

## The COVID-19 Global Pandemic: Implications for People With Schizophrenia and Related Disorders

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**The coronavirus disease-19 (COVID-19) global pandemic has already had an unprecedented impact on populations around the world, and is anticipated to have a disproportionate burden on people with schizophrenia and related disorders. We discuss the implications of the COVID-19 global pandemic with respect to: (1) increased risk of infection and poor outcomes among people with schizophrenia, (2) anticipated adverse mental health consequences for people with schizophrenia, (3) considerations for mental health service delivery in inpatient and outpatient settings, and (4) potential impact on clinical research in schizophrenia. Recommendations emphasize rapid implementation of measures to both decrease the risk of COVID-19 transmission and maintain continuity of clinical care and research to preserve safety of both people with schizophrenia and the public.**

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### Introduction

Starting in January 2020, coronavirus disease-19 (COVID-19) has rapidly developed into a global pandemic with the number of deaths continuing to climb worldwide.<sup>1</sup> The World Health Organization (WHO) and many governments have promulgated social distancing and social isolation to slow the spread of the virus (ie, “flatten the curve”).<sup>2</sup> These public health efforts are targeting the entire population. However, these strategies may be less effective for certain marginalized groups, notably those with schizophrenia and related disorders (referred as schizophrenia in the rest of this manuscript). Features of these disorders, such as delusions, hallucinations, disorganized behavior, cognitive impairment, and poor insight, and

sociodemographic characteristics, including living in congregate housing and homelessness,<sup>3</sup> may put these individuals at higher risk of becoming infected with COVID-19. Furthermore, people living with schizophrenia are at greater risk for adverse outcomes, including death, because compared with the general population, they typically have poorer physical health,<sup>4–6</sup> greater socioeconomic disadvantage,<sup>7</sup> are more socially disconnected,<sup>8</sup> and experience pervasive stigma and discrimination.<sup>9</sup> Here, we discuss (1) why people with schizophrenia are at increased risk of infection with COVID-19 and poor outcomes; (2) possible mental health consequences of COVID-19 infection in people with schizophrenia; (3) possible consequences for health professionals and institutions that serve patients with schizophrenia; and (4) potential adverse impact on clinical research related to schizophrenia.

### Factors That Put People With Schizophrenia at Elevated Risk of Acquiring COVID-19 and of Experiencing Poor Outcomes

People with schizophrenia may be more susceptible to transmission of COVID-19 due to a number of factors: cognitive impairment, lower awareness of risk, and barriers to adequate infection control including congregate living.<sup>10</sup> As schizophrenia is characterized by impairments in insight and decision-making capacity,<sup>11</sup> it may be harder for people with schizophrenia to adopt and adhere to the protective measures recommended to prevent infection (eg, hand washing, social distancing or isolation, confinement).<sup>12</sup> Comorbid substance use disorders, highly prevalent in schizophrenia, may compound impairments in judgment and decision-making.<sup>13</sup> Furthermore, people with schizophrenia are overrepresented in vulnerable populations that are at increased risk for COVID-19 outbreaks,

including prisoners and individuals experiencing homelessness.<sup>14,15</sup> For these groups, as well as people living in congregate housing such as rooming houses and mental health supportive housing, social distancing is near impossible.

Multiple factors increase the risk of poor outcomes from COVID-19 in people with schizophrenia. Smoking, which is prevalent in more than 60% of people with schizophrenia,<sup>16</sup> may increase the risk of disease progression and severe complications from COVID-19, including death, via its effects on lung health and immune responsiveness.<sup>17</sup> Early but robust data indicate that mortality from COVID-19 is particularly elevated in people with comorbid conditions, in particular cardiovascular disease, diabetes, and chronic respiratory disease,<sup>18,19</sup> all of which are more common in people with schizophrenia than the general population.<sup>20–22</sup> Antipsychotic medications commonly prescribed in schizophrenia, particularly clozapine, appear to be associated with risk of death from pneumonia related to impaired swallowing, sedation, and hypersalivation, which worsen during the immune response due to a feedback loop that increases clozapine concentrations<sup>23</sup>; while we are unaware of evidence specifically linking clozapine to deaths from coronaviruses, there is at least a hypothetical risk. Several other factors put people with schizophrenia at risk: they experience substantial disparities in access to health care, related in part to the effects of stigma on help-seeking<sup>24,25</sup> and discrimination when they access care: they are more likely to experience underdiagnosis of comorbid physical illnesses, less likely to receive screening and definitive interventions, and generally receive poorer-quality care.<sup>26</sup> The WHO recommends that “isolating, testing and treating every suspected case, and tracing every contact” is the best way of preventing widespread community transmission.<sup>2</sup> Barriers to uptake of protective measures and appropriate use of health care services among people with schizophrenia could have profound implications for containment of the pandemic. Furthermore, preexisting health disparities could be exacerbated in the context of limited resources. Failure to promote fair and equitable resource allocation could result in more severe complications for people with schizophrenia, including death.<sup>27</sup> Mechanisms and guidelines to uphold the rights to health for people with schizophrenia and promote equitable outcomes are urgently needed.

### **Mental Health Impact of COVID-19 on Schizophrenia**

Previous outbreaks have had persistent mental health effects: following the 2003 Severe Acute Respiratory Syndrome (SARS) pandemic, significantly elevated rates of psychiatric disorders and psychological distress were present.<sup>28</sup> Researchers have already sounded the alarm on how the COVID-19 pandemic may affect the mental health of the general population, and more specifically patients with mental disorders.<sup>10</sup> If the stress related to the COVID-19 pandemic and corresponding public health measures worsens mental health in the general population,

one would expect that their impact might be even higher in people living with schizophrenia.<sup>29</sup> In addition, COVID-19 infection itself may exacerbate symptoms in people with schizophrenia, as coronaviruses may be associated with psychotic symptoms through an immune-related mechanism.<sup>30</sup> Furthermore, symptoms associated with coronaviruses and their treatment have been associated with distress related to symptom severity and isolation, as well as psychosis secondary to steroids and other interventions.<sup>31</sup>

Social distancing, whereby governments have discouraged and imposed restrictions to reduce physical proximity, has been widely adopted in order to decrease community transmission of COVID-19. Fears of contracting COVID-19, along with significant social isolation, have led to more than half of the general public surveyed in China to report that the outbreak had a moderate or severe psychological impact on them.<sup>32</sup> Social distancing practices could have a particularly negative impact on individuals with schizophrenia. Typically, individuals with schizophrenia on average have smaller and poorer-quality social networks than the general population.<sup>33</sup> Thus, they may be more able to comply with, and tolerate, social distancing directives. However, social support has been associated with higher scores on recovery measures in schizophrenia,<sup>34</sup> and broad community supports, including casual contacts at pharmacies, grocery stores, and cafes, have also been associated with improved recovery and community integration scores in schizophrenia.<sup>35</sup> These casual contacts will be disrupted by social distancing, putting patients at risk. Among people with schizophrenia, social isolation may increase the risk for suicide,<sup>36</sup> and stress has been associated with aggressive behavior.<sup>37</sup> Social distancing may also disproportionately impact the ability of people with schizophrenia to maintain their basic needs, given their high reliance on income support and other community services that become more difficult to access.<sup>38</sup> For those with substance dependence, changes in the ability to access substances and their treatments, including agonist therapies, can precipitate crises. Thus, developing approaches to maintain social connection to instrumental supports in the face of social distancing may be especially crucial for people with schizophrenia. Video conferencing apps are widely used to maintain face-to-face connection during the outbreak. Similarly, programs and government agencies that provide essential services to the community should strive to find ways to maintain their efforts to ensure continued and safe delivery of services to vulnerable populations.

### **Impact of the COVID-19 Pandemic on the Management of Inpatients and Outpatients With Schizophrenia**

The COVID-19 pandemic has created challenges for the health professionals and programs that provide services to patients with schizophrenia. Continuity of care is critical for these patients to prevent decompensation and its

consequences, including emergency department visits and hospital admissions resulting in further strain on the health care system, mental and physical deterioration, and even deaths.<sup>39</sup> In February 2020, a cluster of approximately 50 patients and 30 medical staff were diagnosed with COVID-19 at the Wuhan Mental Health Center.<sup>40</sup> Factors hypothesized to have increased the risk of outbreak on an inpatient psychiatric unit included: crowded wards, lack of isolation of suspected or early cases, and lack of clinical pathways to prevent infectious diseases in mental health settings.<sup>40</sup> A COVID-19 outbreak in a South Korean inpatient psychiatric unit infected 100 of its 102 patients and resulted in 7 deaths, at the time accounting for nearly half the COVID-19-related deaths in the country.<sup>41</sup> Factors identified as having contributed to this outbreak were the lack of ventilation due to windows having been sealed shut to prevent suicides, and restrictions on the use of hand sanitizer due to fears that some patients would drink it.<sup>42</sup> The recommendations of the Wuhan group included: use of a preadmission observation ward; screening of admitted patients; screening of hospital staff; temporary prohibition of in-person visitors, external food, and clothing; and improved skills among psychiatric care providers to identify and treat physical diseases.<sup>40</sup> Similar practices—including isolation of at-risk individuals, infection control training and audits—were successfully implemented on some psychiatric inpatient units during the 2003 SARS outbreak.<sup>43</sup> Additional concerns for psychiatric inpatient units include managing agitation, given the risk of contagion, and managing patients and staff who may have been exposed to COVID-19 in the face of shortages of both personal protective equipment and staff.<sup>44</sup> Strategies implemented at the Centre for Addiction and Mental Health in Toronto, Canada, modeled after a system developed during the 2003 SARS outbreak, involve designating different units to segregate patients with suspected infection, diagnosed infection, or absence of infection, and assignment to every inpatient psychiatrist of backup outpatient psychiatrists prepared to seamlessly assume care in the event that an inpatient psychiatrist becomes unable to work.

The immediate impact of COVID-19 could be even greater in outpatient settings, where the majority of mental health care is delivered. Evidence-based models of care for schizophrenia, including assertive community treatment and intensive case management, emphasize in-person contacts in the community and in patients' homes.<sup>45</sup> While outreach visits increase the risk of transmission to both patients and providers, abrupt changes to how mental health services are delivered could increase the risk of service disengagement, medication nonadherence, and distress, all leading to decompensation and relapse.

Phone and video consultations have been rapidly implemented as an alternative to in-person clinical care during the COVID-19 outbreak.<sup>46,47</sup> However,

there is little research examining the suitability of telepsychiatry for schizophrenia compared with other less severe mental disorders (eg, depressive and anxiety disorders) for which it has been typically used to date.<sup>48</sup> A recent randomized-controlled trial of adjunct videoconferencing in patients with severe mental illness compared with usual care found high levels of satisfaction associated with the service, but low use over the 18-month study period.<sup>49</sup> While mobile phone ownership approaches 100% in the general population in North America or Europe, the use of digital technologies is lower in those with psychosis.<sup>50,51</sup> Despite these challenges, outpatient services should strive to reduce in-person contacts when it is safe to do so through the use of telepsychiatry and the provision of longer prescription durations. In addition to digital solutions used to deliver direct patient care, automated text messages<sup>52</sup> and mobile applications<sup>53</sup> can augment care and provide support between appointments. In the midst of the pandemic, providers should be flexible and payers should remunerate care provided over either videoconferencing or phone to ensure access and uptake.<sup>54</sup>

Despite its merits, virtual care cannot completely replace in-person care for schizophrenia. For example, the ability to detain someone involuntarily still requires in person assessment and hearings in many jurisdictions. The COVID-19 pandemic may lead to an increase in the acceptability of telepsychiatry for these quasilegal processes, much as it has facilitated novel funding mechanisms for the expanded delivery of telehealth services.<sup>54</sup> Furthermore, in-person visits are required for the administration of long-acting injectable antipsychotic medications, which are increasingly used in the management of schizophrenia. Given the role of long-acting injectable antipsychotics in reducing hospitalizations compared with oral medications,<sup>55</sup> it is prudent to continue using them, even if these visits may increase the risk of infection for patients and providers. Similarly, clozapine is associated with superior outcomes (and reduced mortality) in treatment-resistant schizophrenia, but it requires regular bloodwork.<sup>56</sup> In response to the COVID-19 pandemic, the US Food and Drug Administration (FDA) has changed some of their regulations for laboratory monitoring requirements on an emergency basis.<sup>57</sup> Thus, during the pandemic, the frequency of blood monitoring required for clozapine maintenance could be reduced. However, the risks and benefits of such a change need to be carefully considered.

### Clinical Research

The FDA<sup>58</sup> and National Institutes of Health (NIH)<sup>59</sup> have provided guidance for researchers conducting clinical trials and human subject studies impacted by COVID-19, emphasizing safety of study participants. Suggestions

include coordination with institutional review boards to limit study visits to those needed for participant safety or coincident with clinical care, conducting virtual study visits, and arranging for required laboratory tests or imaging needed for safety monitoring to occur at local laboratories or clinics. Certain self-administered investigational products typically picked up at the study site may be delivered through alternative secure methods.<sup>58</sup> In addition to upholding the safety of research participants, it is important to safeguard the integrity of research efforts in schizophrenia, which despite its substantial global public health burden, has historically lagged in research funding compared with physical health conditions.<sup>60</sup> Clinical trials in schizophrenia typically have smaller sample sizes than in physical disorders associated with comparable disability and costs, reducing their statistical power and the generalizability of their results. A prolonged cessation of new recruitment into ongoing research studies, coupled with the reduction or elimination of in-person research visits will exacerbate the challenges already present in schizophrenia research, including challenges in study retention. Ensuring the safety of both participants and research staff should be the foremost priority. However, research with participants with schizophrenia should continue through the use of remote assessments and delivery methods in order to prevent worsening disparities in the progress of schizophrenia research.<sup>61</sup>

## Summary

The COVID-19 global pandemic is expected to have an outsized impact on people with schizophrenia, further exacerbating health and economic disparities they experience. Public health interventions designed to slow and curb the spread of the virus (flatten the curve) will likely disproportionately affect people with schizophrenia. We propose the following recommendations for consideration to temper the effect of COVID-19 on people with schizophrenia:

1. Addressing the social determinants of health, including ensuring safe and comfortable housing and implementing strategies to reduce health disparities, should be a foremost priority.
2. Guidelines for resource allocation in the context of the outbreak may help protect vulnerable populations by ensuring fair and consistent decision-making, acknowledging this may be challenging in the short-term, but remains a long-term goal.
3. Families, neighbors, and community-based programs that may comprise the social network for people with schizophrenia should find ways to maintain social connection that adhere to physical distancing, including through the use of video conferencing.
4. Programs and government agencies that provide essential services that address people's basic needs (eg,

income support, food banks) should find ways to continue to safely deliver them.

5. Inpatient mental health settings should develop capacity to rapidly isolate people with suspected and confirmed COVID-19 from each other and nonaffected patients; limit and screen people coming into the facilities; perform infection control training and audits, including proper use of personal protective equipment; and make contingency plans to introduce alternate trained personnel in case frontline staff become ill.
6. Outpatient mental health settings and their funders should embrace the use of telepsychiatry and other digital health interventions to support continuity of care. Prescribers, patients, and caregivers should weigh the risks and benefits of treatments that must be delivered or monitored in person. Long-acting injectable antipsychotics may be safer to continue than to stop, so long as appropriate infection control procedures are followed. Clozapine bloodwork may be completed less frequently to reduce the risk of COVID-19 transmission according with current FDA standards and with ample education provided to the treatment decision-maker.
7. Researchers and institutional review boards should work together to substitute remote assessments and delivery methods to allow studies to safely continue when possible.

We suggest that thoughtful consideration of the implications of COVID-19 for people with schizophrenia may not only reduce the burden of the global pandemic on people with schizophrenia, but also on the population as a whole.

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