

Effectiveness of opioid maintenance programs for treating drug dependence in prisons

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ABSTRACT

Objectives: To evaluate the effectiveness of opioid maintenance programs in treating opioid dependence in Spanish prisons.

Material and method: A narrative bibliographic review was carried out on the following databases: PubMed; Cochrane; IBECs; LILACS; HealthCare. All clinical trials were chosen as a preference, along with systematic review articles and some articles that were considered relevant for their content. The time period was limited to between January 2011 and November 2021. The languages chosen were English, Spanish and Catalan. Repeated articles and those that were not related to the objectives were rejected. The search criteria were: “methadone AND prisons”; “opiate substitution treatment AND prisons”; “methadone AND buprenorphine”; “methadone OR buprenorphine”; “prisons AND Methadone AND buprenorphine”.

Results: 20 articles were selected out of 647 items consulted after applying the corresponding filters and after discarding duplicates.

Discussion: There was a slightly greater effectiveness of buprenorphine versus methadone. The high prevalence of the program was highlighted, as well as the variety of adverse effects of methadone. Usefulness with regard to inmates' behavior showed a range of opinions. The possibility of new treatment alternatives with better pharmacological control is mentioned.

Key words: methadone; buprenorphine; prescription drug monitoring programs; opiates; prisons.

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INTRODUCTION

Opioid use has evolved over the years, changing from their origins in the Second World War, to the 80s and 90s when they became a worldwide problem¹. The use of injected heroin was associated with severe marginalisation, increased crime and a higher risk of infection from diseases such as the human immunodeficiency virus (HIV). Spain saw an exponential growth of HIV+ cases amongst drug addicts in this period, which led to the approval of a range of legislative measures on interventions with methadone for patients with opioid dependency².

The healthcare scenario also brought about a change in the organisational model in Spanish prisons, which led to the introduction of the methadone maintenance program for inmates. A Royal Decree was

published in 1990 that regulated the use of and access to this intervention, which was not enacted for several years. Since then, new treatment programs have been introduced that are geared towards abstinence from substances, such as drug-free programs, and multidisciplinary interventions have also been established³.

These programs are one of the treatments of choice for heroin dependence. They include personalised oral administration of an opioid agonist (methadone). They form part of a set of harm reduction activities and strategies, which consist of individual and collective social and medical measures that set out to eliminate the negative effects of drug use in the dependent population^{4,5}.

According to the results of the 2022 Spanish Survey on Health and Drug Use amongst Prison Inmates (ESDIP), the percentage of opioid users in Span-

ish prisons has gone down in recent years, although there are still many amongst the prison population. According to the 2017 memorandum on drug abuse published by the Ministry of Health and Consumer Affairs, the prevalence of the methadone maintenance program, which was introduced in 1994, dropped over the years and was replaced by other drug rehabilitation approaches in response to the changes in consumption patterns amongst the prison population. The general objective of this study is to evaluate the effectiveness of opioid maintenance programs when treating drug dependence in Spanish prisons⁶.

MATERIAL AND METHOD

For this review, a bibliographical search of the following databases was carried out: PubMed, Cochrane, IBECs, LILACS, HealthCare, all of which were available at the library of the Universitat Jaume I de Castellón. The resources available at other entities such as the Spanish Ministry of Health and Consumer Affairs and the Spanish Journal of Prison Health (*Revista Española de Sanidad Penitenciaria (RESP)*) were also used.

Descriptors included in health sciences in Spanish were used, along with others in English included in medical subject headings, as indicated in Table 1.

The terms used for the bibliographical search were mainly: *methadone*, *prisons*, and *buprenorphine in combination with the connectors AND and OR* as follows: *methadone AND prisons*; *opiate substitution treatment AND prisons*; *methadone AND buprenorphine*; *methadone OR buprenorphine*; *prisons AND methadone AND buprenorphine*.

The language limits established were publications in Spanish, English and Catalan and the period of publication was limited to between January 2011 and November 2021.

The inclusion criteria applied were: freely accessible articles, based on recent studies. The exclusion criteria on the other hand were: articles duplicated in different databases, articles with no relevant information related to opioid rehabilitation programs and articles that were published more than ten years ago.

The results are reflected in Figure 1 after the application of the aforementioned strategies for the obtaining the items.

RESULTS

A total of 647 articles were obtained at the end of the bibliographical search. Filters belonging to each data base were then used and 616 articles were eliminated. Duplicates found in the searches were also rejected ($n = 11$), and finally a reading session of the title and abstract of the articles of interest for the subject matter in question was carried out, after which 20 articles were selected.

Of the 20 selected articles, 70% ($n = 14$) were reviews of the literature, 5% were cohort studies ($n = 1$), another 5% were cross-sectional studies ($n = 1$), 10% were studies of cases and controls ($n = 2$), 5% were quasi-experimental studies and 5% were field research articles.

Table 2 contains a summary of the characteristics of each article selected for this review: the type of study, the date and country of publication, and the aims and conclusions reached.

DISCUSSION

The predominance of methadone based interventions is highlighted in a study by Martínez⁷, who indicates that the most widely used programme for opioid rehabilitation in Spanish prisons is the methadone maintenance program (MMP), which

Table 1. Terms used in literature search. Key words.

MeSH		DeCS	
Spanish	English	Spanish	English
Metadona	<i>Methadone</i>	Metadona	<i>Methadone</i>
Prisiones	<i>Prisons</i>	Prisiones	<i>Prisons</i>
Tratamiento	<i>Terapeutics</i>	Tratamiento	<i>Terapeutics</i>
Opiáceos	<i>Opiate</i>	Opiáceos	<i>Opiate</i>
Buprenorfina	<i>Buprenorphine</i>	Buprenorfina	<i>Buprenorphine</i>

Note. DeCs: health sciences descriptors; MeSH: medical subject headings.

was used by a large sector of the prison population in the years immediately following its introduction, while the number of participants in this type of program has since gone down. In similar studies, Martín *et al.*⁸ and Torrens *et al.*⁹ also comment on the large number of inmates who receive this treatment. However, Narezo *et al.*¹⁰, while agreeing with the number of individuals who participate in the program, states that other methods of detoxification are growing in terms of the number of users, while there is a gradual decrease in the popularity of MMPs .

Several studies highlight the different adverse effects of treatment with methadone. One of the most frequently mentioned of these is the prolongation of the QT interval . Bart *et al.*¹¹ state that this

effect can lead to a type of cardiac arrhythmia called *torsade de pointes*, although the repercussions for the heart are not clinically significant, given that the rate of associated cardiovascular events is very low. Barbosa *et al.*¹² also mention this effect, but add that there is insufficient evidence to back up this effect on patients with no previous history of cardiovascular risk, although at the same time they recommend a preventive electrocardiogram for users.

Salsitz *et al.*¹³ likewise concur with this side effect, and include other adverse effects, such as a certain degree of sedation, excessive sweating, increased appetite and a reduction in testosterone levels caused by the inhibitory action on the gonadotropin-releasing hormone of methadone, which may lead to sexual dysfunctions.

Table 2. Articles included in the selection.

Title	Authors	Year	Origin	Study	Objective	Conclusion
Evolution of the most prevalent pathologies in prisons. In the last decades	Martínez C ⁷	2019	Spain	Book chapter	Describe the evolution of the most prevalent pathologies, as well as the programs established to treat them.	Entering prison has led to an improvement in prisoners' pathologies over the years thanks to the various interventions associated with treating them.
Drug Addiction and Prison: Study on the situation of people with drug problems in prison	Martin J ⁸	2017	Spain	Mixed research and analytical study	Act on the problems suffered by drug addicts, such as social and labor marginalization, deterioration of physical and mental health, prison and judicial situation, and promote treatment.	Given the high incidence of drug addiction problems in prisoners, we must conclude that many efforts must be directed to providing assistance in this matter so that equal attention is guaranteed.
Methadone maintenance treatment in Spain: the success of a harm reduction approach	Torrens M ⁹	2013	Spain	Literature Review	Present the evolution and characteristics of the Methadone Maintenance Program in Spain.	The MMP in Spain meant a decrease in drug consumption, as well as sexually transmitted diseases at a time when they were considered two major epidemics.
Prison, drugs and social education	Narezo R ¹⁰	2014	Spain	Literature Review	Approach the penitentiary reality and its relationship with drugs from an educational perspective.	Emphasize the importance of a qualified intervention that includes the reeducation and reintegration of people deprived of liberty.

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Table 2. Articles included in the selection (*continuation*).

Title	Authors	Year	Origin	Study	Objective	Conclusion
Methadone and the QTc Interval: Paucity of Clinically Significant Factors in a Retrospective Cohort	Bart G ¹¹	2017	USA	Retrospective cohort study	Demonstrate the association of methadone with prolongation of the cardiac QT interval.	Methadone is associated with prolongation of the cardiac QT interval, but it is not clinically relevant.
Revisiting methadone: pharmacokinetics, pharmacodynamics and clinical indication	Barbosa J ¹²	2015	Brazil	Literature Review	Show the pharmacodynamic and pharmacokinetic aspects of methadone, and in addition, its therapeutic indication.	Methadone is a unique opioid due to its lower likelihood of tolerance, prevention of hyperalgesia, and higher quality in treating neuropathic pain.
Pharmacotherapy of Opioid Addiction: "Putting a Real Face on a False Demon"	Salsitz E ¹³	2016	USA	Literature Review	Present the history of methadone, its effectiveness and the associated stigmas.	There is a variety of evidence that affirms the effectiveness and safety of methadone.
Recent advances in the treatment of opioid use disorders-focus on long-acting buprenorphine formulations	Soyka M ¹⁴	2021	Germany	Literature Review	Discuss the pharmacological activity, clinical efficacy, and prospects of methadone, buprenorphine, and depot treatments.	The new buprenorphine depot treatments may become one of the best alternatives.
Methadone: A Review - Oral Health	Green R ¹⁵	2011	USA	Literature Review	Show the impact of methadone on oral health.	The maintenance of oral health can be compromised by methadone treatments.
Underrepresentation of diverse populations and clinical characterization in opioid agonist treatment research: A systematic review of the neurocognitive effects of buprenorphine and methadone treatment	Mindt M ¹⁶	2021	USA	Literature Review	Examine the neurocognitive effects of buprenorphine and methadone.	Both methadone and buprenorphine are associated with neurocognitive improvement, but especially buprenorphine.
Oral substitution treatment of injecting opioid users for prevention of HIV infection	Gowing L ¹⁷	2011	Australia	Literature Review	To evaluate the effect of oral substitution treatment for opiate-dependent injecting drug users on risk behaviors and rates of HIV infections.	Reductions in risk behaviors related to drug use translate into reductions in cases of HIV.

(*continued*)

Table 2. Articles included in the selection (continuation).

Title	Authors	Year	Origin	Study	Objective	Conclusion
Voluntary treatment, not detention, in the management of opioid dependence	Clark N ¹⁸	2013	USA	Literature Review	Demonstrate the effectiveness of methadone maintenance treatment.	The therapeutic use of methadone reduces heroin abuse, the risk of HIV transmission and criminal behavior.
Is it necessary to have Buprenorphine/ Naloxone treatments for opioid-dependent prisoners?	Marco A ¹⁹	2013	Spain	Literature Review	Evaluate the advantages and disadvantages of the substances used in agonist substitution treatments, as well as review the aspects related to equality of treatment in prison and in the community.	Both the methadone option and the buprenorphine option have sufficient evidence, but the buprenorphine option has a greater safety profile and fewer drug interactions.
Initiating methadone in jail and in the community: Patient differences and implications of methadone treatment for reducing arrests	Schwartz R ²⁰	2019	USA	Retrospective case-control study	Compare the characteristics of patients in methadone substitution treatment from two prison programs and those in the community.	They suggest that patients who initiate methadone in a jail-based program may have a higher likelihood of future arrest compared to patients who enter community-based treatment.
Pharmacotherapy for opioid addiction in community corrections	Schwartz R ²¹	2018	USA	Literature Review	To examine the effectiveness of pharmacological treatments for opioid addiction in people under court supervision in US.	Afirman que disminuyen la actividad delictiva y el índice de arrestos relacionado con el consumo de opioides.
Personality disorders, addictions and psychopathy as predictors of criminal behavior in a prison sample	Flórez G ²²	2019	Spain	Retrospective cross-sectional study	To analyze the relationship between personality, addictions and criminal behavior with a sample of inmates at the Pereiro de Aguiar Penitentiary Center in Ourense.	It is observed that inmates have a higher prevalence of personality disorders, psychopathy and consumption of addictive substances. Significantly increasing the risk of committing crimes.
Pharmacological interventions for drug-using offenders	Perry A ²³	2015	USA	Literature Review	To evaluate the effectiveness of pharmacological interventions in drug-dependent patients to reduce criminal behavior, substance abuse, or both.	Interventions with agonists appear to have no effect and those with antagonists showed a slight reduction in criminal activity but not substance abuse.

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Table 2. Articles included in the selection (continuation).

Title	Authors	Year	Origin	Study	Objective	Conclusion
Prolonged-release buprenorphine formulations: Perspectives for clinical practice.	Chappuy M ²⁴	2020	France	Literature Review	Describe the main characteristics and effectiveness of opioid substitution methods.	There are certain risks of this type of long-term treatment, but professionals affirm that the new treatments represent an improvement in stable patients.
Effectiveness of changing treatment from Methadone to Buprenorphine/ Naloxone in opiate dependents	Fuentes J ²⁵	2017	Spain	Quasi-experimental, quantitative, longitudinal, prospective study	To determine the effectiveness of treatment with Buprenorphine/ Naloxone as a replacement for methadone in opiate-dependent patients.	Changing maintenance therapy from Methadone, in opioid-dependent patients, to buprenorphine/ naloxone is a good option, as it has similar effectiveness in terms of adherence and retention, and produces a greater reduction in the use of illicit opioids, while that improves the patient's quality of life.
What place for prolonged-release buprenorphine depot-formulation Buvidal [®] in the treatment arsenal of opioid dependence? Insights from the French experience on buprenorphine	Vorspan F ²⁶	2019	France	Literature Review	Show the characteristics and effectiveness of the new treatment with Buvidal [®] .	Buvidal may be a promising treatment for patients on oral opioid replacement therapy.
Detainees and prisoners: challenging the role of mental health nurses	Vera-Remartínez EJ ²⁷	2022	Spain	Book chapter	Delve into suicide prevention programs, as well as established drug cessation programs.	There are several difficulties that limit the possibilities of action; the increasing lack of health professionals in penitentiary centers, as well as the lack of mental health nursing protocols that unify and facilitate care.

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Table 2. Articles included in the selection (*continuation*).

Title	Authors	Year	Origin	Study	Objective	Conclusion
Economic evaluation: A comparison of methadone versus buprenorphine for opiate substitution treatment	Maas J ²⁸	2013	United Kingdom	Cases and controls study	To evaluate the cost and effectiveness of methadone and buprenorphine in patients on substitution treatment in Norfolk, UK.	Methadone is estimated to have a slightly lower cost than buprenorphine; However, when the clinic contact cost and pharmacy dispensing costs are taken into account, the differences became quite small.

Note. HIV: human immunodeficiency virus; MMP: methadone maintenance programme.

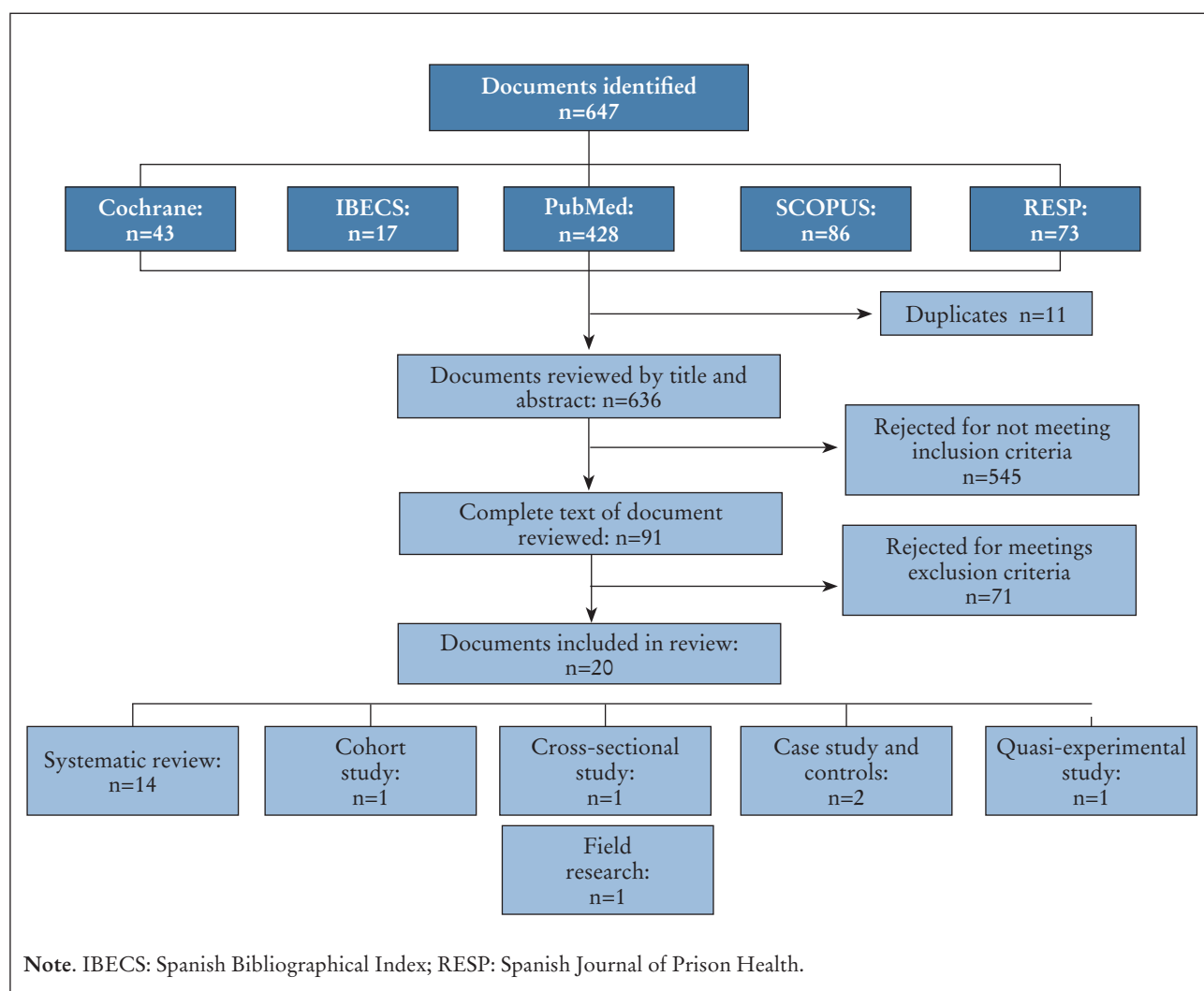


Figure 1. Flow chart of study.

Soyka *et al.*¹⁴ adds other symptoms and signs to the ones mentioned by Salsitz *et al.*¹³, respiratory depression, sensations of euphoria and possible tolerance and physical dependence. When considering the last of these adverse effects, Barbosa *et al.*¹² comments that methadone, within the parameters of potential tolerance or dependence that any opioid can cause after someone has been taking a different one, is a less sensitive substance in this regard and so the risk of this condition arising is minimal.

Green *et al.*¹⁵ state that there is a link between methadone consumption and poor dental conditions, as there is a high prevalence of caries, poor dental hygiene, dry mouth and bruxism amongst subjects receiving treatment.

Another possible adverse effect mentioned by authors is the impact on cognitive functions. Mindt *et al.*¹⁶ comment that methadone maintenance treatment has a low effect on such functions, but it can interfere with executive functioning (abstract thinking, the ability to make plans, initiate actions and complex behaviours, etc.), memory, learning, visuospatial functions, language, speed of processing stimuli and attention span.

Several authors, such as Gowing *et al.*¹⁷, Clark *et al.*¹⁸ and Marco *et al.*¹⁹, agree that this program has been very effective in reducing illegal opioid consumption and HIV transmission, since it has brought about a change in high risk behaviours of consumption and has reduced the incidence of IDU and syringe exchanges.

Schwartz *et al.*²⁰ likewise state that such interventions have reduced criminality and the number of arrests related to opioid use, affirmation which they agree in another article by Schwartz *et al.*²¹, as well as Flórez *et al.*²². On the other hand, Perry *et al.*²² did not find enough evidence to conclude that there is a link to reduced criminal behaviour. They consider that it would be a variable that depends on the type of offence, the likelihood of rehabilitation and the setting of the person receiving treatment, rather than just being in a program.

One new alternative treatment option for rehabilitation was recently placed on the market: extended-release buprenorphine/naloxone. Soyka *et al.*¹⁴ comment that the program consists of a depot release drug of buprenorphine/naloxone, based on weekly injections of a range of doses that can be extended to monthly ones. This implies better pharmacological management and control and greater ease of administration, unlike methadone. Chappuy *et al.*²⁴ support this assertion.

Marco *et al.*¹⁹ and Fuentes *et al.*²⁵ compared the effectiveness of MMPs with other rehabilitation treatments used in the prison setting, and indicate that both methods have obtained similarly favourable results, although they mention some important differences. Both studies showed that inmates treated with buprenorphine are usually more likely to continue with the treatment once they are released. On the other hand, Vera-Remartínez²⁷, states that treatment with buprenorphine/naloxone is safer, thanks to the naloxone in the composition, which is an antagonist for overdoses of opioids and maintains the levels of buprenorphine within therapeutic ranges. For the same reason Soyka *et al.*¹⁴ affirm that, unlike methadone, buprenorphine/naloxone entails a lower risk of overdose and respiratory depression, making the use of this combination safer than methadone.

Salsitz *et al.*¹³ add that buprenorphine/naloxone has a lower incidence of adverse effects related to prolonged QT intervals and reduced libido.

Along the same lines, Vorspan *et al.*²⁶ add another advantage of buprenorphine/naloxone over methadone in dosage adjustment. According to the authors, methadone requires a period of progressive increases of the dosage until the right one is reached in the first weeks of treatment, while buprenorphine/naloxone has just three different doses, making it easier to adapt to the individual. The final significant differences according to Maas *et al.*²⁸ is the difference in price between the two products; methadone is cheaper than buprenorphine, which implies a better cost/effectiveness ratio for methadone.

Some limitations to this study have been identified, such as the lack of recent and useful information about methadone maintenance programs in the Spanish prison setting, and so we recommend more rigorous research to obtain more up to date information and to carry out a better cost/effectiveness balance between the different interventions. Training of professionals in management and safety of this type of therapy is also recommended.

CONCLUSION

After reviewing the bibliography, the conclusion is that MMPs are a widely used interventional approach in Spanish prisons, and that they have been shown to improve inmates' quality of life by reducing the illegal use of opioids and improving their behaviour. However, adverse effects associated with the use of methadone were also observed.

Buprenorphine/naloxone appears to be a better option when compared to methadone because it is safer in cases of overdosing and also reduces some adverse effects. The new extended-release pharmaceutical forms also offer greater patient comfort, avoid misuse of the product and facilitate adherence and reintegration into society once inmates are released.

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