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Evidence based Psychiatric Care
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Editorial

Società Italiana di Psichiatria

# Back to the brain: for a third-millennium psychiatry

Liliana Dell'Osso

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Liliana Dell'Osso

Last century's psychiatry left us with an important and heavy legacy. A legacy of great changes, but also of unfulfilled goals and unsatisfactory assumptions. We thought that neuroscience would have provided an answer to all our questions, like a *deus ex-machina*, but those answers never came. Neuroscientific research tirelessly focused on the hope of isolating specific biological markers of diseases, conceptualized as genetically pure phenotypes. Genetic research focused on identifying possible specific mutations associated with the main categories of mental disorders. But despite the unthinkably wide literature production, we reached the conclusion that, in most cases, mental disorders are instead underlain by complex polygenic inheritances, which interact with epigenetic modifications and environmental factors for determining the actual manifestations of the disorder. Although highlighting an undeniable basis of hereditability, the possibility of pure determinism in the field of psychiatry has progressively faded. It is no coincidence that research is now increasingly focusing on the interaction between neurobiological asset and environment, because this is actually the direction in which we need to proceed. On the other hand, the failure of the goal of finding a correspondence between the nosographic categories provided by the Diagnostic and Statistical Manual of Mental Disorders (DSM) and specific biological markers, played a role in the current crisis of the nosographic system itself. In the absence of a well-defined biological counterpart, it could be hypothesized that a given nosological category, defined on a syndromic basis, should be better conceptualized as a pattern, a dimension without a well-defined threshold, and whose diagnostic boundaries are blurred. In light of the increasingly spreading dimensional approach to psychopathology, the issue of psychiatric diagnoses should be regarded critically. It should be noted that the difficulties in finding a specific correspondence between real-life clinical cases and DSM categories are not only a research paradigm problem, but it is an issue that challenges all of us during the clinical practice on a daily basis: all psychiatrists have experienced that, in order to assess most of their patients, they have to refer to multiple comorbid diagnoses, including also personality disorders. Since early 2000s, the operative model of "spectrum" allowed overcoming this problem [1]. Through the spectrum model, it is possible to identify and measure those mild manifestations and symptoms that, although below the clinical threshold, isolated or atypical, are not qualitatively different from the full-fledged disorders described in the DSM. A dimensional approach allows us to describe a clinical case by specifying which symptomatologic clusters are fully expressed and which are instead detectable in a sub-clinical form. During daily clinical practice, the psychiatrists are still pushed to focus on what is called the index episode, and on identifying the clinically prevalent symptoms, ignoring the broad range of sub-threshold manifestations and traits that the subject may show at the time of clinical assessment, having likely been present in various degrees throughout her/his life. Sub-threshold comorbidity, on the other hand, is of the utmost importance for truly understanding the clinical picture, often constituting the vulnerability ba-

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sis for the entire psychopathological trajectory: hence the need to focus on sub-clinical symptomatology. From this perspective, the stereotype of episodic course of psychiatric disorders also needs to be reconsidered. As a matter of fact, the arbitrarily identified clinical thresholds give an episodic appearance to a chronic and life standing condition with different grades of severity during lifetime. While the episode is identified only when symptoms exceed the diagnostic threshold, broader and milder manifestations of the same sign persist and shape subjects' life, often anticipating the clinical onset and remaining as an inter-episodic and residual condition. A third-millennium medicine, prevention-oriented, should certainly change this paradigm and focus on addressing sub-clinical manifestations, rather than simply on treating the acute phases, thus contributing on the prevention of the so called clinical onset. As described above, the spectrum model is based on a dimensional approach to psychopathology, according to which the chronic presence of sub-clinical traits, usually detectable since the developmental period, significantly contribute in shaping the subject's personality, conditioning life choices and constituting the vulnerability basis for developing a full-fledged psychopathological trajectory. It would be wrong to believe, however, that this model is in contrast with a neurobiological approach to psychiatry. It is, in fact, quite the opposite: the spectrum model may allow a novel approach to neurobiological research in psychiatry that, without trying to push neurobiology into abstract categories, or to link the latters to specific brain circuits whose specificity appears equally abstract, would be more compliant with the most recent findings in the field of brain functioning. Recent researches pointed out how the central nervous system is a tightly interconnected and flexible structure, where a given function is underlain by complex interactions between different areas, overcoming the concept of compartmentalization. On the basis of this model, which seems in agreement with the dimensional presentations of psychiatric conditions, it has been proposed that mental disorders might be better conceptualized not as alterations of specific brain mechanisms, but as "globalopathies", which would feature an impairment of the whole brain functioning and of its complex network of connections [2]. A further advancement in this hypothesis has been made through the study of neurodevelopmental disorders, and in particular through the autism spectrum model. Familial aggregation studies have long emphasized the heritability of Autism Spectrum Disorder (ASD) not only considering its clinical presentation, but also as a "Broad autism phenotype", a condition very common among first degree relatives of ASD patients, featuring manifestations qualitatively similar to the full-blown disorder but of reduced intensity. Growing research is stressing how autistic traits seems to be distributed along a continuum in the general population, being particularly common among patients with other kinds of mental disorders. The presence of autistic traits, even when sub-threshold, seems to be associated with increased risk for the development of other mental disorders as well as suicidal ideation and behaviors, enhancing vulnerability toward stressful life events. Based on these findings, and in accordance with the "globalopathies" theory, it has been hypothesized that a neurodevelopmental alteration could be at the basis of different psychiatric conditions: the interaction of the specific type, severity and timing of the alteration with prenatal and postnatal environmental influences, including stressful life events, may shape the specific psychopathological trajectory, including the pattern of mental disorders developed [3]. In this framework, the recently renewed focus on the catatonia spectrum, and its associations with the autism spectrum, may provide additional insights to the proposed model [4,5]. To date, we find us at a turning point in the field of psychiatry: through the matter of neurodevelopment, we glimpse the chance to finally merge psychopathological and neurobiological approaches in a coherent model, possibly as never happened before. It is, now, all about understanding whether we can meet this challenge, and to which new frontiers this may lead us.

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Original article

Società Italiana di Psichiatria

# Considerations on treatment pathways for psychiatric offenders: critical points and Piedmont's regional coordination

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Giovanna Crespi

## Summary

**Objectives.** This work addresses the evolution of psychiatric offenders pathways from Law 81/2014 to the current day, analysing critical points and highlighting Piedmont's experience on regional coordination.

**Methods.** The main consequences of Law 81/2014 are analysed and the situation of REMS in Italy is outlined, explaining function of security measures, treatment by mental health departments and the relationship between the latter and the judicial authority.

**Results.** The analysis of current situation in Italy reveals some critical points, to which the authors also aim to provide possible solutions, taking as an example the experience of managing waiting list and admissions to REMS in Piedmont. The establishment of Regional Single Points (PUR), through the Unified Conference of the Italian Presidency of the Council of Ministers of 30 November 2022, will encourage a multidisciplinary take-over by DSMs.

**Conclusions.** REMS are useful detention health rehabilitation facilities when placed within a patient care pathway that starts with the detention centre, passes through REMS and continues with a community based program. PURs can be useful tools that help different actors involved in the treatment pathway of psychiatric offenders.

**Key word:** psychiatric offenders, treatment pathways, REMS, waiting list, PUR

## Introduction

As a result of Law 81/2014, assessment and treatment pathways for people with mental disorders who have committed a criminal offence have changed without amending the Penal Code. An offender undergoing psychiatric evaluation during pre-trial phase may remain in custody in prison or be sent to a treatment facility by public prosecutor. Whether the patient is acquitted, after psychiatric evaluation and according to Article 88 of the Penal Code, he or she cannot stay in prison and, when considered socially dangerous, must be subjected to a security measure. When the patient has a diminished mental capacity/diminished responsibility, security measure is carried out after detention in prison. Security measures are mostly non-custodial, consisting of territorial therapeutic pathways for patients on probation carried out in 80% of the cases by the Department of Mental Health (DSM) of the competent Local Health Agencies (ASL).

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Whilst detention security measures are carried out in therapy-intense facilities called REMS, which are healthcare facilities with a maximum of 20 beds per module depending on Regional Authority [1,2]. There are 33 REMS in Italy, placed in almost every region, other than Umbria, Molise and Valle d'Aosta, which lean on REMS in nearby regions. The highest concentration of REMS is located in Castiglione della Stiviere, Lombardia, with 6 modules of 20 beds in the former OPG area [3].
Two (new) REMS were built in 2022. One of the last REMS built, Santa Maria Calice di Cornoviglio in Liguria, works differently than other REMS on national territory: waiting list is managed at a national level and aims to reduce waiting time for inmates patients to access regional REMS. Last REMS being built is in Girifalco (CZ), which opened after years of delays and postponements.

## Definitive security measures

An article published in 2022 on the "Rassegna Italiana di Criminologia" [4] analysed the evolution of security measures in the register of final sentences from 2001 to 2019, when the overcoming of forensic psychiatric hospitals (OPGs) process (Supreme Court decision of 2003) has begun. In almost 20 years non-custodial security measures increased from less than 10% to more than 80% of total security measures. This raise leads to an enormous burden on Italian Mental Health Services (DSM). We are talking about 800 final sentences per year, with a steady increase due to the sharp rise of non-custodial security measures. Since 2014 Italian DSMs have also struggled in replacing retiring specialists and in managing economic constraints occured in health care. This evidence shows that REMS are not a replacement for old Forensic Psychiatric Hospitals (OPGs) and according to Law 81/2014, they should be considered as the end of the line for patients who are deemed to be socially dangerous and a non-custodial territorial pathway is not possible.
Unfortunately, the failure to reform the Italian Penal Code and the difficult dialogue between judiciary and health services have led to a REMS assignment which far exceeds their ability to take in patients, resulting in a waiting list.
According to a recent study led by the Prisoners' Guarantor [5], on the 31 December 2021 there were 31 Italian REMS with a capacity of 656 places. 87% of all were occupied by 573 internees, of whom 512 (91%) were men and 61 (9%) women; 451 (79%) were Italians and 122 (21%) foreigners; 305 (53%) had a definitive measure and 243 (42%) a provisional one; 25 (5%) were (in the process of) changing from a provisional to a definitive measure. The average time spent in REMS, at national level, (nationally) was 708 days, and there were 630 patients with a REMS assignment on waiting list on the 31 December 2021, of whom 42 (7%) were incarcerated.
According to the intention of Law 81/2014 bed in REMS were not intentionally equal to the OPG. Unlike the Public Health System, which involves the basic concept of waiting list, Judiciary does not accept when issuing orders are not carried out immediately. The conflict of competences arose because REMS system, which was designed for permanent internees, was extended by the Minister of Justice to temporary internees as well, whom would be more appropriately located in mental health protection areas (ATSM) in prisons. The correctional system has opposed to this solution and has demanded that REMS could accommodate temporary inmates, which constitute the 42% of the inmates accessing REMS. In a census carried out on REMS residents, Catanesi et al. described the population present in 2018: 89% male, mean age 41.7 years, with a duration of mental disorder of more than 11 years; 82 % of the internees were already known to the DSM before entering the REMS and 71 % had previously been admitted to a specialised psychiatric setting. 60% of patients had a diagnosis of schizophrenia spectrum disorder and 30% a personality disorder; 21% showed a comorbid substance use disorder [3].

## Critical points

In 2019, the National Bioethics Committee (CNB) presented an opinion on mental health and psychiatric care in prisons, which contained elements of undoubted interest in analysing the issues resulting by the effects of Law 81/2014 [6]. The expert opinion pointed out that closure of OPGs was carried out without a comprehensive treatment plan for psychiatric offenders and without overcoming concepts and terminology that are outdated with current knowledge: "folle-reo" and "reo-folle"*, "licenza finale di esperimento"**, social dangerousness etc.
In order to properly manage the clinical situation of mentally disordered offenders would have been important the adaptation of national standards to healthcare regional realities: for example, the organisation of DSMs differs from region to region, whereas people with mental disorders who have commetted a criminal offense often

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* The term "folle-reo" was used in the Penal Code of 1930 to describe an offender who was mentally ill, unaccountable and considered socially dangerous. The offender, if found insane, was declared insane, incapable of defending himself in court, incompetent to serve a sentence of imprisonment, and sanctioned by an ad hoc institution, the OPG, run by the Ministry of Justice. The security measure imposed continuous social and psychiatric surveillance, even for life. Whereas the term 'folle-reo' was understood to mean the offender who commits an offence as a result of his mental disorder, the term 'reo-folle' was understood to mean the offender who commits an offence completely independently of his mental disorder and is therefore fully culpable.

** It is a (maximum) six-month licence that can be granted in the period immediately prior to the date set for the social dangerousness re-assessment.

require a unified response from the ASLs, with the involvement of addiction services (SerDs) and territorial services dealing with elderly and disabled, in addition to those of psychiatry.

OPGs' closure has not been sustained by an adequate review of current legislation, which still refer to the OPGs and it severely restrict the possibility to build appropriate treatment pathways both for people who commit crimes with excluded or severely diminished mental capacity and for people diagnosed with a mental illness while in custody.

The biggest unsolved problem of mental health in prison is the persistence of the so-called 'double track' (doppio binario), whereby the offender who was mentally incapacitated had to be committed to the OPG and could not stay in prison. With the overcoming of OPG, it has not been clarified where the offenders considered unaccountable and a danger to society should be placed. Incorrectly, judges frequently consider REMS as a replacement for OPG. The abolition of the asylum in 1978 and current abolition of the OPG should have overcomed the 'double track' by giving back dignity and responsibility to the mentally ill offender. As long as they need to be detained because they are a danger to society, they should be kept in an appropriate secure facility. Once OPG is overtaken, REMS should be considered more like rehabilitative facilities than restrictive. The eccessive use of REMS assignment ensure that patients considered to be socially dangerous are placed on waiting lists and are managed in different ways: prison, residential facilities, hospital services for the diagnosis and treatment of psychiatric disorders (SPDCs), home, etc. This can lead to risky situations, precisely because the Penal Code has not been revised.

The concept of "psychiatric" social dangerousness must be revised: it is a very difficult prediction even for an experienced psychiatrist, who could express more competently about patients' prognosis. Only judges should decide on social dangerousness, with an expert opinion on possible outcomes of the patient's treatment. Human behaviour, and even more so the behaviour of patients who have committed a crime, is affected by a large number of individual variables. Therefore, illness alone does not explain the behaviour of psychiatric patients who have committed a crime. It is incorrect to predict the future behaviour of a subject solely taking into account only symptom development or resolution.

One of the possible solutions is to set up health care facilities within prisons; at present, prisons have designated areas for the 'protection of mental health' (ATSM), where socially dangerous psychiatric patients can be hold while waiting the admission to REMS. Indeed, the Italian Psychiatry Society (SIP) promotes to improve quality of life of inmates improving the quality of medical care in prisons and through the creation of units within prisons maneged by the DSM [7]. Mental illness should be considered as physical illness, and it is necessary to allow suspended sentences for inmates who become ill and need treatment in facilities outside prison. This requires investment in DSMs, in order to establish forensic psychiatry units (UPFs)*** in each ASL, also including the Penitentiary Psychiatry in all of those ASLs hosting a correctional facility on their territory. In order to be able to identify community network resources for treatment of serious diseases, these units should be an integral part of the DSMs.

A continous cooperation with the Judiciary of Cognition and Surveillance is necessary for a more attentive and precise use of security measures, consistently with the therapeutic purpose of REMS, limiting the access to REMS to individuals towards whom a definitive custodial security measure has been applied. For defendants in the cognitive phase and inmates with temporary psychiatric treatment needs, psychiatric observation units within prisons can be used. The existence of special prison psychiatric units run by DSMs within forensic psychiatric units structured using specialised resources might improve mental health in prisons, REMS and community-based treatments [8].

In REMS and community-based pathways an accurate selection of patients eligible for a specific treatment must be carried out, for example using a few REMS for people with mental disabilities and for people with substance dependence comorbid with a personality disorders. It is also essential to improve communication between psychiatric experts and mental health services, which must be mandatory in order to improve custodial and non-custodial treatment pathways, balancing as far as possible therapeutic needs with containment of behavioural changes that may lead to criminal misconduct [1,2].

The recent Constitutional Court decision 22/2022[9] is very critical towards the current situation related to Law 81/2014 and proposes to increase the number of REMS and to have them run by the Judiciary, which is inappropriate because these are health facilities. In health care, an increase in supply matches with an increase in demand: an increase in the number of REMS does not necessarily correspond to a reduction in waiting lists[10]. An improved management in terms of assignments and resignations for REMS is mandatory. Patients with a provisional security measure should be adressed to psychiatric observation units or ATSM in prisons, together with an improvement of health care in correctional facilities.

## Piedmont's experience of regional coordination

The model of REMS allocation in the Piedmont region is virtuous: it does not delete waiting list but it highlights legal and clinical aspects in the priority of REMS admissions. In Piedmont, UPFs have been set up in all the ASLs, whose

*** Multidisciplinary teams of psychiatrics, psychologists, social workers and nurses who manage and plan the care of mentally ill offenders.

representatives meet every three weeks, coordinated by regional officials, with the directors of the two Piedmont REMS and the ATSM psychiatric liaison officer at the Lo Russo and Cutugno Prison in Turin. The establishment of Regional Single Points (PUR), through the Unified Conference of the Italian Presidency of the Council of Ministers of 30 November 2022 [11], through managing and assessing the situation of REMS assignments and patients already interned, will encourage a multidisciplinary take-over by DSMs. This conference formalized, regarding Piedmont, the existing management of waiting lists and patients in REMS, ensuring a homogeneity of interventions and health and treatment services throughout the country. Piedmont's waiting list and REMS management model has resulted in a shorter average REMS stay of eight months and a waiting list stay of REMS assignees of less than two months on average: this shows that this continuous dialogue between ASL representatives and REMS directors is useful for REMS management and allows to focus on territorial treatment pathways. The majority of probation and discharge projects from REMS take place largely within psychiatric residential facilities (SRPs): only 6% of patients return home directly from REMS****.

Thanks to the REMS assignment assessment in Piedmont, from 2016 to 2022, 25% of the patients on the waiting list were never interned, precisely because of the work of regional governance. The latter identified effective alternative territorial pathways that convinced the competent judge to review the REMS assignment and transform it into a non-custodial territorial pathway, according to Law 81/2014. Another way to reduce the number of REMS admissions is to provide in the REMS Discharge Plan for an aggravation of the security measure, other than re-entry into the REMS, for possible non-compliance with the probationary or final licence conditions.

Essentially, in order to reduce the waiting lists of those assigned to REMS, instead of increasing the number of places in REMS, we can a) ensure that psychiatric experts cooperate on treatment pathways with DSMs operators; b) through regional governance, examine the accuracy of REMS assignments; c) actively involve DSMs operators in taking charge of inmates in REMS in order to reduce length of stay.

## Conclusions

In conclusion, authors believe that collaboration between DSM, REMS and ATSM professional through the implementation of PURs is a useful tool to reduce length of stay and verify the adequacy of the assignment to the REMS and therefore make better use of them. Priority of entry into REMS must be based not only on a chronological order, but also on legal and clinical criterias. REMS are useful detention health rehabilitation facilities when placed within a patient care pathway that starts with the detention centre, passes through REMS and continues with a community based program. PURs can be useful tools that help different actors involved in the treatment pathway of psychiatric offenders. After a reasonable period of time it will be necessary to assess how they are implemented and managed in different regions, especially where they are not already in place, and whether they allow us to reduce waiting time for REMS allocation, which is the main criticism of the current system that replaced OPG.

**** Data processing by Unità di Monitoraggio e Programmazione Clinica (UMPC) of the Mental Health Department ASL TO3 & A.O.U. San Luigi Gonzaga.

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Original article

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

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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

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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-to-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

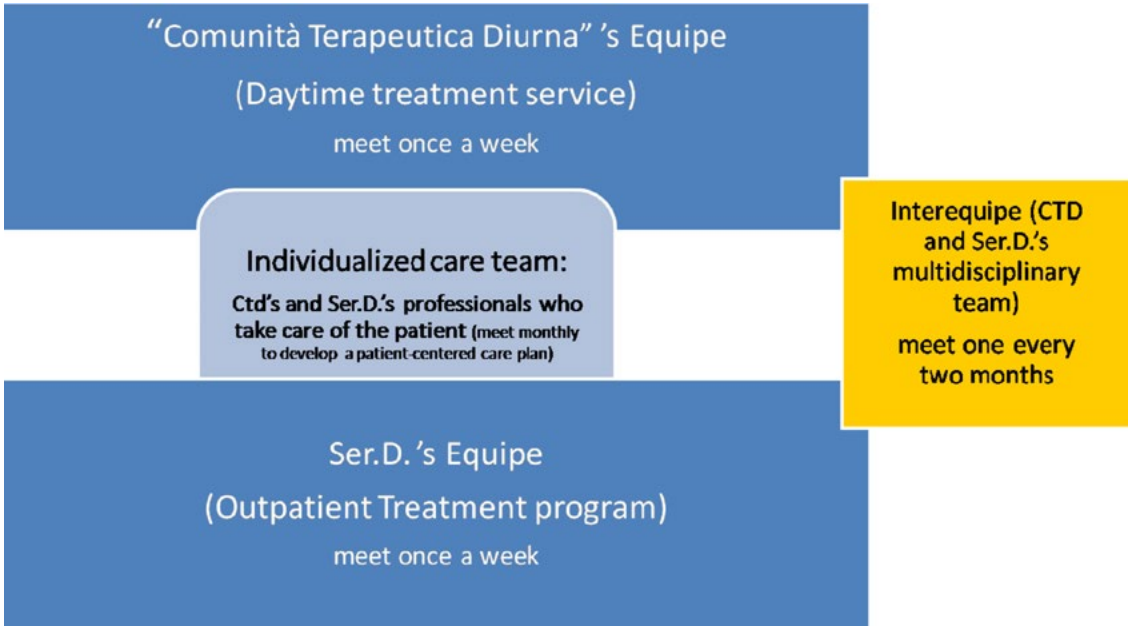


**Figure 1.** Integration Model CTD-SerD.

**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. SerD'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 SerD 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 literature [12]. 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 it's 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 toxological 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

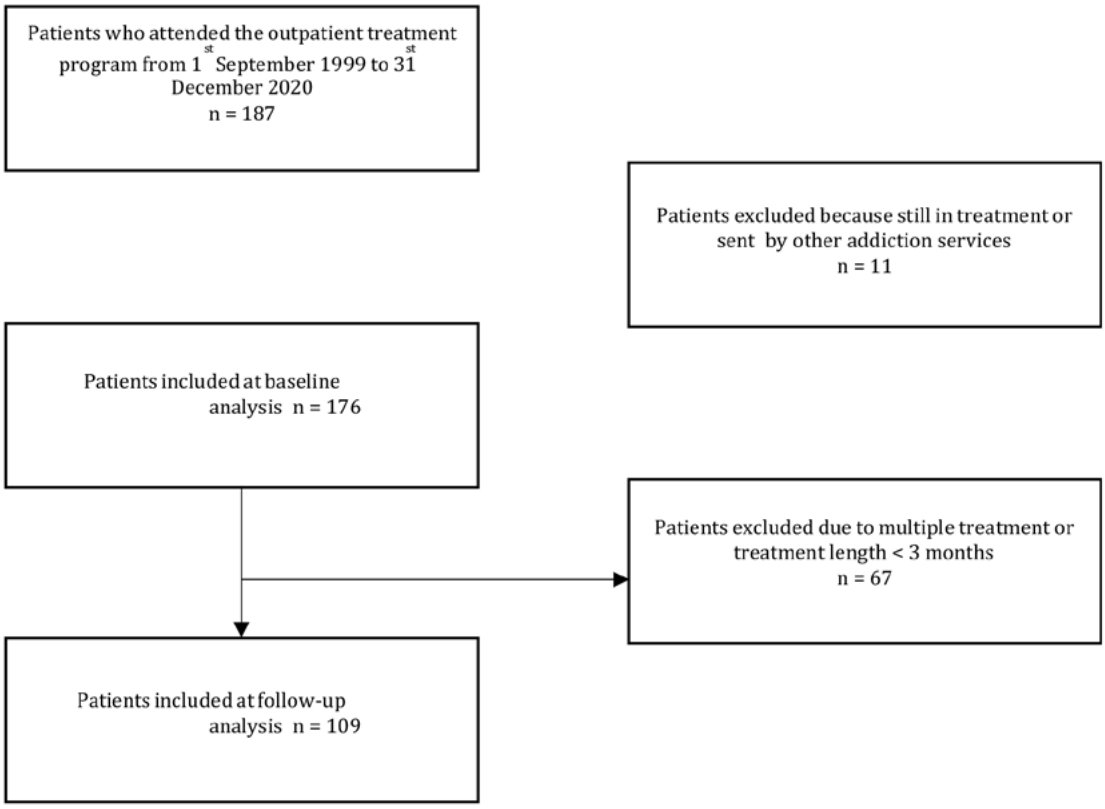


**Figure 2.** Flowchart of the participants of the retrospective cohort study.

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 heroine (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 management [17] and community reinforcement [9]. In addition, psychosocial interventions (i.e., CBT or mindfulness-based stress reduction) have an observable positive effect, especially in terms of relapse prevention [18]. 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

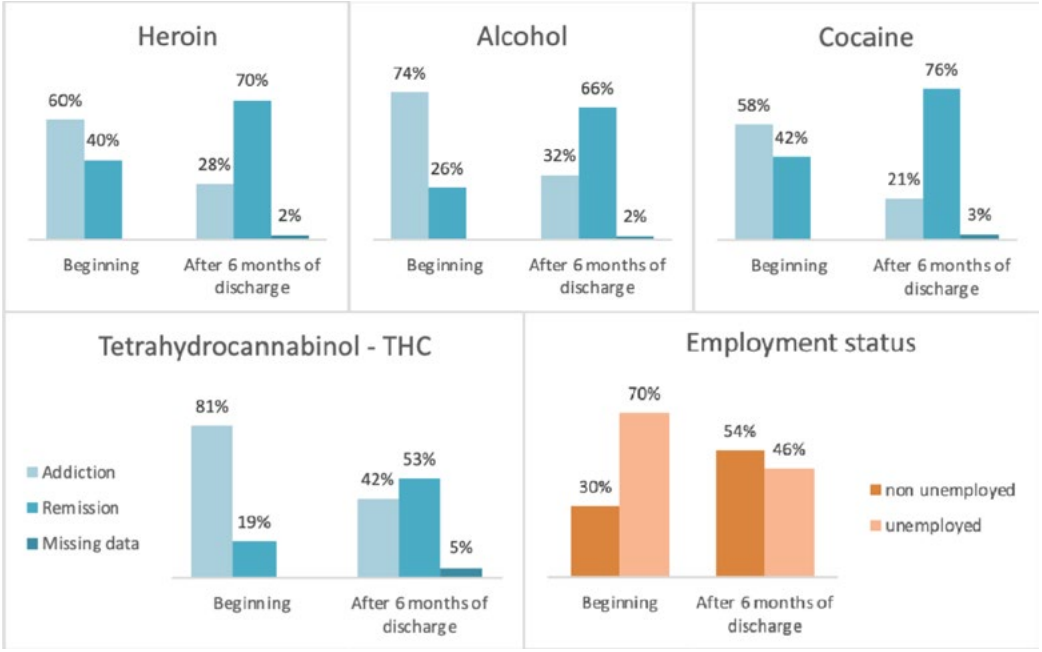


**Figure 3.** Percentage of participants at baseline and follow-up analysis related to SUD status for each substance (blue) and employment status (orange).

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.

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# Sedative, hypnotic and anxiolytic drug use disorder: prevalence and treatment perspectives in a population of young detainees

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## Summary

Psychotropic drug dependency among the prisoner population from 18 to 25 years of age represents a growing and epidemiologically relevant phenomenon. The behaviour of abuse may begin before incarceration or during its course. The loss of personal freedom and the prison environment seem to be instrumental contributing factors in the increase of use and abuse of psychotropic drugs, with consequent clinical criticality associated with the chronic use of sedatives. Psychotropic drug use in prison, together with the appropriate prescriptions for mental disorders, appears in effect to constitute at times a simplistic and partial response to suffering and to aggressive and dysfunctional behaviours. Treatment perspectives are complex, and must necessarily be multidimensional, founded on solid therapeutic combinations. They must consider both the patient and the prison environment in which the disorders emerge.

**Key words:** psychotropic drug dependency, sedative-related disorders, young detainees, mental health

A recent study, undertaken within Turin's penitentiary, namely the Casa Circondariale Lorusso e Cutugno, and promoted by the Municipality of Turin's Office of the Guarantor of the Rights of Detainees, ascertained a significant predominance of dependency on psychopharmaceuticals in the prison's young adult population. This phenomenon especially concerns substances with a sedative and anxiolytic action: benzodiazepines (especially with a short or mid-range half-life), benzodiazepine-like drugs (*z-drugs*) and gabapentinoids, although psychotropics belonging to other pharmacological classes also serve as abused substances, such as, for example, antidepressants and second-generation antipsychotics.
In this paper we will describe the prevalence and the treatment perspectives of sedative, hypnotic, or anxiolytic drug use disorder in a population of young detainees.

## Diagnosis, epidemiological and clinical indications

According to the most widely recognized and shared nosography in psychiatry, i.e., the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [1], the dependency on pharmaceutical sedatives can be placed within the sedative, hypnotic, or anxiolytic drug use disorder. According to the diagnostic criteria of the DSM-5, this disorder is defined as a problematic

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*Conflict of interest*
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pattern of sedative drug use, which entails significant distress or impairment, manifesting in at least two of the following conditions: intake of greater quantities or of greater duration than initially predetermined, the desire or unsuccessful efforts to limit use, extensive expenditure of time in the pursuit or use of the drug, the presence of craving, failure to fulfil family and work obligations, work and social problems, or the abandonment of important work or social activities due to usage, consumption of sedatives in potentially dangerous situations (like driving), continual use despite the awareness that it may lead to physical or psychological health problems, the development of tolerance or withdrawal phenomena.

The estimated prevalence of the disorder in the adult population is 0.2%, with a slight predominance among males, and a spike in the 18-29 age group (0.5%). The onset of use most usually occurs in adolescence and early adulthood[1]. However, it is possible that this data underestimates the true extent of the disorder, one which often escapes medical attention. As regards benzodiazepines and *z-drugs*, it has been ascertained that there is a prevalence in drug consumption for a duration longer than 6 months, which means that, realistically speaking, it exceeds the length of consumption advised by the guidelines and evidenced-based data and could even reach 15% [2]. This figure further rises if we consider populations of patients associated with psychiatric services, with values reaching beyond 30% for benzodiazepine use, and primarily consumed in a chronic manner, something widely discouraged [3,4]. The data on gabapentinoids indicate a prevalence of abuse at around 1%, with a risk of developing forms of abuse or dependence on gabapentin reaching 50% in patients who began use with a medical prescription [5,6].

Of note, especially with respect to the population entering a prison, are the data around comorbidity: often the disorder goes hand in hand with the intake of other psychotropic substances of abuse (alcohol, cocaine, amphetamines, opioids). Sedative-anxiolytic pharmaceuticals are in fact frequently used in a progression with cocaine, amphetamines, or other stimulants in order to shut down excessive psychophysical activation or to reduce symptoms linked to the end of their effect, or in association with opioids or alcohol in order to amplify their sedative effect, or to counter insufficiency [7]. Other disorders, which are often found in comorbidity with dependence on sedatives, are those pertaining to personality, mood, and anxiety [1].

The main risk factors for the development of dependency on sedative and anxiolytic drugs are the presence of some mental disturbance, a positive anamnesis for the use of alcohol or substances, the absence of an explicit diagnosis justifying an initial prescription or co-prescription with opioid drugs [6,8].

The onset of the disorder is in general attributable to two distinct patterns: one which anticipates the procurement of drugs illegally, and a consumption often associated with other substances of abuse, and the second, which coincides with a doctor's prescription, followed by a progressive dose increase and frequency of use, self-directed or supported by repeat prescriptions. The risk of developing dependency is directly related to the dosage and duration of the treatment and is greater for the chemicals that have a shorter half life, meaning those which reach peak effect first and are metabolized more rapidly (for example clonazepam) [1,7]. That is why it is evident that chronic usage of these drugs should be avoided.

Intoxication from benzodiazepine or pharmaceuticals with a similar profile can result in excessive sedation or the development of respiratory depression, which can be lethal, especially if in the presence of other organic disorders, or in conjunction with the consumption of alcohol or opioids. It should also be highlighted that decreased impulse control and behavioural disinhibition (including episodes of autodirected or heterodirected aggressivity) can be manifested – possible adverse effects that arise especially after acute consumption. If, in fact, on the one hand, these drugs are taken for the management of anxiety and agitation, on the other, they can lead to an increased risk of aggressive acts through the facilitation of behavioural disinhibition. The withdrawal from benzodiazepine and other hypnotic and anxiolytic drugs may manifest in the emergence of anxiety, epileptic seizures, agitation, hallucinations, and ultimately in the development of delirium, with the possibility of even a fatal outcome in the absence of proper treatment. It is also possible that, over the course of withdrawal, suicidal behaviours can develop. Lastly, it is necessary to emphasize the consequences of chronic use, which, due to a slow and insidious onset, can be clinically just as relevant as they are underestimated: emotional blunting, depression, negative effects on cognitive and mnesic functions [1,3,6,7,9].

## Substance dependency in the young adult population of the prison

The predominance of abuse and dependency on psychopharmaceuticals observed in prison should be included within the wider phenomenon of a recent rapid quantitative and qualitative increase in the use of prescription medications as substances of abuse, on both the national and international level. This phenomenon, which often goes hand in hand with the use of "traditional" substances, is of particular interest to the adolescent and the early adult populations and appears to be only partially definable and traceable [10]. In addition, considering, as shown above, that substance abuse and youth are risk factors for dependency on sedative-anxiolytic drugs, it is not surprising to discover a higher prevalence of the phenomenon in young detainees [6-8].

As seen with respect to the general population, it is apparent that, within the prison population too, it is possible to trace two different profiles that lead to the development of

disorders linked to the use of sedative and anxiolytic drugs, which often overlap in the stories of single individuals. Drug consumption can in fact begin in the context of behaviours of alcohol or substance abuse, through illegal acquisition, or via a doctor's prescription in the event of a mental disturbance. Some of the detainees obtain the prescription before entering the prison, while in other instances, the disorder, for which benzodiazepine or other anxiolytics may be prescribed, arises during detention. The disorder can be represented by the withdrawal from other substances consumed before incarceration, or from the onset, a relapse or an exacerbation of anxiety or sleep disorders, or from the manifesting of symptoms – different from those of anxiety – attributable to personality disorders (for which benzodiazepines have no reported indications). At any rate, as previously mentioned, chronic usage is to be avoided [3,4]. Moreover prescriptions of sedatives within the prison do not always correspond to specific diagnoses but can play a role in diminishing behavioural alterations and aggressivity, representing more than a cure of a specific disorder – in other words, a form of behaviour control for the purpose of maintaining order [11]. However, resuming what was said about clinical manifestations of abuse of benzodiazepine and similar drugs, it must be remembered how the intake itself of the drug may contribute to the surfacing of those stresses that therapy wishes to hinder [3,6]. In relation to mental disturbances, it is necessary to give thought to how much our prison system, due to its structural and systemic characteristics, may constitute a greater pathogenic harm than the privation of personal freedom. If we assume that distress and how the manifestations of aggression and behavioural changes originate, not only from an individual predisposition and other psychosocial factors, but also from the prison environment in which they develop, it is necessary to consider the importance, simultaneously with, or as an alternative to a medical response, of interventions on the environment, on the living conditions, as well as the implementation or consolidation of other forms of support, providing more valid alternatives to a mere pharmacological management of the suffering [11].

## Treatment suggestions

Before exploring available therapeutic options, two preliminary considerations are necessary. First and foremost, studies to date on the efficacy of the possible treatments for the disorder, caused by using sedatives, are largely of poor quality, according to what has been confirmed by authoritative literature reviews [3,7], and are therefore of only partial value in guiding responsible therapeutic choices.

Furthermore, the available scientific literature takes into consideration heterogenous populations, with the possibility that the effectiveness of the data observed in particular populations (for instance composed of patients that have developed dependence as a result of medical prescriptions) may not be valid in clinical practice with patients, who, instead, began their drug intake for recreational purposes, or together with other substances of abuse, or who may be included in different treatment contexts. In other words, it is difficult to say how much the results of the current studies in the literature may be extrapolated to include the prison population.

The resolution of dependency can not but have as its goal drug discontinuation, which must be conducted by means of a gradual tapering to avoid withdrawal symptoms. For this to happen successfully, it is necessary for the patient to demonstrate awareness of the problem and be motivated to get treatment, and that this is supported by a solid therapeutic relationship. The process of decreasing drug intake is to be defined based on the half life of the drug, the dosage and duration of consumption. This reduction must also be gradual because some withdrawal symptoms (anxiety, insomnia) can overlap those that instigated the prescription of the drug in the first place, with the subsequent difficulty for the clinician to distinguish between a relapse, which could benefit from a revitalization of the therapy, and symptoms of deficiency. In the case of benzodiazepine with a short half life – which, as previously stated, should be avoided, but are often the most requested – a valid option is that of including longer-lasting benzodiazepine, whose discontinuation, to be carried out after the discontinuation of the initial chemical, will be less challenging because of its pharmacokinetic profile [3,8].

Various treatments have been suggested to support drug tapering and they can be categorized in pharmacological and psycho-social interventions.

The efficacy of numerous drugs, belonging to different pharmacological classes, and administered in coordination with benzodiazepine weaning, has been investigated and has resulted in possible, albeit modest, benefits particularly from the dispensing of valproate and some anti-depressants [3,12].

Psychological treatments associated with gradual drug discontinuation have been, as a whole, more effective in relation to tapering not combined with other interventions. Some evidence suggests the utilization of cognitive behavioural psychotherapy, relaxation techniques, and of counselling or motivational psychoeducational interventions [2,3,7,8,13].

In the prison context, numerous and relevant factors of obstacles to treatment are present. The environment does not provide adequate social support and indeed can represent a pathogenic factor for the establishment of a possible "contagion" regarding the use of and dependency on drugs linked to cohabitation with individuals who already manifest abuse practices or dependence. The creation of significant therapeutic relationships is sometimes undermined by an institutional context that induces "relational structures (…) {that are} responsibility-negating and infantilizing" and within which "the valorization of the therapeutic relationship must conflict not only with

certain strategies for the maintenance of internal order, but also with the systematic reproduction of 'diminished' individualities" [11]. The offer of specific interventions in conjunction with the services for dependencies is challenging. Meanwhile, providing therapeutic continuity as well, after release from prison with support measures for the discontinuation or reduction of sedative drugs [11] would be of fundamental clinical importance.

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# Sleep quality and sleep duration in the acute and remission phase of mood disorders

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## Summary

**Introduction**. Sleep disturbances are a common and significant issue in mood disorders, including both bipolar and major depressive disorders. The impact of sleep problems can be observed during acute depressive episodes as well as in the euthymic phase. This study aims to investigate the quality and duration of sleep in patients with mood disorders, examining the differences between the acute depressive phase and euthymic phase, and their potential consequences on patients' well-being and symptom severity.

**Objectives**. The objectives of this study are to evaluate the presence, frequency, and characteristics of sleep disorders in patients with different mood disorders (Major Depressive Disorder, Bipolar Disorder I and II), both during acute phases of a depressive episode and during euthymia.

**Methods**. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), while sleep duration was evaluated using a specific item (number 4) from the PSQI to define the manifestation of insomnia (< 6.5h), hypersomnia (> 9h), and normal sleep duration (6.5-9h). Descriptive and statistical analyses were performed using SPSS version 26.0 software.

**Results**. We discovered that sleep disturbances are highly prevalent not only during the acute phase of the depressive episode but also during the euthymic phase of mood disorders. Ninety-six percent of patients with mood disorders experienced poor sleep quality (PSQI global score greater than 5) during the acute phase, and 53% of patients had poor sleep quality in the euthymic phase. In the acute phase, 22.9% of our patients had normal sleep duration, 62.5% had reduced sleep duration, and 14.6% had increased sleep duration-hypersomnia. A percentage of 39.8% of euthymic patients had normal sleep duration (6.5-9 hours), while 27.6% had reduced sleep duration (less than or equal to 6.5 hours), and 32.7% had increased sleep duration - hypersomnia (sleep duration greater than or equal to 9 hours).

**Conclusions**. Sleep disturbances are very frequent both in the acute and remission phases of mood disorders. More studies are necessary to establish the role of sleep disturbances as a possible cause or predictor of acute mood episodes or a worse course of mood disorders.

**Key words:** sleep, bipolar disorder, major depressive disorder

## Background

Mood disorders, encompassing bipolar and major depressive disorders, are often accompanied by sleep disturbances, which can exacerbate symptoms

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and impair overall functioning [1]. Sleep problems, including insomnia, hypersomnia, and irregular sleep-wake patterns, have been linked to a range of adverse outcomes such as decreased quality of life, cognitive deficits, and increased risk of relapse [2]. During acute depressive episodes in both bipolar and major depressive disorders, sleep disturbances are frequently reported, which can further worsen the severity of depressive symptoms [3]. These sleep problems may manifest as difficulties falling asleep, maintaining sleep, or experiencing a nonrestorative sleep [4]. Moreover, research has shown that persistent sleep disturbances during the acute phase can contribute to poorer treatment outcomes and a more prolonged recovery process [4]. In the euthymic phase, when individuals with mood disorders are not experiencing acute symptoms, sleep disturbances may still persist [3]. These residual sleep problems can negatively impact the overall well-being of the affected individuals and increase the risk of relapse into a depressive or manic episode [1]. Understanding the nature of sleep disturbances during both the acute depressive phase and euthymic phase is crucial for developing targeted interventions that can improve sleep quality and promote long-term recovery in individuals with mood disorders.

## Methods

This observational study encompassed 146 patients diagnosed with major depressive disorder (n = 42), bipolar disorder type 1 (n = 65) with the most recent depressive episode, or bipolar disorder type 2 (n = 39) with the most recent depressive episode. Participants were recruited at the Division of Psychiatry, Department of Molecular and Developmental Medicine, University of Siena, Italy. Of the total cohort, 98 participants were enrolled as outpatients in the euthymic phase, characterized by a Montgomery-Asberg Depression Rating Scale (MADRS) score of less than 7 and by a Young Mania Rating Scale (YMRS) score of less than 7, while 48 participants were recruited as inpatients during the initial day of hospitalization in the acute phase of a depressive episode, defined by a MADRS score exceeding 22. Diagnostic validation was carried out utilizing the Mini-International Neuropsychiatric Interview (M.I.N.I.). The investigation assessed sleep characteristics via the Pittsburgh Sleep Quality Index (PSQI), with a score greater than 5 indicative of suboptimal sleep quality. Item number 4 of the PSQI: “During the past month, how many hours of actual sleep did you obtain at night? (This may differ from the number of hours spent in bed.)” was used to evaluate sleep duration and to define the manifestation of insomnia (sleep equal to or less than 6 and a half hours), hypersomnia (sleep equal to or greater than 9 hours), or normal sleep duration (between 6 and a half hours and 9 hours). Statistical analyses were performed using SPSS version 26.0 software.

## Results

The euthymic group consisted of 98 subjects aged between 18 and 78 years, with a mean age of 48.82 years and a standard deviation of 14.5. Of these patients, 42 were male (42.9%), 23 had a diagnosis of major depressive disorder (23.5%), 46 had type 1 bipolar disorder (46.9%), and 29 had type 2 bipolar disorder (29.6%). The acute phase (depressive episode) group included 48 subjects aged between 18 and 79 years, with a mean age of 49.35 years and a standard deviation of 15.642. Of these patients, 17 were male (35.4%), 19 had a diagnosis of major depressive disorder (39.6%), 19 had type 1 bipolar disorder (39.6%), and 10 had type 2 bipolar disorder (20.8%).

All the study participants were treated with psychotropic medications, and many were taking more than one drug (with an average of 3.08 medications). Specifically, 54,79% of them were taking antipsychotics, 82,19%% were taking classic mood stabilizers such as lithium, valproate, and carbamazepine, 81,5% were taking antidepressants, 13,69% were taking hypnotics and/or benzodiazepines, 23,97% were taking anticonvulsants (e.g., gabapentin, pregabalin, topiramate) that were not included in the classes mentioned above, and only 4% were taking bupropion or stimulants (e.g., methylphenidate, atomoxetine, etc.). It’s worth noting that many patients were taking medications (e.g., sedating antipsychotics, trazodone, low dose benzodiazepines, etc.) that are more likely to decrease rather than increase the percentage of people with insomnia. Only a few patients (4%) were taking medications such as stimulants, bupropion, etc. that may increase the percentage of patients with insomnia. However, this percentage is quite low, and these medications were all administered in the morning.

We found that 53% of patients in the euthymic phase and 96% of those experiencing acute depressive episodes had poor sleep quality, endorsing a PSQI Global Score of more than 5. The euthymic patients had a mean Global Score of 6.32 (SD = 3.986), while the acute phase patients had a mean Global Score of 11.52 (SD = 3.679). The mean PSQI Global Scores for MDD, BD1, and BD2 subgroups were 9.05 (SD = 3.679), 7.58 (SD = 4.736), and 7.73 (SD = 5.070), respectively.

A comparison of the mean PSQI Global Scores between the two groups (euthymic and acute depressive episode) was conducted using an independent t-test. The analysis yielded a t-value of -7.598 ($df = 144$, $p < 0.001$), indicating a statistically significant difference in the mean scores. The mean difference was -5.205 (95% CI: -6.559 to -3.850). The resulting p-value was found to be highly significant ($p < 0.001$). This indicates a statistically significant difference in the mean Global Scores between the euthymic patients and those in the acute phase of a depressive episode.

To investigate a potential correlation between the three diagnostic subcategories examined (Major Depressive Disorder [MDD, Bipolar Disorder Type 1 [BD1, and

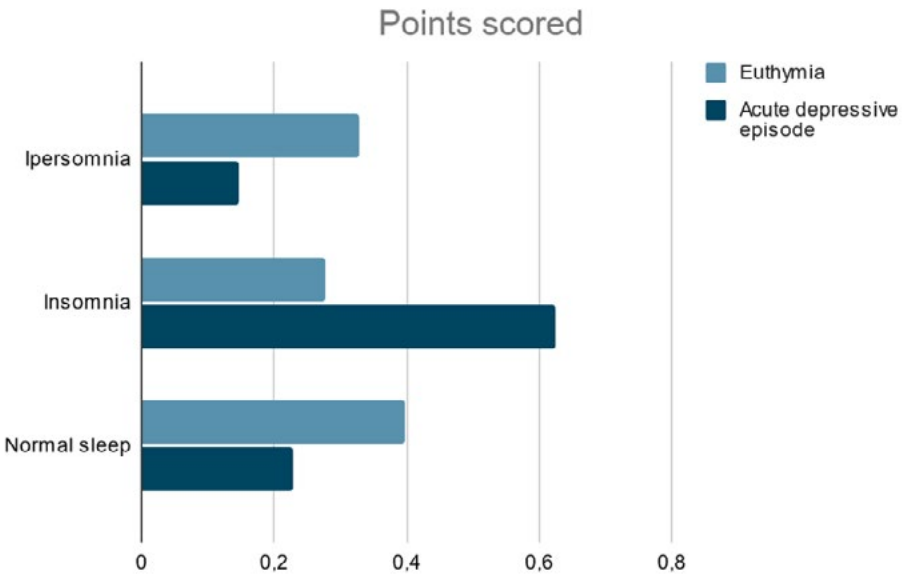


**Figure 1.** Sample characterization based on disease status and sleep duration.

Bipolar Disorder Type 2 [BD2) and the severity of sleep disturbances, we employed a one-way ANOVA analysis. Each diagnostic subgroup (independent variable) was compared to the Global Score of the Pittsburgh Sleep Quality Index (PSQI) (dependent variable). This analysis was carried out for both euthymic and acute patient groups. In both cases, no statistically significant differences were found (F-value: 1,390; p < 0,252), suggesting that the *diagnostic subcategory may not be* a major factor influencing sleep disturbance severity within our sample.

Regarding sleep duration (Fig. 1), 39.8% of euthymic patients had normal sleep duration (6.5-9 hours), 27.6% had reduced sleep duration (less than or equal to 6.5 hours), and 32.7% had increased sleep duration - hypersomnia (sleep duration greater than or equal to 9 hours). Among the patients in the acute phase, 22.9% had normal sleep duration, 62.5% had reduced sleep duration, and 14.6% had increased sleep duration-hypersomnia.

In the euthymic state, insomnia was reported by 55.0% of MDD patients, 69.2% of BD1 patients, and 75.6% of BD2 patients, while hypersomnia was reported by 50.0% of MDD patients, 94.4% of BD1 patients, and 90.9% of BD2 patients. In contrast, normal sleep patterns were observed in 54.5% of MDD patients, 76.2% of BD1 patients, and 94.4% of BD2 patients in the euthymic state. In the acute depression state, insomnia was reported by 45.0% of MDD patients, 30.8% of BD1 patients, and 24.4% of BD2 patients, whereas hypersomnia was experienced by 50.0% of MDD patients, 5.6% of BD1 patients, and 9.1% of BD2 patients. In this state, normal sleep patterns were observed in 45.5% of MDD patients, 23.8% of BD1 patients, and 5.6% of BD2 patients.

In addition, we performed a two-factor ANOVA to examine the interaction between diagnostic subgroups (MDD, BD1, BD2) and patient groups (eutymic or acute) on the sleep polarity variable (insomnia, hypersomnia, normal sleep pattern). The results showed no statistically significant differences in sleep polarity among the diagnostic subgroups (F = 0.448, p = 0.640) or between eutymic and acute depressed patients (F = 0.044, p = 0.835). The low R-squared value (0.006) suggests that the model may not adequately explain the variance in the sleep polarity data. Our findings indicate that, in the euthymic state, insomnia and hypersomnia were more prevalent among BD1 and BD2 patients than MDD patients, while normal sleep patterns were more common among BD1 and BD2 patients. Conversely, in the acute depression state, MDD patients experienced higher rates of both insomnia and hypersomnia, with normal sleep patterns being less prevalent than in BD1 and BD2 patients. However, when assessing the interaction between diagnostic subgroups and mood states through a two-factor ANOVA, we found no statistically significant differences in sleep polarity among the diagnostic subgroups (F = 0.448, p = 0.640) or between eutymic and acute depressed patients (F = 0.044, p = 0.835). The low R-squared value (0.006) implies that the model may not adequately explain the variance in the sleep polarity data.

## Discussion

This study highlights the ubiquitous presence of sleep disturbances in patients with mood disorders, not only during acute episodes but also during euthymic periods [3].

More than half of the participants had suboptimal sleep quality during remission, with only 39.8% reporting normal sleep duration. As expected, these percentages were even higher in the acute depressive phase. These findings support previous research showing the persistence of sleep disturbances in mood disorders, regardless of the current phase of illness [1,3]. The persistent nature of poor sleep quality and altered sleep duration during remission highlights the need for a broader understanding of sleep abnormalities as potential precursors or contributors to new acute episodes [2]. These results suggest that, although there are observable trends in sleep disturbances across mood disorder diagnoses and mood states, the interaction between these factors may not be statistically significant. Furthermore, given the well-established negative impact of sleep disturbances on overall functioning and quality of life in patients with mood disorders, it is crucial that these issues are identified early and addressed with appropriate interventions [4]. Our findings highlight the need for clinicians to be vigilant in monitoring and addressing sleep disturbance in people with mood disorders, even during periods of symptom remission. Future research, including larger and longitudinal studies, should be undertaken to investigate the role of sleep disturbance as a potential predictor of relapse and to identify optimal treatment strategies for managing these disturbances at different stages of mood disorders [1].

## Limitations

Our study has several limitations, including the relatively limited number of patients in the acute phase of a depressive episode and the lack of follow-up, which prevents us from observing the long-term course of these subjects. Other limitations include the absence of a control group of subjects without a mood disorder and the lack of an objective measurement of sleep duration and quality.

## Conclusions

In conclusion, our study highlights the persistent nature of sleep disturbances in individuals with mood disorders, both in the acute phase of major depression and during the euthymic phase [3]. These findings emphasize the importance of addressing sleep disturbances as a key component of mood disorder treatment, even during periods of symptom remission. Future research should aim to elucidate the mechanisms underlying these sleep disturbances and identify effective interventions to improve sleep and overall outcomes in individuals with mood disorders [1,2].

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