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Drugs Misuse in custodial settings: a systematic review and meta-analysis

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SUMMARY

Background: Increasing evidence suggests that custodial settings are at risk for the misuse of psychoactive drugs (DM) outside their prescription. The purpose of this systematic review and meta-analysis was to determine the extent of this phenomenon of psychoactive drug misuse in prisons, exploring the classes of drugs commonly used, the characteristics of inmates who are affected, and focusing on studies that have identified the phenomenon in an evidence-based manner.
Methods: From January 1 2025 to June 1 2025, we reviewed the scientific literature following PRISMA guidelines. 8826 studies were analyzed, 6 met the inclusion criteria.
Results: The overall rate of DM was 24%. Prisoner characteristics associated with DM included mental disorders, psychoactive substance use, and individual characteristics of prisoners. Social factors associated with DM included significant problems with the law, drug dealing, and arrests.
Conclusions: The DM issue is a non-negligible public health problem in custodial settings. Related factors can be identified and preventive actions taken.

Keywords: Drug Misuse; Problematic drug use; Custodial setting; Prison; Inmates.

INTRODUCTION

In 2022, the United Nations Office on Drugs and Crime (UNODC) defined "Misuse" as the misuse, or nonmedical use of prescription drugs, i.e., we refer to the intentional repurposing of prescribed drugs outside the intended indication, or the use of prescription drugs of illicit origin [1–3]. The drugs with the greatest potential for misuse are opioids, benzodiazepines, Z-drugs, and gabapentinoids [1),(4),(5]. The UNODC 2022 Report identified the misuse of these drugs, as a growing public health threat [6]. In addition, the report listed benzodiazepines and Z drugs, used to treat insomnia and anxiety [7], as the most commonly abused prescription drugs [8]. However, given the low toxicity profile [9,10], Gabapentinoids (the analogs of γ-aminobutyric acid, GABA) (pregabalin and gabapentin) are licensed for the treatment of epilepsy, neuropathic pain, and anxiety disorder. Evidence from recent systematic reviews shows that gabapentinoids are, in some individuals, misused to achieve sedation, dissociation, or euphoria [11,12]. Of particular importance is the finding on the effects of benzodiazepines or gabapentinoids which, when taken in combination with prescription opioids, could cause dangerous respiratory depression resulting in mortality [13]. Prison custody settings, whether prisons or judicial psychiatric hospitals are reported to be at high risk for the misuse of psychoactive drugs, estimating their use in 30 percent of male prisoners and 51 percent of female prisoners [14,15]. The consequences of this serious public health problem range from increased admissions to treatment and emergency rooms to increased addiction and overdose deaths [16]. The ease of obtaining them compared to illicit drugs and the ability to avoid controls could

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explain the prevalence of prescription drug abuse in prison settings [17]. The misuse of psychoactive drugs in prisons also worsens prisoners' well-being: in fact, it is associated with bullying, violence, organized crime and indebtedness [18], suicide and self-harm [19]. The undetectability by most traditional drug tests, wide availability compared to traditional illicit drugs, and greater affordability being the reasons behind the misuse of psychoactive drugs [20]. So the international literature is becoming increasingly interested in this issue [17], which has become relevant especially in recent years [21]. Measures that aim to detect, assess, understand, and hopefully prevent adverse effects or any other drug-related problems come under pharmacovigilance. There is increasing attention to date on prescription drugs and their levels of dependence/potential for diversion [22–25]. Because the intended and actual use of drugs differ between clinical trials and actual use, pharmacovigilance activities focus on the post-marketing phase. In Europe, these activities are coordinated by the European Medicines Agency (EMA) [26] through EudraVigilance (EV), which is the system for collecting, managing, and analyzing information on suspected adverse reactions to drugs authorized in the European Economic Area (EEA) [26]. Therefore, prescribing can be very challenging because of the complex health needs of inmates and the risks to the prison population associated with the abuse and diversion of prescribed drugs and other illicit substances [21,27–29]. Despite widespread concern about prescription drug diversion in prisons, few studies have examined trends in prison drug misuse [17]. This study is a first step toward identifying the phenomenon of psychoactive drug misuse in prisons, exploring the classes of drugs commonly used, the characteristics of inmates who are affected, and focusing on studies that have identified the phenomenon in an evidence-based manner.

METHODS

Study design

A systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses [30]. This work was recorded on PROSPERO, International prospective register of systematic reviews (ID: CRD42024530273).

Search strategy

An electronic search in Medline, Scopus and Cochrane Library (Wiley) databases was performed from January 01, 2025 to June 01, 2025, looking for relevant studies that could be included in this study. The search was performed by setting the following terms: "misuse" OR "problematic drugs use [MeSH terms]" OR "substance misuse [MeSH terms]" AND "prison" OR "inmates" OR "custodial setting [MeSH terms]" OR "prison medicine [MeSH terms]". The Boolean operator "AND" was used to combine parts of the subject terms and "OR" was used to expand the search. Two independent reviewers (SM and MCN) screened titles and abstracts, assessed full-text versions, and extracted data. Disagreements were resolved by re-extraction or third-party adjudication. Where overlapping registries were identified or suspected, the more recent or informative study was included for analysis.

Data Extraction

The literature search was performed by two independent reviewers (SM and MCN) using a predefined search strategy. Duplicate studies were removed manually. Each reviewer then examined the titles, abstracts and/or full texts of included manuscripts to ensure that all inclusion criteria were met before extracting the following data: [1] first author's name, [2] year of publication, [3] study design, [4] country of origin, [5] purpose of the study, [6] nature and size of the sample, [7] inmates' characteristics, [8] number of inmates who did develop drugs misuse, [9] psychiatric comorbidities associated with drugs misuse, [10] addictive behavior associated with drugs misuse, [11] inmates' factors associated with drugs misuse [12]. Collected inmates' factors, were age, gender, employment, marital status, university degree, and type of drugs misuse.

Study selection

We defined our study eligibility using the populations-interventions-comparators-outcomes study design (PICO) framework. The PICO was defined as follows: the included population consisted of inmates, ≥ 18 years old who have been treated with psychoactive drugs and who have been diagnosed with drugs misuse. Outcomes of interest included inmates' characteristics and different types of drugs misuse. The primary outcome of the present study was to estimate the rate of drugs misuse, defined as misuse or nonmedical use of psychoactive prescription drugs, in custodial setting. Secondary outcomes included addictive behaviors, psychiatric comorbidities and inmate factors associated with drugs misuse. Primary outcome was defined at the time of the first studies' selection, while secondary outcomes were included following title and abstract review in order to capture a complete and accurate representation of the patient and surgical characteristics that have been evaluated by current literature. We included studies evaluating the impact of psychoactive drugs prescription on the development of drugs misuse, on inmates' ≥18 years of age, which enrolled more than 10 adults, with no limits of language. Studies meeting any of the following exclusion criteria were excluded from the

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present review: [1] comments, [2] animal studies, [3] abstracts, [4] review articles, [5] case reports or case series including less than 10 subjects; [6] editorials or letters, [7] studies not evaluating the impact of psychoactive drugs prescription on drugs misuse; [8] patient age < 18.

Risk of bias assessment

The Risk of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool was used to rate risk of bias for non-randomized included studies [31]. This tool assesses seven domains: risk of bias from confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported results [31]. A proposed judgment about the risk of bias arising from each domain is generated by an algorithm, based on answers to the signaling questions. Judgment can be "Low", "Moderate" or "High" risk of bias, or can express "Some concerns" [31].

Data analysis and data synthesis

Patients' characteristics and outcomes were summarized and described as means or medians for continuous variables or percentages for categorical variables. Quantitative data synthesis was conducted while always keeping the drug abuse rate as the baseline outcome, in terms of the proportion of inmates manifesting drug misuse in prison. Pooled proportions were estimated through a proportional meta-analysis with random-effects models according to DerSimonian and Laird [32]. Results were expressed in proportions with 95% confidence intervals and prediction intervals. In cases of significant heterogeneity, prediction intervals will be wider than confidence intervals, offering a more cautious approach to integrating uncertainty into the analysis [33]. Heterogeneity was inspected using the I2 statistic, with a threshold level for significant heterogeneity of 50% [34]. Methods for assessing publication bias, such as Egger's and Begg's tests alongside funnel plots, were originally designed for comparative data, assuming a bias toward publishing positive results over negative ones. While it is possible to apply these tests to proportional meta-analyses, there is insufficient evidence to suggest they effectively account for such data. Additionally, the assumption of positive results being preferentially published may not hold true for proportional studies, given the absence of a standardized definition or consensus regarding positive outcomes in meta-analyses of proportions [33]. Statistical analyses were conducted adopting the R statistical software (version 4.4.0) [35]. Particularly, for the meta-analysis of proportions, the "meta" package (version 5.0.0) was employed. Statistical significance was determined at a threshold of two-sided p-values < 0.05.

RESULTS

Study selection

A total of 8826 studies were retrieved, and 7035 unique results remained for the initial title and abstract screening. Results were screened and 519 manuscripts underwent full-text review. Finally, only 6 articles met full inclusion criteria (Figure 1). Studies included 2 survey, 2 prospective cohort studies and 1 observational study (Table 1). All studies were conducted in Europe [36–40], except one in the US [41], and they presented a study period that collectively extended from 2006 to 2020. The study purposes of the included articles are presented in Table 1.

Risk of bias assessment

By using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I), there was low-to-moderate risk of bias among the included studies. Overall, 4 of the included studies had low risk of bias (80%) [37,38,40,41], while just 2 of the studies included illustrated some concerns for bias (20%) [36,39]. None of the included studies were concerned to have a high risk of bias. Risk of bias assessment using the ROBINS-I tool is demonstrated in Table 2.

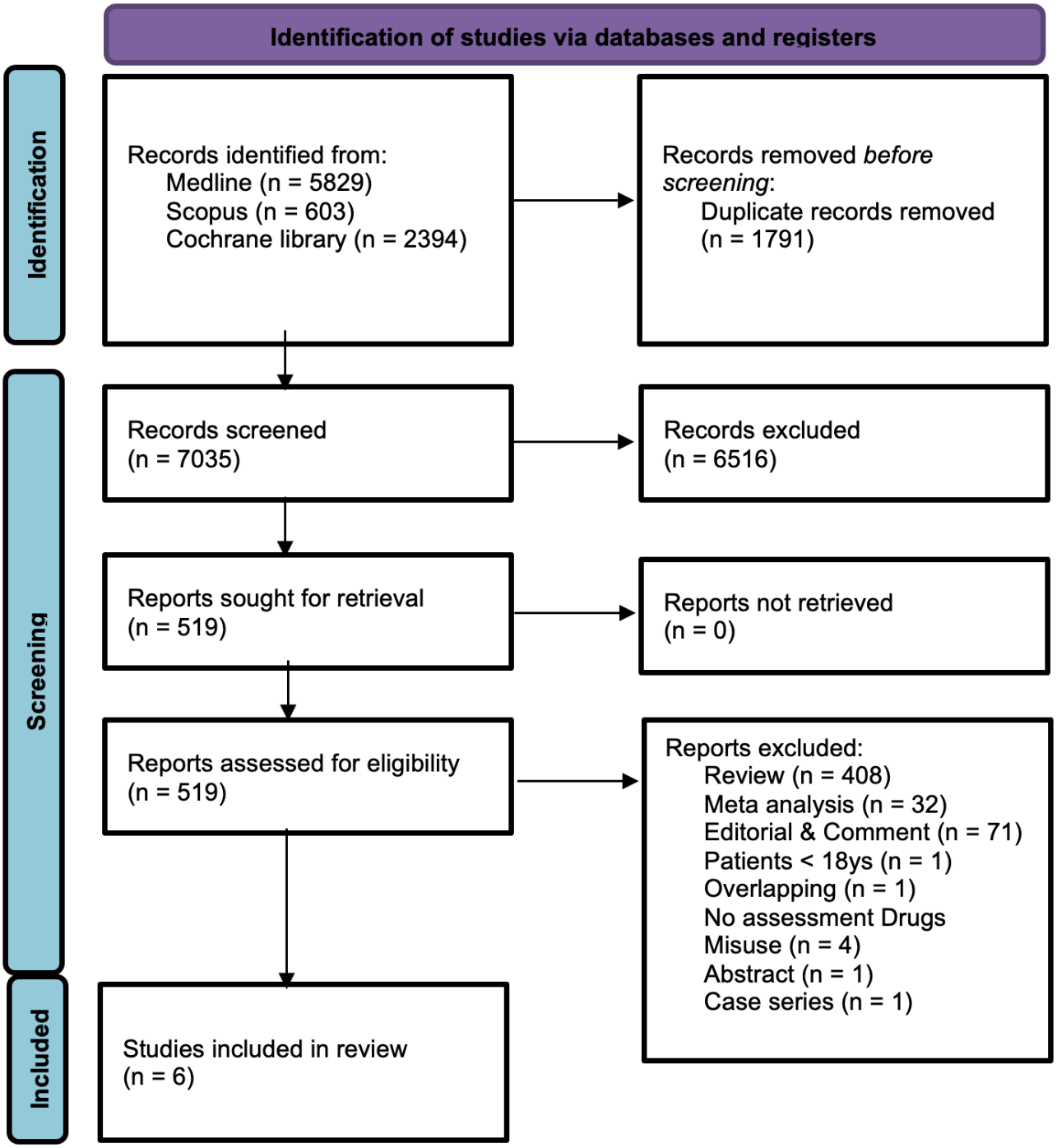
Inmates' characteristics and type of drugs misuse

Overall, 17023 inmates were included for analysis. Inmate' demographics from the included studies are displayed in Table 3. Female sex ranged from 0% to 33.8% in studies reporting sex. Age ranged from 18 to >50 years in the included studies and employed status ranged from 15.57 to 58.2%. Among the studies reporting the type of drugs misuse, 4 were focusing on opioids misuse [36–38,41], whereas 2 studies reported Gabapentinoids misuse and 1 Z-drugs misuse [39,40].

Rate of drugs misuse and predisposing factors

The prevalence rate of pooled drug misuse was 24% (95% CI: 35 44,2) (Fig. 2). The estimated 95% prediction intervals ranged from 35% to 44,2%. All the included studies evaluated the rate of drugs misuse following psychoactive drugs prescription [36–41]. The observational study by Plojovic et al [38]. reported a drugs misuse rate as high as 67.3% after psychoactive drugs prescription, which was consistent across other studies. The lowest reported rate of drugs misuse was 9.2% in the study by Sec et al. [37]. A prospective cross-sectional study by Durand et al. [40] determined rates of drugs misuse and demonstrated that the adjusted time trends across genders show prescribing rates were increasing for Gabapentinoids. The follow-up periods in the included studies are

Figure 1. Flowchart according to PRISMA guidelines



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For more information, visit: http://www.prisma-statement.org/

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Table 1. Design and characteristics of the included studies

References	Country	Inclusion period	Design	Purpose of the study	Nature and size of the sample
Sec, 2009	France	2006-2007	PCS	To identify which psychotropic medication are misused in custodial population	659 inmates
Plojovic, 2016	Serbia	2013	OBS	To investigate the misuse of psychologically active substances of convicts being in prisons and their treatment in the District Prison in Novi Pazar, Serbia	55 inmates
Soni, 2019	UK	2017-2018	Survey	To examine prescribing rates and the compliance for gabapentinoids in English Prisons	109 inmates
Franchetti, 2023	Germany	/	PCS	To provide an objective estimation of the prevalence of illicit use of methadone and buprenorphine in two German prisons	678 urine samples
Morrison, 2023	US	2015-2020	Survey	To explore patterns of opioids misuse among prison patients.	5154 individuals
Durand, 2023	Ireland	2012-2020	PCSS	To examine prescribing rates and trends for opioids, benzodiazepines, Z-drugs, and gabapentinoids in Irish Prisons between 2012 and 2020 using electronic health records data from the Irish Prison Services; to examine whether prescribing rates and trends vary by gender and if a person has a history of OUD; to determine rates of co-prescribing of opioids, benzodiazepines, Z-drugs, or gabapentinoids among people receipt of OAT medications.	10371 inmates

PCS: prospective cohort study
OBS: observational study
PCSS: prospective cross-sectional study
RCSS: retrospective cross-sectional study

Table 2. Methodological quality evaluation of the included non-randomized studies according to ROBINS-I

Author	Bias due to confounding domains relevant to the setting of the study	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported results
Plojovic	Low	Moderate	Low	Low	Moderate	Low	Moderate
Soni	Low	Moderate	Moderate	Low	High	Moderate	Moderate
Franchetti	Low	Moderate	Low	Low	High	Moderate	Moderate
Morrison	Low	Moderate	Low	Low	Moderate	Moderate	Moderate
Durand	Low	Low	Low	Low	Moderate	Moderate	Low
Sec	Low	Low	Low	Low	Moderate	Moderate	Low

Table 3. Inmates' characteristics and type of drug misuse

Author	Age	Female sex, %	Employed, %	Not Married, %	University Education, %	Type of drug misuse
Sec	35.4*	9.8	26.3	NA	NA	Opioids, Z-drugs
Plojovic	20-35 range	0	58.2	56.4	1.8	Opioids
Soni	NA	NA	NA	NA	NA	Gabapentinoids
Franchetti	NA	NA	NA	NA	NA	Opioids
Morrison	#19.16* (18-29ys); 16.28* (30-40ys); 15.30* (>50ys)	18.42#	15.57#	18.72#	8.62#	Opioids
Durand	34.4*	33.8	NA	NA	NA	Gabapentinoids

**mean value*
 # Inmates with Drug Misuse
NA: not assessed

Table 4. Drugs Misuse rates and associated factors

Author	Inmates included n.	Inmates developing DM n. (%; 95%CI)	Follow-up period (%)	Inmates' social factors associated with DM	Addictive behavior associated with DM	Psychiatric factors associated with DM
Sec	659	61 (9.2)	NA	Drug selling; theft	Alcohol use	NA
Plojovic	55	37 (67.3)	1 year	Significant problems with the law	Alcohol use; Cannabis use; Cocaine use; LSD use	Serious or Mild problems with Mental Status
Soni	109	14 (13) diverting of prescribed drugs	8 month	NA	NA	NA
Franchetti	675	100 samples (14.8)	1 years	NA	NA	NA
Morrison	5154	919 (17.12; 15.22-19.21)	1 years	Arrest; drug selling; higher risk propensity	Tobacco use; marijuana use; cocaine use; binge drinking	Major depressive episode; serious psychological distress
Durand	10371	Adjusted time trends across genders show prescribing rates were increasing for Gabapentinoids (ARR [95% CI] 1.07 [1.05–1.08]).	1 year	NA	NA	NA
Tot	17023		/	/	/	/

NA: not assessed
DM: drugs misuse

reported in Table 4. Three studies provided insight into secondary outcomes evaluating inmates and addictive behaviors associated with drugs misuse [37,38,41]. Two studies demonstrated an association between drugs misuse and mental health problems in adults in custodial setting as reported in Table 4 [38,41]. Inmate characteristics associated with drugs misuse included arrest, drug selling, theft, higher risk propensity and generally significant problems with the law (Table 4). Psychiatric comorbidities and addictive behaviors

ISSN 2282-0930 • Epidemiology Biostatistics and Public Health - 2025, Volume 20, Issue 2

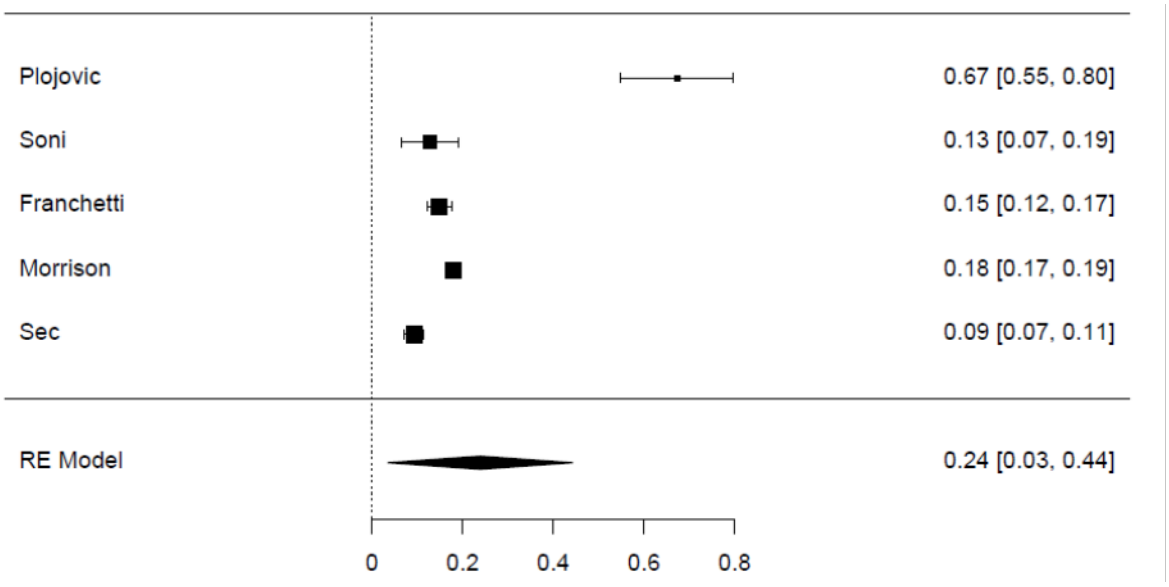
linked with drugs misuse included major depressive episode, serious psychological distress,

DISCUSSION

The present study demonstrates an incidence of drugs misuse as high as 24% as shown in Figure 2.

This finding is important as it highlights the need of identifying inmates at high risk of developing drugs misuse, as they may develop even lethal complications due to drugs abuse. Second, the present study identifies some factors that predispose to drugs misuse in custodial settings. Some of them are not modifiable (e.g., level of education, age) but can allow us to select categories at higher risk, which could benefit from multidisciplinary management (e.g., psychiatric, psychosocial specialists) after imprisonment in order to minimize the occurrence of drugs misuse. Others (e.g., psychiatric illnesses, addiction behaviors) may be identified at prison entry and treated/stabilized immediately and reevaluated frequently. Drug prevention work in prisons is critically important. Recent research points out that adult prisoners often continue to use psychologically active substances and commit criminal acts because they lack effective treatment and supervision [42,43]. Psychologically active substance abuse is a significant factor reflecting criminal behavior, and therefore treatment of the disease of addiction plays an important role in the prevalence of recidivism [38]. The effectiveness of treatment is mainly reflected in improved psychological interventions [44]. A combined treatment is possible in prisons and some authors evaluate that a treatment of addiction disease in combination with methadone therapy, counseling and treatment reduces the use of psychologically active substances within convicts that can go under such treatment, different from those who did not have any treatment [45]. Given that illicit use of methadone and buprenorphine is highly prevalent in the prison population, and that buprenorphine has been found to originate from the community setting, we believe that the methods currently implemented to prevent and counter illicit drug entry from the outside and inadvertent use of prescribed drugs in prison (e.g., inspection by prison officers or drug-sniffing dogs on visitors and inmates, and random urine screening on inmates) should be increased and expanded. This could be achieved by identifying those involved in the black market for substances inside and outside prison, or by prescribing forms of drugs less suitable for illicit use (e.g., buprenorphine-naloxone). In addition, our results indicate a high number of inmates with an untreated opioid use disorder. This underscores the need for widespread implementation of treatment of substance abuse in correctional institutions. In addition, the use of illicitly obtained opioids while in prison carries a higher risk of overdose [27]. Therefore, for people who die during detention or shortly after release, postmortem examination should routinely include systematic toxicological testing. Regarding the other pharmaceutical class affected by "drug misuse," gabapentinoids (pregabalin and gabapentin), they are increasingly being reported for drug misuse at the European level, in parallel with increasing prescription levels, related deaths, and black market [11,46–48]. Gabapentinoids are anticonvulsants, but they are also prescribed for a range of clinical conditions in neurology, psychiatry, and rheumatology, as well as being used off-label to treat benzodiazepine and alcohol dependence [20]. Their effects are due to binding to calcium channels, resulting in reduced levels of central excitability [20]. In addition, gabapentinoids are believed to possess GABA-mimetic properties, with possible direct/indirect effects on the dopaminergic "reward" system [22]. Typical psychoactive effects include a sense of well-being/relaxation, euphoria, and

Figure 2. Meta-analysis



even hallucinations [49]. The data that emerged in our study in this regard confirm those in the literature on the general population that gabapentinoids are increasingly abused or misused for self-medication, and it is also necessary to pay particular attention in the prison setting to the fact that these drugs can produce desirable effects on their own but are often used in conjunction with other drugs with unfavorable health outcomes. Therefore, multidisciplinary and multi-professional assessment remains critical in relation to the development of psychoactive drug misuse, to select which inmates are at risk and how to take action to reduce their risk of developing psychoactive drug misuse.

Strengths and Limitations

The main limitation of this study is the nature and scarcity of the included studies. Many were survey studies with risk of selection bias and underreporting. By its nature, the pooling of information from multiple studies has limitations due to the significant variability in patient populations and study designs, as well as different psychiatric assessment methods, thus a meta-analysis was not feasible. Instead, a pooled proportion approach was used. Several type of drugs misuse was included in this study, increasing the heterogeneity of the patient population. Prospective studies had limited size and numbers and were at risk for inclusion of nonconsecutive patients and nonresponse bias. Self-reported questionnaires were subject to recall bias or inaccurate responses regarding drug misuse. The majority of the included studies had chronic opioid use as their focus while there were scarce data on drugs misuse from other problematic drug misuse. Furthermore, the precise diagnosis of the type of associated mental disorder, which would be useful to further describe the impact of the development of drug misuse in these prisoners, is rarely specified in the included studies. Despite these limitations, this is the first systematic review to examine the phenomenon of psychoactive drug misuse in the prison setting. Another systematic review recently published in the literature addressed the topic of drug use within prisons, but unlike our study, which addressed the topic in a broader public health manner, the systematic review by Chiappini et all. [50], focused more in the area of clinical neurological-psychiatric symptomatology reported by inmate users. In addiction, the systematic review mentioned above, included articles that did not exactly center the context of the topic, for example, they dealt with drug misuse in the general population and not in the prison setting. In other cases, it added articles that used wastewater analysis as a methodology, a use that only allows for drug detection and not for discerning between prescription-induced use and psychoactive drug misuse, invalidating the validity of the conclusions reached. On the contrary, our work included only papers in the literature that addressed the issue of prison misuse of psychoactive drugs with reliable methodology with respect to the conclusions of identifying the phenomenon. This study is notably strengthened by its meticulous method, which involved the thorough screening of articles by clinical experts in emergency medicine during the literature review phase. Through rigorous appraisal, where each study quality was evaluated, and thorough assessment, involving rigorous data synthesis and analysis, we ensured a robust foundation to support the meta-analysis. Finally, our work is the only work that provided a meta-analysis with a prevalence data on the issue.

Further Issues

Illicit drug use was widespread in the surveyed prison population. Although the participation rate was high, this figure may still be underestimated. Further cross-sectional experimental studies that provide data on the prevalence of illicit drug use in prisons are needed to explore trends in this phenomenon and put in place appropriate measures to counter it, both at the level of public health interventions and ministerial measures. What emerges from this work suggests that future research should focus, in particular, on toxicological analyses of biological samples that allow longer detectability of drug use (e.g., hair). Furthermore, given the imbalance in the gender ratio observed in prisons, it is critical to perform gender-sensitive analyses, as women-specific findings would otherwise remain invisible. In addition, more in-depth analyses should be done with respect to poly-drug use, a type of intake that is potentially lethal to the abuser. As already indicated by a recent review of the literature on the subject [50], the increase in drug misuse in detention settings urgently requires more attention from public health and governments. New research is needed, such as understanding the long-term effects of new psychoactive substances on human health, and preventive strategies, such as figuring out how to enable better risk management to improve early warning systems for law enforcement and policy makers [50]. Prevention strategies should include not only training health personnel and educating prisoners, but also implementing stricter substance control policies and regulations [50]. Interventions such as the implementation of new prescribing guidelines involving substances with reduced abuse potential and diversion rates should be considered [50].

CONCLUSION

It is evident that the misuse and abuse of prescription drugs is a problem that affects the entire prison population, not just those with mental disorders, which, moreover, have not been extensively described as previously mentioned. Therefore, it is important not to consider drug misuse and abuse merely as a mental health issue, but rather to promote a dialogue at the intersection of these two distinct realities. This

would enable the development and implementation of joint interventions by mental health services and addiction services for individuals facing these challenges. Such shared pathways should be based on a logic of empowerment and aim at promoting health, while avoiding the risk of neo-institutionalization in mental health and the use of the penal system to manage social phenomena. The misuse and abuse of prescription drugs in the prison setting is a global problem that requires urgent action. The modern pharmacovigilance, in order to look at how medicines are actually used in real life, should identify a range of technical tools and approaches to go beyond spontaneous reporting systems. Physicians should be vigilant when prescribing drugs with an abuse/misuse/diversion potential and carefully evaluate the possibility for inmates to be more vulnerable to these misuse activities. To effectively address these problems, prison institutions, health care providers, and policy must work together to implement preventive measures, provide appropriate treatment and support, and improve monitoring and reporting systems. It is imperative to recognize the seriousness of this problem and take concrete steps to address it comprehensively, starting with a methodological approach to develop research in the context of vulnerable people.

AUTHOR CONTRIBUTIONS

Silvia Martinelli, Mario Cesare Nurchis, Kıvanç Kok: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Roles/Writing - original draft; and Writing - review & editing. Emanuele Caroppo, Gianfranco Damiani: Investigation; Methodology; Software; Validation; Visualization; Writing - review & editing (should always state something when more than one author).

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STATEMENT OF ETHICS

An ethics statement is not applicable because this study is based exclusively on published literature.

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DISCLOSURE STATEMENT

The authors report no conflicts of interest.

DATA AVAILABILITY STATEMENT

All data used in the preparation of this manuscript is derived from published materials and can be accessed via literature search as outlined in methods and supplemental material.

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SUPPLEMENTAL MATERIAL

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Pages 2-3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Pages 4
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Pages 4
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Pages 5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Pages 5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 5
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 6

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Section and Topic	Item #	Checklist item	Location where item is reported
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 6-7
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 6-7
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 6-7
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 6-7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 6-7
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 6-7
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 6-7
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 6-7
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 7
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 7
Study characteristics	17	Cite each included study and present its characteristics.	Page 7-8 Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 7 Table 2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Page 8-9 Figure 2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 8-9 Table 3-4
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 8-9 Figure 2
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 8-9 Figure 2
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page 8-9 Figure 2
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 8-9 Figure 2
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Page 8-9

Section and Topic	Item #	Checklist item	Location where item is reported
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 9-10-11
	23b	Discuss any limitations of the evidence included in the review.	Pages 11-12
	23c	Discuss any limitations of the review processes used.	Pages 11-12
	23d	Discuss implications of the results for practice, policy, and future research.	Page 12-13
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 4
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Page 4
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 14
Competing interests	26	Declare any competing interests of review authors.	Page 14
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Pages 4-5

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Heterogeneity Statistics

Tau	Tau²	I²	H²	R²	df	Q	p
0.230	0.0529 (SE = 0.0381)	99.67%	302.652	.	4.000	114.416	< .001

Random-Effects Model (k = 5)

	Estimate	se	Z	p	CI Lower Bound	CI Upper Bound
Intercept	0.238	0.104	2.30	0.022	0.035	0.442
	.	.	.	.	.	.

Note. Tau² Estimator: Restricted Maximum-Likelihood