# Treatment for Outpatients with Comorbid Schizophrenia and Substance Use Disorders: A Review

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## Abstract

*Aims:* This review provides evidence of which interventions need to be part of effective outpatient integrated treatment for patients with comorbid schizophrenia and substance use disorders. *Methods:* A total of 14 randomized controlled trials were included. Effect sizes are provided to assess the magnitude of the treatments' efficacy. *Results:* Despite the studies' heterogeneity, we can conclude that certain programs (e.g. Behavioral Treatment for Substance Abuse in Severe and Persistent Mental Illness ) and specific interventions (e.g. motivational interviewing, family interventions) seem to be effective. Moreover, programs integrating multiple interventions are more likely to be positively related to better outcomes than single interventions. Finally, the lack of difference between effect sizes of assertive community treatment compared to case management suggests that a lower caseload is not necessary for positive treatment outcomes. *Conclusion:* Integrated treatment seems advantageous, although effect sizes are mostly modest. More homogeneous and qualitative sound studies are needed.

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## Introduction

Schizophrenia is a severe psychiatric disorder that can cause long-standing impairments in several life domains. The overall outcome of schizophrenia is notably heterogeneous. Several clinical characteristics are related to better or worse outcomes [1], with concurrent substance use disorder (SUD) being consistently associated with worse outcome. In fact, patients with schizophrenia and SUD, when compared to patients with a single diagnosis, have more severe (positive) symptoms, less treatment compliance, more re-hospitalizations, a higher degree of homelessness, and more legal, medical and social problems [2–7]. These factors are associated with worse overall outcome and higher treatment and societal costs.

A sizeable portion of patients with schizophrenia suffers from comorbid SUD. Indeed, both high lifetime (47%) [8] and current (27%) [9] prevalence of SUD has been reported by epidemiological studies. However, these dual disorder (DD) patients do not fit in the traditional treatment systems, where addiction and mental healthcare do considerably differ [10] so that healthcare professionals continuingly demand for specialized treatment settings for these difficult-to-treat patients. As a consequence, the last two decades have seen the development

of the paradigm of integrated treatment (IT), i.e. treatment programs in which addiction and mental health interventions are offered at the same time and by the same team. However, the interpretation of the effectiveness of these programs is ambiguous and particularly complicated by the great variety of different interventions, the heterogeneity of the patient samples, and the lack of consistent reports of effect sizes of the outcome studies.

First, apart from the target population (i.e. DD patients), there are very few similarities between different integrated programs. They vary greatly in terms of the number and type of interventions they include, the degree of comprehensiveness, duration and intensity of treatment, and the setting in which they are offered. Interventions that have often been implemented in IT are motivational interviewing (MI), cognitive behavioral therapy (CBT), relapse prevention (RP), case management (CM), assertive community treatment (ACT), and family interventions (FI). MI is aimed at increasing the motivation for change by emphasizing personal choice, responsibility and consciousness about the risks and advantages of continued substance use. CBT is focused at learning specific behavioral skills to cope with stress and certain problems and to accomplish well-set goals. RP is a form of CBT specifically focused on preventing relapse. CM is an intervention in which a treating agency coordinates the care of a patient by ensuring access to different types of interventions. ACT (often considered to be a subtype of CM) not only coordinates care, but also offers mobile assertive outreaching. ACT consists of several components: care in the community, assertive engagement, high intensity, small caseload, continuous responsibility and availability, consistent multidisciplinary team, team approach, and cooperation with the patient's support network [11]. The content of FI is very diverse, but it is often aimed at increasing the family's knowledge about DD and ameliorating communication between the family and the team and/or patient. Finally, there recently has been an increase in attention for contingency management (CoM) in this patient group. In CoM, adaptive behavior (e.g. negative urine sample) is rewarded by positive consequences.

In addition to the heterogeneity of treatment programs, interpretation of the effectiveness of IT is hampered by the great heterogeneity of patients included in the different outcome studies. Most outcome studies include mixed patient samples, with only a relatively small proportion of patients with schizophrenia and SUD. For example, the review by Brunette et al. [12] concluded that residential IT is more effective than treatment as usual (TAU). Furthermore, Drake et al. [13] also conclude that IT seems advantageous. However, both reviews reflect studies with very heterogeneous patient populations (different diagnostic groups), making it difficult to transfer the results to the specificities of patients with schizophrenia [14]. An additional problem within the existing outcome studies is that the effect sizes of IT are only fragmentarily (e.g. only SUD or psychiatric outcome variables) or not at all reported, making it difficult to interpret the findings. Furthermore, most studies do not assign patients randomly to the treatment conditions.

Finally, it needs to be taken into account that most of the existing IT programs are offered within the context of outpatient services and rarely in residential treatment settings. This is in accordance with the current mental healthcare developments supported by the World Health Organization (WHO) and other leading healthcare organizations, putting a focus on outpatient, community-based treatment organization for patients with severe mental illnesses [15, 16]. The focus in mental healthcare is currently shifting from traditional residential treatment centers to outpatient, community-based settings in which the patient is being treated in an integrative way. Given these (societal) evolutions, the fact that most studies focus on outpatient programs, and the need for homogeneity when comparing the effectiveness between studies, we focus in this review specifically on outpatient programs.

Although the concept of IT is widely acclaimed and has been well received from the perspective of patient's treatment satisfaction [17], the evidence remains mainly expert-driven. In addition, there is still a lack of consensus about which specific interventions should be included in an IT approach. This review provides much-needed information on the efficacy of outpatient treatment for patients with schizophrenia and comorbid SUD by offering an overview of available randomized controlled trials (RCTs) on this topic and reporting treatment effect sizes, which will help in comparing studies and coming to a consensus regarding specific interventions that need to be included in an IT program.

## Materials and Methods

*Study Sources and Selection*
Internet databases (PsycInfo, PubMed, and Web of Knowledge) were searched for RCTs with specific treatment interventions for patients suffering from comorbid schizophrenia and SUD (limited to the English language) until December 2012. Additionally, cross-references of the selected articles were checked and re-

**Table 1.** Overview of the selected RCTs on the addition of a single intervention to standard treatment in patients with schizophrenia and comorbid SUD and their outcomes

| Study | Inter-vention | Sample, n | Primary drug use | Duration of the intervention (intensity) | FU | Outcomes | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | reduction in substance use (ES) | reduction in psychiatric symptom severity (ES) | other (ES) |
| Graeber et al. [19][a] | MI vs. PE | 15 vs. 15 | alcohol | 3 weeks (1 h/week) | 24 weeks lost to FU: 7% | MI > PE (1.29) | unknown | unknown |
| Ries et al. [21] | CoM vs. non-CoM | 22 vs. 19 | various | 27 weeks (variable) | none | alcohol: CoM > CM (0.87) drugs: CoM > CM (0.74) | unknown | money management: CoM > CM (1.41) |
| Martino et al. [22][a] | MI vs. SI | 24 vs. 20 | various | 1 week (2 × 1 h/week) | 12 weeks lost to FU: 23% | cocaine: MI > SI (0.5) marijuana: MI < SI (1.11) | PANSS negative: MI < SI[b] | medication and treat-ment adherence: MI = SI |

Effect sizes (ES) are presented in parentheses in the last three columns, representing the following magnitude of the effect: small (≤0.20), medium (>0.20 and <0.80), and large (≥0.80). PANSS = Positive and Negative Syndrome Scale.
[a] This study included inpatients as well as outpatients. [b] Could not be calculated.

trieved. Articles were selected for review when they included an RCT with (a) a sample consisting of participants with schizophrenia/psychotic disorder and comorbid SUD; (b) participants diagnosed according to DSM or ICD criteria; (c) interventions offered in outpatient settings; (d) a comparison between treatment interventions with primary treatment outcome measures, and (e) interventions delivered by a trained professional according to existing protocols. Finally, since the vast majority of articles report on samples with a variety of severe mental illnesses (e.g. schizophrenia, bipolar disorder) and SUD, we additionally limited the selection to articles of which the sample included a sizeable (at least one third of patients) proportion of patients with schizophrenia or a psychotic disorder. Other patients' diagnoses were severe mental illnesses such as bipolar disorders or other severe affective disorders.

*Statistical Analysis*
Treatment effect sizes (Cohen's *d*) of the primary outcome measures were retrieved from the articles or were calculated according to Thalheimer and Cook [18]. Effect sizes (expressed in Cohen's *d*) vary from small (up to 0.20) to medium (from 0.21 to 0.79) or large (0.80 and above).

**Results**

*Literature Search*
Our search retrieved 119 titles that were further consulted. Of these, 14 were selected for review according to the above-mentioned selection criteria and can be classified in four categories: first, a total of 3 RCTs investigated the effect of a single intervention compared to a standardized alternative; second, 4 RCTs investigated the effect of adding a set of interventions (SoI) to TAU; third, another 4 RCTs included ACT. Finally, 3 RCTs involved pro-

grams that were designed specifically for DD patients. The subsequent paragraphs discuss these 14 RCTs according to the four categories. The study details and effect sizes of the primary outcome measures are reported in tables 1–4.

*RCTs Implementing a Single Intervention*
In a pilot study by Graeber et al. [19], MI was associated with a reduction in drinking days and positive outcomes in terms of abstinence compared to psycho-education (PE; table 1). The authors concluded that MI was a useful intervention in patients with schizophrenia and comorbid SUD, with an effect size in the same range as found in non-DD SUD patients [19, 20]. Unfortunately, no outcomes were reported on schizophrenic symptom reduction. In contrast to the other studies, this was the only study that included solely alcohol-abusing SUD patients.

Ries et al. [21] observed that CoM had a positive effect on treatment outcomes regarding substance use and money management compared to non-CoM (non-contingent management of monetary benefits; table 1). The small sample size and the lack of registration of psychiatric outcomes and follow-up (FU) data suggest that replication is needed to ascertain whether the effects on SUD are long-lasting and whether psychiatric pathology is affected by CoM. The effect size in terms of money management is large, which makes it important to investigate whether these effects are long-lasting and how they impact the patient's financial situation and quality of life.

**Table 2.** Overview of the selected RCTs adding a standardized set of interventions to treatment as usual in patients with schizophrenia and comorbid substance use disorders and their outcomes

| Study | Added set of interventions (SoI) | Sample, n | Primary drug use | Duration of the intervention (intensity) | FU | Outcomes | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | reduction in substance use (ES) | reduction in psychiatric symptom severity (ES) | other (ES) |
| Barrowclough et al. [23][a] | MI + CBT + FI | 18 vs. 18 | various | 9 months (variable) | 12 months lost to FU: 13% | SoI > TAU[b] | PANSS positive: SoI > TAU (1) | GAF: SoI > TAU (1.42) |
| Haddock et al. [24][a] | MI + CBT + FI | 18 vs. 18 | various | 9 months (variable) | 18 months lost to FU: 22% | SoI = TAU | PANSS negative: SoI > TAU (1.21) | GAF: SoI > TAU (0.81) |
| James et al. [27] | MI + PS + RP + PE | 32 vs. 31 | various | 6 weeks (1–1.5 h/ week) | 3 months lost to FU: 8% | DAST: SoI > TAU (1.09) AUDIT and SDS: SoI = TAU | BPRS: SoI > TAU (0.73) GSI: SoI = TAU | hospitalization: SoI < TAU (unknown) |
| Barrowclough et al. [25] | MI + CBT | 164 vs. 163 | various | 12 months (variable) | 24 months lost to FU: 25% | SoI = TAU | SoI = TAU | hospitalization: SoI = TAU |

Effect sizes (ES) are presented in parentheses in the last three columns, representing the following magnitude of the effect: small (≤0.20), medium (>0.20 and <0.80), large (≥0.80). PANSS = Positive and Negative Syndrome Scale; GAF = Global Assessment of Functioning Scale; PS = peer support; DAST = Drug Abuse Screening Test; AUDIT = Alcohol Use Disorder Identification Test; SDS = Severity of Dependence Scale; BPRS = Brief Psychiatric Rating Scale; GSI = Global Severity Index.
[a] These trials report on the same patient sample. [b] Could not be calculated.

Martino et al. [22] investigated MI compared to a standard psychiatric interview (SI) and found significantly improved treatment outcome in the MI group for SUD patients with cocaine as their primary drug (table 1). In contrast, SUD patients with cannabis as their primary drug reported significantly more benefits from SI, an unexpected finding since these patients reported less motivation to change at baseline and were thus expected to benefit more from MI. However, these patients had more legal involvements (i.e. were on probation) and the authors assume that the contradicting results could be a consequence of external pressure to alter drug use.

In summary, MI was found to be more effective than PE, but it was not consistently better than SI in terms of substance use outcome [19, 22]. This inconsistency may reflect a difference between subgroups of DD patients. MI seems to be effective in patients with an alcohol or cocaine use disorder but not in patients with a cannabis use disorder. CoM was also found to be effective, but nothing is known about its long-term outcome in DD patients [21].

*RCTs Adding a Standardized SoI to TAU*
Barrowclough et al. [23] reported that adding MI, individual CBT, and FI to TAU was associated with a significantly reduced risk of relapse, an improvement in positive symptoms, and improved global functioning compared to TAU alone (table 2). The data were re-analyzed at 18 months' FU and reported that the difference between treatment conditions remained statistically significant regarding global functioning, but that the difference in substance use (i.e. relapse rate) was not significant anymore (table 2) [24]. Furthermore, patients that received the standardized SoI had improved outcome in terms of negative symptoms at 18 months' FU but not immediately after treatment. According to the authors, caregivers may have learned to adequately support the patients by FI and continued doing so after treatment, hereby improving functioning and reducing negative symptoms. Barrowclough et al. [25] replicated this study with a much larger sample size, but without FI. Relapse rate, psychotic symptoms, functioning, and self-harm were similar between treatment conditions (table 2). There was, however, a significant positive effect of the added interventions regarding abstinence (a secondary outcome measure). The authors suggest that a longer duration of treatment could possibly lead to better outcomes. However, other studies described in this review report positive treatment outcomes with even shorter duration of treatment than the Barrowclough study [19, 22, 26]. The differences in outcome between the studies of the Barrowclough group may suggest that FI was important in improving psychiatric and functioning outcomes, since all other interventions were alike.

**Table 3.** Overview of the selected RCTs implementing assertive community treatment in patients with schizophrenia and comorbid SUD and their outcomes

| Study | Intervention | Sample, n | Primary drug use | Duration of the inter-vention | FU | Outcomes | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | reduction in substance use (ES) | reduction in psychiatric symptom severity (ES) | other (ES) |
| Drake et al. [10] | I-ACT vs. I-CM | 105 vs. 98 | various | unlimited | 3 years lost to FU: 15% | I-ACT > I-CM (0.19) | BPRS: I-ACT = I-CM | stable housing: I-ACT = I-CM |
| Essock et al. [28] | I-ACT vs. I-CM | 99 vs. 99 | various | unlimited | 3 years lost to FU: 10% | I-ACT = I-CM | BPRS: I-ACT = I-CM | stable housing: I-ACT = I-CM |
| Morse et al. [29] | I-ACT vs. ACT vs. SC | 46 vs. 54 vs. 49 | various | unlimited | 24 months lost to FU: 12% | I-ACT = ACT = SC | BPRS: I-ACT = ACT = SC | stable housing: I-ACT + ACT > SC (0.34) I-ACT = ACT |
| Petersen et al. [6] | Enriched ACT vs. TAU | 74 vs. 74 | various | unlimited | 2 years lost to FU: 44% | ACT > TAU[a] | positive symptoms: ACT = TAU negative symptoms: ACT > TAU (0.43) disorganized symptoms: ACT > TAU (0.20) | hospitalization: ACT < TAU (0.32) |

Effect sizes (ES) are presented in parentheses in the last three columns, representing the following magnitude of the effect: small (≤0.20), medium (>0.20 and <0.80), and large (≥0.80). I-ACT = Integrated assertive community treatment; I-CM = integrated case management; BPRS = Brief Psychiatric Rating Scale; SC = standard care.

[a] Could not be calculated.

James et al. [27] compared a DD program consisting of stage-wise intervention, MI, peer support, PE, harm minimization and RP, with PE alone and found less hospitalizations at FU in patients in the DD program compared to PE alone (table 2). The different outcome measures of substance use and psychiatric symptoms were inconsistent. When considering primary SUD outcome measures, a reduction in drug abuse was observed in the DD program compared to PE, but no differences were found for psychological dependence or alcohol abuse. Moreover, the primary psychiatric outcome measures indicated that there was a reduction in psychiatric symptoms following the DD program compared to PE alone but not in the severity of the illness. These inconsistencies may be associated with the duration of the DD program, which was considerably shorter than most other studies in this review (6 weeks compared to often 9 months or more).

In summary, adding a standardized SoI had mixed effects without consistent outcomes. Furthermore, the selection of outcome measures seems to be crucial to capture improvement in outcomes. It is interesting to note that three out of four studies are conducted by the same research group and that the outcomes of these three studies were incidentally very diverse.

*RCTs Implementing (Integrated) ACT*

Drake et al. [10] and Essock et al. [28] did not find differences in treatment outcomes between the integrated ACT model and integrated CM (table 3). Apart from caseload and thus how many services they offer directly, ACT and CM were approximately equal in content, suggesting that a lower caseload per staff seems not to be associated with better outcomes.

Morse et al. [29] compared integrated ACT (i.e. staff trained in IT principles and services, having a substance use specialist as a team member, and SUD-focused treatment) with standard ACT and with standard outpatient treatment. Outcomes of the two ACT modalities did not differ from one another, but the two differed significantly from TAU in terms of housing conditions (table 3). The absence of difference in treatment outcomes between the ACT models could be explained by the great similarities in content and the lack of treatment fidelity (i.e. deviation from the proposed manual, e.g., standard ACT also provided patients with SUD-focused treatment).

Petersen et al. [6] observed that a modified ACT model including SUD treatment, extended family PE (FPE), social skills training, and caseload 1:10 was associated with significantly better outcomes than standard treatment (consisting of FPE and caseload 1:20 to 1:30) in terms of psychiatric symptoms, number of days in the

**Table 4.** Overview of the selected RCTs comparing integrated treatment programs in patients with schizophrenia and comorbid SUD and their primary outcomes

| Study | Intervention | Sample, n | Primary drug use | Duration of the intervention (intensity) | FU | Outcomes | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | reduction in substance use (ES) | reduction in psychiatric symptoms (ES) | other (ES) |
| Burnam et al. [30] | RIT vs. AIT vs. no intervention | 67 vs. 144 vs. 65 | various | 3 months (intensive) + 3 months (optional) | 9 months lost to FU: 42% | RIT = AIT = no intervention | RIT = AIT = no intervention | housing: RIT = AIT = no intervention |
| Bellack et al. [26] | BTSAS vs. STAR | 61 vs. 49 | alcohol, cocaine, heroin, cannabis | 6 months (2×/week) | end of treatment lost to FU: 25% | BTSAS > STAR (0.76) | unknown | attendance: BTSAS > STAR (0.64) |
| Mueser et al. [31] | FIDD vs. FPE | 52 vs. 56 | various | FIDD: 9–18 months (20–30 sessions) FPE: 2–3 months (6–8× 1 h/week) | 36 months lost to FU: 55% | FIDD = FPE | BPRS total: FIDD > FPE (0.17) BPRS psychoses: FIDD > FPE (0.32) | GAS: FIDD > FPE |

Effect sizes (ES) are presented in parentheses in the last three columns, representing the following magnitude of the effect: small (≤0.20), medium (>0.20 and <0.80), and large (≥0.80). RIT = Residential integrated treatment; AIT = ambulatory integrated treatment; BPRS = Brief Psychiatric Rating Scale; GAS = Global Assessment Scale.

hospital, and number of patients fulfilling SUD criteria at FU. The effect sizes are nevertheless modest (table 3). Enriched ACT had better outcomes in terms of patients' treatment adherence than TAU, which was reflected in a significantly smaller number of patients without outpatient visits. Petersen et al. furthermore observed that there was a lower rate of participation at FU among patients without an interview with relatives at baseline, concluding that FI can have a positive impact on retention.

In summary, ACT was not associated with better outcomes than CM, probably due to the model's similar contents. Lower caseload does not seem associated with better outcome. ACT provided better treatment outcomes than TAU. Although small in effect sizes, DD patients seem to benefit from FI in terms of treatment adherence.

*RCTs Comparing IT Programs*

Burnam et al. [30] compared outpatient IT (consisting of group interventions, self-help, individual consultations and CM) with identical treatment offered residentially and with a control condition (no intervention). Remarkably, the authors did not find any clinically relevant differences between these three conditions (table 4), although they report sufficient power. However, effective interventions that are often implemented in other DD programs were not implemented in this IT program. This suggests that interventions such as MI or FI are necessary for positive outcomes. An interesting FU study would be to compare the program in combination with other interventions (e.g. MI, FI or a combination of both interventions) to the original program.

Bellack et al. [26] observed that patients in Behavioral Treatment for Substance Abuse in Severe and Persistent Mental Illness (BTSAS; a combination of social skills training, MI, PE, RP and CoM) achieved significantly better outcomes in terms of abstinence from substance use (reported as drug-free urine samples) and of percentage of patients with at least one 4- or 8-week block of continuous abstinence than patients in Supportive Treatment for Addiction Recovery (STAR; PE and supportive group therapy) (table 4). Also, BTSAS was associated with significantly improved attendance and retention. Additional exploratory analyses indicated that the number of inpatient admissions and arrests significantly decreased and that social functioning, quality of life, life satisfaction, and financial situation significantly improved in patients in BTSAS compared to patients in STAR. BTSAS indeed seems very promising, but only short-term effects were found.

Mueser et al. [31] compared a Family Intervention for DD (FIDD; comprising of PE, skills training, stage-wise intervention and single and multiple family groups) with an FPE program. FIDD was associated with better outcomes for patients in terms of general functioning, overall psychiatric symptoms, and psychotic symptoms revealing small effect sizes (table 4). Furthermore, mental health and knowledge of DD improved significantly in

family members receiving FIDD compared to FPE. This could, in turn, improve patient outcomes, since a more stable and well-informed family environment can help preventing relapse and improving quality of life [32]. Both programs, FPE and FIDD, improved psychiatric, substance use, psychosocial, and family functioning outcomes, but FIDD improved psychiatric outcomes and functioning significantly more than FPE.

The content of the three IT programs obviously is very diverse and makes a general conclusion about the efficacy of IT difficult. BTSAS was effective [26], while the Burnam program was not [30]. A program that includes family members' involvement was associated with positive treatment outcomes anyhow [31].

## Discussion

This review provides an overview of the efficacy of outpatient care for patients with schizophrenia and comorbid SUD. The results reflect the great heterogeneity in the field of DD treatment. Most of the interventions and IT models nevertheless show beneficial effects over TAU, but the effect sizes vary substantially.

The first question is whether a broader SoI is related to significantly better treatment outcome compared to a limited SoI. We identified three RCTs implementing a single intervention [19, 21, 22], four using a more extensive SoI [23–25, 27] and three using a fully integrated SoI [26, 30, 31]. Improved substance use outcomes were observed in two out of three studies including only one intervention (MI or CoM) [19, 21]. This is in accordance with two other studies on patient populations that did not fulfill inclusion criteria, which also found positive effects of CoM on SUD [33, 34]. In terms of psychiatric symptoms, Martino et al. [22] reported that MI improved negative symptoms, but results in terms of various SUD outcomes were inconsistent in this study. Adding a single intervention, particularly CoM, is associated with better SUD outcome.

When offering a combination of interventions, one out of four studies showed improvements in both substance use and psychiatric symptoms [27]. Two other studies reported discrepant results of their program at 12 and 18 months' FU [23, 24]: the effect on SUD improvement diminished over time, while a significant effect on psychiatric outcomes was found at 18 months' FU and improvement of global functioning remained. However, by far the largest study only found minor improvements in SUD outcomes [25].

Finally, one out of four studies on a fully integrated program found improvements on psychiatric symptomatology (with a small effect size) [31] and one other study (that unfortunately did not assess psychiatric outcomes) observed large effects in terms of SUD at the end of treatment [26], in contrast to another study that found no evidence for the efficacy of IT [30].

Despite a large variability in outcome and its measurement, one may conclude that more elaborated programs are more positively related to a broader spectrum of improvement (i.e. SUD, psychiatric, and/or functioning outcomes) compared to more limited interventions. In addition, some studies suggest that intensity and program duration could play an important role in achieving better outcomes [e.g. 27]. These factors should be investigated further.

ACT or CM is often suggested to be an essential part of treatment for SUD patients. In this review, we could identify four studies comparing ACT with other interventions [6, 10, 28, 29]. When a program with ACT was compared to a program without ACT or CM, results were inconsistent: one study demonstrated better outcomes of ACT on both SUD and psychiatric outcomes [6], whereas another study found very little difference between ACT and TAU outcomes (i.e. only in terms of stable housing) [29]. The authors of an excluded study concluded that ACT significantly improved quality of life compared to TAU but that outcomes of ACT appeared similar to outcomes of an intervention based on group therapy [35]. Another study that also did not fulfill inclusion criteria revealed that ACT outperformed an intervention focused on self-help meetings in terms of psychiatric outcomes, family interaction and global life satisfaction, but SUD was not affected [36]. Overall, ACT programs do not seem to be associated with better outcomes than CM [10, 29]. Moreover, CM and ACT programs are very similar in content with the exception of their caseload. Also, integrated ACT compared to standard ACT did not result in better treatment outcomes [29]. Finally, McHugo et al. [11] reanalyzed the data of Drake et al. [10] and showed that patients receiving an ACT program implemented with high treatment model fidelity had significantly superior outcomes in terms of days of alcohol and drug use, stage of substance abuse treatment, percentage of patients with stable remission, and hospital admissions compared to patients in programs implemented with low treatment model fidelity. In conclusion, both ACT and CM seem effective. The lack of difference indicates that lower patient-staff ratio was not associated with better outcomes. Furthermore,

high treatment model fidelity is important for improvement.

Given the wide variety and combinations of interventions, it remains difficult to assess the effectiveness of each single intervention. All described interventions implemented in IT programs are known to be effective in the treatment of (non-DD) SUD patients, but effectiveness in DD patients needs to be confirmed. A large number of included studies (n = 7) [19, 22–26, 28] implemented MI, and most of these studies reported that the experimental condition had significantly better treatment outcomes (mostly in terms of SUD). Another frequently implemented intervention was FI (n = 5) [6, 23, 24, 28, 31]. Although the content of these interventions varied greatly, the outcomes mostly seemed positive. FI seems especially promising in terms of ameliorating real-life functioning. Some evidence was found for the efficacy of stage-wise interventions [28, 31], but one other study (with ACT) did not find improved treatment outcomes [10]. Finally, few studies implement RP [26, 27] and CoM [21, 26], but these studies do show very encouraging results. To affirm the impact and efficacy of a single intervention to treatment outcomes, one should investigate a combined program compared to the program with a single intervention withheld.

One of the major strengths of our review consists of the strict selection of RCTs with the consequence that informative studies were excluded because they did not meet our selection criteria. Of importance, the outcomes of these excluded studies were consistent with our results, providing support for our findings. A second important strength is that this review has managed to bring some structure in the heterogeneous field of DD treatment by focusing on the programs and specific interventions used in the different studies. Several limitations warrant careful interpretation of our results. Most of these limitations are well-known caveats when studying the outcome of complex, real-world, multidisciplinary psychosocial interventional programs. First, most studies included patients with a psychotic disorder combined with patients with other severe mental disorders (mostly bipolar disorders). If we had strictly excluded studies with diagnostically mixed samples, only eight studies would have been selected for review [i.e. 6, 19, 22–25, 27, 28]. In our opinion, excluding a large number of patients with schizophrenia would be a serious bias in the results. Thus, we believe that including studies with mixed samples with a sizeable portion of patients with schizophrenia (at least one third) is a justifiable decision when the interpretation of the results is carefully done due to samples' heterogeneity. However, DD patients with other severe mental illnesses might need slightly different integrated interventions or programs than DD patients with schizophrenia. Secondly, two studies included inpatients as well as outpatients [19, 22] and it was not possible to dismantle the setting effect in these studies. Thirdly, it was not always possible to elaborate on the required intensity of a program due to lack of information or because treatment programs provided unlimited care. Furthermore, we found a large variability between studies as to the types of interventions offered (and also with respect to the content of the specific interventions), the outcome variables used, and the TAU conditions. This variability is, however, inherent to the field of DD treatment and clinical practice. Finally, we focused on outpatient programs, a choice we believe is justified given the present and future relevance of and focus on community-based service provision [16, 17]. We did not include studies on residential programs [37–42] so that results cannot be transferred to inpatient services. The outcomes of two of these RCTs on inpatient treatment were consistent with the results of this review [39, 40].

Taken together, and in spite of the above-mentioned limitations, we do think the mayor strength of our study is its comprehensiveness, reflective of the current outcome research on DD patients in real-world patient samples. Our findings clearly highlight the enormous diversity within the clinical and research field both as to the differences of the patient samples included as to the different treatment interventions offered in these DD programs. This manifest heterogeneity leads us to conclude that future research should focus on narrowing patients' characteristics (e.g. patients with 'pure' schizophrenia, poly- vs. single-substance use) and tailoring specific interventions or programs related to their expected outcomes (i.e. type of substance abused). In addition, one should try to assess which specific interventions most strongly drives the positive effects of the treatment. This could be done by taking an elaborate program and comparing it with and without each intervention. Furthermore, patient (and family) treatment satisfaction needs to be incorporated as relevant outcome factors in clinical decision-making.

We conclude that IT, in particular BTSAS and FIDD, is effective in treating DD patients with schizophrenia and SUD. However, this conclusion should be taken carefully as only one study investigated these two programs. Additionally, the current evidence supports the use of MI, CoM, FI, and RP or a combination of the foregoing in IT programs. Finally, both ACT and CM seem similarly ef-

fective, suggesting that a lower caseload did not promote better outcome. Although our review revealed useful insights in the efficacy of outpatient DD treatment, the low number of included studies clearly illustrates the need for additional high-quality research.

## Acknowledgements

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