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Socio-demographic variables affect the management and administration of opioid agonists in patients under medication for addiction treatment during pandemic

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Abstract

The pandemic crisis and the restriction measures applied detrimentally affected several aspects of life of patients under medication for addiction treatment (MAT), potentially influencing the management and administration of methadone and buprenorphine. In total, 444 patients were divided into two groups based on medication and completed an anonymous self-reported Pandemic Medication-Assisted Treatment Questionnaire (PANMAT/Q) to assess the impact of the COVID-19 pandemic on the management and administration of MAT. The findings revealed that “Mood”, “Sociability”, and “Substitute administration and pandemic measures” were affected more in patients taking methadone than in those taking buprenorphine. The variables, namely, “Age”, “Place of residence”, “Years attending MAT”, “Living in high-risk area for SARS-CoV-2 infection” and “Educational status”, were correlated with the dimensions “Mood” and “Sociability”, affecting the substance administration context. Sociodemographic variables play a key role in retention in treatment and prevention of drug-seeking behavior, influencing dimensions that mediate the management and administration of MAT during the pandemic outbreak.

Introduction

Addiction refers to a psychiatric condition that is defined not only as using drugs but also as the loss of control over use (Pelloux et al., 2019) because of reward system activation through dopaminergic nerves (Strathearn et al., 2019). Interestingly, the increase in dopamine levels induced by stimuli that are outcomes of opioid substance use and associated with pleasure leads to memorizing signals announcing the reward and is linked to environmental and psychosocial factors (Schultz, 2015). Recent experimental evidence indicates that the number of patients with opioid use disorders (OUDs) is equal to 40.5 million worldwide (Degenhardt et al., 2019). However, only 25% of patients facing OUDs participate in medication for addiction treatment (MAT) programs (Saloner & Karthikeyan, 2015). Medication for opioid use disorders (MOUD), namely, methadone and buprenorphine, which are critical components of the therapy process (Del Pozo & Rich, 2020), aim to reduce the harmful effects due to heroin use, morbidity and mortality, and illegal activities as well (Timko et al., 2016).

It has been demonstrated that there are several putative obstacles that negatively affect the entrance and adherence of patients to MAT programs and thus hinder or inhibit their beneficial effects on patients with OUDs (Khazaee-Pool et al., 2018). In particular, it has been observed that patients with OUDs tend to offer and acquire illicit substances on the black market (Baillargeon et al., 2021), modifying the recommended MOUD schemes and hence intensifying relapse through craving and misuse (Lambert, 2020). Moreover, economic and health disparities, inadequacy of the supportive environment, homelessness, imprisonment, psychological trauma and stigma have resulted in the adoption of unsafe practices that disturb the management and administration of MOUD (Vasylyeva et al., 2020). Furthermore, specific barriers related to availability, accessibility or acceptability have been found to affect retention to treatment and the risk for relapse, especially in rural areas (Lister et al., 2020).

It appears that this situation is further complicated during pandemic or public health crises through the imposement of social restrictions and health measures by a state. Indeed, patients with OUD seem to be vulnerable to the impact of the COVID-19 pandemic at the psychosocial and medical levels (Harris et al., 2021). As a result, they have an increased risk for relapse and infections such as human immunodeficiency virus (HIV) and hepatitis C virus due to social distancing that is responsible for isolation and stress situations, as well as disruption of harm confinement and accessibility to treatment services (Harris et al., 2021). Additionally, factors including homelessness, increased rates of depression and anxiety are related to social and physical isolation (Columb et al., 2020) and to fear and fear-induced behaviors in the general public (Dong & Bouey, 2020), resulting in increased stress levels that play a key role in drug misuse and relapse (Sinha, 2001). Moreover, parameters that exacerbate the negative impact of pandemic crises, such as social stigma, lack or confinement in the availability of the services (i.e., medical care and psychosocial support) of MAT programs and difficulties in the accessibility (e.g., residence in remote areas) of the patients in MAT programs, negatively affect treatment retention and overdose prevention (Corace et al., 2022; Krawczyk et al., 2022; Lister & Lister, 2021; Nunes et al., 2021; Rosenblum et al., 2011). Anomalies induced by the COVID-19 pandemic, such as the enhancement of stress at the financial level, isolation and fear, exacerbate the social vulnerability of patients under MAT (Bart et al., 2022). Thus, the management of MOUD is modified, the possibilities for craving are increased, and misuse as well relapse are the main outcomes (Lambert, 2020).

Given that the COVID-19 pandemic is a very recent, global public health issue, the evidence that describes its impact on parameters affecting the needs of patients under MAT in such an unstable situation is extremely scarce. However, there is a great need for the acquisition of such information by professionals in MAT programs to avoid patients being at high risk for relapse and fatal drug overdose in an evolving context such as the COVID-19 pandemic. On that basis, this study aimed to apply an already validated instrument, such as the self-reported PANdemic Medication-Assisted Treatment Questionnaire (PANMAT/Q) (Leventelis et al., 2022), to offer insight towards the parameters/dimensions that mediate the management and administration of MAT during the COVID-19 pandemic outbreak in correlation

to sociodemographic variables. It is expected that PANMAT/Q could serve as a valuable tool for patients under MAT to avoid craving and opioid overdose.

Material and methods

Participants

A total of 444 patients attending 54 MAT programs of Organization against Drugs (OKANA), Greece, participated in this investigation. The volunteers were divided into two groups, namely, patients under methadone maintenance treatment (MMT) and patients under buprenorphine maintenance treatment (BMT). All participants were completely informed about the purpose and objectives of the investigation. The confidentiality of personal data was fully ensured, whereas each patient signed a consensus form before enrollment in the study. According to the inclusion criteria, the patients should be over 20 years of age, long-term users of opioid substances suffering from physical and mental dependence, and active members in MAT programs for at least three quarantine periods during the COVID-19 pandemic. Patients with severe psychopathology and serious pathological disorders, which impaired their ability to attend the MAT program, were excluded from the study. All patients anonymously completed the self-reported PANMAT/Q to evaluate the impact of the COVID-19 pandemic on the management and administration of MAT (Leventelis et al., 2022).

Description of the instrument

The PANMAT/Q is consisted of 25 items concerning six dimensions: mood, substance administration and pandemic measures, sociability, accessibility to therapeutic programs, biopsychosocial support by therapeutic programs, and wellness. Through these dimensions, the questionnaire is a valuable and recently validated instrument for the measurement of the impact of the COVID-19 pandemic on the management and administration of MOUD by patients themselves. Each dimension consisted of items referring to the impact of the COVID-19 pandemic on wellness (i.e., physical and mental health), on the mood for concurrent illicit drug use and seeking illegal substances, on the need for biopsychosocial support from programs, on MOUD management and administration (i.e., dose management, dose exchange, changes in the way MOUD has taken, control of overdose, MOUD diversion to black market), on accessibility to therapeutic programs due to restrictive measures applied because of the pandemic (i.e., difficulties in accessibility, feelings of insecurity for MOUD nondaily intake), and on sociability (i.e., social distancing, social isolation, stress, insecurity). Every item is calculated with a 5-point Likert scale ranging from 1 (i.e., not at all) to 5 (i.e., very much). The reliability of the questionnaire was high, as indicated by the value of Cronbach's $\alpha = 0.85$ (Leventelis et al., 2022). Demographic data, including gender, age, educational level, nationality, family status, place of residence, time attending OKANA programs, age at opioid drug use initiation, duration of addictive substance use before MAT, chronic diseases, and inflammation due to SARS-CoV-2 infection, were obtained.

Medications for addiction treatment

The patients were given either methadone hydrochloride solution (10 mg/ml) or buprenorphine tablets (2–8 mg). The mean doses of methadone and buprenorphine were 69.09 mg/24 h and 15.77 mg/24 h, respectively. According to the literature, daily doses of methadone between 40 mg − 100 mg and buprenorphine between 12 mg − 16 mg are considered effective (Saxon et al., 2013).

Ethical considerations

This study was performed in line with the European Union guidelines under the 1975 Helsinki Declaration as revised in 2013 and was approved by the Nursing Department of the University of Peloponnese, Tripoli, Greece, and the scientific committee of OKANA.

Statistical analysis

The dataset is composed of 463 samples from individuals containing a total of 52 different variables. To minimize outliers and ensure statistical integrity, only variables that had less than 50 percent missing values were chosen. Furthermore, for the 51 remaining variables, we had to address misspelling correction, misspelt duplicates of equivalent level in categorical values, and correct and unify the scale and typos for the numeric values. Lastly, identifying entirely wrong values and different symbolism for missing values was done and replaced with the Catholic "NA" (nonapplicable) value and removing samples that had wrong values in multiple variables. The final dataset comprised 444 samples and 51 variables.

Quantitative variables were expressed as the mean values ± standard deviation (SD), and qualitative variables were expressed as absolute and relative frequencies. The Spearman correlation was computed to assess how well the relationship between two variables can be described using a monotonic function. To assess whether a dimension is independent of more than one variable, two-way ANOVA was conducted. The Kruskal-Wallis test, as a nonparametric method, was used to measure the differences between two or more independent

sample groups. All reported p values are two-tailed. Statistical significance was set at $p < 0.05$, and analyses were conducted using R language Version 4 for Statistical Computing.

Results

The sociodemographic data of the 444 patients (76.6% males; 23.6% females) under MAT who participated in this study are presented in Table 1. According to them, their mean age was 44.3 years; their nationality was almost exclusively (97.5%) Greek, most of them were not married (65.8%) and were living in urban areas (82.2%). The mean age at first use was 18.2 years, and the mean duration in MAT programs and drug use was 7.5 and 16.7 years, respectively. Moreover, 15.8% of the participants had been diagnosed with COVID-19, and 39% of them were living in a high-risk area for SARS-CoV-2 infection. Regarding MOUD, 75.2% of the patients were under BMT, and 24.8% of them were under MMT.

Table 1
Sociodemographic data of the participants

Demographic data		MMT N (%)	BMT N (%)
Gender	Females	30 (27.3)	74 (22.1)
	Males	80 (72.7)	260 (77.8)
Educational status	None	0 (0)	6 (1.8)
	Primary school	16 (14.6)	37 (11.1)
	Secondary school	-	-
	Undergraduate studies	-	-
	Postgraduate studies	2 (1.8)	1 (0.3)
Nationality	Greek	110 (100.0)	323 (96.7)
	Other	0 (0)	11 (3.3)
Insurance		82 (74.6)	222 (66.5)
Marital status	Married	27 (24.6)	42 (12.6)
	Unmarried	60 (54.6)	232 (69.5)
	Widowed	3 (2.7)	8 (2.4)
	Divorced	11 (10.0)	41 (12.3)
	Separated	9 (8.2)	11 (3.3)
Work status	Full-time	30 (27.3)	64 (19.2)
	Part-time	8 (7.3)	32 (9.6)
	Temporarily out of work	7 (6.4)	17 (5.1)
	Unemployed	65 (59.1)	221 (66.2)
Place of residence	Urban	101 (91.8)	264 (79.0)
	Rural	9 (8.2)	70 (21.0)
Chronic disease	Diabetes	1 (0.9)	9 (2.7)
	Neoplasmatic disease	4 (3.6)	1 (0.3)
	Cardiovascular disease	6 (5.5)	12 (3.6)
	COPD	12 (10.9)	18 (5.4)
	Systematic disease	2 (1.8)	6 (1.8)
	Other (e.g., HIV, HCV)	29 (26.4)	94 (28.1)
	None	56 (50.9)	194 (58.1)
COVID-19 data	COVID-19 cases	31 (28.2)	39 (11.7)
	Living in high-risk area for SARS-CoV-2 infection	77 (70.0)	96 (28.7)
	Travelled in high-risk area for SARS-CoV-2 infection	5 (4.6)	20 (6.0)

MMT: Methadone maintenance treatment; BMT: Buprenorphine maintenance treatment;

COPD: Chronic obstructive pulmonary disease; HIV: Human immunodeficiency virus;

HCV: Hepatitis C virus

Demographic data	MMT N (%)	BMT N (%)
	MMT Mean (SD)	BMT Mean (SD)
Age	48.9 (7.9)	42.9 (7.8)
Years in OKANA	10.3 (6.4)	6.7 (4.8)
Age at first use	19.3 (6.2)	17.8 (4.8)
Years of drug use (before admission in OKANA)	18.2 (0)	16.2 (0)
MMT: Methadone maintenance treatment; BMT: Buprenorphine maintenance treatment;		
COPD: Chronic obstructive pulmonary disease; HIV: Human immunodeficiency virus;		
HCV: Hepatitis C virus		

Figure 1 presents the relative percentages of answers in each dimension for each substitute (i.e., MMT and BMT) discretized as “High”, “Med”, and “Low”. The relative percentages depict the percentage of answers for every dimension that had either high, medium, or low values on the Likert scale (“High”: 4,5; “Med”: 3; “Low”: 1,2) of the questionnaire. The dimensions “Mood”, “Sociability”, and “Substitute administration and pandemic measures” showed very different distributions of answer values between those who were administered MMT and those with BMT. In particular, the patients under MMT were able to better handle the impact of the COVID-19 pandemic, as the results indicated in the three aforementioned dimensions. Most notable examples were the answers for “Sociability”, wherein those that were under MMT had a unimodal distribution in their answer range, while those under BMT had multimodal distributions. Moreover, “Substitutes administration and pandemic measures” in the MMT patients had a multimodal distribution in their answer range, whereas those under BMT had a unimodal distribution. Furthermore, Fig. 1 presents Boxplots with respect to a selection of Varimax dimensions. Varimax rotation is an orthogonal rotation yielding factor that has significant loadings only on a subset of variables. Each boxplot represents the distribution of the projected samples onto the corresponding varimax coordinates. A Boxplot depicts the median (horizontal lines) value, inner-quartile range of 50% of values (boxes), and the values outside of the 50% middle (whiskers). The above observations were further confirmed when we conducted Kruskal-Wallis tests for the distributions of the two groups. The results of the tests concluded that the aforementioned groups regarding the dimensions “Mood”, “Sociability”, and “Substitutes administration and pandemic measures” had statistically significant different distributions with p-values < 0.05 and < 0.01, respectively. The results of the Kruskal-Wallis tests are also used to depict those differences in Fig. 2, illustrating the mean values, inner-quartile (50% of all samples) range and outliers for the PANMAT dimensions for each group of substitutes.

Table 2depicts the association between the dimensions of the questionnaire and the obtained demographic variables. According to the results, statistically significant positive correlations were observed between the dimension “Substance administration and pandemic measures” and the demographic variables “Age”, “Years in OKANA” and “Living in high-risk area for SARS-CoV-2 infection”, whereas negative correlations were observed for the demographic variables “Place of residence” and “Travelled in high-risk area for SARS-CoV-2 infection”. Moreover, there were statistically significant negative correlations between the dimension “Biopsychosocial support from therapeutic programs” and “Age” as well as “Years in OKANA”. Finally, the dimension “Mood” was significantly positively correlated with “Educational status”, “COVID-19 cases” and “Place of residence” and was negatively correlated with “Security”.

Table 2
Correlations between demographic variables and questionnaire dimensions

		Questionnaire dimensions					
Demographic variables		Substitute administration and pandemic measures	Biopsychosocial support	Mood	Wellness	Sociability	Accessibility to the therapeutic programs
Gender	r	-0.064	-0.039	-0.050	-0.015	0.001	-0.013
	p	0.17	0.41	0.29	0.74	0.97	0.77
Age	r	**0.098**	**-0.110**	0.017	-0.034	0.060	0.014
	p	**0.03**	**0.02**	0.71	0.46	0.20	0.76
Educational status	R	0.034	-0.011	**0.148**	0.04	-0.002	-0.031
	p	0.47	0.81	**0.001**	0.34	0.95	0.50
Nationality	r	0.004	-0.036	0.011	0.018	-0.053	0.059
	p	0.91	0.43	0.81	0.70	0.25	0.21
Security	r	0.025	-0.039	**-0.114**	0.029	-0.073	-0.036
	p	0.58	0.40	**0.01**	0.53	0.12	0.43
Marital status	r	-0.016	0.037	0.081	-0.075	0.049	0.016
	p	0.73	0.43	0.08	0.11	0.29	0.72
Work status	r	-0.048	-0.048	-0.026	0.058	-0.037	-0.067
	p	0.31	0.31	0.57	0.22	0.43	0.15
Place of residence	r	**-0.137**	0.074	-0.033	-0.055	-0.086	0.027
	p	**0.003**	0.11	0.47	0.24	0.06	0.56
Chronic disease	r	-0.059	0.067	0.039	-0.011	-0.041	0.044
	p	0.21	0.15	0.40	0.81	0.38	0.34
Years in OKANA	r	**0.127**	**-0.129**	0.036	-0.041	0.079	-0.040
	p	**0.007**	**0.006**	0.43	0.38	0.09	0.39
Age at first use	r	0.044	-0.010	0.058	-0.009	0.011	-0.0003
	p	0.34	0.82	0.21	0.83	0.81	0.99
Years of drug use (before admission in OKANA)	r	0.005	-0.030	-0.003	-0.029	-0.005	0.031
	p	0.90	0.52	0.94	0.53	0.90	0.50
COVID-19 cases	r	0.010	-0.013	**0.114**	0.083	0.083	0.033
	p	0.82	0.77	**0.015**	0.07	0.07	0.48
Living in high-risk area for SARS-CoV-2 infection	r	**0.132**	-0.047	**0.107**	0.075	0.041	-0.032
	p	**0.005**	0.31	**0.02**	0.11	0.38	0.49
Travelled in high-risk area for SARS-CoV-2 infection	r	**-0.107**	-0.023	0.030	-0.014	0.059	-0.022
	p	**0.02**	0.61	0.51	0.76	0.21	0.63

r: Spearman's rank coefficient; p: Statistical significance level < 0.05

The associations between the obtained demographic variables and the dimensions of the questionnaire divided on the basis of MMT and BMT groups are presented in Table 3. In the MMT group, statistically significant positive correlations were observed between the dimension

of “Biopsychosocial support from therapeutic programs” and the variables “Years in OKANA” and “Travelled in high-risk area for SARS-CoV-2 infection”, whereas the aforementioned dimension was negatively correlated with “Chronic disease”. Furthermore, “Mood” was positively correlated with “COVID-19 cases”, while negative correlations between “Sociability” and “Educational status” as well as between “Accessibility” and “Security” were found. Regarding the results of the BMT group, the dimensions “Substitute administration and pandemic measures” and “Biopsychosocial support from therapeutic programs” were negatively correlated with “Travelled in high-risk areas for SARS-CoV-2 infection”. Moreover, “Mood” was positively correlated with “Educational status” and “Living in high-risk area for SARS-CoV-2 infection” and negatively correlated with “Security”. Finally, “Wellness” was positively correlated with “Work status”.

Table 3
Correlations between demographic variables and questionnaire dimensions grouped by medications for opioid use disorders (MOUD)

		Questionnaire dimensions											
Demographic variables		Substitute administration and pandemic measures		Biopsychosocial support		Mood		Wellness		Sociability		Accessibility to the therapeutic programs	
		MMT	BMT	MMT	BMT	MMT	BMT	MMT	BMT	MMT	BMT	MMT	BMT
Gender	r	-0.033	-0.052	0.032	-0.075	-0.068	-0.034	0.106	-0.041	0.064	0.006	0.073	-0.039
	p	0.72	0.33	0.73	0.17	0.47	0.52	0.26	0.44	0.50	0.90	0.44	0.47
Age	r	0.009	-0.043	-0.094	-0.090	0.032	-0.041	-0.100	-0.056	-0.088	-0.025	0.108	0.006
	p	0.92	0.42	0.32	0.10	0.73	0.45	0.29	0.3	0.35	0.64	0.26	0.90
Educational status	r	-0.021	0.0019	0.017	-0.014	0.178	**0.118**	-0.016	0.058	**-0.180**	0.002	-0.042	-0.026
	p	0.82	0.97	0.85	0.78	0.06	**0.03**	0.86	0.28	**0.05**	0.95	0.65	0.62
Nationality	r	NA	0.0473	NA	-0.051	NA	0.025	NA	0.027	NA	-0.033	NA	0.063
	p	_+	0.389	-	0.34	-	0.64	-	0.61	-	0.54	-	0.25
Security	r	-0.128	0.089	-0.140	-0.002	-0.084	**-0.123**	0.017	0.035	-0.119	-0.061	**-0.200**	0.003
	p	0.18	0.10	0.14	0.96	0.38	**0.02**	0.85	0.52	0.21	0.26	**0.03**	0.95
Marital status	r	-0.083	0.013	0.116	-0.001	0.051	0.096	-0.073	-0.077	0.125	0.036	0.057	0.004
	p	0.38	0.80	0.22	0.97	0.59	0.07	0.44	0.15	0.19	0.51	0.55	0.93
Work status	r	-0.093	0.005	-0.135	-0.008	-0.007	-0.016	-0.085	**0.106**	-0.089	0.006	-0.100	-0.061
	p	0.33	0.92	0.15	0.87	0.93	0.76	0.37	**0.05**	0.35	0.90	0.29	0.26
Place of residence	r	-0.059	0.074	0.033	-0.038	0.008	-0.030	0.111	-0.068	-0.001	0.007	0.027	0.013
	p	0.57	0.173	0.73	0.48	0.93	0.57	0.24	0.20	0.99	0.88	0.77	0.80
Chronic disease	r	-0.122	0.005	**0.211**	-0.001	0.126	0.026	-0.103	0.021	0.079	-0.042	0.083	0.034
	p	0.20	0.92	**0.02**	0.98	0.18	0.63	0.28	0.69	0.41	0.44	0.38	0.52
Years in OKANA	r	-0.002	0.018	**-0.200**	-0.070	-0.074	0.033	-0.101	-0.063	-0.032	0.001	0.014	-0.052
	p	0.98	0.73	**0.03**	0.19	0.43	0.53	0.29	0.25	0.73	0.97	0.88	0.34
Age at first use	r	-0.006	-0.003	-0.028	0.012	0.076	0.028	-0.053	-0.011	-0.042	-0.023	-0.006	0.005
	p	0.94	0.95	0.76	0.82	0.42	0.59	0.57	0.83	0.66	0.66	0.94	0.92
Years of drug use	r	0.002	-0.045	-0.067	-0.009	0.051	-0.036	0.063	-0.058	-0.115	-0.021	0.082	0.022
(before admission in OKANA)	p	0.97	0.40	0.48	0.85	0.59	0.51	0.50	0.28	0.22	0.70	0.39	0.68
COVID-19 cases	r	-0.095	-0.067	0.015	-0.007	**0.241**	0.022	0.004	0.092	0.075	0.013	0.040	0.039
	p	0.32	0.22	0.87	0.88	**0.01**	0.68	0.96	0.09	0.43	0.81	0.67	0.46
Living in high-risk area for SARS-CoV-2 infection	r	-0.051	-0.004	-0.068	-0.005	-0.115	**0.131**	-0.030	0.065	-0.019	-0.089	-0.077	-0.011
	p	0.59	0.93	0.47	0.92	0.22	**0.01**	0.74	0.23	0.83	0.10	0.42	0.83
Travelled in high-risk area	r	-0.032	**-0.126**	**0.226**	**-0.111**	-0.151	0.091	-0.104	0.007	0.173	0.050	-0.064	-0.014

r: Spearman's rank coefficient; p: Statistical significance level; NA: Not applicable; +: Not calculated due to no distribution

		Questionnaire dimensions											
for SARS-CoV-2 infection	p	0.70	**0.02**	**0.01**	**0.04**	0.11	0.09	0.27	0.88	0.06	0.35	0.50	0.79

r: Spearman's rank coefficient; p: Statistical significance level; NA: Not applicable; +: Not calculated due to no distribution

Furthermore, concerning the dimensions of the association of the questionnaire dimensions with each substance (i.e., MMT and BMT) grouped in COVID-19 cases and healthy patients, statistically significant positive correlations were observed only in the dimension "Accessibility to the therapeutic programs" with BMT patients and non-COVID-19 patients (as well as with all patients) (Table 4).

Table 4
Correlations between the dimensions of the questionnaire and the substance received grouped in COVID-19 cases and healthy patients.

Questionnaire dimensions		MMT	BMT	All patients	Covid-19 cases	Non-COVID-19 patients
Substitute administration and pandemic measures	r*	-0.015	-0.038	-0.002	0.045	-0.012
	P**	0.87	0.48	0.96	0.71	0.81
Biopsychosocial support	r	0.022	0.074	0.052	0.050	0.052
	P	0.81	0.17	0.27	0.67	0.31
Mood	r	-0.058	-0.003	-0.011	-0.092	0.008
	P	0.54	0.95	0.81	0.44	0.87
Wellness	r	-0.116	0.002	-0.018	-0.052	-0.011
	P	0.22	0.95	0.69	0.66	0.83
Sociability	r	0.025	-0.083	-0.034	0.09	-0.057
	P	0.79	0.12	0.46	0.42	0.26
Accessibility to the therapeutic programs	r	0.087	**0.120**	**0.108**	0.136	**0.103**
	P	0.36	**0.02**	**0.02**	0.26	**0.04**

r: Spearman's rank coefficient; p: Statistical significance level < 0.05

Discussion

The present study approached the issue of the impact of the COVID-19 pandemic, which has led to date to three quarantine periods and to restriction measures characterized by social distancing and housing isolation, on the management and administration of received MOUD by patients under MAT. The main findings indicate that the management and administration of MOUD by patients themselves during prolonged periods of quarantine were affected by sociodemographic variables, such as "Age", "Educational status", "Place of residence", "Security level" and "Years in OKANA", as indicated through alterations in the dimensions "Substitute administration and pandemic measures", "Mood" and "Biopsychosocial support" and "Accessibility to the therapeutic programs". Furthermore, patients under MMT were able to cope with dimensions "Mood", "Sociability" and "Substitute administration and pandemic measures" compared to their BMT counterparts.

According to the literature, patients with OUDs have been affected by the COVID-19 pandemic and subsequent restriction measures to a great extent, experiencing increased stress, loneliness, and insecurity, as well as serious health concerns due to opioid use (Tracy et al., 2021). Furthermore, factors that exacerbate the negative impact of COVID-19, such as social stigma, lack or restriction in the availability of MAT program services (i.e., medical care and psychosocial support), and residency in rural areas, appear to have a negative impact on treatment retention and overdose prevention (Corace et al., 2022; Krawczyk et al., 2022; Lister & Lister, 2021; Nunes et al., 2021; Rosenblum et al., 2011). Moreover, changes in mood are directly linked to factors such as stress and craving and could potentially encourage members of a vulnerable group (e.g., OUD patients) to use alcohol or drugs to cope with the COVID-19 pandemic (Taylor et al., 2021). Additionally, changes in mood state were observed in BMT patients, which is in line with recent results prior to the pandemic era in OUD patients. These

changes were positively related to educational status and negatively related to security level, whereas higher educational status was accompanied by enhancement in mood for seeking drug substances and parallel illicit drug use in BMT patients. The insecurity was linked to mood, a result that is in agreement with research findings that have indicated the relation of bad mood with the administration and retention in treatment leading BMT patients to dropout from MAT programs (Hser et al., 2014; Mattick et al., 2014; Panlilio et al., 2019). However, to our knowledge, herein is presented for the first time relevant evidence regarding patients under MAT during the COVID-19 pandemic.

Conversely to BMT patients, pandemic restriction measures seem to affect MMT patients to a greater extent in the PANMAT/Q dimensions “Substitute administration and pandemic measures”, “Biopsychosocial support from the therapeutic programs”, “Sociability” and “Accessibility to therapeutic programs”, which are correlated to variables, namely, “Educational status”, “Security”, “Chronic disease” and “Years in MAT programs”. These findings indicate that MMT patients can more efficiently cope with the intention often encountered in patients to self-manage their substitute administration under stressful periods that can easily lead to overdose risk. Similarly, the dimension “Accessibility to the therapeutic programs” was related to the magnitude of the buprenorphine dose. In particular, the patients receiving higher doses faced more intense accessibility difficulties. In this context, it has been implied that financial stressors, social isolation and disruptions in the MOUD supply chain increase the social vulnerability of patients under MAT, leading to MOUD manipulation and poor outcomes of the medication (Bart et al., 2022).

The findings of the present study have revealed that many stressors and social variables potentially lead to manipulation of the MOUD by patients themselves, which is in line with recent data that have demonstrated increased dispensation of MOUD during the COVID-19 pandemic (Haggerty et al., 2022). Indeed, barriers to retention on treatment, including stigma, lack of treatment availability and lack of biopsychosocial support, led to drug-seeking behaviors and dropout from MAT programs (Nunes et al., 2021).

Although methadone and buprenorphine are key substances widely applied as treatments in OUD patients, lowering craving, stress and depression, MAT patients were marked with high levels of psychological consequences that provoked social disruptions during an outbreak such as the COVID-19 pandemic (Liu et al., 2021). The adverse effects of stress are mediated through the reward system, leading to the activation of biological factors (i.e., corticotrophin-releasing factor, cortisol, pro-inflammatory agents), which promote the development of negative emotions interrupting the decision-making process and increasing the risk for relapse and overdose (Bardo et al., 2021; Liu et al., 2021; Ruisoto, & Contador, 2019). Research findings imply that there is an underpinned relationship between drug dependence and environmental factors interacting with psychoendocrine systems, as these systems have been demonstrated to be more sensitive to social disruptions with a dysregulation of hippocampal glucocorticoid receptors (Ajonijebu et al., 2017; Fattore & Melis, 2016). Furthermore, the interaction between socioeconomic level and DNA alterations has been demonstrated and indicates the impact of environmental stimuli on the physiological and behavioral responses related to drug-seeking regimens (Ajonijebu et al., 2017). It has been shown that craving and drug-seeking behavior that are triggered by social factors, such as social isolation, induce neurogenic changes in the function of domanimergic and serotonergic systems that potentially lead to modified neurotransmission (Araujo et al., 2005; Matsuda et al., 2001), affecting retention on treatment and increasing the risk for relapse.

Indeed, the COVID-19 pandemic is not the first extreme situation with a severe impact on MAT patients and services. Previous studies have shown that natural disasters, socioeconomic and health crises were correlated with disrupted MAT services, the emergence of barriers confining access of the patients to clinical settings and the lack of clinical planning resulted in increased drug use, especially when medication access was interrupted (Bart et al., 2022; Maxwell et al., 2009; Pouget et al., 2015). Of note, extreme or disastrous situations are accompanied by disruptions in several social parameters whose consequences last for many years, influencing vulnerable populations in their societal progress or integration (Friedman et al., 2006).

Several aspects of our study may limit the generalizability of the findings. First, there was a difference in the population of MMT and BMT patients. Second, our sample lacked racial diversity (most of them were Greek) and adult participation. Finally, the results related to MOUD manipulation did not intersect with urine results to exclude concurrent illicit drug use.

Conclusions

The findings of the present study revealed that sociodemographic variables, especially educational, work and marital status, place of residence and years in MAT programs, are key factors affecting retention in treatment and prevention of drug-seeking behavior, influencing dimensions that mediate the management and administration of MOUD during the COVID-19 pandemic crisis. Furthermore, accessibility to MAT programs, patient mood, and social distancing along with insecurity seem to be the main factors that are directly related to medication management by patients themselves. These parameters have a high impact on treatment retention and MOUD manipulation, thus potentially leading to craving and relapse. On that basis, it appears that both psychosocial support, as it is associated with higher

retention and treatment completion (Dobkin et al., 2002), and improvement in MOUD administration play a pivotal role in the prevention of drug-seeking behaviour and substance dispersion.

Declarations

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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Figures

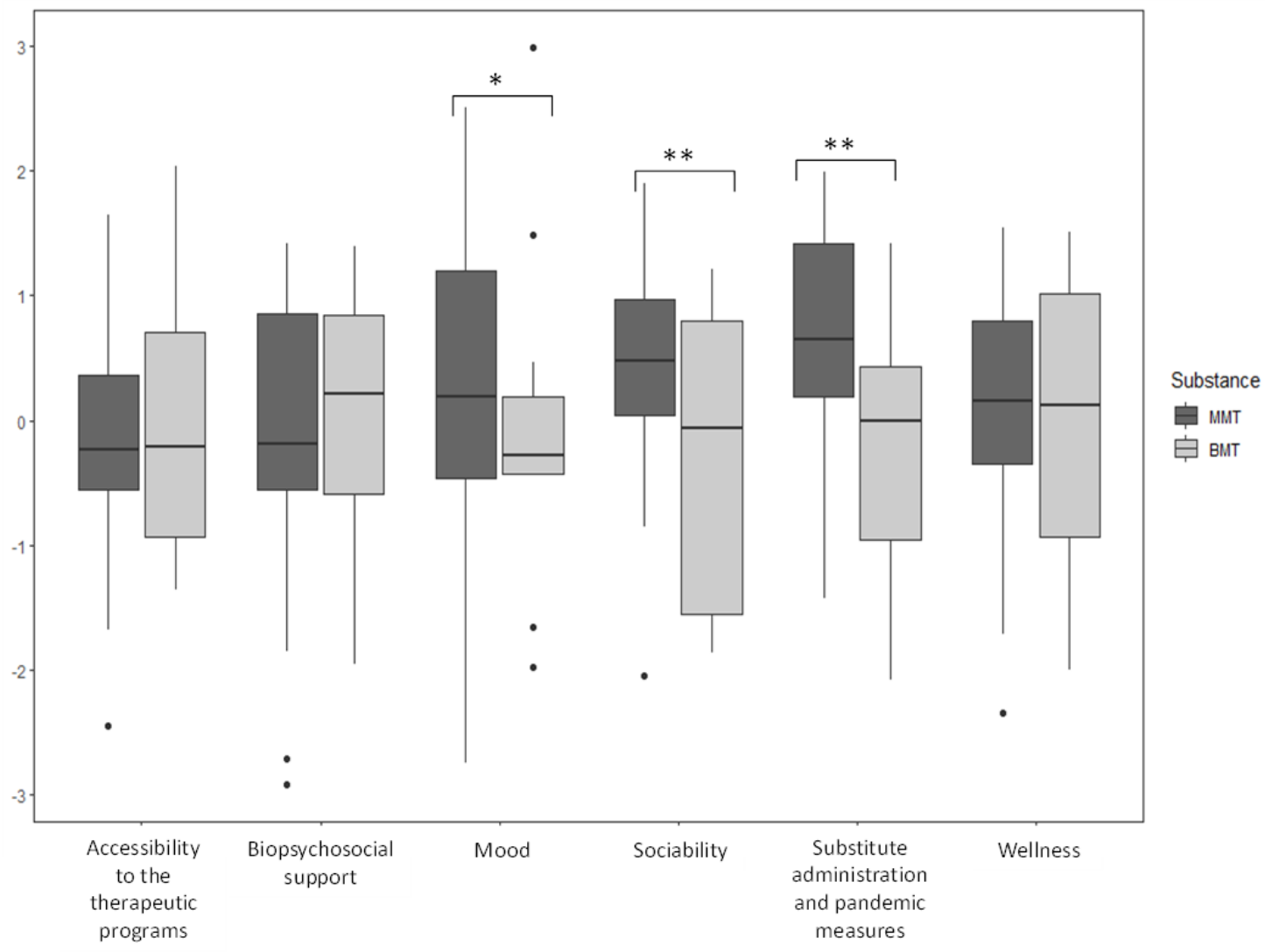

Figure 1

Boxplots with respect to each Varimax dimension and substance.

This figure presents the distribution characteristics of the substance admission groups (i.e., MMT, BMT) on the Varimax rotated Principal Components linear transformation, namely, the dimensions of PANMAT (Leventelis et al. 2022). Each dimension name represents the corresponding subset of variables.

*, ** Statistically significant difference between the two medication substances, i.e., methadone (methadone maintenance treatment, MMT) and buprenorphine (buprenorphine maintenance treatment, MMT) (p<0.05 and p<0.001, respectively).

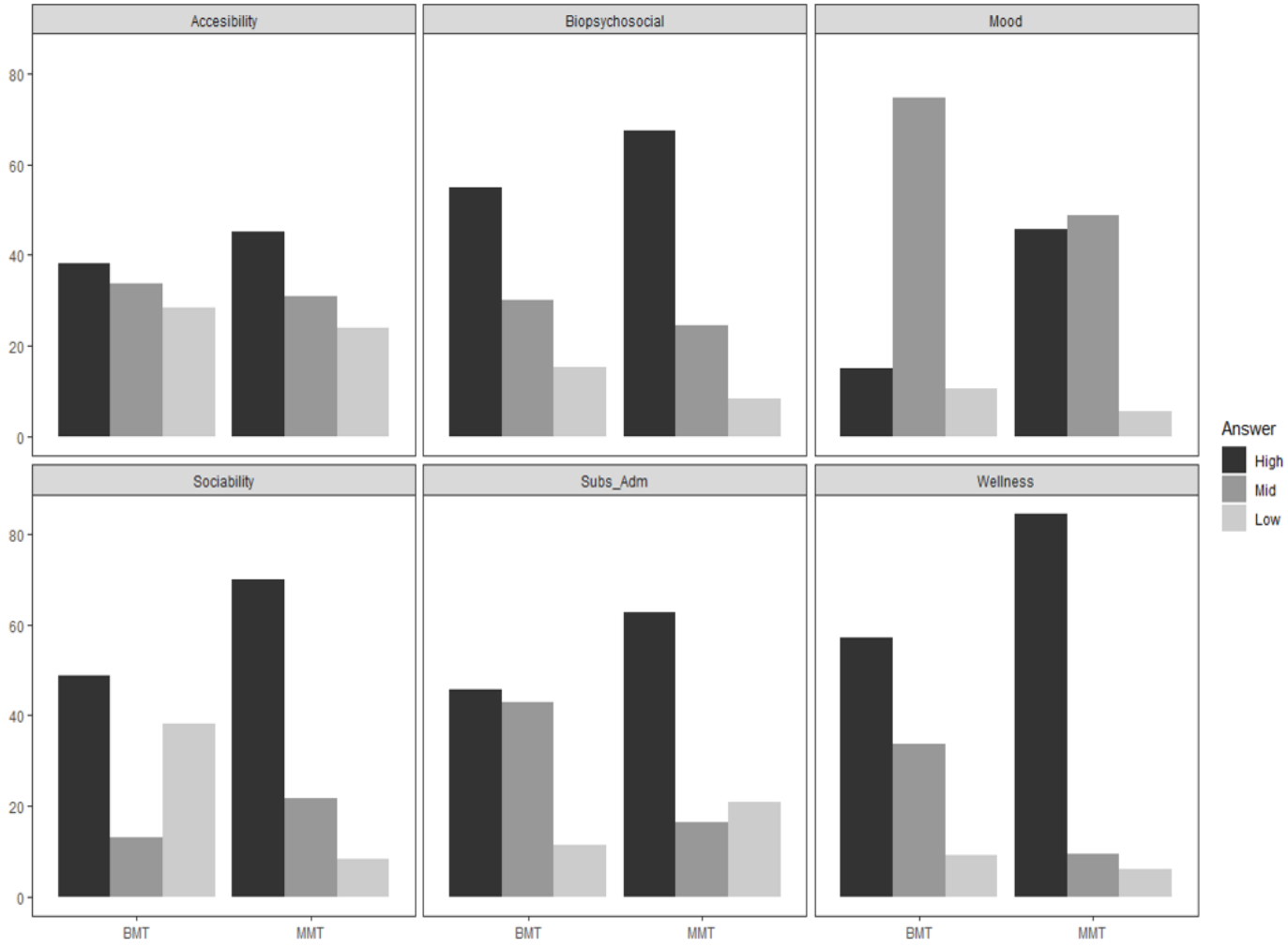

Figure 2

Answer frequencies per medication substance and PANMAT/Q dimensions