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Recommendations for the care of patients with bipolar disorder during the COVID-19 pandemic

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ABSTRACT
In recent months, there has been a rapid spread of coronavirus disease (COVID-19), being now regarded as a global pandemic. In this context, the governments of different countries have established strict containment measures, and subsequent deconfinement measures, with consequential alterations in the rhythms and living habits of the population, including patients with bipolar disorder (BD), who are in an extremely vulnerable situation. The present paper aims to propose a number of recommendations, based on scientific evidence, for mental health professionals who may be in charge of BD patients during this health crisis in the coming months. Among these recommendations, careful monitoring of pharmacological treatment, reinforcing medication adherence, and surveillance of drug-drug interaction risk in cases where the patient is being treated for COVID-19 are of utmost importance.

1. Introduction
In recent months, the coronavirus SARS-CoV-2 causing coronavirus disease (COVID-19) has spread throughout more than 100 countries in a matter of weeks and has been classified as a pandemic by the World Health Organization (WHO). In the current context characterized by the lack of effective treatments for this disease, each country has put in place strict containment measures, such as confining the population for weeks. Scientific evidence from previous pandemics (e.g., SARS in 2003) highlights the harmful psychological effects of lockdown and social isolation on the general population, along with the worsening of symptoms and the risk of relapse in individuals with a previous mental disorder (Chatterjee et al., 2020; Mahase, 2020; Pacchiarotti et al., 2020).

Nowadays, governments of different countries are implementing precautionary deconfinement measures with the hopeful aim of returning to pre-pandemic normality; this inevitably leads us to more uncertainty arising from the return to normal life after months of lockdown, the adoption of new social distancing measures, and the fear of a possible resurgence (Vieta et al., 2020). In these circumstances, the changes in daily rhythms and living habits make BD patients an at-risk population, especially vulnerable to episode recurrence. Although there are recommendations for dealing with schizophrenia patients during the COVID-19 outbreak (Fonseca et al., 2020; Kozloff et al., 2020), to the best of our knowledge no recommendations have been developed for professionals who work with BD patients. Only a few articles deal with the nuances of bipolar disorder in the context of COVID-19 (Gil-Badenes et al., 2020; Stefan et al., 2020; Youngstrom et al., 2020) without developing specific recommendations. Therefore, it is necessary to provide clear and consistent advice for mental health professionals on how to manage the risks generated by COVID-19 and the subsequent deconfinement for BD patients.
Consequently, the main goal of this work is to provide several recommendations to clinicians who have to treat BD adult patients during this period and in the coming months.

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Table 1: Evidence-based recommendations for mental health professionals treating BD patients.

| Sections | Objectives |
|----------|------------|
| Start of the interview | To debrief and validate the patient's emotional experience and emotional reactions (e.g., fear, anxiety) during confinement. |
| Anticipate stress reactions that may arise when returning to normal activity after quarantine. | |
| To reduce emotional distress | 1. Inform the patient of the benefits of adopting the preventive and social distancing measures recommended by the health authorities (e.g., handwashing, use of masks, social distancing) (Güner et al., 2020). |
| To promote adherence to pharmacological treatment during quarantine, and adjust or amend medication depending on the patient's current state. | 1. Review adherence to pharmacological treatment during quarantine, and adjust or amend medication depending on the patient's current state. |
| To promote healthy lifestyle choices | 1. Recommend a healthy and low-salt diet, exercise appropriate to the patient's physical conditions, and weight reduction if there is overweight/obesity (Bobes et al., 2008). |
| To monitor social and family functioning before the COVID-19 pandemic outbreak. | 2. Assess the frequency of interpersonal contact between the patient and other people before the COVID-19 outbreak and at the present time, in order to maintain stable interpersonal relationships. |
| To provide the tools | 1. Assess the patient's psychological functioning before the COVID-19 pandemic outbreak. |
| To monitor the risk of relapse | To reduce the stigma associated with being BD patients treated for COVID-19 disease. |

Pharmacological section

1. Determine systolic and diastolic blood pressure, weight, height, body mass index (BMI = weight/height in m²), and waist circumference, and perform blood tests for glucose, total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol, triglycerides, and thyroid-stimulating hormone (Bobes et al., 2008).
2. Assess and discuss the patient's experience and emotional reactions (e.g., fear, anxiety, sadness) during confinement.
3. Assess whether the patient is consuming other substances (e.g., tobacco, alcohol, drugs) and rule out the risk of substance abuse (Bobes et al., 2008).

Behavioral section

1. To reduce the feeling of isolation caused by the health crisis, and establish a plan to maintain and strengthen the patient's social support network (e.g., by telephone or internet) (Fiorillo and Gorwood, 2020). Interpersonal contacts should be regular and of limited duration.
2. To promote information to the family members. |

Social and family section

1. Validate the emotional experience and subsequent decompensation of the patient (e.g., fear, uncertainty, anxiety) (Ormel et al., 2003).
2. To establish a therapeutic alliance with the patient and the family, in order to coordinate care. |

Conclusion

By following these recommendations, mental health professionals can help BD patients during the COVID-19 pandemic. These measures aim to reduce the risk of relapse and improve the patients' quality of life, while also promoting a sense of normalcy in their daily lives. It is crucial to continue monitoring and adjusting treatment as needed, while also addressing any new emotional or physical symptoms that may arise. The goal is to help BD patients maintain their mental health and well-being during these challenging times.
Table 1 (continued)

| Sections | Objectives | Clinical recommendations |
|----------|------------|--------------------------|
| 1        | To promote both healthy activities and regulate them | 1. Assess sleep habits, their regularity, and the patient’s daily activities (e.g., schedules and frequency of these activities). Objectives Clinical recommendations. 2. If alterations in these areas are identified, promote sleep hygiene practices (Frank, 2007a), and—with the patient—decide on a behavioral activation program, to be reviewed at the subsequent consultation. 3. It may be useful to agree with the patient on some stimuli that can control other responses in order to comply with proposed schedules and activities (e.g., warnings on a refrigerator, alarms on a mobile phone). |
| 2        | To stimulate to reduce environmental stimulation, to educate about medications, and alcohol consumption, upon important decisions. | 1. Spend a few minutes teaching patients how to identify relapse prodromes. The four most frequent manic prodromes are sleep disturbances/decreased need for sleep, elevated mood, agitation, and increased performance. 2. Devise an action plan. If the patient experiences prodromes of mania/hypomania, he/she will increase the hours of sleep, limit the number of activities, reduce environmental stimulation, and stop smoking. |
| Relapse prevention | | 3. Offer a resource to the family and/or the patient (e.g., phone number of the nearest mental health center) in case they need support for an illness episode or if they detect a risk of relapse. |
| Farewell and closure | | 1. Offer a resource to the family and/or the patient (e.g., phone number of the nearest mental health center) in case they need support for an illness episode or if they detect a risk of relapse. |

2. Recommendations

The following recommendations are based on a body of scientific research and can be applied in-person or via the phone or internet. This set of recommendations contains suggestions that should consider during the first consultation of an adult patient during the COVID-19 pandemic (see Table 1).

The drug-drug interactions that should be taken into account when the BD patient is being treated for COVID-19 are presented in Table 2. It is suggested to avoid starting pharmacological treatment for BD in patients with COVID-19 treated with drugs that have shown interactions (see Table 2). In BD patients who are already under treatment, the risk-benefit of withdrawal should be evaluated (Anmella et al., 2020).

3. Discussion

The COVID-19 pandemic outbreak, the lockdown measures for weeks, and the subsequent deconfinement aimed at its containment imply an alteration in the rhythms and living habits that can present a challenge to the health of BD patients. This paper outlines the areas that mental health professionals who treat these patients should consider during this health crisis and the subsequent deconfinement. Therefore, there is a great need to provide clinical recommendations, which will necessarily have to accommodate the idiosyncrasies of each BD patient.

These recommendations should be adapted to the usual psychiatric comorbidity of the BD patient, to the degree of family support and family stress, and to the patient’s current physical health. The pandemic generated by COVID-19 represents a circumstance capable of provoking intense emotions (Montemurro, 2020), which may overwhelm BD patients and thereby necessitate special professional attention. Therefore, validating the emotional experience of these patients caused by confinement is of paramount importance to successfully managing the stress reactions elicited by the COVID-19 outbreak. Adherence to social distancing, hand hygiene, and respiratory measures may be more difficult to adopt in this population, since it involves the strict establishment of new habits and the abandonment of previously established ones. Detection of relapse prodromes, monitoring of pharmacological treatment, and enhancement of medication adherence in these patients will contribute to reducing the possibility of relapses marked by the instability provoked by this health crisis. At this stage it is important that the clinicians that prescribe medication to patients with BD who are being treated for COVID-19 consider the risk of adverse pharmacological interactions. On the other hand, promoting regular healthy sleep habits and living habits will serve to normalize the emotional highs and lows brought on by the COVID-19 lockdown measures, and the subsequent deconfinement. Likewise, the reduction of social isolation feeling as well as social relationships regularization will avoid a drastic decrease and/or increase in social stimulation that could compensate for these patients. In addition, learning a technique for coping with stressful situations will allow the BD patient not only to cope better with deconfinement but also to cope better with the possibility of a new outbreak that may necessitate another period of confinement. For the family, the COVID-19 outbreak and the changes elicited by this pandemic may raise doubts about how best to support the patient as well as how to manage family stress arising from different types of changes (e.g., due to the loss or illness of family members or the presence of financial difficulties). In this context, ensuring patient follow-up and offering healthcare resources makes perfect sense; the fight against a pandemic in the digital era makes it necessary to have in place high-quality resources and solid recommendations that can be utilized not only face to face but also via the telephone or internet (Golinelli et al., 2020). Finally, the situation generated by COVID-19 poses new challenges for children and adolescents with BD that can represent sources of stress, such as teleschooling and the drastic change in their lifestyle habits (e.g., lack of contact with classmates and teachers, or a reduction in activity due to cancellation of extracurricular
activities; Wang et al., 2020b), which reinforces the need to provide recommendations for dealing with this population.

In conclusion, BD patients are vulnerable to experiencing stress from the profound changes in their living habits, and in addition can experience intense emotions resulting from the severe health crisis caused by the COVID-19 outbreak. Mental health professionals who are required to treat BD patients should pay special attention to this population and their families to ensure their emotional stability and reduce the likelihood of relapse.

Authors’ contribution

AHG and NAG designed the study. GL and EV checked the recommendations. AHG prepared Table 1 and prepared the first draft for review. GL and EV provided input into the development of the manuscript, including the final version. EV critically revised the manuscript for intellectual content and reviewed the first and second draft. All authors contributed significantly to the discussion and approved the final draft.

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Table 2

| COVID-19 treatment | Clinical recommendations and drug-drug interactions |
|--------------------|-----------------------------------------------------|
| Dexamethasone      | 1 Monitor the occurrence of relapses, especially manic ones in short term treatment (Bolanos et al., 2004; Wada et al., 2001). Adverse effects also include depression, agitation, mood lability, anxiety, insomnia, catatonia, depersonalization, delirium, dementia, and psychosis (Bilbil et al., 2020; Warrington and Bostwick, 2006). 2 Avoid carbamazepine and oxcarbazepine (potential induction of CYP3A4 may decrease dexamethasone concentrations) (University of Liverpool, 2020). 3 Monitoring of lithium effects may be required, particularly in patients with renal impairment. 4 Caution with bupropion (lowers seizure threshold). |
| Remdesivir         | 1 Totally avoid carbamazepine (University of Liverpool, 2020). 2 Risk of elevatedaminotransferase level—caution with potentially hepatotoxic psychotropics (Bilbil et al., 2020). |
| Tocilizumab        | 1 Potential weak interaction with carbamazepine (Drugs.com, 2020) Esteve et al., 2020; University of Liverpool, 2020). |
| Favipiravir         | 1 Possible QTc prolongation (Chinello et al., 2017). These drugs may produce psychosis, mood change, mania, and suicidal ideation (Nevin and Croft, 2016). 2 Risk of QTc prolongation—caution with QT-prolonging drugs (McGhie et al., 2018). 3 Metabolized by CYP3A4—potential drug interactions with CYP3A4 inhibitors (e.g., fluvoxamine) and inducers (e.g., carbamazepine, oxcarbazepine, modafinil) (Bilbil et al., 2020). |
| Chloroquine/hydroxychloroquine | 1 Totally avoid carbamazepine, haloperidol, quetiapine, clozapine, risperidone, and escitalopram. 2 Avoid as far as possible lithium salts, valproic acid, lamotrigine, topiramate, risperidone, and trazadone. 3 Use with extreme caution sertraline, paliperidone, and mirtazapine. 4 Use with caution aripiprazole, olanzapine, duloxetine, gabapentin, pregabaline, and venlafaxine (Drugs.com, 2020; Esteve et al., 2020; University of Liverpool, 2020). |
| Chloroquine         | 1 Totally avoid carbamazepine, haloperidol, quetiapine, clozapine, risperidone, and escitalopram. 2 Avoid as far as possible lithium salts and risperidone. 3 Use with great caution mirtazapine, and sertraline. 4 Use with caution aripiprazole, olanzapine, paliperidone, amisulpride, venlafaxine, and trazadone (Drugs.com, 2020; Esteve et al., 2020; University of Liverpool, 2020). |
| Hydroxychloroquine sulfate | 1 Totally avoid haloperidol, quetiapine, clozapine, risperidone, and escitalopram. 2 Avoid as far as possible lithium salts and risperidone. 3 Use with great caution mirtazapine, and sertraline. 4 Use with caution aripiprazole, olanzapine, paliperidone, amisulpride, venlafaxine, and trazadone (Drugs.com, 2020; Esteve et al., 2020; University of Liverpool, 2020). |

Note: QTc = corrected QT.
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