ORIGINAL

Patients' satisfaction and experience in treatment with opioid substitution therapy in Spain. The PREDEPO study

Satisfacción y experiencia de pacientes en tratamiento con sustitutivos opioides en España. Estudio PREDEPO

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Abstract

The aim of this study was to compare patients' satisfaction, experience, objectives, and opinion based on their current opioid substitution therapy (OST) (buprenorphine/naloxone (B/N) or methadone). The PREDEPO study is an observational, cross-sectional, multicentric study performed in Spain. Adult patients diagnosed with opioid use disorder (OUD) receiving OST were included. They were asked to fill in a questionnaire regarding their current OST. A total of 98 patients were enrolled (B/N: 50%, methadone: 50%). Mean age was 47 ± 8 years old and 80% were male. Treatment satisfaction was similar between groups. The most frequently reported factor for being "very/quite satisfied" was "being able to distribute the dose at different times throughout the day" (44% B/N vs. 63% methadone; p = .122). A significantly lower proportion of patients in the B/N group versus the methadone group reported that having to collect the medication daily was "very/quite annoying" (19% vs. 52%, p = .032). Treatment objectives reported by the majority of patients were similar between groups ("not feeling in withdrawal anymore", "reduce/definitely stop drug use", "improve my health", and "stop thinking about using daily") except for "not having money problems anymore" (73% B/N vs. 92% methadone; p = .012). These results suggest there are several unmet expectations regarding current OST. There is a need for new treatments that reduce the burden of OUD, avoid the need for daily dosing, and are less stigmatizing which in turn could improve patient management, adherence and, quality of life.
Key words: opioid use disorder, patient satisfaction, opioid substitution therapy, methadone, buprenorphine/naloxone

Resumen

El objetivo es comparar la satisfacción, experiencia, objetivos y opinión de los pacientes con trastorno por consumo de opioides (TCO) en base a su tratamiento sustitutivo de opioides (TSO) actual (metadona o buprenorfina/naloxona (B/N)). El estudio PREDEPO es un estudio observacional, transversal, multicéntrico desarrollado en España que incluyó pacientes adultos, diagnosticados de TCO y en TSO, quienes contestaron una encuesta sobre su tratamiento actual. Se incluyeron 98 pacientes (B/N:50%, metadona:50%): edad media de 47 ± 8 años y el 80% varones. A nivel de la satisfacción con su tratamiento, los resultados fueron similares entre grupos. El factor "muy/bastante satisfactorio" que se reportó con mayor frecuencia fue "poder repartir las dosis en varios momentos del día" (44% B/N vs. 63% metadona; p = ,122). Se encontraron diferencias significativas en "tener que recoger la medicación diariamente" donde una menor proporción en el grupo B/N contestaron "muy/bastante molesto" versus el grupo metadona (19% vs. 52%, p = ,032). Los objetivos reportados por la mayoría de los pacientes fueron similares entre grupos ("no sentir más síndrome de abstinencia", "disminuir o dejar definitivamente mi consumo de drogas", "mejorar mi estado de salud" y "dejar de pensar en consumir todos los días") excepto en "no tener más problemas de dinero" (72% B/N vs. 92% metadona; p = ,012). Estos resultados evidencian que existen expectativas no cubiertas con los TSO actuales y la necesidad de nuevos tratamientos que disminuyan la carga de la enfermedad, eviten la necesidad de una dosificación diaria y reduzcan el estigma, mejorando así el manejo del paciente, su adherencia y calidad de vida.
Palabras clave: trastorno por consumo de opioides, satisfacción de pacientes, sustitutivo de opioides, metadona, buprenorfina/naloxona

Opioid use disorder (OUD) is a major chronic and complex health problem, characterised by repeated opioid use and frequent relapse (American Psychiatric Association, 2013; Dematteis et al., 2017), potentially leading to medical, social and economic problems for both the individual and society (Canadian Agency for Drugs and Technologies in Health, 2013).

OUD affects millions of people worldwide (World Health Organization, 2018). In the European Union, the prevalence in 2018 of high-risk opioid use among adults was estimated at 1.3 million users (European Monitoring Centre for Drugs and Drug Addiction, 2020) and it is estimated that over 100,000 people die each year as a result of opioid use (World Health Organization, 2018). The prevalence of high-risk opioid use among adults in Spain is estimated to be around 2.2% per 1,000 inhabitants (European Monitoring Centre for Drugs and Drug Addiction, 2019) and in 2017, more than 1,000 deaths due to opioid overdose were reported (Salazar et al., 2020).

OUD is associated with a high rate of morbidity and mortality, with infectious diseases and psychiatric disorders being the most frequent comorbidities (González-Saiz et al., 2011; Mateu, Astasls & Torrens, 2005; Roncero et al., 2016). Many long-term opioid users in Europe engage in polydrug use, so OUD is also associated with drug-related problems such as overdose, crime, unemployment, social exclusion and disadvantage, among others (European Monitoring Centre for Drugs and Drug Addiction, 2020).

Overcoming addiction and reintegrating into society usually requires long-term treatment (Dematteis et al., 2017; European Monitoring Centre for Drugs and Drug Addiction, 2020; Observatorio Vasco de Drogodependencias, 2004; Roncero et al., 2017). Although there are abstinence-based treatments for OUD, pharmacotherapy with opioid substitution treatments (OST) and psychosocial support is recommended (Dematteis et al., 2017), with methadone and a sublingual buprenorphine and naloxone (antagonist) combination (B/N) being the most widely used OST in Spain (Roncero et al., 2015). Both treatments reduce opioid craving, thus allowing better control of psychiatric and organic comorbidities. In addition, they are associated with a reduction in the rate of infectious diseases and hospitalizations, increasing overall survival (Koehl, Zimmerman & Bridgeman, 2019; Sordo et al., 2017; Volkow, Frieden, Hyde & Cha, 2014).

However, lack of adherence and treatment abandonment are common (Calvo et al., 2018; Strang et al., 2017), with a high percentage of patients restarting treatment (European Monitoring Centre for Drugs and Drug Addiction, 2019). Methadone and B/N are daily dosage treatments and require frequent visits by patients to addictive behaviour units or pharmacy services to collect the medication. For many patients, this is a stigmatizing process which limits their freedom and quality of life, making work, vacations, and other everyday activities difficult. Patients with OST thus increasingly want more free time that they can spend on normalizing their lives (Harris & McElrath, 2012; Treloar & Valentine, 2013). To find the most suitable pharmacological strategy, it is important to take into account not only the condition of the patients but also their satisfaction and/or experiences when establishing a treatment. Evaluating patients' experience, as captured by Patient Reported Experiences Measures (PREMs) is thus becoming increasingly important. PREMs assess the perception, satisfaction and/or experience of patients regarding the care, treatment and support received and are therefore an indicator of received care quality and an essential element for medicine and patient-centred research (Alonso-Caballero & Ferrer-Forés, 2017).

Satisfaction with treatment and with the medical care received reflects the degree to which a patient's experience matches their expectations (Iftikhar et al., 2011). Knowing the degree of patient satisfaction is an increasingly used indicator to achieve therapeutic success and improve the quality of life of patients (Florek, Wang & Armstrong, 2018). The objective of this study was therefore to compare the satisfaction, experience, objectives and opinion of patients with OUD based in their current OST (methadona or B/N).

Method

Study design
The PREDEPO study is an observational, cross-sectional and multicentre study carried out in six addiction care centres belonging to the Spanish National Health System in six Autonomous Communities of Spain. This study was approved by the Euskadi Drug Research Ethics Committee (CEIm-E) (Basque Country, Spain) and was carried out in accordance with the Declaration of Helsinki principles regarding medical research on human beings.

Study population
Adult patients were recruited who were diagnosed with OUD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2013), and on OST treatment (with prescription) for OUD, and who provided written informed consent. Patients unable to read and/or understand the questions in the patient diary or informed consent were not included, as were those patients with evident mental dysfunction that could lead to a lack of willingness or inability of the patient to comply with study procedures.

Data Collection
To avoid bias in information gathering, patients were recruited consecutively as they came to their consultation

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appointments until each treatment group was completed. Data collection was carried out between September and October 2020. The researchers from each centre completed a data collection notebook (DCN) retrospectively with sociodemographic and clinical data obtained from the clinical records and computerized records of the centre. For their part, patients filled in a cross-sectional patient diary with questions to give their opinion and experiences regarding their OST.

Design of the DCN and patient diary
A scientific committee was formed which included the president of the Spanish Scientific Society for the Study of Alcohol, Alcoholism and Other Drug Dependencies (SOCIDROGALCOHOL), an expert in health psychology, management and evaluation, and a patient with OUD worked with two members who were expert in health outcomes research on the design of the DCN and the patient diary. In addition, the OUD patient helped in adapting the language of the questions in the patient diary to make them easy to understand for participants.

The patient's diary consisted of fixed-choice questions and various Likert scales. To reveal patients' objectives, a graded Likert Scale with four response options was used, with results grouped according to the level of agreement ["not at all" and "not really" vs. "yes, quite a bit" and "yes, absolutely"]. To determine patient satisfaction with possible situations associated with their OST at the time of the study, a five-step Likert scale was used, with results grouped according to the degree of satisfaction ["very annoying" and "quite annoying" vs. "neither annoying nor satisfying" vs. "quite satisfactory" and "very satisfactory"]. Continuous Likert scales (1-10) were used to determine the degree of patient satisfaction with the care received from the professionals, as well as with the OST at the time of the study and the assessment of its efficacy, with 1 the least positive and 10 the most positive value.

Objectives of the study
The main objective of this study was to compare the satisfaction and experience of patients with OUD based on their current OST (methadone or B/N). The secondary objectives were to determine, based on treatment group, the objectives and opinions of the patients, as well as their sociodemographic and clinical characteristics.

Sample size
The results of this article were obtained from an extension to the main PREDEPO study analysis, which is why the entire methodology, including design, the variables included and sample size was taken from the same study. The necessary sample size for the main PREDEPO analysis was calculated with 10% precision and 95% confidence to estimate the percentage of patients who would be willing to change treatment. This estimate was based on the study by Bendimerad, Kosim and Trojak (2019), in which 53.2% of patients undergoing treatment for OUD were willing to change or modify their treatment. According to these data, 96 patients would be required, to which an additional 10% would be added to cover possible losses, making a total of 106 patients.

Statistical analysis
For the descriptive study, absolute and relative frequencies were calculated for qualitative variables, as well as means and standard deviations for quantitative variables and the 95% confidence interval (CI = 95%) for the result of the main objective. For the inferential analysis comparing the characteristics of the patients according to whether they received methadone or B/N, Pearson's chi-square test was applied on qualitative variables, with Fisher's exact test used in the case of non-compliance with any of its requirements, and Student's T test was used with quantitative variables, assuming normality on exceeding 30 cases per group. The type I error threshold for accepting or rejecting null hypotheses was 5%. Calculations were carried out with R 4.0.4 software.

Results

Study population
Of the 99 patients recruited from the six participating centres, 98 were analyzed (50% on methadone treatment and the other 50% on B/N). One patient on naltrexone was excluded from the analysis for non-compliance with the study selection criteria.

Sociodemographic and clinical characteristics
The sociodemographic and clinical characteristics of the patients included in the study analysis are shown in table 1 and 2, respectively. Patient mean age was 46.9 ± 8.4 years and 79.6% of the participants were men. The rate of HCV infection was found to be significantly lower in patients with B/N compared to those on methadone (2.04% with B/N vs. 22.45% with methadone; p = .002). In addition, the percentage of patients with children was significantly higher in the group with B/N, compared to the methadone group (50.0% with B/N vs. 26.5% with methadone; p = .022) Statistically significant differences were also observed in relation to years in OUD treatment (10.4 ± 7.6 years with B/N vs. 16.7 ± 9.3 years with methadone; p <.001) and the start of OST at the time of the study (4.6 ± 4.2 years with B/N vs. 9.7 ± 8.6 years with methadone; p <.001), as well as in the collection of medication frequency (p <.001), with a higher proportion of patients on methadone collecting the medication with a frequency less than one month (89.8%) compared to patients on B/N (23.40%), most of whom (42.6%) collected the medication monthly (Figure 1).

Table 1
Sociodemographic characteristics

Variable	TOTAL (n=98)	Methadone (n=49)	B/N (n=49)	*p*-value
Age, years				
Mean (DE)	46.9 (8.4)	46.7 (7.7)	47.0 (9.2)	.873
Sex, n (%)				
Male	78 (79.6)	40 (81.6)	38 (77.6)	.616
Female	20 (21.4)	9 (18.4)	11 (22.4)	
Marital status, n (%)				
Single	49 (50.0)	26 (53.1)	23 (46.9)	
Married or with partner	31 (31.6)	16 (32.6)	15 (30.6)	.576
Separated or divorced	18 (18.4)	7 (14.3)	11 (22.5)	
Stable family situation, n (%)				
Has children	37 (37.8)	13 (26.5)	24 (49.0)	**.022**
Stable home situation	70 (71.4)	36 (73.5)	34 (69.4)	.655
Living arrangements, n (%)				
With parents	36 (36.7)	18 (36.7)	18 (36.7)	
With partner	29 (29.6)	16 (32.7)	13 (26.5)	
Alone	27 (27.6)	13 (26.6)	14 (28.7)	.898
Shared flat	2 (2.0)	1 (2.0)	1 (2.0)	
Other	4 (4.1)	1 (2.0)	3 (6.1)	
Level of education, n (%)				
Primary school	54 (55.1)	31 (63.3)	23 (46.9)	
Secondary school	34 (34.7)	13 (26.5)	21 (42.9)	.333
No schooling	7 (7.1)	4 (8.2)	3 (6.1)	
University studies	3 (3.1)	1 (2.0)	2 (4.1)	
Employment, n (%)				
On benefits	48 (49.0)	24 (49.0)	24 (49.0)	
Unemployed	22 (22.4)	13 (26.5)	9 (18.4)	
In work	21 (21.4)	9 (18.4)	12 (24.5)	.666
Unpaid work	3 (3.1)	2 (4.1)	1 (2.0)	
Other	4 (4.1)	1 (2.0)	3 (6.1)	

Note. B/N: buprenorphine/naloxone; SD: standard deviation.

Patient satisfaction with their OST

Figure 2 shows the results of patient satisfaction with possible situations associated with their OST. The factor most frequently reported in both treatment groups as "very or quite satisfactory" was "being able to distribute the doses at different times throughout the day" (44.4%, 12/27 with B/N vs. 63.0%, 17/27 with methadone; p =. 122). The factors that patients reported more frequently as "very annoying" or "quite annoying" in the B/N group was "being able to not take the medication from time to time in order to use illicit substances in other places", "being able to sell the treatment" and "feeling ashamed/stigmatized by having my treatment administration supervised daily". In contrast, the factor that methadone group patients most frequently reported as "very annoying" or "quite annoying" was "having to pick up the medication daily", followed by "having to pick up the treatment frequently (daily, weekly)" and "feeling ashamed/stigmatized by having my treatment administration supervised daily". The only variable where significant differences were found between groups was "having to pick up the medication daily" where a smaller proportion of B/N group patients answered "very annoying" or "quite annoying" compared to the methadone group (19.0%, 4/21 vs. 52.2%, 12/23 p = .032, respectively).

In both treatment groups, patients scored above 8/10 when asked about satisfaction with their OST at the time of the study (8.9/10 with B/N vs. 8.4/10 with methadone; p = .107). Assessment by B/N patients were more positive compared to those of methadone patients both for care received from health professionals (9.2/10 with B/N vs. 8.7/10 with methadone; p = .048), and OST efficacy at the time of the study (9.2/10 with B/N vs. 8.5/10 with methadone; p = .014) (Table 3).

Patient experience with their OST

No statistically significant differences were found between treatment groups when analyzing the experiences of patients with their treatment, although almost twice as many patients with methadone indicated that their circumstances/conditions made it difficult to take their treatment (14.9% with B/N vs. 28.6% with methadone). Most patients in both treatment groups indicated that they never, or rarely, forgot to take their medication (77.1%

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Table 2
Clinical characteristics

Variable	TOTAL (n=98)	Methadone (n=49)	B/N (n=49)	*p*-value
Onset of opioid use, years				
Mean (SD)	21.4 (11.5)	23.1 (11.2)	19.6 (11.6)	.148
Missing values	7	4	3	
Start of first OST, years				
Mean (DE)	13.5 (9.0)	16.7 (9.3)	10.4 (7.6)	**<.001**
Start of current OST, years				
Media (DE)	7.3 (7.2)	9.7 (8.6)	4.6 (4.2)	**<.001**
Nº of previous treatments, n (%)				
1 or more	56 (57.1)	25 (51.0)	31 (63.3)	.640
None	42 (42.9)	24 (49.0)	18 (36.7)	
Stage of current OST, n (%)				
Maintenance	87 (88.8)	45 (91.8)	42 (85.7)	.337
Reduction	11 (11.2)	4 (8.2)	7 (14.3)	
Changes in dosage over the last year, n (%)				
No	70 (71.4)	32 (65.3)	38 (77.6)	.180
Yes	28 (28.6)	17 (34.7)	11 (22.4)	
Dependence on other substances, n (%)				
No dependence	11 (11.2)	3 (6.1)	8 (16.3)	.110
Dependence on 1 or more substances	87 (88.8)	46 (93.9)	41 (83.7)	
Substances, n (%)#				
Tobacco	72 (73.5)	39 (79.6)	33 (67.4)	.170
Cocaine	43 (43.9)	26 (53.1)	17 (34.7)	.067
Cannabis	21 (21.4)	13 (26.5)	8 (16.3)	.218
Anxiolytics	15 (15.3)	9 (18.4)	6 (12.2)	.400
Alcohol	14 (14.3)	6 (12.2)	8 (16.3)	.564
Stimulants	6 (6.1)	3 (6.1)	3 (6.1)	1.000
Organic pathology, n (%)#				
HIV	19 (19.3)	9 (18.4)	10 (20.4)	.798
HCV	12 (12.2)	11 (22.5)	1 (2.0)	**.002**
Lung disorder	9 (9.2)	5 (10.2)	4 (8.2)	1.000
HBV	6 (6.1)	5 (10.2)	1 (2.0)	.111
Heart disease	1 (1.0)	0 (0.0)	1 (2.0)	1.000
Other	10 (10.2)	4 (8.2)	6 (12.2)	.487
Psychiatric comorbidities, n (%)#				
Personality disorder	26 (26.5)	13 (26.5)	13 (26.5)	1.000
Major depressions	18 (18.4)	6 (12.2)	12 (24.5)	.118
Schizophrenia/psychosis	14 (14.3)	5 (10.2)	9 (18.4)	.248
ADHD	5 (5.1)	4 (8.2)	1 (2.0)	.362
Other	7 (7.1)	4 (8.2)	3 (6.1)	1.000
Other treatments, n (%)				
No treatments	26 (26.5)	12 (24.5)	14 (28.6)	.647
One or more treatments	72 (73.5)	37 (75.5)	35 (71.4)	
Treatments, n (%)#				
Anxiolytics/hypnotics	57 (58.6)	31 (63.3)	26 (53.1)	.306
Antidepressants	32 (32.7)	15 (30.6)	17 (34.7)	.667
Antipsychotics	25 (25.5)	12 (24.5)	13 (26.5)	.817
Other	10 (10.2)	4 (8.2)	6 (12.2)	.487

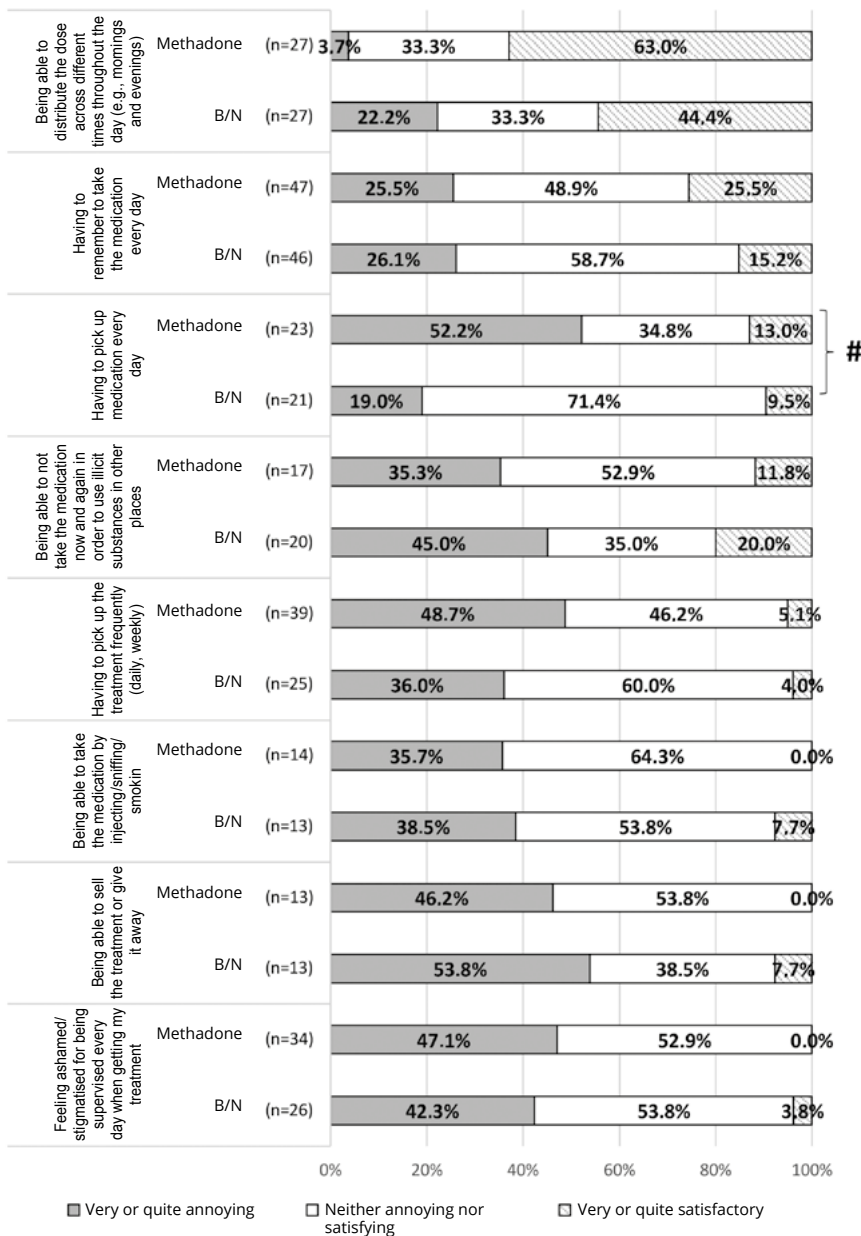*Note.* #Patients could mark more than one option.
ADHD: Attention deficit hyperactivity disorder; B/N: buprenorphine/naloxone; HBV: hepatitis B virus; HCV: hepatitis C virus; HIV: human immunodeficiency virus; OST: opioid substitution treatment; SD: standard deviation.

Figure 1
Frequency of medication collection

Total (n= 98)**

Methadone (n=49)

B/N (n=49)**

■ < Month   □ Monthly   ▨ > Month   ▨ Electronic prescription
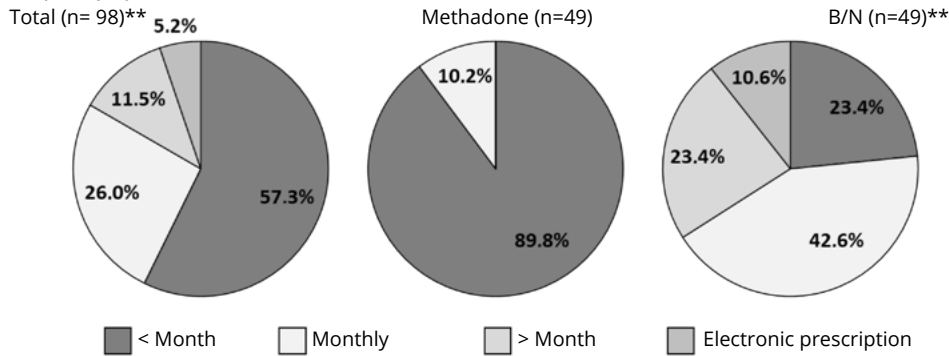
Note. **2 midding values. B/N: buprenorfina/naloxona. Comparison between treatment groups: p-value < 0.001-. Coparison between groups and monthly frequency and < month: p-value <0.001.

Figure 2
Patient satisfaction with their OST

□ Very or quite annoying   □ Neither annoying nor satisfing   □ Very or quite satisfactory

Note. #p = .032. B/N: buprenorphine/naloxone; OST: opioid substitution treatment

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Table 3
Patient experience and satisfaction with OST

Variable	TOTAL (n=98)	Methadone (n=49)	B/N (n=49)	*p*-value
Do you forget to take your medication? n (%)				
No, never or rarely	74 (76.3)	37 (75.5)	37 (77.1)	.855
Yes, sometimes or often	23 (23.7)	12 (24.5)	11 (22.9)	
Missing value	1	0	1	
Have you found yourself in circumstances/conditions which made it difficult or impractical for you to follow your treatment? n (%)				
No, never or rarely	75 (78.1)	35 (71.4)	40 (85.1)	.105
Yes, sometimes or often	21 (21.9)	14 (28.6)	7 (14.9)	
Missing value	2	0	2	
Do you take the prescribed medicine? n (%)				
No, never	1 (1.0)	1 (2.0)	0 (0.00)	
Yes, sometimes	3 (3.1)	1 (2.0)	2 (4.1)	.273
Yes, often	11 (11.2)	3 (6.1)	8 (16.3)	
Yes, always	83 (84.7)	44 (89.8)	39 (79.6)	
What do you do with the medication you don't take on a daily basis? n (%)				
I keep it because I prefer to have reserves for personal use	16 (16.3)	5 (10.2)	11 (22.4)	
I sell it from time to time or regularly	1 (1.0)	1 (2.0)	0 (0.0)	
I prefer to keep some in reserve so I can help someone	3 (3.1)	1 (2.0)	2 (4.1)	.210
It does not apply because I always take the dose of medication that they indicate to me	76 (77.6)	40 (81.6)	36 (73.5)	
Other	2 (2.0)	2 (4.1)	0 (0.0)	
Do you take the medication in one go or distribute it? n (%)				
I always distribute the medication throughout the day	20 (20.4)	13 (26.5)	7 (14.3)	
I often distribute medication throughout the day	5 (5.1)	2 (4.1)	3 (6.1)	
I sometimes spread the medication throughout the day	3 (3.1)	2 (4.1)	1 (2.0)	.579
I rarely distribute medication throughout the day	4 (4.1)	2 (4.1)	2 (4.1)	
I always take my medication in one go	66 (67.3)	30 (61.2)	36 (73.5)	
Satisfaction with the care provided by professionals*				
Mean (SD)	8.9 (1.3)	8.7 (1.5)	9.2 (1.0)	**.048**
Satisfaction with current OST*				
Mean (SD)	8.6 (1.4)	8.4 (1.5)	8.9 (1.3)	.107
Assessment of efficacy of current OST*				
Mean (SD)	8.9 (1.5)	8.5 (1.7)	9.2 (1.1)	**.014**

Note.*Likert rating scale from 1 to 10, with 1 = more negative and 10 = more positive.
B/N: buprenorphine/naloxone; OST: opioid substitute treatment; SD: standard deviation.

with B/N vs. 75.5% with methadone), and always took the prescribed medication (79.6 % with B/N vs. 89.8% with methadone) as well as the prescribed dose. However, 22.5% and 10.2% of patients with B/N and methadone, respectively, indicated that they saved the untaken daily dose to have reserves for their personal use (Table 3).

Patient goals

Stopping the use of all types of opioids, including OST, was something that 80.6% of all patients said they would like to do (73.5% with B/N vs. 87.8% with methadone; p =. 109) (data not shown). No significant differences were found between groups when analyzing patient goals with respect to their OST, except in "not having more money problems" (72.3% with B/N vs. 91.8 with methadone; p = .012). The goals reported by the majority (~90%) of the patients were similar between groups: "no more withdrawal symptoms" (97.9% with B/N vs. 93.9 with methadone), "decrease or definitively stop my drug use" (91.7% with B/N vs. 93.9

with methadone), "improve my health" (89.6% with B/N vs. 91.8% with methadone) and "stop thinking about using every day" (89.6% with B/N vs. 91.8% with methadone) (Figure 3).

Patient opinions about their OST

The opinions of patients regarding their treatments are shown in figure 4. In both treatment groups, most patients indicated that their treatment did not cause increased consumption of alcohol (93.9% with B/N vs. 100% with methadone; p = .106), or of illegal substances (95.6% with B/N vs. 91.8% with methadone; p = .679), or other drugs (91.1% with B/N vs. 83.7% with methadone; p = .280), and that they did not want to continue using (93.2% with B/N vs. 87.7% with methadone; p = .492). Significant differences between treatment groups were only observed when patients were asked if they considered their dose to be lower than needed. Approximately three times more patients with methadone felt that their dose was less than

Figure 3
Patient objectives regarding their OST
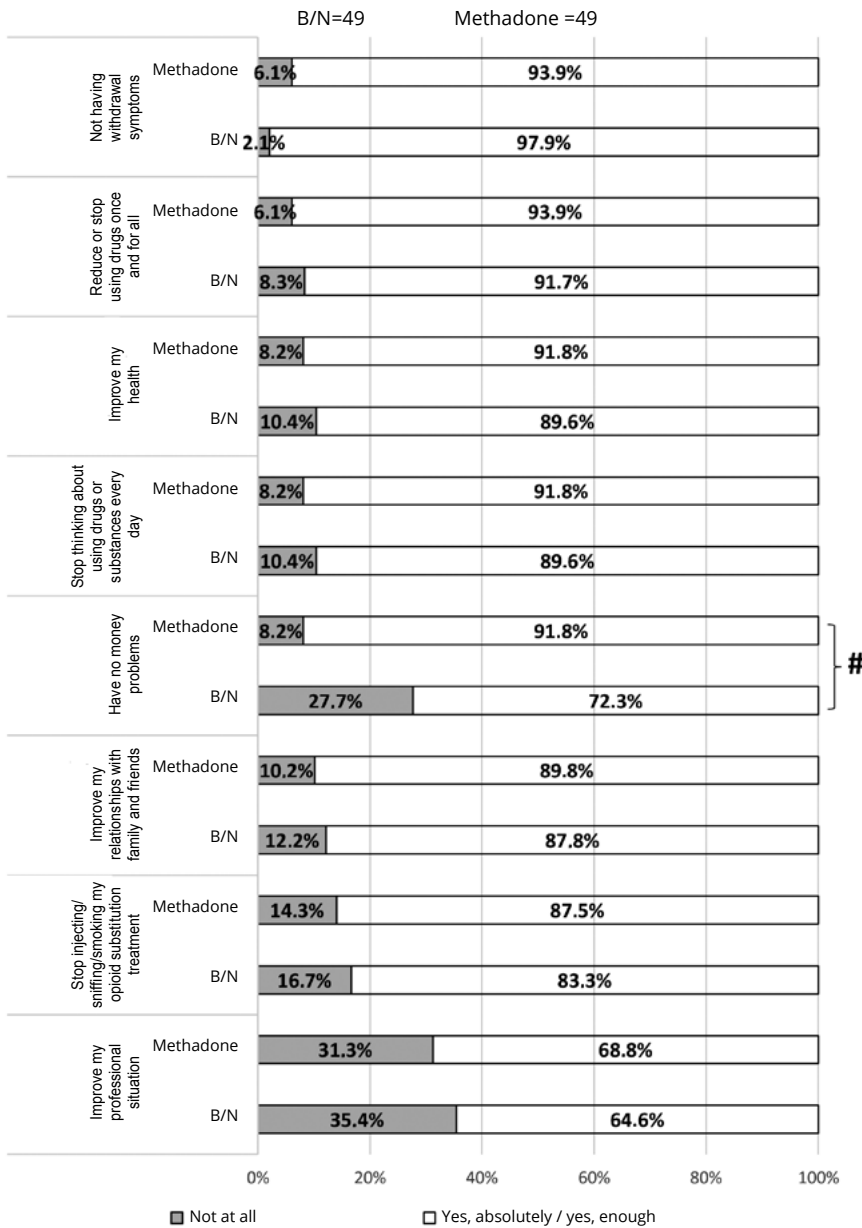
Note. #p = .012. B/N: buprenorphine/naloxone; OST: opioid substitution treatment.

needed, compared to patients with B/N (13.3% with B/N vs. 34.7% with methadone; p = .016).
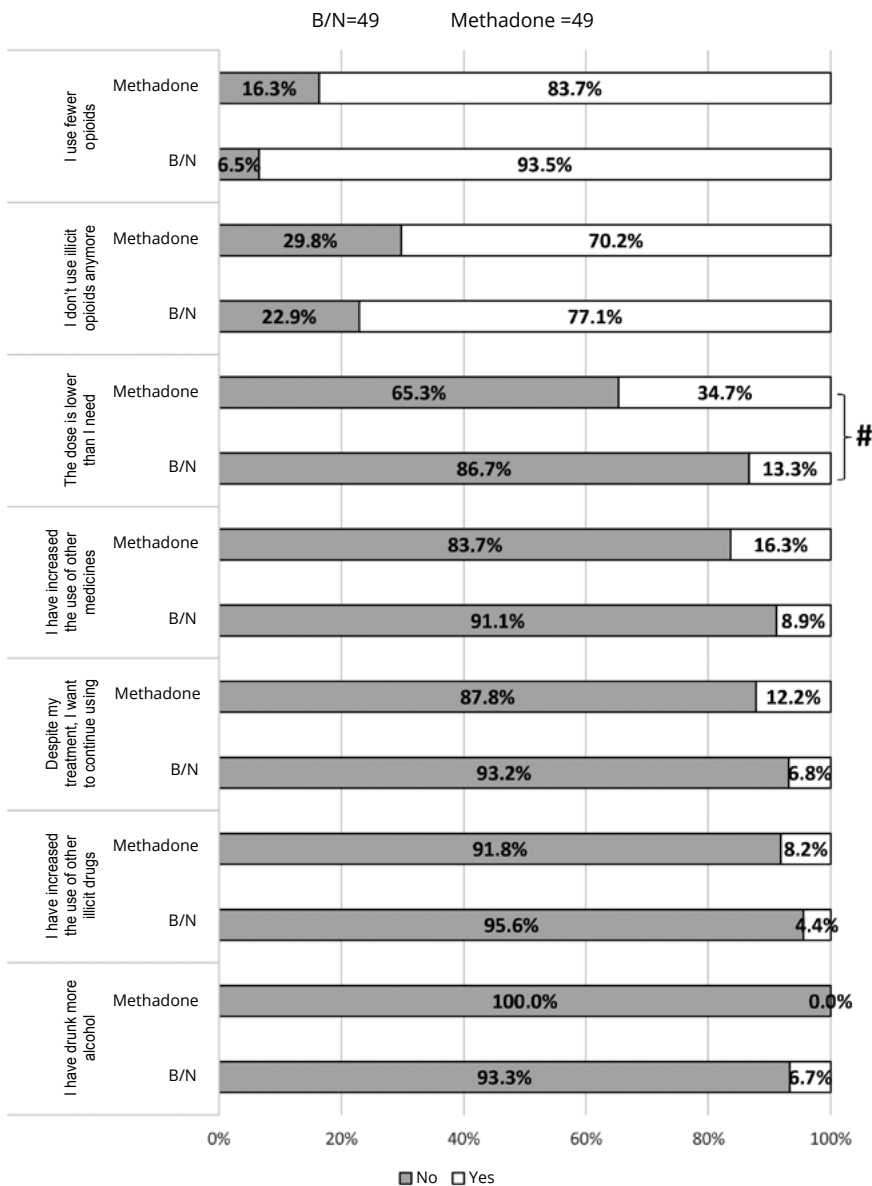
Discussion

This study reports interesting results with regard to treatment satisfaction reported by patients. Aspects such as having to collect the medication daily, stigma, the possibility of consuming illicit opioids during treatment and being able to sell the medication were the most frequently reported reasons for dissatisfaction with their current treatment in both groups of patients (methadone and B/N). Conversely, the reason for the greatest satisfaction was being able to distribute the doses across different times of the day. As far

as the authors are aware, the PREDEPO study is the first in Spain to assess the satisfaction, experience, objectives and opinion of patients with OUD with regard to their treatment depending on the OST prescribed.

The profile of sociodemographic and clinical characteristics was similar to that reported in the national statistics for the population with OUD and OST in Spain, with no large differences observed between treatment groups.

Satisfaction with the received OST appeared to be high, and its efficacy was positively rated in both groups, with scores above 8/10 in both cases. However, based on patient responses, there is evidence of a lack of satisfaction with certain aspects. Approximately 20% to 50% of patients in

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Figure 4
Patients' opinion of their OST

Note. #p = .016; B/N: buprenorphine/naloxone; OST: opioid substitution treatment.

both groups indicated that their current OSTs did not meet their expectations because they had to collect the medication daily or frequently (which also caused embarrassment or made them feel stigmatized in connection with the treatment), the medication could be misused, other illicit substances could be taken occasionally and they had to remember to take the medication on a daily basis. More than 50% of the methadone patients were dissatisfied with

having to pick up the medication daily (more than twice the number of B/N patients). This statistically significant difference was to be expected, since a significantly greater number of patients with methadone (89.9%) collected the medication with a frequency of less than one month, compared to patients with B/N (23.4%).

The need to pick up medication or having to take medication daily is a stigmatizing process for OST patients. This has been reported in other studies in which patients claim that the process of frequent collection and daily dosage of the medication is stigmatizing and, therefore, demand a less frequent dosage of the treatment, which would allow them more free time to normalize both their personal and professional lives (Harris et al., 2012; Neale, Tompkins, McDonald & Strang, 2018; Treloar et al., 2013). The dispensing of treatments at frequently rigid times which are difficult to reconcile with working hours, and dispensing in health centres or in addictive behaviour units where patients with different degrees of addiction coexist would be negative factors for patients who are stabilized

(Socidrogalcohol, 2018). In a study of the opinions of patients with different OST formulations, participants considered that reducing the burden of treatment (both in delivery and administration) would have a series of indirect benefits, such as reduced stigma, improved quality of life and increased time available to complete other life activities (Gilman et al., 2018).

An important limitation of the current OSTs, requiring daily administration, is that the medication can be sold or not taken so that illicit substances can be used from time to time, which results in poor treatment adherence and risk of relapse (Socidrogalcohol, 2018). In this study, around 50% of the patients treated with B/N did not like the fact that they had the possibility of giving away or selling their OST or occasionally being able to stop taking the medication to use illicit substances instead. The need for daily administration with current OSTs, added to the nature of the addiction disorder itself, increases the potential of the drug being abused or used for illicit trafficking, consequently leading to a greater number of relapses (Socidrogalcohol, 2018).

Patients in both groups showed a high predisposition to stop opioid use, including OST (74% with B/N vs. 88% with methadone). In terms of the aim's patients had regarding their treatment, the desire to live without withdrawal symptoms, reduce drug use and improve their health was reported. In addition, a high proportion of patients said they wanted to "have no more money problems" (72% with B/N vs. 92% with methadone). All of the above is in line with results reported in a recent European expert consensus, which recommended that improving physical and mental health, well-being and limiting the social or economic damage for the individual and society associated with the use of illicit drugs were among the treatment goals for these patients (Dematteis et al., 2017).

Most patients reported not forgetting to take the medication, taking the prescribed dose, and not finding it difficult to take. However, this contrasts with published data on lack of adherence in patients with OUD and the high percentage of treatment abandonment, ranging from 23% to 50% of patients treated in outpatient centres for at least four months in severely opioid-dependent patients who had not responded to at least four months of methadone maintenance treatment (McHugh et al., 2013) and 17% to 57% in residential centres over a nine-month period in patients with a DSM-IV diagnosis of substance abuse or lifetime dependence (Samuel, LaPaglia, Maccarelli, Moore & Ball, 2011).

According to these results, patients want to have no more withdrawal symptoms, reduce the number of visits to the centres and the need to take medication every day, stop thinking about using every day, reduce the risk of selling medication and to have the option of not taking the medication to continue using from time to time, and to be able to stop having money problems. Barriers associated with current OUD treatments, along with poor adherence to existing medications, suggest the need for new types of treatments offering advantages over current therapies that reduce the burden of treatment and avoid diversion and misuse, providing another treatment option and increasing the proportion of patients starting a treatment that matches their expectations (Vorspan et al., 2019).

Strengths of this study to be noted are that it was carried out in a context of real clinical practice and with a sample with broad geographic representation across six Autonomous Communities in Spain. Nevertheless, this project has a series of limitations that need to be taken into account. The study used a questionnaire designed specifically for this study based on the one published by Rolland et al. (2021). Other validated questionnaires such as the one by Pérez de los Cobos et al. (2020) were not considered given the very complex population and the authors' awareness that a questionnaire with a specific design could better capture the study information. It would be interesting for further research to carry out a psychometric validation of the questionnaire used to assess its possible applications in other studies. Treatment adherence of the participants was not determined; this would have made it possible to control the results for this factor and could have provided additional information. Although the estimated sample size was reached, it may be that in some of the variables analyzed no significant differences were observed between the treatment groups due to small sample size. Multiple comparisons were not performed by post-hoc procedures in the case of ANOVA to try to reduce the number of comparisons. Given the exploratory or hypothesis-generating nature of the study, it was thought that the most appropriate option was to clarify the objectives of future research. The selection of patients was not carried out randomly, which would have contributed more evidence to the results of the study. Consecutive selection was chosen because it was understood to be more practical for data collection due to the different medication collection periods and the emergency situation resulting from the COVID-19 pandemic.

Conclusion

Based on patient experiences, there appears to be a need for new treatments that address unmet expectations and dissatisfaction with currently available treatments. Patients reported the need for treatments that reduced stigmatization and avoided the need for daily administration; this could potentially improve patient management, adherence to treatment, and quality of life.

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Conflict of interests

References

Alonso-Caballero, J. & Ferrer-Fóres, M. M. (2017). Resultados reportados por los pacientes (PROs). https://fundaciongasparcasal.org/wp-content/uploads/2021/02/Monografia-4-Politica_Resultados-reportados-por-los-pacientes.pdf.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders:* DSM-5. *5th ed.* Washington, DC: APA.

Bendimerad, P., Kosim, M. & Trojak, B. (2019, October). *Patient acceptance and acceptability of a new long-acting form of buprenorphine - AMBRE survey results*. Poster presented at the 14th International Congress of Addiction, Hepatitis and AIDS, Biarritz.

Calvo, F., Carbonell, X., Valero, R., Costa, J., Turró, O., Giralt, C. & Ramírez, M. (2018). Abandono precoz y retención en servicios ambulatorios de drogodependencias: Análisis transversal comparativo de factores que aumentan o disminuyen la adherencia. *Atención Primaria*, 50, 477–485. doi:10.1016/j.aprim.2017.06.006.

Canadian Agency for Drugs and Technologies in Health. (2013). *Rapid response reports. Suboxone® versus methadone for the treatment of opioid dependence: A review of the clinical and cost-effectiveness*. http://www.ncbi.nlm.nih.gov/books/NBK195153/.

Dematteis, M., Auriacombe, M., D'Agnone, O., Somaini, L., Szerman, N., Littlewood, R.,… Soyka, M. (2017). Recommendations for buprenorphine and methadone therapy in opioid use disorder: A European consensus. *Expert Opinion on Pharmacotherapy*, 18, 1987–1999. doi:10.1080/14656566.2017.1409722.

European Monitoring Centre for Drugs and Drug Addiction. (2020). *Informe europeo sobre drogas 2020: Cuestiones clave*. Luxemburgo: Oficina de publicaciones de la Unión Europea. https://www.emcdda.europa.eu/system/files/publications/6343/20174796_TD0117699ESN_PDF.pdf.

European Monitoring Centre for Drugs and Drug Addiction. (2019). *Informe sobre drogas en España 2019*. Madrid: Delegación del Gobierno para el Plan Nacional sobre Drogas. https://www.emcdda.europa.eu/system/files/publications/11353/20190725_InformeDrogasEspana2019_EMCDDA_DGPNSD.pdf.

Florek, A. G., Wang, C. J. & Armstrong, A. W. (2018). Treatment preferences and treatment satisfaction among psoriasis patients: A systematic review. *Archives of Dermatological Research*, 310, 271–319. doi:10.1007/s00403-018-1808-x.

Gilman, M., Li, L., Hudson, K., Lumley, T., Myers, G., Corte, C. & Littlewood, R. (2018). Current and future options for opioid use disorder: A survey assessing real-world opinion of service users on novel therapies including depot formulations of buprenorphine. *Patient Preference and Adherence*, 12, 2123–2129. doi:10.2147/PPA.S180641.

González-Saiz, F., Lozano Rojas, Ó. M., Martín Esteban, J., Bilbao Acedos, I., Ballesta Gómez, R. & Gutiérrez Ortega, J. (2011). Psychiatric comorbidity in a sample of opiate-dependent patients treated with sublingual buprenorphine in a therapeutic community regime. *Revista de Psiquiatría y Salud Mental*, 4, 81–87. doi:10.1016/S2173-5050(11)70013-9.

Harris, J. & McElrath, K. (2012). Methadone as social control: Institutionalized stigma and the prospect of recovery. *Qualitative Health Research*, 22, 810–824. doi:10.1177/1049732311432718.

Koehl, J. L., Zimmerman, D. E. & Bridgeman, P. J. (2019). Medications for management of opioid use disorder. *American Journal of Health-System Pharmacy*, 76, 1097–1103. doi:10.1093/ajhp/zxz105.

Iftikhar, A., Allah, N., Shadiullah, K., Habibullah, K., Muhammad, A. R. & Muhammad, H. K. (2011). Predictors of patient satisfaction. *Gomal Journal of Medical Sciences*, 9, 183-188.

Mateu, G., Astasls, M. & Torrens, M. (2005). Comorbilidad psiquiátrica y trastorno por dependencia de opiáceos: Del diagnóstico al tratamiento. *Adicciones*, 17,111-121.

McHugh, R. K., Murray, H. W., Hearon, B. A., Pratt, E. M., Pollack, M. H., Safren, S. A. & Otto, M. W. (2013). Predictors of dropout from psychosocial treatment in opioid-dependent outpatients. *The American Journal on Addicti*ons, 22, 18–22. doi:10.1111/j.1521-0391.2013.00317.x.

Neale, J., Tompkins, C.N.E., McDonald, R. & Strang, J. (2018). Patient views of opioid pharmacotherapy biodelivery systems: Qualitative study to assist treatment decision making. *Experimental and Clinical Psychopharmacology*, 26, 570–581. doi:10.1037/pha0000217.

Observatorio Vasco de Drogodependencias. (2004). *Perfil del Drogodependiente que no responde a los programas de mantenimiento con metadona*. País Vasco: GABIA. https://www.osakidetza.euskadi.eus/ataria/.

Pérez de Los Cobos, J., Alcaraz, S., Siñol, N., González-Saiz, F., Vergara-Moragues, E., Trujols, J. & Buprenorphine Naloxone Survey Group. (2020). Towards a common metric for assessing heroin-dependent patient satisfaction with medications: Testing methadone and buprenorphine-naloxone. *Drug and Alcohol Dependence*, 212, 108010. doi:10.1016/j.drugalcdep.2020.108010.

Rolland, B., Trojak, B., Nourredine, M., Bachellier, J., Chappuy, M., Bendimerad, P.,… Brousse, G. (2021). Determinants of interest in extended-released buprenorphine: A survey among 366 French patients treated with buprenorphine or methadone. *Drug and Alcohol Dependence*, 220, 108492. doi:10.1016/j.drugalcdep.2020.108492.

Roncero, C., Barral, C., Rodríguez-Cintas, L., Pérez-Pazos, J., Martínez-Luna, N., Casas, M.,… Grau-López, L. (2016). Psychiatric comorbidities in opioid-dependent patients undergoing a replacement therapy programme in Spain: The PROTEUS study. *Psychiatry Research*, 243, 174–181. doi:10.1016/j.psychres.2016.06.024.

Roncero, C., Domínguez-Hernández, R., Díaz, T., Fernández, J. M., Forcada, R., Martínez, J. M.,… Oyagüez, I. (2015). Management of opioid-dependent patients: Comparison of the cost associated with use of buprenorphine/naloxone or methadone, and their interactions with concomitant treatments for infectious or psychiatric comorbidities. *Adicciones*, 27, 179–189.

Roncero, C., Fuster, D., Palma-Álvarez, R. F., Rodríguez-Cintas, L., Martínez-Luna, N. & Álvarez, F. J. (2017). HIV And HCV infection among opiate-dependent patients and methadone doses: The PROTEUS study. *AIDS Care*, 29, 1551–1556. doi:10.1080/09540121.2017.1313384.

Salazar, A., Moreno, S., De Sola, H., Moral-Muñoz, J. A., Dueñas, M. & Failde, I. (2020). The evolution of opioid-related mortality and potential years of life lost in Spain from 2008 to 2017: Differences between Spain and the United States. *Current Medical Research and Opinion*, 36, 285–291. doi:10.1080/03007995.2019.1684251.

Samuel, D. B., LaPaglia, D. M., Maccarelli, L. M., Moore, B. A. & Ball, S. A. (2011). Personality disorders and retention in a therapeutic community for substance dependence. *The American Journal on Addictions*, 20, 555–562. doi:10.1111/j.1521-0391.2011.00174.x.

Sordo, L., Barrio, G., Bravo, M. J., Indave, B. I., Degenhardt, L., Wiessing, L.,… Pastor-Barriuso, R. (2017). Mortality risk during and after opioid substitution treatment: Systematic review and meta-analysis of cohort studies. *BMJ*, 357, 1550. doi:10.1136/bmj.j1550.

Socidrogalcohol. (2018). *Guía de adicciones para especialistas en formación*. Valencia: Socidrogalcohol. https://socidrogalcohol.org/wp-content/Pdf/publicaciones/manuales-guias/guia-adicciones-para-especialistas.pdf.

Strang, J., Reed, K., Bogdanowicz, K., Bell, J., van der Waal, R., Keen, J.,… Knight, A. (2017). Randomised comparison of a novel buprenorphine oral lyophilisate versus existing buprenorphine sublingual tablets in opioid-dependent patients: A first-in-patient phase II randomised open label safety study. *European Addiction Research*, 23, 61–70. doi:10.1159/000456612.

Treloar, C. & Valentine, K. (2013). Examining structural violence in opioid pharmacotherapy treatment in Australia: Sweating the "small stuff" in a liberal paradise. *The International Journal on Drug Policy*, 24, 11–13. doi:10.1016/j.drugpo.2013.04.010.

Volkow, N. D., Frieden, T. R., Hyde, P. S. & Cha, S. S. (2014). Medication-assisted therapies-tackling the opioid-overdose epidemic. *The New England Journal of Medicine*, 370, 2063–2066. doi:10.1056/NEJMp1402780.

Vorspan, F., Hjelmström, P., Simon, N., Benyamina, A., Dervaux, A., Brousse, G.,… Rolland, B. (2019). What place for prolonged-release buprenorphine depot-formulation Buvidal® in the treatment arsenal of opioid dependence? Insights from the French experience on buprenorphine. *Expert Opinion on Drug Delivery*, 16, 907–914. doi:10.1080/17425247.2019.1649252.

World Health Organization. (2018). *Information sheet on opioid overdose*. Ginebra: World Health Organization. https://www.who.int/substance_abuse/information-sheet/en/.