COVID-19 Infection and Psychotic Experiences: Findings From the Healthy Minds Study 2020

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ABSTRACT

BACKGROUND: Clinical reports from across the world have documented psychosis in the context of COVID-19 infection; however, there has yet to be a large-scale epidemiological study to confirm this association.

METHODS: We analyzed data from the Healthy Minds Study (N = 15,935; conducted between September and December 2020), which was administered online to students attending one of 28 colleges in the United States. Using multivariable logistic regression, we examined the associations between COVID-19 infection/severity and psychotic experiences over the past 12 months, adjusting for age, gender, race/ethnicity, and international student status as well as anxiety and depression.

RESULTS: More than one fifth of the analytic sample reported COVID-19 infection, and about one in six students with COVID-19 infection reported psychotic experiences over the past 12 months. In weighted multivariable logistic regression models, COVID-19 infection was associated with significantly greater odds of having psychotic experiences (adjusted odds ratio 1.36, 95% CI 1.19–1.48). Compared with being asymptomatic, having moderate (adjusted odds ratio 1.85, 95% CI 1.03–3.31) or severe (adjusted odds ratio 1.76, 95% CI 1.11–2.77) symptoms was associated with significantly greater odds of having psychotic experiences. These associations became statistically nonsignificant when adjusting for depression and anxiety. Hospitalization was not significantly associated with psychotic experiences among students with COVID-19 infection.

CONCLUSIONS: Psychotic experiences are associated with COVID-19 infections, though much of the association is attenuated when accounting for anxiety and depression. Findings based on this sample of college students should be replicated outside of the college context to determine whether psychosis is a neuropsychiatric symptom during and after COVID-19 infection.

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Historically, mental well-being often declines across general populations following disastrous events (1), including epidemics and pandemics. A systematic review found that common symptoms among patients admitted to the hospital for severe acute respiratory syndrome or Middle East respiratory syndrome included confusion, depression, anxiety, memory impairment, and insomnia (2). Studies have shown that coronavirus disease 2019 (COVID-19) infection produces similar psychiatric and neuropsychiatric presentations (3), with the possible addition of psychosis. Numerous individual client reports have described the occurrences of psychotic symptoms in the context of COVID-19 among people with no known history of psychosis prior to infection (4–8); in general, the reports described individuals presenting with hallucinations, delusions, disorganized thinking, confusion, and cognitive problems (3), and several of these individuals had no personal or familial history of psychiatric illness (9). In light of the emerging findings, rapid reviews and opinion pieces have questioned whether COVID-19 is linked to psychosis (5,10,11), consistent with the increased risk for psychosis observed in prior epidemics and pandemics (12), putatively via several direct and indirect pathways, such as inflammatory responses (cytokine storms) that are profound enough to produce hallucinations and delusions (13).

The extent to which anxiety or depression explains the association between COVID-19 infection and psychosis has yet to be investigated. Mental health screenings in the general population increased by as much as 200% in 2020 compared with 2019 (14)—an escalation that corresponded with increases in reported moderate to severe anxiety and depression attributable to a host of factors, including economic distress, social isolation and loneliness, and fear of illness or death (15–17). Taquet et al. (18) found that in patients with no prior psychiatric history, a diagnosis of COVID-19 was associated with increased incidence of first psychiatric diagnosis within 14 to 90 days. Immune response and systemic inflammation have been positively associated with measures of anxiety and depression among COVID-19 survivors (19) and may explain, at least in part, the link between COVID-19 infection and psychosis (20).

To date, anecdotal reports have yet to be corroborated in large samples, given the limited availability of epidemiological
data collected on the topic during the pandemic. Therefore, we used a large sample of college students [whose average age overlapped with the peak age range for the onset of psychosis (21)] to study the following: 1) whether COVID-19 infection is associated with psychotic experiences; 2) whether symptom severity is associated with increased odds of psychotic experience among people who are infected; and 3) whether the association between COVID-19 infection and psychotic experiences is explained by general psychopathology (anxiety and depression).

METHODS AND MATERIALS

Sample

We analyzed data from the fall cohort of the 2020 Healthy Minds Study (HMS), a cross-sectional, web-based survey examining mental health and related factors in undergraduate and graduate student populations. The survey was administered at 28 universities in September through December 2020. At each university, a random sample of 8000 students was invited by e-mail to participate except at smaller universities (< 8000 students), where all students were invited to participate. The response rate was 14%, which is typical of online surveys of college populations (17). Sample probability weights were used to adjust for nonresponse using administrative data on full student populations with respect to gender, race/ethnicity, academic level, and grade point average. The HMS was approved by the Health Sciences and Behavioral Sciences institutional review board at the University of Michigan and at all participating campuses. The current study is a secondary data analysis of de-identified data collected by the HMS, the entirety of which was made available to the authors on request at https://healthymindsnetwork.org/hms/.

Measures

COVID-19 Infection. COVID-19 infection was measured by asking participants whether they had COVID-19 (the novel coronavirus disease). Responses included the following:

- Yes (confirmed by a test)
- Probably (e.g., a health care provider told me that I likely had COVID-19)
- Maybe (e.g., I have had symptoms consistent with COVID-19, but it was not confirmed by a test)
- No (no symptoms or other reason to think I have had it)

It is widely accepted that rates of COVID-19 infection are underestimated. The U.S. Centers for Disease Control and Prevention (22) stated that the confirmed COVID-19 cases likely represent only a fraction of the true number of cases that have occurred in the population, given delays or unavailability of testing, reluctance to get tested, barriers to formal treatment, false-negative test results, and the prevalence of mild/asymptomatic infections. Thus, responses of “yes,” “probably,” and “maybe” were combined to form a binary variable indicating likely COVID-19 infection. Further, sensitivity analyses used different thresholds of certainty about COVID-19 infection.

COVID-19 Severity. Participants who responded “yes/probably/maybe” were then asked a question about COVID-19 severity using two items. The first item asked about the severity of the symptoms. Respondents’ answers included the following:

- Severe (e.g., difficulty breathing or speaking, low blood pressure, fever of 103°F [39.4°C] or higher)
- Moderate (e.g., some shortness of breath, cough, fever of 100.4°F [38°C] or higher)
- Mild (e.g., coldlike symptoms)
- No symptoms (asymptomatic)

The second item asked whether (yes/no) respondents were hospitalized because of COVID-19 symptoms.

Psychotic Experiences

Psychotic experiences were measured using an abbreviated version of the World Health Organization Composite International Diagnostic Interview Psychosis Screen (23), which is a reliable and valid measure that has been used in large global epidemiology studies across multiple countries (24). Respondents were asked if they had ever experienced the following: 1) a feeling that something strange and unexplainable was going on that other people would find hard to believe; 2) a feeling that people were too interested in them or that there was a plot to harm them; 3) a feeling that their thoughts were being directly interfered with or controlled by another person or that their mind was being taken over by strange forces; and 4) an experience of seeing visions or hearing voices that others could not see or hear when they were not half asleep, dreaming, or under the influence of alcohol or drugs. Endorsing any of these experiences constituted lifetime psychotic experience. Respondents were then asked a single binary question asking whether these experiences occurred over the past 12 months. Only psychotic experiences within 12 months were used in these analyses as this period coincided with the timing of the COVID-19 pandemic.

Depression and Anxiety. Depression was measured using the 9-item Patient Health Questionnaire (25), and anxiety was measured using the 7-item Generalized Anxiety Disorder Scale (26), both of which are reliable, validated, and widely used measures.

Sociodemographic Covariates. Respondents self-reported sociodemographic characteristics, including gender identity (man, woman, other), race/ethnicity (White, Black, Latinx, Asian American/Pacific Islander, multicultural, other), age (continuous), and international student status (yes/no).

Analysis

In the HMS sample, 15,935 respondents completed the COVID-19 module and psychotic experiences items. Missing data for individual variables were handled using listwise deletion, which is appropriate for these survey data given the low frequency of missingness (< 3%). Sample sizes were allowed to vary depending on the variables that were available. Multivariable logistic regression analyses were used to test for
associations between COVID-19 infection and psychotic experiences over the past 12 months. Among those with COVID-19 infection, multivariable logistic regression analyses examined COVID-19 symptom severity and psychotic experiences, and COVID-19 hospitalization and psychotic experiences. All models were adjusted for age, gender, race/ethnicity, and international student status. Models were then hierarchically adjusted for depression and anxiety. All logistic regression models were repeated using two different thresholds for COVID-19 infection: the first threshold defined COVID-19 infection as “1” only if respondents answered yes (confirmed by a test); the second threshold defined COVID-19 infection as “1” if respondents answered “yes” (confirmed by a test) or “probably” (a health care provider told the respondent that they likely had COVID-19). In addition, all analyses were repeated without using survey weights. All results were presented as odds ratios with 95% confidence intervals.

RESULTS
In the sample of college students who completed the COVID-19 items, approximately one fifth of the sample (22.03%, n = 3450) reported COVID-19 infection, and 14.44% (n = 2215) reported having at least one psychotic experience over the past year. COVID-19 infection was significantly more prevalent among people with psychotic experiences than among those without psychotic experiences, and about 17.7% (n = 582) of people with COVID-19 infection reported psychotic experiences, which is significantly higher than the 13.51% (n = 1633) of people without COVID-19 infection who reported psychotic experiences. When restricting the sample to only people with COVID-19 infection, respondents with psychotic experiences tended to have more severe symptoms and had higher prevalence of hospitalization than respondents without psychotic experiences, though the difference was not statistically significant for hospitalization (Table 1).

In multivariable logistic regression models (Table 2), having COVID-19 infection was associated with a 1.36 times greater odds of having psychotic experiences, adjusting for gender, age, race/ethnicity, and international student status. When additionally controlling for depression and anxiety, having COVID-19 infection was associated with 1.14 times greater odds of having psychotic experiences, though this association did not reach a conventional level of statistical significance. In unweighted models, COVID-19 infection was significantly associated with 1.33 times greater odds of psychotic experiences adjusting for basic sociodemographic characteristics and 1.14 times greater odds of psychotic experiences after additionally controlling for depression and anxiety.

In sensitivity analyses, we considered COVID-19 infection to be only that which was confirmed through test or diagnosed by a medical professional. We found no statistically significant associations with psychotic experiences in weighted models; however, COVID-19 infection was associated with 1.25 times greater odds of having psychotic experiences in unweighted models, though this association lost statistical significance with the additional adjustment for depression and anxiety. If we consider COVID-19 infection as only that which is confirmed through a COVID-19 test, then COVID-19 infection was not significantly associated with psychotic experiences.

Among individuals with COVID-19 infection (Table 3), having greater severity of symptoms was associated with greater odds of having a psychotic experience when adjusting for sociodemographic characteristics. Compared with being asymptomatic, having mild symptoms was not associated with psychotic experiences, but having moderate or severe symptoms was associated with significantly greater odds of having psychotic experiences. However, the association was no longer statistically significant after adjusting for anxiety and depression. In unweighted models, compared with individuals who were asymptomatic, those who had severe COVID-19 were 2.25 times as likely to have psychotic experiences, though this association did not remain statistically significant after adjusting for depression and anxiety.

Being hospitalized for COVID-19, which arguably represents the most severe instances of COVID-19 illness, was not significantly associated with psychotic experiences compared with being infected with COVID-19 but not being hospitalized.

DISCUSSION
To our knowledge, this was the first large-scale cross-sectional descriptive study to examine the association between COVID-19 infection and 12-month psychotic experiences. While several published clinical reports have suggested the emergence of psychotic symptoms in the context of COVID-19 illness [e.g. (4,7,8)], this study was among the first to show the relationship in a large sample of people, most of whom belong to an age range when psychotic experiences often first emerge (21). The effects of COVID-19 infection attenuated and lost statistical significance when accounting for anxiety and depression in weighted models, suggesting that the relationship may be explained by other psychopathology. Among individuals with COVID-19 infection, mild symptoms were not significantly associated with psychotic experiences, but significant associations did exist for moderate and severe symptoms. However, these associations were not statistically significant after adjusting for anxiety and depression. We did not find evidence to suggest that respondents hospitalized for COVID-19 infection were any more likely to have psychotic experiences than those who were not hospitalized for COVID-19 infection, though this may have been due to inadequate power given the small cell counts.

While psychotic disorders are rare, a growing body of research has shown that individuals in the general population will report mild psychotic experiences and yet never develop a psychotic disorder (27). In the United States, the lifetime prevalence of psychotic experiences can range from roughly 10% to 20% of the general adult population (28–30). Psychotic experiences have become a public health concern because they appear to be linked to a host of mental and physical health problems, disability, suicidal thoughts and behaviors, and mortality (31).

There are several pathways by which COVID-19 infection may be related to psychotic experiences. It is possible that COVID-19 may have a direct impact on the central nervous system operating through immunologic mechanisms and neurotoxicity (32,33). Indeed, prior studies have noted that certain viral infections may play a critical role in the development of subsequent psychotic experiences (34,35).
Depression Scale, PHQ-9 7.83
Anxiety Scale, GAD-7 6.85

COVID-19 infection can produce several neuropsychiatric symptoms, and these symptoms may be indicative of COVID-19. However, it is also possible that COVID-19 may produce psychotic experiences indirectly through various psychosocial mechanisms, such as social isolation. Moreover, COVID-19 symptoms (such as nocturnal cough) may cause sleep disturbances, which are linked to psychotic experiences.

Studies of previous pandemics have noted that acute viral infection can produce several neuropsychiatric symptoms, including psychosis, which can linger after recovery by weeks or longer. Our results suggested that the association was mediated by anxiety and depression, although this can be indicative of COVID-19-related inflammation as a common cause for all three of these psychiatric outcomes.
experiences (40,41). While we cannot distinguish between these mechanisms using these data, we found evidence to suggest that the associations between COVID-19 and psychosis in individual case reports may generalize to a broader population, raising the possibility that this risk is due to direct neurological or inflammatory effects of the infection on mental health.

Findings from this study should be interpreted bearing in mind several potential limitations. First, data were cross-sectional and did not allow for us to ascertain the temporal order of events or make causal inferences. It seems unlikely that psychotic experiences would necessarily lead to COVID-19 infection, though psychotic experiences are associated with other common mental disorders, including substance use, which allows for the possibility that people with these disorders may be less likely to observe quarantine mandates and social distancing, thus being more vulnerable to COVID-19 infection. Substance use in particular may result in risky behaviors that increase the risk of COVID-19 infection. Further research is needed to understand the mechanisms underlying the association between COVID-19 and psychotic experiences.

### Table 2. Multivariable Logistic Regression Showing Associations Between COVID-19 Infection and Psychotic Experiences Over the Past 12 Months (Healthy Minds Study, September–December 2020)

|                      | Weighted No Adjustments for Depression or Anxiety | Weighted Adjusted for Depression or Anxiety | Unweighted No Adjustments for Depression or Anxiety | Unweighted Adjusted for Depression or Anxiety |
|----------------------|--------------------------------------------------|---------------------------------------------|-----------------------------------------------------|-----------------------------------------------|
| COVID-19 Infection   | aOR (95% CI) p Value                             | aOR (95% CI) p Value                        | aOR (95% CI) p Value                                 | aOR (95% CI) p Value                          |
| Yes                  | 1.36 (1.12–1.63) .002                            | 1.14 (0.93–1.40) .210                       | 1.33 (1.20–1.47) .000                               | 1.14 (1.02–1.28) .018                        |
| No                   | 1.00                                             | 1.00                                        | 1.00                                                | 1.00                                          |
| n                    | 15,930                                           | 15,532                                     | 15,930                                              | 15,532                                       |

Sensitivity Analysis 1: COVID-19 Infection

|                      | Weighted No Adjustments for Depression or Anxiety | Weighted Adjusted for Depression or Anxiety | Unweighted No Adjustments for Depression or Anxiety | Unweighted Adjusted for Depression or Anxiety |
|----------------------|--------------------------------------------------|---------------------------------------------|-----------------------------------------------------|-----------------------------------------------|
| Yes                  | 1.14 (0.91–1.43) .238                            | 1.03 (0.79–1.33) .851                       | 1.25 (1.08–1.46) .004                               | 1.15 (0.97–1.35) .100                        |
| No                   | 1.00                                             | 1.00                                        | 1.00                                                | 1.00                                          |
| n                    | 15,930                                           | 15,532                                     | 15,930                                              | 15,532                                       |

Sensitivity Analysis 2: COVID-19 Infection

|                      | Weighted No Adjustments for Depression or Anxiety | Weighted Adjusted for Depression or Anxiety | Unweighted No Adjustments for Depression or Anxiety | Unweighted Adjusted for Depression or Anxiety |
|----------------------|--------------------------------------------------|---------------------------------------------|-----------------------------------------------------|-----------------------------------------------|
| Yes                  | 0.89 (0.67–1.17) .388                            | 0.96 (0.72–1.26) .736                       | 1.10 (0.90–1.35) .353                               | 1.14 (0.92–1.40) .242                        |
| No                   | 1.00                                             | 1.00                                        | 1.00                                                | 1.00                                          |
| n                    | 15,930                                           | 15,532                                     | 15,930                                              | 15,532                                       |

All models were adjusted for gender, age, race/ethnicity, and international student status. Sample probability weights adjust for nonresponse using administrative data on full student populations in terms of gender, race/ethnicity, academic level, and GPA.

aOR, adjusted odds ratio.

1COVID-19 infection was coded “yes” if respondents answered “yes,” “probably,” or “maybe.”

Sensitivity analysis 1: COVID-19 infection was coded “yes” or “probably.”

Sensitivity analysis 2: COVID-19 infection was coded “yes” only if respondents answered “yes.”

### Table 3. Multivariable Logistic Regression Showing Associations Between COVID-19 Infection Severity and Psychotic Experiences Among Individuals With COVID-19 Infection Over the Past 12 Months (Healthy Minds Study, September–December 2020)

|                      | Weighted No Adjustments for Depression or Anxiety | Weighted Adjusted for Depression or Anxiety | Unweighted No Adjustments for Depression or Anxiety | Unweighted Adjusted for Depression or Anxiety |
|----------------------|--------------------------------------------------|---------------------------------------------|-----------------------------------------------------|-----------------------------------------------|
| COVID-19 Severity    | aOR (95% CI) p Value                             | aOR (95% CI) p Value                        | aOR (95% CI) p Value                                 | aOR (95% CI) p Value                          |
| Asymptomatic         | 1.00                                             | 1.00                                        | 1.00                                                | 1.00                                          |
| Mild                 | 1.17 (0.65–2.09) .588                            | 1.32 (0.70–2.48) .384                       | 1.12 (0.78–1.61) .533                               | 1.09 (0.75–1.59) .634                        |
| Moderate             | 1.85 (1.03–3.31) .039                            | 1.63 (0.92–2.88) .093                       | 1.69 (1.17–2.45) .005                               | 1.31 (0.89–2.13) .169                        |
| Severe               | 1.76 (1.11–2.77) .017                            | 1.41 (0.82–2.40) .203                       | 2.25 (1.42–3.55) .001                               | 1.48 (0.92–2.40) .107                        |
| n                    | 3438                                             | 3376                                       | 3438                                                | 3376                                         |
| COVID-19 Hospitalization |                                                |                                             |                                                     |                                               |
| Yes                  | 1.51 (0.56–4.12) .404                            | 1.46 (0.46–4.66) .509                       | 1.50 (0.75–2.99) .255                               | 1.37 (0.66–2.83) .401                        |
| No                   | 1.00                                             | 1.00                                        | 1.00                                                | 1.00                                          |
| n                    | 3468                                             | 3405                                       | 3468                                                | 3405                                         |

All models are adjusted for gender, age, race/ethnicity, and international student status. Sample probability weights adjust for nonresponse using administrative data on full student populations in terms of gender, race/ethnicity, academic level, and GPA.

aOR, adjusted odds ratio.
behaviors (e.g., not wearing masks, congregating in close quarters, flouting lockdown restrictions). Further, psychotic experiences (delusional ideation) may make one mistakenly perceive illness or overestimate symptom severity. Future epidemiological surveys could attempt to ascertain the timing of the onset of psychotic experiences relative to the onset of COVID-19 symptoms, while accounting for common mental disorders. Second, the data were self-reported and may have been vulnerable to recall and social desirability biases (e.g., reluctance to disclose COVID-19 infection or psychotic experiences). More research is needed on this topic that assesses the presence of COVID-19 through polymerase chain reaction or antigen testing or through more comprehensive assessments of symptoms of COVID-19 and health behaviors that could be linked to psychosis (e.g., delirium secondary to fever, using anticholinergic medications to treat respiratory infections resulting in intoxication, sleep disturbances, decrements in oxygenation). Third, the sample consisted of college students, and it remains to be seen whether findings are applicable to other populations. That being stated, college students are typically within the peak age range for the onset of psychotic experiences (21), making them an appropriate population for this study. While college students as a whole may be less likely to experience psychotic experiences than individuals with less education, our study showed that a significant percentage of the sample still reported psychotic experiences. Moreover, the relationship between COVID-19 infection and psychotic experiences may even be stronger outside of the university context. Fourth, the response rate was 14%, which raises concerns about selection bias and generalizability of findings, though this response rate is comparable to surveys of this nature (42) and survey weights were used to adjust for nonresponse. To be thorough, we also provided unweighted analyses. Finally, we did not have data on the past-year prevalence of individual psychotic experiences, only the composite measure, preventing an item-by-item analysis. This study adds to an emerging body of literature that shows COVID-19 infection can potentially impact mental health, specifically psychosis. Studies have already noted the neuropsychiatric and cognitive effects of COVID-19, including difficulty concentrating and memory problems (3,18,36,43,44). Our findings suggest that COVID-19 infection may be linked to psychotic experiences among college students as well as potentially the larger population and that these associations are largely explained by anxiety and depression. While it is not yet clear if findings are attributable to the biological effects of the virus (e.g., inflammation) or social consequences of the pandemic (e.g., social isolation), best practices in the delivery of tele-psychotherapy [see (45)] may provide guidance on how to support people affected (directly or indirectly) by the COVID-19 pandemic, including individuals experiencing symptoms of psychosis throughout the course of illness or even after recovery from acute illness in the context of long-haul syndrome.

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Codebooks and datasets are available at https://healthymindsnetwork.org/

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