

Original article

Retrospective study in a cohort of subjects with substance use disorders in Veneto, Italy: real-world outcomes of an addiction daytime program treatment

Diego Saccon¹, Alice Valdesalici², Elena Boatto¹, Giovanna Bortoluzzi¹, Susan De Nardi¹, Chiara Lazzarato¹, Francesco Moret¹, Andrew Smith⁴, Sally Paganin⁵, Marco Solmi^{3,5-7}

¹ Addiction Department, AULSS 4 Veneto Orientale, San Donà di Piave (VE), Italy; ² Department of General Psychology, University of Padua, Padova, Italy; ³ Department of Psychiatry, University of Ottawa, Ottawa, Canada; ⁴ Department of Mental Health, The Ottawa Hospital, Ottawa, Canada; ⁵ Department of Biostatistics, Harvard T.H. Chan School of Public Health, Harvard University, USA; ⁶ Clinical Epidemiology Program, Ottawa Hospital Research Institute (OHRI), University of Ottawa, Ottawa, Canada; ⁷ Department of Child and Adolescent Psychiatry, Charité Universitätsmedizin, Berlin, Germany



Diego Saccon

Summary

Background. Treatments for substance use disorders (SUDs) can be delivered in outpatient, residential or daytime treatment settings. Existing literature on the efficacy of addiction treatment programs is scarce and mainly regards randomized control trials (RCTs). However, it is of great importance to conduct research in ecological contexts to gather valuable real-world effectiveness data and to inform clinicians and policymakers.

Objectives. The present study evaluates real-world clinical outcomes in an Italian addiction day treatment program.

Methods. We conducted a retrospective naturalistic study on a cohort of patients with SUDs enrolled in a day treatment program offered by the local health unit “ULSS 4 Veneto Orientale”, located in the Veneto region of Italy, from the beginning of September 1999 to the end of December 2020. Data were collected at the time of admission to the program, during the program period and 6 months after its conclusion. Descriptive socio-demographic data, diagnoses (SUDs and comorbid disorders), pharmacological treatments, and psychiatric hospitalization data of patients enrolled in the program were collected. Primary outcomes of remission of SUD and employment status were measured in patients who completed at least 3 months of treatment. McNemar’s nonparametric test for paired data was used to analyze these outcomes. Results with a p-value < 0.05 were considered statistically significant. Reporting referred to STROBE checklist.

Results. The average age of patients was 42 (range: 18-77). Most patients were not married, lived alone, had no children, and attended middle school as the highest level of education achieved. Diagnostically, most reported a clinical history consistent with heroin (42.04%), alcohol (34.1%), tetrahydrocannabinol (THC; 11.93%), cocaine (9.65%), ecstasy (1.71%) or benzodiazepine (0.57%) use disorder. We found a significant increase in employment levels in patients having completed at least 3 months in the day treatment program compared to their pre-treatment baseline (p-value 0.0001). There was also a significant decrease in the number of patients meeting clinical criteria for heroin (p-value 0.0003), alcohol (p-value < 0.0001), cocaine (p-value 0.0026), and

How to cite this article:

Saccon D, Valdesalici A, Boatto E, et al. Retrospective study in a cohort of subjects with substance use disorders in Veneto, Italy: real-world outcomes of an addiction daytime program treatment. Evidence-based Psychiatric Care 2023;9:7-14; <https://doi.org/10.36180/2421-4469-2023-3>

Correspondence:

Diego Saccon
diego.saccon@aulss4.veneto.it

Conflict of interest

The authors declare that they have no conflict of interest nor that they have received compensation from third parties for the creation of this article.

This is an open access article distributed in accordance with the CC-BY-NC-ND (Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International) license. The article can be used by giving appropriate credit and mentioning the license, but only for non-commercial purposes and only in the original version. For further information: <https://creativecommons.org/licenses/by-nc-nd/4.0/deed.en>

Open Access



© Copyright by Pacini Editore Srl

THC (p -value 0.0015) dependence at the 6 month follow-up visits.

Conclusions. This study provides real-world clinical evidence that addiction day treatment programs can improve not only SUD symptoms, but overall function as measured by post-treatment employment status. Results should be interpreted with caution due to the lack of a control group, and the retrospective and observational nature of this study.

Key words: substance use disorder, rehabilitation; addiction daytime program, treatment outcome, real-world study

Introduction

Alcohol and drug consumption is a global health concern with dramatic increases in global prevalence of substance use disorders (SUDs) causing societal burdens due to negative health outcomes around the world ¹. Globally, more than 175 million people suffer from SUDs ², with more than 100 million people being affected by alcohol use disorder alone. In the 2018 National Survey on Drug Use and Health of U.S.A., rates of drug abuse were 49.4% in the severely mentally ill, 36.7% in those with any mental disorder, and 15.7% in individuals without psychiatric disorders ³. Clearly, evidence-based interventions are needed on an unprecedented scale.

Well-recognized treatments for SUDs include pharmacotherapy, psychotherapy, counselling, and psychosocial interventions including mutual help groups ⁴. These can be delivered in various clinical contexts including outpatient, residential or daytime treatment settings. In the Italian context, residential treatment is much more readily available than are day treatment programs. Residential treatment ³ refers to long-term treatment programs in which patients receive 24-hour support and care throughout their recovery while engaging in prescribed therapeutic activities and living and sleeping inside the treatment facility for a period of 12 months, on average ^{3,5}. In contrast, outpatient treatment programs typically require patients to attend the service for regular scheduled visits with treatment team members (nurses, occupational therapists, psychologists, or doctors) during the day, often one or more times per week. Outpatient programs consist of therapeutic activities ranging from pharmacological treatments to socio-educational and rehabilitation interventions ⁴ to psychotherapeutic treatment ⁴.

Residential treatment programs are conducted in highly structured, protective environments within which triggers and relapse-inducing cues are reduced or removed entirely. In the residential setting, patients can focus on their recovery following carefully organized daily schedules. On the other hand, outpatient programs are far less restrictive and allow patients to experience more

freedom, thus relying far more on the patient's skills and internal motivation to recover ⁶. In both cases, the goal of addiction treatment programs is to achieve SUD remission and patient recovery including improvement in autonomy and functioning, and the promotion of social reintegration ^{5,7}.

Existing literature on the efficacy and outcome data from addiction treatment programs of various sorts has not yet been conclusive, especially when considering the Italian research framework. In Italy, programs and patients may differ from international cohorts in significant ways, potentially leading to different results. Most prior research is focused on randomized control trials (RCTs) to understand what type of intervention is most efficacious in treating people with SUDs ^{8,9}. Nonetheless, it remains important to examine and study contexts in which RCTs have not been conducted, as research in these areas can provide valuable real-world effectiveness data to inform and guide clinicians and policymakers in decision-making and evidence-based health resource allocation.

The present study evaluates outcomes related to an Italian day treatment program in an Addiction Department, which carries out therapeutic and rehabilitative treatments for patients with SUDs and comorbid mental disorders (dual diagnosis). This is of particular importance as very few programs will accept patients with dual diagnoses, and the all-too-frequent norm being rather that dual diagnosis patients are declined from both general psychiatric and addictions treatment programs instead of being offered the specialized treatment that they need.

The aim of the study is to examine the real-world effectiveness of a day treatment program for persons with comorbid SUD and mental disorders, with regard to both SUD symptoms and overall functioning as measured by post-treatment employment levels as a surrogate outcome measure.

Materials and methods

Study design and setting

We conducted a retrospective study on a cohort of patients with SUDs enrolled in an outpatient addiction treatment program in Italy from the beginning of September 1999 to the end of December 2020. The flow of participants is reported according to the STROBE cohort reporting guidelines ¹⁰.

Offered by the local health unit "ULSS 4 Veneto Orientale", located in the Veneto region of Italy, our program called "Comunità Terapeutica Diurna" consists of an integrated multimodal therapeutic program developed in collaboration with the addiction treatment outpatient service (i.e. Servizio per le Dipendenze - Ser.D.) (CTD; Fig. 1). As an outpatient day treatment program, patients do not stay overnight, and we do not operate during weekends or

holidays; however, a telephone line connected with the occupational therapist is available 24/7. The team following patients consists of different healthcare professionals. For each patient, a highly individualized treatment plan is designed, implemented, monitored, and adjusted to optimize for symptom control and functional recovery. Daily and weekly activities are organized to offer a range of therapeutic and occupational interventions (Tab. I).

Previously ¹¹, we described the treatment model of the CTD as characterized by a connection between the real-life context of the patient and a partially protected environment as a starting point from which the individual can establish safer relationships and improved life skills. In this sense, the outpatient program maintains continuity with the natural context of the patient, therefore serving as a safe setting for self- reflection, developing tools for

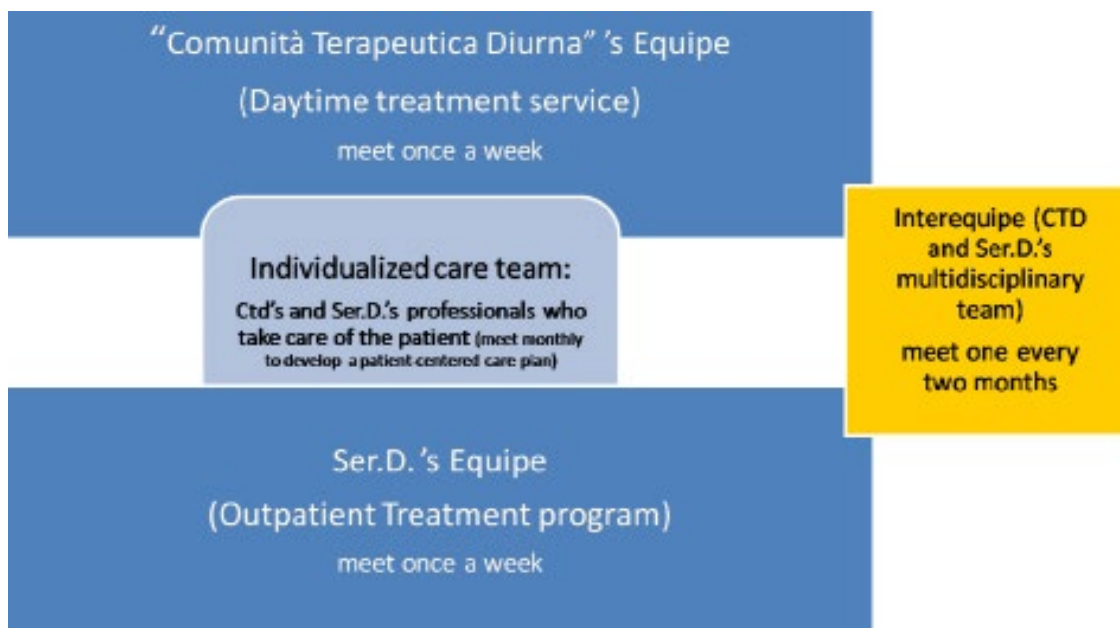


Figure 1. Integration Model CTD-SerD.

Table I. Description of the rehabilitative and therapeutic activities in "Comunità Terapeutica Diurna".

Type of intervention	Activities conducted	Description (time, professionals involved ...)
Occupational therapy	Assembly activities, cartonnage, horticulture	Every day, tutored by educator
Psycho-educational interventions	Psychoeducational group to plan and check the weekend. Social skills and relapse prevention training, personal coaching	Every Friday and Monday, conducted by educator, weekly conducted by educator, managed by educator
Therapeutics interventions	Psychotherapy group	Weekly, conducted by psychologist-psychotherapist
Recreational activities	Sport activities, day trips	Weekly, monthly managed by educators
Therapeutic activities in the outpatient service ("Servizio per le Dipendenze")		
Psychiatric/medical doctor activities	Assessment, test prescriptions, pharmacotherapy prescriptions, follow up	Psychiatrist. Intake; as needed, monthly almost.
Nurse's activities	Administer and dispense pharmacotherapy, carry out toxicological and hematological screening, ECG, etc.	Nurse; as needed.
Psychological and psychotherapeutic activities	Psychological assessment, individual psychotherapy	Psychologist/psychiatrist. Intake; only some patients

self-regulation, and learning to navigate the difficulties encountered during their rehabilitative journey.

CTD and Ser.D. services are composed and integrated as follows. The CTD team is composed of four occupational therapists and a clinical psychologist who meet once a week. Ser.D.'s multidisciplinary team is composed of MDs, psychologists, occupational therapists, nurses and social workers who meet once a week. The two teams work together once every two months to share common patient goals. Individual patient teams are also created and are composed of the CTD and Ser.D. professionals who provide care for the patient. This individualized care team meets with each patient monthly to review clinical progress and develop a patient-centered care plan for ongoing clinical management.

Data collection and participants

Socio-demographic information, current and historical diagnoses, pharmacological treatments, and psychiatric hospitalization data for day treatment program patients was collected retrospectively, through Ser.D. clinical records review. Once collected, data were entered into a database created for the purpose of the present study, but also to follow the patients and their treatment course prospectively. Data were collected at the time of admission to the program, during the program and at a 6-month follow-up visit. We analyzed outcomes of only those patients who underwent treatment for at least 3 months, as suggested by the literature¹². The diagnoses of psychiatric comorbidity were made by psychiatrists from Ser.D. originally in reference to the clinical criteria of the DSM-IV-R and, subsequently, from its Italian edition in 2013 to the DSM-5. Having analyzed a long period of time (from 1999 to 2020) the DSM-4 and DSM-5 criteria were used to diagnose. Two levels of gravity are indicated in the DSM IV substance use which were, namely, "Abuse" and "Dependency". These largely correspond to the "mild" and "moderate to severe" levels of severity indicated in DSM 5. Structured interviews were not conducted for this study.

We excluded from the baseline evaluation patients still under treatment and patients who attended the outpatient facility sent by other Addiction Departments of other healthcare units, as the program attended was different to the standard one. For the follow-up analysis, we excluded patients who had multiple treatments as well as those who attended the program for less than 3 months.

Outcomes

Remission of SUD. For the formulation of SUD diagnoses, we referred to the diagnostic classification of the DSM IV-R, and of the DSM-5 for patients treated in 2014 onwards. The SUD diagnosis was made by the Ser.D. psychiatrists at the beginning of the therapeutic program through clinical assessment including toxicological tests and blood markers of alcohol abuse. A stringent clinical

interview coupled with clinical observations of the state and behaviours of the patient along with urine toxicological tests are used to evaluate remission outcomes. Keratin matrix examinations are not normally available to Italian national health service patients (*i.e.*, *Servizio Sanitario Nazionale-SSN*) in the Veneto Region as an indicator of remission in clinical practice.

Six months after the end of the treatment, data on SUD remission was collected by considering the results of the patients' toxicological examinations and a thorough review of individual medical records. There are very few outpatient experiences in the literature with respect to those of semi-residential structures. The patients in this study are not in residential programs and, that is, programs held in protected structures. The patients included in this study live in the real world and face the issue of renewed substance use on a daily basis. For this reason, patients are evaluated during the whole treatment period as well as in the 6 month period after remission. However, a longer follow-up period would be preferable in future evaluations. *Employment status.* We examined the dichotomous variable of employed or unemployed using information collected from individual medical records and work contracts supplied by the patients.

Statistical analysis

Descriptive analyses were conducted to characterize the study sample. Change in occupational status was assessed by considering only those subjects for whom there was continuity over the time of the survey and by comparing the dichotomous status of employed/unemployed variable between time t_0 (onset) and t_1 (6 months after discharge) using McNemar's nonparametric test for paired data. The same analysis was conducted to assess remission of SUD (abuse or dependence vs. remission) at 6 months after discharge. Results with a p -value < 0.05 were considered statistically significant.

Results

Overall, 187 subjects attended CTD from September 1, 1999 to December 31, 2020. We excluded 10 patients from the study who were still in treatment, and one patient attending the program who was sent by other services. Therefore, a total of 176 patients were considered for the baseline analysis, including those who had been in treatment for less than 3 months (Fig. 2).

The average age of patients entering the program was 42 with a minimum age of 18 and a maximum of 77. Most of the patients were not married, were living alone, had no children, and attended middle school as their highest level of education.

Most of the patients suffered from heroin (42.04%), alcohol (34.1%), tetrahydrocannabinol (THC; 11.93%), cocaine (9.65%), ecstasy (1.71%) or benzodiazepine (0.57%) use disorder. Concerning psychiatric comorbidities, 56.23% of

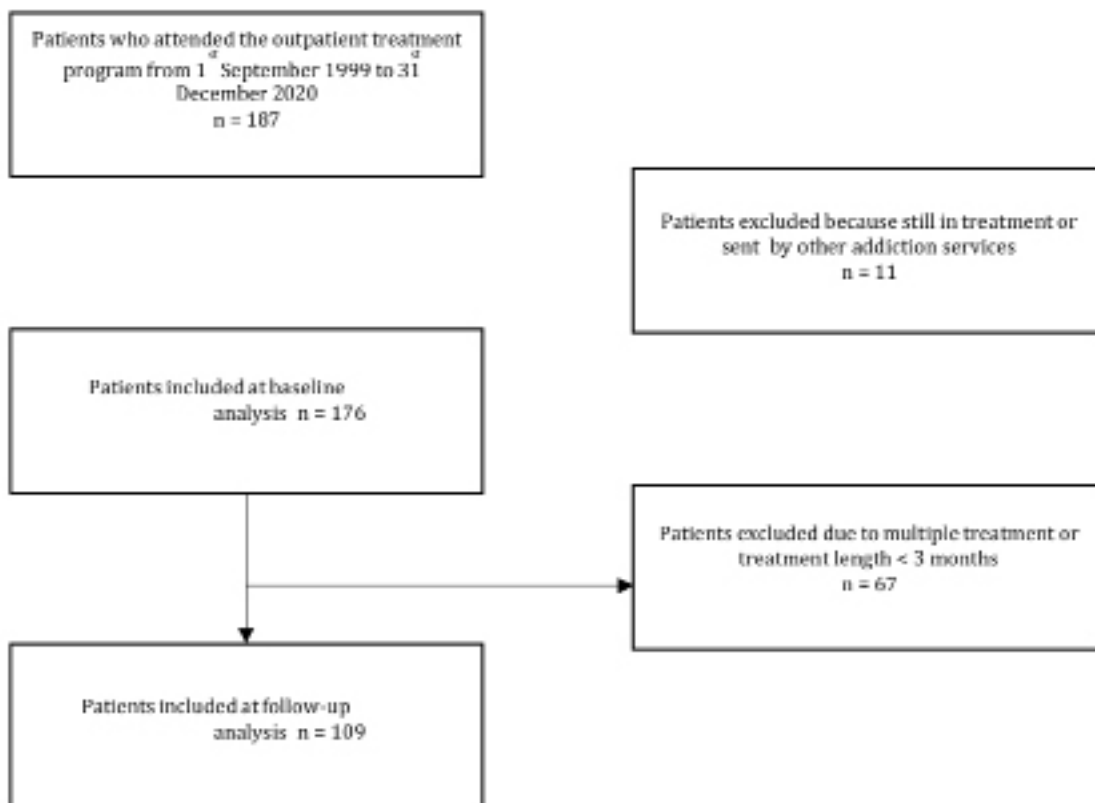


Figure 2. Flowchart of the participants of the retrospective cohort study.

the patients were diagnosed with a personality disorder, 12.5% with a psychotic disorder, 11.93% with depressive disorders, 7.95% with anxiety disorders. Most of the patients received pharmacological treatments either for the SUD or comorbid diagnoses. Of the 176 patients included in the study, 38.1% (n = 67) had at least one psychiatric hospitalization, while approximately 10% (n = 18) underwent one or more involuntary admissions. Patients' length of stay in the program ranged from a few days to more than 3 years, however, about half of the patients (49.5%; n = 87) attended the facility for between 3 and 18 months. Overall, 38.1% (n = 67) of patients attended the program for less than 3 months, and 12.5% (n = 22) attended for more than 18 months. Demographic and clinical characteristics of the sample at baseline are represented in Table II.

Follow-up analysis

Two outcomes related to the treatment were evaluated at the beginning of the program and 6 months after discharge. In this analysis, only patients who completed at least three months of CTD treatment were considered, for a total of 109 subjects (Fig. 2).

The first outcome evaluated is the employment status of the patients attending the outpatient treatment program. These patients' declared status is supported by copies of their work contract which are supplied during the

Table II. Demographic and clinical characteristics of the patients at baseline.

N = 176	N	%
Marital Status		
Unmarried	124	70.45%
Divorced	21	11.93%
Married	18	10.23%
Cohabiting	11	6.25%
Missing data	2	1.14%
Educational Level		
Primary school	24	13.60%
Middle school	97	55.10%
Vocational courses	20	11.40%
High school	26	14.80%
Degree	3	1.70%
Missing data	6	3.40%
Number of children		
None	141	80.11%
1	20	11.36%
2+	13	7.39%
Missing data	2	1.14%
N = 176	N	%

SUD Diagnosis – main substance		
Heroin	74	42.04%
Alcohol	60	34.1%
Cocaine	17	9.65%
THC	21	11.93%
Benzodiazepines	1	0.57%
Ecstasy	3	1.71%
Psychiatric comorbidities		
Psychotic disorders	22	12.5%
Depressive disorders	21	11.93%
Anxiety disorders	14	7.95%
Somatic symptoms and related disorders	1	0.56%
Sexual and gender identity disorders	1	0.56%
Cluster A personality disorders	10	5.68%
Cluster B personality disorders	52	29.54%
Cluster C personality disorders	13	7.38%
Other personality disorders	24	13.63%
DUDs pharmacological treatments		
Methadone	53	30.11%
Buprenorphine	8	4.55%
Naltrexone	2	1.14%
No treatment	108	61.36%
Missing data	5	2.84%
AUD pharmacological treatments		
Disulfiram	21	11.90%
Disulfiram and oxibatoNa	9	5.10%
OxibatoNa	2	1.10%
No treatment	144	81.81%
Psychiatric comorbidities pharmacological treatments		
Single pharmacological treatment	67	38.1%
Combined pharmacological treatment	64	36.00%
No pharmacological treatment	45	26.00%
Antipsychotics	61	28.90%
Antidepressants	54	25.60%
Mood stabilizers	12	5.70%
Benzodiazepines	84	39.80%

SUD: substance use disorder; DUD: drug use disorder; AUD: alcohol use disorder; THC: tetrahydrocannabinol.

interviews. At the beginning of the program, 70% of this subgroup was unemployed while in subsequent surveys, taken at the end of the outpatient program, there is a decrease in the percentage of unemployed individuals (46%) in favor of employment or a pension (Fig. 3). Personal growth objectives pursued in the program also include patient movement towards economic autonomy. When comparing the number of unemployed users versus those employed at the time of entry into the program and 6 months after discharge, a significant difference was found (non-parametric McNemar test, p-value 0.0001). There was also a significant difference (p-value 0.022) when comparing the number of employed people after 6 months from discharge from the CTD program.

Regarding remission, we found an increase in the number of patients in remission for each of the substances examined (Fig. 3). There was a significant decrease in the number of patients with heroin (non-parametric McNemar test, p-value 0.0003), alcohol (p-value < 0.0001), cocaine (p-value 0.0026), and THC (p-value 0.0015) dependence at 6 months after the end of the program.

Discussion

The present study examined outcomes related to a day treatment program for individuals diagnosed with SUDs in the Veneto region of Italy. The aim was to determine whether this specific service can be considered an effective treatment solution, with respect to remission of the patients' SUD and their employment status at 6 months post discharge.

According to our analysis, there is a significant reduction in the number of unemployed individuals after treatment, confirming an improvement in the employment status of patients that attend treatment facilities, as has been found in previous studies^{11,13}. Moreover, it can be concluded that there is a significant reduction in the number of patients affected by SUDs, as evidenced by the increase of the patients in remission after the end of the program for each examined substance (i.e., alcohol, heroin, cocaine, THC), a result that confirms findings in previous studies^{11,14}.

According to recent network metanalysis, the most effective intervention to treat SUDs is pharmacotherapy^{8,15,16} together with contingency management¹⁷ and community reinforcement⁹. In addition, psychosocial interventions (i.e., CBT or mindfulness-based stress reduction) have an observable positive effect, especially in terms of relapse prevention¹⁸. The treatment program examined in this study provides psychosocial interventions that focus on occupational activities, skills training, relapse prevention, and emotional management, which can complement pharmacotherapy.

The primary limitations of the present study are its retrospective design, the lack of a control group in this study, and the fact that outcomes were analyzed on a subgroup of patients who attended the facility for at least 3 months. Further, a single diagnosis is evaluated as an

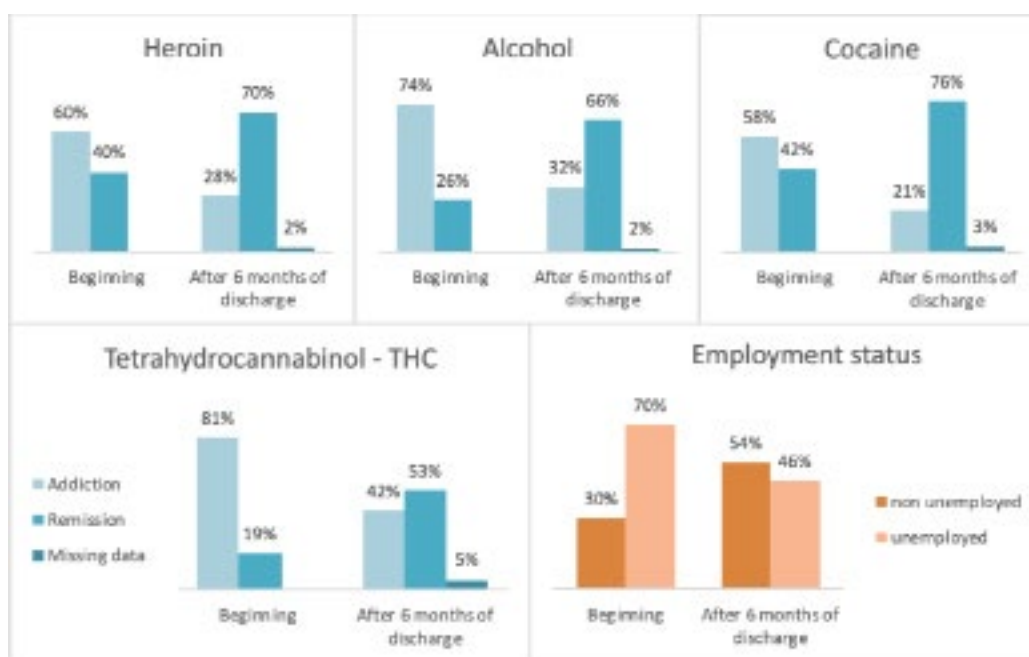


Figure 3. Percentage of participants at baseline and follow-up analysis related to SUD status for each substance (blue) and employment status (orange).

outcome as subgroup numbers are too small to allow for an analysis of the patterns of substance use. In addition, a longer follow up period could be advisable. Although studies using real-world data cannot provide evidence on the efficacy of treatments as can be done by RCTs, they are informative in terms of evaluating the effectiveness of treatment programs and should be conducted more often to guide more structured service-evaluation programs in Italy, with the ultimate goal of implementing evidence-based services to cost-effectively optimize patients' health outcomes. In addition, cost-effectiveness analyses are also needed.

Conclusions

The results of this study indicate that, following completion of at least 3 months of an outpatient-based day treatment program, patients with SUDs and other co-morbid mental health diagnoses showed significant improvement in terms of SUD remission rates and employment status as a surrogate outcome for overall level of functioning. Given the promising results presented herein, further study is warranted in this area, potentially including health economic analysis comparing the cost-effectiveness of day treatment programs and residential treatment settings to guide future health policy and resource allocation.

References

- Degenhardt L, Charlson F, Ferrari A, et al. The global burden of disease attributable to alcohol and drug use in 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Psychiatry* 2018;5:987-1012. [https://doi.org/10.1016/S2215-0366\(18\)30337-7](https://doi.org/10.1016/S2215-0366(18)30337-7)
- James SL, Abate D, Abate KH, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018;392:1789-858. [https://doi.org/10.1016/S0140-6736\(18\)32279-7](https://doi.org/10.1016/S0140-6736(18)32279-7)
- SAMSHA, National Survey of Mental Health, 2018. <https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHNationalFindingsReport2018/NSDUHNationalFindingsReport2018.htm#mhisud2>
- NIDA. Therapeutic Communities Research Report. What Are Therapeutic Communities? 2015;(July):2-25.
- NIDA. Principles of Drug Addiction Treatment: A Research-Based Guide (Third Edition). National Institute on Drug Abuse 2018. <https://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/frequently-asked-questions/what-are-unique-needs-pregnant-women-substance-use>
- Karriker-Jaffe KJ, Klinger JL, Witbrodt J, et al. Effects of treatment type on alcohol consumption partially mediated by alcoholics anonymous attendance. *Subst Use Misuse* 2018;53:596-605. <https://doi.org/10.1080/10826084.2017.1349800>
- Lamonaca P, Berlini A, Il progetto terapeutico per gli utenti inseriti nelle comunità terapeutiche. Sestante: i nodi tra consumi e dipendenze, Rivista scientifica a carattere divulgativo della rete dei servizi per le dipendenze patologiche in Area Vasta Romagna. 2010; 33:12-15
- Cheng HY, McGuinness LA, Elbers RG, et al. Treatment interventions to maintain abstinence from alcohol in primary care: systematic review and network meta-analysis. *BMJ* 2020;371:m3934. <https://doi.org/10.1136/bmj.m3934>

- ⁹ De Crescenzo F, Ciabattini M, D'Alò GL, et al. Comparative efficacy and acceptability of psychosocial interventions for individuals with cocaine and amphetamine addiction: a systematic review and network meta-analysis. *PLoS Med* 2018;15:e1002715. <https://doi.org/10.1371/journal.pmed.1002715>
- ¹⁰ von Elm E, Altman DG, Egger M, et al. The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol* 2008;61:344-9. <https://doi.org/10.1016/j.jclinepi.2007.11.008>
- ¹¹ Saccon D, Banon D, Boatto E. Evoluzioni nelle dipendenze da sostanze - il problema delle cronicizzazioni. Padova: CLEUP, 2013.
- ¹² Dowd ET, Rugle L. La tossicodipendenza: trattamenti a confronto. Milano: McGraw-Hill Libri Italia 2001.
- ¹³ De Leon G. Is the Therapeutic community an evidence based treatment? What the evidence says. *International Journal of Therapeutic Communities* 2010;31, 2,;31, 2, summer 104-128.
- ¹⁴ European Monitoring Centre for Drugs and Drug Addiction, Broekaert E, Vanderplasschen W, Vandeveldel S. Therapeutic communities for treating addictions in Europe – Evidence, current practices and future challenges. 2014 <https://data.europa.eu/doi/10.2810/25291>
- ¹⁵ Bahji A, Meyyappan AC, Hawken ER, et al. Pharmacotherapies for cannabis use disorder: a systematic review and network meta-analysis. *Int J Drug Policy* 2021;97:103295. <https://doi.org/10.1016/j.drugpo.2021.103295>
- ¹⁶ Lim J, Farhat I, Douros A, et al. Relative effectiveness of medications for opioid-related disorders: a systematic review and network meta-analysis of randomized controlled trials. *PLoS One* 2022;17:e0266142. <https://doi.org/10.1371/journal.pone.0266142>
- ¹⁷ Bentzley BS, Han SS, Neuner S, et al. Comparison of treatments for cocaine use disorder among adults: a systematic review and meta-analysis. *JAMA Netw Open* 2021;4:e218049. <https://doi.org/10.1001/jamanetworkopen.2021.8049>
- ¹⁸ Rice D, Corace K, Wolfe D, et al. Evaluating comparative effectiveness of psychosocial interventions adjunctive to opioid agonist therapy for opioid use disorder: a systematic review with network meta-analyses. *PLoS One* 2020;15:e0244401. <https://doi.org/10.1371/journal.pone.0244401>