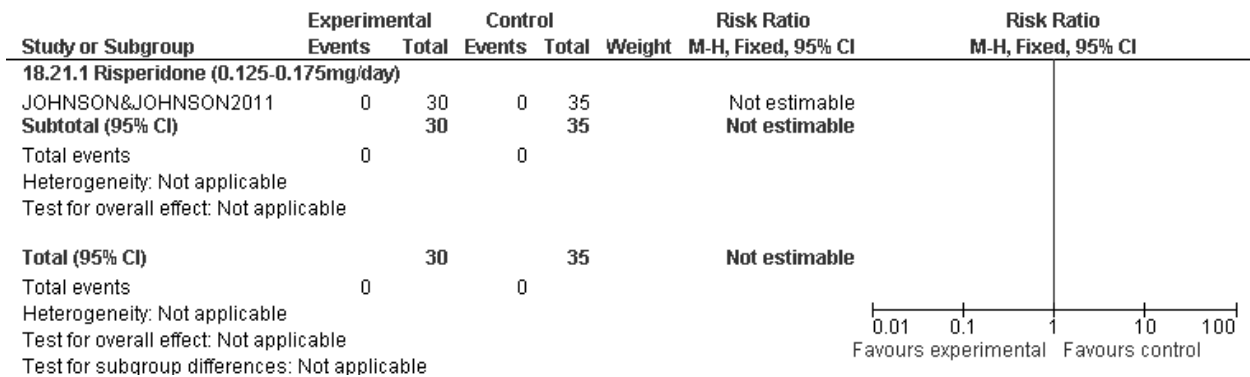
**Aggression**



### Agitation

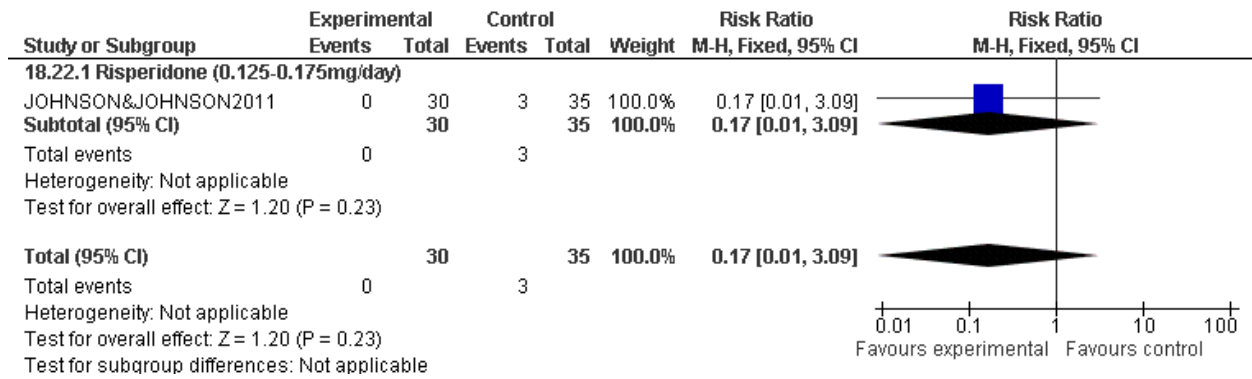


### Depression

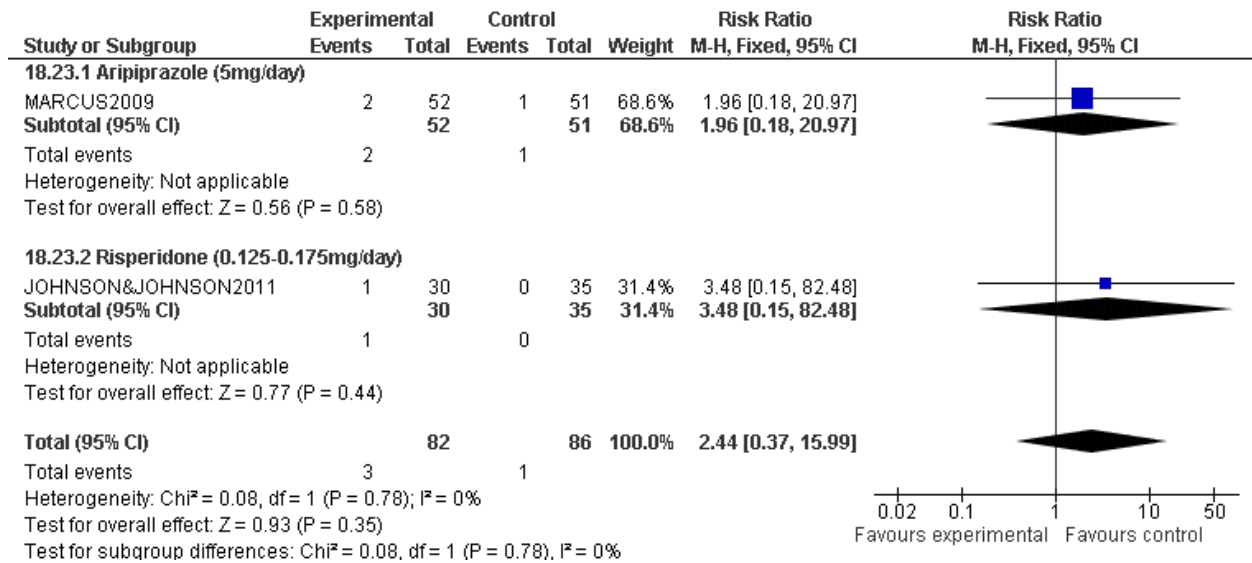


### Abdominal discomfort

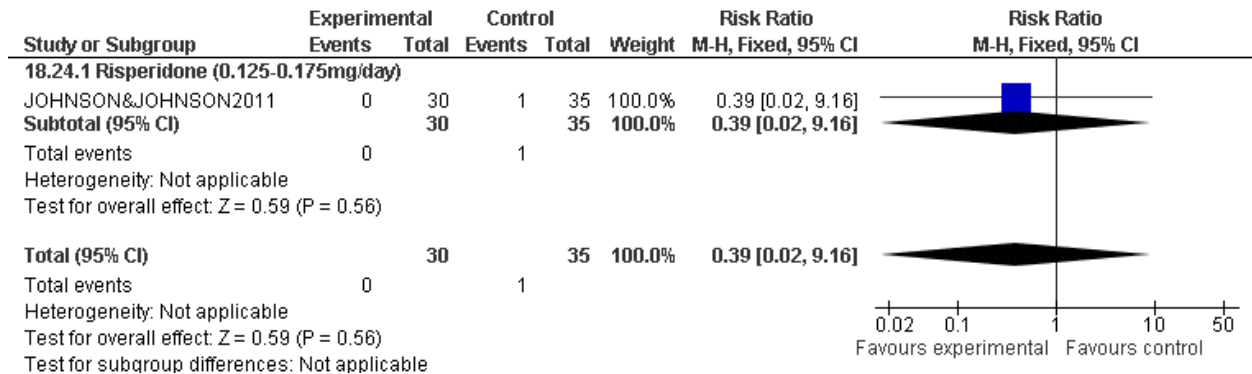




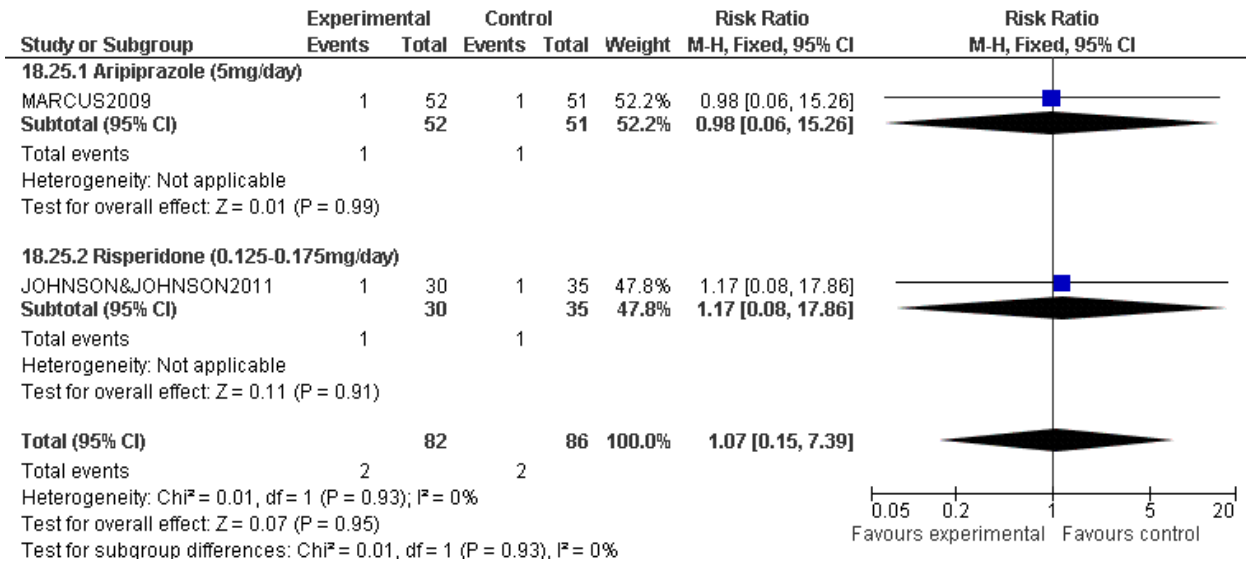
### Abdominal pain (upper)



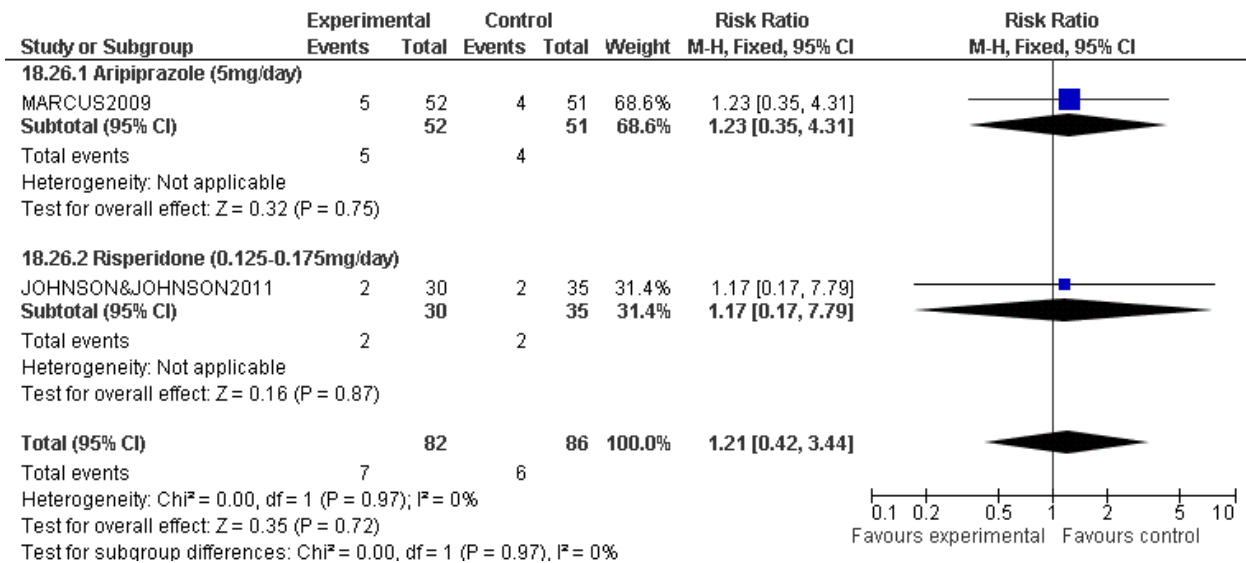
### Constipation



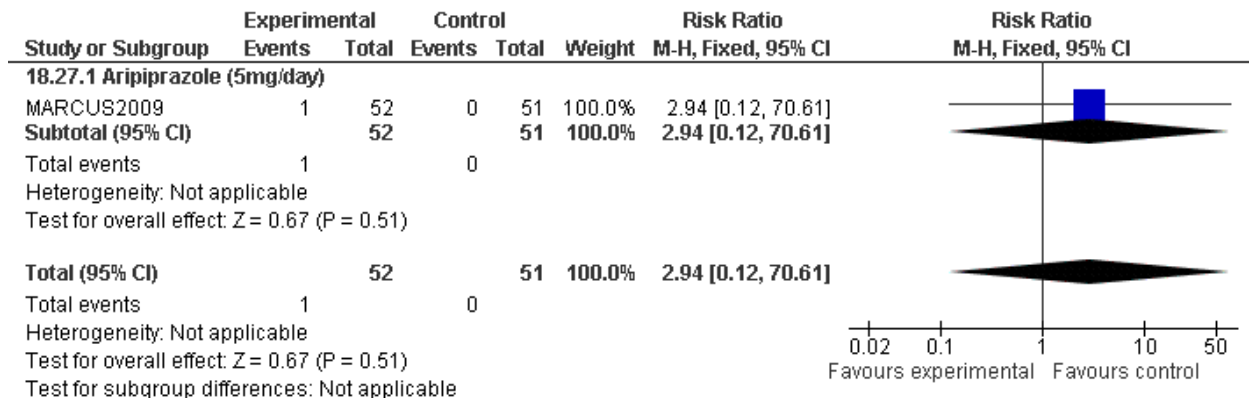
**Nausea**



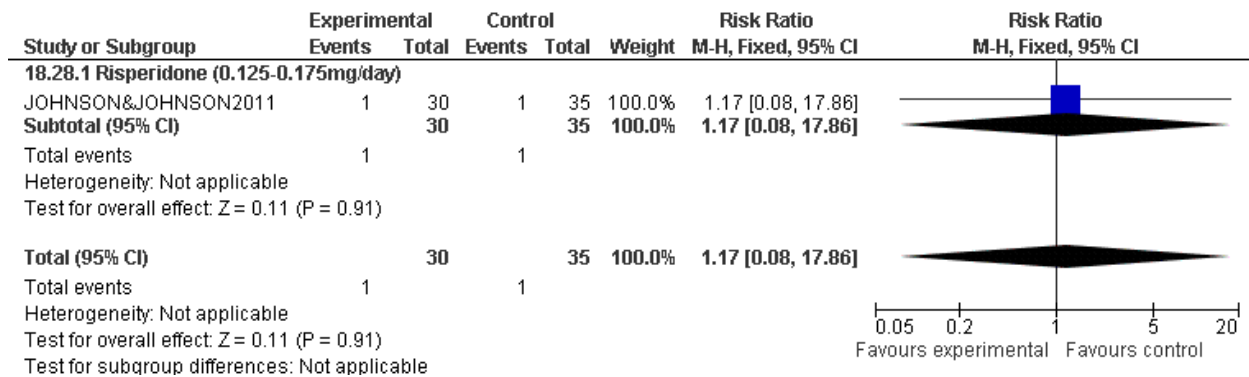
**Vomiting**



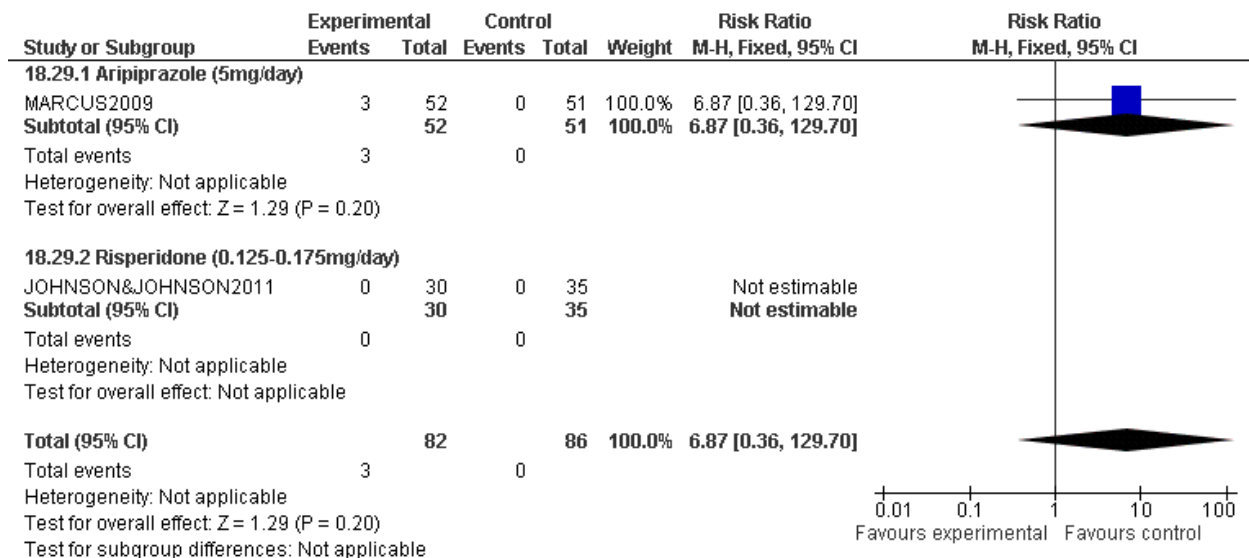
**Gastroenteritis viral**



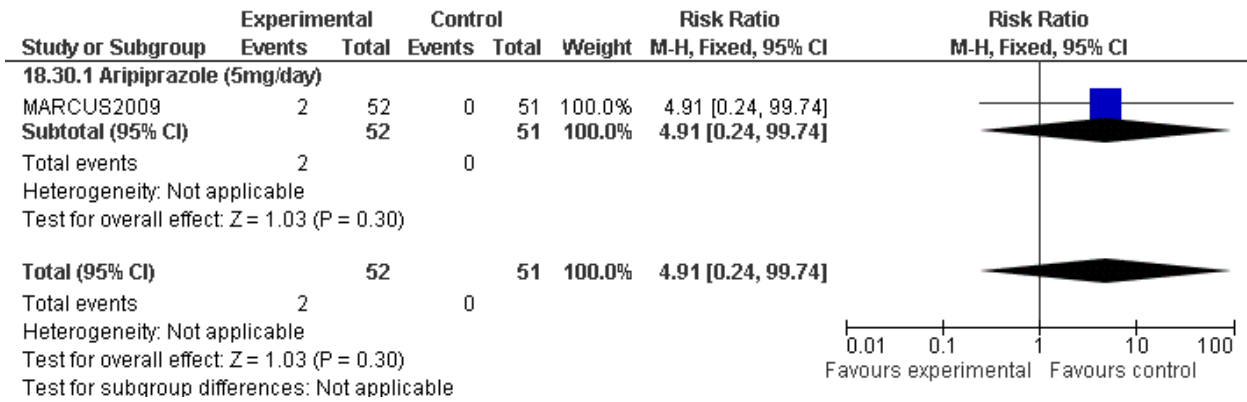
### Diarrhoea



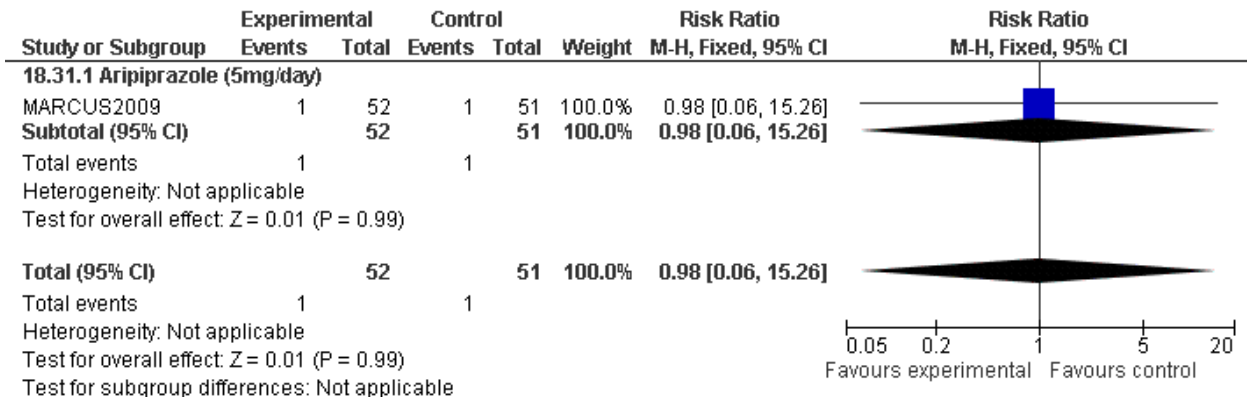
### Pyrexia



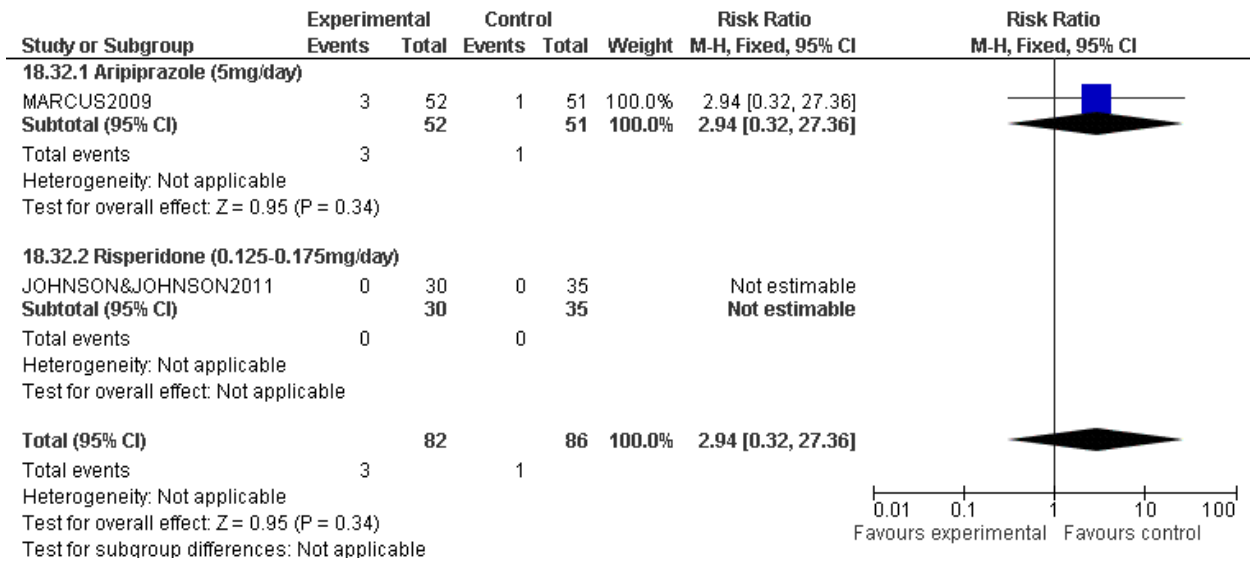
## Drooling



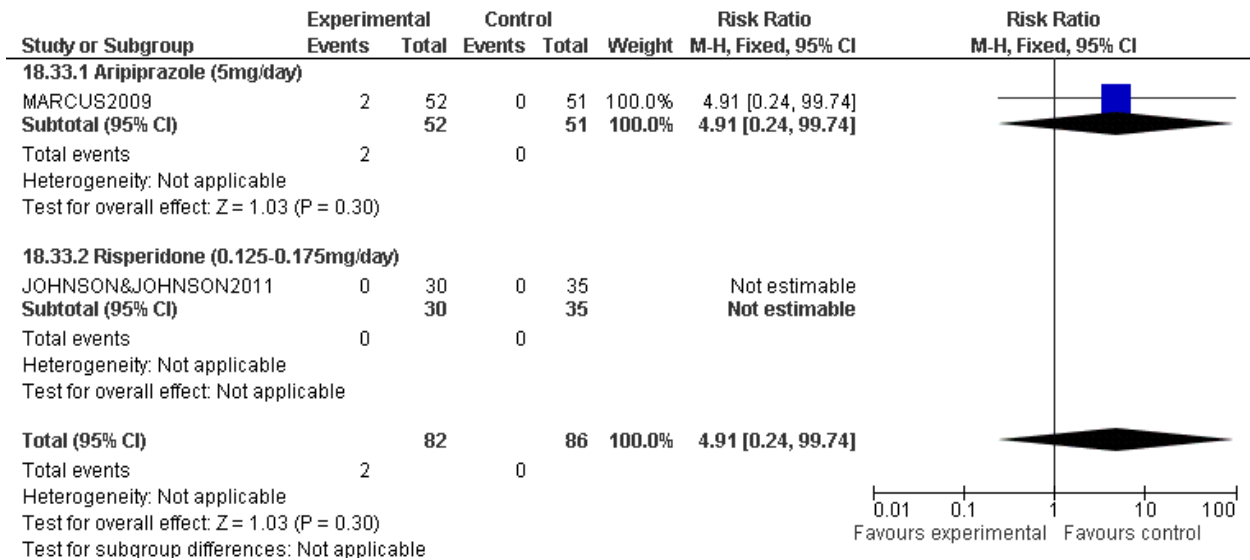
## Increased salivation



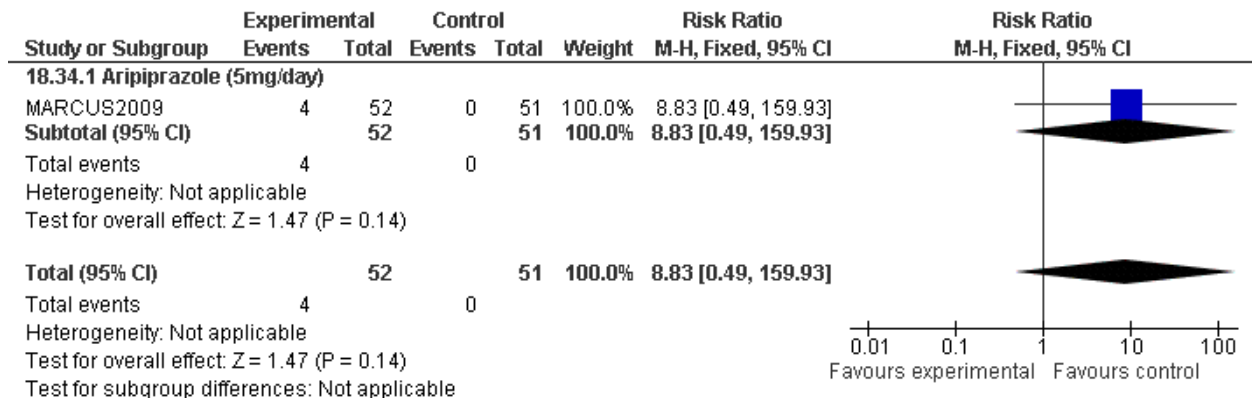
## Thirst



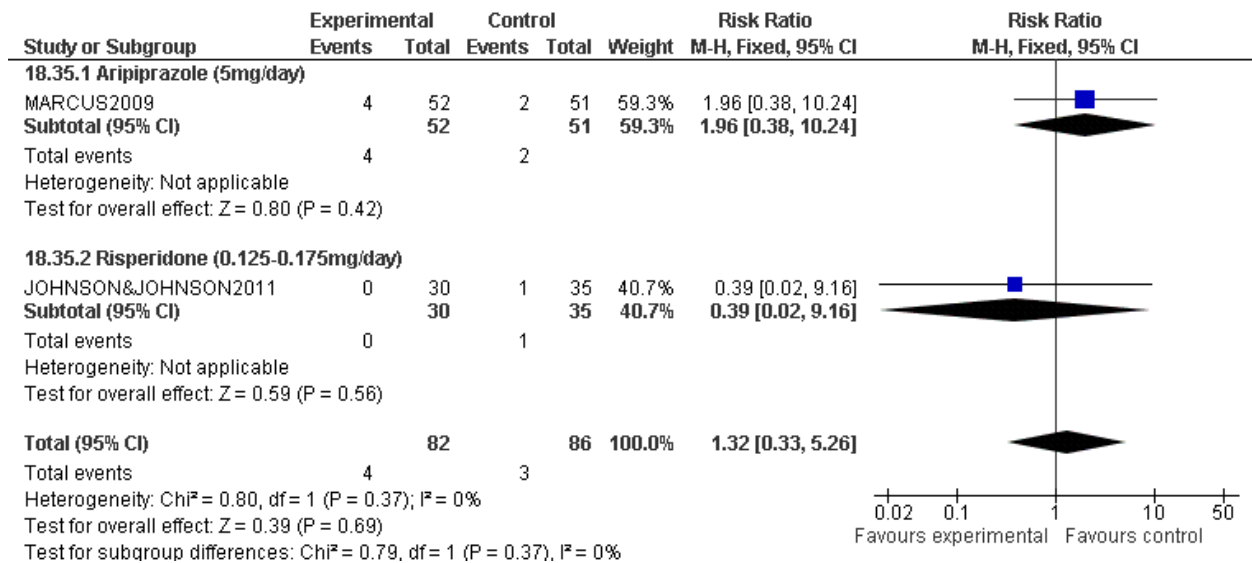
## Fatigue



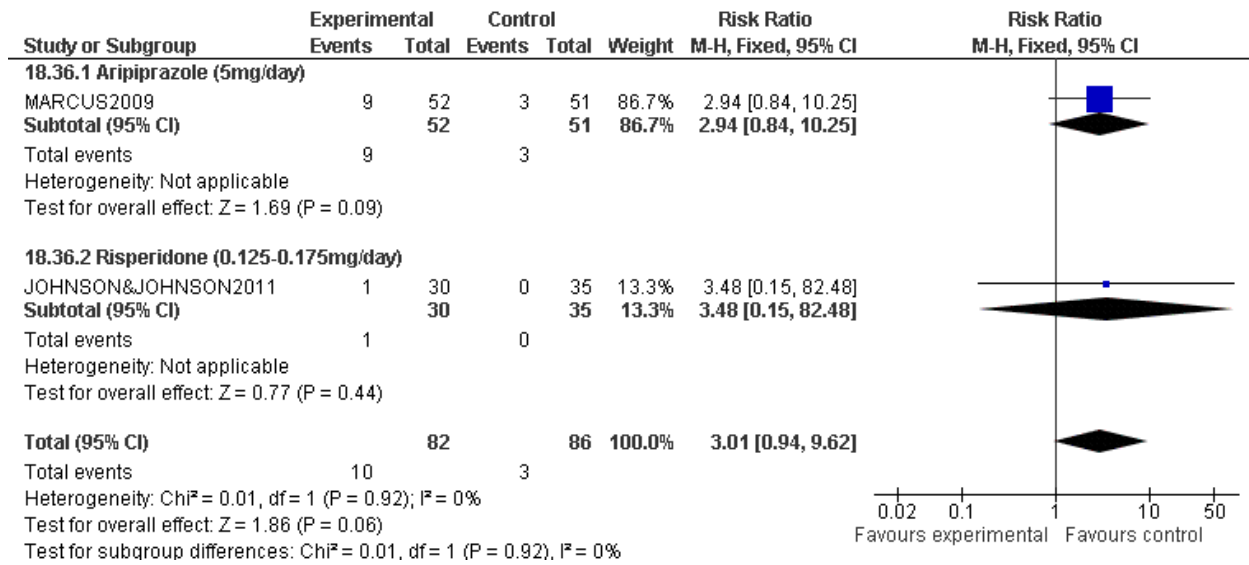
## Lethargy



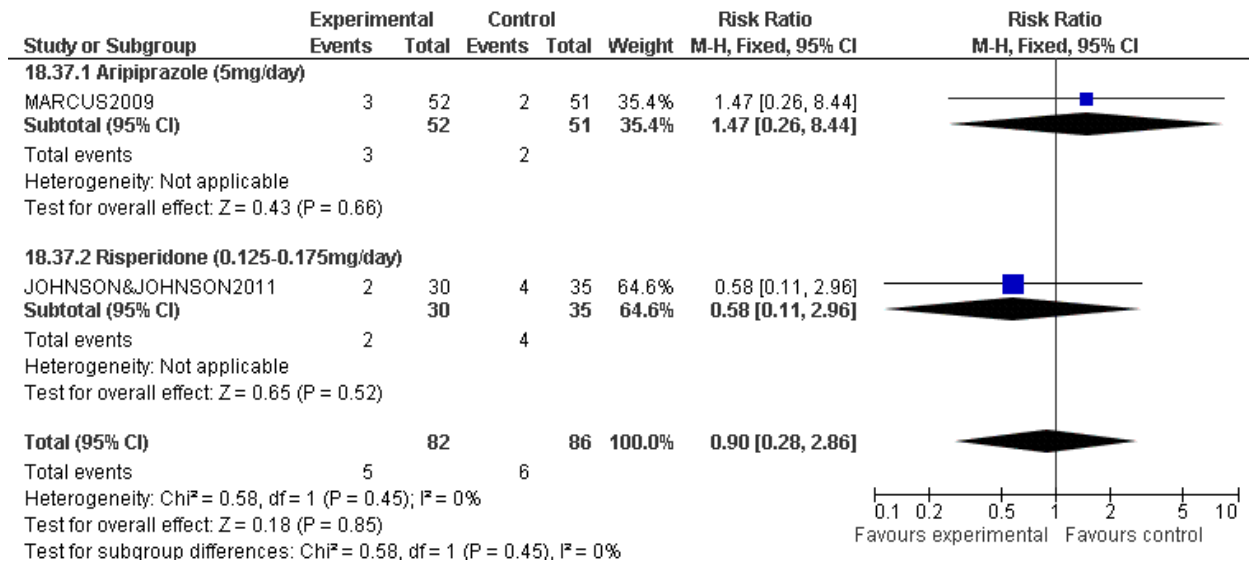
### Somnolence



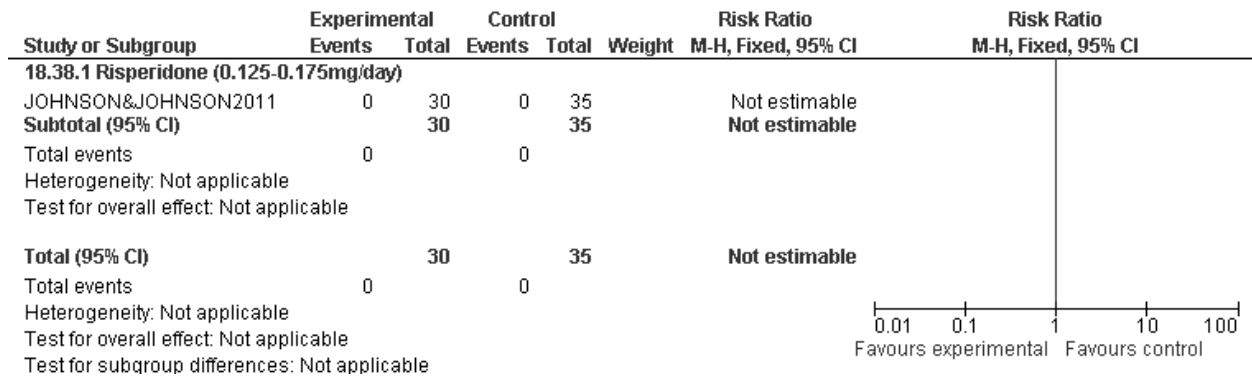
### Sedation



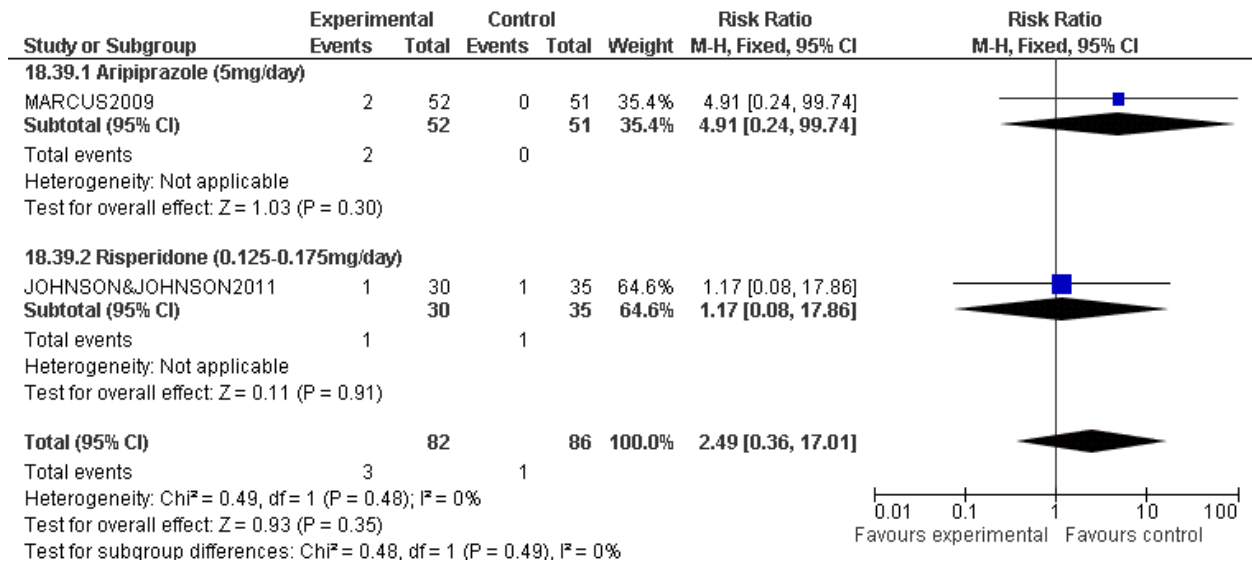
## Headache



## Ear infection

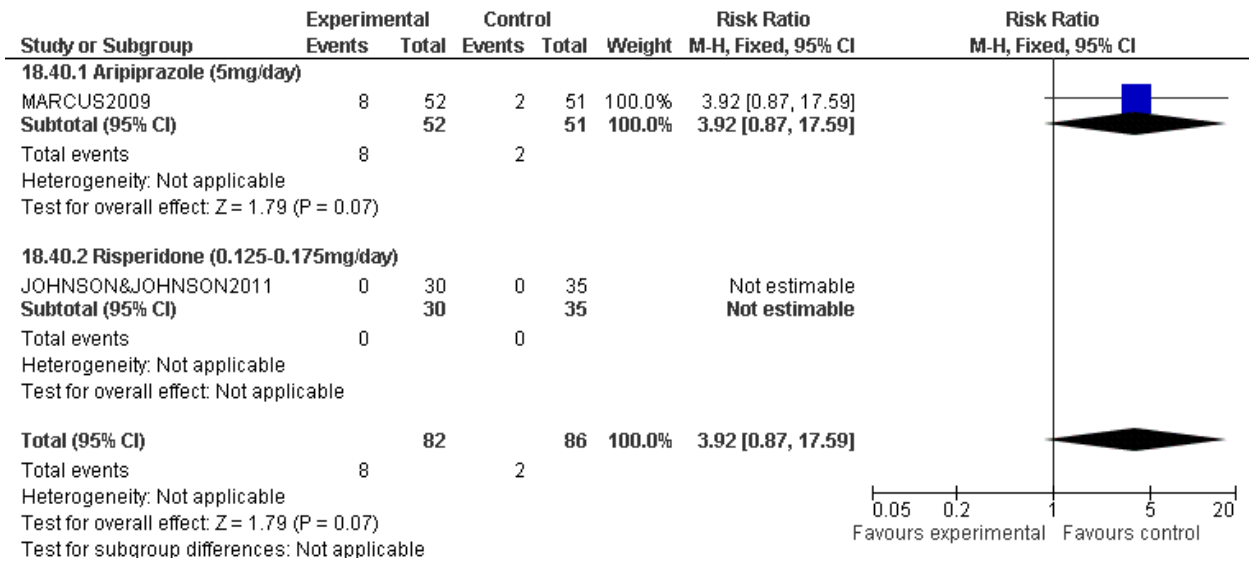


### Upper respiratory tract infection

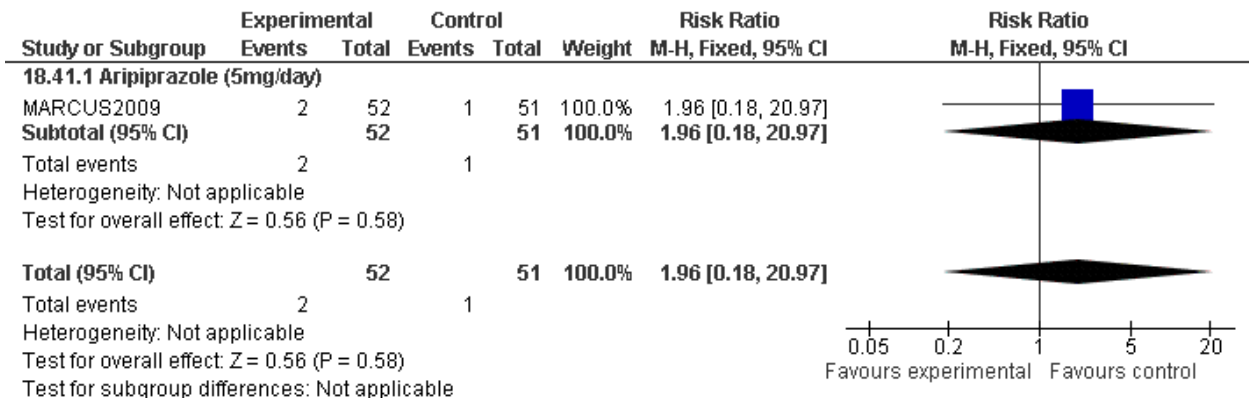


### Cough

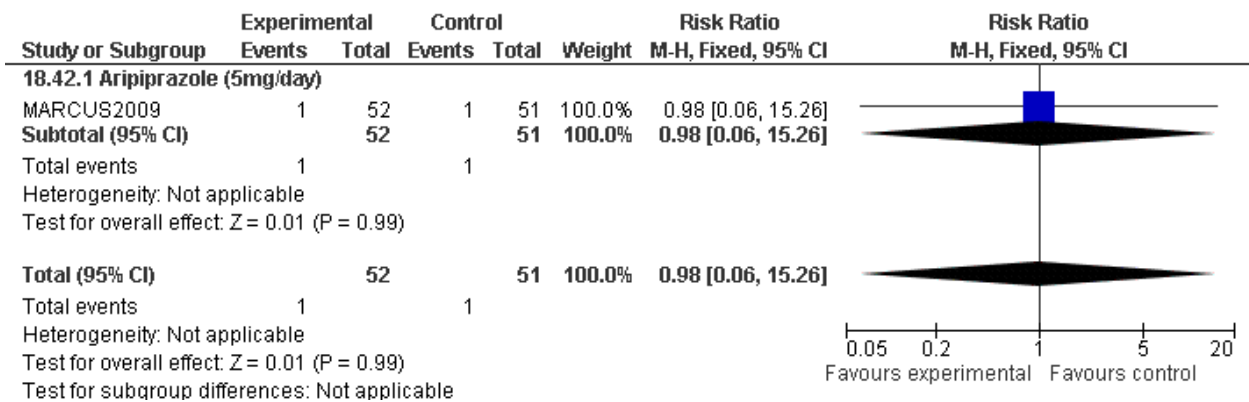




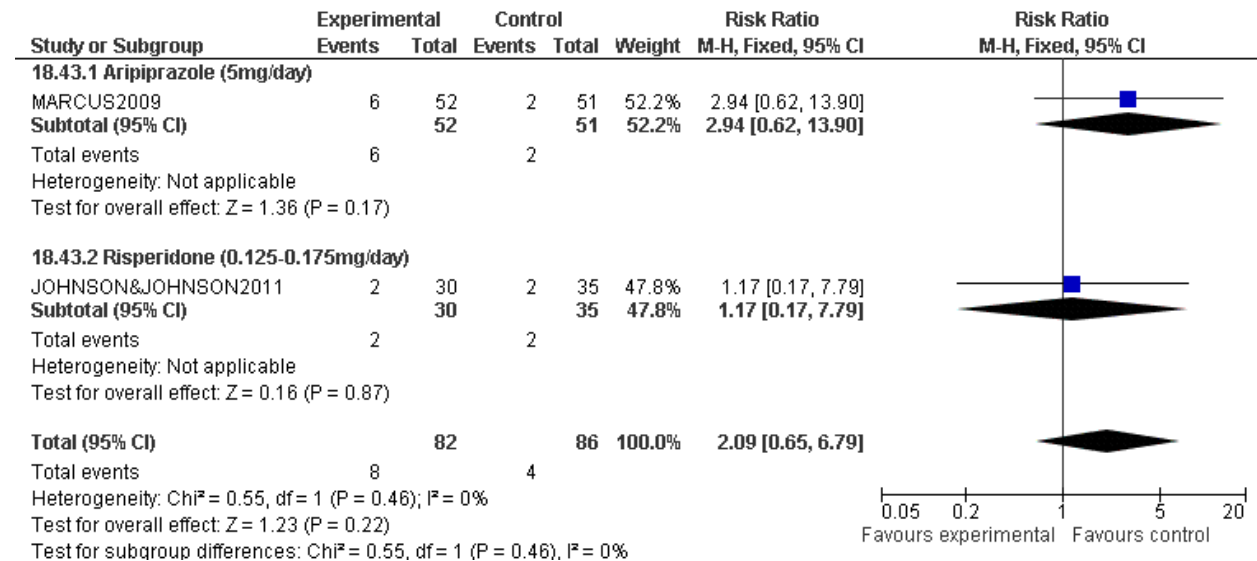
### Rhinorrhea



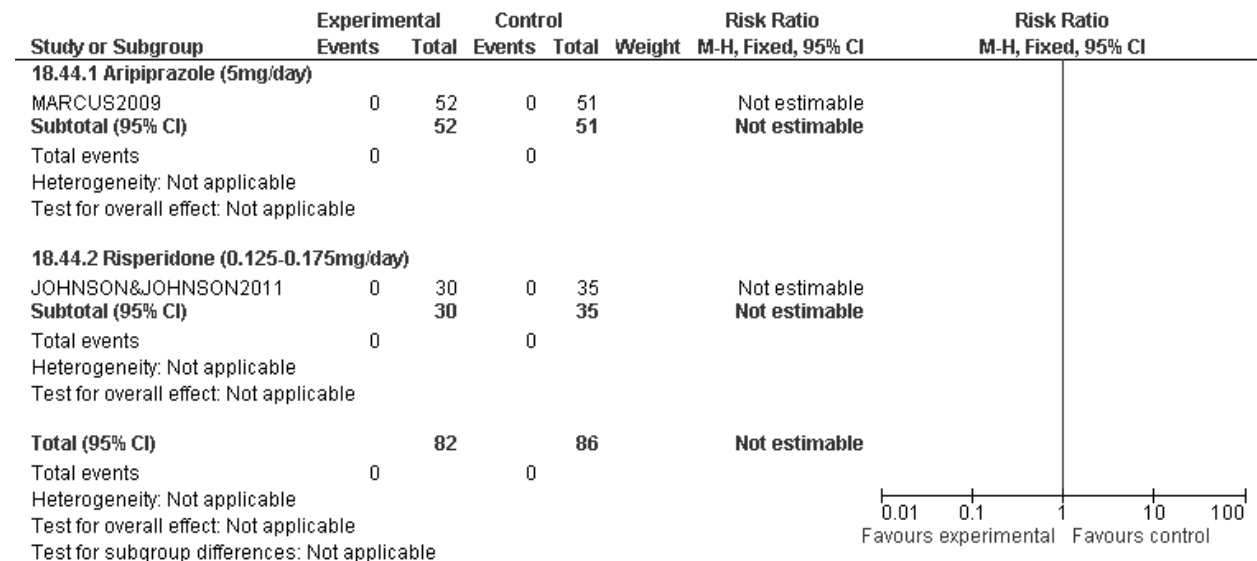
### Nasal congestion



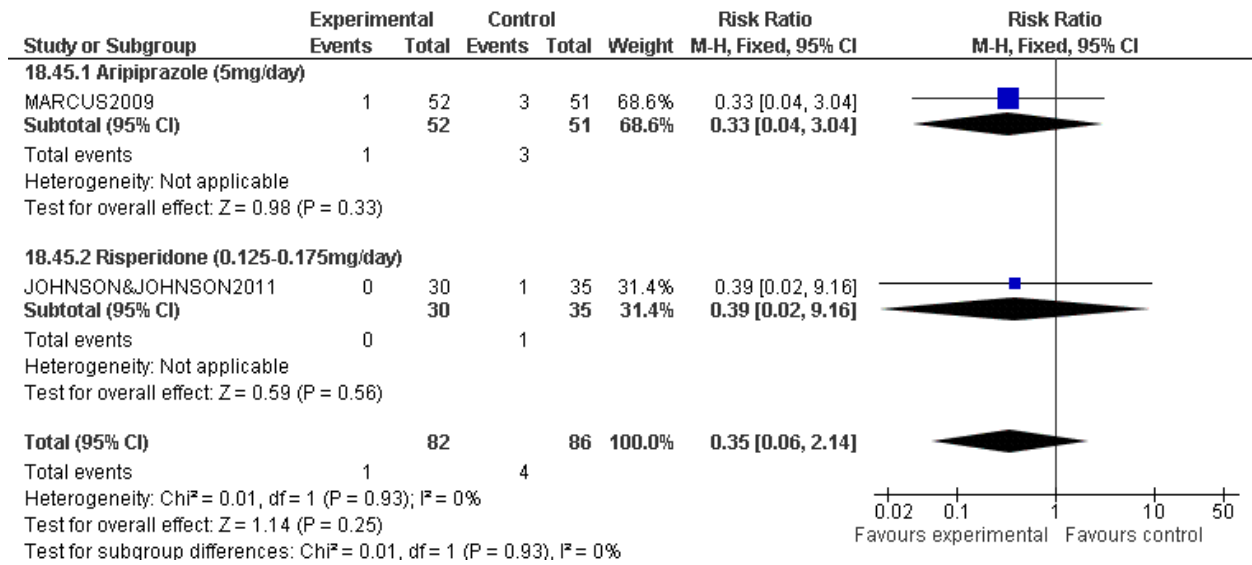
## Nasopharyngitis



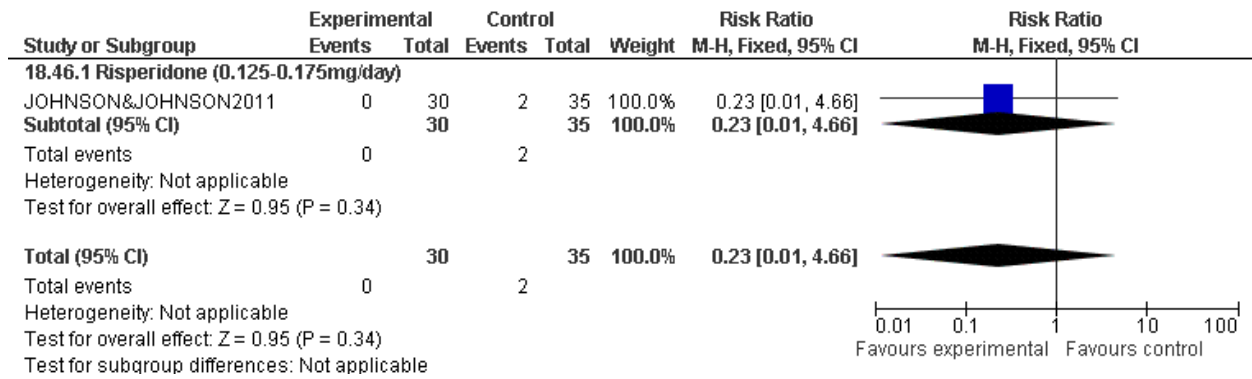
## Nose bleed



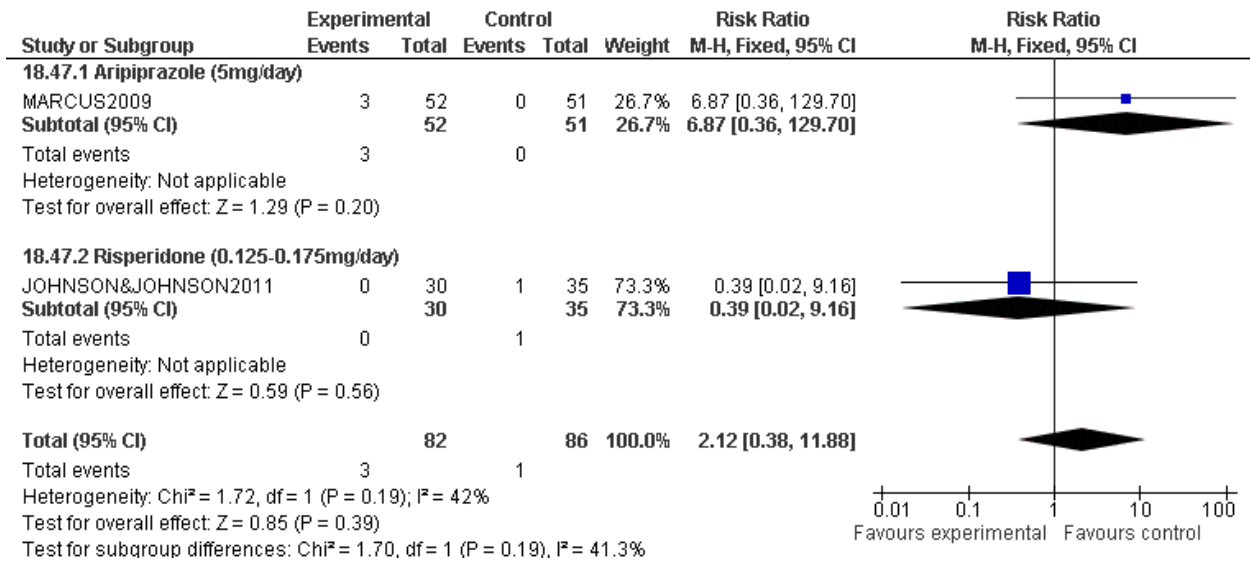
## Akathisia



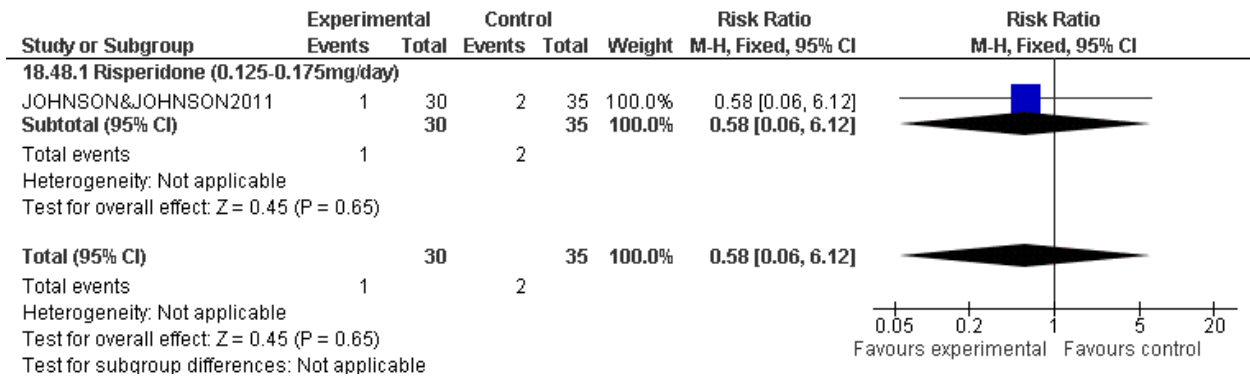
### Insomnia



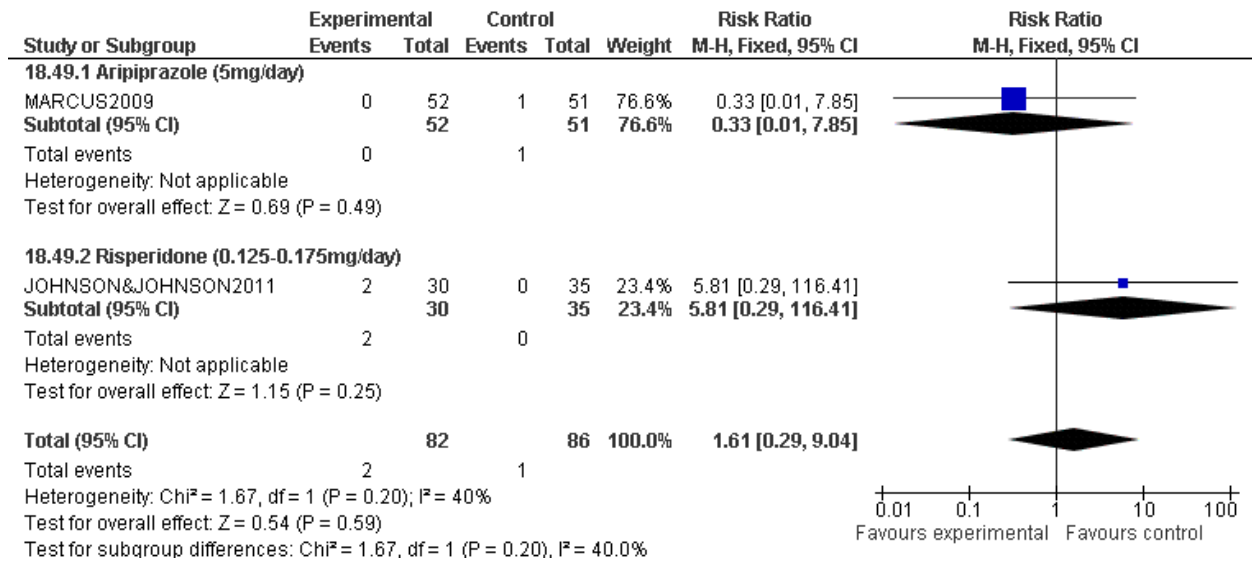
### Hypersomnia



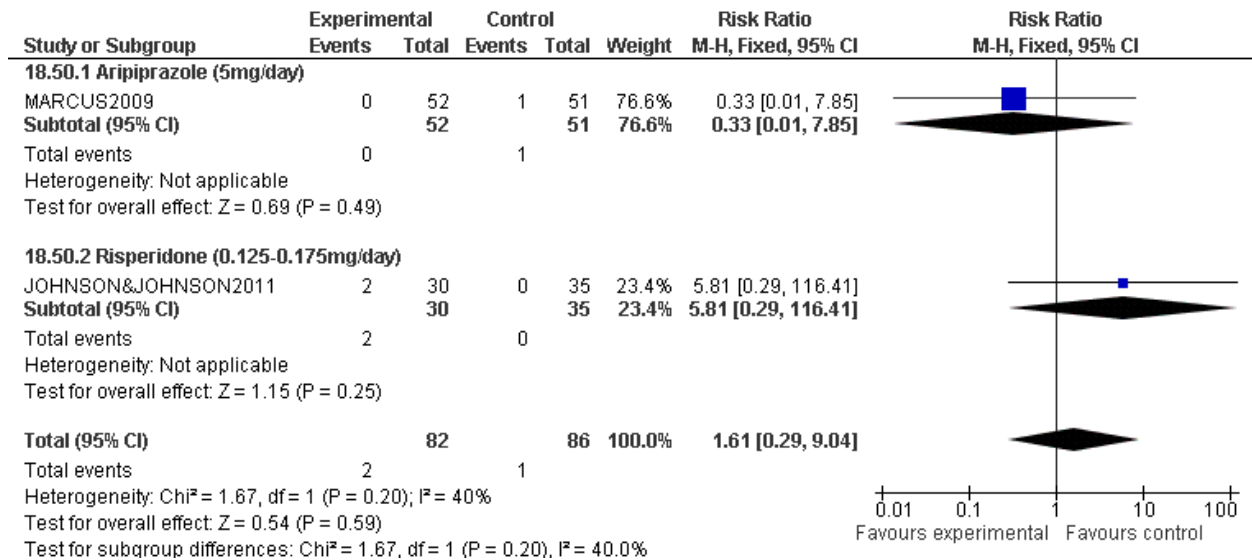
### Psychomotor hyperactivity



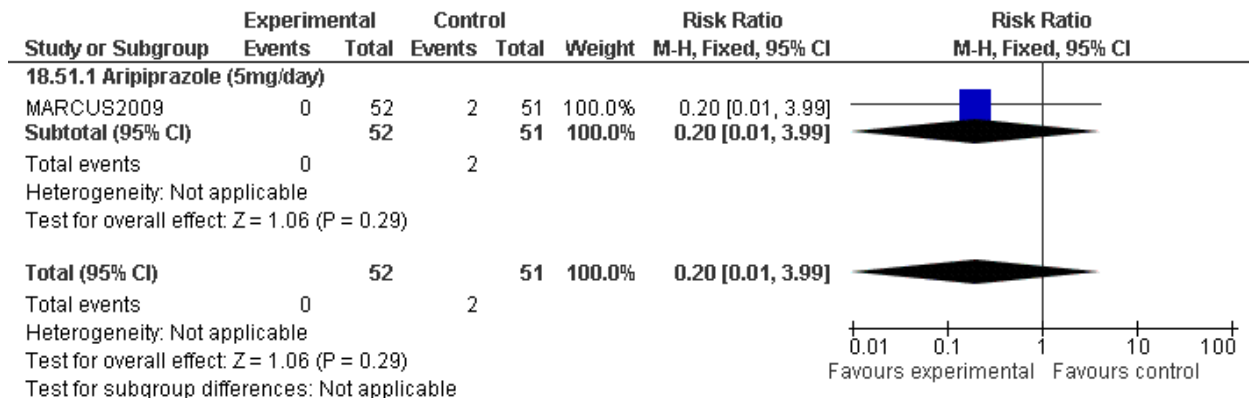
### Enuresis



## Rash

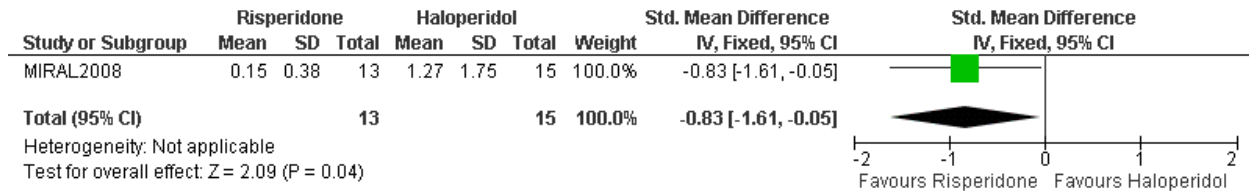


## Clinically relevant prolactin elevation (above upper limit of normal)

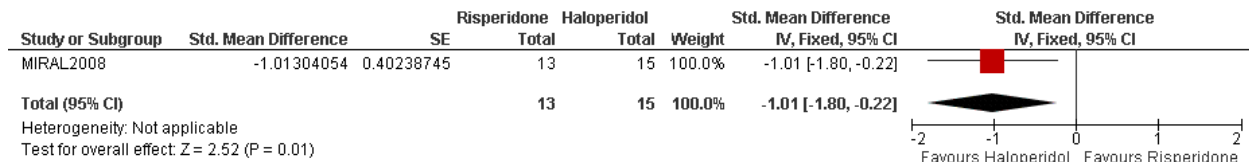


*Adverse events associated with risperidone versus placebo*

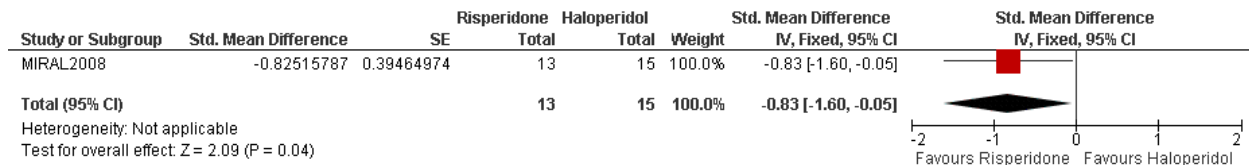
**Treatment-emergent extrapyramidal symptoms**



**Prolactin (change score)**



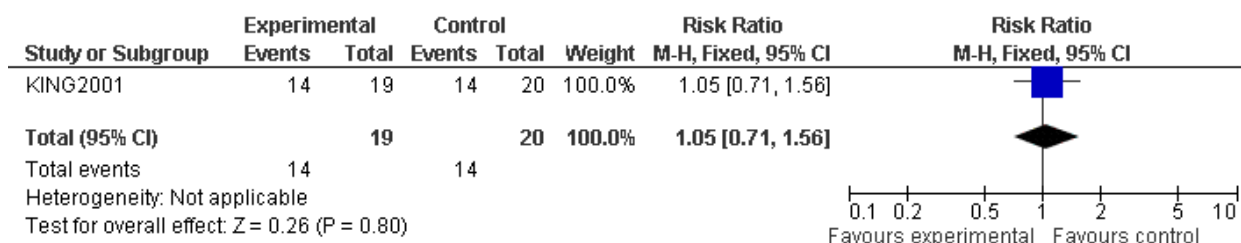
**Liver problems (change in alanine transaminase [ALT])**



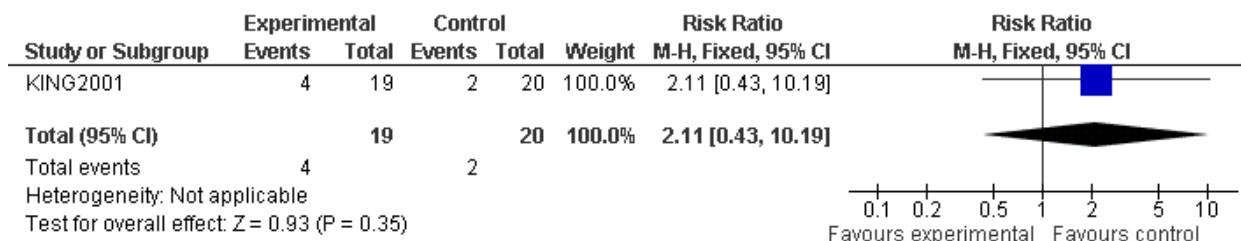
**1.33.6 Adverse events associated with antivirals**

*Adverse events associated with amantadine hydrochloride versus placebo*

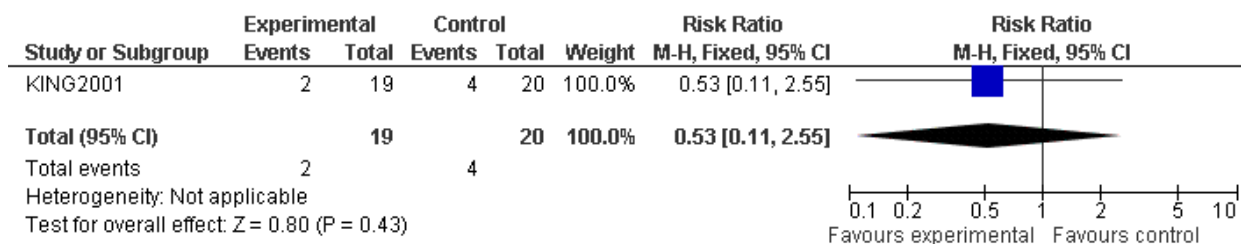
**Any adverse event**



### Insomnia



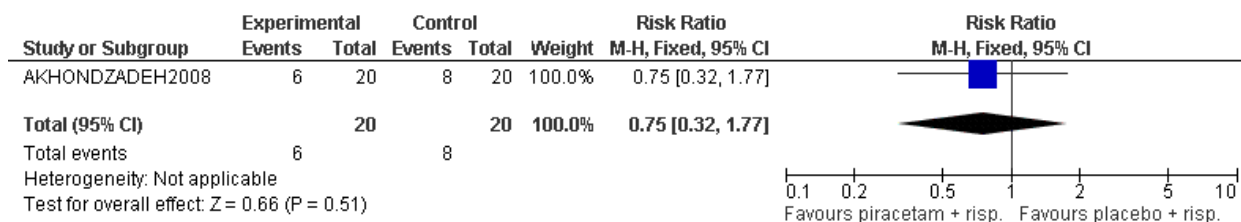
### Antisocial behaviour



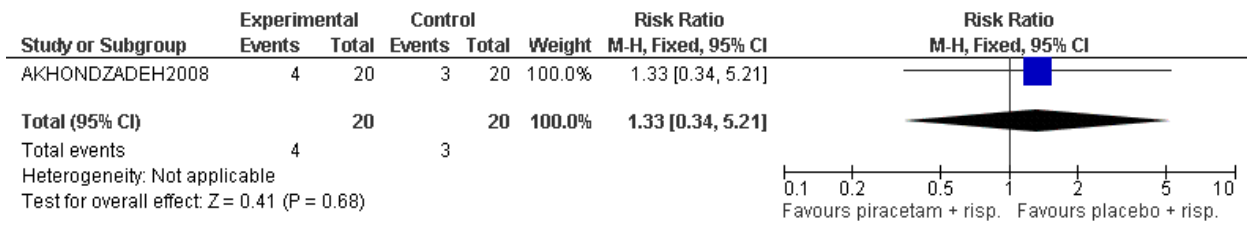
## 1.33.7 Adverse events associated with cognitive enhancers

*Adverse events associated with piracetam and risperidone versus placebo and risperidone*

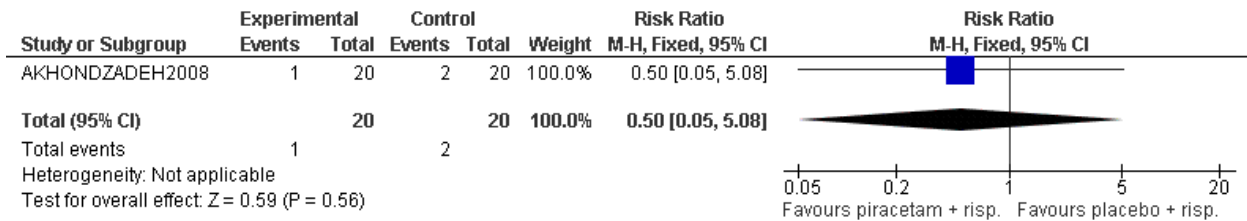
### Any treatment-emergent extrapyramidal symptom



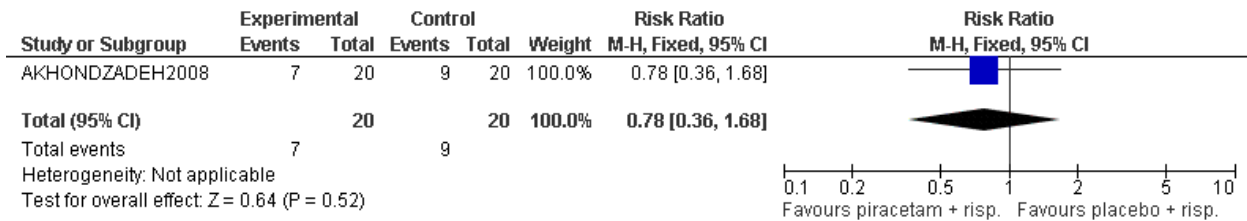
### Constipation



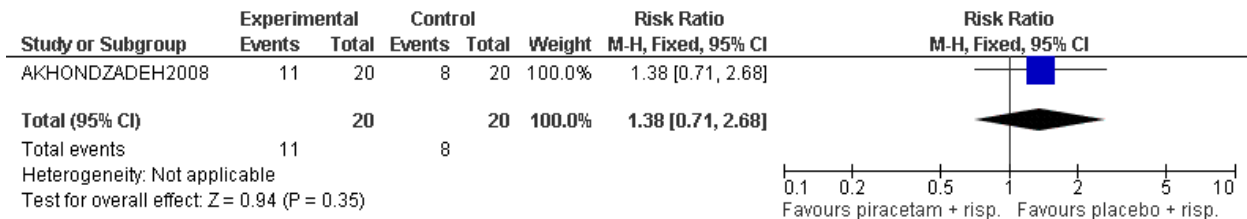
### Nervousness



### Day time drowsiness

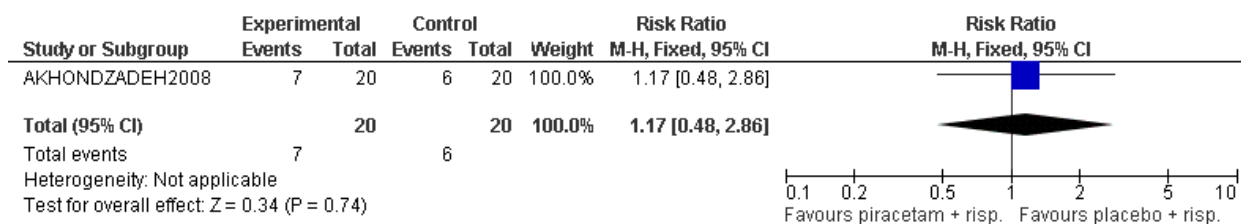


### Morning drowsiness

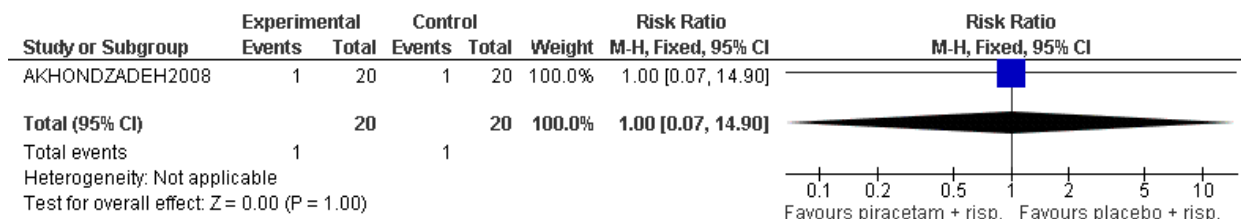


### Increased appetite

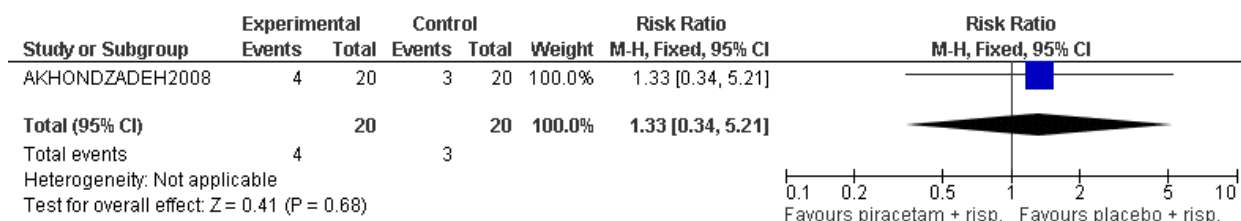




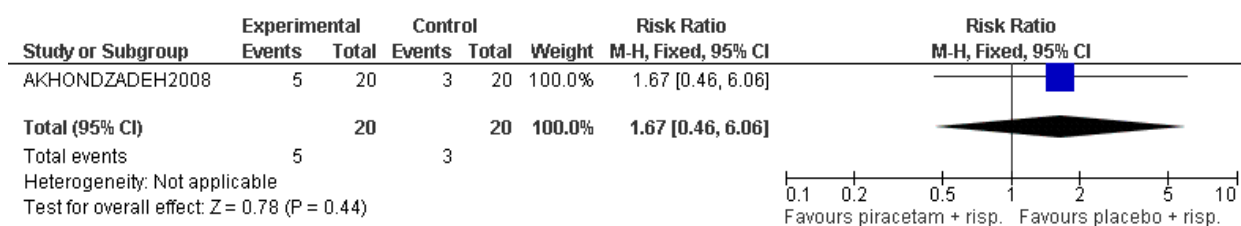
## Loss of appetite



## Dry mouth



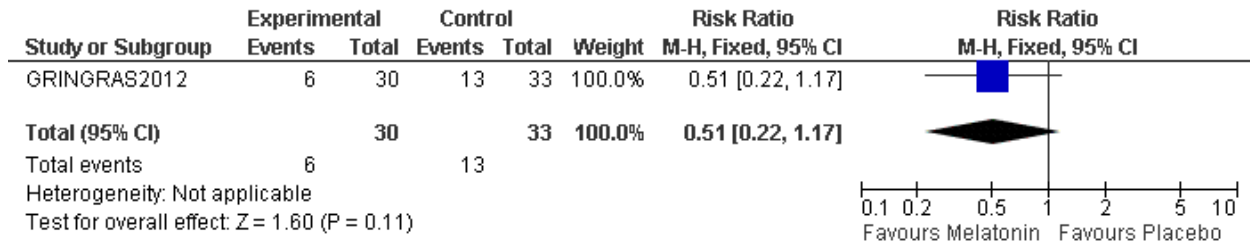
## Fatigue



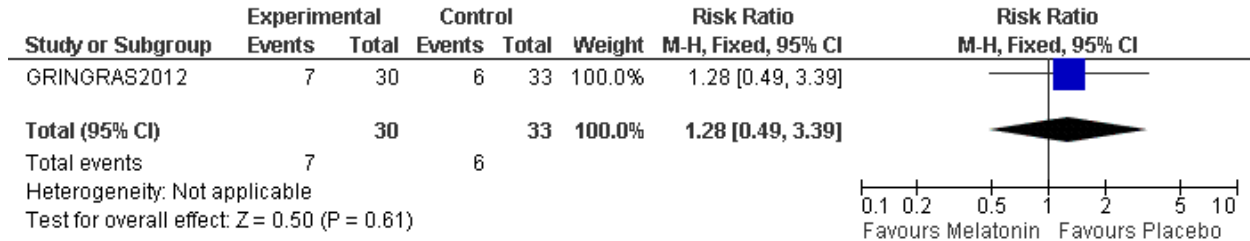
### 1.33.8 Adverse events associated with melatonin

#### *Adverse events associated with melatonin versus placebo*

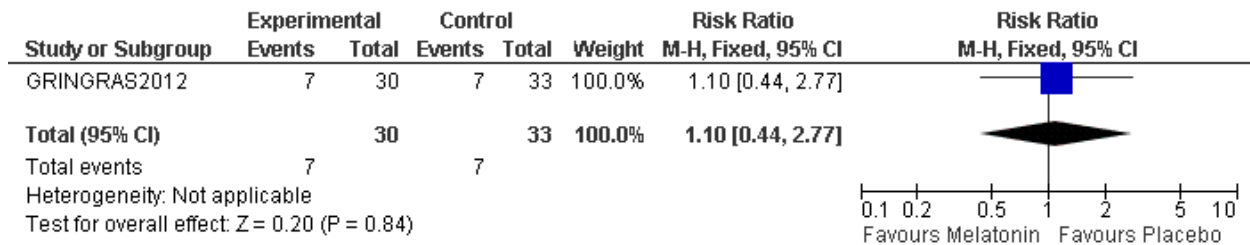
#### Coughing



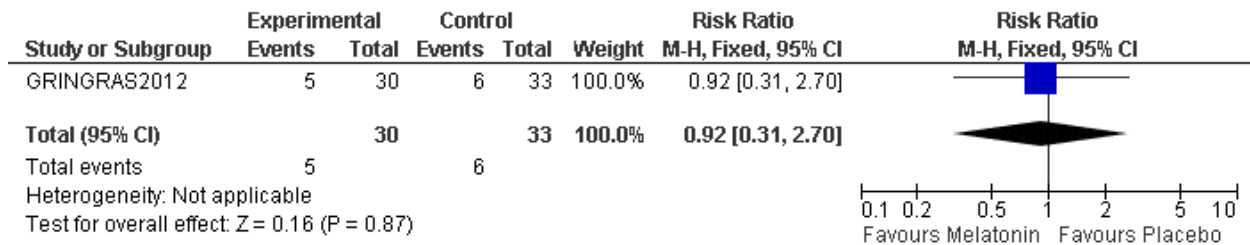
### Mood swings



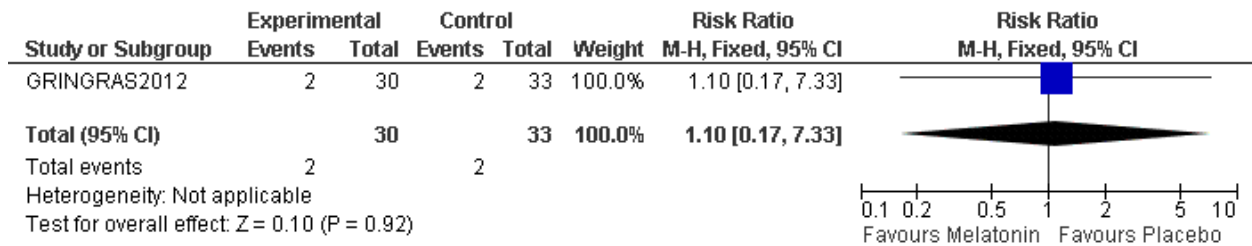
### Vomiting



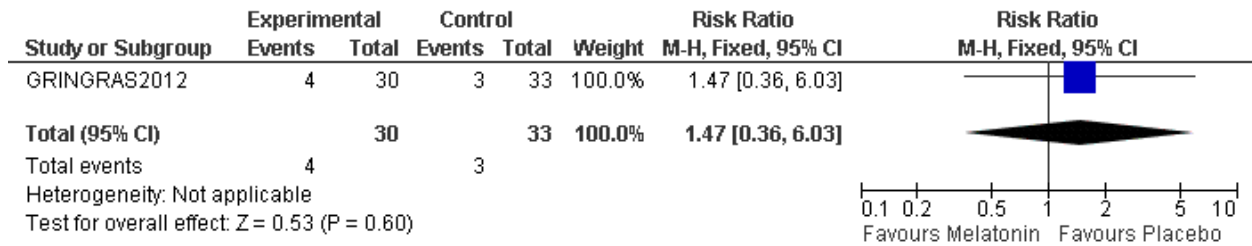
### Increased excitability



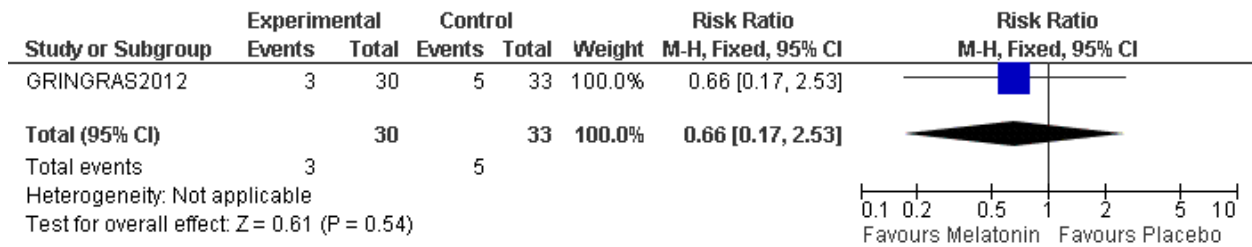
### Headache



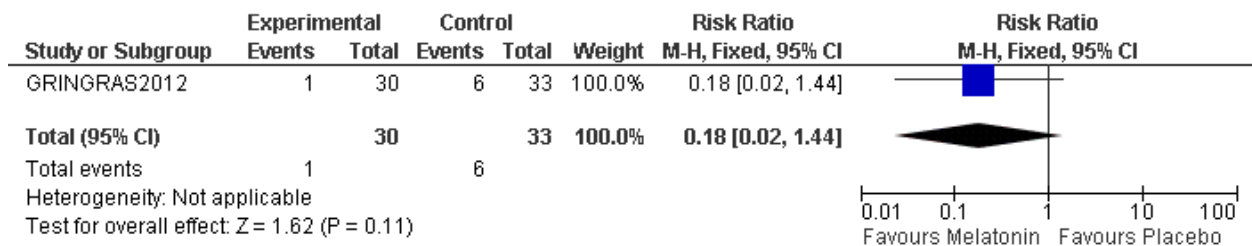
### Rash



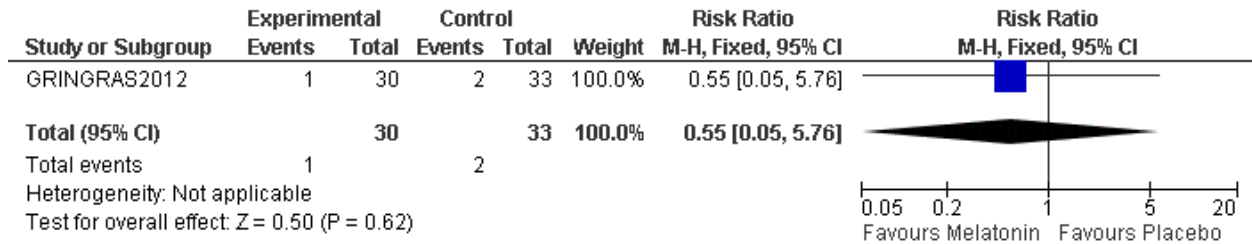
### Somnolence



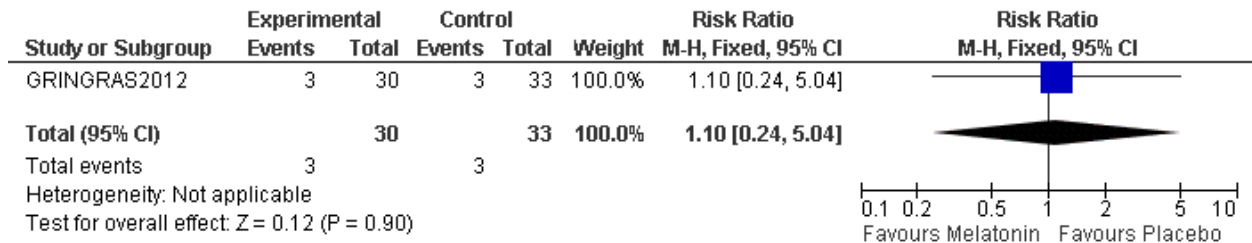
### Fatigue



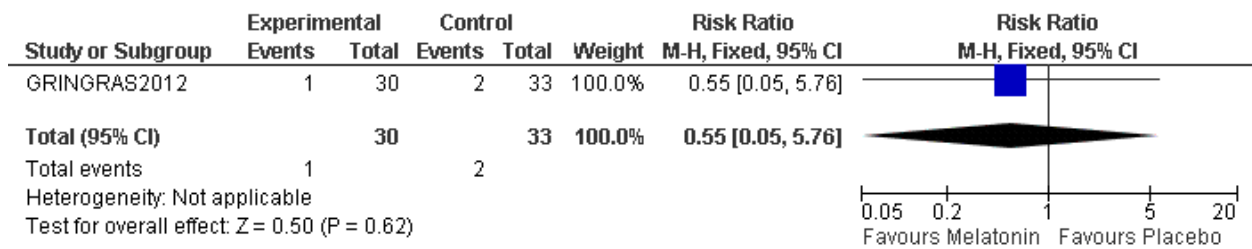
### Hypothermia



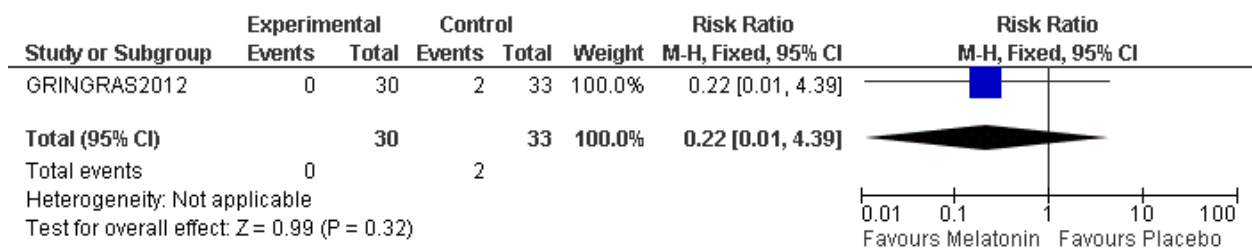
### Increased activity



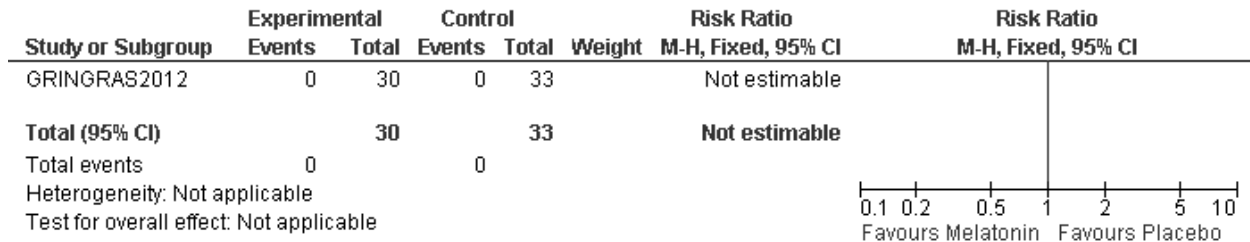
### Nausea



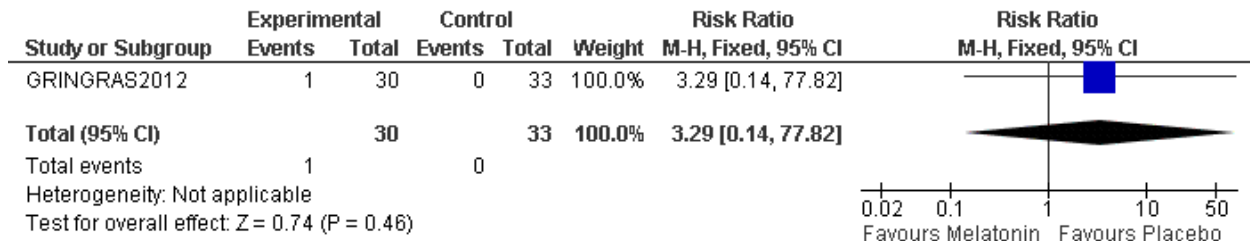
### Dizziness



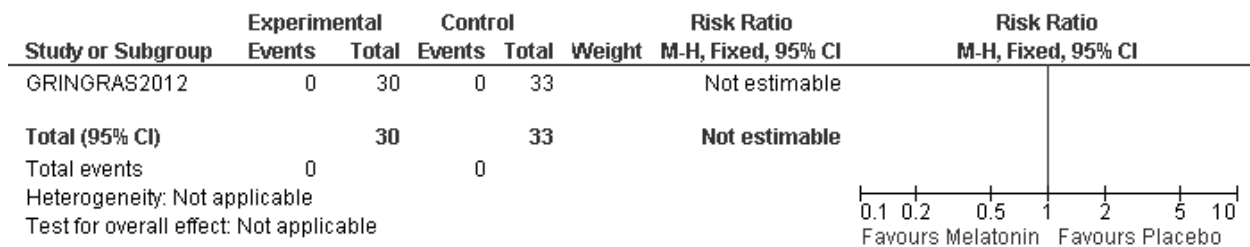
### Breathlessness



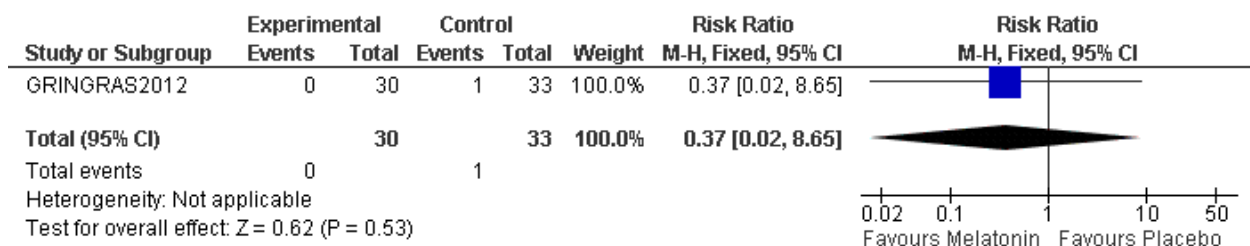
### Hung-over feeling



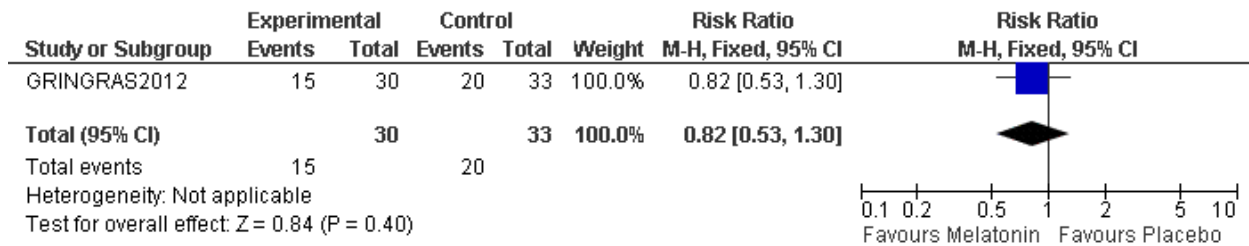
### Tremor



### Seizures



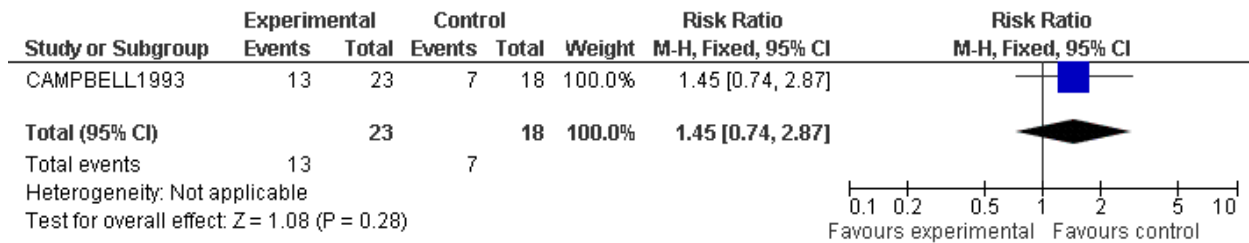
### Other



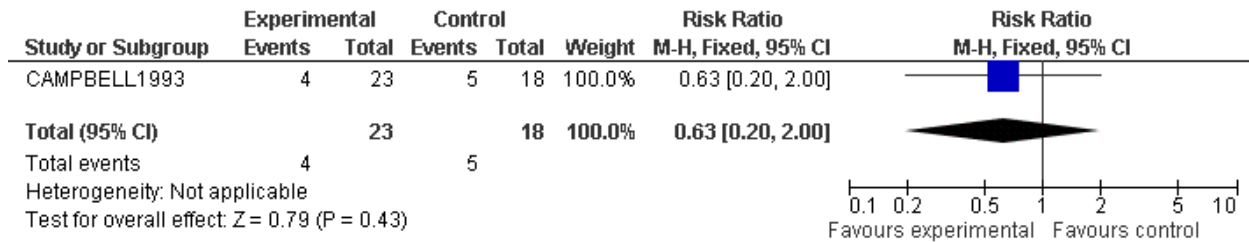
### 1.33.9 Adverse events associated with opioid antagonists

#### *Adverse events associated with naltrexone versus placebo*

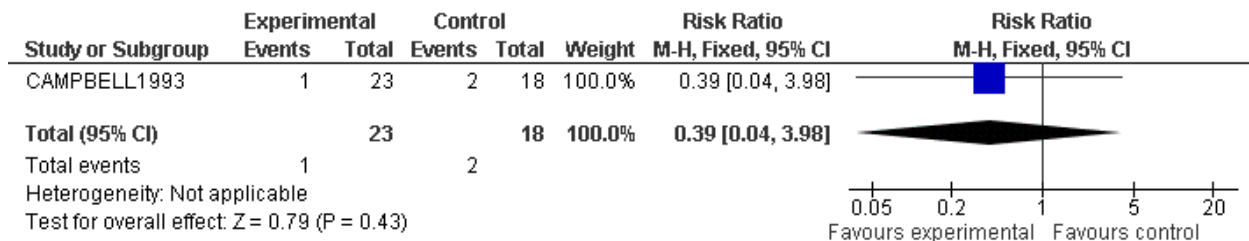
##### Any side effect



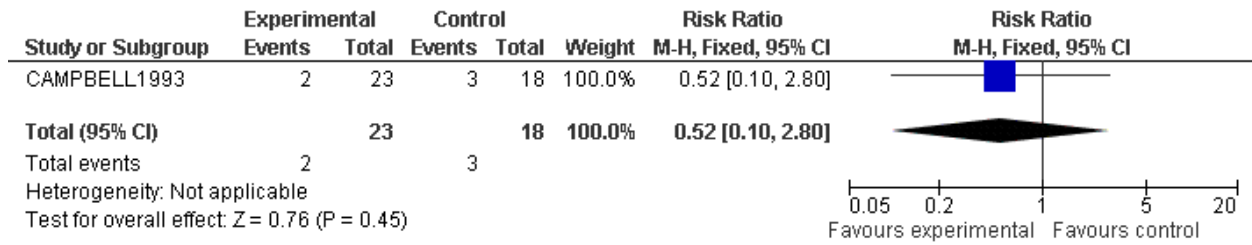
##### Aggressiveness



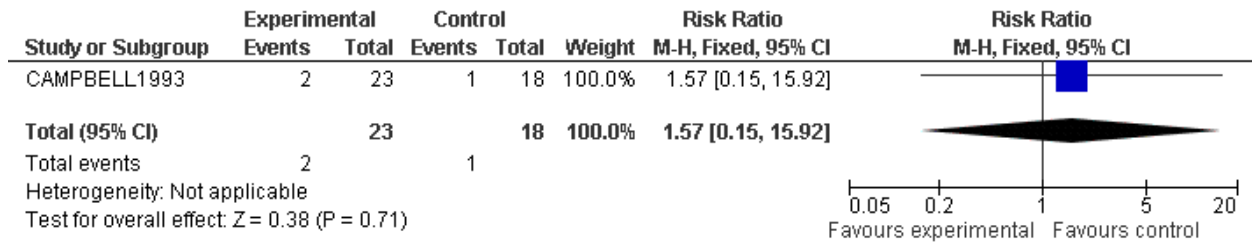
##### Self-injurious behaviour



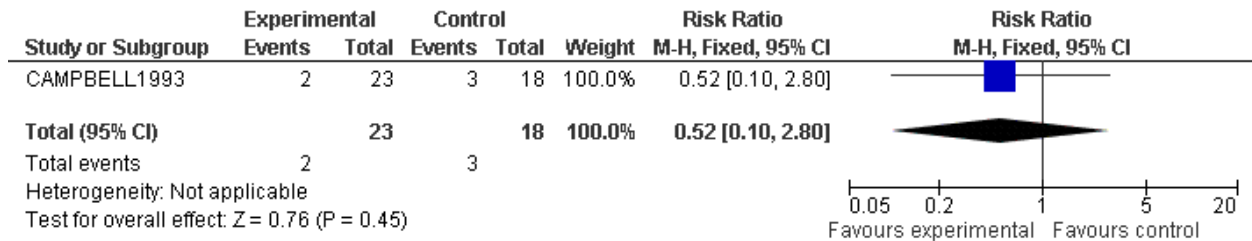
### Hyperactivity



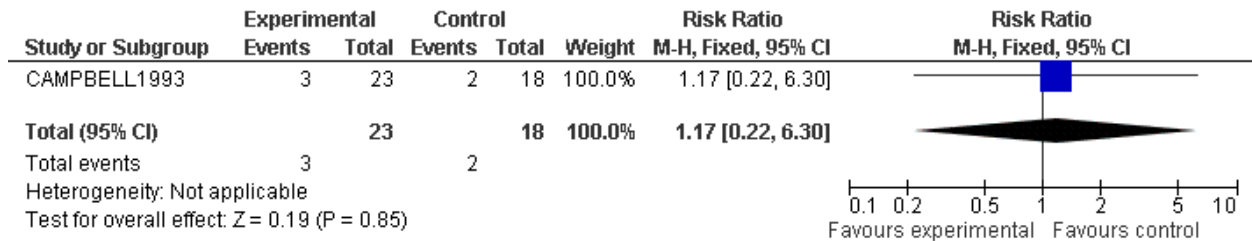
### Temper tantrums



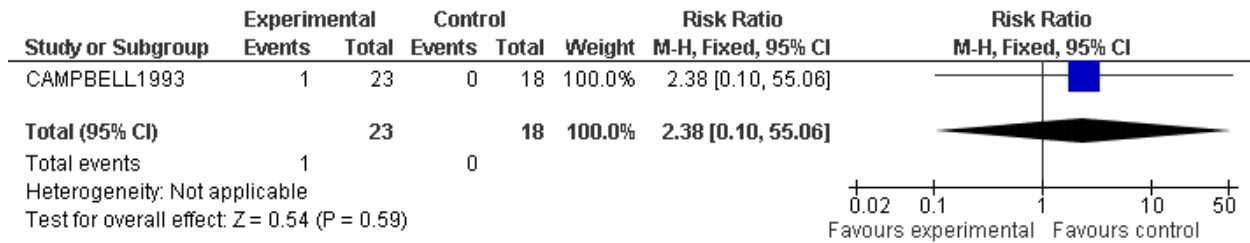
### Stereotypes



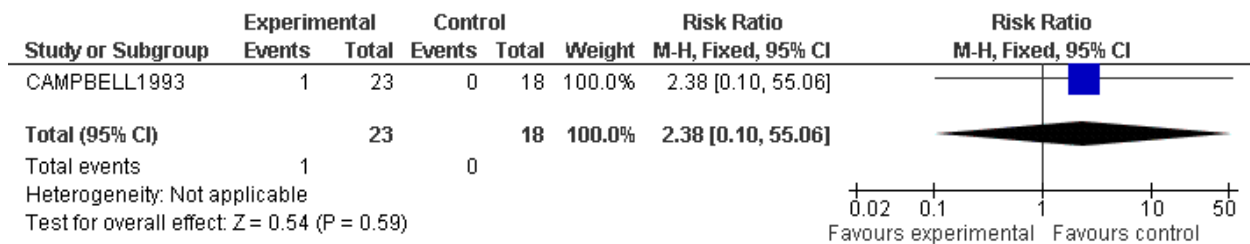
### Irritability



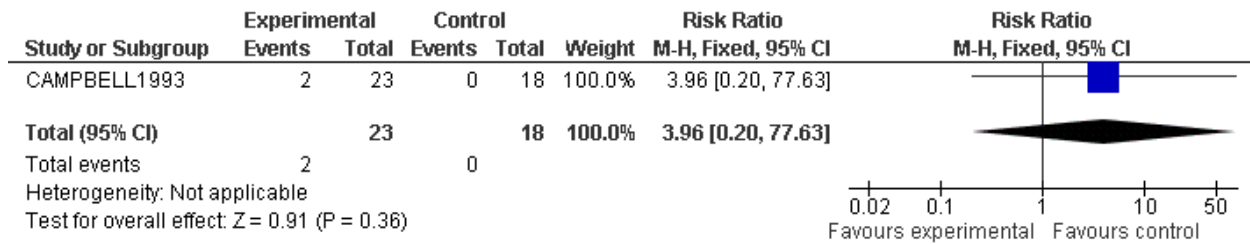
### Decreased verbal production (transient)



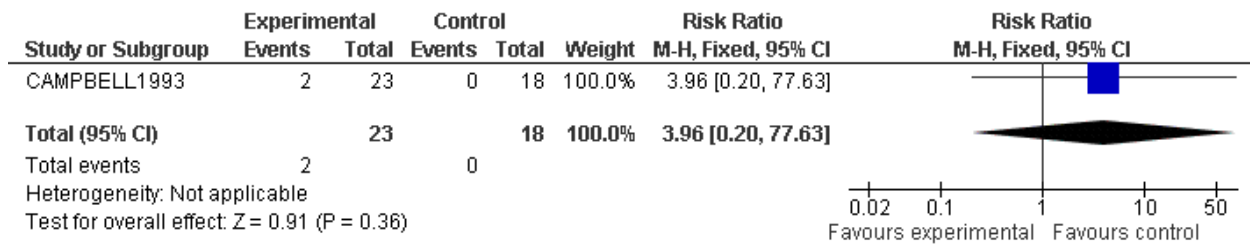
### Slight sleepiness



### Falling asleep

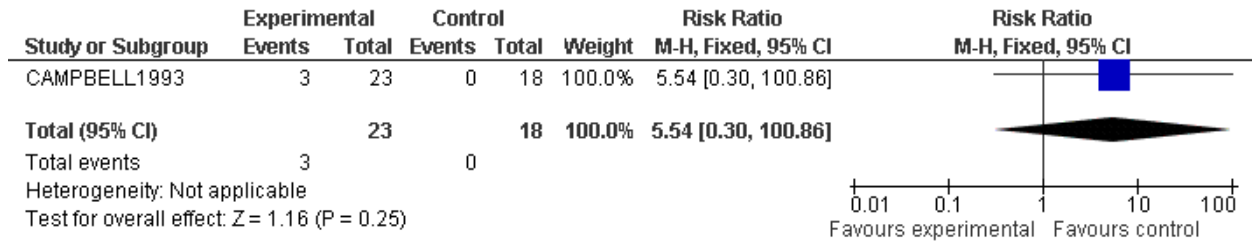


### Decreased appetite



### Vomiting

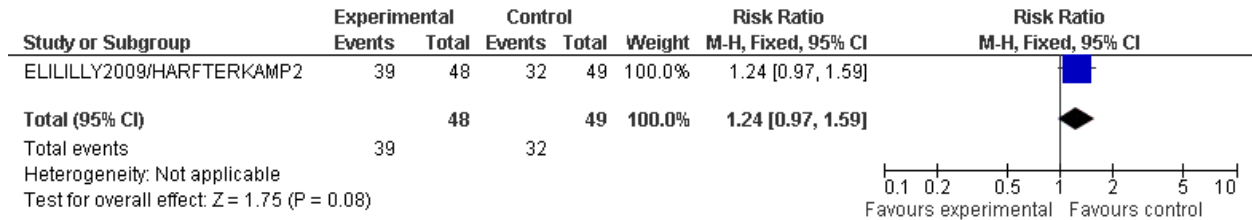




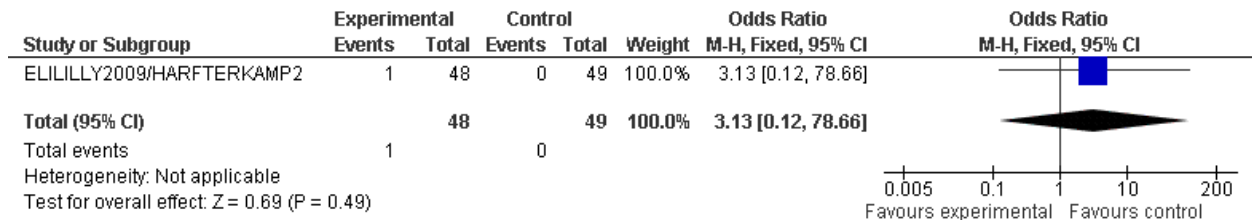
### 1.33.10 Adverse events associated with SNRIs

#### *Adverse events associated with atomoxetine versus placebo*

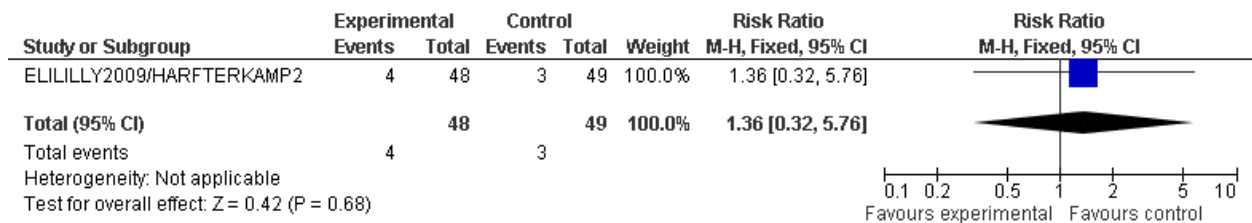
##### Any adverse event



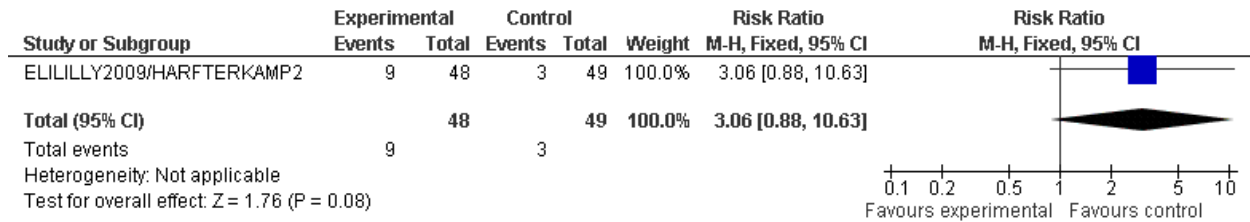
##### Discontinuation due to adverse events



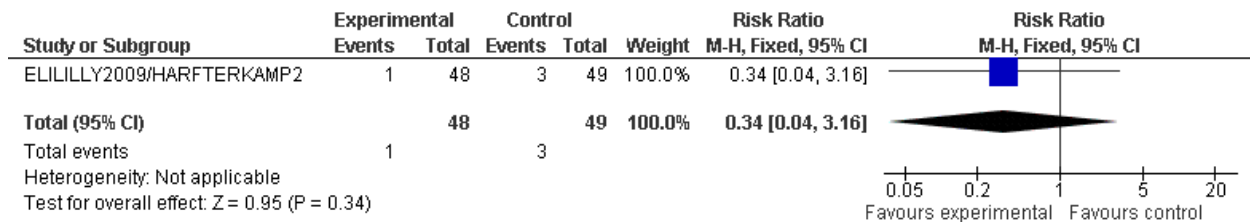
##### Abdominal pain



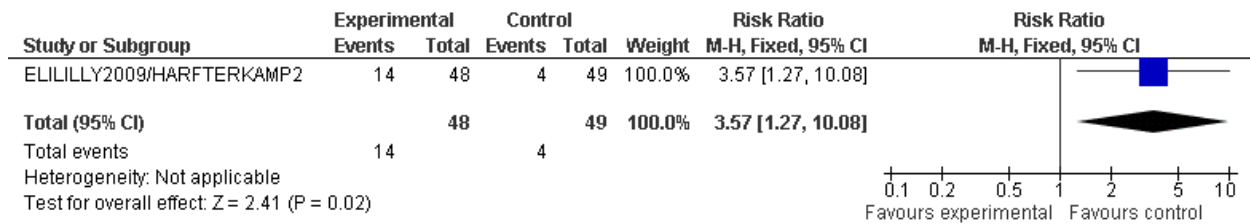
## Upper abdominal pain



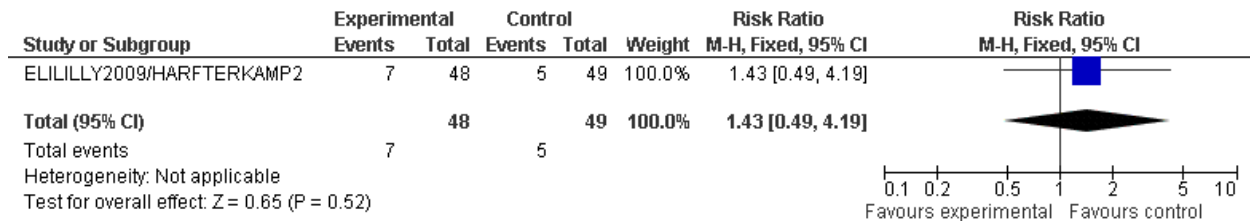
## Diarrhoea



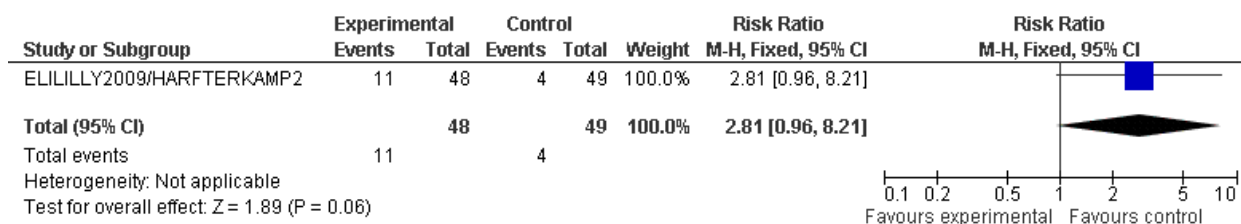
## Nausea



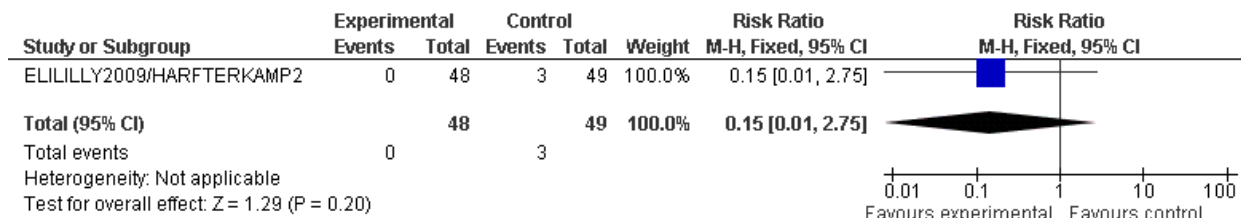
## Vomiting



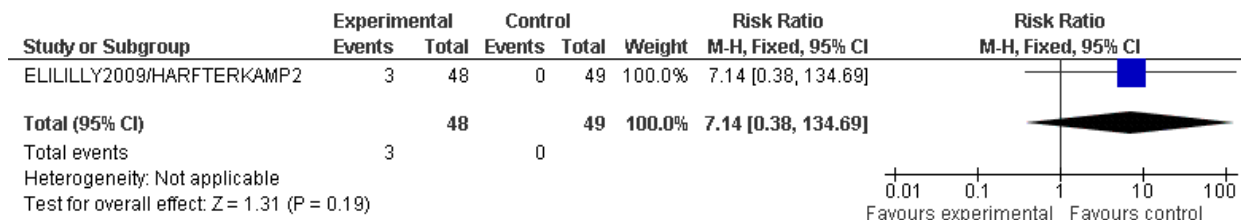
## Fatigue



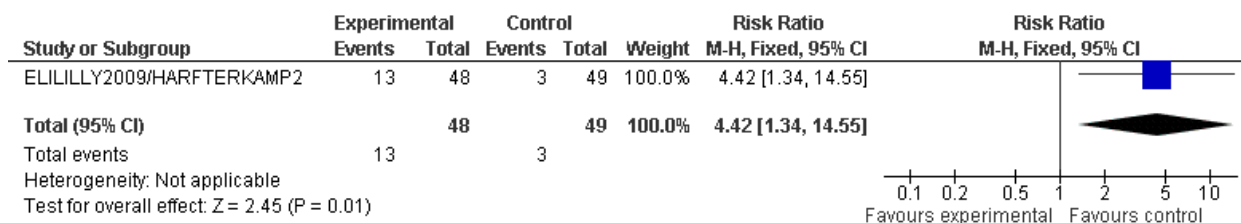
### Pyrexia



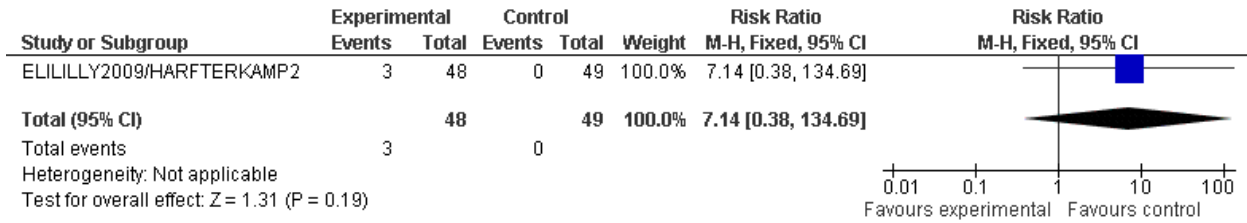
### Influenza



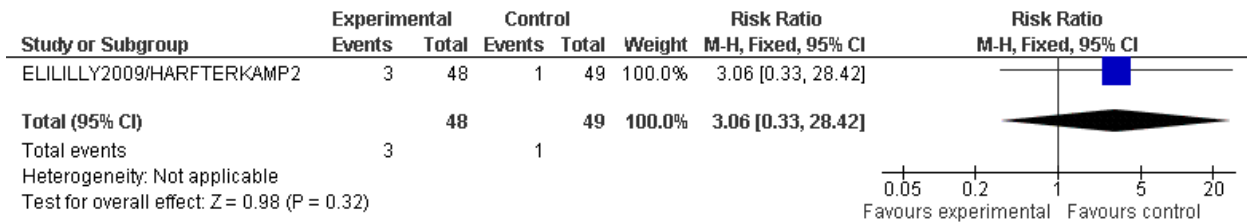
### Deceased appetite



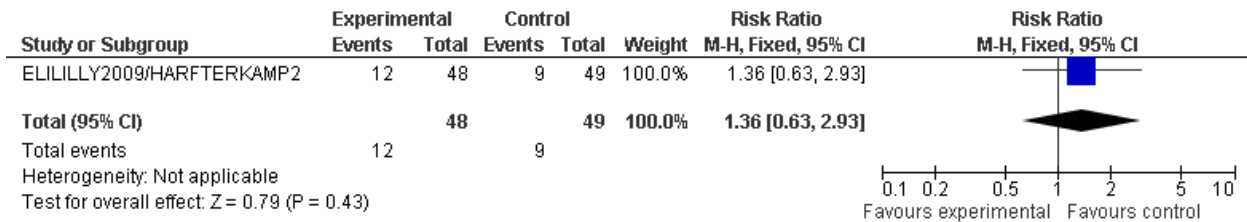
### Myalgia



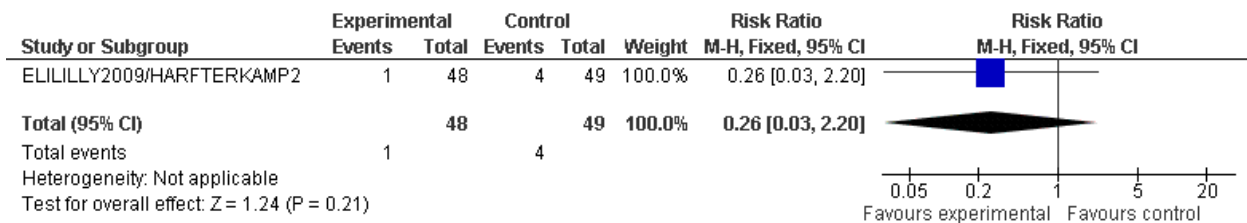
### Dizziness



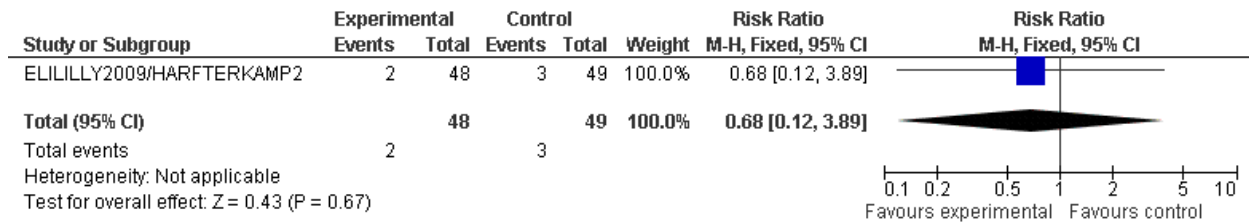
### Headache



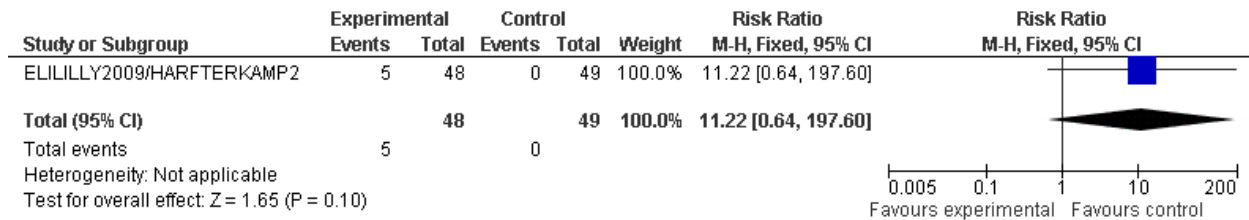
### Psychomotor hyperactivity



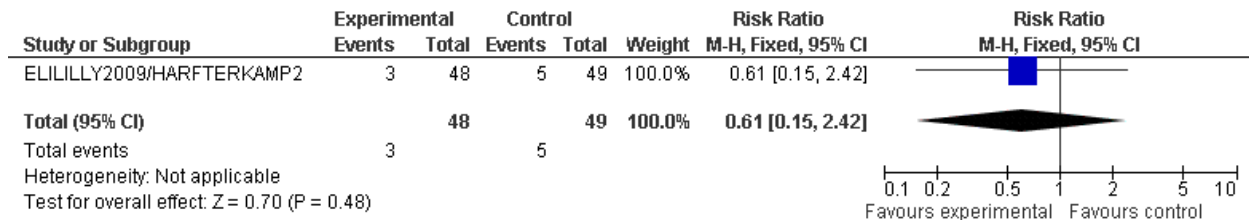
### Aggression



### Early morning awakening



### Initial insomnia

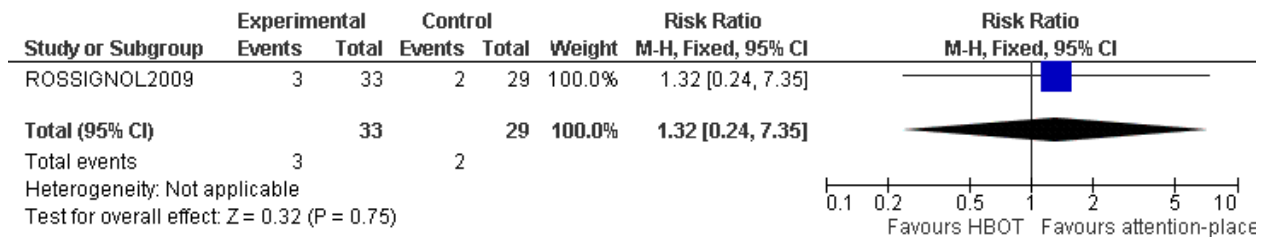


## 1.34 ADVERSE EVENTS ASSOCIATED WITH BIOMEDICAL INTERVENTIONS

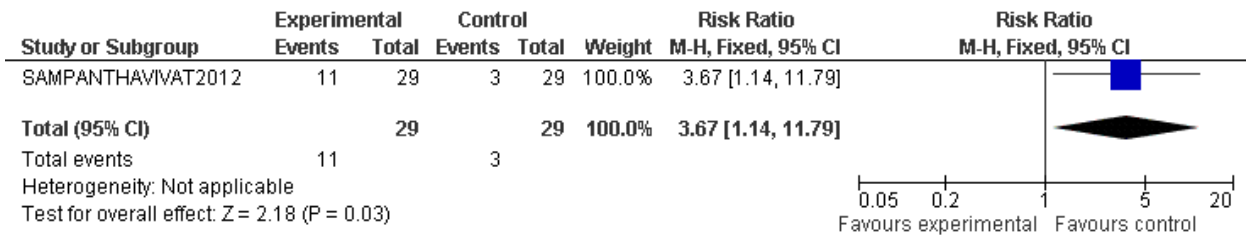
### 1.34.1 Adverse events associated with medical procedures

#### *Adverse events associated with HBOT versus attention-placebo*

#### Any adverse event



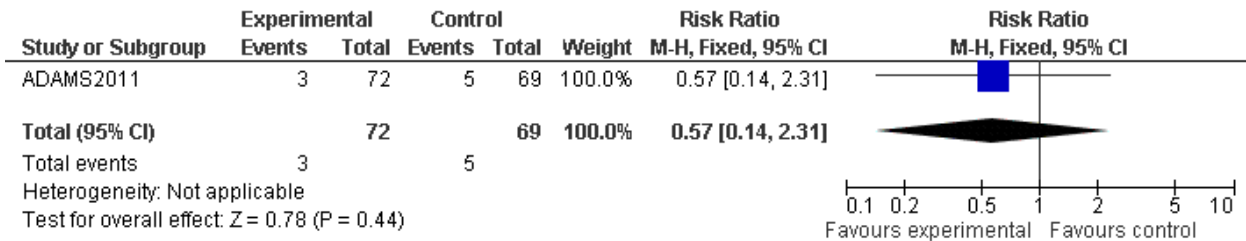
### Minor-grade ear barotrauma



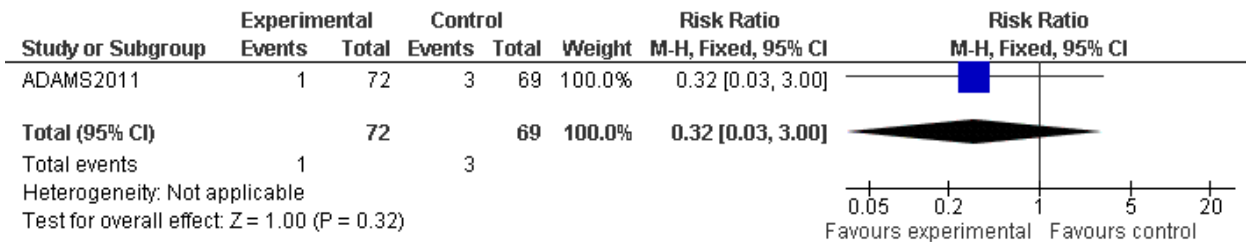
## 1.34.2 Adverse events associated with nutritional interventions

### *Adverse events associated with multivitamin/mineral supplement versus placebo*

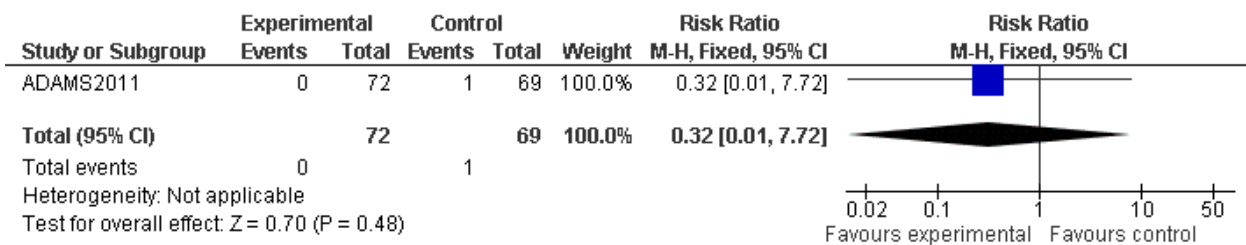
#### Discontinuation due to adverse events



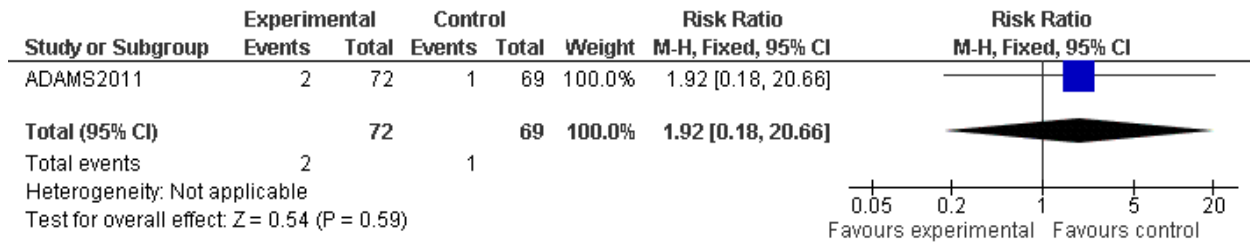
#### Discontinuation due to diarrhoea



#### Discontinuation due to increased stimming

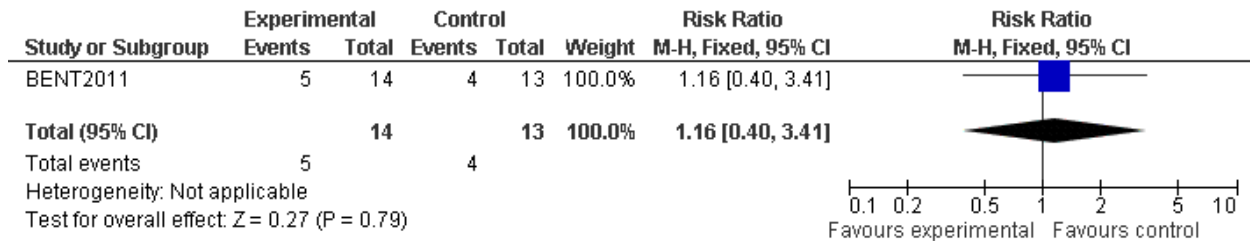


### Discontinuation due to behaviour problems

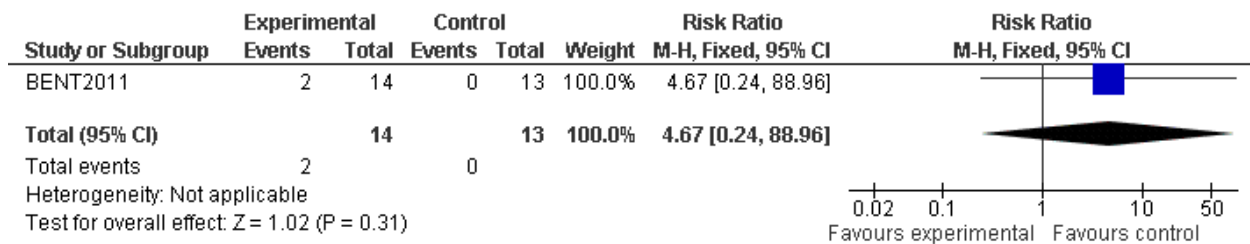


### Adverse events associated with omega-3 fatty acids versus placebo

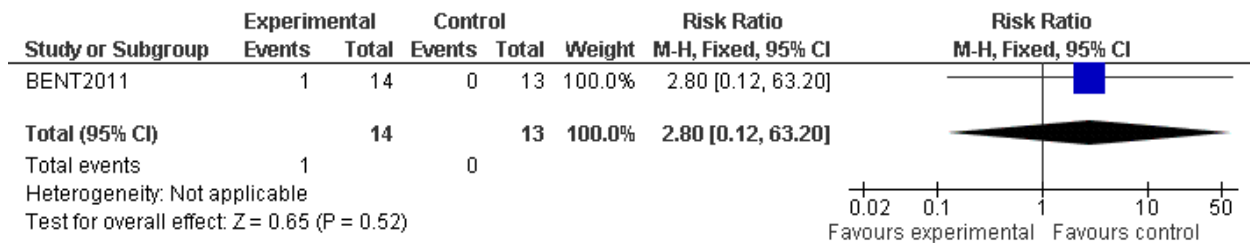
#### Any adverse event



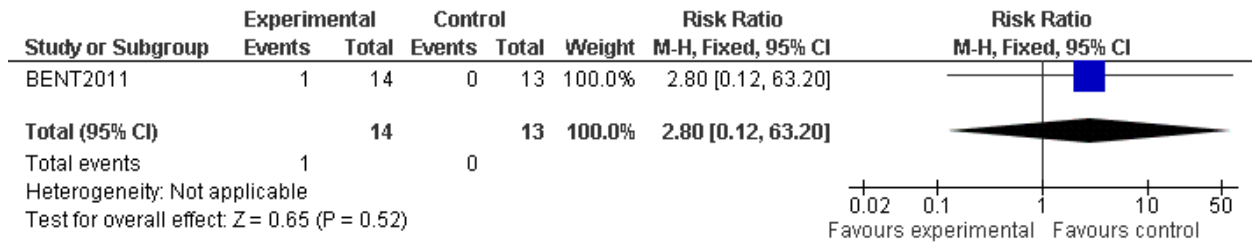
#### Rash



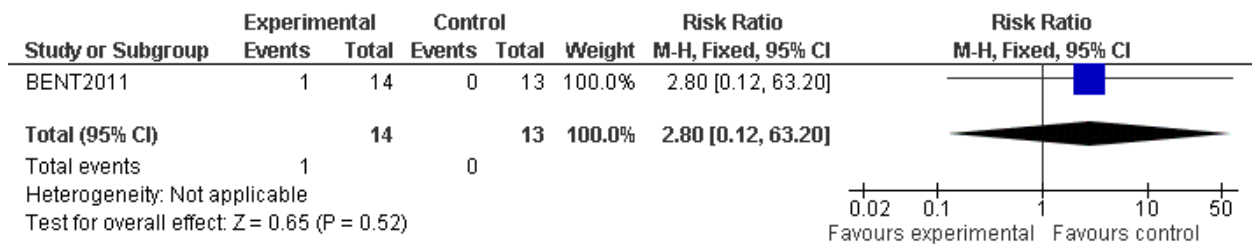
#### Upper respiratory infection



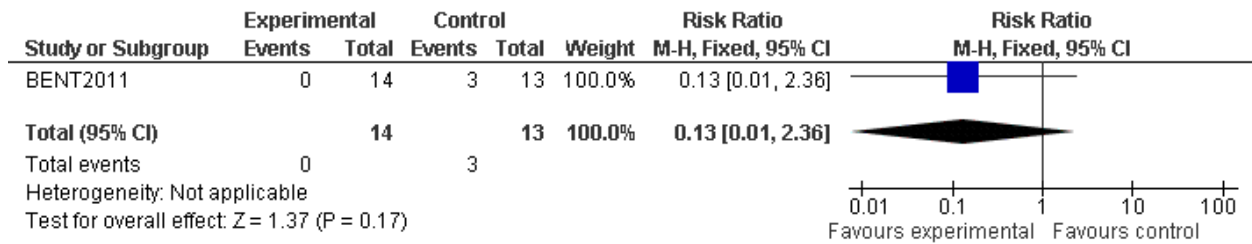
### Nose bleeds



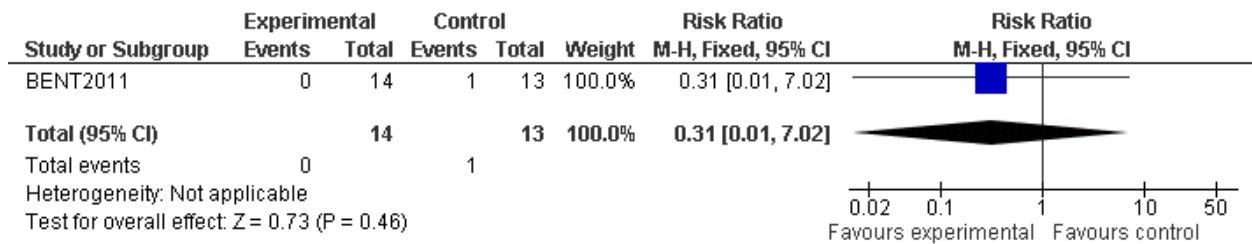
### GI symptoms



### Hyperactivity



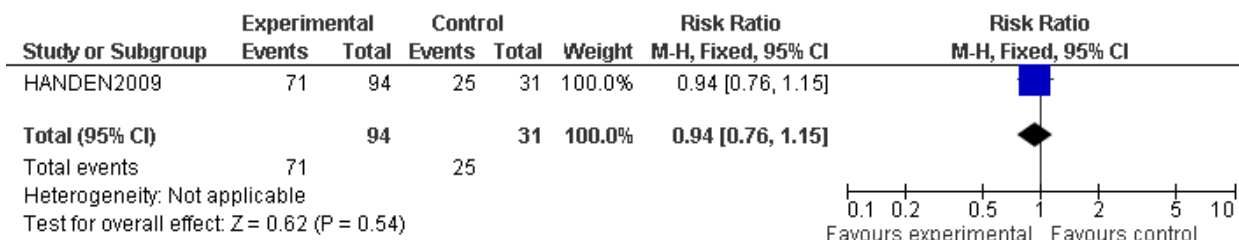
### Self-stimulatory behaviour



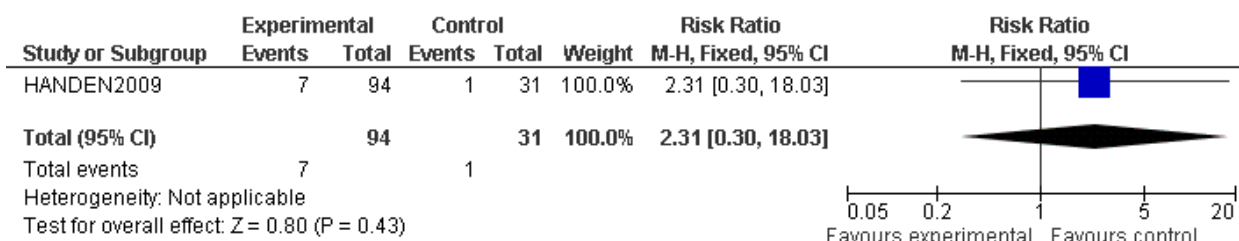


*Adverse events associated with immunoglobulin (dosages combined) versus placebo*

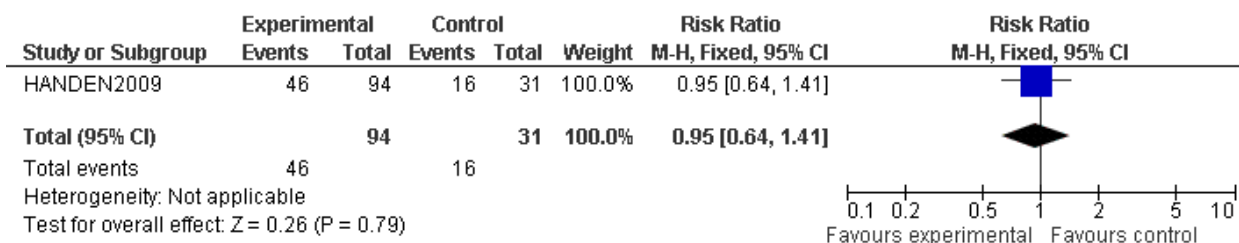
**Any side effect**



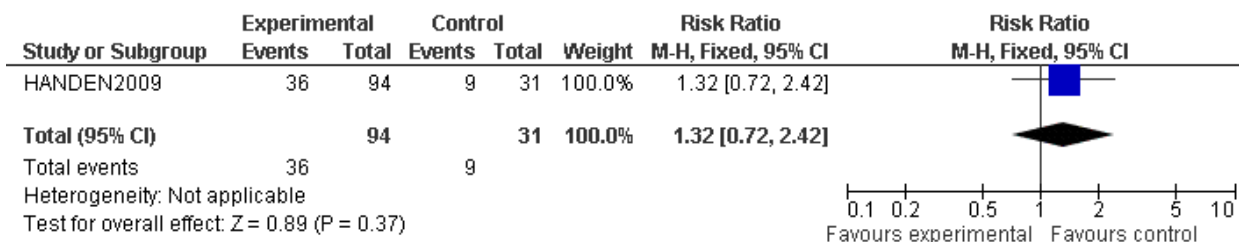
**Discontinuation due to adverse events**



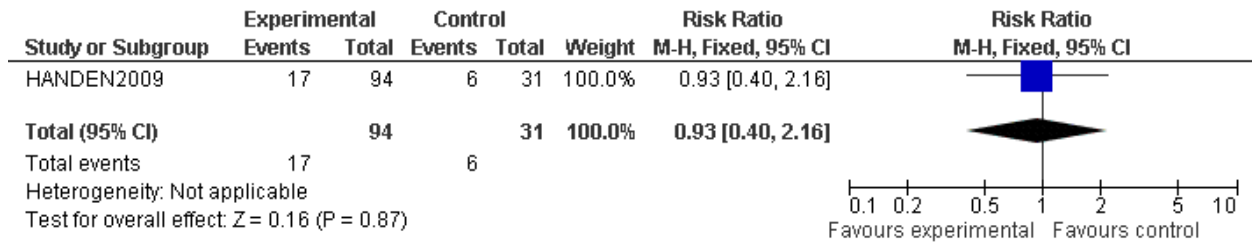
**Infections or infestations**



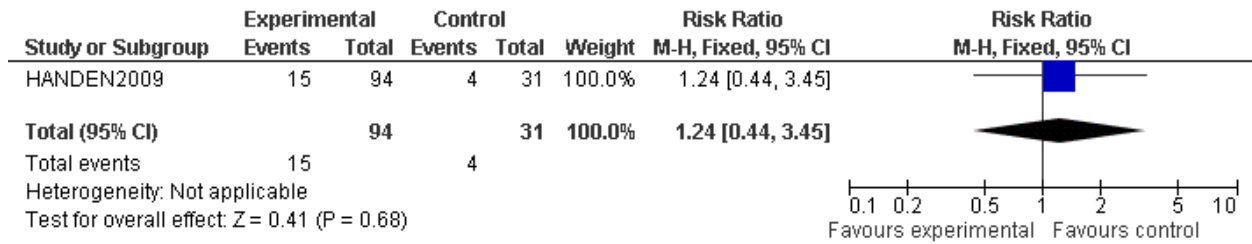
**Gastrointestinal disorders**



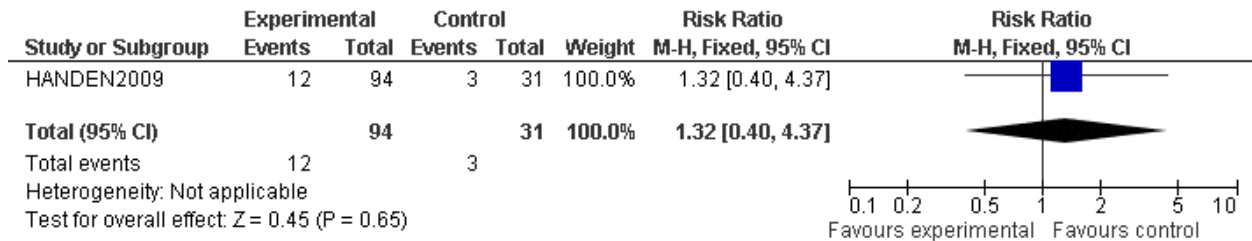
**Psychiatric disorders**



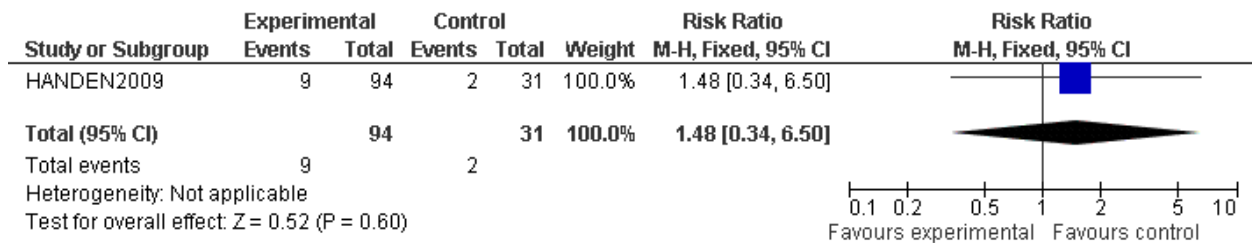
**Respiratory, thoracic or mediastinal disorders**



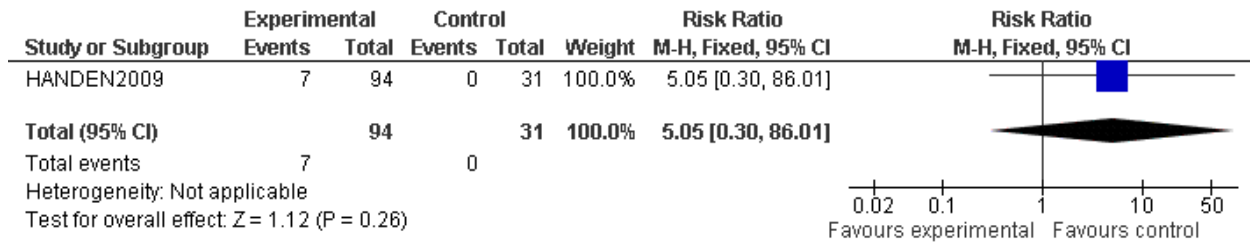
**Skin or subcutaneous tissue disorders**



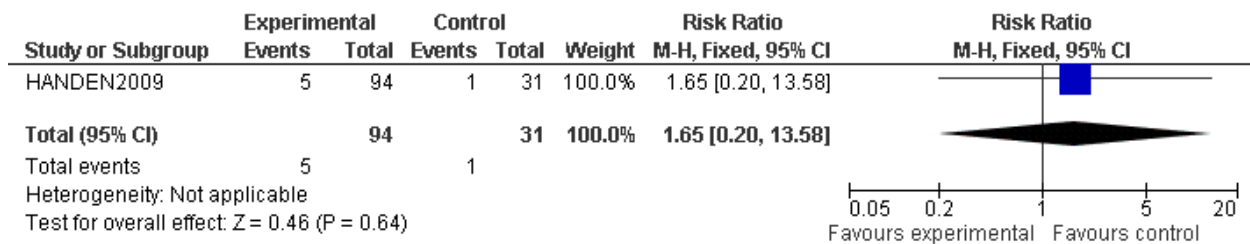
**General disorders or administration site conditions**



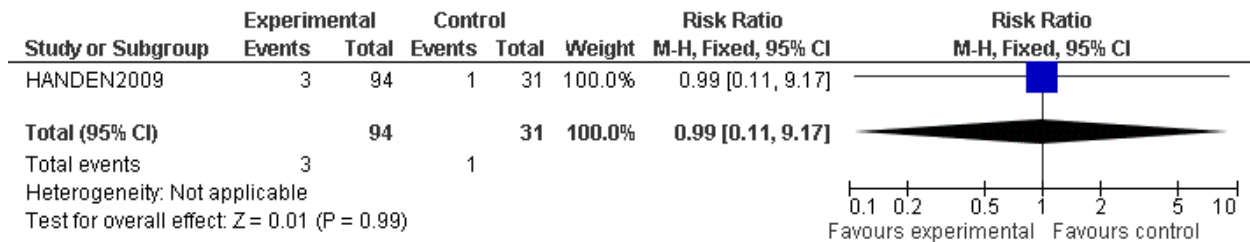
### Nervous system disorders



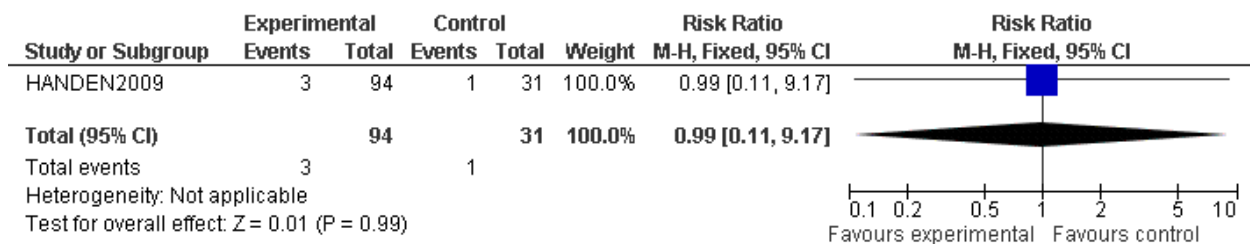
### Injury, poisoning or procedural complications



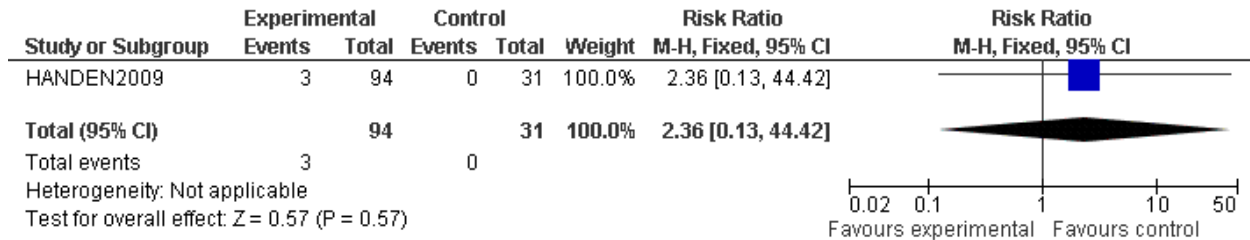
### Investigations



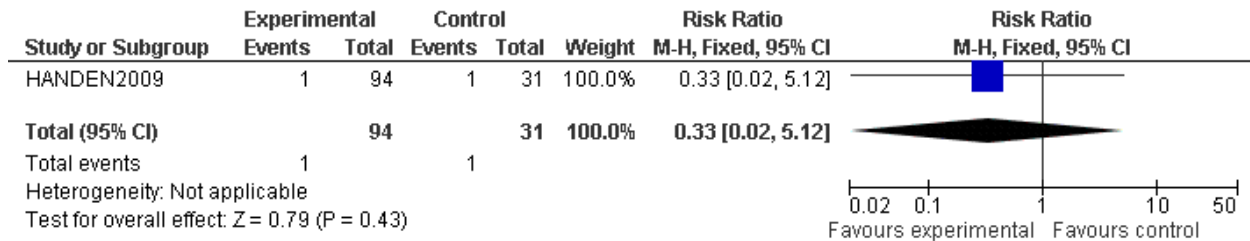
### Metabolism or nutrition disorders



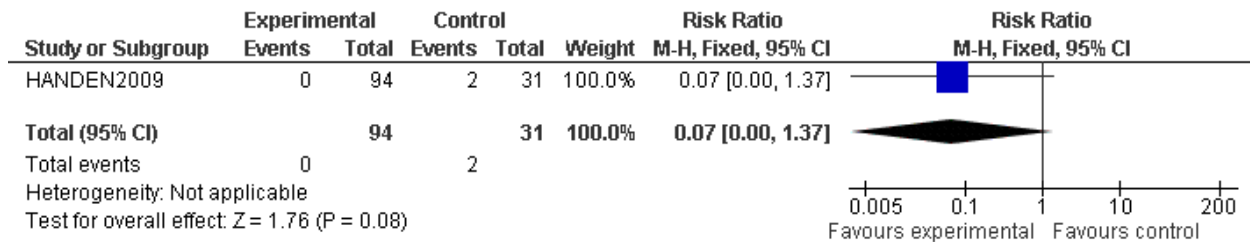
### Eye disorders



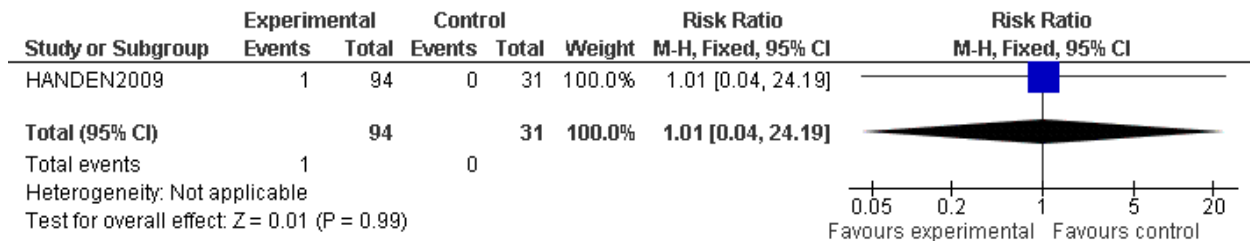
### Blood or lymphatic system disorders



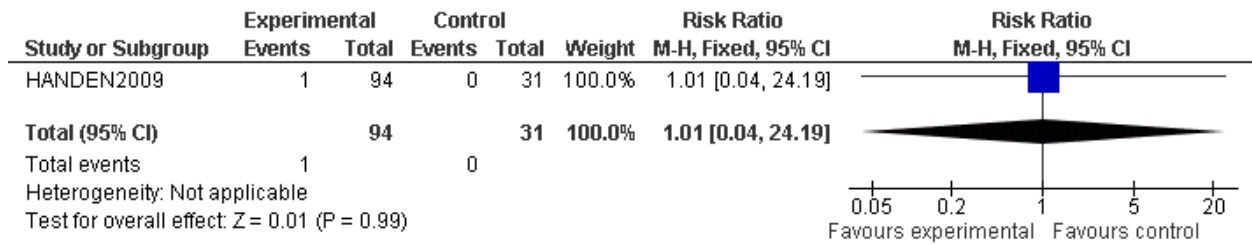
### Renal or urinary disorders



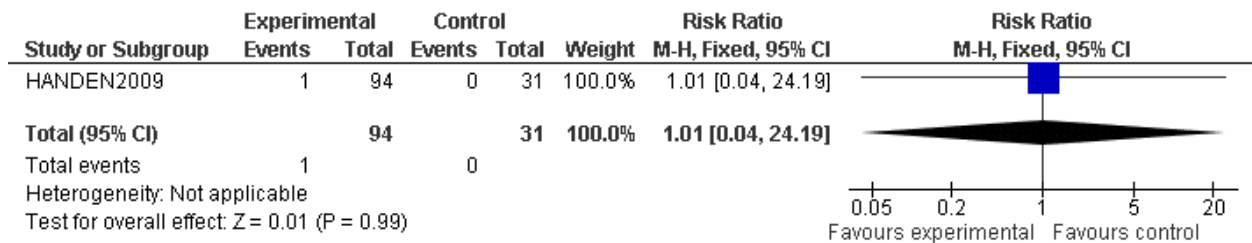
### Ear or labyrinth disorders



### Immune system disorders



### Vascular disorders

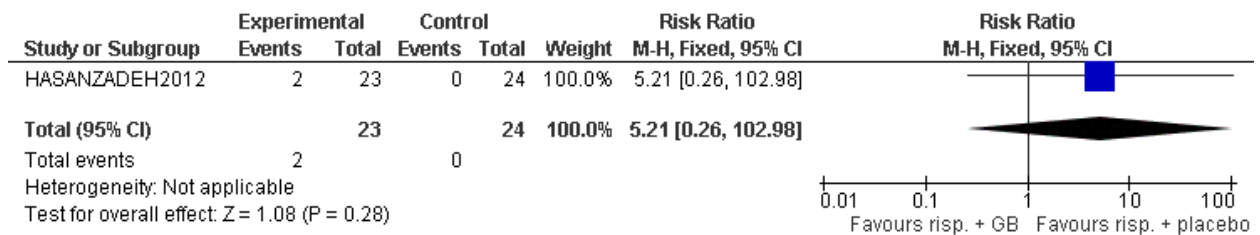


### *Adverse events associated with ginkgo biloba and risperidone versus placebo and risperidone*

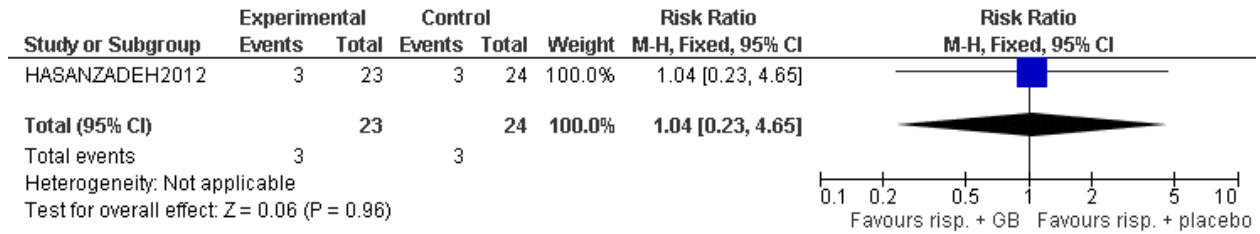
#### Day time drowsiness



#### Morning drowsiness



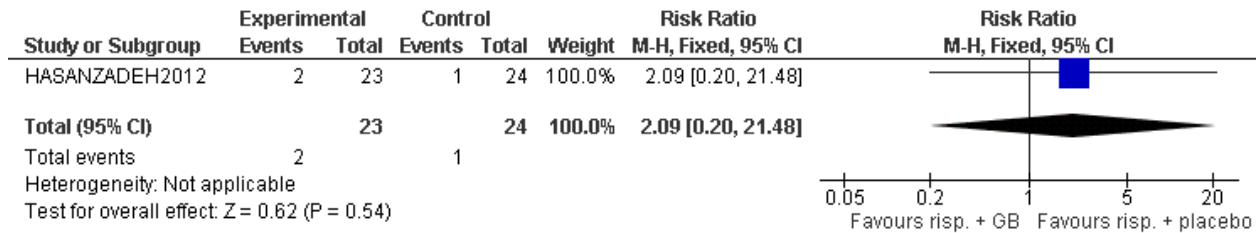
#### Constipation



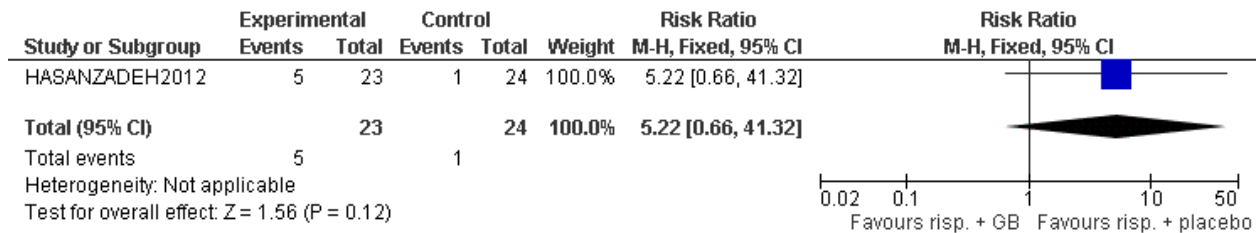
### Dizziness



### Slow movement



### Nervousness



### Restlessness



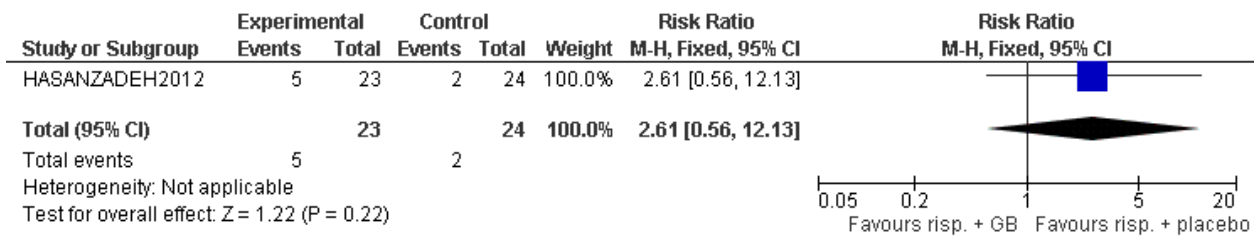
### Increased appetite



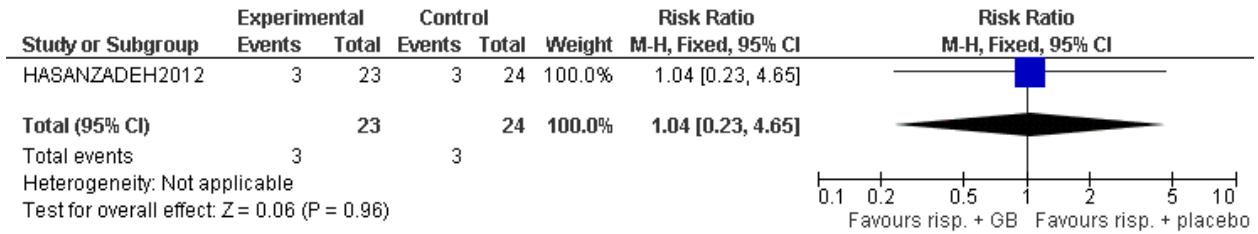
### Loss of appetite



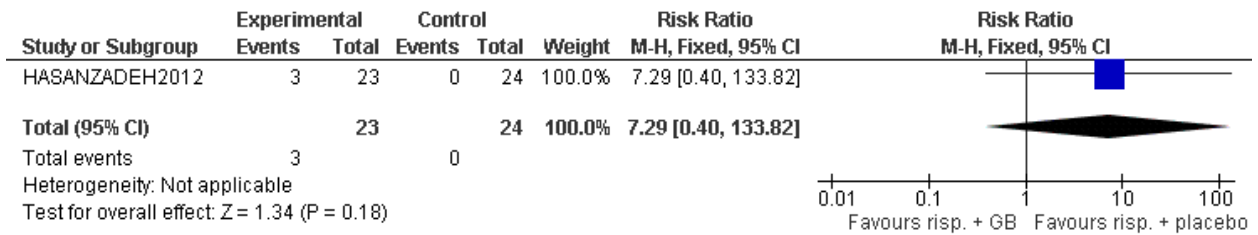
### Fatigue



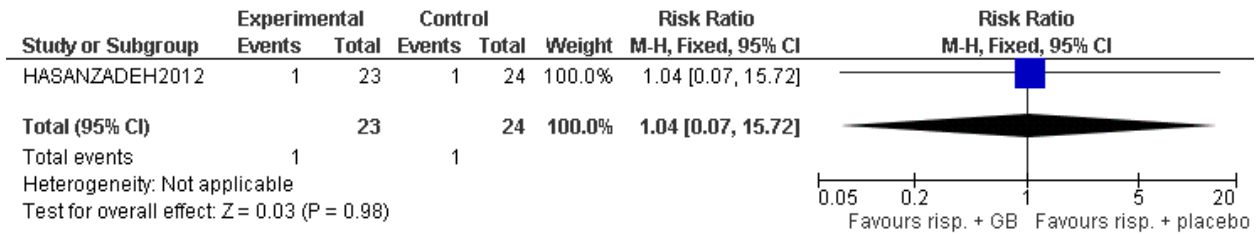
### Diarrhoea



### Twitches



### Dry mouth



### Trouble swallowing



### Sore throat/tongue





### Abdominal pain



### *Adverse events associated with gluten-free and casein-free diet versus treatment as usual*

