Efficacy of Motivational Interviewing in Treating Co-occurring Psychosis and Substance Use Disorder:
A Systematic Review and Meta-Analysis

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ABSTRACT

Objective: A wealth of evidence has supported the efficacy of motivational interviewing (MI) in reducing substance use as well as other addictive behaviors. In view of the common co-occurrence of substance use disorder among individuals with schizophrenia spectrum disorders, there has been increased attention to applying MI in psychological interventions for individuals with co-occurring psychosis and substance use disorder. This review aims to synthesize the evidence on the efficacy of MI interventions (either as a stand-alone intervention or in combination with other psychological interventions) in reducing substance use and psychotic symptoms.

Data Sources: MEDLINE, PsycINFO, EMBASE, CENTRAL, and CINAHL were searched using keywords related to "psychosis," "substance addiction," and "motivational interviewing" to identify studies published in English from 1984 to May 2021.

Study Selection: Of 1,134 articles identified in the literature, we selected 17 studies for review: 5 studies examined stand-alone MI ("MI-pure"), and 13 studies assessed MI as a major treatment component ("MI-mixed").

Data Extraction: Demographics of participants, intervention characteristics, and outcome data were extracted by the first author and checked by the second author. Random-effects models were used for substance use and psychotic symptom outcomes.

Results: MI-pure interventions did not significantly reduce severity of substance use ($g = 0.06$, $P = .81$) or psychotic symptoms (g's for 2 individual studies = 0.16, $P = .54$; and 0.01, $P = .96$). The effect of MI-mixed interventions on substance use decrease was statistically significant but small in size ($g = 0.15$, $P = .048$), whereas the effect on psychotic symptom improvement was not significant ($g = 0.11$, $P = .22$).

Conclusions: With the caveat that only a small number of comparisons were available for the review on MI-pure interventions, the efficacy of MI in treating co-occurring psychosis and substance use disorder was heterogeneous and modest.

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Psychosis is a psychiatric condition that affects nearly 1% of the population, and approximately half of individuals with psychosis meet the diagnostic criteria for a substance use disorder, a rate about 3 times higher than that in healthy individuals.[1–3] Of all types of substances, alcohol and cannabis are the most commonly used,[1,2] with polydrug use being a common pattern of use.[4] Substance use disorder not only poses a clinical challenge in and of itself but also exacerbates the existing psychotic symptomatology.[5–7] Coexisting psychosis and substance use disorder are associated with a wide spectrum of problems, including severe mental distress, suicidal ideations, poor psychosocial functioning, low antipsychotic adherence, delayed treatment seeking, heightened risks of medical diseases, frequent hospitalizations, housing problems, violence, and victimization.[7]

Clinical guidelines for schizophrenia spectrum disorders recommend evidence-supported psychological interventions such as cognitive behavioral therapy (CBT) and family intervention alongside antipsychotic medication, which forms the first-line treatment.[8,9] However, special considerations are required for individuals with a dual diagnosis. First, substance use may be adopted by individuals as coping behaviors in response to the distressing psychotic symptoms[7,10] or contribute directly to the psychotic symptomatology, such as in the case of substance-induced psychosis.[11,12] Second, individuals with a dual diagnosis typically present with perceived social stigma, low motivation to maintain abstinence and self-management, and high resistance, which are common obstacles in effective treatment.[7,13] Therefore, an intervention that has a motivational component and targets substance use will be conducive to overall clinical outcome for individuals with co-occurring psychosis and substance use disorder.[8,14]

Motivational interviewing (MI), first developed as a treatment approach for alcohol addiction,[15] is a clinical method that aims at promoting behavior change by eliciting people's intrinsic motivation to change.[16–18] MI is conducted through 4 key processes: engaging (establish a working relationship), focusing (maintain a direction of change), evoking (elicit motivations for change), and planning (develop commitment and plan for action).[16] A wealth of evidence has supported the efficacy of MI in reducing substance use as well as other addictive behaviors.[18–22] It has been argued that MI effects changes among individuals with substance use disorder by increasing change talk (arguments for change),

Clinical Points

- There has been increased attention to applying motivational interviewing (MI) to treating co-occurring psychosis and substance use disorder, although the treatment efficacy remains unclear.
- In this analysis, MI showed a small effect on decreasing substance use when integrated with other treatment components but not when used alone. Reducing substance use behaviors may further produce improvement in psychotic symptoms.

softening sustain talk, and strengthening commitment.[23,24] MI has also been shown to increase healthy behaviors among people with long-term medical conditions by enhancing adherence to treatments (eg, weight-loss programs).[18–20] While MI can form a stand-alone brief psychological intervention with behavior change as the key outcome, it is more typically delivered as part of a more extensive treatment (integrating both MI and non-MI components) or as a prelude to other interventions such as CBT.[18,25] When MI is combined with other treatment components, the therapeutic outcomes usually encompass both behavior changes and clinical improvement.[17]

Building on the wealth of evidence of MI on substance use disorder, there has been an increase in attention in applying MI to psychological treatment for individuals with psychosis who had coexisting substance addiction or a substance use disorder. These treatments range from brief stand-alone MI intervention for behavior changes[26,27] to longer treatment integrating MI components with other treatments such as CBT and family therapy.[28] In view of the unique characteristics of this population such as cognitive impairments and disordered thinking, adaptations might be made to the content and delivery of the intervention.[13] Therapeutic outcomes such as psychotic symptomatology, substance abstinence, and medication adherence are most commonly evaluated. Other treatment goals include reduction of perceived social stigma and increase in motivation to change.[13]

Although a number of reviews have recently been published on psychological interventions for individuals with co-occurring psychosis and substance use,[29–33] these studies cover a wide range of treatment modalities and do not focus on MI. Barrowclough et al[4] reviewed 7 MI studies in psychosis and co-occurring substance use disorder and found evidence for the general effectiveness of MI either used in isolation or combined with CBT. On the contrary, Lubman et al[32] argued that MI alone had limited effects but might be useful when integrated with other treatment elements. While previous meta-analyses on MI[18–22] cover a range of populations with a single psychological condition, none have targeted individuals with co-occurring psychosis and substance use disorder. In the only meta-analysis on psychosocial interventions for individuals with severe mental illness and substance use (including MI), only an effect of substance use but not of psychiatric symptom outcomes was reported.[29] With numerous treatment trials involving MI being conducted in recent years, it is time for us to quantitatively synthesize the effects of MI interventions on psychosis and substance use disorder. The aim of this systematic review and meta-analysis is to provide an up-to-date summary of the effects of MI in reducing psychotic symptoms and substance use, in comparison with control conditions, among individuals with co-occurring psychosis and substance use disorder. To enhance clinical implications of this study, we report effect sizes for trials that tested MI as a stand-alone treatment ("MI-pure") separately from those that had MI as a core component within an integrated treatment ("MI-mixed") among individuals with co-occurring psychosis and substance use disorder. On the basis of the existing literature, we derived the following hypotheses: (1) compared to control conditions, MI will produce higher reductions in severity of substance use disorder; (2) compared to control conditions, MI will produce higher reductions in severity of psychotic symptoms; and (3) MI-mixed interventions will yield a greater efficacy than MI-pure interventions. Associations between treatment effects and study characteristics were also explored.

METHOD

We followed the PRISMA guidelines for reporting the current systematic review and meta-analysis.[34,35]

Eligibility Criteria

To be eligible for inclusion in this review, a study had to meet the following criteria: (1) it was a published clinical trial written in English; (2) participants had coexisting psychosis (ie, *DSM* or *ICD* schizophrenia spectrum and other psychotic disorders, mania/severe depression/bipolar disorders/personality disorders with psychotic features) and substance use disorder; (3) a type of motivational intervention was delivered either as a stand-alone treatment or as a major treatment component as indicated by the authors; (4) there was at least 1 non-MI condition for comparison; and (5) effect of the treatment on either severity of psychotic symptoms or severity of substance use was reported.

A motivational intervention is defined as any type of intervention based on motivational interviewing principles.[16,25,36] Studies that adopted stand-alone MI were identified as MI-pure studies, whereas studies that integrated MI into a comprehensive treatment with other psychological treatment components (eg, CBT, family interventions) were identified as MI-mixed studies. Studies that added stand-alone MI to treatment-as-usual (TAU) were classified as MI-pure studies if the TAU included no active treatment component.

Electronic Literature Search

The electronic databases MEDLINE, PsycINFO, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), and the Cumulative Index of Nursing and Allied Health Literature (CINAHL) were searched for articles using the following search terms: (psychosis OR psychoses OR psychotic OR schizoaffective OR schizophreni*

OR paranoia OR hallucination* OR delusion* OR delud* OR negative symptoms OR positive symptoms) AND (substance OR drug OR alcohol OR cannabis OR amphetamine OR cocaine OR tobacco OR misuse OR abuse OR dependen* OR addict*) AND (motivational interviewing OR motivational enhancement OR motivation* intervention* OR motivational counsel*). The terms were searched as title and abstract. The search was limited to studies published from 1984 to May 2021.

Study Selection

Titles and abstracts of articles identified by the electronic searches were screened by the first two authors, and studies irrelevant to the topic of the current review were excluded. The first 2 authors independently read the full-text versions of the remaining articles and excluded those that did not meet the inclusion criteria. Reference lists of the included articles and major reviews and important journals were then checked for secondary search. Articles identified as relevant to the current topic were subjected to full-text screening and final analysis. A unanimous decision was reached between the first two authors to exclude a study during both title/abstract and full-text review. Disagreements between the authors were resolved by consensus via the corresponding author.

Data Extraction

A data extraction sheet was used to capture study characteristics and study data. Data were extracted by the first author and checked by the second author. Inconsistencies were resolved by consensus between the authors. Information extracted included demographic details of participants, service settings, randomization procedure, intervention characteristics, and outcome data.

Statistical Analyses

Data were analyzed in Comprehensive Meta-Analysis 2.0 (CMA).[37] Continuous outcomes were analyzed using standard mean difference (SMD) compared between conditions. Effect sizes were presented as the Hedges *g*,[38] with approximately 0.8 considered as large, 0.5 moderate, and 0.2 small.[39] Logged odds ratio (LOR) was used for dichotomous outcomes. To combine 2 types of effect sizes, LORs were converted to SMDs.[40] Where group means and standard deviations (SDs) were not reported in the original article, study authors were approached; where only medians and ranges were available, means and SDs were estimated following procedures recommended by Hozo et al[41]; otherwise, other statistics were used to calculate the effect sizes based on procedures implemented in the software CMA.

Separate effect sizes for substance use and for psychotic symptoms were calculated. For the analysis of psychotic symptomatology, total scores of clinical rating scales, such as the Positive and Negative Syndrome Scale (PANSS)[42] and the Brief Psychiatric Rating Scale (BPRS)[43] were entered into analysis. Where PANSS positive, negative, and general psychopathology subscale scores were reported as separate, a total score was calculated by summing the 3 subscale scores. For studies that only reported PANSS positive and negative symptom scores, we did not average the scores to create an overall score.[44] For studies with multiple comparisons (1 control condition compared with more than 1 MI condition), all comparisons were reported separately in the meta-analysis.

If more than 1 substance use or psychotic symptom outcome measure was reported in a single study, the best target measure was selected according to psychometric properties and common usage. For example, established measures on continuous scales such as the Alcohol Use Disorders Identification Test (AUDIT),[45] the Drug Abuse Screening Test (DAST),[46] and the Addiction Severity Index (ASI)[47] were preferred over researcher-created, binary measures (eg, cones of cannabis used in the past month); outcomes for the primary substance used were preferred over those for all substances. Data from intention-to-treat (ITT) analyses were preferred over completer-only (CO) data. Where several outcome measures were equally good, or effect sizes for several types of substances (eg, tobacco and alcohol) within the same sample were reported, an average effect size was created and entered into the meta-analysis. For studies with more than 1 post-treatment assessment, the earliest was selected to ensure maximum consistency in follow-up durations.

Random-effects models were used to summarize results. Heterogeneity between studies was examined by observing the *Q* statistic, which indicates whether the heterogeneity was significant. The I^2 statistic was also calculated, with a value of 0% indicating no observed heterogeneity and larger values showing increasing heterogeneity: 25% as low, 50% as moderate, and 75% as high.[48] Publication bias was examined by visually inspecting the funnel plot, where the effect representing each trial was plotted by the inverse of its standard error. The Egger test for funnel plot asymmetry[49] and the Duval and Tweedie trim and fill method[50] were also used. Outliers were detected by examining the residuals, with studies with larger than 2.0 standard residuals removed from subsequent analyses.

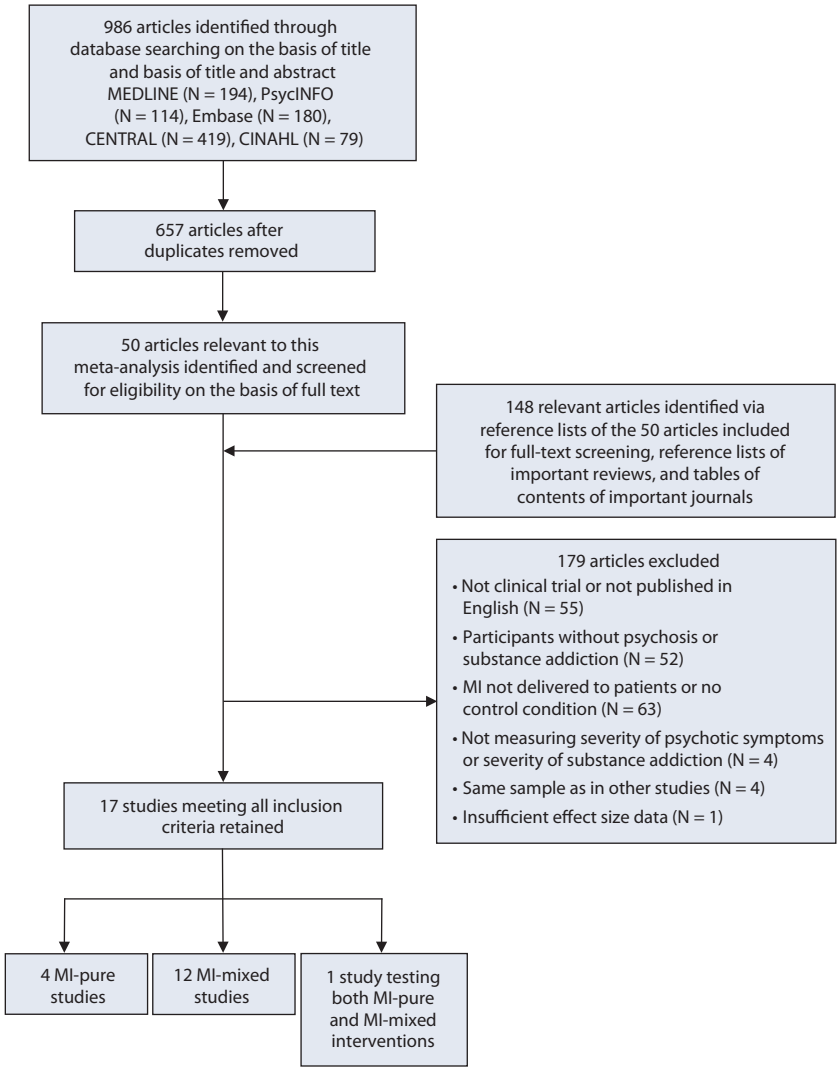
Moderator Analyses

As exploratory research questions, moderator analyses were conducted to identify any associations between effect sizes and the following study characteristics: the mean age of participants, percentage of participants who were male, dual diagnosis (all participants with diagnosable psychosis and diagnosable substance use disorder versus not all participants qualify for dual diagnosis), treatment duration (in minutes), total number of sessions, year of publication, risk of bias (low risk vs others), and analysis (ITT vs CO). Meta-regression analyses were conducted to examine the association between effect sizes for substance use decrease and those for overall psychotic symptom improvement.

Assessment of Methodological Quality and Sensitivity Analyses

Methodological quality of the included studies was evaluated according to the Cochrane Collaboration's tool for assessing risk of bias.[51] Domains assessed were as follows: selection bias, performance bias, detection bias, attrition

Figure 1. Flowchart Illustrating Study Selection Process



Abbreviation: MI = motivational interviewing.

bias, reporting bias, and other bias. Methodological quality of each included study was rated by the first 2 authors, and disagreement was resolved through discussion (the criteria for rating risks of bias and the detailed ratings are accessible from the corresponding author upon request).

The impact of "high risk" studies was examined by sensitivity analyses using the "one study removed" function in CMA, which displayed changes in effect size as each study was removed from the meta-analysis. Sensitivity analyses were also performed for studies with multiple comparisons, considering the potential dependence between comparisons might affect heterogeneity of the pooled effect sizes.[40]

RESULTS

Study Selection

Figure 1 displays a flowchart that illustrates the study selection process. Of all 986 records identified through database searches, we identified 657 articles after excluding the duplicates and selected 50 articles after examining titles and abstracts. A secondary search rendered 148 more articles, such that a total of 1,134 studies were identified in the literature. One hundred seventy-nine of all 198 potentially relevant articles were excluded after full-text screening. A final set of 17 studies reported by 19 articles that met the inclusion criteria were selected for analysis, among which 4 studies used MI as a stand-alone treatment (MI-pure studies) and 12 studies employed a comprehensive treatment that incorporated MI as a major component (MI-mixed studies). One study[52] compared an MI-pure condition and an MI-mixed condition separately against a single non-MI condition and was thus included in both MI-pure and MI-mixed reviews, resulting in 5 comparisons for MI-pure studies and 13 for MI-mixed studies.

MI as a Stand-Alone Treatment (MI-Pure Interventions)

Characteristics of included studies. The included MI-pure studies had a total of 390 participants (190 in treatment conditions and 200 in control conditions). Most

Table 1. Characteristics of Included Studies That Compared MI With Non-MI Control

Study (country)	Design	Conditions	N (% male)	Age, y	Diagnosis (substances used)	Treatment duration	MI information	Outcome measures	Measurements	Risk of bias
MI-pure interventions										
Graeber et al, 2003[26] (US)	Randomized in a yoked fashion	1. MI 2. ET	1. 15 (93.3%) 2. 15 (100%)	1. 42.87 2. 45.00	*DSM-IV* SCZ, *DSM-IV* AUD (primary: alcohol; concurrent cannabis/ cocaine use: N = 14 [47%])	1. 3 sessions, each 1 h (weekly, over consecutive weeks) 2. 3 sessions, each 1 h (weekly, over consecutive weeks)	Version: MI Target: alcohol use disorder Therapist: an experienced psychologist	SU: Drinking frequency % participants abstinent Drinking intensity Drinking quantity (BDP)	Baseline 4, 8, and 24 wk after treatment completion	Unclear
Kavanagh et al, 2004[53] (Australia)	RCT	1. SOS + TAU 2. TAU	25 (60%) 1. 13 2. 12	22.6	*DSM-IV* PD, *DSM-IV* SUD (alcohol, tobacco, cannabis)	1. 6–9 sessions, each 3 h (completed within 7–10 d)	Version: ME Target: SU and related harm Manualized Therapists: trained therapists	SU: % participants abstinent/ improved % participants unimproved (AUDIT, SDS, DrugCheck)	Baseline 6 wk and 3, 6, and 12 mo	Moderate
Bonsack et al, 2011[54] (Switzerland)	RCT	1. MI + TAU 2. TAU	1. 30 (86.7%) 2. 32 (87.5%)	1. 25 2. 25.5	*DSM-IV* PD, ≥ 3 joints of cannabis per week (51 [82.3%] with *DSM-IV* cannabis dependence) (primary: cannabis; on average 2.5 types of substances being used)	1. 4–6 sessions, each 30–60 min	Version: AMI (optional GMI) Target: harmful cannabis use Therapists: trained psychologists Fidelity: monitored via supervision by a senior psychiatrist	SU: Cannabis use frequency No. of days abstinent past month "Index of severity" of cannabis use Reduction in cannabis use frequency No. of days with binge use (TLFB, CSUAS) PS: PANSS	Baseline 3, 6, and 12 mo	Low
Tantirangsee et al, 2015[52] (Thailand)	RCT	1. BI + TAU 2. TAU	1. 54 (96.3%) 2. 57 (100%)	1. 35.52 2. 35.49	*ICD-10* PD, ASSIST substance misuse of moderate severity (tobacco: N = 108 [97%], alcohol: N = 4 [3%], illicit drugs: N = 2 [2%])	1. 1 session, 30–45 min 2. 1 session, 5 min	Version: BI Target: SU Manualized Therapists: trained nurses Fidelity: ensured with a checklist of techniques used (examined weekly by the first author) and additional training input	SU: Substance involvement score No. of cigarettes per day (ASSIST, TLFB) PS: BPRS	Baseline 6 mo after treatment completion	Low
Brunette et al, 2020[55] (US)	RCT	1. MI 2. ET	1. 78 (62.8%) 2. 84 (70.2%)	1. 47.63 2. 44.32	*DSM-IV* SSD, daily smokers (primary: tobacco; in the past 6 mo, alcohol use: N = 67 [41.4%], drug use: N = 29 [17.9%])	1. 1 session, 30–90 min 2. 1 session	Version: WBMI Target: smoking	SU: No. of participants with quit attempt No. of participants with abstinence No. of participants with biologically verified abstinence (TLFB, expired air carbon monoxide)	Baseline 3 and 6 mo	Low

(continued)

Table 1 (continued).

Study (country)	Design	Conditions	N (% male)	Age, y	Diagnosis (substances used)	Treatment duration	MI information	Outcome measures	Measurements	Risk of bias
MI-mixed interventions										
Barrowclough et al, 2001[28] Haddock et al, 2003[56] (UK)	RCT	1. MI-CBT-FI + TAU 2. TAU	36 (92%) 1. 18 2. 18	31.1	*ICD-10* SCZ/SZA, *DSM-IV* substance dependence/ abuse (alcohol, cannabis, amphetamine; used > 1 substance: N = 21 [58%])	1. Weekly, over 9 mo (5 sessions of MI, 24 sessions of CBT, 16 sessions of FI)	Form: MI as prelude, MI style integrated into subsequent treatment Target: SU Manualized Therapists: trained clinicians Fidelity: monitored via weekly supervision based on audiotaped sessions	SU: Change in % days abstinent from most frequently used substance Change in % days abstinent from all substances SU dependence Severity of SU (TLFB) PS: PANSS	Baseline 9, 12, and 18 mo after beginning of treatment	Moderate
James et al, 2004[57] (Australia)	RCT	1. Group intervention (encompassing ME strategies) 2. ET	1. 32 (71.9%) 2. 31 (71%)	1. 28.50 2. 26.87	*ICD-10* non-organic PD, *ICD-10* harmful drug use/drug dependence (alcohol, illicit drugs; on average 2.12 types of substances being used)	1. 6 sessions, each 1.5 h 2. 1 session, 1 h	Form: ME strategies incorporated into treatment Target: SU Manualized Fidelity: ensured via cofacilitation by experienced therapists	SU: Polydrug use (OTI) DAST AUDIT SDS PS: BPRS	Baseline 3 mo after treatment completion	Low
Baker et al, 2006[58] (Australia)	RCT	1. MI-CBT + TAU 2. TAU	130 (78.2%) 1. 65 2. 65	28.83	*ICD-10* non-acute PD, regular users (in the past 12 mo, alcohol dependence: N = 72 [55.5%], cannabis dependence: N = 85 [65.5%], amphetamine dependence: N = 41 [31.9%])	1. Weekly, over 15 wk (4 sessions of MI, 6 sessions of CBT, each 1 h)	Form: MI as prelude Target: SU Manualized Therapists: state-registered psychologists Fidelity: assessed with a therapist checklist adapted from NIDA	SU: Estimated daily SU quantity Polydrug use Aggregate SU index score % participants above SU intervention threshold % participants abstinent (OTI, SCID-I-RV) PS: BPRS	Baseline 15 wk, 6 mo, and 12 mo after initial assessment	Low
Kemp et al, 2007[27] (Australia)	RCT	1. MI-CBT + TAU 2. TAU	1. 10 (70%) 2. 6 (100%)	1. 20.6 2. 20.8	*DSM-IV* PD, DAST/ AUDIT substance abuse (alcohol, illicit drugs)	1. 4–6 sessions, each approximately 1 h	Target: SU Manualized	SU: Cones of cannabis per month Frequency of cannabis and alcohol use per month Quantity of alcohol per month DAST-10 AUDIT PS: PANSS	Baseline 6 mo after treatment completion	High
Johnson et al, 2007[59] Craig et al, 2008[60] (UK)	Cluster RCT	1. Training staff to deliver substance misuse intervention (MI as central training source) + TAU 2. TAU	1. 127 2. 105		*ICD-10* SCZ/SZA/ delusional disorder (N = 208 [90%]) or bipolar disorder with psychotic symptoms (N = 24 [10%]), CADUS substance dependence/ misuse (alcohol only: N = 77 [33%], cannabis only: N = 52 [22%], both alcohol and cannabis: N = 29 [13%], stimulants: N = 55 [24%], all other drugs: 19 [8%])	Information not reported	Form: MI elements as a central source Manualized Therapists: trained community mental health team staff Fidelity: not monitored	SU: Alcohol, cannabis, and other drug use quantity % participants who used alcohol, cannabis, and other drugs (MAP) PS: BPRS	Baseline 18 mo after initial assessment	High

(continued

Table 1 (continued).

Study (country)	Design	Conditions	N (% male)	Age, y	Diagnosis (substances used)	Treatment duration	MI information	Outcome measures	Measurements	Risk of bias
Barrowclough et al, 2010[61] (UK)	RCT	1. MI-CBT + TAU 2. TAU	1. 164 (89%) 2. 163 (84%)	1. 37.4 2. 38.3	*ICD-10* and/or *DSM-IV* non-affective PD, *DSM-IV* substance misuse/ dependence (alcohol dependence only: N = 157 [48%], illicit drug use only: N = 116 [35%], both alcohol and drug misuse: N = 54 [17%])	1. Up to 26 sessions, over 1 y	Form: MI as prelude, MI techniques integrated into subsequent treatment Target: substance misuse and mental health issues Manualized Therapists: trained psychologists, nurses, and a social worker Fidelity: monitored via supervision based on therapy audiotapes and a scale designed to assess integrated MI and CBT (number of items rated as compliant ranged from 13/16 [81%] to 16/16 [100%] across 40 sessions audiotaped sessions rated)	SU: % days abstinent from main substance and all substances Ranked change scores for main substance and all substances (TLFB) PS: PANSS	Baseline 6, 12, 18, and 24 mo after treatment completion	Moderate
Williams et al, 2010[62] (US)	RCT	1. TANS (incorporating MI skills) 2. MM	1. 45 (64.4%) 2. 42 (61.9%)	1. 43.5 2. 47.1	*DSM* SCZ/SZA, ≥ 10 cigarettes per day (primary: tobacco; in the past 30 d, alcohol/other substance use: N = 26 [30%])	1. 24 sessions, each 45 min, over 26 wk 2. 9 sessions, each 20 min, over 26 wk	Form: MI skills incorporated into treatment Manualized Therapists: trained experienced clinicians Fidelity: monitored via weekly supervision (casework discussions, review of audiotaped sessions) by doctoral-level staff	SU: % participants with continuous abstinence Time to first cigarette relapse Quitting on the quit date Reduction in expired carbon monoxide Reduction in cigarettes per day (TLFB, hand-held carbon monoxide monitor) PS: PANSS	Baseline 12 wk, 26 wk, and 1 y after target quit date	Moderate
Morrens et al, 2011[63] (Belgium)	Comparative study	1. IDDT (integrating MI) 2. TAU	1. 85 (87.1%) 2. 35 (85.3%)	1. 28.4 2. 27.8	*DSM-IV* non–drug-induced PD, *DSM-IV* SUD (AUD: N = 60 [50%], CUD: N = 81 [68%], other SUDs: cocaine, opiates, etc)	Information not reported	Therapists: a multidisciplinary and fully cross-trained team	SU: ASI-alcohol ASI-drugs AUS DUS PS: PANSS	Baseline 3, 6, and 12 mo after initial assessment	High
Hjorthøj et al, 2013[64] (Denmark)	RCT	1. MI-CBT + TAU 2. TAU	1. 52 (73.1%) 2. 51 (78.4%)	1. 26.6 2. 27.1	*ICD-10* SSD, *ICD-10* CUD (primary: cannabis; concurrent other substance abuse/ dependence: N = 23 [22%])	1. 24 sessions, each about 1 h, over 6 mo	Form: MI as prelude and returned to when required Target: cannabis use Manualized Therapists: a psychologist, a master psychology student, and an occupational therapist who are trained and experienced Fidelity: monitored via meetings and supervision	SU: No. and % days with cannabis use past month No. of joints past month % participants abstinent (TLFB) PS: PANSS	Baseline 6 mo after beginning of treatment 4 mo after treatment completion	High

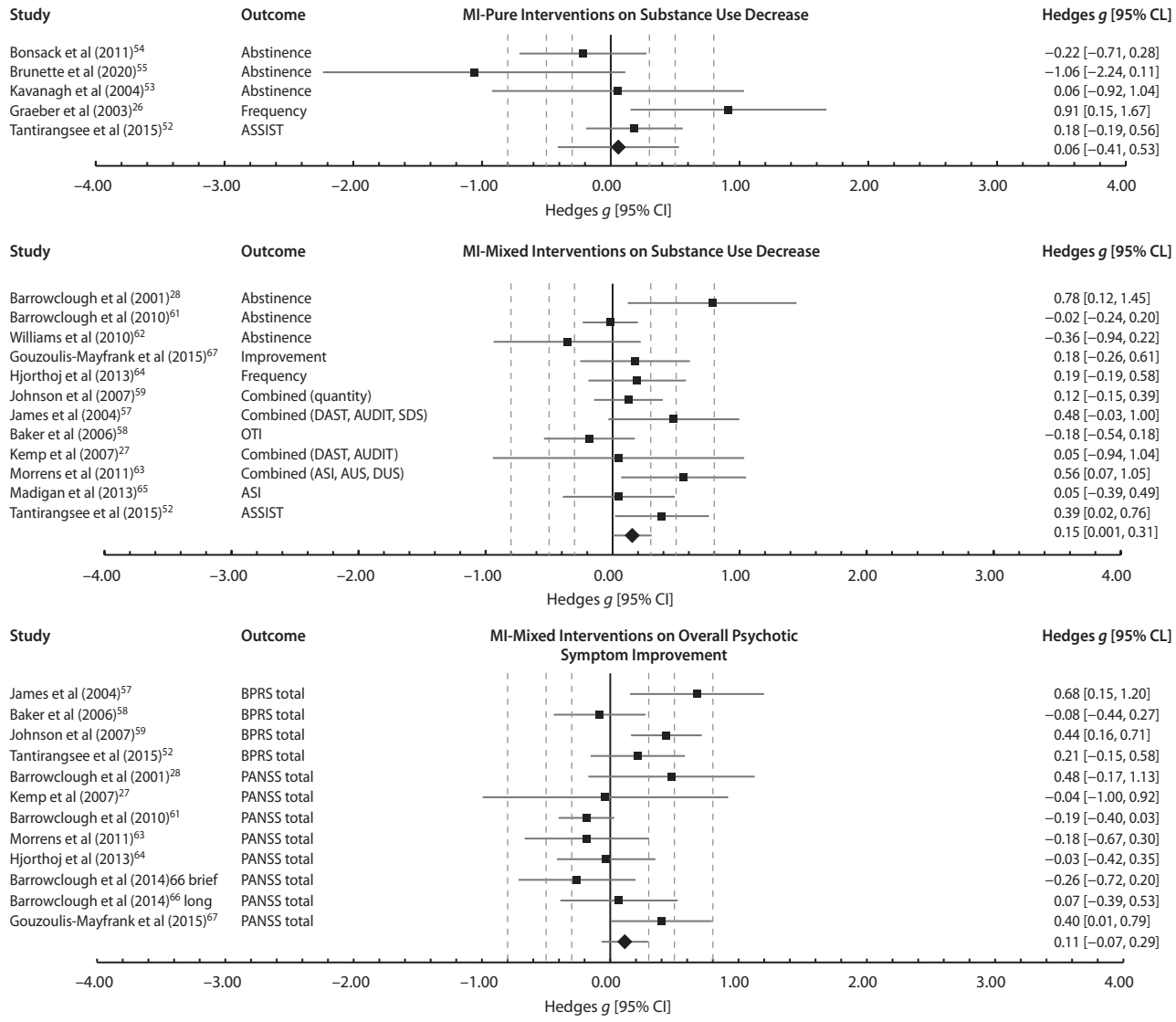
(continued)

Table 1 (continued).

Study (country)	Design	Conditions	N (% male)	Age, y	Diagnosis (substances used)	Treatment duration	MI information	Outcome measures	Measurements	Risk of bias
Madigan et al, 2013[65] (Ireland)	RCT	1. Group MI-CBT + TAU 2. TAU	1. 59 (78%) 2. 29 (79%)	1. 27.6 2. 28.2	*DSM-IV* psychosis (PD: N = 74 [84%], bipolar disorder: N = 14 [16%]), *DSM-IV* cannabis dependence (primary: cannabis)	1. First 12 wk: 1 session per week; 6 wk later: 1 "booster" session	Form: MI techniques incorporated into treatment Target: cannabis dependence Manualized Therapist: an experienced clinical psychologist	SU: Cannabis use frequency (ASI) PS: PANSS	Baseline 3 mo and 1 y	Low
Barrowclough et al, 2014[66] (UK)	RCT	1. Brief MI-CBT + TAU 2. Long MI-CBT + TAU 3. TAU	1. 38 (89.5%) 2. 37 (91.9%) 3. 35 (85.7%)	1. 24.9 2. 24.1 3. 23.4	*DSM-IV* non-affective PD, *DSM-IV* cannabis dependence/abuse (primary: cannabis; polysubstance use: N = 40 [36%], eg, alcohol, cocaine, amphetamine)	1. Up to 12 sessions, over 4.5 mo 2. Up to 24 sessions, over 9 mo	Form: MI as prelude, MI techniques integrated into subsequent treatment Target: cannabis use Manualized Therapists: trained therapists Fidelity: monitored via weekly supervision based on recorded therapy sessions and the MI-CBT fidelity scale (number of items rated as compliant ranged from 14/16 [87.5%] to 16/16 [100%] across 20 recorded sessions rated)	SU: % days abstinent from cannabis and all substances Cannabis use quantity Average cannabis use quantity per using day Reductions in above outcomes (TLFB) PS: PANSS	Baseline 4.5, 9, and 18 mo after treatment allocation	Low
Gouzoulis-Mayfrank et al, 2015[67] (Germany)	RCT	1. IntT (MI, PE, CBT) + TAU 2. TAU	1. 50 (86%) 2. 50 (82%)	1. 31.14 2. 30.8	*DSM-IV* SCZ/schizophreniform disorder/SZA, *DSM-IV* substance dependence/misuse (cannabis, alcohol, amphetamine; on average 1.5 diagnoses of substance-related disorder)	1. Inpatient phase: 2 group therapies, 1 60-min session of each per week; outpatient phase: inpatient phase treatment plus 1 session of CBT per week, each 90 min	Form: GMI (modified according to the MI principles)	SU: Quantity of main substance use Ranked change score in main substance use (ASI) PS: PANSS	Baseline 3, 6, and 12 mo after inclusion in the program	Low
Tantirangsee et al, 2015[52] (Thailand)	RCT	1. BI-FS (feedback give using MI techniques) + TAU 2. TAU	1. 58 (98.3%) 2. 57 (100%)	1. 34.98 2. 35.49	*ICD-10* PD, ASSIST substance misuse of moderate severity (tobacco: N = 111 [99%], alcohol: N = 20 [18%], illicit drugs: N = 8 [7%])	1. 1 session, 45–75 min 2. 1 session, 5 min	Form: BI (supplemented with family support topics) Target: SU Manualized Therapists: trained nurses Fidelity: ensured with a checklist of techniques used (examined weekly by the first author) and additional training input	SU: Smoking involvement score Cigarettes per day (ASSIST, TLFB) PS: BPRS	Baseline 6 mo after treatment completion	Low

Abbreviations: AMI = adapted motivational interviewing, ASI = Addiction Severity Index, ASSIST = Alcohol, Smoking and Substance Involvement Screening Test, AUD = alcohol use disorder, AUDIT = Alcohol Use Disorders Identification Test, AUS = Alcohol Use Scale, BDP = Brief Drinker Profile, BI = brief intervention, BI-FS = brief intervention with family support, BPRS = Brief Psychiatric Rating Scale, CBT = cognitive behavioral therapy, CI = confidence interval, CSUAS = Cannabis and Substance Use Assessment Scale, DAST = Drug Abuse Screening Test, CUD = cannabis use disorder, *DSM* = *Diagnostic and Statistical Manual of Mental Disorders*, DUS = Drug Use Scale, ET = educational treatment, GMI = group motivational interviewing, *ICD* = *International Classification of Diseases*, IDDT = Integrated Dual Diagnosis Treatment, IntT = integrated treatment, MAP = Maudsley Addictions Profile, ME = motivation enhancement, MI = motivational interviewing, MM = medication management, NIDA = National Institute on Drug Abuse, OTI = Drug Use Scale of the Opiate Treatment Index, PANSS = Positive and Negative Syndrome Scale, PD = psychotic disorder, PE = psychoeducation, PS = psychotic symptoms, RCT = randomized controlled trial, SCID = Structured Clinical Interview for *DSM-IV* Axis I Disorders, SCZ = schizophrenia, SDS = Severity of Dependence Scale, SOS = Start Over and Survive, SU = substance use, SUD = substance use disorder, SSD = schizophrenia spectrum disorder, SZA = schizoaffective disorder, TANS = Treatment of Addiction to Nicotine in Schizophrenia, TAU = treatment as usual, TLFB = timeline follow-back, WBMI = web-based motivational intervention.

Figure 2. Forest Plots for Effect Sizes for Substance Use and Overall Psychotic Symptom Outcomes



Abbreviations: ASI = Addiction Severity Index, ASSIST = Alcohol, Smoking and Substance Involvement Screening Test, AUDIT = Alcohol Use Disorders Identification Test, AUS = Alcohol Use Scale, BPRS = Brief Psychiatric Rating Scale, DAST = Drug Abuse Screening Test, DUS = Drug Use Scale, MI = motivational interviewing, OTI = Drug Use Scale of the Opiate Treatment Index, PANSS = Positive and Negative Syndrome Scale, SDS = Severity of Dependence Scale.

studies (N = 4) adopted a randomized controlled design (see Table 1 for details). Two of the 5 studies examined an exclusive sample with dual diagnosis, and the remaining 3 recruited patients with *DSM*/*ICD* psychosis but undiagnosable substance use. Regarding substance use, all 5 studies involved participants with polysubstance use: 3 studies targeted a specific type of substance (alcohol: N = 1; tobacco: N = 1; cannabis: N = 1), and 2 studies examined miscellaneous substances (eg, alcohol, tobacco). As for interventions in comparison, 3 studies compared MI plus TAU (simple advice, pharmacotherapy, case management) with TAU, and 2 studies compared MI with an educational treatment. Up to 9 MI sessions were delivered, each lasting from 30 minutes to 3 hours. MI targeted substance use behaviors in all 5 studies. The version of MI, manual usage, therapist characteristics, and treatment fidelity checking varied across studies. Various substance use outcome measures were used, such as frequency and abstinence measured by timeline follow-back (TLFB).[68] PANSS was used to measure psychotic symptom severity in all included studies. The earliest outcome assessment points ranged from the end of treatment to 6 months after treatment. As summarized in Table 1, risk of bias was generally low, with 3 studies being rated as "low risk," 1 as "moderate risk," and 1 as "unclear risk."

Effects of MI-pure interventions on substance use. MI-pure interventions did not significantly decrease substance use ($g = 0.06$; 95% CI, −0.41 to 0.53; $P = .81$; Figure 2). There was significant, moderate heterogeneity ($I^2 = 59.76$; $Q_4 = 9.94$, $P = .04$). Effect sizes were not predicted by age, percentage of males, year of publication, or treatment duration (see Table 2). No publication bias was suggested

Table 2. Sensitivity Analyses for Effect of MI on Substance Use and Overall Psychotic Symptom Outcomes and Moderator Analyses of Associations Between Study Characteristics and Effect Sizes (Hedges *g*)

	No. of comparisons	*g*	*b*	95% CL [LL, UL]	*P*	Heterogeneity I^2	Heterogeneity *P* (*Q*)
MI-pure interventions on decrease in substance use							
Continuous moderators							
Age	5		0.02	[−0.02, 0.06]	.246		.035
Percentage of males	5		2.08	[−0.22, 4.38]	.076		.079
Treatment duration	5		−0.0001	[−0.0009, 0.0007]	.790		.020
Year of publication	5		−0.05	[−0.11, 0.006]	.080		.076
MI-mixed interventions on decrease in substance use							
Sensitivity analyses							
All ESs included	14	−0.004		[−0.25, 0.24]	.974	79.37	.000
Barrowclough et al, 2014[66] excluded	12	0.15		[0.001, 0.31]	.048	39.18	.080
Continuous moderators							
Age	12		−0.02	[−0.04, 0.004]	.110		.114
Percentage of males	12		1.35	[−0.18, 2.87]	.083		.129
Number of sessions	9		−0.01	[−0.02, 0.01]	.557		.044
Treatment duration	6		−0.0004	[−0.001, 0.0001]	.138		.123
Year of publication	12		0.001	[−0.03, 0.03]	.932		.054
Effect on psychotic symptoms	10		0.33	[−0.05, 0.72]	.089		.141
Categorical moderators							
Dual diagnosis	12				.167		
Yes	6	0.27		[0.05, 0.49]	.019	50.06	.075
No	6	0.01		[−0.18, 0.27]	.710	28.76	.219
Low risk of bias	12				.959		
Yes	5	0.16		[−0.08, 0.41]	.195	40.55	.151
No	7	0.15		[−0.06, 0.37]	.158	46.58	.080
Analysis	12				.719		
ITT	7	0.13		[−0.06, 0.32]	.169	42.06	.110
CO	5	0.20		[−0.10, 0.50]	.198	44.03	.128
MI-mixed interventions on overall psychotic symptom improvement							
Sensitivity analyses							
All ESs included	12	0.11		[−0.07, 0.29]	.219	57.89	.006
Barrowclough et al, 2014[66] long treatment condition removed	11	0.12		[−0.08, 0.32]	.237	61.71	.004
Barrowclough et al, 2014[66] brief treatment condition removed	11	0.15		[−0.04, 0.33]	.129	58.03	.008
MI-mixed interventions on overall psychotic symptom improvement							
Continuous moderators							
Age	12		0.002	[−0.02, 0.02]	.825		.004
Percentage of males	12		−0.73	[−2.57, 1.10]	.435		.004
Number of sessions	9		−0.01	[−0.03, 0.01]	.342		.066
Treatment duration	5		−0.0003	[−0.0009, 0.0003]	.318		.135
Year of publication	12		−0.02	[−0.05, 0.008]	.146		.008
Effect on substance use	12		0.25	[0.01, 0.49]	.038		.016
Categorical moderator							
Low risk of bias	12				.651		
Yes	6	0.16		[−0.11, 0.42]	.243	51.92	.065
No	6	0.07		[−0.20, 0.34]	.612	66.29	.011

Abbreviations: CL = confidence limit, CO = completer-only analysis, ES = effect size, ITT = intent-to-treat analysis, LL = lower limit, UL = upper limit.

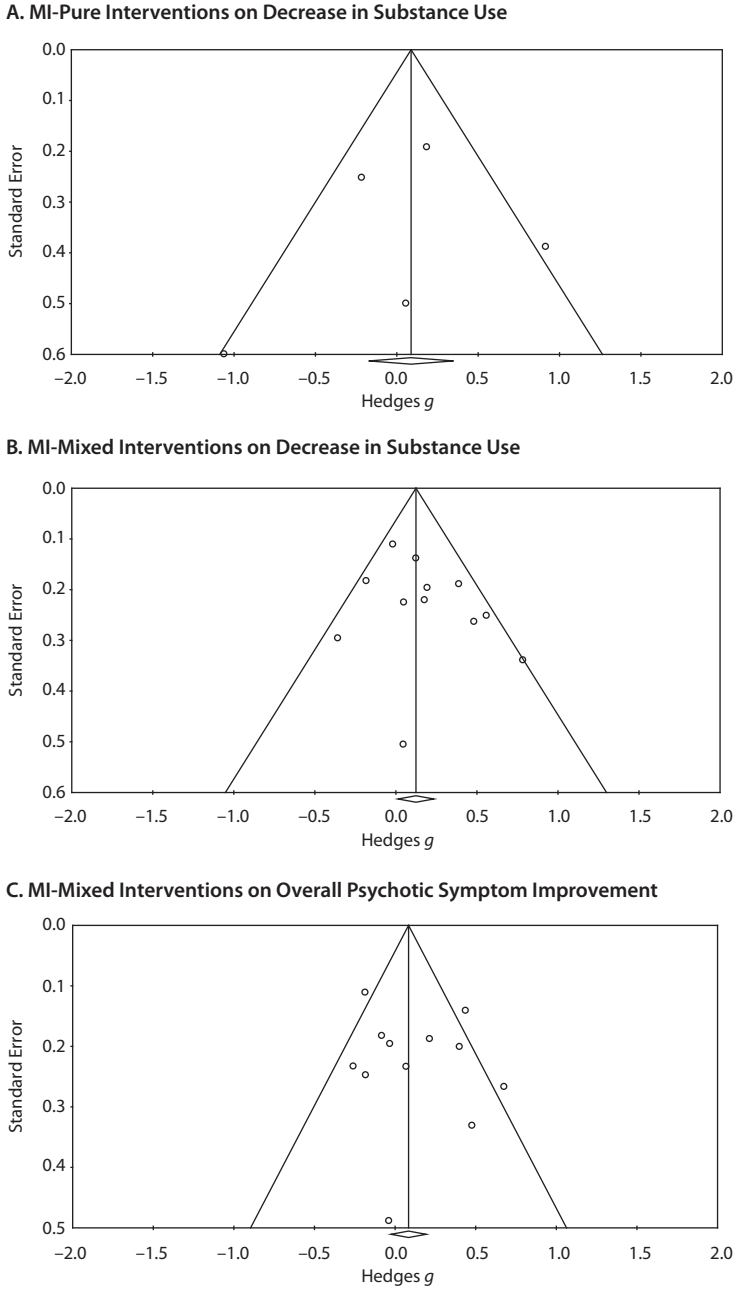
based on (1) visual inspection of the funnel plot (see Figure 3), (2) no plot asymmetry ($P = .37$) on the Egger test, and (3) no adjustment for missing studies identified by the trim-and-fill method.

The effect of MI-pure interventions on psychotic symptom improvement was not meta-analyzed because effect size data were available for only 2 studies[52,54] (personal communications: P. Golay, PhD, 2019; N. Tantirangsee, PhD, 2019). Effect sizes separately calculated for Bonsack et al[54] and Tantirangsee et al[52] revealed a nonsignificant treatment effect at 3 months ($g = 0.16$; 95% CI, −0.34 to 0.65; $P = .54$ and $g = 0.01$; 95% CI, −0.37 to 0.38; $P = .96$, respectively).

MI as a Major Treatment Component (MI-Mixed)

Characteristics of included studies. A total of 1,527 participants were involved (840 in treatment conditions and 687 in control conditions). Most studies reported randomized controlled trials (N = 11; detailed in Table 1). Eight of the 13 studies examined an exclusive sample with dual diagnosis, and the rest recruited patients with *DSM*/*ICD*

Figure 3. Funnel Plots (Standard Error by Hedges *g*) for Effect Sizes for Substance Use and Overall Psychotic Symptom Outcomes



psychosis but undiagnosable substance use.* Concerning substance used, most studies (N = 11) reported involving patients with polysubstance use. Four of the 13 studies targeted a specific type of substance (eg, cannabis: N = 3; tobacco: N = 1), and the rest examined miscellaneous substances. Regarding interventions in comparison, 11 studies compared MI-mixed interventions plus TAU with TAU (eg, psychiatric management, self-help materials), 1 compared MI with an educational session, and 1 compared MI with medication management. Total treatment lengths ranged from 1 session to over 26 sessions, each lasting from 45 to 75 minutes. Nine studies reported the target behavior of MI: 1 targeted both substance use and mental health issues, and 8 targeted substance use. Eleven studies reported the form of integrating MI with other treatment components: as a prelude to other interventions (N = 1), incorporated into the whole treatment (N = 6), or both (N = 4). Most studies reported using a manual (N = 11). Eight studies reported monitoring treatment fidelity: 4 used a checklist or scale and 4 ensured fidelity via supervision only. The characteristics of therapists were heterogeneous (eg, trained master students, experienced psychologists). A variety of substance use outcome measures were used, including self-reported outcomes such as frequency and quantity of use measured by TLFB, DAST, and AUDIT and clinician-rated instruments such as ASI and the Opiate Treatment Index (OTI).[69] Psychotic symptoms were assessed with valid clinician-rated assessment tools such as PANSS, BPRS, the Scale for the Assessment of Positive Symptoms (SAPS),[70] and the Scale for the Assessment of Negative Symptoms (SANS).[71] The earliest timepoints for outcome assessments ranged from 3 to 24 months. The selected MI-mixed studies had varied risks of bias, with 6 studies being rated as "low risk," 3 as "moderate risk," and 4 as "high risk" (see Table 1).

Effect of MI-mixed interventions on substance use. Twelve studies reported sufficient data for at least 1 substance use outcome to be entered into meta-analysis. Unpublished outcome data were obtained for 1 study[64] (C. Hjorthøj, PhD, personal communication, 2019). Means and SDs were estimated from medians and ranges for 2 studies.[28,66] Four studies[27,57,59,63] reported more than 1 equally good outcome, and an average outcome score was produced to represent each study. Two comparisons from 1 study[66] were substantial outliers (*g*'s = −1.06 and −1.19) and were excluded from subsequent analyses.

As shown in Figure 2, MI-mixed interventions had a significant small effect on substance use decrease ($g = 0.15$; 95% CI, 0.001 to 0.31; $P = .048$). Heterogeneity was low and nonsignificant ($I^2 = 39.18$; $Q_{11} = 18.09$, $P = .08$). Separately removing 4 "high risk" studies[27,59,63,64] did not significantly change the pooled effect size or heterogeneity. Despite the nonsignificant between-group test ($P = .17$; Table 2), the subgroup of studies that recruited an exclusive sample with dual diagnosis reported a significant treatment effect ($g = 0.27$;

*Only 2 of the 13 studies selected for this meta-analysis (references 59, 60, 65) reported including patients with bipolar disorders with psychotic features in their samples (percentages = 10% and 16%, respectively).

95% CI, 0.05 to 0.49; $P = .02$), whereas the subgroup of studies involving participants with mixed diagnoses did not ($g = 0.01$; 95% CI, −0.18 to 0.27; $P = .71$). Effect sizes were not significantly associated with age, percentage of males, year of publication, number of treatment sessions, treatment duration, or a low risk of bias (see Table 2). No publication bias was indicated by visual inspection of the funnel plot (see Figure 3), the Egger test for plot asymmetry ($P = .24$), or the trim-and-fill method.

Effect of MI-mixed interventions on psychotic symptoms. Twelve studies measured overall psychotic symptoms, and 9 reported sufficient data to be meta-analyzed. Unpublished outcome data were obtained for 3 studies[52,64,67] (personal communications: N. Tantirangsee, PhD, 2019; C. Hjorthøj, PhD, 2019; E. Gouzoulis-Mayfrank, PhD, 2019). No outliers were detected.

As shown in Figure 2, MI-mixed interventions had a small and nonsignificant effect in improving overall psychotic symptoms at post-treatment ($g = 0.11$; 95% CI, −0.07 to 0.29; $P = .22$). There was moderate heterogeneity across studies ($I^2 = 57.89$; $Q_9 = 26.12$, $P = .01$). Separately removing the "high risk" studies[27,59,63,64] did not significantly change the pooled effect size or heterogeneity. Sensitivity analysis conducted for Barrowclough et al,[66] which compared 2 MI-mixed treatment conditions (brief vs long treatments) against a single control condition, yielded no significant difference in effect sizes (see Table 2). A larger effect on psychotic symptom improvement was significantly associated with a larger effect on substance use decrease ($b = 0.25$; 95% CI, 0.01 to 0.49; $P = .04$). We detected no other significant moderators (see Table 2). Visual inspection of the funnel plot (see Figure 3), the Egger test ($P = .46$), and the trim-and-fill method indicated no publication bias.

One study[65] only reported PANSS positive and negative symptom scores, and an overall score was not calculated. Effect sizes separately calculated for positive and negative symptom outcomes suggested nonsignificant treatment effects ($g = -0.25$; 95% CI, −0.70 to 0.19; $P = .27$ and $g = 0.08$; 95% CI, −0.37 to 0.52; $P = .73$, respectively).

DISCUSSION

The current systematic review and meta-analysis investigated the efficacy of MI as a stand-alone treatment and MI as a major part of integrated treatments for individuals with co-occurring psychosis and substance use disorder. As opposed to previous meta-analyses that examined individuals with a single psychological condition (ie, alcohol use disorder), the current review targeted a population with co-occurring psychosis and substance use disorder.

A meta-analysis based on 5 studies revealed a nonsignificant effect of stand-alone MI in decreasing substance use ($g = 0.06$), with substantial heterogeneity across studies. Neither did stand-alone MI improve psychotic symptoms in 2 studies[52,54] that reported effect size data (g's = 0.16 and 0.01). MI, when applied to people with alcohol dependence or alcohol use disorder but no psychosis, could achieve small to moderate efficacy in reducing alcohol use ($d = 0.18$ when compared with no treatment and $d = 0.43$ when compared with another treatment).[22] Patients with co-occurring psychosis and substance use disorder are probably so severely impaired that psychological interventions cannot achieve the expected potency[26] or even effectively engage the patients in the treatment, which might explain the small treatment effect despite the relatively weak control intervention used (eg, TAU, psychoeducation). In fact, psychosocial interventions in general (including MI) have small effects where psychiatric disorders and substance use disorder coexist (eg, Dumaine[72]: effect size = 0.22; Riper et al[73]: g's = 0.17 and 0.27). In line with previous suggestions,[4] polysubstance use is common in our samples (up to 58% of participants used more than 1 substance), which could further increase the difficulty in treating patients with coexisting psychosis and substance use disorder.

There is a nuanced suggestion that MI, when combined with other treatment components, may be more effective than when used alone. Despite the moderate level of heterogeneity, our meta-analysis yielded a small but significant superiority of MI-mixed interventions over control conditions on improving substance use outcomes ($g = 0.15$; $P = .048$). In particular, the study that directly compared 2 MI-based treatment conditions (1 stand-alone and 1 combined) against a single TAU condition[52] supported the hypothesized superiority of MI-mixed interventions over MI-pure interventions. Such superiority, albeit of a small size, is consistent with those reported by previous meta-analyses.[18,20–22] As Miller and Rollnick[25] originally conceptualized, MI might be particularly useful when integrated into a comprehensive treatment, where its effects could be boosted by other treatment components. Although the advantage of MI-mixed interventions may also be explained by the longer treatment duration involved, the non-MI treatments used for comparison were also substantially longer; neither did our moderator analyses support the association between treatment lengths and efficacy.

The superiority of MI-mixed interventions is not evident for psychotic symptom improvement, though. Almost half of our included studies[27,58,61,63,64,66] reported no superiority of MI-mixed interventions over control conditions in improving psychotic symptoms. Whenever there were multiple follow-up assessments, we entered the first assessment result in the meta-analysis only. Looking at outcomes at multiple time points may help us understand the results more comprehensively. For example, Barrowclough et al[28] found a significant effect of MI-mixed interventions on psychotic symptoms at 12 months but not at 9 months. A similar finding was reported by Baker et al.[58] The effect of MI on psychotic symptoms may need a longer time to emerge, possibly after the intervention has fully exerted its effect on substance use. Of 9 MI-mixed studies that reported the target behavior of MI, only 1[61] targeted both substance use and mental health issues. The effect of MI on psychotic symptoms is therefore likely to be indirect, that is, through

its effect on substance use. As preliminary evidence, we found the effects of MI-mixed interventions on psychotic symptom improvement were significantly associated with those on substance use decrease ($b = 0.25$; $P = .04$). This distal effect, if empirically validated, may lend support to the clinical practice of targeting first the substance use behaviors of clients with co-occurring psychosis and substance use disorder, with the expectation that a decrease in substance use severity would bring about improvement in psychotic symptoms and the overall clinical outcome in the long run.

Our subgroup analysis tentatively suggests that effect of MI-mixed interventions on substance use disorder may be more prominent in samples with dual diagnosis (vs samples with mixed diagnostic statuses), a finding that warrants further research. The nonsignificant moderation by treatment duration or number of sessions challenges the view that long-term interventions are more effective with patients with co-occurring psychological conditions than briefer ones.[32,66,74] If this result can be further replicated, it might have implications for policy making because lengthy interventions often involve higher costs.[75]

Limitations

Interpretability of our results is limited by the small number of studies in this area. The variations in participant characteristics and treatment design, such as diagnostic status, dosage of MI, identity of therapists, and the combination of treatment components in MI-mixed interventions, further add to the heterogeneity of our samples. Such methodological heterogeneity is nevertheless common in the field of dual diagnosis.[73] Second, to maximize consistency across studies, only treatment effects at the earliest post-treatment assessment point were selected for review, whereas the effects of MI might take a longer time to develop and to be measurable (eg, Baker et al[58] and Barrowclough et al[28]). Future reviews could consider addressing the longer-term efficacy of MI by computing effect sizes at longer-term follow-ups. Third, we were not able to determine the relative efficacy of MI-pure versus MI-mixed interventions due to a lack of studies that directly compare them within a clinical trial. Finally, a question remains over how much treatment efficacy of MI-mixed interventions could be attributed to the MI component. The contribution of MI to an integrated intervention should be examined in future research for better understandings of the mechanisms behind MI when integrated with other treatment components.

CONCLUSION

The current systematic review and meta-analysis revealed a modest and heterogeneous effect of MI in treating co-occurring psychosis and substance use disorder. While stand-alone MI did not significantly improve either substance use or psychotic symptom severity, integrated treatments with an MI component did exhibit a small effect on substance use. In summary, psychological interventions for coexisting psychosis and substance use disorder may benefit from including an MI component, with a primary effect in decreasing substance use. Further research is needed to enhance the efficacy of MI in treating patients with co-occurring psychosis and substance use disorder.

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Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Psychosis section. Please contact Ann K. Shinn, MD, MPH, at ashinn@psychiatrist.com.