

COVID-19 vaccination coverage and vaccine hesitancy among people with opioid use disorder in Barcelona, Spain.

Running title: COVID-19 vaccination among people with opioid use disorder.

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Abstract

Introduction: People with substance use disorders are considered a priority group for SARS-CoV-2 vaccination as they are at elevated risk of COVID-19 and its severe complications. However, data are scarce about vaccination coverage in a real-world setting.

Methods: A descriptive study was conducted in people with opioid use disorder (OUD) from three public centres for outpatient drug addiction treatment in Barcelona (Spain), who received brief medical advice and were referred to vaccination clinic sites.

Results: Three hundred sixty-two individuals were included: 277 (77%) were men with a mean age of 48.1 ± 8.9 years and 77% were Spanish. Most (90%) participants engaged in polysubstance use and all individuals were on opioid agonist therapy. Psychiatric comorbidity was present in 56% subjects and 32% individuals had ≥ 1 chronic diseases, 30% were infected with HIV and 13% with hepatitis C. There were 258 fully vaccinated individuals (71%; 95%CI:67,76). Age (OR:1.04; CI95%:1.01,1.08; $p < 0.01$) and Charlson Comorbidity Index (OR:1.67; CI95%: 1.11,2.5; $p < 0.01$) were associated with full vaccination. The vaccination hesitancy causes cited were complacency in 53 (51%) individuals, convenience in 40 (39%) and confidence in 11 (10%).

Discussion and conclusions: More than two thirds of our sample of people with OUD were fully vaccinated. Complacency and convenience represented a significant barrier to complete vaccination among people with OUD on opioid agonist therapy referred to vaccination clinic sites. Additional measures are necessary to increase vaccination, especially for younger individuals and those with less medical comorbidity. Integrating vaccination services in drug outpatient centres could be a useful alternative.

Keywords: COVID-19, vaccine, drugs; opioid, hesitancy.

Key points

- More than two thirds of the patients who received brief counselling regarding vaccination were vaccinated.
- Complacency and convenience represented a significant barrier to complete vaccination among people with OUD on opioid agonist therapy referred to vaccination clinic sites.
- Additional measures are necessary to increase vaccination, especially for younger individuals and those with less medical comorbidity.

Introduction

Vaccines against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are an effective means of controlling the clinical impact of the current COVID-19 (coronavirus disease 2019) pandemic, including disease transmission, hospitalisations, deaths, and chronic sequelae [1-4]. A high coverage of COVID-19 vaccines is essential to ensure a successful vaccination program, especially for vulnerable populations [5-6]. However, vaccine hesitancy has led to delay in acceptance or refusal of vaccination despite availability of vaccination services, and is a limiting factor that reduces the effectiveness of vaccination programs, resulting in failure in disease control [7]. Vaccine hesitancy is complex and context-specific, varying across time, place and vaccines [7-9]. In a recent systematic review, the rates of COVID-19 vaccine hesitancy across high-income countries ranged from 7–77.9%, depending on the definitions and populations, with rates of 30% or more in half of the studies conducted [10].

People with substance use disorders are considered a priority group for SARS-CoV-2 vaccination as they are at an elevated risk of COVID-19 and its severe complications, especially those with a recent diagnosis of substance use disorder and opioid use disorder (OUD) [11-13]. However, they are a population characterized by low estimated vaccination coverage for other recommended vaccines, including pneumococcal, diphtheria, tetanus and pertussis vaccine, hepatitis A, hepatitis B and influenza [14-16]. In the case of the COVID19 vaccine, previous studies regarding the vaccine roll-out in developed countries have shown a high prevalence of hesitancy among people with SUD [17-19]. Data from an Australian National Drug Surveillance System showed that only 57% of the people who inject drugs would definitely or probably receive a COVID-19 vaccine if available, which was significantly lower than the 77% observed in the broader Australian population [17]. And less than half of the individuals from a

Californian residential SUD treatment program trusted that a COVID-19 vaccine would be safe and effective [18]. Finally, in an American methadone clinic, one-fifth of the individuals were unwilling to be vaccinated, especially Black subjects [19].

Nevertheless, there are no studies published yet analysing vaccine coverage in a real-world setting among people with SUD. These studies are necessary to determine causes of vaccination hesitancy, identify barriers to vaccination and design additional measures to increase vaccine uptake in a population with a high risk COVID-19 and its severe complications.

Therefore, this study analysed COVID-19 vaccine coverage and causes of vaccination hesitancy among people with OUD who attended an outpatient drug treatment centre in Barcelona (Spain), one of the European cities with the highest incidence of the virus [20].

Methods

This cross-sectional study was conducted in three outpatient treatment centres for drug addiction (CAS: Centro de Atención y Seguimiento a las Drogodependencias: Drug Addiction Attention and Follow-up Centre) located in or near central Barcelona, Spain: CAS Barceloneta, CAS Fòrum Sant Martí and CAS Santa Coloma. The centres are part of the public health system and provide integrated patient care to patients, including medical and psychosocial support, through a multidisciplinary team composed of a psychiatrist, a psychologist, an addiction physician, a social worker, and addiction nurses. More details on the functioning of CAS have been published elsewhere [21].

In Barcelona, SARS-CoV-2 vaccines were freely distributed and coordinated by the local health system (Catalonian Health Service), which is integrated within the Spanish National System Health. The National Vaccination Plan was based on international

recommendations and began on December 27, 2020 with priority populations, including frontline healthcare workers and the elderly and the disabled from residential homes. The following phases included older individuals and younger individuals with underlying medical conditions and high-risk workers, and finally, later phases included people of younger ages [22]. Patients with SUD were referred from the drug outpatient centres to vaccination clinic sites in Barcelona [23]. According to local health authority protocols and vaccine availability, individuals could receive any of the mRNA (Comirnaty, BioNTech/Pfizer Laboratories; Spikevax, Moderna Laboratories) or non-replicating adenovirus vaccines (Vaxzevria, AstraZeneca Laboratories; Vaccine Janssen, Janssen Laboratories) [22-23]. A person was considered fully vaccinated if they had received the two doses of a mRNA vaccine or two or one doses of a recombinant adenovirus according to trademark. Vaccine doses were reported in the local health registry after vaccine administration [22-23].

Brief counselling on COVID-19 vaccine was offered by CAS nurses to all individuals when they came for opioid agonist therapy intake.

Individuals who indicated that they wanted to be vaccinated were referred to vaccination sites via a phone call with the coordination of the vaccination centre.

For the purposes of the study, only the individuals over 18 years of age with OUD, from the three CAS, who were offered the brief counselling on COVID-19 vaccination were included. The inclusion period started after June 2021, the vaccination start date for substance-using populations according to the national vaccination schedule for specific populations, and ended on October 31, when all patients had received counselling and had time to complete the second dose. It was decided to exclude the group of patients with alcohol use disorder receiving care in the CAS because it was a group that basically came from primary care, where they already received medical care that could

have facilitated the use of vaccines. Sociodemographic and clinical information was extracted from the patients' medical records from the CAS and the local health registry, and the data were registered anonymously in the study database. Opioid use disorders, and other psychiatric conditions were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders (5th Edition) [DSM-5]; chronic diseases were diagnosed according to the International Statistical Classification of Diseases and Related Health Problems (ICD) [ICD-10] and grouped into seven conditions: hypertension, diabetes, respiratory, cardiovascular, renal, hepatic and oncologic diseases. Comorbidity was classified using the Charlson Comorbidity Index as low (scoring ≤ 2) or high (> 3).

Hesitancy was defined arbitrarily for this study as a refusal of vaccination despite availability of vaccination services and having received brief counselling on vaccination in the CAS [7]. Causes of vaccine hesitancy were classified as: confidence (mistrust in the effectiveness and safety of vaccines, the system that delivers them, including the reliability and competence of the health services and health professionals and the motivations of policy-makers who decide on the needed vaccines); complacency (a low perceived risk of contracting or severity of the disease being prevented) and convenience (problems in physical availability, affordability and willingness-to-pay, geographical accessibility, ability to understand, appeal of immunization services and time someone has to spend to get vaccinated) [7]. Reasons of hesitancy were registered in the medical records after patients received the brief counselling. A thematic analysis was undertaken to group the causes of hesitancy.

The primary outcome of the study was the rate of vaccination coverage, which was calculated as the number of patients who received a complete COVID-19 vaccination divided by the total number of patients who were offered the vaccination. We examined

associations between the primary outcome and a range of social and clinical factors as well as causes of vaccination hesitancy. Descriptive statistics were expressed as mean and standard deviation for the quantitative variables, and percentages for the qualitative variables. The Mann-Whitney test was used to compare quantitative variables and the Fisher's exact test to compare categorical variable proportions. Multivariate analyses of factors related to vaccination included those which were significant in the bivariate analyses. $p < 0.05$ were considered statistically significant. Statistical analyses were performed using R (3.5.2 version).

The study was approved by the local ethics committee (2020/9355/I, CEIC Parc de Salut Mar, Barcelona).

Results

A total of 362 individuals who were receiving clinical care at the three CAS were included in the study: 49% in CAS Barceloneta, 29% in CAS Santa Coloma and 22% in CAS Forum. Social and substance use characteristics of individuals are shown in Table 1. Most of the individuals were male, middle age Spanish natives, living at home. Half of them had criminal records and three quarters were unemployed.

All individuals with opioid use disorder included in the study had heroin as the main opioid used before seeking treatment and 90% were polysubstance users. The other substances were cocaine, reported as being used by 88% of participants, followed by cannabis (58%) and alcohol (42%). One third of individuals had positive drug urine tests. Half of the individuals had mental disorders and all of them were on opioid agonist therapy: 83% with methadone and 17% with buprenorphine, with a median follow-up of 19.3 (IQR: 12,25) years in drug addiction centres.

One or more chronic medical conditions were observed in 39% of individuals: hypertension in 15%, chronic respiratory diseases in 16%, diabetes in 7%, liver disease in 5%, kidney chronic diseases in 3%, cancer in 3% and vascular diseases in 3%.

Twelve individuals who initially indicated that they would be vaccinated later rejected vaccination (nine because of convenience causes and three because of complacency) and six individuals who initially indicated that they would not accept a vaccine were later vaccinated. Eighteen individuals received the second doses later than indicated (range 12-27 days). Finally, two hundred fifty-eight (71%; 95%CI: 66-76) individuals were fully vaccinated according to the vaccine schedule: 76% individuals with two doses of mRNA vaccine 56% BioNTech/Pfizer Laboratories and 20% Moderna laboratories), 11% with one dose of recombinant adenovirus (Jansen Laboratories) and 9% with two doses of recombinant adenovirus (AstraZeneca Laboratories). The multivariable analyses of factors associated with being fully vaccinated are shown in Table 2. In adjusted analyses, age and the Charlson Comorbidity index were associated with being fully vaccinated, while criminal records, origin and hepatitis C infection, significantly associated in bivariate analyses, were not. Hesitancy vaccine causes are shown in Table 3.

Discussion

The results of this study showed that more than two thirds of people with OUD on opioid agonist, who received a brief counselling on COVID-19 vaccination and were referred to vaccination sites, were fully vaccinated. However, complacency and convenience represented a significant barrier to achieving complete vaccination coverage, especially among younger individuals and those with less medical comorbidity. In addition, the vaccination coverage rate was lower than the 87%

recorded in the general reference population of Barcelona and the end of the inclusion period of the study [24].

Previous studies on vaccine intentions related to the COVID-19 vaccine in developed countries showed an acceptance rate of less than half among people with OUD, mainly related to concerns about vaccine safety [17-19]. The higher vaccination rates in this study may be explained by the fact that people were engaged in opioid agonist therapy, which is a factor that has been associated with increased uptake of other vaccines among people with OUD [16, 25]. In addition, individuals who receive a direct recommendation from a health professional are often reported to be more likely to be vaccinated for other diseases [26-27], as medical recommendations change negative attitudes about vaccine safety concerns [28]. Indeed, safety concerns about COVID-19 vaccine were an unusual reason for vaccination hesitancy in this study. In addition, this study was done after the start of the global vaccination campaign and data on efficacy and safety of the COVID-19 vaccines had already become available, which may have decreased vaccine hesitancy over time.

Vaccination convenience was one of the other main factors associated with hesitancy in the study and this may be related to the method of the vaccine rollout in Barcelona for people with OUD, which was based on referring individuals to vaccination clinic sites from drug addiction centres [22, 23]. Geographical difficulties in accessing the centre, the schedule of the centre and mistrust in healthcare workers underpinned reasons for vaccination convenience in this study. In this regard, fragmentation of clinical care is one of the contributing factors to subject losses during referral and poor outcomes in clinical care [29-32]. So, integrating clinical care and vaccination services in one place may improve vaccination coverage among people with OUD. Integrative models could be located in primary care or infectious disease units as well as in addiction units.

However, the integration at drug addiction centres may offer a model to eliminate structural barriers, where individuals feel more comfortable and less stigmatized and discriminated by healthcare professionals, and schedules are more flexible to suit the patient's needs [29-32].

Finally, vaccination complacency was the other main reason for not being vaccinated in this study, which is a common barrier cited in studies of influenza vaccine hesitancy in people with OUD [14-17]. In the case of COVID-19 vaccines, this finding may be a result of increased public health focus on vaccinating the elderly and populations with underlying chronic conditions [33] and the lack of outreach on COVID-19 vaccination using social media platforms targeting younger populations [10, 34]. By contrast, people with OUD, particularly older people, have a higher prevalence of comorbidities compared to the general population [35, 36], which represent a primary health concern, given the projections regarding the progressive aging of these individuals [37]. Therefore, it is necessary to change the public health message for people with OUD and deliver it through closer and more trusted sources such as drug treatment centres.

However, complacency about vaccination is influenced by many factors, including other life/health responsibilities that may be seen to be more important at that point in time [8-10]. For people with OUD, vaccination complacency could reflect their more immediate concerns relating to substance use, food, housing and legal issues, which are more prevalent in younger adults [38, 39] and highlights the importance of the comprehensive clinical care for people with OUD, including not only medical care, as well as psychosocial support to improve vaccine coverage.

The present study was limited by selection bias where participants were people who voluntarily came to the CAS and were engaged in opioid agonist therapy. Participants who were most concerned for their own medical health and more motivated to get

vaccination could be overrepresented among this cohort, so that results may not be generalisable to other hard-to-reach populations. Importantly information about COVID-19 vaccination was well documented through the review of the local health registry.

Conclusion

The results of this study showed a high rate of vaccine uptake among people with OUD on opioid agonist therapy who received brief counselling on vaccination and were referred to vaccination clinic sites. However, complacency and convenience represented a significant barrier to complete vaccination coverage for people with OUD, which may result in an increased incidence of COVID-19 related morbidity and mortality at both an individual and population level. Given the increasing number of people affected by opioid use disorder [40], additional public health measures are necessary to improve vaccination coverage in this population, particularly among younger individuals and those with less medical comorbidity. Integrating COVID-19 vaccination services in drug addiction centres could be a useful alternative.

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Table 1. Social and clinical characteristics of the 362 participants with opioid use disorder included in the study.

Characteristic	total	vaccinated	non-vaccinated	p
n	362	258	104	
Age (SD) ¹	48.06 (9.25)	49.63 (9.48)	44.15 (7.38)	<0.01
Origin				
Spanish	279(77%)	211 (82%)	68 (65%)	<0.01
non-Spanish	83(23%)	47 (18%)	36 (35%)	
Gender				
male	277(77%)	197 (76%)	80 (77%)	1.00
female	85(23%)	61 (24%)	80 (23%)	
Studies				
primary	237 (65%)	165 (64%)	72 (69%)	0.33
secondary	112 (31%)	85 (33%)	27 (26%)	
tertiary	13 (4%)	8 (3%)	5(5%)	
Housing				
home	294(81%)	211 (82%)	83 (80%)	0.18
shelter	41(1%)	25 (10%)	16 (15%)	
homeless	27(8%)	22 (8%)	5 (5%)	
Employment				
employed	93(26%)	72 (28%)	21 (20%)	0.14
unemployed	269(74%)	186 (72%)	83 (80%)	
Criminal records				
yes	186(51%)	117 (45%)	69 (66%)	<0.01
no	176(49%)	141 (55%)	35 (34%)	
Substance administration				
intravenous	204(56%)	143 (55%)	61 (59%)	0.64
others	158(44%)	115 (45%)	43 (41%)	
Drug urine test				
negative	229(66%)	170 (66%)	59 (57%)	0.48
positive	133(37%)	88 (34%)	45 (43%)	
Mental health disorders				
yes	206(57%)	143 (55%)	63 (60%)	0.41
no	156(43%)	115 (45%)	41 (40%)	
HIV infection				
yes	106(29%)	79 (31%)	27 (26%)	0.44
no	256(71%)	179 (69%)	77 (74%)	
Chronic hepatitis C infection				
yes	46(13%)	27 (11%)	19 (18%)	0.05
no	316(87%)	231 (90%)	85 (82%)	
High Comorbidity*				
no	346 (96%)	243 (94%)	103 (99%)	0.05
yes	16 (4%)	15 (6%)	1 (1%)	
Prior COVID-19				
yes	17(5%)	13(5%)	4(4%)	0.62
no	345(95%)	245(95%)	100(96%)	

Data are presented as No. (%) unless otherwise indicated.¹ Data presented as mean \pm standard deviation.

*According to Charlson Comorbidity Index: scoring <2 for low comorbidity and ≥ 3 for high.

Table 2. Unadjusted and adjusted analyses of factors associated with fully COVID-19 vaccination among the 362 individuals with opioid use disorder included in the study.

Characteristic	Unadjusted analysis		Adjusted analysis	
	O.R.(C.I.95%)	p	OR(C.I.95%)	p
Age (SD) ¹	1.02(1.01,1.1)	<0.01	1.04(1.01,1.08)	<0.01
Spanish	2.37(1.42,3.96)	0.01	1.19(0.63,2.23)	0.59
Male	3.22(2.11,4.92)	1.00		
Studies primary secondary tertiary	1 0.9(0.31,2.37) 1.42(0.84,5.62)	0.33		
Housing home shelter homeless	1 0.82(0.73-2.15) 0.51(0.26-1.78)	0.18		
Employed	1.53(0.88,2.65)	0.14		
Criminal records	0.42(0.26,0.67)	<0.01	0.64(0.37,1.13)	0.12
Intravenous drug use	0.87(0.55,1.39)	0.64		
Positive drug urine test	1.47(0.92,2.34)	0.48		
Mental health disorders	0.81(0.51,1.28)	0.41		
HIV infection	1.25(0.75,2.1)	0.44		
Chronic hepatitis C infection	0.52(0.27,0.98)	0.05	0.82(0.41,1.62)	0.56
Charlson Comorbidity Index	1.53(1.22,2.9)	0.05	1.67(1.11,2.50)	<0.01
Prior COVID-19	1.32(0.42,4.16)	0.62		

Abbreviations: O.R., odds ratio; C.I., confidence interval.

Table 3. Causes of hesitancy vaccine among 104 individuals with opioid use disorder.

Hesitancy	n (%)	Causes (n)
complacency	53(51%)	low perceived risk of COVID-19 (53)
convenience	40 (38.%)	geographical difficulties to access (23) visiting centre schedule (17)
confidence	11 (11%)	mistrust in healthcare workers (6) vaccine safety concerns (5)

Abbreviations: n, number