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A real-world ten-week follow-up of the COVID outbreak in an outpatient drug clinic in Salamanca (Spain)

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ABSTRACT

Objective: To compare over ten weeks the number of relapses, hospital admissions, calls made, admissions to therapeutic communities, face-to-face visits, treatment adjustment, number of injectables administered, and number of emergencies attended due to emotional and behavioral alterations and/or substance use disorder, and to describe and quantify social emergencies in an outpatient drug clinic (ODC) in Salamanca (Spain) from March 16, 2020, to May 22, 2020.

Methods: This is an ecological study of the COVID pandemic over ten weeks. The study examines the set of alcohol or other drug-dependent or dual disorder patients in the population of Salamanca, Spain. The measurements were: professionals; calls made; percentage of successful calls; face-to-face visits; first visits made; reviews made; techniques; injectable treatments; other treatments; evolution; relapses. The ODC includes about 375 new patients each year and another 650 other patients annually.

Results: The study found the number of relapses to be greater in the last five weeks of the 10-week study period. Patients' psychopathological instability also increased, and face-to-face visits were necessary. The most frequent psychopathology that required face-to-face intervention was depressive disorder. The number of interventions with patients increased. In parallel, social workers' efforts were greater after the seventh week. There was a decrease in response to calls. Throughout this time, the ODC attended to patients who needed to be treated for the first time.

Conclusions: Confinement due to the coronavirus pandemic generated maladaptive emotional responses and other behaviors, such as excessive alcohol consumption. The number of face-to-face consultations, admissions, and referrals to therapeutic communities increased. Patients under stress and in social isolation resorted more often to substance use. The ODC had to adopt a flexible approach to evaluate patients with more serious problems, by using face-to-face assessments.

1. Introduction

Starting in December 2019, cases of an acute respiratory disease were being reported in Wuhan (China). The agent responsible was identified as a new coronavirus, previously unknown in humans, called COVID-19, which causes a syndrome called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (ECDC, 2020). The characteristics of this disease include, apart from pulmonary involvement, the involvement of other organs (Li et al., 2020), including the central

nervous system (CNS) (Asadi-Pooya & Simani, 2020). The virus is very easily transmitted between humans (Li et al., 2020). At the time of this writing (July 7, 2020), the disease had been identified in more than 239,228 cases of coronavirus that had been diagnosed with PCR in Spain, and it had caused more than 27,125 deaths (Ministry of Health, Consumption and Social Welfare, 2020). This situation led to the confinement of the population (Official Bulletin of Castile and Leon (BOE), 2020) and it has had a major impact that has involved the restructuring of health services, including mental health care, as

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suggested by some authors from China (Li et al., 2020; Xiang et al., 2020). Many patients with addictions suffer respiratory problems derived from the consumption of opioids, cannabis, or other substances (Volkow, 2020). The presence of preexisting conditions is associated with a higher risk of suicide (Liu et al., 2020).

Individuals with mental disorders present a higher risk of infection due to their lower capacity to protect themselves, because in some cases they may have lower self-control (Xiang et al., 2020). They are also at a higher risk of worsening their preexisting medical problems, including other infections that are usually present (Roncero et al., 2017), and they are more likely to overdose because they buy substances that are more adulterated or to consume substances manufactured in their homes (EMCDDA, 2020; Jenkins et al., 2019; Kar et al., 2020).

The confinement measures have led to a situation in which, except under very serious circumstances, communication with patients has been carried out over the telephone. Videoconference-based telepsychiatry would have been an ideal solution (Hollander & Carr, 2020), but, considering the relatively fast pace with which the restrictions have been imposed over several resources, the required equipment was not available. Telephone consultations may be as effective as face-to-face interaction (Urness, Wass, Gordon, Tian, & Bulger, 2006). This is particularly relevant in the cases of addiction during the pandemic, in which patients' external support structures to maintain the rehabilitation process were less accessible (Cowan, McKean, Gentry, & Hilty, 2019). A flexible approach was necessary to assess the patients despite concerns related to COVID-19 (Marsden et al., 2020).

Obligatory confinement, which was necessary to prevent further spreading of the virus, is a potentially critical situation that can lead to substance consumption. Given the circumstances, alcohol and other drugs could be used as a means for self-medication (Kontopantelis et al., 2018). The following may be considered risk factors for addictive behavior and relapses: anxiety, uncertainty about the future, loneliness, depression, and even suicidal tendencies induced by social distancing (Marsden et al., 2020). On the other hand, the lower availability of alcohol (with bars and restaurants closed and the impossibility to leave the house) and of money (with increased unemployment rates) could be considered factors that promote a decrease in consumption. The fact that all the alcohol sales outlets are closed may improve overall health and reduce domestic violence and other types of violence (Rehm et al., 2017).

However, there are no real data available on substance use disorders that reveal an increase in consumption as a consequence of confinement. For this reason, we have analyzed the multidisciplinary intervention carried out in an outpatient drug clinic (ODC) throughout the first ten weeks of strict confinement. The objectives of this research were: (1) to compare throughout this period the number of relapses, hospital admissions, calls made, admissions to therapeutic communities, face-to-face visits, treatment adjustment, and number of injectables administered; (2) to analyze the number of emergencies attended throughout this period due to emotional and behavioral alteration and/or substance use disorder; and (3) to describe and quantify social emergencies: homeless patients, lack of bonds with which to maintain active communication, patients living in risk environments, domestic violence, loneliness, lack of support networks, job losses, and economic precariousness.

2. Materials and methods

2.1. Data source

There are 165 professionals linked to the psychiatric service (PS), 32 of whom are working in the Addiction and Dual Disorders Unit (ADDU) that develops care programs for addictive disorders and dual disorders (C. Roncero et al., 2020). The ADDU includes one outpatient unit for the treatment of alcohol- and cocaine-related disorders (the alcohol treatment unit, ATU), an outpatient dual disorders program (ODDP), and a

hospitalization service fulfilling the roles of a hospital detoxication unit and an inpatient dual disorder unit (HDU/IDDU), which is a reference unit for the region of Castile and León, and which closed on March 16, 2020.

After the declaration of the state of alarm in Spain, the treatment program put into practice a contingency plan on the week of March 16. The program established a system of regular communication with all the specialists in the PS in all services and units. An intense re-adaptation process took place in three ways: reorganization of human resources, physical shutdown of some health care resources such as the IDDU, and implementation of telemedicine programs in the ODC and the ODDP.

Some of the measures that the ADDU adopted in the health area of Salamanca (Spain) include the implementation of telemedicine. Simultaneously, two new health care programs were initiated: one aimed at mental health care for professionals and patients (PASMICOR) and another program for homeless people (HP) (Martin et al., 2020). The staff in the ADDU have maintained face-to-face assessment with patients who required an immediate check-up, and they implemented different protective measures: the patient answered questions aimed at detecting symptoms of COVID-19 before the patient came for consultation, patients and staff wore face masks during the entire check-up, and they maintained social distance at all times. Group activities had been canceled on March 10. This study assesses phone consultations, the number of relapses, and the number patients transferred to the emergency room in a naturalistic 10-week follow-up.

2.2. Subjects

The activity of the ODC is the subject of this study, which includes the alcohol treatment unit (ATU) and the outpatient dual disorders program (ODDP), from March 16, 2020, to May 22, 2020. Both services (ATU and ODDP) belong to the PS of the Salamanca University Hospital. The ODC provides treatment to approximately 375 new patients each year and to another 650 different patients annually, all of them for alcohol use problems. Normally, in a year, treatment the ODC provides treatment to more than 1000 patients with alcohol dependence. The ODDP started to operate in October 2019, and it provides treatment to approximately 25 patients per year. The ODDP has established three weekly groups with approximately 25 patients.

2.3. Design

We carried out a longitudinal ecological study (which studies the group of users who are consumers of alcohol and other drugs in the population of Salamanca, Spain), throughout 10 weeks. This study based its analysis on the work that the addiction treatment services ATU and ODDP carried out; their main patients present with alcohol use disorder, either by itself or in combination with other drugs. They also see patients with dual disorder. The objective was to assess the health care provided in the interventions that took place during the COVID outbreak, the evolution of patients, and the influence of confinement on patients with alcohol or other drug use disorders. The period of 10 weeks was divided into two 5-week subperiods for later comparison. We established the hypotheses for this study as follow:

- If the crisis improves, then number of professionals attending the ATU and PAPPD will increase;
- Number of calls will increase as time passes;
- Number of relapses will increase gradually; and
- Injectable treatment will not vary because of its importance.

We pre-registered the hypotheses in ORCID: <https://osf.io/b4g2k>.

2.4. Measures

The recorded variables of interest for the study include:

- Professional workers: Number and type of professionals who worked in that week in the different units. This variable is an indicator of the state of the crisis, because as the number of workers approaches the normal figures, we can observe a lower contagion rate.
- Calls attempted: Number of times that a user of the unit was called. This variable is associated with the workload of the unit.
- Successful calls: Number of times that the calls managed to reach the users. This variable shows the response rate of the patients.
- Percentage of successful calls: The result of dividing the number of successful calls by the number of calls attempted, expressed as a percentage. This is a secondary outcome calculated from the data, which shows the effectiveness of the contact attempts.
- Face-to-face visits: Number of face-to-face user visits to the unit. Similar to the number of professionals, face-to-face visits are related to lower mobility restrictions and, therefore, a lower risk of contagion.
- First visits: Number of contacts with new users who come voluntarily or are transferred to the unit by another center. This factor shows the effects of the crisis on individuals who had not used this resource before to treat their problems with alcohol.
- Reviews: Number of contacts with users who were already registered in the unit. This variable, together with the number of first visits, provides information about the increase or decrease of the proportion of new cases.
- Techniques: Type of main technique used in the interventions. The type of technique provides information about the needs of the patients and the type of professionals who were in the unit each week.
 - o Support techniques
 - o Psychotherapy techniques: Number of psychotherapeutic interventions.
 - o Pharmacological adjustment techniques: Number of pharmacological interventions.
- Injectable treatments: Number of injectable treatments administered in the unit. It shows the importance of depot treatments in a health crisis.
- Other treatments: Number of treatments other than injectable treatments. It shows the importance of the pharmacological treatment in a health crisis.
- Progress: shows the evolution in each of the cases. These measures show the consequences of the health crisis on the patient population throughout these 10 weeks:
 - o Steady progress: Number of cases contacted who maintained abstinence and continued with their established treatment.
 - o Unstable progress: Number of cases contacted who showed a worsening in their symptoms and required some type of adjustment.
 - o Progress to emergency: Number of cases contacted who were transferred to emergency services because of the severity of the symptoms (either psychological or medical).
- Relapses: Number of confirmed cases of relapse into consumption. As with the factor analyzing patient progress, this factor indicates the consequences of the health crisis on patients' consumption during the crisis.
- Social work: Number and type of interventions that social workers carried out throughout these 10 weeks.
 - o Transfer to therapeutic communities (Transfer to community): Number of requests for transfer from the unit to a residential therapeutic community.
 - o Processed documents for admission into therapeutic communities (Processed admission into community): Number of times in which the documents were processed for patients to be admitted into a residential therapeutic community.
 - o Contact with PAPT (PAPT): Number of times that the personal autonomy protection team (PAPT) was contacted to manage patients in our unit.

- o Reports for the Regional Child Protection Office (Child protection reports): Number of times that cases that could involve minors were detected and the authorities were contacted through official reports.

2.5. Analysis

This study carried out a descriptive analysis (Table 1), with the main variables mentioned in the previous section. The study divided the 10-week period into two parts, one prior to the declaration of the state of emergency (weeks 1–5) and one in the acute stage (weeks 6–10), so as to compare the results from each of these groups as independent samples. The analysis used Student's *t*-test to compare the mean values in each of these periods. For this analysis, nonparametric tests confirmed the assumptions (Table 2).

3. Results

Along the 10 weeks included in our study, the mean number of professionals working at the ODC was 3.6 (SD = 1.17), with an increasing trend as the crisis continued. The maximum number of professionals at work within the same week was 5 (1 psychiatrist, 1 psychologist, 1 nurse, 1 social worker, and 1 nursing assistant).

The number of relapses was irregular, and there were weeks with and without relapses within the first 5 weeks (Fig. 1). From week 6 onward, the study observed at least one relapse every week. The study observed the maximum number of relapses in week 7. The study observed no changes between the two periods of the study.

The study first observed cases of unstable progress in week 4 (two cases with depression and anxiety) (Fig. 2). From week 6 onward, the study found cases of unstable progress in all weeks, with depression, anxiety, and insomnia. None with schizophrenia. The study found the maximum number in week 9. However, the frequencies are still very low, and the study found a tendency when comparing both periods (*p* = 0.051). Only two patients had to be transferred to the emergency services: one of them in week 5 and one in week 6.

Table 1
Summary of interventions/variables.

	Minimum	Maximum	Total/ Avg	Average (SD)
Descriptive variables				
Total no. of professionals/ week	2	5	–	3,6 (1,17) 164,5
Calls made	118	226	1645	(32,7) 141,4
Successful call	110	177	1414	(20,184) 86,9
% of successful calls	74,41	98,67	–	(17,10) 17,1
In-person consultation	0	35	171	(10,67)
First consultations	0	3	13	1,3 (1,05)
Follow-up consultations	103	189	1480	14 (28,36) 110,9
Support techniques	23	160	1109	(49,87) 36,9
Psychotherapy techniques	9	98	369	(30,31)
Pharmacological adjustment techniques	5	24	117	11,7 (6,53)
Injectable treatments	0	9	41	4,1 (2,88)
Other pharmacological treatments	4	24	117	11,7 (7,07) 147,5
Favorable evolution	110	183	1475	(23,28)
Unstable evolution	0	6	16	1,6 (2,01)
Relapses	0	7	21	2,1 (2,12)

Most important variables registered with minimum and maximum frequency reached, total frequency in 10 weeks period and average by week.

Table 2
Comparison between 1 and 5 and 6–10 weeks with t-student.

	Compared periods				P-value
	Weeks 1–5		Weeks 6–10		
	Mean	SD	Mean	SD	
Total no. of professionals	7,6	0,54	9,2	2,58	0.213
Calls made	147,2	21,33	181,8	34,68	0.094
Successful calls	138,2	18,39	144,6	23,51	0.644
% of successful calls	94,036	3,65	79,92	4,24	0.000**
In-person consultations	10	9,08	24,2	6,90	0.024*
First consultations	1,4	1,14	1,2	1,09	0.784
Follow-up consultations	142,8	22,02	153,2	35,45	0.593
Support techniques	99,2	69,83	122,6	19,45	0.505
Psychotherapy techniques	46,8	41,33	27	10,7	0.352
Pharmacological adjustment techniques	14,8	41,33	27	10,7	0.141
Injectable treatments	2,4	1,81	8,6	3,36	0.055
Other pharmacological treatments	14,6	8,93	8,8	3,42	0.212
Favorable evolution	146,2	26,01	148,8	23,21	0.872
Unstable evolution	0,4	0,89	2,8	2,16	0.051
Relapses	1	1225	3,2	2,38	0.104

First column shows most important variables registered. Means and standard deviations are compared between 1 and 5 weeks and 6–10 weeks period using T for Student. Significant values appeared with * ($P < 0.05$) and ** ($P < 0.01$).

The type of techniques and treatments show irregular curves with a slightly decreasing trend during the middle weeks (psychotherapy techniques) or an increasing trend (support techniques). Injectable treatments and pharmacological adjustment techniques remained relatively stable (Fig. 3).

The study recorded almost no specific interventions from social workers within the first 6 weeks, with the exception of one intervention for admission into a residential community in week 5. A similar intervention was carried out in week 7. From this point, Fig. 4 shows a progressive increase in area of social work. The study registered the maximum number of interventions in week 9. The most common type of intervention was contact with the personal autonomy protection team (35 contacts in total). The study found that two reports for the Regional

Child Protection Office were prepared in week 9.

The percentage of successful calls (successful calls/attempted calls *100) increased progressively over the first 4 weeks (98.67%) and then decreased progressively down to a 78.32% success rate in week 10 (Fig. 5). The study observed differences regarding the successful calls between the first 5 weeks and the last 5 weeks ($p = 0.000$).

The study observed an increasing trend regarding the number of in-person consultations. After the first two weeks (with stricter confinement measures), in person consultations started to rise and reached their peak in week 10 ($p = 0.024$).

4. Discussion

There is contradiction among certain studies about the increase of alcohol consumption in situations that can cause stress and anxiety, such as the confinement that the COVID-19 pandemic imposed. In our case, there was a clear upturn in consumption and relapses in week 7, partly because the hours in which people were allowed to go out increased, the psychopathological instability was greater, and small food stores started to open again, as some authors have suggested (North, Kawasaki, Spitznagel, & Hong, 2004; Shimizu et al., 2000). Other authors, however, claim that consumption decreases due to the lower access to alcohol and drugs (Boscarino, Adams, & Galea, 2006; Lebeaut, Tran, & Vujanovic, 2020).

As weeks passed, psychopathological instability increased, as did the number of patients consulted with depressive disorders and anxiety, which matches the previous descriptions on the most common effects of confinement: stress, depression, irritability, insomnia, fear, confusion, anger, frustration, and boredom. There is also concern that these symptoms may persist after the quarantine period (Brooks et al., 2020). One study recently demonstrated a correlation between the coronavirus diagnosis and a history of anxiety and alcohol/drug coping (Lee, Mathis, Jobe, & Pappalardo, 2020). These measures may have a significant impact on the increased risk of suicide in the population (Reger, Stanley, & Joiner, 2020), which is already elevated in addicted patients and patients with dual diagnoses (Senior et al., 2020). This situation could also lead to a lack of compliance with the established measures and to substance use (Pfefferbaum & North, 2020). Psychopathological

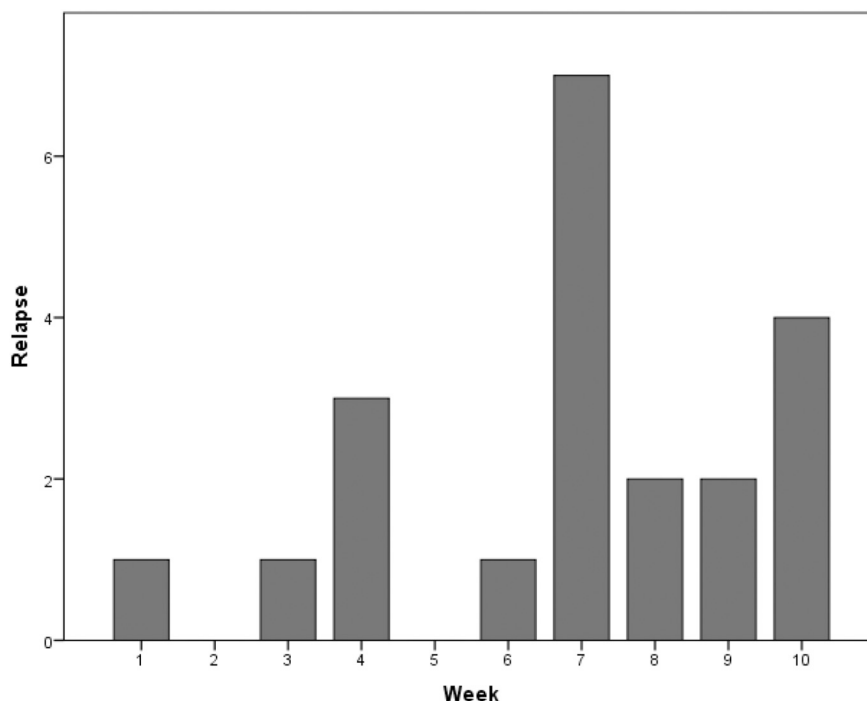


Fig. 1. Relapses (weeks 1–10).

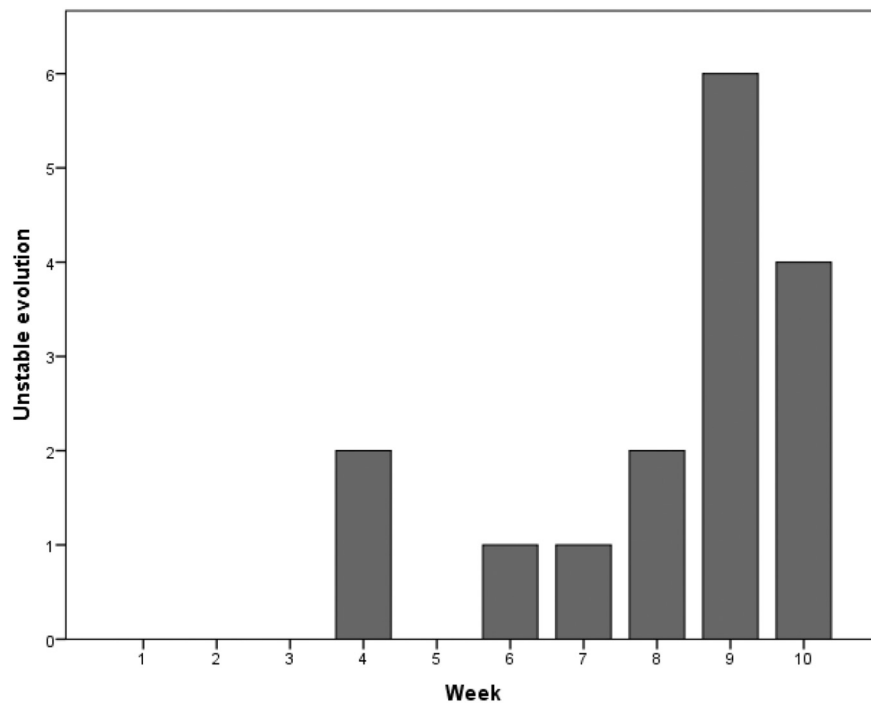


Fig. 2. Cases of unstable evolution (week 1–10).

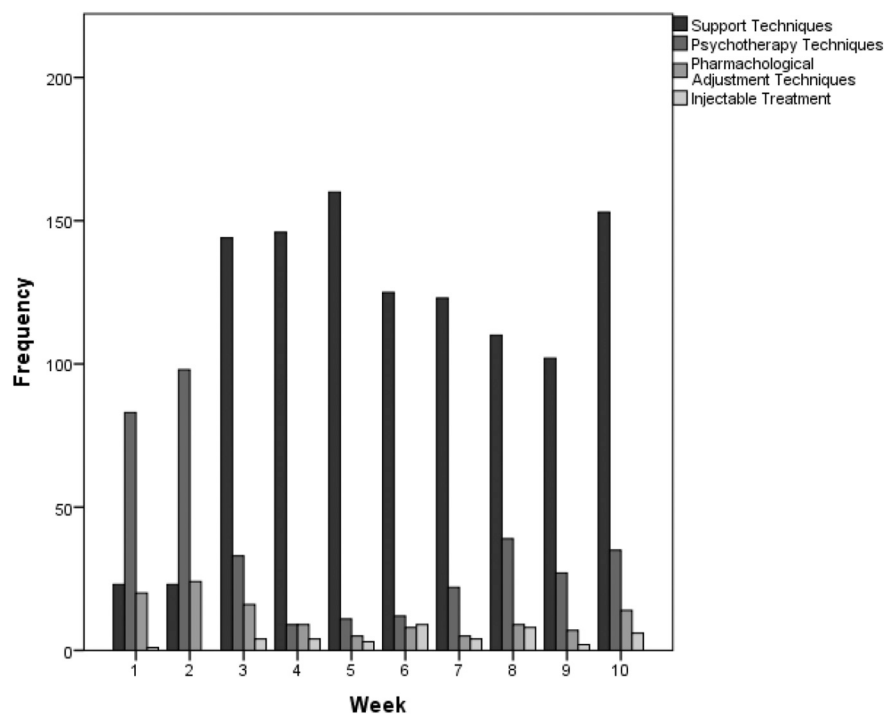


Fig. 3. Intervention (week 1–10).

instability could account for the increased number of face-to-face visits. However, we should note that there were no episodes of decompensation in patients with psychotic disorders, which may be because the unit administered long-acting antipsychotics for dual psychotic patients, which made it possible to control their evolution and to carry out a telephonic monitoring in which they were reminded of the administration date.

China has put forward different psychological support measures for the COVID-19 pandemic, which include a multidisciplinary approach

that includes, among others, psychologists, psychiatrists, and nurses specialized in mental health; providing reliable and updated information on the pandemic; and establishing different services to provide psychological support (Bilal, Latif, Bashir, Komal, & Tan, 2020), which may include online treatment programs (Xiang et al., 2020). This study shows that the number of interventions by our team increased over the last weeks of the study: more psychotherapy sessions with each patient; a higher number of calls within a narrower margin of time; on-site administration of medication in the adherence unit; more

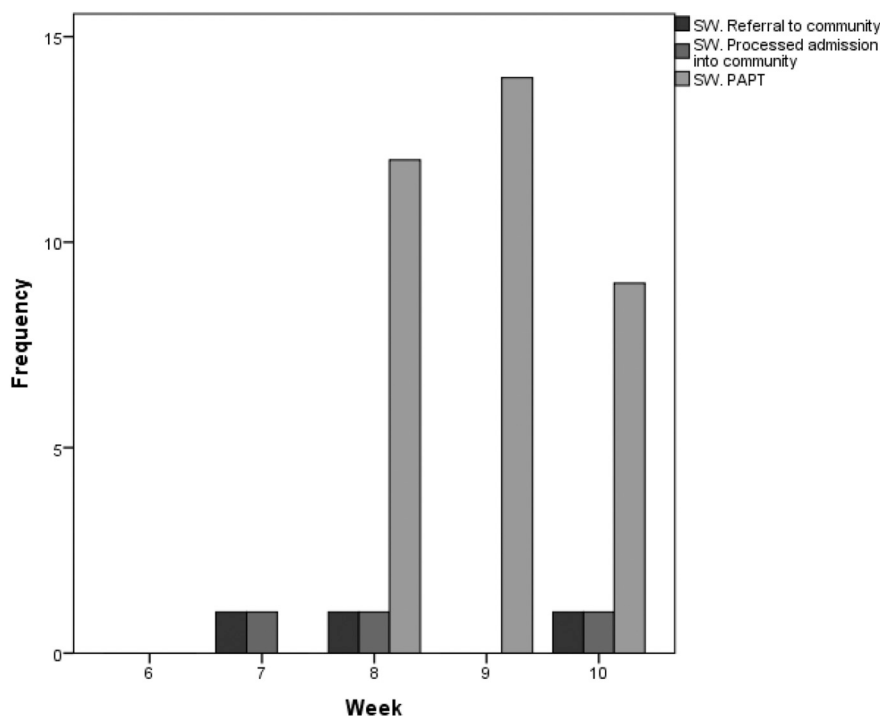


Fig. 4. Social work interventions (week 6–10).

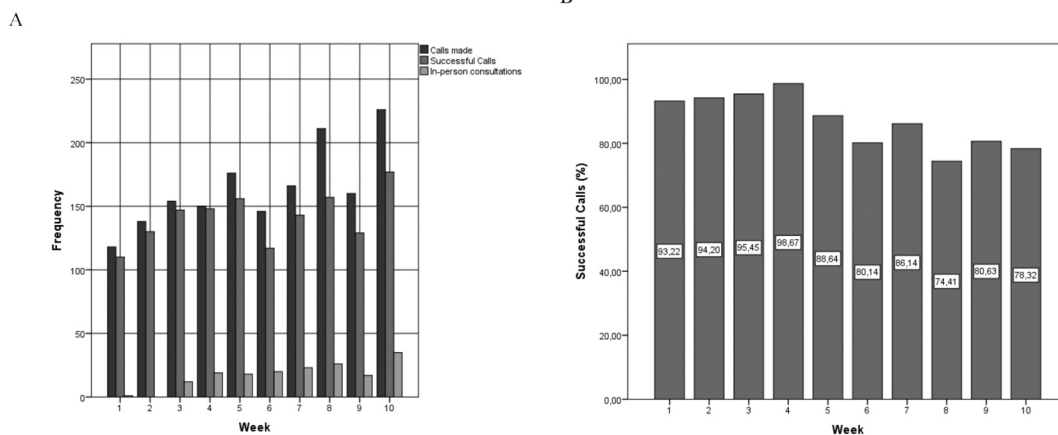


Fig. 5. Intervention modality applied (Week 1–10).

prescriptions requested; and changes of treatment for anxiety, depression, and insomnia.

When facing such a radical change in behavior and routines (social distancing, telecommuting, limitation of sport and leisure activities outside the house, etc.), people should find alternative activities, such as the expression of negative emotions, keeping in contact with relatives and friends, taking up regular hobbies and new leisure activities, and so on (Park & Park, 2020).

Addressing social problems that emerged as some of the shelters for the homeless closed down was essential, and the study observed an increase in the number of relapses and episodes of psychopathological destabilization among this population. Treatment providers and social workers had to find them housing, to manage their admission into therapeutic communities, and to maintain constant contact with the psychosocial support team of the city council. These homeless patients with substance use problems find it more difficult to access the health system and to maintain self-isolation and social distancing, even when

they present symptoms of COVID-19 (Lima et al., 2020).

The decrease in telephone calls, particularly in weeks 6 and 7, could be due to the fact that some patients had started to work in some essential services, to a decrease in the restrictions of curfew during those weeks, and to the fact that the patients did not require as much support as during the first weeks of confinement.

Based on previous crises, some authors have suggested that the main mechanism that affects the increase in alcohol consumption is the increase in stress levels, promoted by the economic difficulties, social isolation, and uncertainty about the future (de Goeij et al., 2015; Rehm et al., 2017). After the SARS crisis of 2003, in a group of 800 Hong Kong residents who were regular drinkers, 4.7% of the men and 14.8% of the women reported an increase in alcohol consumption after 1 year (Lau, Kim, & Tsui, 2005). Research should consider this population’s capacity for self-regulation and self-awareness, because individuals with AUD who are more interoceptively sensitive may have problems controlling their behaviors while experiencing negative emotional states

(Jakubczyk et al., 2020). In our case, the number of first visits motivated by an increased consumption of drugs during the confinement was very similar in the two periods considered in our study: most of the cases were transferred from the emergency department and from different mental health care teams after being discharged from the short-stay unit of the hospital. On the other hand, the easy access and contact with the team explains why so few patients were transferred to the emergency room, which confirms the findings from previous studies that increasing access to ambulatory care, and care continuity in outreach programs for acute MH disorders, including substance-related disorders, may reduce ED visits (Gentil, Huynh, Grenier, & Fleury, 2020).

The social distancing guidelines that were required to prevent the spread of the virus have made it necessary to reassess our plans and protocols. Group therapies are a significant part of the treatment that we provide; these group sessions were canceled. In the future, we will have to reduce the number of participants in each group, and we will have to reduce the number of groups. Separating members within the groups may alter the dynamics that the previous group had, which is another important aspect in this type of therapy (Columb, Hussain, & O'Gara, 2020). Therefore, we will have to consider the implementation of online therapy; some authors have already reported that group telepsychiatry may have a clinical effectiveness similar to that of traditional group therapies (Chakrabarti, 2015). Telepsychiatry could also be useful to limit anxiety and to address addiction during confinement.

Treatment providers should consider patients' emotional changes and their changes in substance consumption, and assess treatment protocols prospectively to design specific interventions that fit current needs. The COVID-19 pandemic poses significant challenges to health care services.

One limitation of this study is that it is a single-center study and, therefore, may not be representative of all patients. However, this is a real-world study that we developed during the pandemic, despite the difficulties in carrying out longitudinal studies, even under normal conditions (Azcárate-Jiménez et al., 2019; C. Roncero et al., 2019). The study conducted most patient interviews by phone. That made it hard to assess anxiety, so the study conducted clinical evaluations. We placed special attention on those who had a history of multiple relapses and those who required more frequent contact.

The ODC responded to the pandemic in a noticeably short timeframe, and we believe that its execution of that response was successful, considering the low number of relapses among patients. The response was coordinated with the other services in the health care system, including primary care and other resources in the drug-dependence assistance network (Roncero, 2020). Using telephone support and therapy looks promising for patients with mental disorders, and we believe it should be implemented beyond the current crisis (Bilal et al., 2020; O'Brien & McNicholas, 2020). There is an urgent need to provide services to patients with addiction disorders (Marsden et al., 2020).

We can conclude that: (1) The period of confinement that the coronavirus pandemic caused has led to nonadaptive emotional responses and other behaviors, such as excessive consumption of alcohol. As the weeks in confinement went by, the number of face-to-face visits, admissions, and transfers to therapeutic communities increased. (2) Patients in social isolation reverted to substance use more frequently, and showed greater psychopathological instability, particularly as depression, anxiety, and insomnia. (3) The ODC had to establish telephone communication with patients, except for 10% of the severe cases, which it treated in face-to-face visits. The effectiveness of therapy via telephone was similar to that of face-to-face visits in cases that required a check-up, treatment adjustment, or psychological support. This kind of therapy was particularly relevant in patients with substance use disorder because they were less able to access external support structures to maintain rehabilitation. (4) ODC required a flexible approach for onsite assessment of its more severe patients, despite concerns related to the pandemic.

The response to the pandemic described here will surely change, and

thus research will need to continue to evaluate it. The COVID-19 pandemic has been a challenge for clinicians, due to new clinical presentations (Majadas et al., 2020) and new treatment approaches. Research should continue to study the impact of COVID-19 on drug dependence and its treatment.

CRediT authorship contribution statement

Lourdes Aguilar: Writing - Original Draft, Conceptualization, Investigation

Begoña Vicente-Hernández: Conceptualization, Methodology, Investigation

Diego Remón: Formal analysis, Software, Validation.

Llanyra García-Ullán: Writing - Review & Editing

Isabel Valriberas-Herrero: Writing - Review & Editing

Ana Maciá-Casas: Data Curation

Ana Pérez-Madruga: Investigation

Maria Ángeles Garzón: Supervision, Resources

Ana Álvarez-Navares: Supervision, Resources

Carlos Roncero: Funding acquisition, Project administration

Declaration of competing interest

Dr. Begoña Vicente-Hernández declares that in the last years she has received remuneration as a speaker from Janssen-Cilag and Lundbeck.

Dr. Carlos Roncero has received fees to give lectures from Janssen-Cilag, Indivior, Lundbeck, Otsuka, Servier, GSK, Astra, Gilead, MSD, Sanofi, Excelsis, Abbvie, Takeda Rubio and Casein. He has received financial compensation for his participation as consultant or a board member of Lundbeck, Gilead, MSD, Mundipharma, INDIVIOR, Excelsis, Martindale, Camurus, Gebro and Abbvie board.

He has carried out the PROTEUS project, which was funded by a grant from Reckitt-Benckiser/Indivior and the COSTEDOPIA project, which was funded by INDIVIOR. He received two medical education grants by Gilead.

The rest of authors declare that they have not participated in activities in which they had any conflict of interest.

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Authors' contributions

All authors helped to conceptualize the paper. C.R and L.A did the first draft of the original paper. D.R undertook the analyses. All authors refined the various versions of the paper and approved the final manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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