

**APPENDIX 14A: CLINICAL EVIDENCE FOREST PLOTS:
AT RISK MENTAL STATES FOR PSYCHOSIS AND
SCHIZOPHRENIA IN CHILDREN AND YOUNG PEOPLE:
RECOGNITION AND MANAGEMENT**

PHARMACOLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 25 YEARS AND YOUNGER 3

1. Olanzapine versus placebo: 52 weeks post-treatment efficacy outcomes..... 3
2. Olanzapine versus placebo: 52 weeks post-treatment (leaving the study for any reason)..... 5
3. Olanzapine versus placebo: 52 weeks post-treatment side effect outcomes 5
4. Olanzapine versus placebo: 104 weeks’ follow-up (change scores from post-treatment until follow-up when no treatment was received) 6
5. Risperidone + cognitive behavioural therapy (CBT) versus supportive counselling (SC): post-treatment efficacy outcomes..... 6
6. Risperidone + CBT versus supportive counselling (SC): post-treatment side effect outcomes.. 8
7. Risperidone + CBT versus supportive counselling (SC): 52 weeks’ follow-up efficacy outcomes 9
8. Risperidone + CBT versus supportive counselling (SC): 52 weeks’ follow-up side effect outcomes 11
9. Risperidone + CBT versus supportive counselling (SC): 156 to 208 weeks’ follow-up efficacy outcomes 11
10. Risperidone + CBT versus supportive counselling (SC): 156 to 208 weeks’ follow-up side effect outcomes..... 13
11. Risperidone + CBT versus placebo + CBT: 52 weeks post-treatment efficacy outcomes 14
12. Risperidone + CBT versus placebo + CBT: 52 weeks post-treatment side effect outcomes 15

DIETARY INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 25 YEARS AND YOUNGER15

13. Omega-3 fatty acids versus placebo: 12 weeks post-treatment efficacy outcomes..... 15
14. Omega-3 fatty acids versus placebo: 52 weeks’ follow-up efficacy outcomes 16
15. Omega-3 fatty acids versus placebo: 52 weeks’ follow-up side effect outcomes..... 17

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

16. CBT versus supportive counselling (SC): post-treatment (within/at 26 weeks) 18
17. CBT versus supportive counselling (SC): post-treatment (leaving the study for any reason).. 21
18. CBT versus supportive counselling (SC): 52 weeks’ follow-up 22
19. CBT versus supportive counselling (SC): 52 weeks’ follow-up (leaving the study for any reason)..... 25
20. CBT versus supportive counselling (SC): follow-up of 78 weeks or more 25
21. CBT versus supportive counselling (SC): follow-up of 78 weeks or more (leaving the study for any reason) 28

PSYCHOLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 25 YEARS AND YOUNGER28

22. Integrated psychological therapy (IPT) versus supportive counselling (SC): 52 weeks post-treatment 28

23. Integrated psychological therapy (IPT) versus supportive counselling (SC): 52 weeks post-treatment (leaving the study for any reason).....	29
24. Integrated psychological therapy (IPT) versus supportive counselling (SC): 104 weeks' follow-up	29
25. Integrated psychological therapy (IPT) versus supportive counselling (SC): 104 weeks' follow-up (leaving the study for any reason).....	29

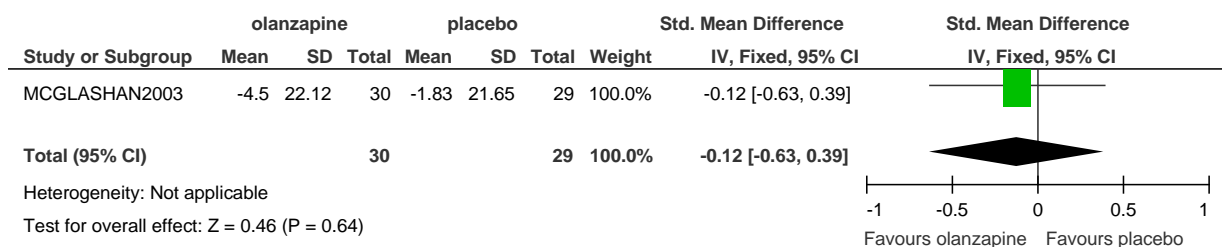
Abbreviations

BDI-PC	Beck Depression Inventory for Primary Care
BPM	beats per minute
BPRS (-P)	Brief Psychiatric Rating Scale (- Psychotic Subscale)
CAARMS	Comprehensive Assessment of At Risk Mental States
CBT	cognitive behavioural therapy
CDSS	Calgary Depression Scale for Schizophrenia
CI	confidence interval
EPS	extrapyramidal symptoms
GAF	Global Assessment of Functioning
DSM-IV	<i>Diagnostic and Statistical Manual of Mental Disorders, 4th edition</i>
HAM-A	Hamilton Anxiety Rating Scale
HAM-D	Hamilton Depression Rating Scale
IPT	integrated psychological therapy
MADRS	Montgomery-Åsberg Depression Rating Scale
MANSA	Manchester Short Assessment of Quality of Life
PANSS	Positive and Negative Syndrome Scale
QLS	Quality of Life Scale
SANS	Scale for the Assessment of Negative Symptoms
SAPS	Scale for the Assessment of Positive Symptoms
SC	supportive counselling
SD	standard deviation
SIAS	Social Interaction Anxiety Scale
SOPS	Scale of Prodromal Symptoms
UKU	Udvalg for Kliniske Undersøgelser
YMRS	Young Mania Rating Scale

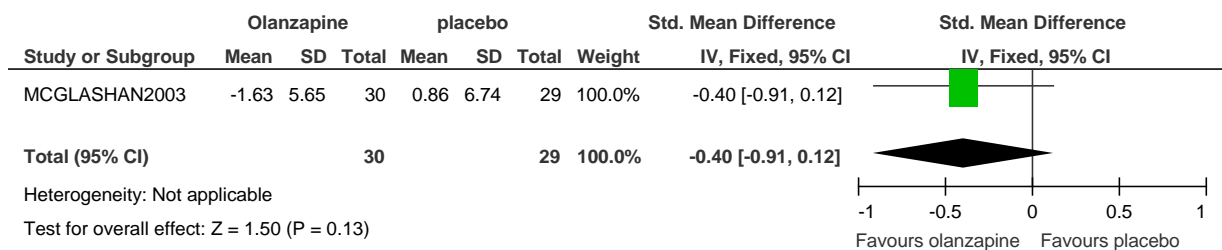
PHARMACOLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 25 YEARS AND YOUNGER

1. Olanzapine versus placebo: 52 weeks post-treatment efficacy outcomes

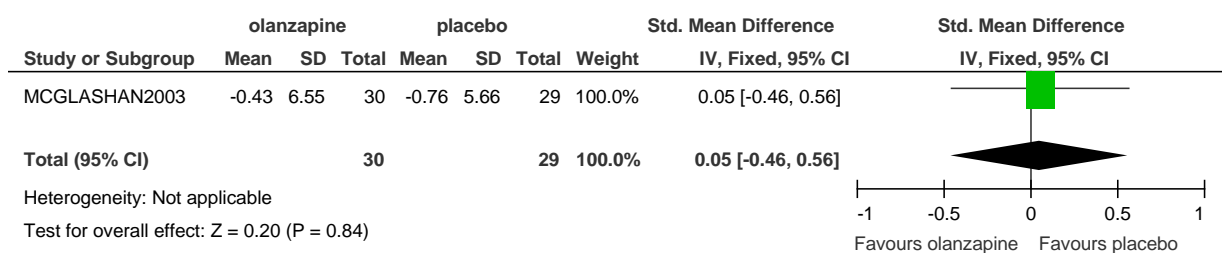
1.1 Mental state: change in mean total symptoms (Positive and Negative Syndrome Scale [PANSS])



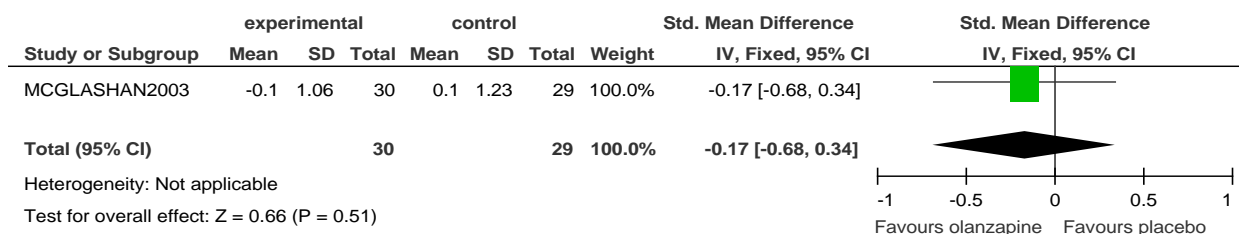
1.2 Mental state: change in mean positive symptoms (Scale for the Assessment of Positive Symptoms [SAPS])



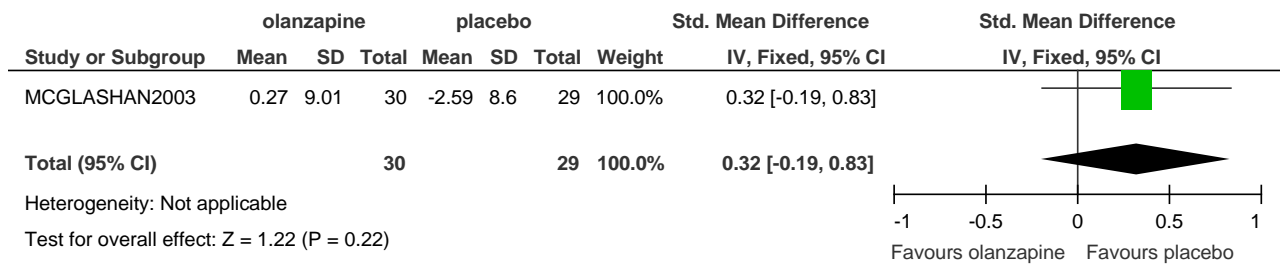
1.3 Mental state: change in negative symptoms (Scale for the Assessment of Negative Symptoms [SANS])



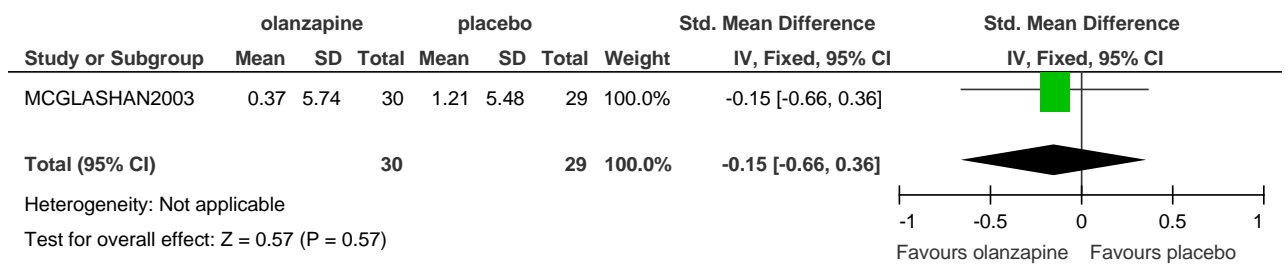
1.4 Change in global state: severity (Clinical Global Impression- Severity [CGI-S])



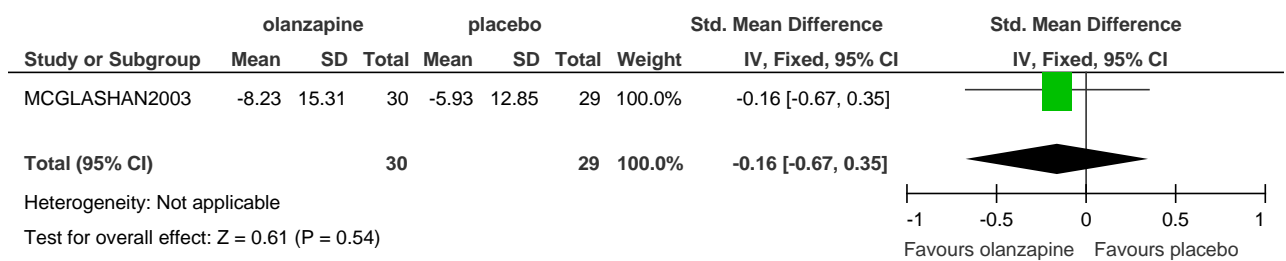
1.5 Mental state: change in depression symptoms (Montgomery-Åsberg Depression Rating Scale [MADRS])



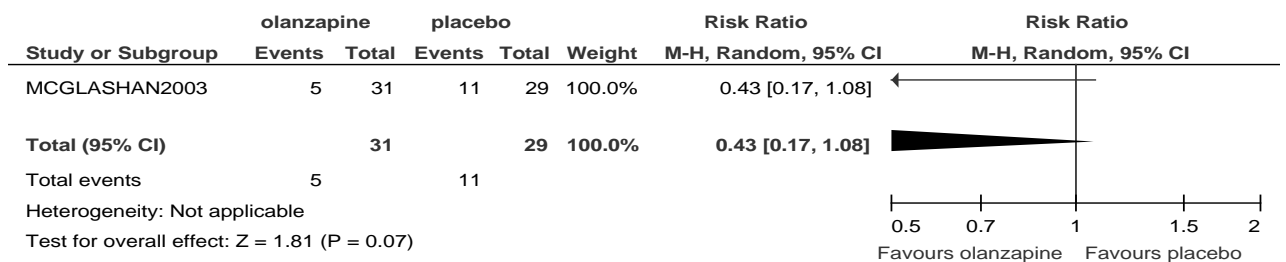
1.6 Mental state: change in mania (Young Mania Rating Scale [YMRS])



1.7 Change in psychosocial functioning (Global Assessment of Functioning [GAF])

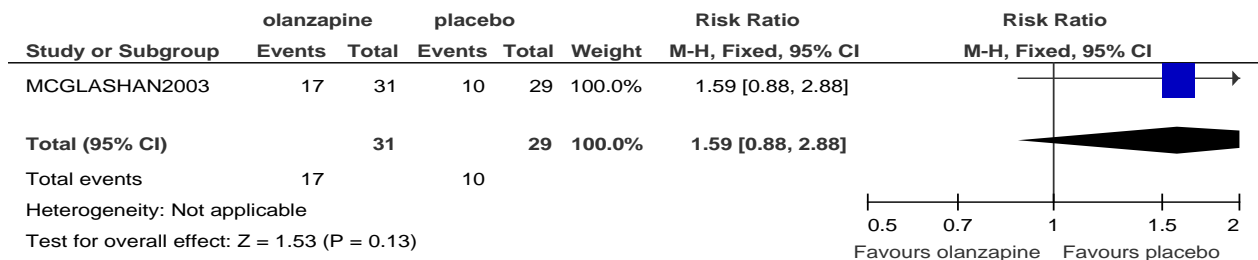


1.8 Transition to psychosis (presence of psychosis scale [author developed measure])



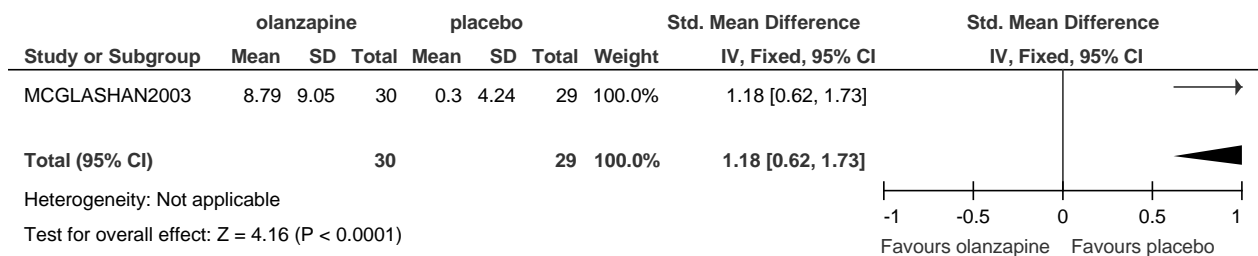
2. Olanzapine versus placebo: 52 weeks post-treatment (leaving the study for any reason)

2.1 Leaving the study early for any reason

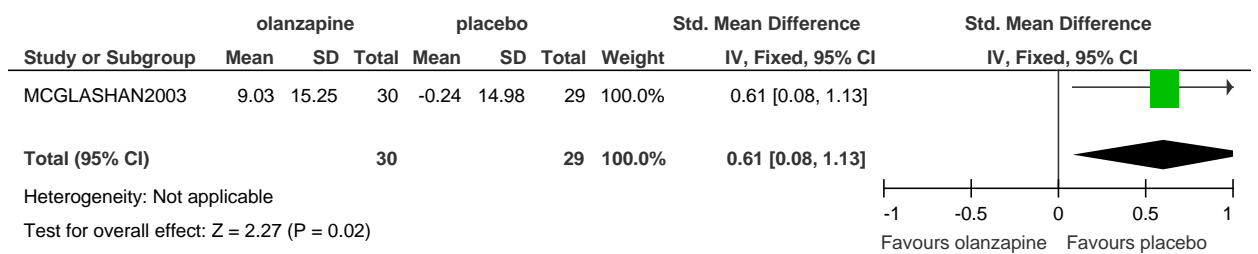


3. Olanzapine versus placebo: 52 weeks post-treatment side effect outcomes

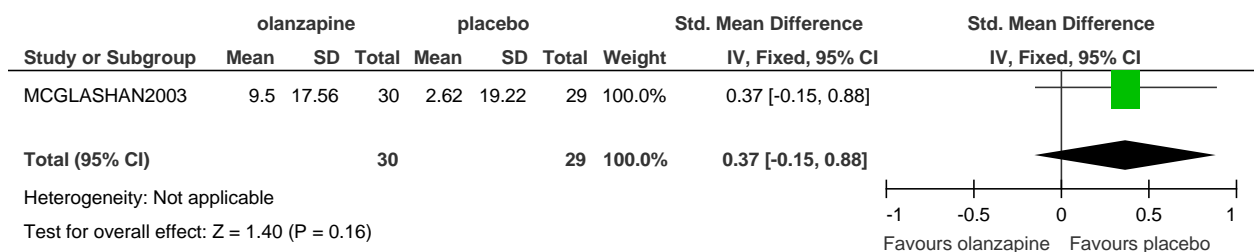
3.1 Mean change in weight (kg)



3.2 Mean change in sitting pulse (BPM)

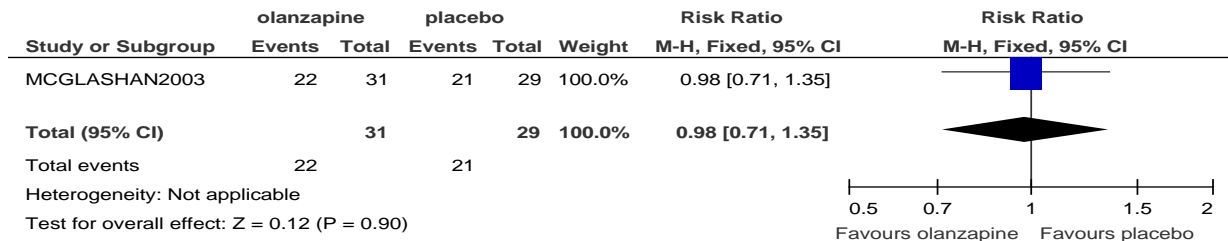


3.3 Mean change in standing pulse (BPM)



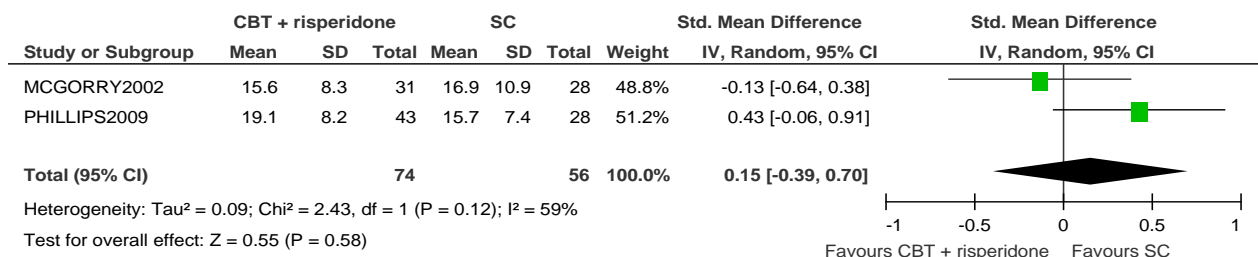
4. Olanzapine versus placebo: 104 weeks' follow-up (change scores from post-treatment until follow-up when no treatment was received)

4.1 Leaving the study early for any reason

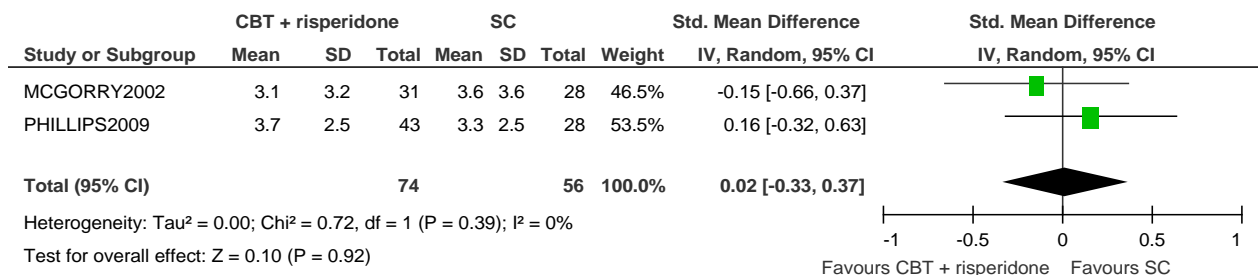


5. Risperidone + cognitive behavioural therapy (CBT) versus supportive counselling (SC): post-treatment efficacy outcomes

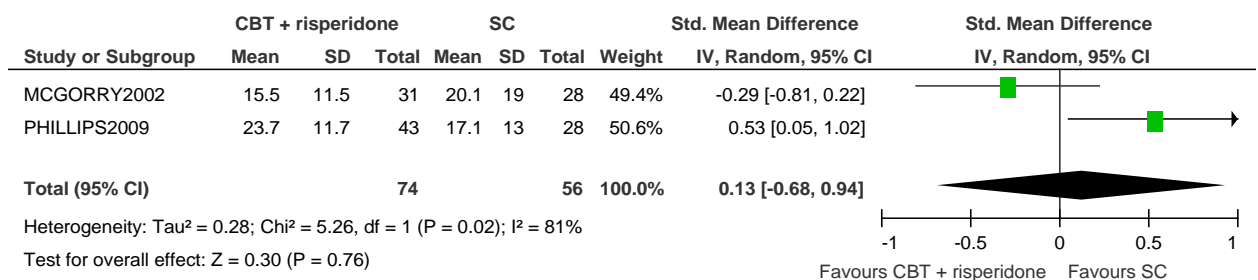
5.1 Mental state: mean endpoint total symptoms (Brief Psychiatric Rating Scale [BPRS])



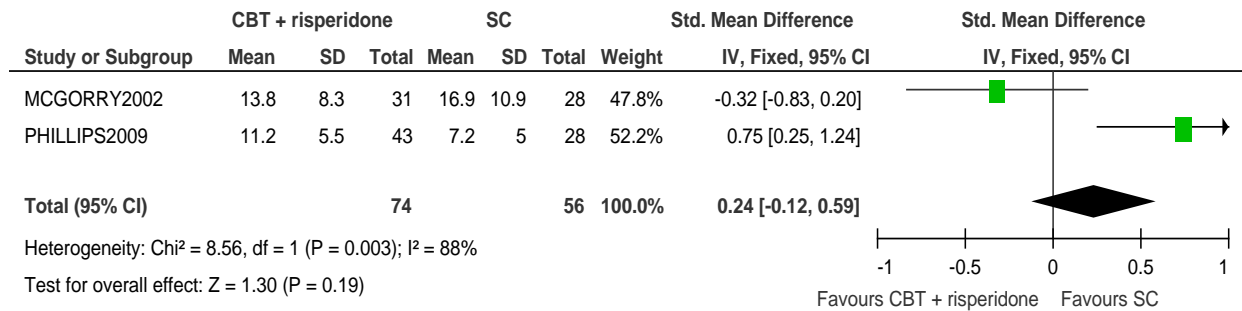
5.2 Mental state: mean endpoint positive symptoms (BPRS-P)



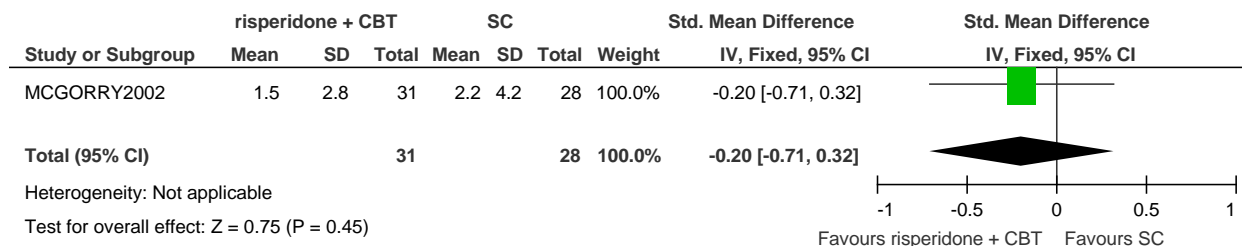
5.3 Mental state: mean endpoint negative symptoms (SANS, Scale of Prodromal Symptoms [SOPS] Negative)



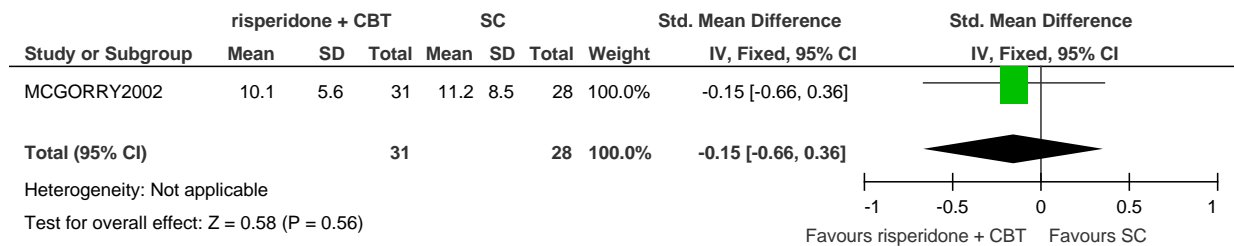
5.4 Mental state: mean endpoint depression symptoms (Hamilton Depression Rating Scale [HAM-D])



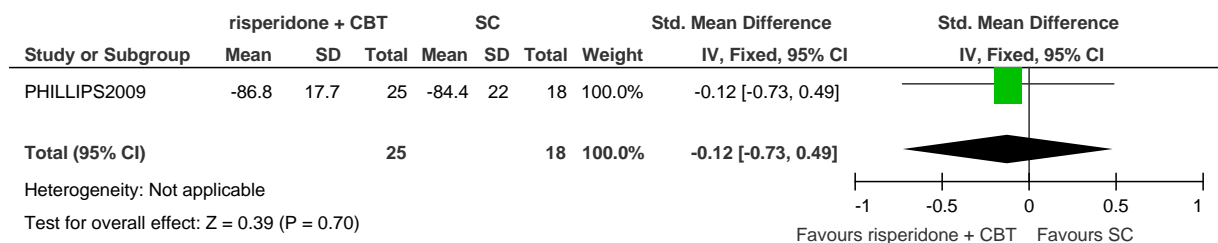
5.5 Mental state: mean endpoint mania symptoms (YMRS)



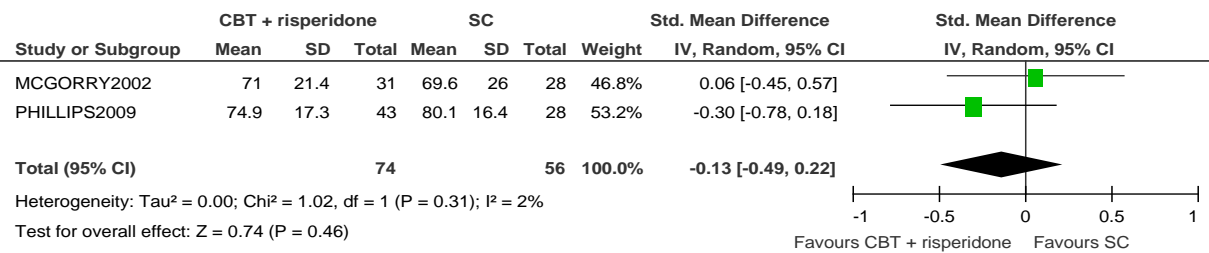
5.6 Mental state: mean endpoint anxiety symptoms (Hamilton Anxiety Rating Scale [HAM-A])



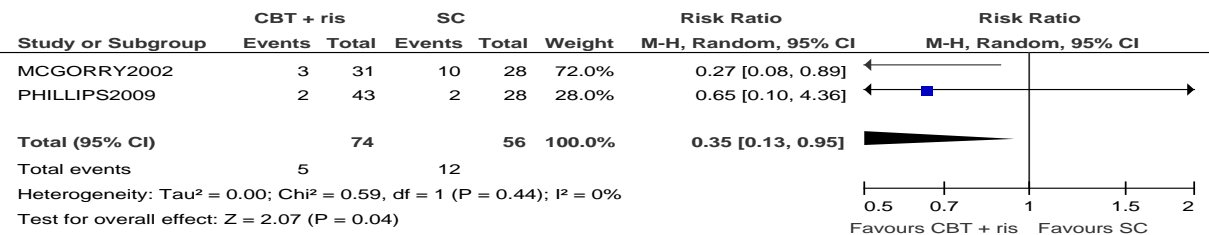
5.7 Mean endpoint psychosocial functioning (GAF)



5.8 Mean endpoint quality of life (Quality of Life Scale [QLS])

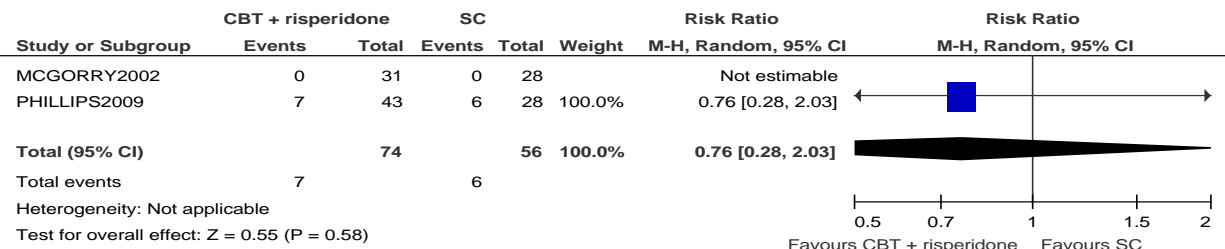


5.9 Transition to psychosis (a predetermined threshold of positive symptoms, Comprehensive Assessment of At Risk Mental States [CAARMS])

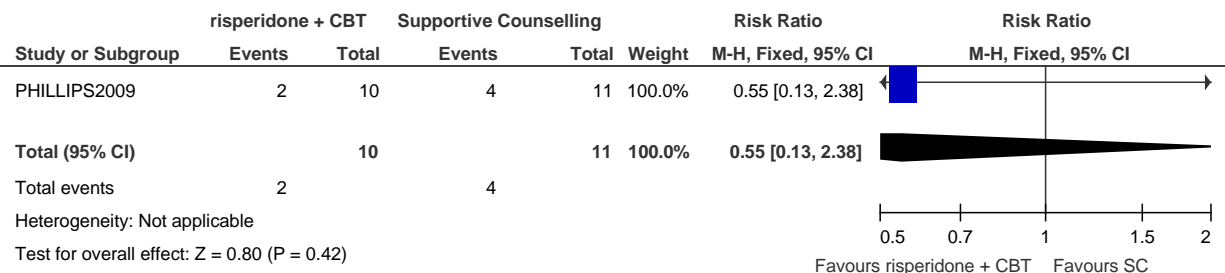


6. Risperidone + CBT versus supportive counselling (SC): post-treatment side effect outcomes

6.1 Leaving the study early for any reason

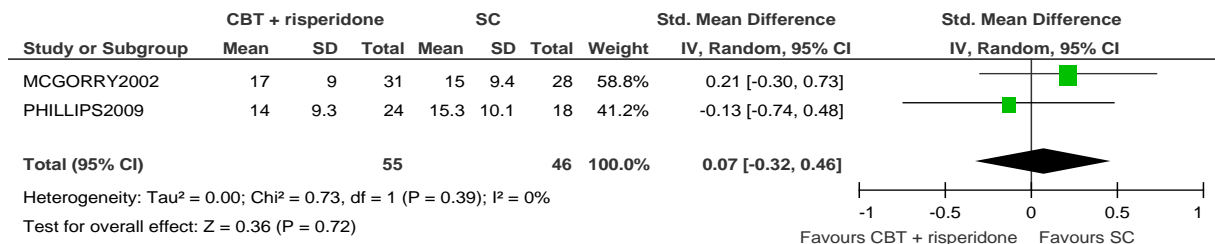


6.2 Extrapyramidal symptoms (EPS) (mean endpoint Udvalg for Kliniske Undersøgelser [UKU] scores)

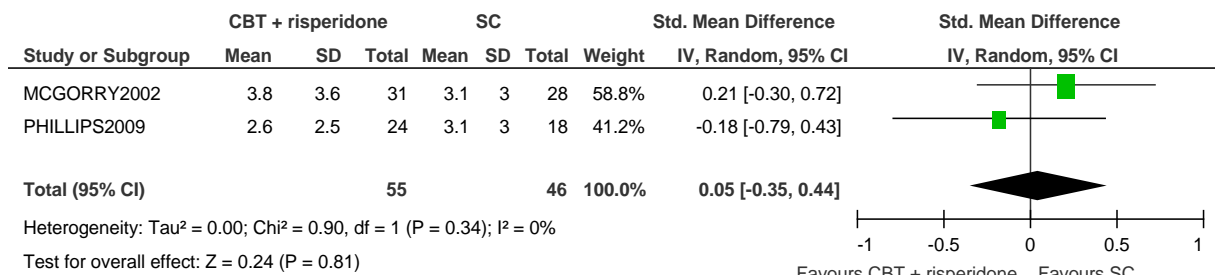


7. Risperidone + CBT versus supportive counselling (SC): 52 weeks' follow-up efficacy outcomes

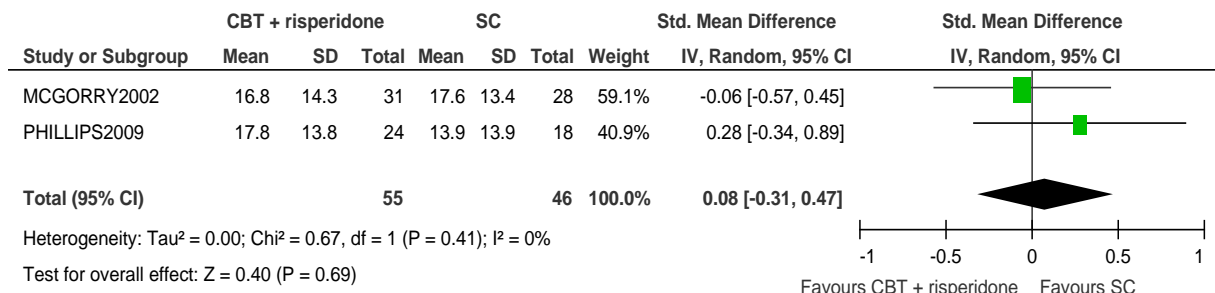
7.1 Mental state: mean endpoint total symptoms (BPRS)



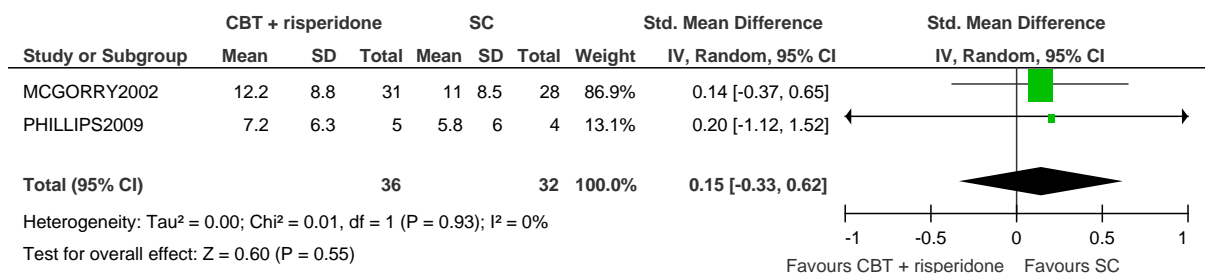
7.2 Mental state: mean endpoint positive symptoms (BPRS-P)



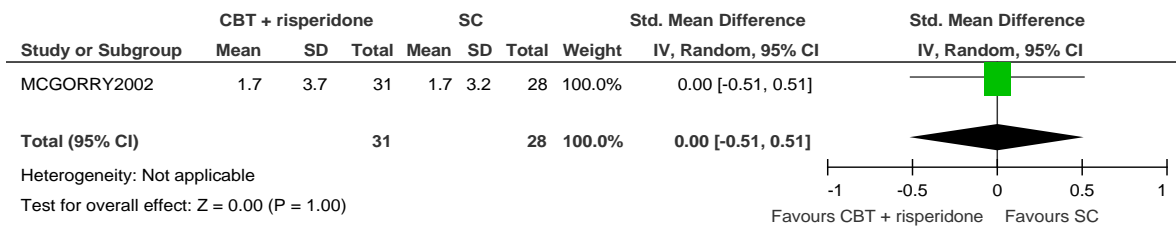
7.3 Mental state: mean endpoint negative symptoms (SANS)



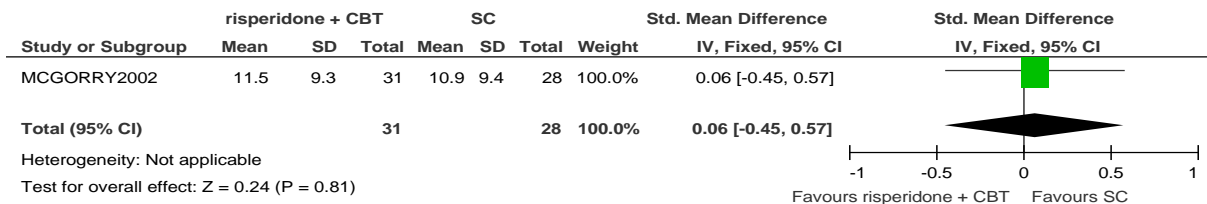
7.4 Mental state: mean endpoint depression symptoms (HAM-D)



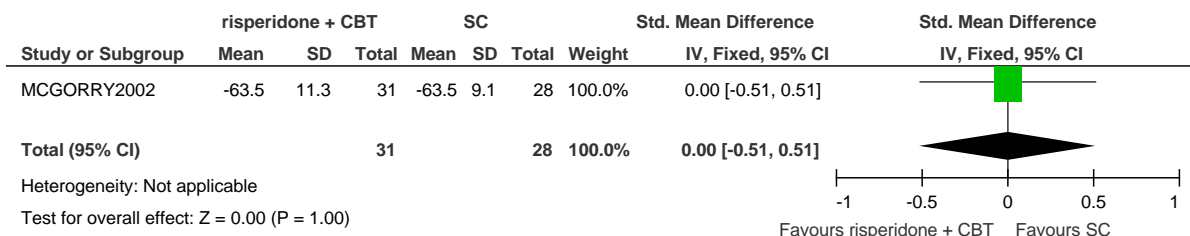
7.5 Mental state: mean endpoint mania symptoms (YMRS)



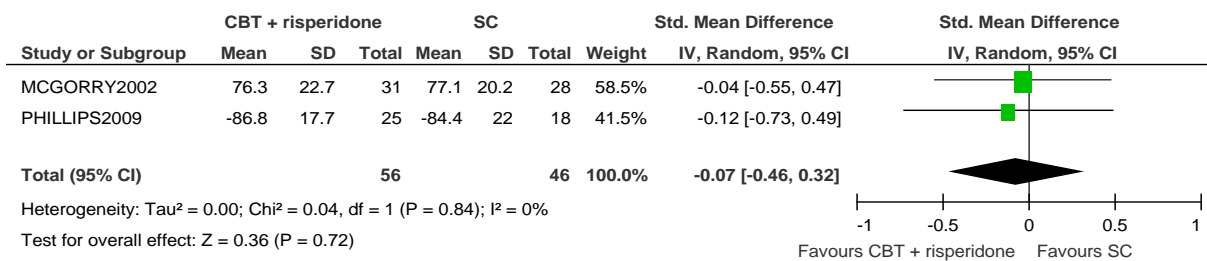
7.6 Mental state: mean endpoint anxiety symptoms (HAM-A)



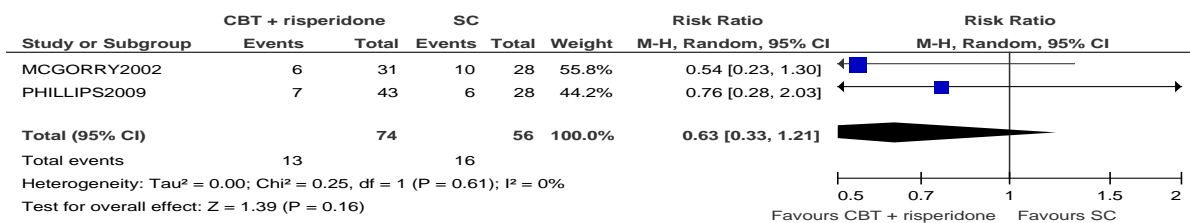
7.7 Mean endpoint psychosocial functioning (GAF)



7.8 Mean endpoint quality of life (QLS)

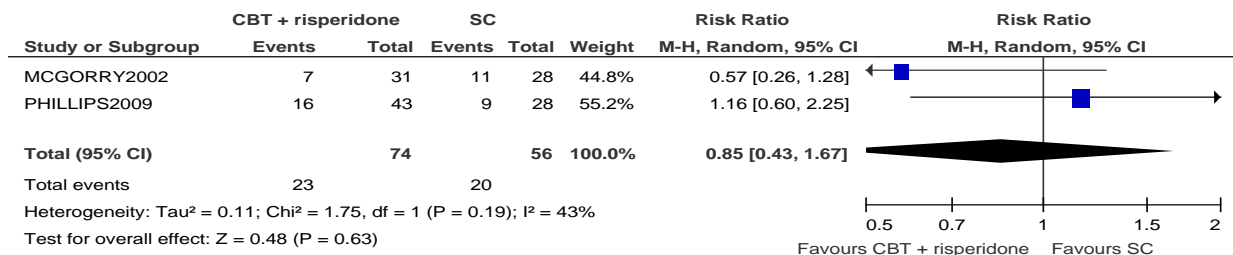


7.9 Transition to psychosis (assessed using a categorical model, to the predetermined threshold of positive psychotic symptoms)



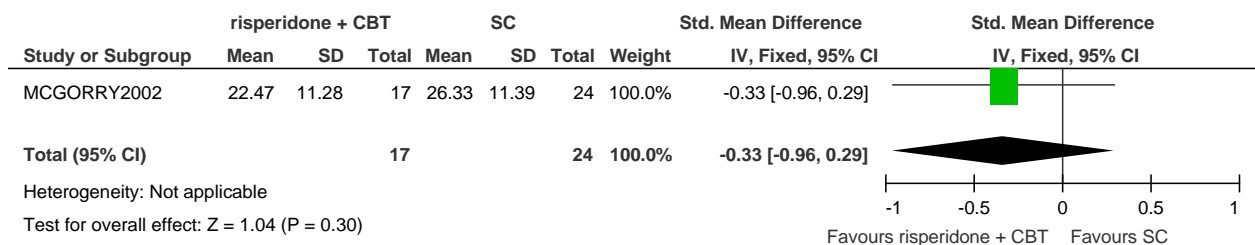
8. Risperidone + CBT versus supportive counselling (SC): 52 weeks' follow-up side effect outcomes

8.1 Leaving the study early for any reason

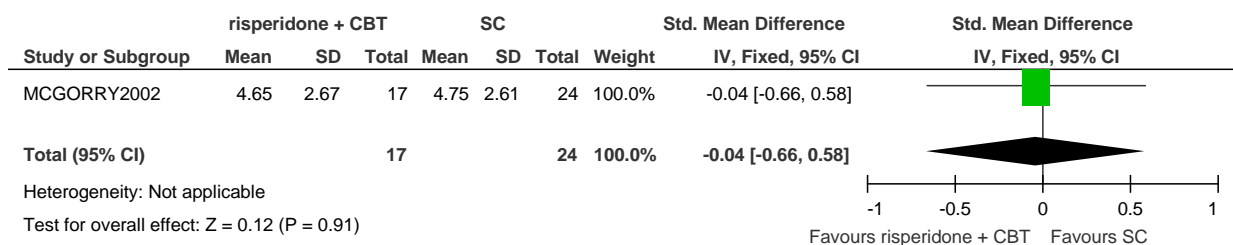


9. Risperidone + CBT versus supportive counselling (SC): 156 to 208 weeks' follow-up efficacy outcomes

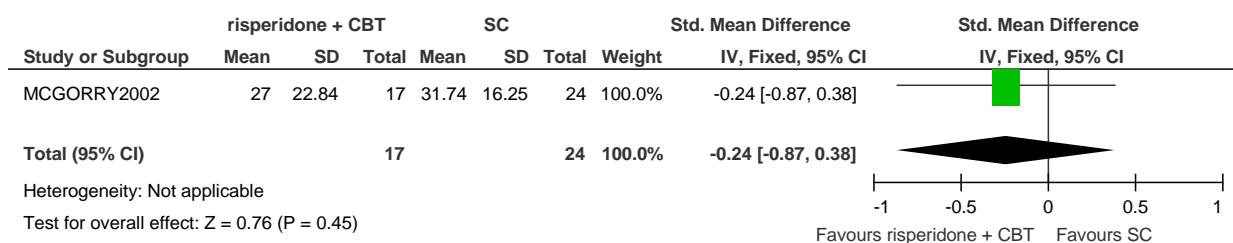
9.1 Mental state: mean endpoint total symptoms (BPRS)



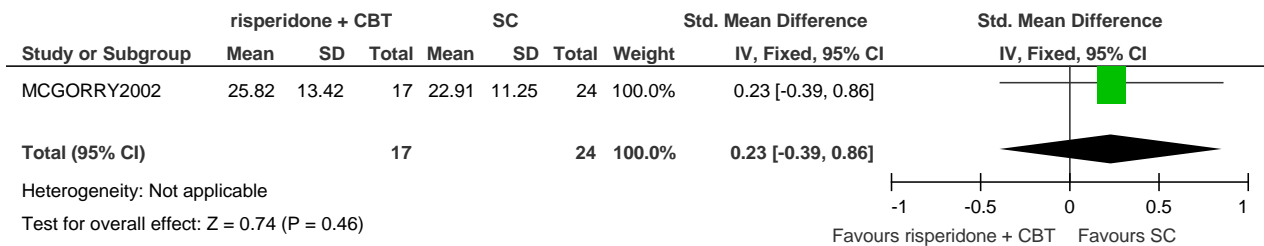
9.2 Mental state: mean endpoint positive symptoms (BPRS-P)



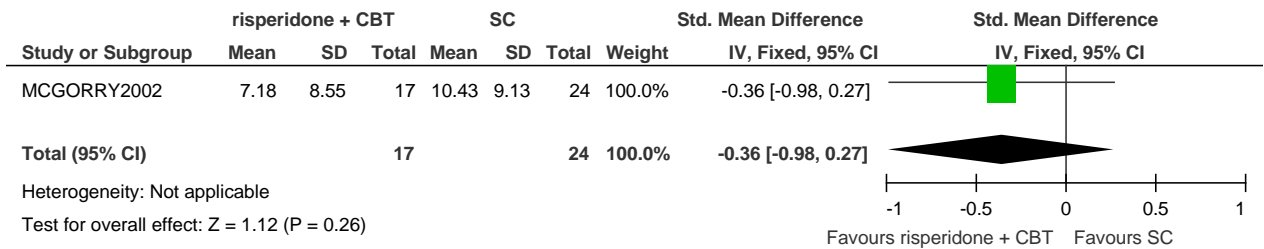
9.3 Mental state: mean endpoint negative symptoms (SANS)



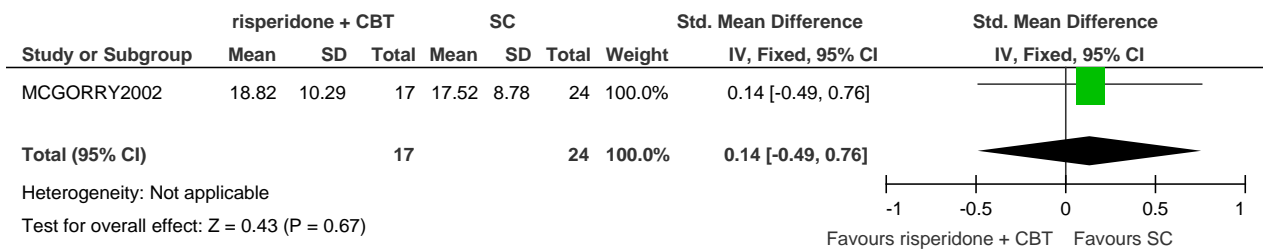
9.4 Mental state: mean endpoint depression symptoms (HAM-D)



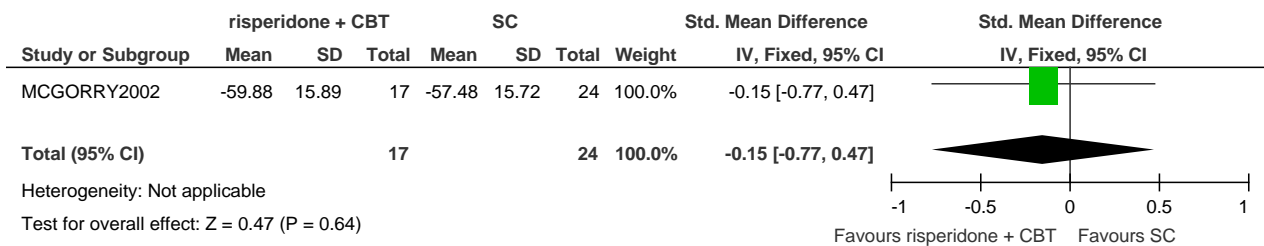
9.5 Mental state: mean endpoint mania symptoms (YMRS)



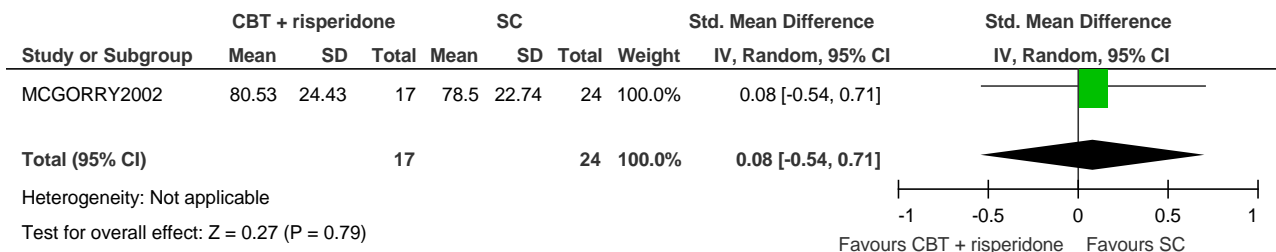
9.6 Mental state: mean endpoint anxiety symptoms (HAM-A)



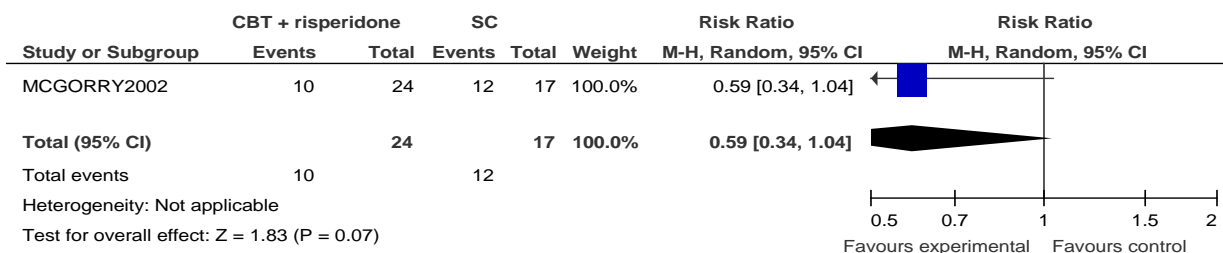
9.7 Mean endpoint psychosocial functioning (GAF)



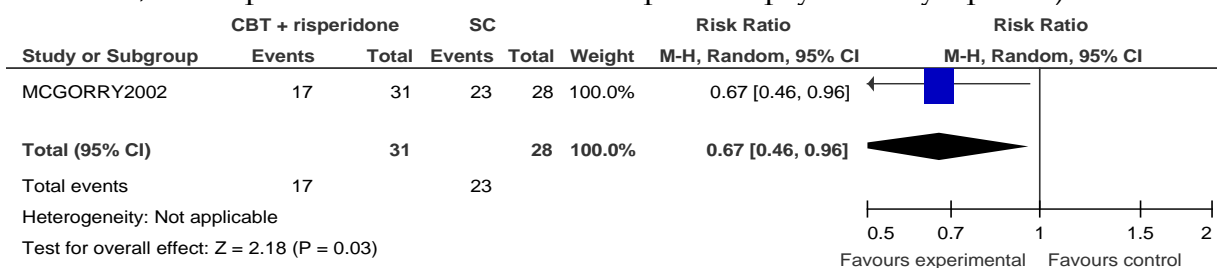
9.8 Mean endpoint quality of life (QLS)



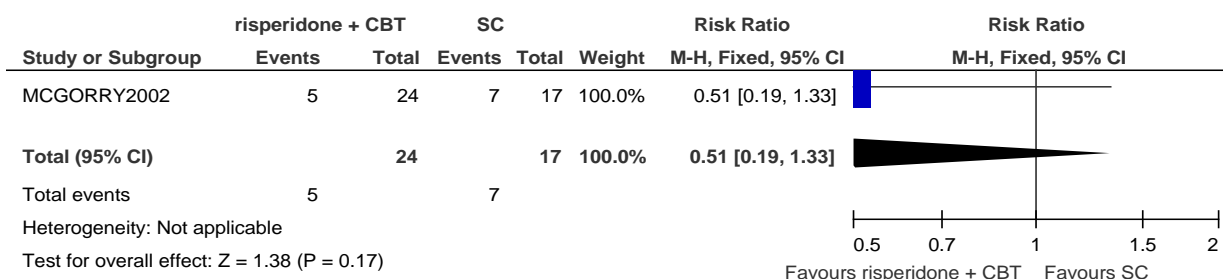
9.9 Transition to psychosis (completer analysis) (assessed using a categorical model, to the predetermined threshold of positive psychotic symptoms)



9.10 Transition to psychosis (sensitivity analysis) (assessed using a categorical model, to the predetermined threshold of positive psychotic symptoms)

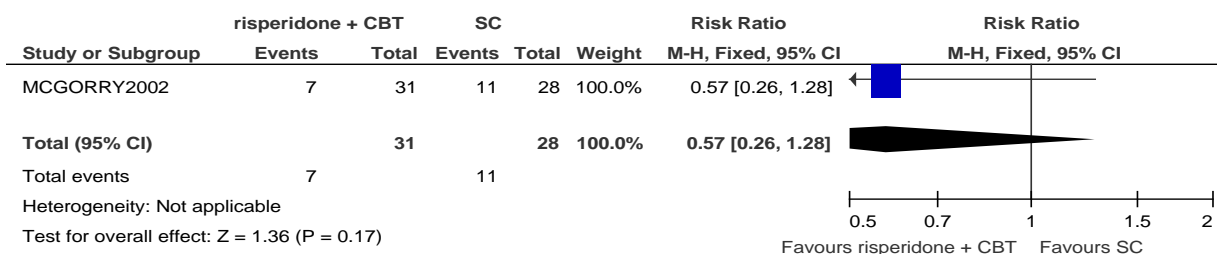


9.11 Number of participants requiring hospitalisation



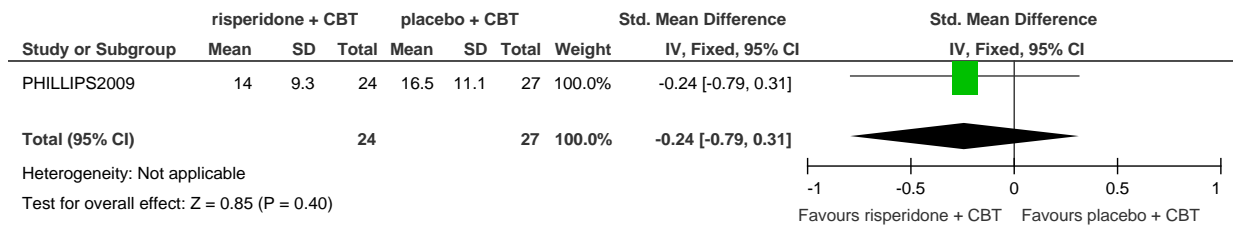
10. Risperidone + CBT versus supportive counselling (SC): 156 to 208 weeks' follow-up side effect outcomes

10.1 Leaving the study early for any reason

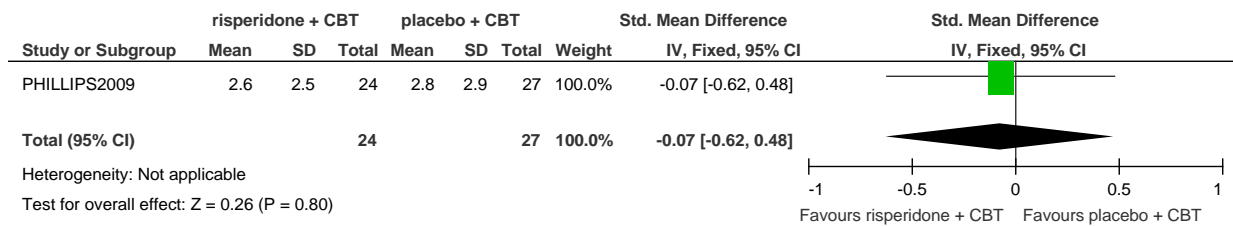


11. Risperidone + CBT versus placebo + CBT: 52 weeks post-treatment efficacy outcomes

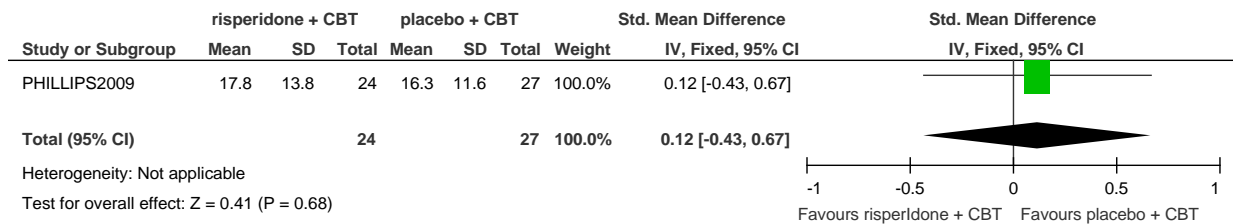
11.1 Mental state: mean endpoint total symptoms (BPRS)



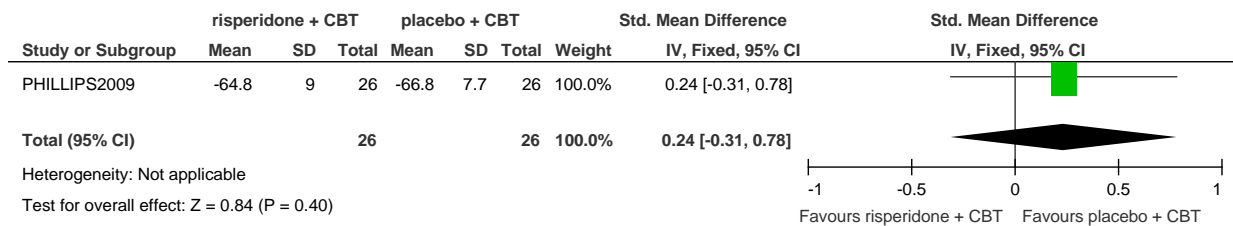
11.2 Mental state: mean endpoint positive symptoms (BPRS-P)



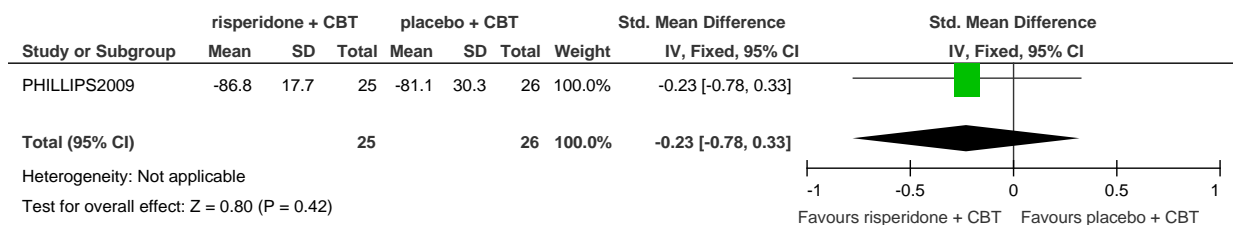
11.3 Mental state: mean endpoint negative symptoms (SANS)



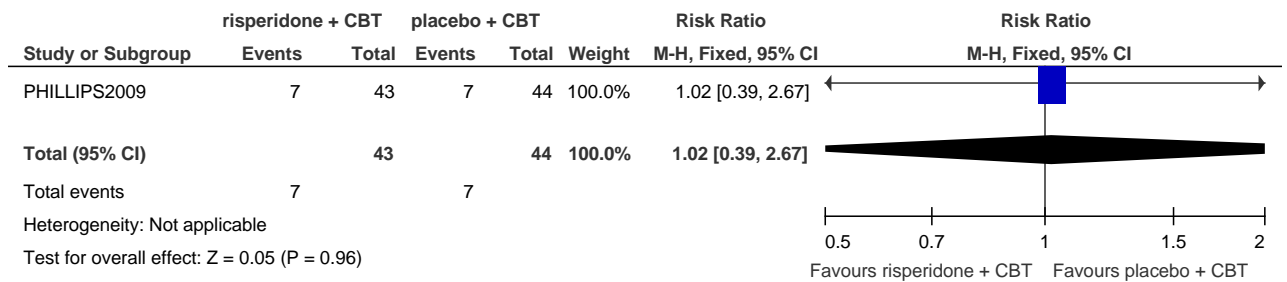
11.4 Mean endpoint psychosocial functioning (GAF)



11.5 Mean endpoint quality of life (QLS)

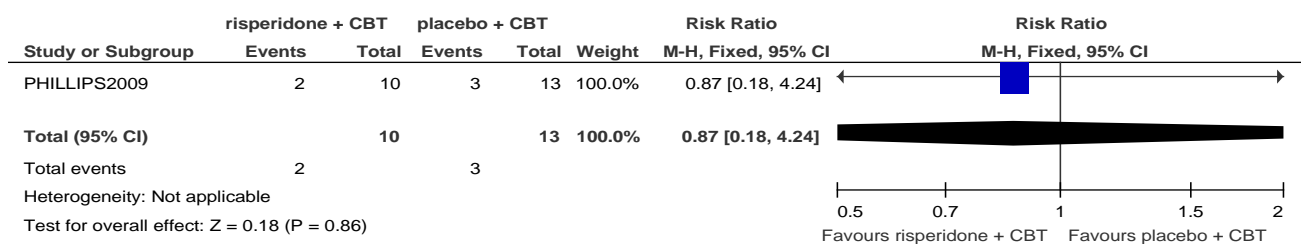


11.6 Transition to psychosis (CAARMS)

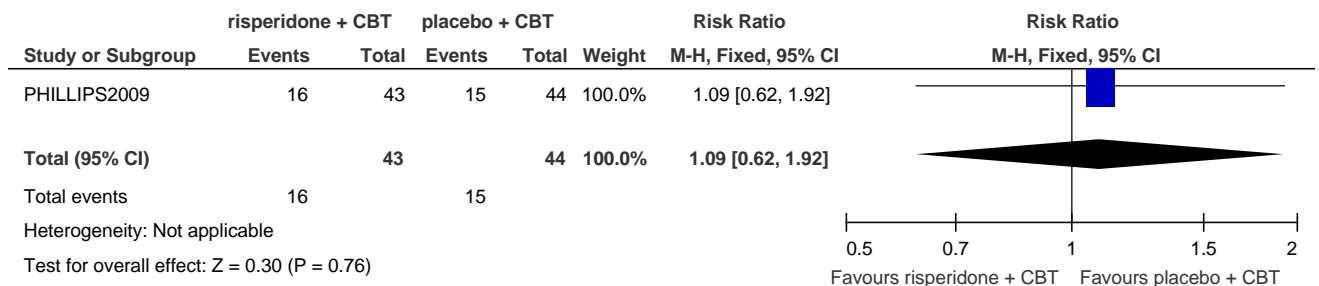


12. Risperidone + CBT versus placebo + CBT: 52 weeks post-treatment side effect outcomes

12.1 EPS (mean endpoint UKU scores)



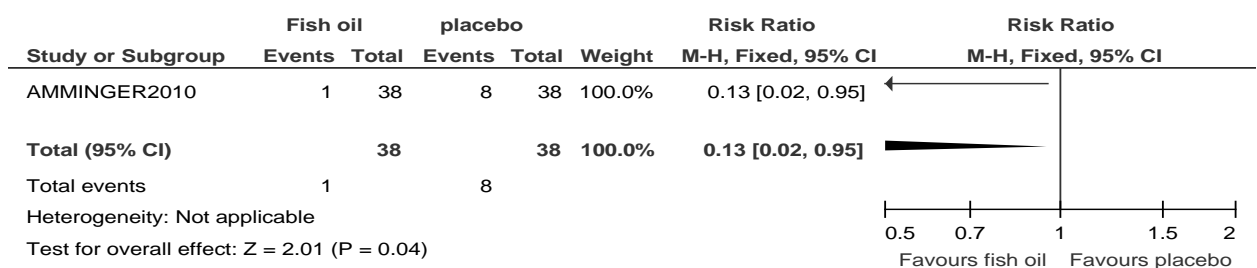
12.2 Leaving the study early for any reason



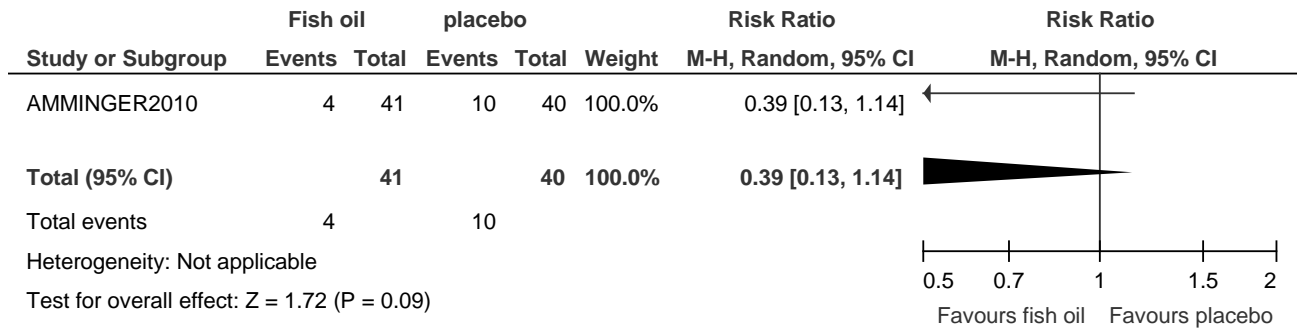
DIETARY INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 25 YEARS AND YOUNGER

13. Omega-3 fatty acids versus placebo: 12 weeks post-treatment efficacy outcomes

13.1 Transition to psychosis (DSM-IV) (completer analysis)

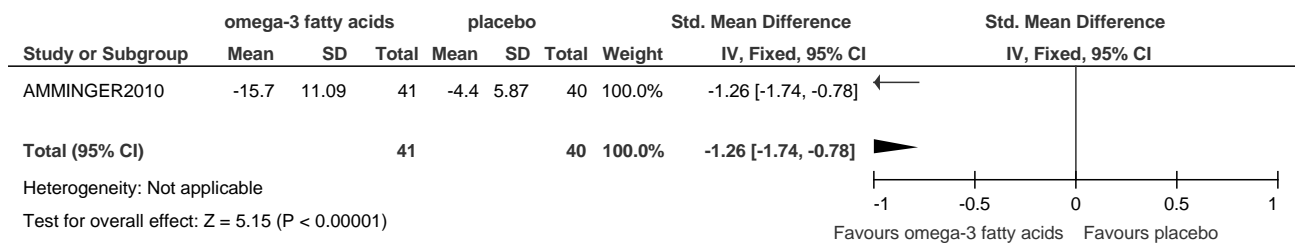


13.2 Transition to psychosis (DSM-IV) (sensitivity analysis)

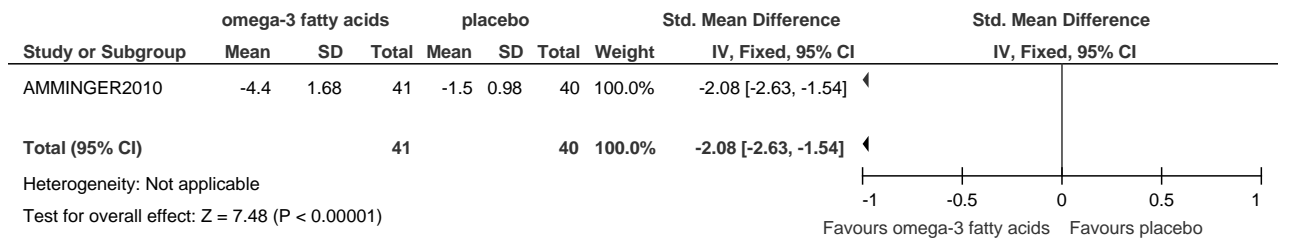


14. Omega-3 fatty acids versus placebo: 52 weeks' follow-up efficacy outcomes

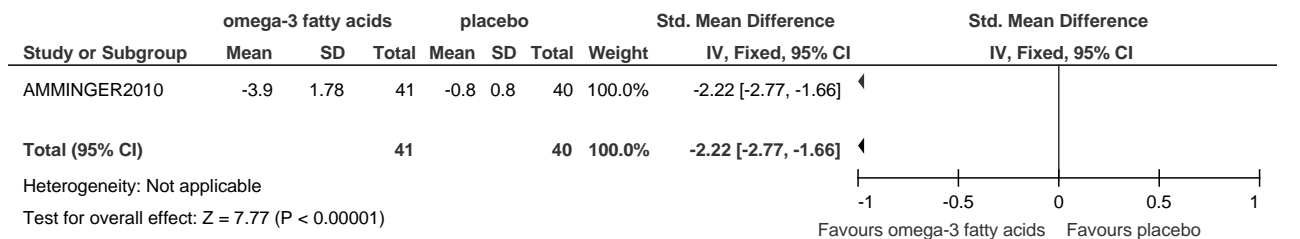
14.1 Mental state: mean endpoint total symptoms (PANSS)



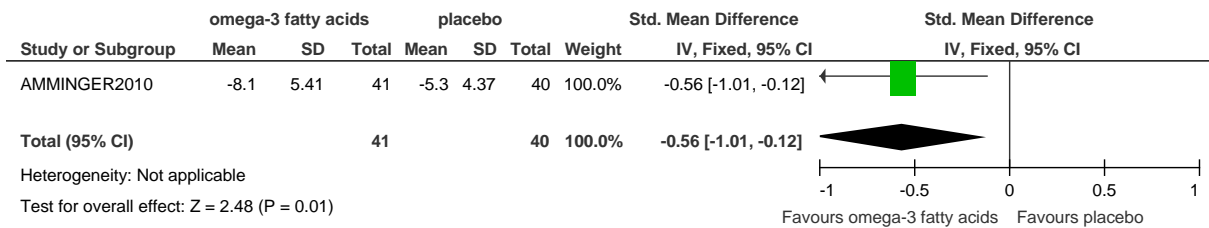
14.2 Mental state: mean endpoint positive symptoms (SAPS)



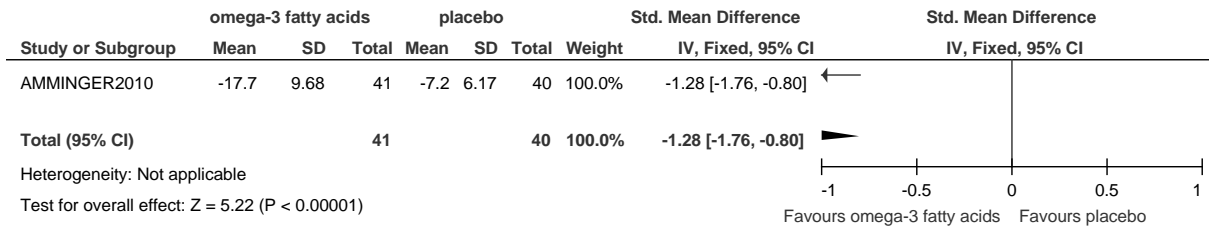
14.3 Mental state: mean endpoint negative symptoms (SANS)



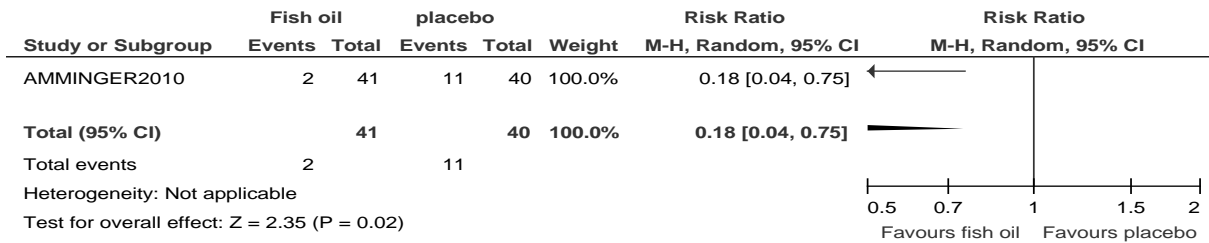
14.4 Mental state: mean endpoint depression symptoms (MADRS)



14.5 Mean endpoint psychosocial functioning (GAF)

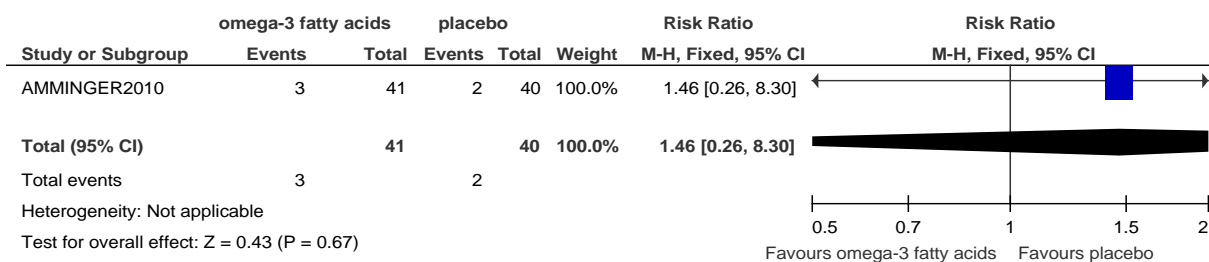


14.6 Transition to psychosis (DSM-IV)



15. Omega-3 fatty acids versus placebo: 52 weeks' follow-up side effect outcomes

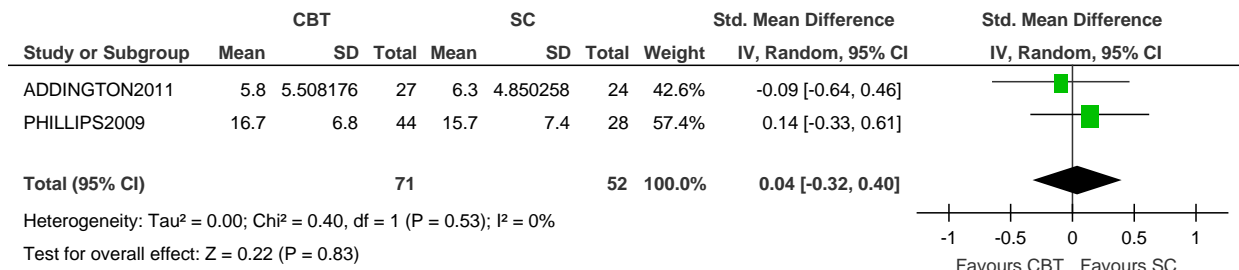
15.1 Leaving the study early for any reason



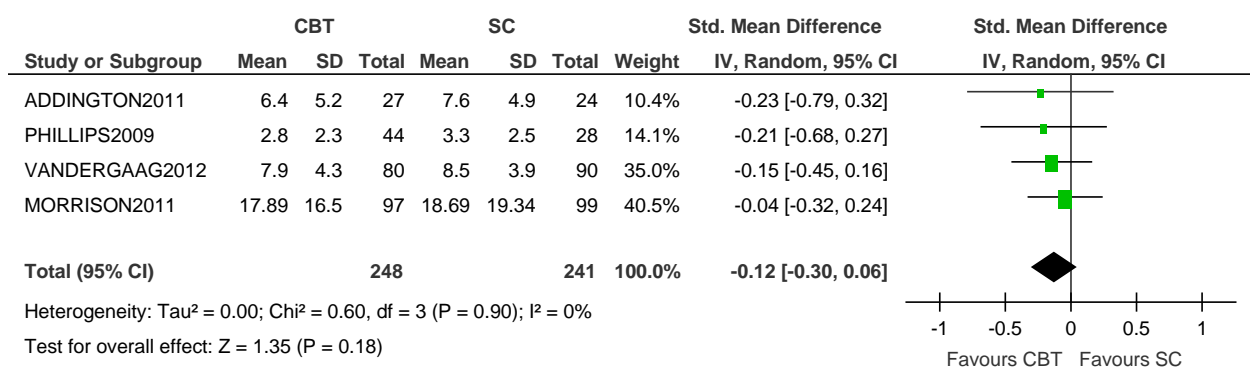
PSYCHOLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 18 YEARS AND YOUNGER COMBINED WITH THOSE AGED 25 YEARS AND YOUNGER

16. CBT versus supportive counselling (SC): post-treatment (within/at 26 weeks)

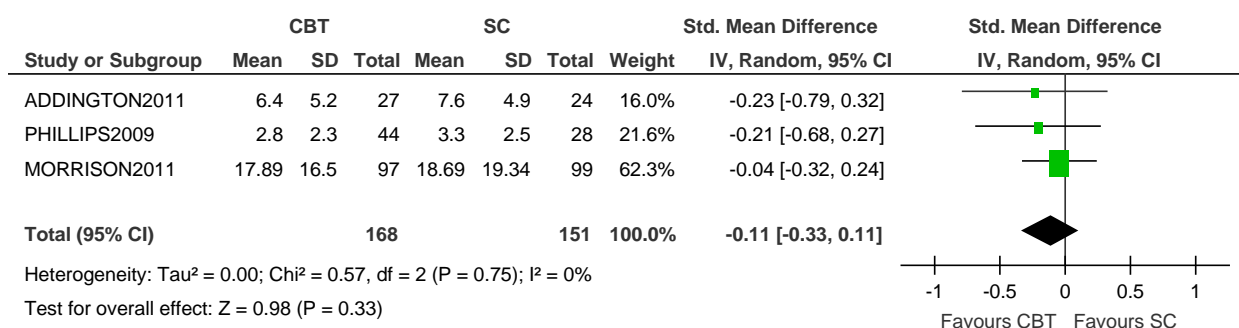
16.1 Mental state: mean endpoint total symptoms (BPRS, SOPS, PANSS, CAARMS severity)



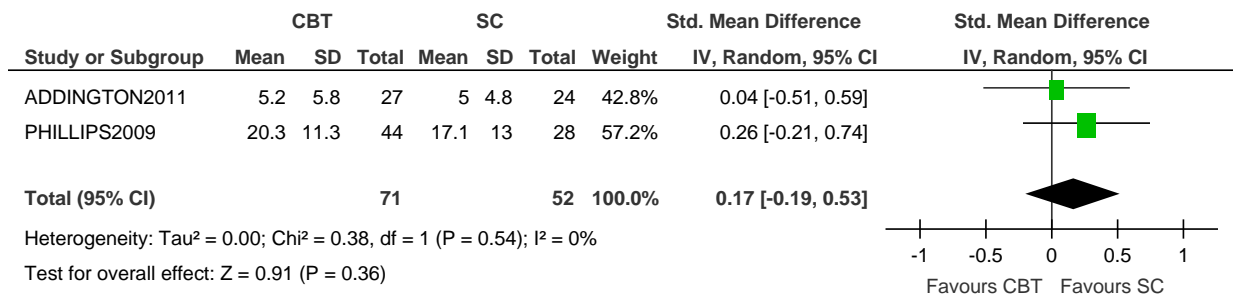
16.2 Mental state: mean endpoint positive symptoms (BPRS positive, SOPS positive, PANSS positive)



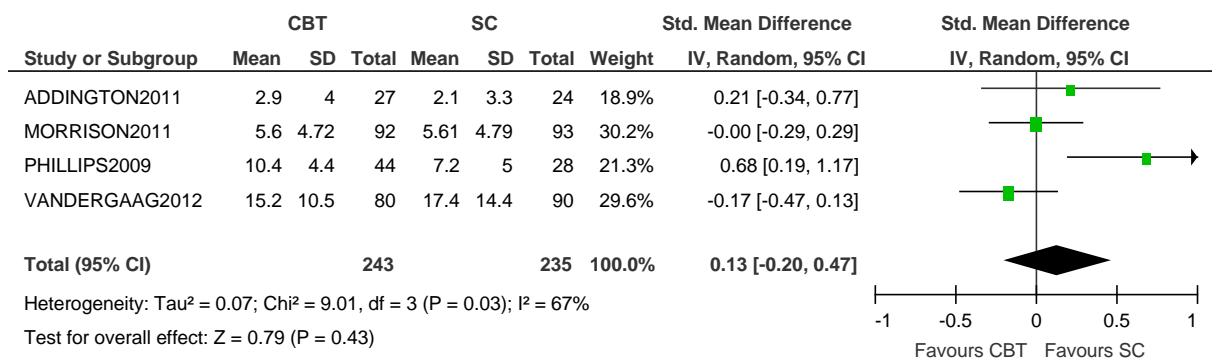
16.3 Sensitivity analysis: mental state: mean endpoint positive symptoms (BPRS positive, SOPS positive, PANSS positive) (without VANDERGAAG2012)



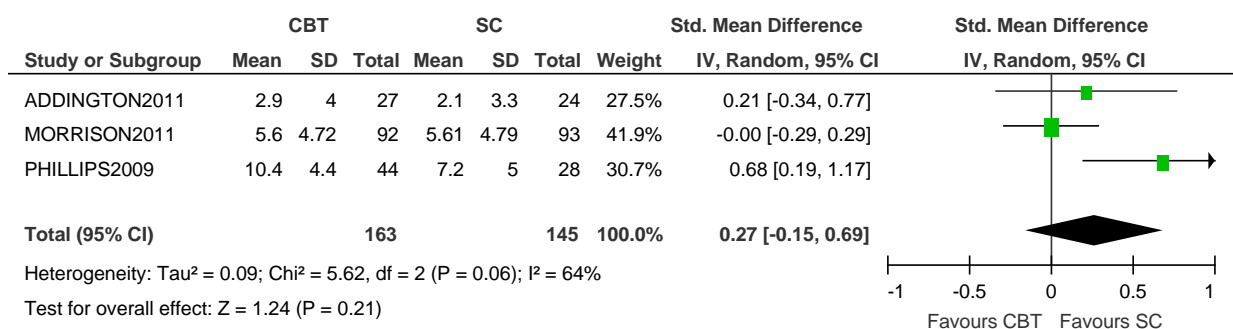
16.4 Mental state: mean endpoint negative symptoms (SOPS negative, PANSS negative)



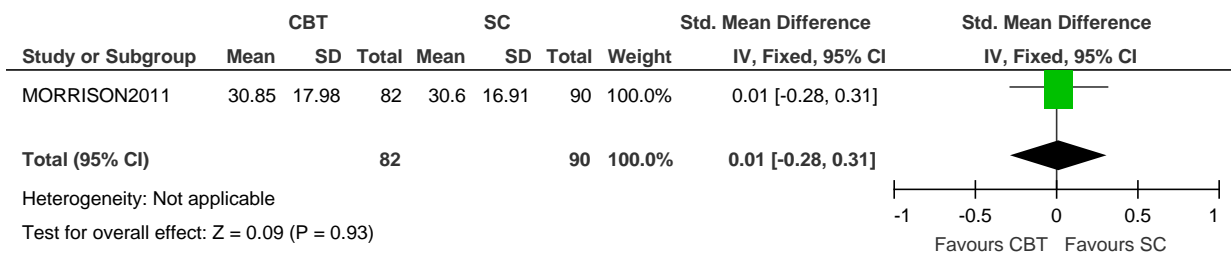
16.5 Mental state: mean endpoint depression symptoms (Beck Depression Inventory for Primary Care [BDI-PC], Calgary Depression Scale for Schizophrenia [CDSS])



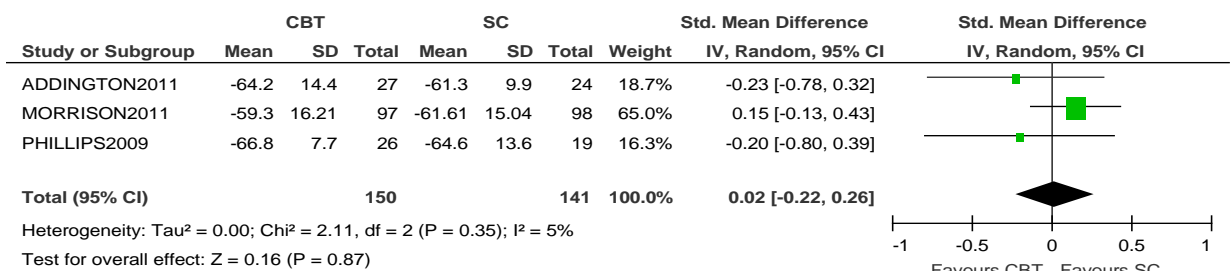
16.6 Sensitivity analysis: mental state: mean endpoint depression symptoms (BDI-PC, CDSS) (without VANDERGAAG2012)



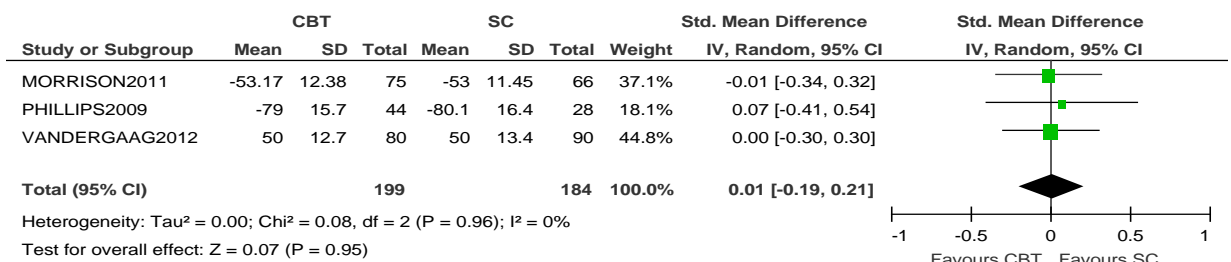
16.7 Mental state: mean endpoint social anxiety symptoms (Social Interaction Anxiety Scale [SIAS])



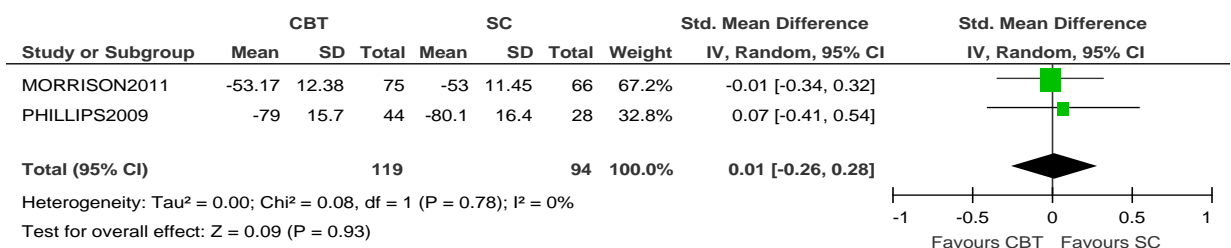
16.8 Mean endpoint psychosocial functioning (GAF)



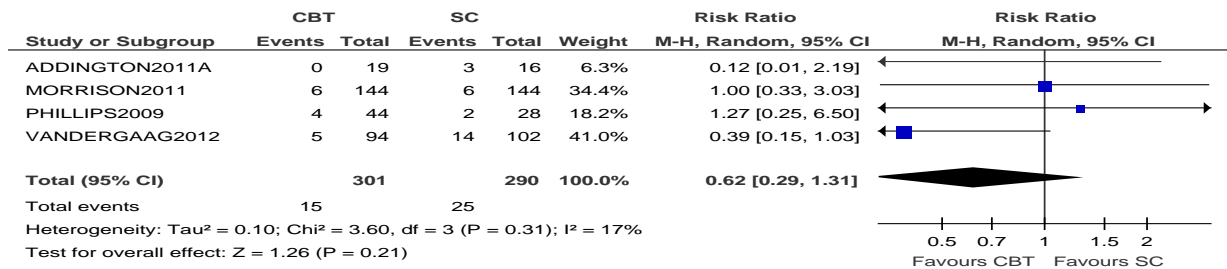
16.9 Mean endpoint quality of life (Manchester Short Assessment of Quality of Life [MANSA], QLS)



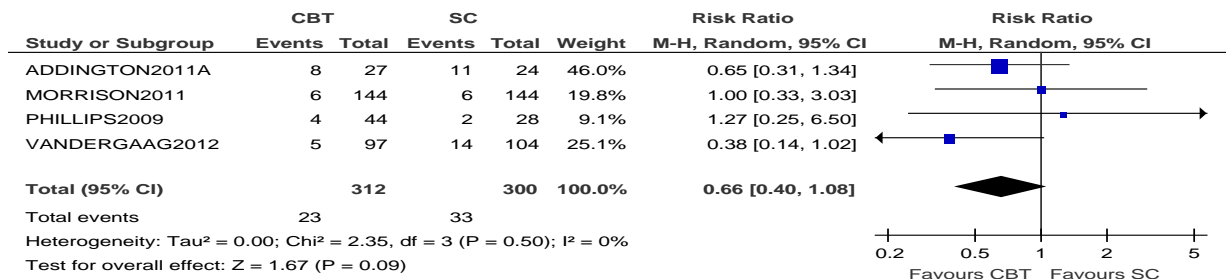
16.10 Sensitivity analysis: mean endpoint quality of life (MANSA, QLS) (without VANDERGAAG2012)



16.11 Completer analysis: transition to psychosis (DSM-IV, PANSS, CAARMS, PANSS)

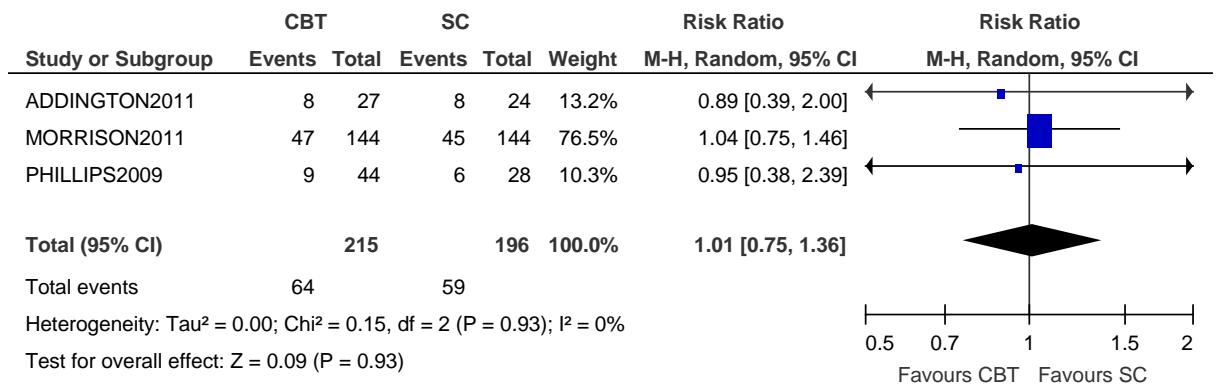


16.12 Sensitivity analysis: transition to psychosis (DSM-IV, PANSS, CAARMS, PANSS)



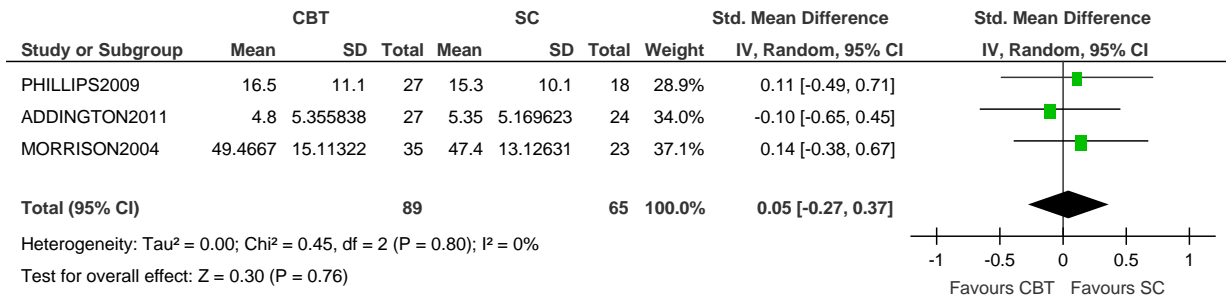
17. CBT versus supportive counselling (SC): post-treatment (leaving the study for any reason)

17.1 Leaving the study early for any reason

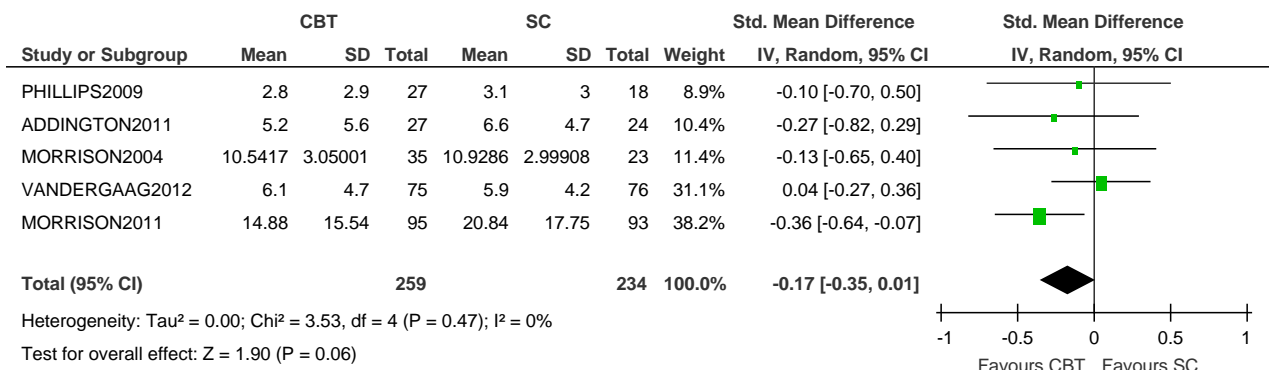


18. CBT versus supportive counselling (SC): 52 weeks' follow-up

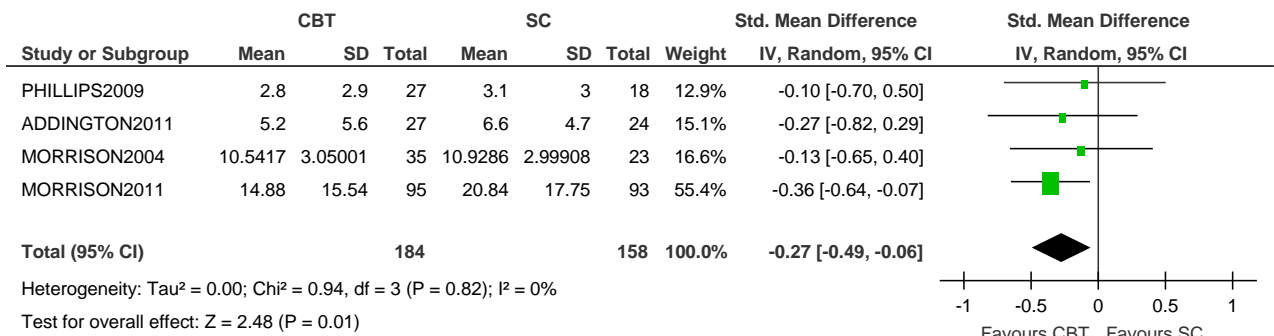
18.1 Mental state: mean endpoint total symptoms (SOPS, CAARMS severity)



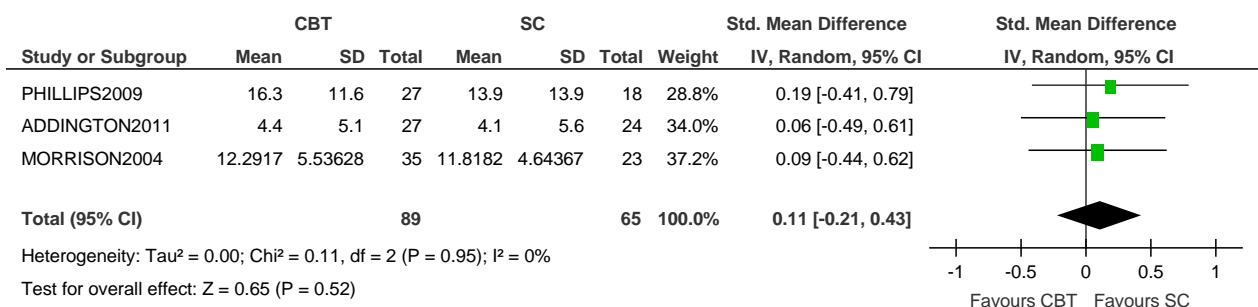
18.2 Mental state: mean endpoint positive symptoms (SOPS positive)



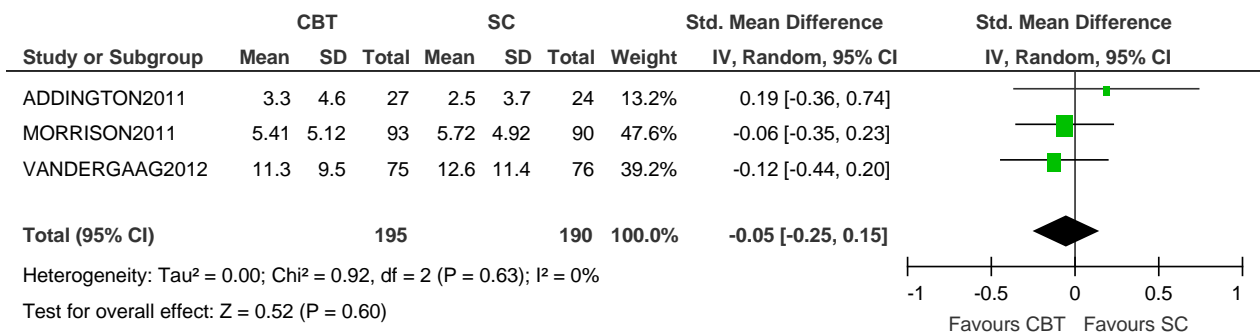
18.3 Sensitivity analysis: mental state: mean endpoint positive symptoms (SOPS positive) (without VANDERGAAG2012)



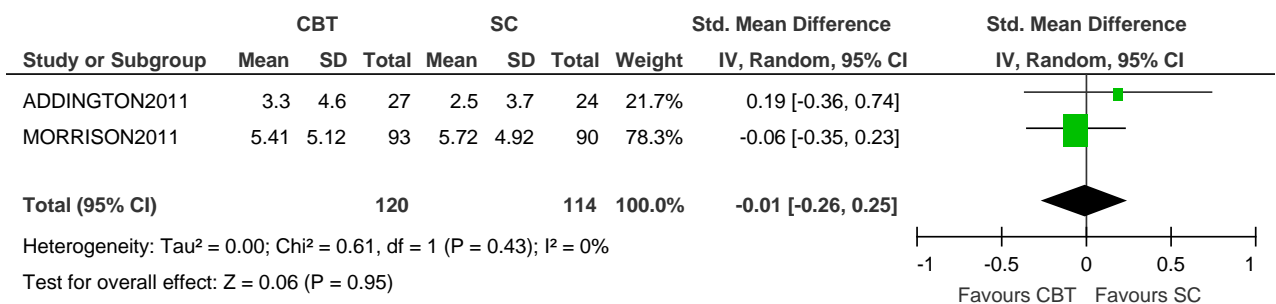
18.4 Mental state: mean endpoint negative symptoms (SOPS negative)



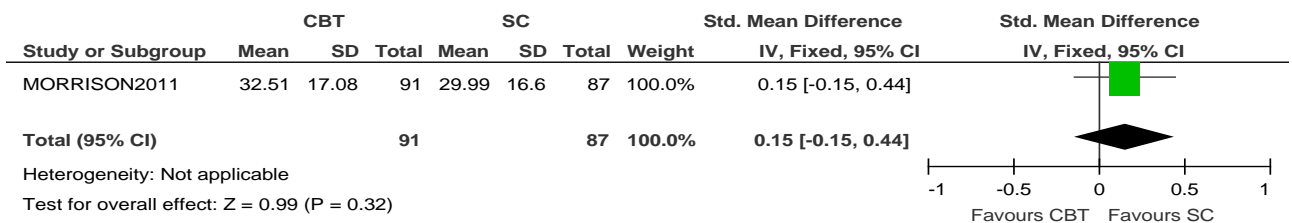
18.5 Mental state: mean endpoint depression symptoms (CDSS, BDI-PC)



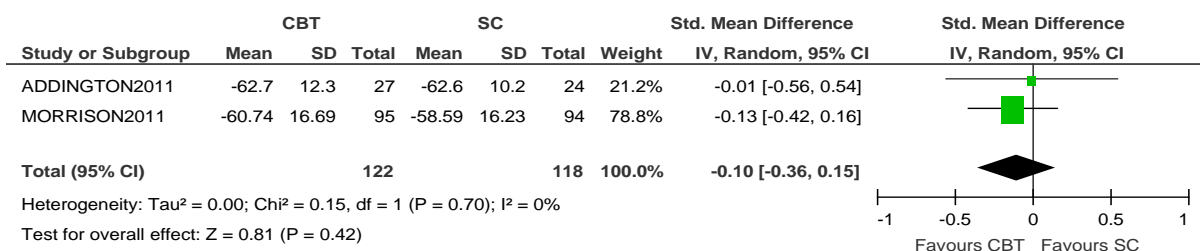
18.6 Sensitivity analysis: mental state: mean endpoint depression symptoms (CDSS, BDI-PC) (without VANDERGAAG2012)



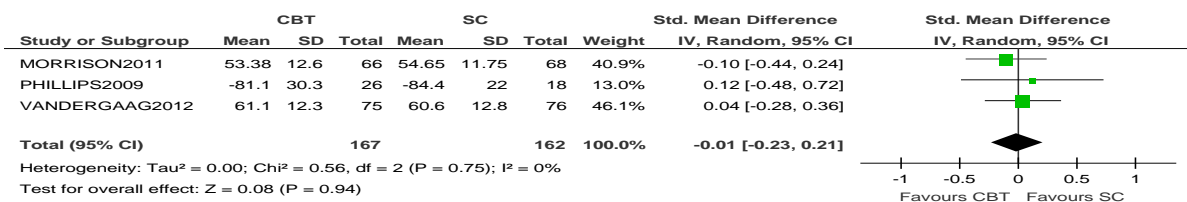
18.7 Mental state: mean endpoint social anxiety symptoms (SIAS)



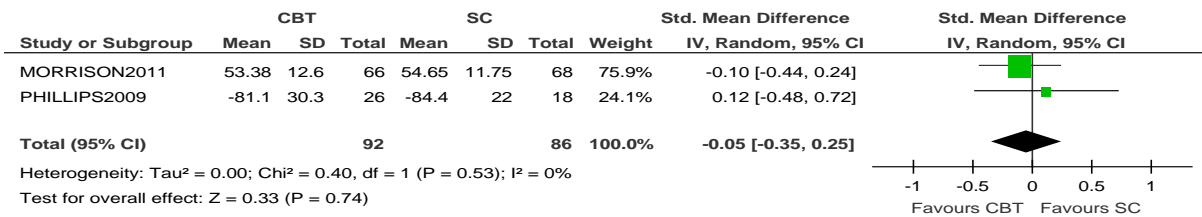
18.8 Mean endpoint psychosocial functioning (GAF)



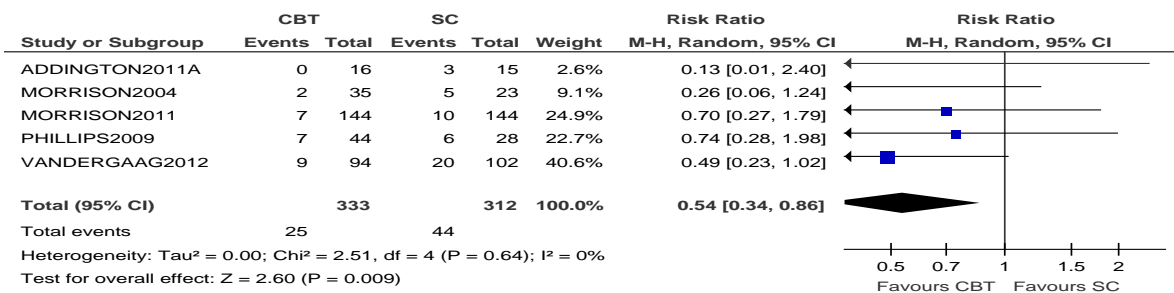
18.9 Mean endpoint quality of life (MANSA)



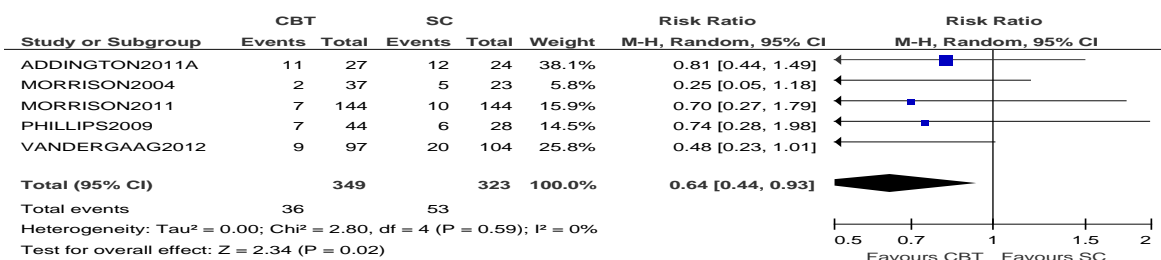
18.10 Sensitivity analysis: mean endpoint quality of life (MANSA) (without VANDERGAAG2012)



18.11 Completer analysis: transition to psychosis (DSM-IV, PANSS)

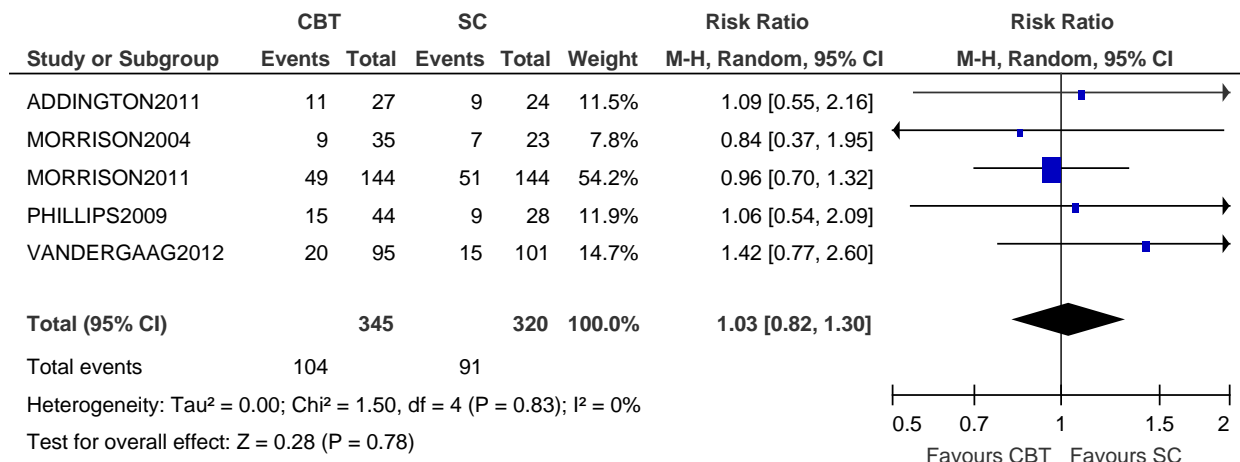


18.12 Sensitivity analysis: transition to psychosis (DSM-IV, PANSS)



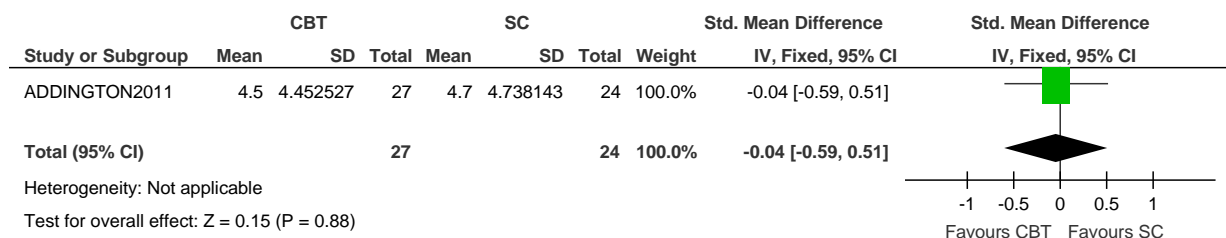
19. CBT versus supportive counselling (SC): 52 weeks' follow-up (leaving the study for any reason)

19.1 Leaving the study early for any reason

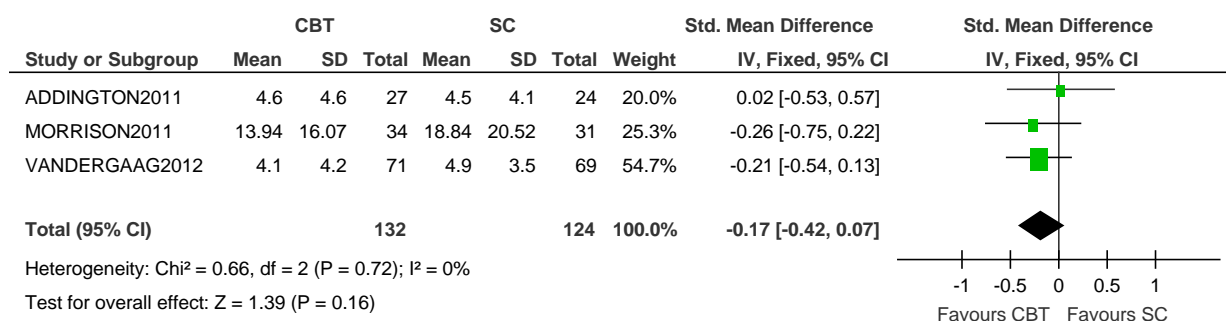


20. CBT versus supportive counselling (SC): follow-up of 78 weeks or more

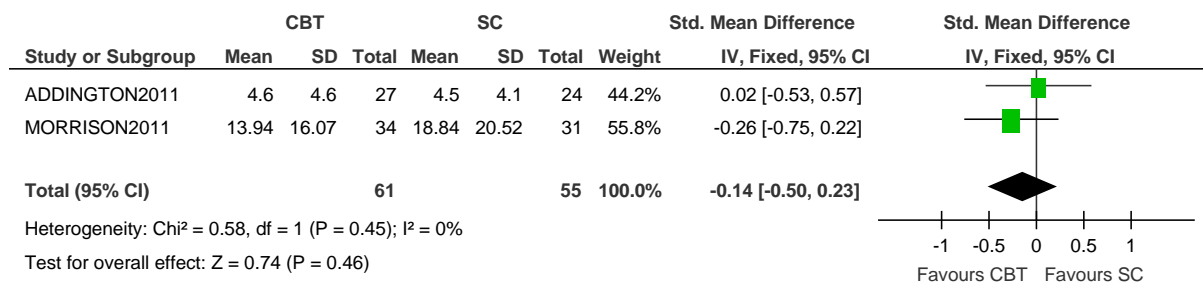
20.1 Mental state: mean endpoint total symptoms (SOPS, CAARMS Severity)



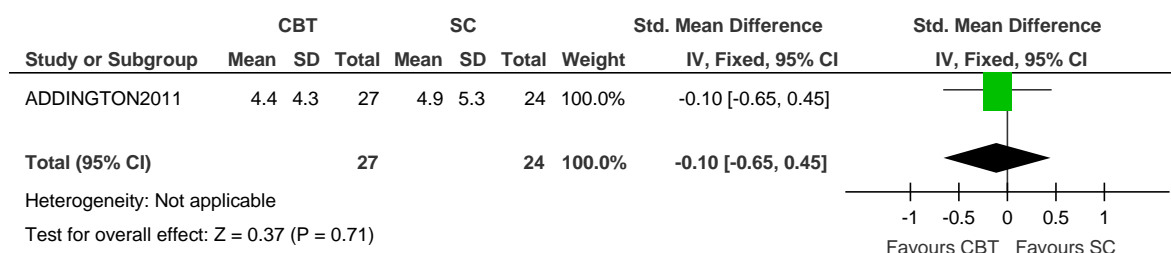
20.2 Mental state: mean endpoint positive symptoms (SOPS Positive)



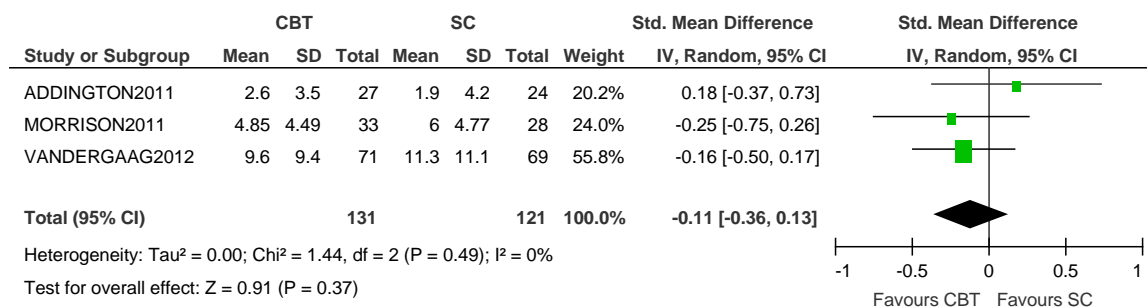
20.3 Sensitivity analysis: mental state: mean endpoint positive symptoms (SOPS Positive)



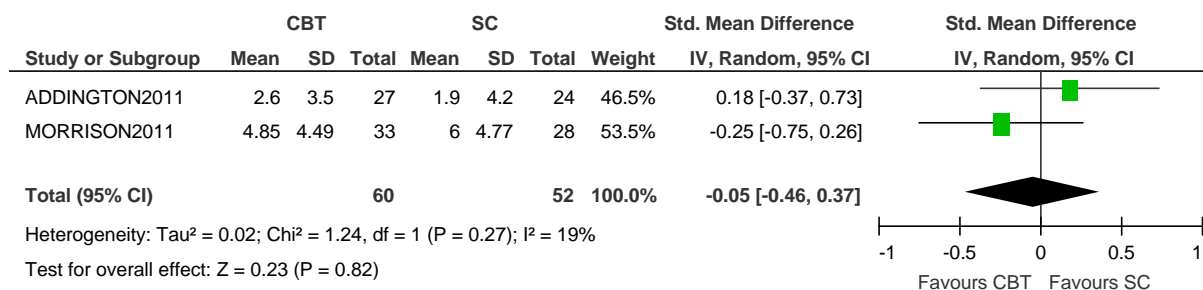
20.4 Mental state: mean endpoint negative symptoms (SOPS Negative)



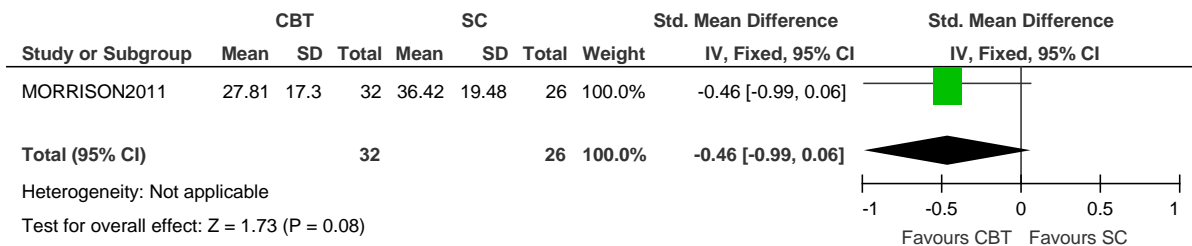
20.5 Mental state: mean endpoint depression symptoms (CDSS, BDI-PC)



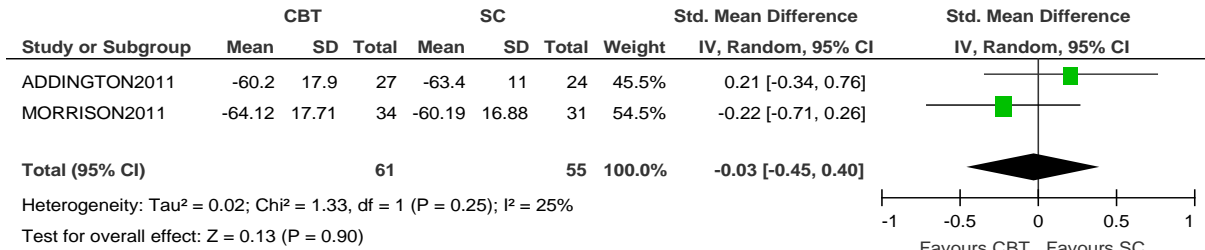
20.6 Sensitivity analysis: mental state: mean endpoint depression symptoms (CDSS, BDI-PC)



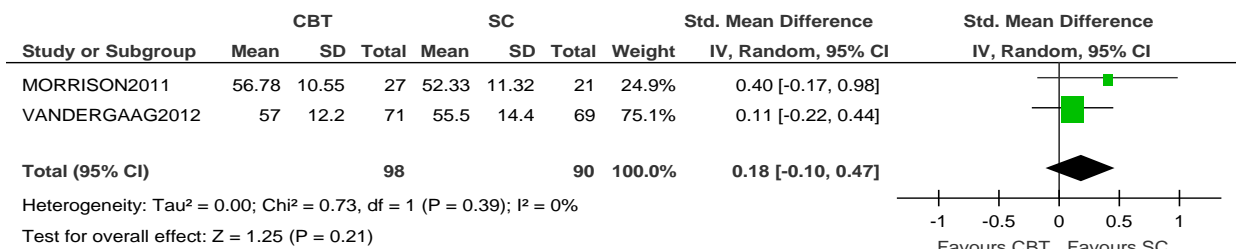
20.7 Mental state: mean endpoint social anxiety symptoms (SIAS)



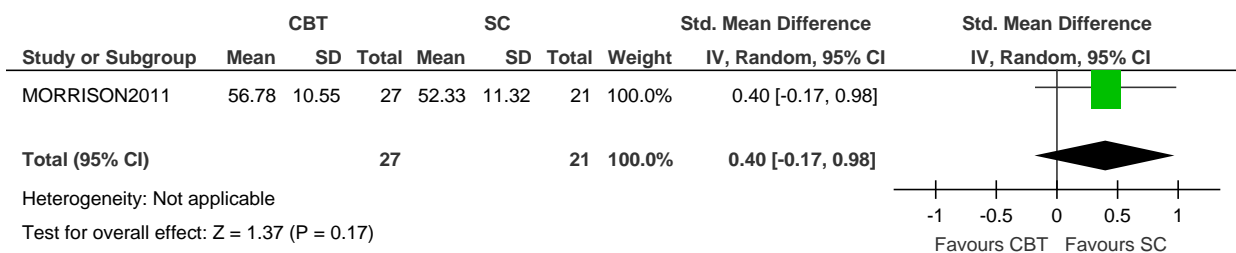
20.8 Mean endpoint psychosocial functioning (GAF)



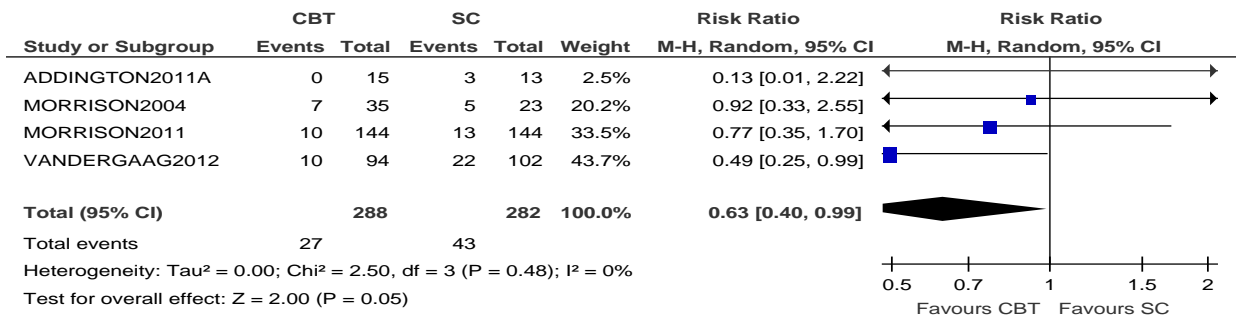
20.9 Mean endpoint quality of life (MANSA)



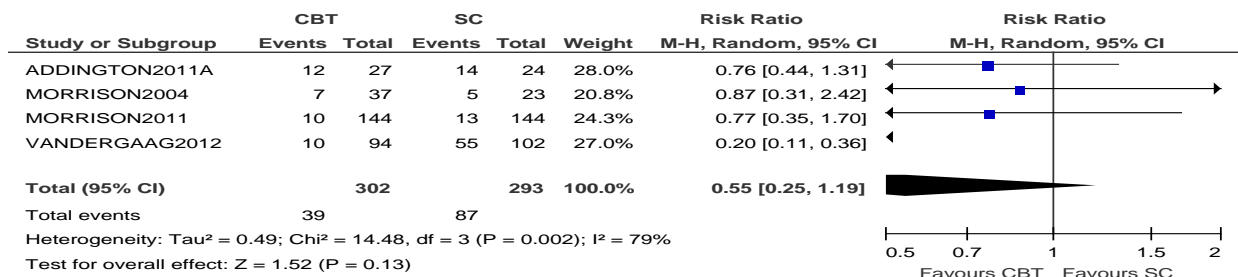
20.10 Sensitivity analysis: mean endpoint quality of life (MANSA)



20.11 Completer analysis: transition to psychosis (DSM-IV, PANSS)

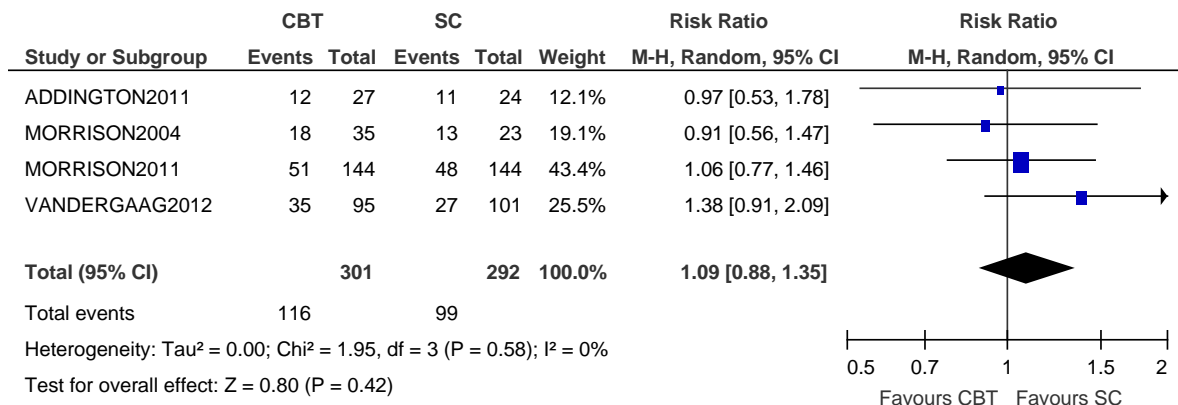


20.12 Sensitivity analysis: transition to psychosis (DSM-IV, PANSS)



21. CBT versus supportive counselling (SC): follow-up of 78 weeks or more (leaving the study for any reason)

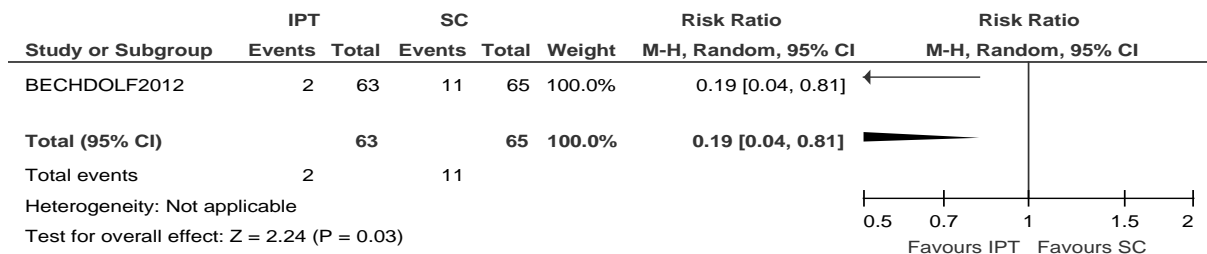
21.1 Leaving the study early for any reason



PSYCHOLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 25 YEARS AND YOUNGER

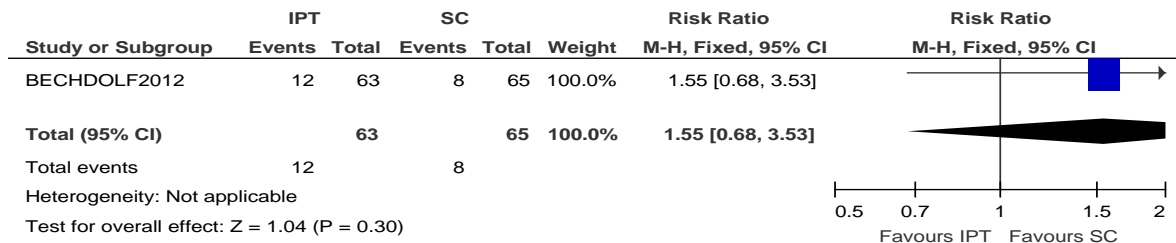
22. Integrated psychological therapy (IPT) versus supportive counselling (SC): 52 weeks post-treatment

22.1 Transition to psychosis (PANSS)



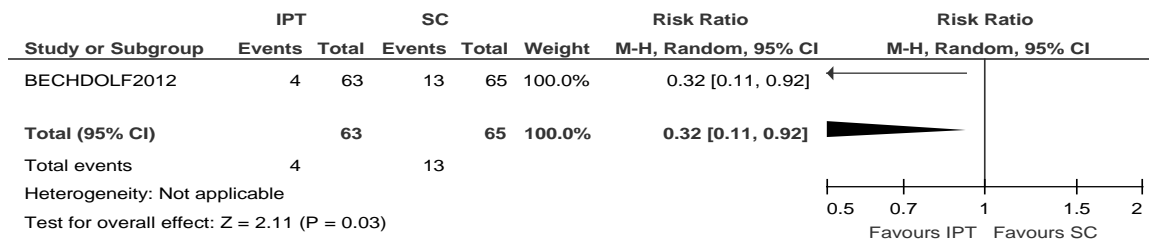
23. Integrated psychological therapy (IPT) versus supportive counselling (SC): 52 weeks post-treatment (leaving the study for any reason)

23.1 Leaving the study early for any reason



24. Integrated psychological therapy (IPT) versus supportive counselling (SC): 104 weeks' follow-up

24.1 Transition to psychosis / subthreshold psychosis (PANSS)



25. Integrated psychological therapy (IPT) versus supportive counselling (SC): 104 weeks' follow-up (leaving the study for any reason)

25.1 Leaving the study early for any reason

