# **Practitioner's Corner**

Barriers to Long-acting Injectable Antipsychotic Adherence During the COVID-19 Pandemic: Observations From One Site SARAH E. FORSTER, PhD NAOMI N. GANCZ MARCI L. GAITHER, PhD GRETCHEN L. HAAS, PhD KELLY D. STARVER, PhD STUART R. STEINHAUER, PhD

*Objective:* Long-acting injectable antipsychotics (LAI-As) are a crucial treatment option for individuals with serious mental illness. However, due to the necessity of in-person administration of LAI-As, pandemics pose unique challenges for continuity of care in the population prescribed these medications. This project investigated the impact of the coronavirus disease 2019 (COVID-19) pandemic on LAI-A adherence at a Veterans Health Administration medical facility in the United States, as well as changes in LAI-A prescribing and administration practices during this period.

*Methods:* Electronic health records were evaluated for 101 patients prescribed LAI-As. A subset of 13 patients also participated in an interview and rated subjective concerns about pandemic-related barriers to medication adherence.

*Results:* Pandemic-related barriers to LAI-A adherence and/or changes to LAI-A medications were documented in 33% of the patients. Within-subjects comparison of an adherence metric computed from electronic health record data further suggested a somewhat higher incidence of missed or delayed LAI-A doses during the pandemic compared with before the pandemic. In contrast, only 2 of the 13 patients interviewed anticipated that pandemic-related concerns would interfere with medication adherence.

*Conclusions:* The results of this study suggest that LAI-A access and adherence can be disrupted by pandemics and other public health emergencies but this finding may not generalize to other sites. As patients may not foresee the potential for disruption, psychiatric service providers may need to assist in proactively problem-solving barriers to access. Improved preparedness and additional safeguards against pandemic-related disruptions to LAI-A access and adherence may help mitigate adverse outcomes in the future. Identifying patients at elevated risk for such disruptions may help support these efforts. (Journal of Psychiatric Practice 2022;28;497-

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KEY WORDS: COVID-19, depot administration, antipsychotics, long-acting injectable antipsychotics, medication adherence, serious mental illness

The coronavirus disease 2019 (COVID-19) pandemic has prompted a radical shift toward service delivery via telemental health in the Veterans Health Administration (VHA) and other health care organizations around the world. Interventions that require in-person contact (eg, depot/long-acting injectable medications) are uniquely challenged by these circumstances.<sup>1</sup> They may, for example, be disrupted by personal protective equipment shortages, travel restrictions, and supply chain issues.

FORSTER, GANCZ, and GAITHER: VA Pittsburgh Healthcare System and VISN 4 Mental Illness Research, Education, & Clinical Center (MIRECC), Pittsburgh, PA; HAAS and STEINHAUER: VA Pittsburgh Healthcare System; VISN 4 Mental Illness Research, Education, & Clinical Center (MIRECC); and Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA; STARVER: VA Pittsburgh Healthcare System, Pittsburgh, PA

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Please send correspondence to: Sarah E. Forster, PhD, VA Pittsburgh Healthcare System, VISN 4 MIRECC, University Drive C, Building 30, Pittsburgh, PA 15240 (e-mail: sarah. forster2@va.gov).

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The authors declare no conflicts of interest. DOI: 10.1097/PRA.000000000000673 Concerns regarding the impact of the COVID-19 pandemic specifically on access to long-acting injectable antipsychotic (LAI-A) medications were voiced early in the crisis.<sup>2</sup> The focus on this type of medication reflects the importance of this therapeutic tool for consistent and effective management of psychotic symptoms,<sup>3,4</sup> despite continued underutilization of LAI-As,<sup>5</sup> including within the VHA.<sup>6</sup>

Persons prescribed LAI-A medications represent a population of special concern during the COVID-19 pandemic due to (1) elevated risk of infection and serious illness from COVID-19, (2) possible pandemic-related exacerbation of psychiatric symptoms, and (3) potential for adverse impacts following abrupt changes in health care delivery.7-11 Individuals with serious mental illness are also more likely to be prescribed an LAI-A if they have risk factors for nonadherence to antipsychotic medications, such as clinical or housing instability or a history of nonadherence.<sup>12,13</sup> A pandemic may introduce new barriers to adherence for such patients, including financial hardship, concerns about infection risk, and restrictions on movement within and between communities.<sup>14,15</sup> Therefore, better understanding the impact of the COVID-19 pandemic on LAI-A adherence could enable improved preparedness for future public health emergencies. Such observations may be especially relevant to the psychiatric providers who prescribe and administer LAI-As and are therefore uniquely positioned to identify early signs of nonadherence and other relevant risk factorsboth during times of crisis and in routine clinical practice. Identification of population-specific risk factors for nonadherence or disruption of access to LAI-As could also equip health system administrators to flag individuals who may require special attention in the context of pandemics and other similar events.

The project described in this article represented an effort to characterize the impact of the COVID-19 pandemic on LAI-A adherence at a VHA medical center in the United States. Veterans receiving LAI-As through outpatient psychiatric services at the VA Pittsburgh Healthcare System (VAPHS) were identified and a retrospective chart review was conducted to identify pandemic-related barriers to adherence and related accommodations. It was hypothesized that the COVID-19 pandemic had introduced new barriers to LAI-A adherence, as well as changes in LAI-A prescribing and administration practices. Subjective self-report data on the perceived impact of the pandemic on healthrelated behaviors, including medication adherence, were also collected from a subset of Veterans.

# METHODS

The effort described here represented one component of an ongoing Quality Assurance/Quality Improvement (QA/QI) project funded through the VHA Innovators Network. All of the activities described here were part of a protocol ruled to be institutional review board-exempt by the VAPHS Institutional Review Board. An administrative data query was conducted to identify Veterans scheduled for outpatient LAI-A administration at VAPHS between January 1, 2020, and May 31, 2020. A total of 101 Veterans were identified by the administrative data query, each of whom received information about the project, as well as information concerning pandemic-related support resources, by mail. A subset of 13 of the identified Veterans also participated in a telephone-based interview about LAI-A treatment experiences during the COVID-19 pandemic and provided written informed consent (obtained by mail) to participate in an audiorecorded interview.

## **Electronic Health Record Review**

For the 101 Veterans identified through our administrative data query, data were extracted for the period from March 12, 2020, to July 1, 2020, through a review of electronic health records and included demographic and clinical characteristics, details concerning the prescribed LAI-A (ie, drug, dose, and frequency of administration), LAI-A appointment attendance, and dates of hospitalization, if applicable. Additional outcomes were coded from a review of documentation related to LAI-A administration and medication management encounters, including the impact of the pandemic on appointment attendance and clinical status (if noted), as well as changes in antipsychotic prescribing and administration practices during the pandemic. The period selected for review began on the day after the World Health Organization

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declared the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic (the first cases of SARS-CoV-2 in the Pittsburgh region were identified 2 days after this date on March 14, 2020); thus this period represented the first 111 days of the COVID-19 pandemic response effort. Data during a "prepandemic" period of the same duration (ie, from November 21, 2019, to March 11, 2020) were also reviewed to quantify baseline LAI-A adherence in the same sample of 101 Veterans.

For both the "prepandemic" and "early pandemic" periods under review, the date of the last injection before the start of the data extraction window was identified, and the number of treatment days between this date and the end date of data extraction was computed. This value was subsequently divided by prescribed injection frequency in days to achieve an estimate of the projected number of injections during each data extraction window. The number of injections attended was then subtracted from this value to provide an adherence metric, so that higher values represented more missed and/or delayed injections. Only individuals for whom LAI-A drug and dose frequency remained consistent during both the "prepandemic" and "early pandemic" review periods were included in within-subjects comparisons concerning changes in adherence during the early pandemic period. Due to evidence of skewness and "heavy tails" in the distribution of adherence metrics, which primarily reflected several individuals with a markedly higher incidence of missed or delayed injections during the "early pandemic" period, a nonparametric paired Wilcoxon signedrank test was used to evaluate differences in the adherence metric between the "prepandemic" and "early pandemic" periods.

#### **Subjective Patient Experience**

To complement the data from the health record, 13 Veterans who were on a 2- to 5-week LAI-A administration schedule participated in a telephone-based qualitative interview. Participants were recruited via a mailing that was sent to all Veterans scheduled within the LAI-A clinic at VAPHS between January 1, 2020, and May 31, 2020. This mailing described the project and included information on staying healthy and engaging in self-care during the pandemic, as well as resources for additional support. Veterans interested in participating in an interview were invited to contact the first author by telephone.

In a manner similar to that employed in previous quality improvement efforts targeting LAI-A adherence,<sup>16</sup> patients were asked to describe their experiences with barriers to LAI-A adherence and provide feedback on strategies to support adherence. While the interview did not focus on challenges specific to the COVID-19 pandemic, a brief assessment was conducted to systemically evaluate pandemic-related health anxiety. Specifically, items from the previously-validated Swine Flu Anxiety Inventory<sup>17</sup> were adapted to reference SARS-CoV-2 and COVID-19. A single item was also added to probe the anticipated impact of the COVID-19 pandemic on medication adherence: "To what extent do you expect your concerns about the novel coronavirus disease (COVID-19) to interfere with taking your prescribed medications on schedule?" While the number of respondents (N = 13) was not sufficient to support the validation of the adapted inventory, the results are presented as anecdotal findings that may inform future research efforts in this area. Participants were compensated \$20 for their time.

## RESULTS

#### Sample from the Electronic Health Records

A total of 101 Veterans (92 male, 9 female) were identified (mean age  $\pm$  SD: 58.6  $\pm$  13.2 y). Additional demographic and clinical characteristics of the sample are summarized in Table 1. During the early pandemic period from March 12, 2020, to July 1, 2020, a total of 291 LAI-As were administered; 74 "no show" and 5 "cancelled" appointments were also documented. A pandemic-related barrier to adherence and/or a change in LAI-A prescribing or administration practices was documented in the electronic health record for 33% of the sample during this period. A total of 27 individuals had a change in medication or administration practices due to the pandemic and 6 additional individuals had a documented pandemic-related problem with adherence (eg, missed appointments due to pandemic-related anxiety or travel restrictions) that did not result in a change in medication or administration practices.

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|  | <i>EHR</i> ( <i>N</i> = 101) (%) | <b>Interview</b> (N = 13) (%) |
|--|----------------------------------|-------------------------------|
| Race                                     |                                  |                               |
| White or Caucasian                       | 55                               | 38                            |
| Black or African American                | 41                               | 62                            |
| Multiracial                              | 2                                | 0                             |
| Native Hawaiian or Pacific Islander      | 1                                | 0                             |
| Unknown or declined to answer            | 1                                | 0                             |
| Diagnosis                                |                                  |                               |
| Schizophrenia                            | 57                               | 54                            |
| Schizoaffective disorder                 | 33                               | 23                            |
| Bipolar disorder                         | 5                                | 15                            |
| Major depressive disorder                | 3                                | 8                             |
| Delusional disorder                      | 1                                | 0                             |
| Borderline personality disorder          | 1                                | 0                             |
| Medication                               |                                  |                               |
| Paliperidone palmitate (Invega Sustenna) | 47                               | 54                            |
| Haloperidol (Haldol) decanoate           | 24                               | 23                            |
| Fluphenazine (Prolixin) decanoate        | 10                               | 8                             |
| Paliperiodone palmitate (Invega Trinza)  | 9                                | 0                             |
| Aripiprazole XR (Abilify Maintena)       | 8                                | 15                            |
| Risperidone XR (Risperdal CONSTA)        | 1                                | 0                             |
| Aripiprazole lauroxil (Abilify Aristada) | 1                                | 0                             |
| Housing                                  |                                  |                               |
| Independent housing                      | 69                               | 84                            |
| Personal care home (PCH)                 | 22                               | 0                             |
| Transitional housing                     | 6                                | 8                             |
| Psychosocial residential rehab program   | 2                                | 0                             |
| Unstable/homeless                        | 1                                | 8                             |

Of the 27 individuals requiring a change in medication or administration practices, 18 were unable to attend in-clinic injection appointments due to pandemic-related health precautions. Thirteen of these individuals were residing in a personal care home subject to lockdown; injections were mailed to the personal care homes for administration in 11 of these cases and the 2 remaining patients were converted to oral medication. Two additional patients were residing in communal transitional housing at the onset of the pandemic and were permitted to receive injections in a transport van outside the medical facility. Three additional independently housed individuals were transitioned to in-home injection administration by home care providers. A pandemicrelated change in LAI-A medication was also documented for 9 individuals following shared

decision-making with their providers. A change in medication and/or dosage was made for 5 of these individuals to provide for an extended dosage interval with less frequent clinic visits; 2 other individuals were transitioned from depot to oral medication due to personal preference; and an increase in dose or injection frequency was documented for 2 other individuals due to pandemicrelated exacerbation of psychiatric symptoms.

In the case of the 6 individuals for whom other disruptions to medication access or adherence were documented without a corresponding change in medication or administration practices, the electronic health records revealed evidence of missed appointments attributed to pandemic-related barriers or concerns (eg, loss of transportation, concern about infection risk, confusion about travel restrictions) as well as distress in the context of LAI-A appointments due to concerns about infection risk or pandemic-related delusional content.

The frequency of missed or delayed injections during the early pandemic and prepandemic periods was quantified using the adherence metric (see the Methods section). After excluding individuals with changes in LAI-A drug or dosage interval during either period, which would have made the adherence metric unreliable, a total of 69 individuals were eligible for inclusion. Within-subjects comparison of the adherence metrics derived from the prepandemic review period versus the early pandemic review period was consistent with our prediction of poorer adherence during the pandemic (Z = 1.71, P = 0.044, 1-tailed); however, the effect size was small. The average difference between expected and actual doses of LAI-A during the prepandemic period was 0.82 (SD = 0.68), while this value was 1.41 (SD = 1.83) during the early pandemic period. Importantly, the percentage of patients with adherence metric scores greater than 2 (indicating 2 or more missed doses) increased from 6% during the prepandemic period to 20% during the early pandemic period.

#### **Interview Subsample**

Thirteen Veterans (10 males, 3 females; mean age  $\pm$  SD: 61.5  $\pm$  7.5; see Table 1 for additional details) participated in a telephone-based qualitative interview exploring barriers to attending appointments for LAI-A administration at VA Pittsburgh. These Veterans also completed questionnaire items concerning pandemic-related health anxiety and related behaviors. Notably, 11 of the 13 participants rated the extent to which they expected concerns about the pandemic to interfere with medication adherence as "very little" (0 on a scale of 0-4; mean  $\pm$  SD = 0.31  $\pm$  0.75). Other items assessing the impact of pandemic-related concerns on behavior received higher ratings: influence on social behavior  $1.85 \pm 1.63$ , travel plans  $2.08 \pm 1.80$ , and safety behaviors (eg, hand hygiene)  $2.31 \pm 1.70.$ 

#### DISCUSSION

Pandemic-related barriers to adherence to LAI-As and/ or changes in LAI-A prescribing or administration were documented for 1 in 3 Veterans scheduled for LAI-A administration during early 2020. Nearly half of these cases involved individuals in communal housing (ie, personal care homes or transitional housing facilities) who were no longer able to present to the clinic for injections due to restrictions at their residential facilities. Personal care home residents were not permitted to leave their residential facility for appointments. Individuals in transitional housing, by contrast, were permitted to travel but were required to receive injections in a transport van outside the medical facility. Additional missed appointments were attributed to other pandemic-related barriers to attendance including loss of transportation, confusion about local lockdown policies, and concerns about infection risk.

Pandemic-related changes in LAI-A administration and prescribing were also identified in electronic health records. These changes were primarily made to eliminate or reduce the need for onsite LAI-A administration (ie, mailing injections to personal care homes, transitioning to an extended dosage interval, or conversion to an oral medication). Despite efforts to accommodate the needs of Veterans experiencing barriers to LAI-A adherence during the first months of the pandemic, there were indications of somewhat poorer LAI-A adherence during the early pandemic period (beginning March 2020) relative to a prepandemic period of equivalent duration. While the size of the observed effect was small, there may still be important clinical implications. For example, adherence metric scores indicating 2 or more missed LAI-A doses increased from 6% for the prepandemic period to 20% during the early pandemic period. It was also noted that changes in LAI-A adherence could only be investigated for those who were prescribed the same LAI-A for administration by VA Pittsburgh providers during both review periods. This necessarily excluded individuals who experienced a change in LAI-A medication or administration venue due to the pandemic (eg, those converted to oral medications) and therefore provides an incomplete picture of risks for nonadherence during the early pandemic period.

Our findings add to previously published observations regarding the impact of the COVID-19 pandemic on LAI-A adherence at a non-VA facility in the Pittsburgh area.<sup>18</sup> Specifically, Gannon and colleagues identified that the number of LAI-As administered through an outpatient clinic at the

University of Pittsburgh Medical Center Western Psychiatric Hospital during the first 6 weeks of the pandemic was comparable-demonstrating only a 10% reduction—to the number administered during the 6 weeks preceding the pandemic. While we found evidence of a small but significant change in adherence, we considered longer prepandemic and early pandemic time intervals (~10 wk longer than those used by Gannon and colleagues), as well as a different approach to quantifying adherence that may be more sensitive to intraindividual changes in missed or delayed doses. Interestingly, our finding of an approximate 14% increase in patients with 2 or more missed injections during the early pandemic period is comparable to the 10% reduction in total doses administered reported by Gannon and colleagues. Considering that most LAI-As would be administered once within a given 6-week interval, a 10% reduction in administered injections would be consistent with a 10% increase in patients with missed doses, who may therefore be at increased risk of adverse outcomes including psychotic relapse and hospitalization. The risk of a relapse to psychosis in the context of the COVID-19 pandemic has previously been highlighted in data from Turkey, where a high incidence of LAI-A nonadherence was identified as a contributing factor.<sup>19</sup> While we did not specifically evaluate for negative impacts on patient clinical status in the context of LAI-A nonadherence, such impacts are anticipated and may present unique challenges in a pandemic (eg, safely accommodating a high inpatient psychiatry census).

Our review of electronic health records also revealed documentation of 1 or more pandemicrelated barriers to adherence and/or changes in LAI-A prescribing or administration practices in 33% of our sample. Importantly, these observations provided additional context and insight into patient experiences during the early pandemic period and specifically identified patients residing in communal housing as being at increased risk of disruption to medication access during the initial response to a disease outbreak such at the COVID-19 pandemic. Strategies used to support adherence during this period, such as transitioning to in-home injection providers or longer acting formulations, appropriately reflected guidance concerning the management of LAI-As in a patient with serious mental illness during the COVID-19 pandemic.<sup>20</sup> In most cases, a strategy involving continued maintenance

on an LAI-A was possible, while conversion to oral medications was rare, as was also the case for the Pittsburgh-based community sample described by Gannon et al.<sup>18</sup> However, the overall incidence of pandemic-related changes to LAI-A medication or administration practices was notably lower in our sample (27%) than reported in published data from a Boston area outpatient clinic where 48% of patients experienced such changes.<sup>21</sup> This suggests the potential for more significant pandemic-related disruptions to LAI-A delivery and/or need for pandemic-related adjustments to LAI-As in other treatment contexts.

We also found it important that the Veterans who were interviewed did not anticipate that pandemicrelated concerns would significantly interfere with medication adherence. While these results are presented as anecdotal evidence only, they suggest that potential pandemic-related disruptions to medication adherence are less apparent than potential impacts on travel, social behavior, and safety behaviors (eg, hand hygiene). It should be taken into account that this small subset of 13 individuals may not be representative of the larger sample, and the participants were not prompted to consider external barriers related to community mitigation strategies or other practical considerations like transportation. However, it is likely that proactively addressing potential barriers to medication adherence during an unusual event like a pandemic could be helpful in improving awareness and facilitating problem-solving in this population in the future.

This study had several other limitations. First, pandemic-related problems and concerns were not routinely evaluated or uniformly documented in the electronic health record. For example, some providers noted that a missed appointment was due to the pandemic, but others may have omitted this information. The actual occurrence of pandemicrelated barriers to LAI-A adherence may therefore have been underreported—especially given the high prevalence of pandemic-related concerns among individuals with mental illness documented elsewhere.<sup>22</sup> It should also be noted that only those individuals who were found to be at least partially adherent during the prepandemic period were included in the subset of 69 individuals for whom changes in adherence during the pandemic were evaluated. For this reason, individuals who discontinued LAI-A treatment before the pandemic and/or those who may have re-engaged with LAI-A treatment during the pandemic are not captured in the results reported here.

Taken together, our results add to accumulating evidence that the COVID-19 pandemic has posed unique risks and challenges for individuals with serious mental illness $^{7-11,22}$  and that administration of LAI-A medications may be specifically impacted.<sup>2,7,19,21</sup> Supply chain issues and hospital restrictions during the pandemic have already reduced LAI-A prescribing outside the United States and longterm impacts remain unclear.<sup>2</sup> LAI-A medications are a critical treatment option for many individuals with serious mental illness and have been associated with improved outcomes with respect to adherence, rehospitalization, suicidality, and daily functioning.4,23-25 The COVID-19 pandemic has highlighted the need for improved safeguards against disruption of access to these medications in the context of public health emergencies. Psychiatric providers and staff members are uniquely positioned to identify problems that may disrupt adherence early on and facilitate problemsolving. Evidence of such a proactive response was identified at VAPHS, and the results of our study may also help identify individuals at elevated risk of pandemic-related disruptions to LAI-A access, such as residents in communal housing, in the future.

## CONCLUSIONS

Individuals prescribed LAI-As may be particularly vulnerable and sensitive to pandemic-related disruptions of health care. Improved preparedness for future pandemics may require advance planning for such circumstances through administrative oversight and shared decision-making between patients and providers. Factors that contributed to disruptions to medication access and adherence during early stages of the COVID-19 pandemic may guide future efforts to proactively identify individuals at elevated risk for targeted intervention.

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