NKR24 - PICO9 - Schizophrenia: CBT+MI for schizophrenia and substance use

Characteristics of studies

Characteristics of included studies

Baker 2006

Methods	Allocation: randomised. Design: Single centre. Duration: 12 months. Setting: community. Location: Hunter region, NSW, Australia.
Participants	Diagnosis: 75%ICD-10 schizophrenia or schizoaffective disorderwith SCID-1 diagnosis of abuse or dependence past 12 months (alcohol 69%, cannabis 74%, amphetamine 42%).* N=130. Age: mean 29 years. Sex: 102M, 28F. Ethnicity: not reported. Inclusion criteria: SCID abuse or dependence for alcohol, cannabis or amphetamine during precedingmonth, age at least 15 years, ability to speakEnglish, having a confirmed ICD-10 psychotic disorder, no organic brain impairment, and not intending to move from area within 12 months
Interventions	1. Motivational interviewing and CBT (10 weekly one hour sessions). N=65. 2. Routine care plus self-help books. N=65.
Outcomes	Lost to evaluation. Death. Substance use: OTI (polydrug use only). Other: GAF. Unable to use: Lost to treatment (no control group data). Substance use: OTI (alcohol, cannabis, amphetamine - skewed data). Mental state: BPRS, BDI-II (data skewed).
Notes	Not ITT analysis. Authors report that a separate ITT analysis was run with similar results *Some participants were dependent on more than one of these. Participants paid AUD $20 for each assessment interview.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Participants drew a card from an envelope but no details provided regarding the generation of the random sequence or whether cards were shuffled beforehand
Allocation concealment (selection bias)	Unclear risk	Patients drew a card from an envelope. No further details provided so it is unclear if envelope was opaque and sealed
Blinding of participants and personnel (performance bias)	Unclear risk	Clinician/participant mediated and participants and personnel not blinded. unclear risk
Blinding of outcome assessment (detection bias)	Low risk	Raters blind so detection bias rated as low.
Incomplete outcome data (attrition bias)	Unclear risk	Lost to follow-up 20% (26/130) 1 year. Number and reason formissing data clearly reported in flow sheet. Missing outcome data balanced across groups. Full ITT analysis with imputed data for all missing values not reported
Selective reporting (reporting bias)	Unclear risk	In the report, the results are fully reported. There is no protocol
Other bias	Low risk	Funded by public institution. No evidence other biases are occurring

Barrowclough 2001

Methods	Allocation: randomised. Design: single centre (three sites). Duration: 12, 18* months. Setting: own homes. Location: Tameside & Glossop, Stockport and Oldham, UK.

Participants	Diagnosis: ICD-10 & DSM-IV schizophrenia or schizoaffective disorder with DSM-IV substance abuse or dependence. N=36. Age: 18-65 years, mean ~ 31 years. Sex: 33M, 3F. Ethnicity: white European. Inclusion criteria: current substance abuse, in current contactwithmental health services, min. 10 hours face-to-face contact with the caregiver per week, no organic brain disease or other serious medical illness or learning disability
Interventions	1. Routine care with family support worker plus motivational interviewing, annualised individual CBT for the participant and CBT for family/caregiver for 9 months. N=18. 2. Routine care plus family support worker. N=18.
Outcomes	Lost to treatment. Lost to evaluation. Death. Mental state: PANSS. Relapse: number of participants experiencing relapse. Other: GAF, SFS. Unable to use: Substance use: ASI - % days abstinent (no mean/SD). Mental state: PANSS (some data skewed). Relapse: duration of relapse (only median and range supplied). Other: SFS 18 month (only adjusted means reported).
Notes	Part ITT analysis. *18 month data (see secondary reference Haddock et al 2003).

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated list stratified for sex and three types of substance use
Allocation concealment (selection bias)	Low risk	Allocated by third party.
Blinding of participants and personnel (performance bias)	Unclear risk	Clinician/participant mediated and participants and personnel not blinded. Unclear risk
Blinding of outcome assessment (detection bias)	Low risk	Raters independent and blind so detection bias rated as low.
Incomplete outcome data (attrition bias)	Unclear risk	Lost to follow-up: 22% (8/36) 18 months. Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
Selective reporting (reporting bias)	Low risk	No selective reporting evident between study protocol (N0244032344) and published article
Other bias	Low risk	Funded by public institution (local health authorities). No evidence other bias occurring

Barrowclough 2010

Methods	Allocation: Randomised. Design: Multi-centre (six large NHS mental health trusts). Duration: 24 months. Setting: Community (most patients received home treatment). Location: London, Lancashire and Manchester, UK.
Participants	Diagnosis: ICD-10 & DSM-IV non-affective psychotic disorder (schizophrenia, schizoaffective etc) and DSM-IV diagnosis of dependence on or abuse of drugs, alcohol or both N=327 Age: 17-67 years, mean ~38. Sex: 283M, 44F. Ethnicity: 81% (n=266) white. Inclusion criteria: English speaking, fixed abode, and no significant history of organic factors implicated in the aetiology of psychotic symptoms
Interventions	1. Routine care plus MI + CBT: Up to 26 individual therapy sessions delivered over 12 months (manual based). N=164.* 2. Routine care plus access to community based rehabilitation activities. N=163
Outcomes	Primary outcome: hospitalisation (for psychosis) or death versus not admitted and alive at 12 months follow-up Secondary: Lost to evaluation. Lost to treatment.

	Death Mental state: PANSS, GAF. Relapse: admissions last 12 months. Substance use: Inventory of drug use consequences, days abstinent, readiness to change Unable to use: proportion days abstinent from all substances (skewed data).
Notes	*One case was misdiagnosed (affective) and excluded from the analysis (CBT+MI)

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated, algorithm taking into account substance type (alcohol alone, drugs alone, or alcohol and drugs) and NHS trust
Allocation concealment (selection bias)	Low risk	Researcher not involved in the study generated sequence. Remote independent service
Blinding of participants and personnel (performance bias)	Unclear risk	Clinician/participant mediated and participants and personnel not blinded
Blinding of outcome assessment (detection bias)	Low risk	For the primary outcome of hospital admission data were obtained from participant psychiatric case notes and is unlikely to be affected by blinding. For other outcomes involving self-report, precautions were taken to maintain the blindness. Throughout the trial, 135 breaks in the blindness of an assessor were reported in total. However, only one assessment was completed unblinded; in all other cases a new “blind” assessor was allocated
Incomplete outcome data (attrition bias)	Unclear risk	Lost to follow-up: 25% (81/327) 2 years. Flow sheet provided describing reasons for incomplete data and deaths. Evenly balanced between treatment groups. Nomissing values for primary outcome measure (re-hospitalisation/or death)
Selective reporting (reporting bias)	Low risk	All outcomes of interest fully reported and these match the trial protocol
Other bias	Low risk	Authors independent of funding, No input from funding sources on protocol

Bellack 2006

Methods	Allocation: randomised (adaptive urn procedure). Design: single centre. Duration: 6 months. Setting: community clinics and Veterans Affairs medical center Location: Baltimore, Md, USA.
Participants	Diagnosis: 38% DSM-IV schizophrenia or schizoaffective disorder, 55% major affective disorder. DSM-IV substance abuse or dependence (predominate drug of abuse was 69% cocaine, 25% opiates, 7% cannabis). N=175.** Mean age: 43 years. Sex: 111M, 64F. Ethnicity: 75% African American. Inclusion criteria: meeting criteria for severe and persistent mental illness and current dependence on cocaine, heroin or cannabis
Interventions	1. BTSAS: Behavioural Treatment for Substance Abuse in severe and persistent mental illness (SPMI).BTSAS consisted ofmotivational interviewing at baseline, 3 and 6months and includes motivational interviewing and CBT approaches. N=61.* 2. Routine care: Supportive Treatment for Addiction Recovery (STAR) which includes some psycho education and group discussion regarding substance misuse. N=49
Outcomes	Lost to treatment. **Lost to evaluation. Other: BQOL, arrests by 6 months. Unable to use: Substance use: urinalysis (no means, SDs or time period given). Mental state: ASI (data skewed). Hospitalisation. (psychiatric and substance use admissions combined). Other: SFS (only 1 subscale score used), BQOL money subscale (data skewed)

Notes	Not ITT analysis. *Participants paid for clean urine test average payment per person USD 60 ** n=175 randomised, however 46 patients failed to initiate treatment and 19 failed to become engaged (analysis was based on subset of 110 patients who were engaged in treatment) Authors have kindly provided further data.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised using an adaptive urn procedure adjusted for sex, psychiatric diagnosis, drug of choice and number of substance use disorders. Separate randomisation was conducted for participants from community clinics and VA centre. No further details
Allocation concealment (selection bias)	Unclear risk	No details provided
Blinding of participants and personnel (performance bias)	Unclear risk	Clinician/participant mediated and participants and personnel not blinded. Unclear risk
Blinding of outcome assessment (detection bias)	Low risk	Primary outcome was urinalysis results so the review authors judge that this outcome is not likely to be influenced by a lack of blinding. Moreover, raters were blind to treatment assignment
Incomplete outcome data (attrition bias)	High risk	Lost to follow-up: 25%(27/110) 6months of “engaged” subjects 46 patients failed to initiate treatment and 19 failed to become engaged (analysis was based on subset of 110 patients who were engaged in treatment) so ITT analysis was not completed. Missing data were not balanced across interventions. Missing outcomes are enough to induce clinically relevant bias in observed effect size
Selective reporting (reporting bias)	Unclear risk	No protocol was available. Author states there was conflicting data on substance use between self-report, drug screens and clinical ratings (SCID) of dependence
Other bias	Low risk	Supported by NIDA grant.

Hjorthøj 2013

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	Unclear risk	no info
Blinding of outcome assessment (detection bias)	Low risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	

Kemp 2007

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	
Allocation concealment (selection bias)	Unclear risk	no info
Blinding of participants and personnel (performance bias)	Unclear risk	no info
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	Unclear risk	no info
Selective reporting (reporting bias)	Unclear risk	no info
Other bias	High risk	

Madigan 2013

Methods	Allocation: randomised. Design: single centre (3 sites). Duration: 12 months. Setting: inpatients and community. Location: Dublin, Ireland.
Participants	Diagnosis: DSM-IV diagnosis of psychosis (schizophrenia, n=38; other psychosis, n= 30) major depression (n=6) and bipolar disorder (n=14) and DSM-IV current cannabis dependence. N=88. Age: mean ~ 28 years. Sex: 69M, 19F. Ethnicity: Not stated (homogenous group). Inclusion criteria: without learning disability or organic brain damage
Interventions	1. CBT/MI group sessions once per week for 12 weeks and invited back 6 weeks later (week 18) for a booster session. Interventions were held in community setting. N=59.* 2. TAU, standard care included care from multi-disciplinary team, 5 patients had counselling for opiate more than one year prior to the present trial. N=29
Outcomes	Lost to treatment (3 months). Lost to follow-up (9 months). Frequency of cannabis use last 30 days. GAF global functioning. Subjective quality of life (WHOQOL, BREF). Unable to use: Mental State: SANS. SAPS (positive, negative),CalgaryDepression Scale for Schizophrenia (skewed data)
Notes	* Note: 2:1 randomisation to CBT/MI arm. A token voucher was given to participants to cover costs of attendance of assessments

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated, block randomised, 2: 1 (CBT/MI:TAU) ratio
Allocation concealment (selection bias)	Unclear risk	Randomisation was conducted by a researcher uninvolved in the provision or assessment of interventions. Concealment not described in sufficient detail to allow a definite judgement
Blinding of participants and personnel (performance bias)	Unclear risk	Clinician/participant mediated and participants and personnel not blinded. Unclear risk
Blinding of outcome assessment (detection bias)	Low risk	Raters of clinical outcomes blind to treatment allocation.
Incomplete outcome data (attrition bias)	Unclear risk	Lost to follow-up: 42% (37/88) 1 year. Similar reasons for missing data across groups. Missing values were not imputed for ITT analysis
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement of 'yes' or 'no' as no protocol was available
Other bias	Low risk	No evidence other bias occurring.

Footnotes

Characteristics of excluded studies

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

References to studies

Included studies

Baker 2006

[Empty]

Barrowclough 2001

[Empty]

Barrowclough 2010

[Empty]

Bellack 2006

[Empty]

Hjorthøj 2013

[Empty]

Kemp 2007

[Empty]

Madigan 2013

[Empty]

Excluded studies

Data and analyses

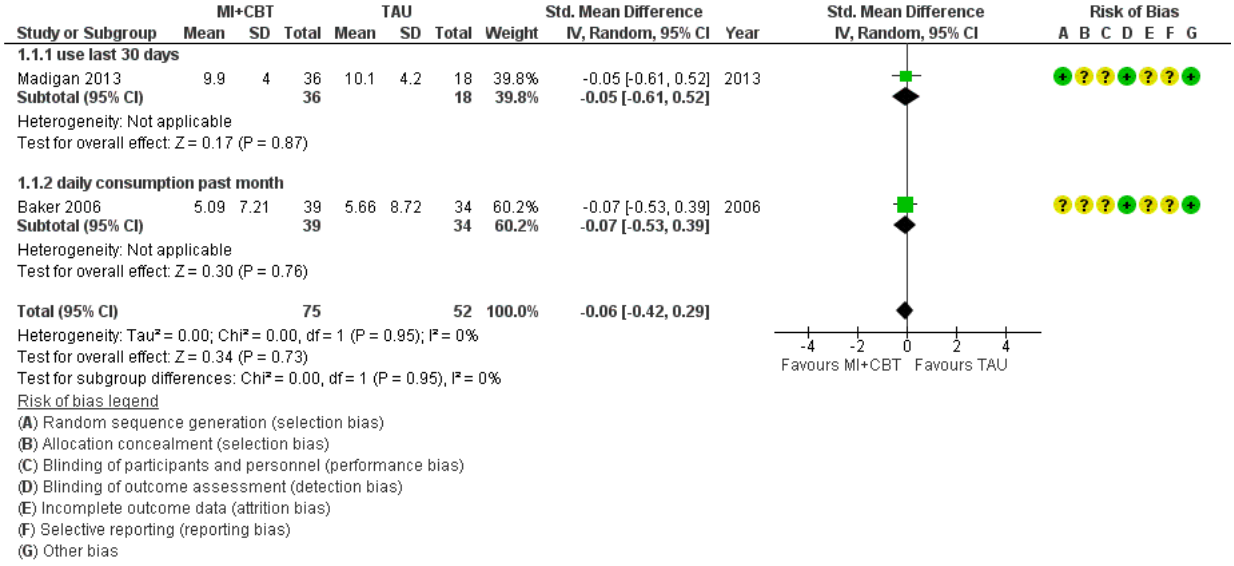
1 MI+CBT

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Cannabis use, end of treatment	2	127	Std. Mean Difference (IV, Random, 95% CI)	-0.06 [-0.42, 0.29]
1.1.1 use last 30 days	1	54	Std. Mean Difference (IV, Random, 95% CI)	-0.05 [-0.61, 0.52]
1.1.2 daily consumption past month	1	73	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.53, 0.39]
1.2 Amphetamine, estimated daily consumption past month, end of treatment	1	20	Std. Mean Difference (IV, Random, 95% CI)	0.16 [-0.73, 1.04]
1.3 Cannabis use, longest FU, min. 4-6 months	3	168	Std. Mean Difference (IV, Random, 95% CI)	0.03 [-0.34, 0.41]
1.3.1 days of use last month	1	68	Std. Mean Difference (IV, Random, 95% CI)	-0.21 [-0.69, 0.27]
1.3.2 daily consumption past month	1	58	Std. Mean Difference (IV, Random, 95% CI)	0.39 [-0.13, 0.90]
1.3.3 use last 30 days	1	42	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.72, 0.57]
1.4 Amphetamine, estimated daily use, 12 months FU	1	17	Mean Difference (IV, Random, 95% CI)	0.13 [-0.11, 0.37]
1.5 Symptoms, end of treatment	2	78	Std. Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.38, 0.51]
1.5.1 PANSS total (high=poor)	2	78	Std. Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.38, 0.51]
1.6 Relapse (mental state), end of treatment	1	36	Risk Ratio (M-H, Random, 95% CI)	0.50 [0.21, 1.17]
1.7 Use of alcohol, end of treatment	2	68	Std. Mean Difference (IV, Fixed, 95% CI)	0.32 [-0.17, 0.81]
1.7.1 estimated daily consumption past month	1	52	Std. Mean Difference (IV, Fixed, 95% CI)	0.36 [-0.20, 0.91]
1.7.2 frequency per month	1	16	Std. Mean Difference (IV, Fixed, 95% CI)	0.20 [-0.82, 1.21]

1.8 Quality of Life, end of treatment	3	190	Std. Mean Difference (IV, Random, 95% CI)	0.17 [-0.13, 0.48]
1.8.1 BQOL, low=poor	1	110	Std. Mean Difference (IV, Random, 95% CI)	0.01 [-0.36, 0.39]
1.8.2 WHOQOL, low=poor	1	16	Std. Mean Difference (IV, Random, 95% CI)	0.75 [-0.30, 1.81]
1.8.3 MANSA, low=poor	1	64	Std. Mean Difference (IV, Random, 95% CI)	0.31 [-0.19, 0.80]
1.9 Social functioning, end of treatment	3	209	Std. Mean Difference (IV, Random, 95% CI)	-0.08 [-0.54, 0.37]
1.9.1 SFS average score (low=poor)	1	32	Std. Mean Difference (IV, Random, 95% CI)	-0.62 [-1.34, 0.09]
1.9.2 GAF average score (low=poor)	2	177	Std. Mean Difference (IV, Random, 95% CI)	0.13 [-0.17, 0.43]
1.10 Death, 12 months FU	3	493	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.22, 2.41]
1.11 Crimes, arrests by 6 months (end of treatment)	1	110	Odds Ratio (M-H, Random, 95% CI)	0.42 [0.16, 1.11]
1.12 Days in hospital	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable

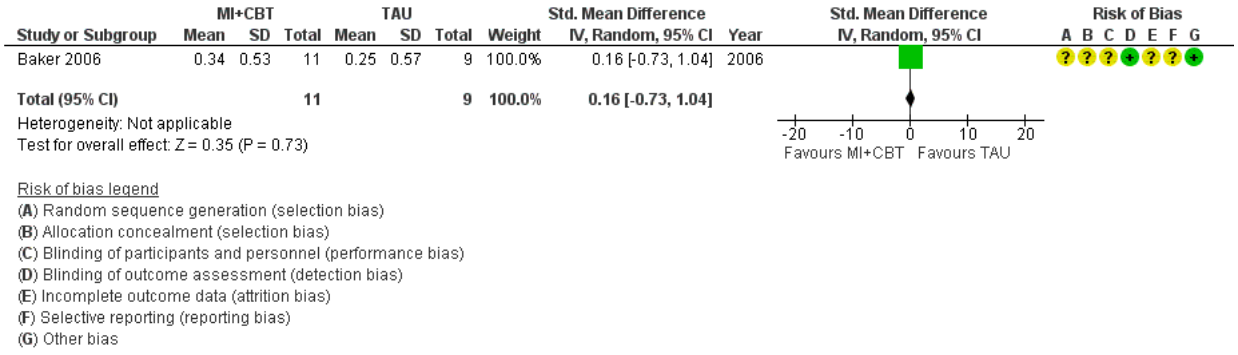
Figures

Figure 1 (Analysis 1.1)



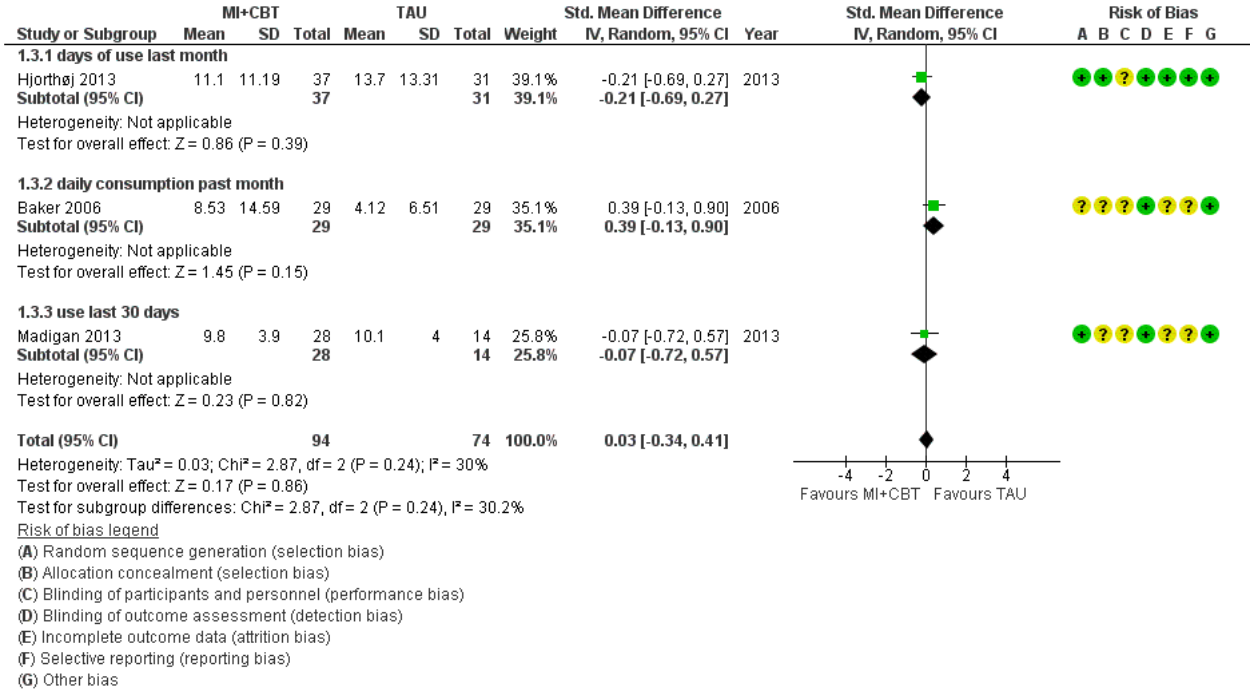
Forest plot of comparison: 1 MI+CBT, outcome: 1.1 Cannabis use, end of treatment.

Figure 2 (Analysis 1.2)



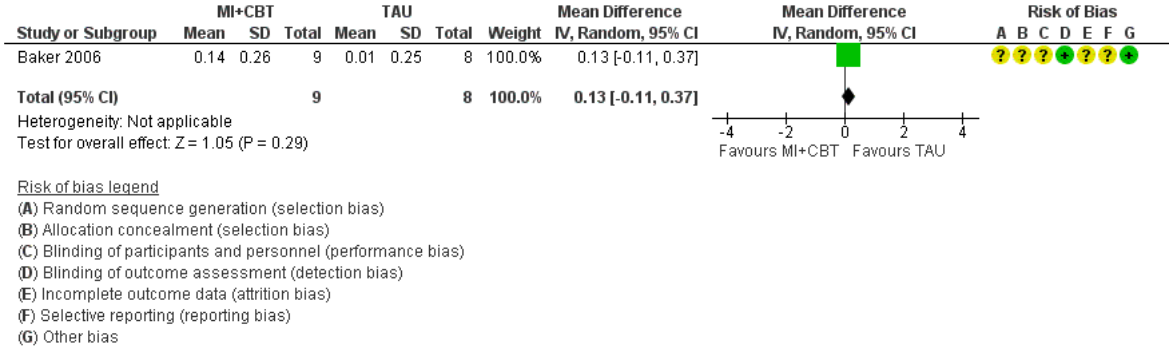
Forest plot of comparison: 1 MI+CBT, outcome: 1.2 Amphetamine, estimated daily consumption past month, end of treatment.

Figure 3 (Analysis 1.3)



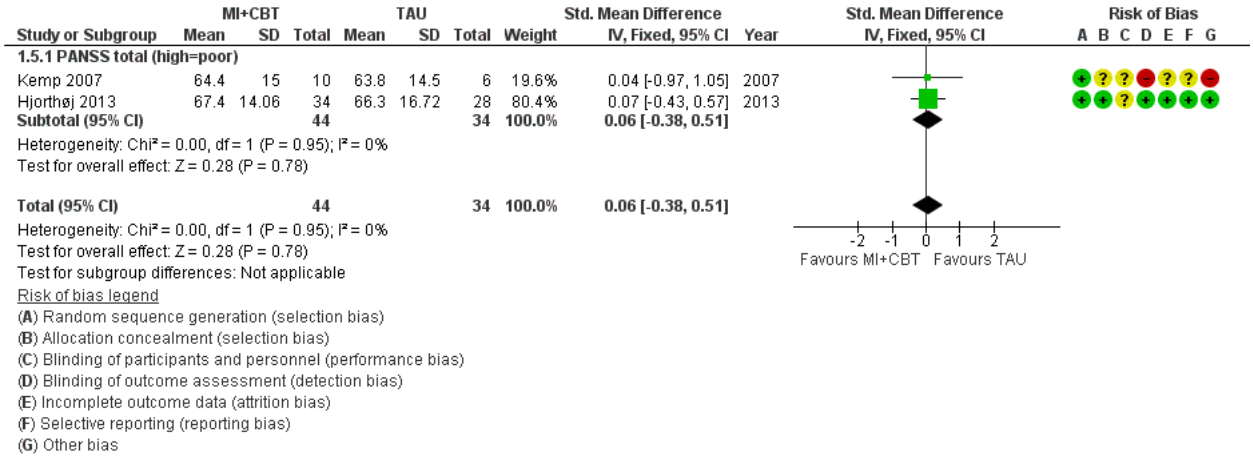
Forest plot of comparison: 1 MI+CBT, outcome: 1.3 Cannabis use, longest FU, min. 4-6 months.

Figure 4 (Analysis 1.4)



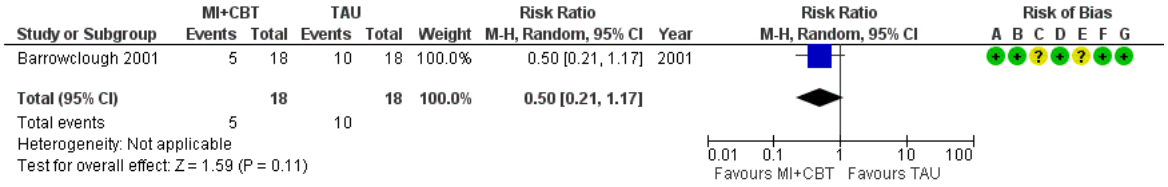
Forest plot of comparison: 1 MI+CBT, outcome: 1.4 Amphetamine, estimated daily use, 12 months FU.

Figure 5 (Analysis 1.5)



Forest plot of comparison: 1 MI+CBT, outcome: 1.5 Symptoms, end of treatment.

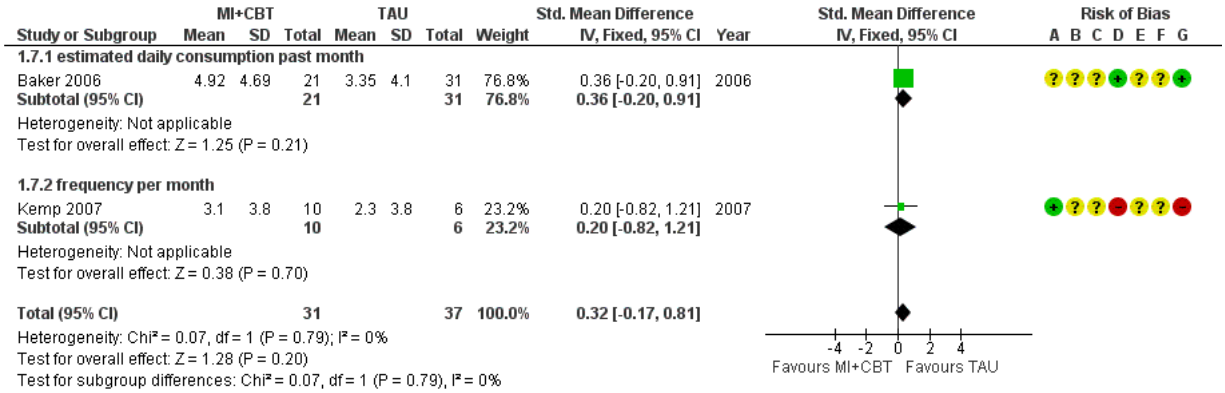
Figure 6 (Analysis 1.6)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 MI+CBT, outcome: 1.6 Relapse (mental state), end of treatment.

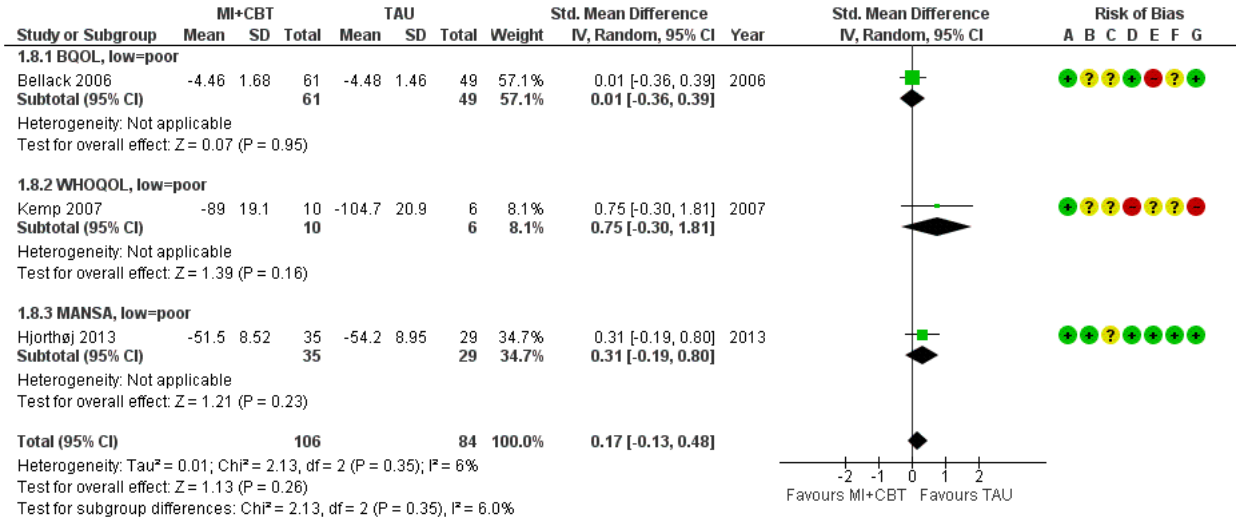
Figure 7 (Analysis 1.7)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 MI+CBT, outcome: 1.7 Use of alcohol, end of treatment.

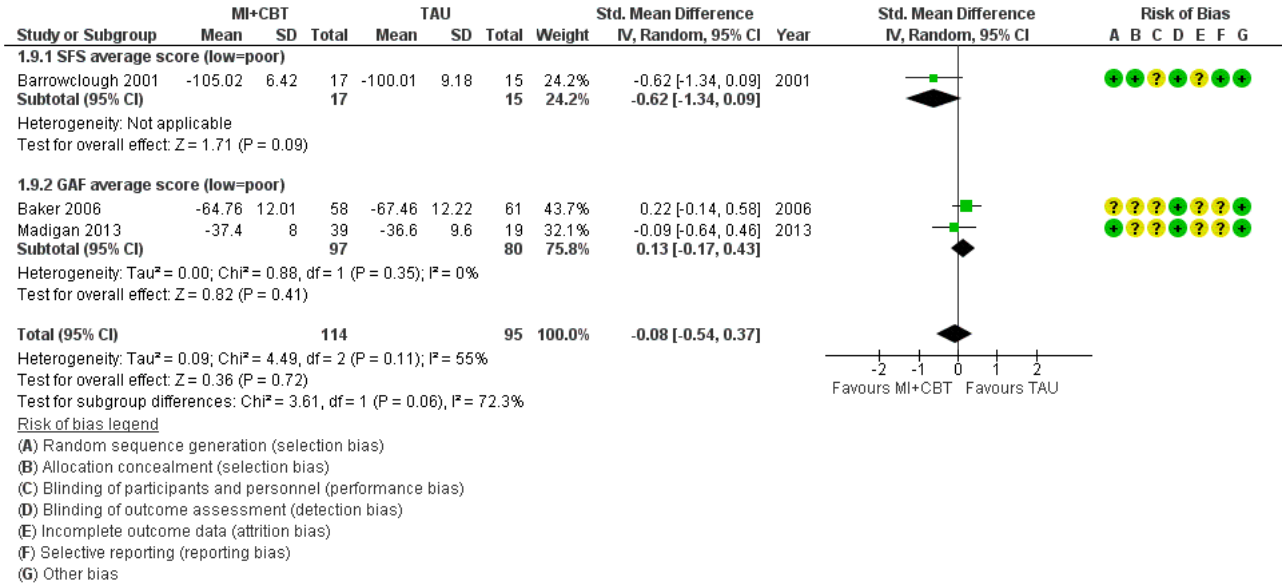
Figure 8 (Analysis 1.8)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 MI+CBT, outcome: 1.8 Quality of Life, end of treatment.

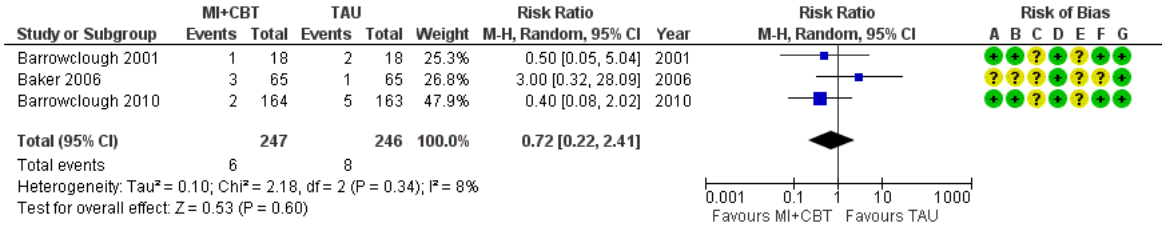
Figure 9 (Analysis 1.9)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 MI+CBT, outcome: 1.9 Social functioning, end of treatment.

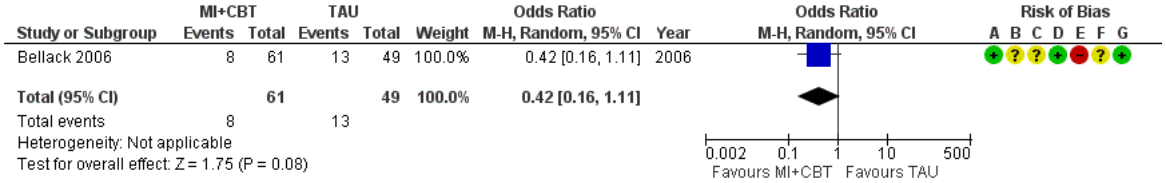
Figure 10 (Analysis 1.10)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 MI+CBT, outcome: 1.10 Death, 12 months FU.

Figure 11 (Analysis 1.11)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 MI+CBT, outcome: 1.11 Crimes, arrests by 6 months (end of treatment).