COVID-19 and severe mental illness in Israel: testing, infection, hospitalization, mortality and vaccination rates in a countrywide study

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The aim of this study was to compare rates of testing, infection, hospitalization, mortality and vaccination for COVID-19 between individuals with a history of hospitalization for a psychiatric disorder and the general population.

INTRODUCTION

Some [1, 2] but not all [3] studies have shown that, compared to controls or to the general population, individuals with a psychiatric disorder were more likely to be tested for COVID-19. Similarly, some [4–7] but not other [1, 3, 8] studies have shown that individuals with a psychiatric disorder were more likely to have a positive test result. If infected with COVID-19, individuals with a psychiatric disorder [3, 6, 7, 9–12], especially bipolar disorder [8] or schizophrenia [2, 13, 14], are at increased risk of suffering from a more severe course of illness and have higher rates of mortality. These studies were limited, in that some [7, 8] did not include entire populations, and others [2, 9] did not control for deaths unrelated to COVID-19 in individuals with a psychiatric disorders [3, 11, 12, 14] Many authors have recommended prioritization of COVID-19 vaccination for people with severe mental illness, and some but not all studies reported lower rates of vaccination in persons with psychiatric disorders [15, 16] compared with controls. To date, no studies have been published on rates of vaccination for COVID-19 of individuals with a history of hospitalization for a psychiatric disorder in an entire country.

The aim of this study was to compare rates of testing, infection, hospitalization, mortality, and vaccinations for COVID-19 between individuals with a history of hospitalization for a psychiatric disorder, and the general population.

MATERIALS AND METHODS

In Israel, the national psychiatric case register (NPCR) is mandated by law, and records all hospitalizations and discharges in any psychiatric inpatient facility in the country, using the patient’s unique identity number. In this study, we followed up a nation-wide cohort of all persons ever hospitalized before March 1st 2020 (the onset of COVID-19 in Israel), aged 18 and above on that date with a psychiatric disorder, defined as an ICD-10 diagnosis of F10-F69 or F90-F99. We looked specifically at persons from this cohort with a last discharge diagnosis of non-affective psychotic disorders (F20-F29), in particular schizophrenia (F20.0-F20.9), and with any affective disorder (F30-F39), in particular bipolar disorder (F30-F31). Where the last-discharge diagnosis was not available the diagnosis at the last admission was used. Israel has national databases on COVID-19, including the results of all tests for COVID-19 using RT-PCR, data on COVID-19 hospitalization, death attributed to COVID-19, all-cause mortality, and data on vaccinations against COVID-19. Persons who tested positive for COVID-19 were further questioned for underlying diseases, and these data were recorded in the COVID-19 database. Data on psychiatric hospitalizations was merged with the COVID-19 databases using the unique identity number of each citizen in the country, utilizing data available until March 31, 2021 for testing.
infection, hospitalization and vaccination, and until April 30, 2021 for
death, to allow for follow up between hospitalization and death of at least
one month.

Israel administered the Pfizer BNT162B2 vaccine, starting on 19 December
2021. The vaccinations were administered free-of-charge in easily accessible
vaccination centers located all over the country to all members of the
population aged 16 and above. We identified all citizens who had had two
doses of vaccine by March 31, 2021, calculating their rate using those alive in
the country on that date as the denominator.

Data analysis
Age-specific and age-adjusted percentages were calculated for testing,
confirmed infection and vaccination, dividing the population into age
groups of 18–24, 25–34, 35–44, 45–54, 55–64, 65–74, 75–84 and 85 and
above, and using the Israeli population in 2019 as the standard population.
Rates of COVID-19 hospitalization, COVID-19 attributed deaths and all-
cause mortality as an age-adjusted percentage of those infected by COVID-
19 over the study period were calculated. These rates were calculated for
individuals with a history of hospitalization for a psychiatric disorder
compared to the total population aged 18 and above on March 1st, 2020, using
population estimates based on data from the Israeli Central Bureau of
Statistics (CBS, https://www.cbs.gov.il). Hospitalization and mortality
among those with a confirmed infection with COVID-19 were further
compared between individuals with a history of hospitalization for a
psychiatric disorder and the total population using two logistic regression
models, one controlling for sex and age (grouped into 18–54, 55–64,
65–74, 75–84 and 85+) and the second with the addition of vaccination
status (if fully vaccinated before COVID-19 diagnosis) and comorbid
medical conditions, including heart disease, diabetes, hypertension, lung
disease, liver disease, immunosuppression, cancer, asthma, kidney disease,
cerebrovascular disease, dementia, digestive system diseases, thyroid
disease, hypercholesterolemia and obesity.

In order to examine the additive effect of COVID-19 on all-cause
mortality, age-adjusted rates of all deaths in individuals with a history of
hospitalization for a psychiatric disorder not infected with COVID-19 during
the study period was calculated.

Finally, among individuals with a history of hospitalization for a
psychiatric disorder, a multiple logistic regression model examined the
effect of demographic and clinical factors on the likelihood of being tested
for or infection with COVID-19, and of being vaccinated. Factors included
in the model were sex, age, psychiatric diagnosis grouped into non-
affective psychotic disorders, affective disorders or other psychiatric
disorders; drug or alcohol abuse, suicide attempt before any psychiatric
hospitalization, having at least one involuntary hospitalization, and the
number of psychiatric hospitalizations.

This study was approved by the IRB of the Israeli Ministry of Health. The
identity number was encrypted in order to protect the identity of the study
participants.

RESULTS
There were 125,273 individuals alive aged 18 and above on March
1st 2020, with a history of hospitalization for a psychiatric disorder.

Rates of COVID-19 testing
Compared with the total population, rates of having at least one
COVID-19 PCR test were lower in individuals with a history of
hospitalization for a psychiatric disorder for those aged under 65,
and aged 85 and over, with no significant differences at ages
65–74, and higher rates of testing in the total population for
persons aged 75–84. Sixty two point three percent (95% CI
62.2–62.4) of the total population had at least one COVID-19 test,
compared to 51.2% (95% CI 50.8–51.7) of individuals with a history
of hospitalization for a psychiatric disorder (age adjusted rates, Fig. 1A, and web supplement).

Age adjusted rates of COVID-19 confirmed infection,
hospitalization and mortality (Table 1)
The confirmed infection rate with COVID-19 was lower among
individuals with a history of hospitalization for a psychiatric
disorder (5.9%; 95% CI 5.8–6.1) than in the total population (8.9%;
95% CI 8.9–8.9).

Among persons with a confirmed infection with COVID-19, the
hospitalization rate in the total population was 8.8% (95% CI:
8.7–8.8), and was significantly higher among individuals with a
history of hospitalization for a psychiatric disorder (15.1%, 95% CI
14.2–15.9), highest for schizophrenia (17.2%, 95% CI 15.5–19.0) and
somewhat lower for bipolar disorder (12.5%, 95% CI 9.8–15.2). The mortality rate both for COVID-19 related deaths and all deaths was
also higher in individuals with a history of hospitalization for a
psychiatric disorder, 2.9% (95% CI 2.5–3.2) and 4.1% (95% CI 3.7–4.5),
respectively, 1.6–1.7 times the rates in the total population (1.8%,
95% CI 1.8–1.9 and 2.4%, 95% CI 2.3–2.4, respectively).

All-cause mortality rates for individuals with a history
hospitalization for a psychiatric disorder with a confirmed
infection with COVID-19 were over twice as high compared to
persons with the same psychiatric diagnoses without COVID-19
(Table 1), particularly for males, 5.1% (95% CI 4.4–5.8), compared
to 2.1% (95% CI 2.0–2.2) for those without COVID-19.

Rates of confirmed COVID-19 infection were slightly lower, and
rates of hospitalization and mortality higher for males than
females in all diagnostic groups.

Rate ratios with 95% CI are presented in the web supplement.

Effect of age on rates of confirmed COVID-19 infection,
hospitalization and mortality
Confirmed COVID-19 infection rates were significantly higher in
the total population compared to individuals with a history of
hospitalization for a psychiatric disorder up to age 65; at ages
75–84 individuals with a history of hospitalization for a psychiatric
disorder had higher rates of confirmed COVID-19 infection. In
persons over age 85 there was no significant difference between the
groups (Fig. 1B and web-supplement).

Hospitalizations and mortality rates attributed to COVID-19, and
all-cause mortality rates were significantly higher in individuals
with a history of hospitalization for a psychiatric disorder up to age
74; at age 75 and above there were no significant differences
between individuals with a history of hospitalization for a
psychiatric disorder and the total population (Fig. 2 and web-
supplement).

Risk of hospitalization and mortality in individuals with
confirmed COVID-19 infection
Among individuals with confirmed COVID-19 infection, the age
and sex adjusted risks of hospitalization and all-cause mortality
were over twice as high for individuals with a history of
hospitalization for a psychiatric disorder compared to the total
population, adjusted odd ratio (AOR) 2.10 (95% CI 1.96–2.25) and
2.02 (95% CI 1.80–2.28), respectively. Risk of death attributed to
COVID-19 was also increased, to a somewhat lesser extent, AOR =
1.76 (95% CI 1.54–2.01). Risk for hospitalization and all-cause
mortality was even higher amongst persons with schizophrenia,
AOR = 2.43 (95% CI 2.16–27.3), and 2.42 (95% CI 2.00–2.94),
respectively (Table 2). When vaccination status and underlying
medical comorbidity were added to the model, the adjusted OR increased, reaching 2.52 (95% CI 2.24–2.84) and 2.69 (95% CI
2.21–3.27) for hospitalization and all-cause mortality amongst
persons with schizophrenia.

Rates of COVID-19 vaccination
Individuals with a history of hospitalization for a psychiatric
disorder were less likely to be vaccinated at all ages. Total age-
adjusted vaccination rate was 74.9% (95% CI: 74.8–75.0) for
the total population aged 18 and over, compared to 60.4% (95% CI:
59.9–60.8) for those with a history of hospitalization for a
psychiatric disorder; 56.9% (95% CI: 56.3–57.6) for persons with
non-affective psychotic disorders, and 66.5% (95% CI 65.3–67.7)
for persons with affective disorders. Rates of vaccination were
especially low in individuals with a history of hospitalization for a
psychiatric disorder aged 85 and above, 48.3% (95% CI 46.5–50.1),

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particularly in persons with non-affective psychotic disorders, 37.2% (95% CI 34.4–39.9), compared to the rates of persons vaccinated in the total population, 80.4% (95% CI 80.2–80.6, Fig. 1C and web-supplement).

Risk for COVID-19 testing, confirmed infection and vaccination among individuals with a history of hospitalization for a psychiatric disorder

Table 3 shows the odds ratios and 95% CI from multiple logistic models predicting whether individuals with a history of hospitalization for a psychiatric disorder would be tested for COVID-19, be infected, or be vaccinated.

The chance of being tested for COVID-19 was lower for males, declined steadily with age, was lowest for those with non-affective psychotic disorders and for those who had at least one involuntary psychiatric hospitalization.

Compared to persons aged 18–24, risk of confirmed infection among individuals with a history of hospitalization for a psychiatric disorder was significantly lower in all other age groups. Persons with substance or alcohol abuse reported at any psychiatric hospitalization had lowest risk for confirmed infection.

Older, compared with younger individuals with a history of hospitalization for a psychiatric disorder were more likely to be vaccinated; persons with affective disorders were more likely and persons with non-affective psychotic disorders were less likely to be vaccinated. Persons with drug/alcohol abuse recorded at any psychiatric hospitalization had lower rates of vaccination, AOR = 0.79 (95% CI 0.77–0.82), and 0.78 (95% CI 0.74–0.81), respectively, as did those with a history of at least one involuntary hospitalization, AOR = 0.67 (95% CI 0.65–0.69).

The chance for an individual with a history of hospitalization for a psychiatric disorder to be tested for COVID-19, have a confirmed infection or to be vaccinated increased significantly with number of hospitalizations, particularly for testing (Table 3).

**DISCUSSION**

This study on the entire population of Israel examined the effect of COVID-19 on all individuals with a history of hospitalization for a psychiatric disorder.
Table 1. Age-adjusted\(^a\) rates with 95% confidence intervals (CI) of COVID-19 infection, hospitalization and deaths by psychiatric diagnosis, and deaths in non-infected patients with SMI.

| Diagnosis                        | Number of patients | Number of patients infected | Age-adjusted % | Number of patients hospitalized| COVID-19 deaths\(^b\) | All deaths\(^c\) | Hospitalized COVID-19 deaths\(^b\) | All deaths\(^c\) | COVID-19 deaths\(^b\) | All deaths\(^c\) |
|----------------------------------|--------------------|-----------------------------|----------------|-------------------------------|---------------------|----------------|----------------------------------|----------------|---------------------|----------------|
| Total                            | 60,590             | 3432                        | 6.1 (5.9–6.3)  | 677                           | 138                 | 204            | 16.4 (15.1–17.6)                  | 4.3 (3.7–4.9)  | 1269                | 1.9 (1.8–2.0)   |
| Non-affective psychotic disorders| 36,859             | 2072                        | 6.2 (5.8–6.5)  | 448                           | 99                  | 146            | 17.2 (15.5–19.0)                  | 3.2 (2.6–3.9)  | 851                 | 2.0 (1.8–2.1)   |
| Schizophrenia                    | 10,413             | 612                         | 6.1 (5.6–6.7)  | 94                            | 26                  | 39             | 12.5 (9.8–15.2)                  | 2.9 (1.8–4.1)  | 185                 | 1.4 (1.2–1.6)   |
| Affective disorders              | 125,273            | 7070                        | 5.9 (5.8–6.1)  | 1278                          | 281                 | 398            | 15.1 (14.2–15.9)                 | 2.9 (2.5–3.2)  | 2616                | 1.8 (1.7–1.9)   |
| Total population                 | 6,143,802          | 548,047                     | 8.9 (8.9–8.9) | 35,952                        | 8259                | 1.9 (1.8–2.0)  | 2.4 (2.3–2.4)                   |                |                     |                |
| Male                             |                    |                             |                |                                |                     |                |                                  |                |                     |                |
| Non-affective psychotic disorders| 36,121             | 1934                        | 5.8 (5.5–6.1)  | 387                           | 85                  | 119            | 18.3 (16.5–20.2)                 | 5.6 (4.6–6.6)  | 717                 | 2.0 (1.9–2.2)   |
| Schizophrenia                    | 23,532             | 1251                        | 6.0 (5.6–6.4)  | 283                           | 63                  | 88             | 19.6 (17.2–22.0)                 | 4.1 (3.1–5.1)  | 528                 | 2.1 (2.0–2.3)   |
| Affective disorders              | 10,282             | 566                         | 5.7 (5.1–6.2)  | 117                           | 33                  | 42             | 14.8 (12.0–17.6)                 | 3.9 (2.5–5.2)  | 259                 | 1.9 (1.7–2.2)   |
| Bipolar disorder                 | 4,976              | 272                         | 5.7 (4.9–6.6)  | 50                            | 16                  | 20             | 15.5 (11.1–20.8)                 | 5.1 (2.5–7.7)  | 102                 | 1.9 (1.5–2.2)   |
| Any SMI                          | 70,181             | 3726                        | 5.6 (5.4–5.8)  | 688                           | 161                 | 219            | 16.6 (15.3–17.8)                 | 3.8 (3.2–4.3)  | 1485                | 2.1 (2.0–2.2)   |
| Total population                 | 2,999,512          | 265,375                     | 8.8 (8.7–8.8) | 18,075                        | 4530                | 9.7 (9.5–9.8) | 2.3 (2.2–2.4)                   | 2.9 (2.9–3.0)  |                     |                |
| Female                           |                    |                             |                |                                |                     |                |                                  |                |                     |                |
| Non-affective psychotic disorders| 24,469             | 1498                        | 6.6 (6.2–7.1)  | 290                           | 53                  | 85             | 14.3 (12.5–16.2)                 | 5.5 (4.0–5.9)  | 552                 | 1.7 (1.5–1.8)   |
| Schizophrenia                    | 13,327             | 821                         | 6.6 (5.9–7.3)  | 165                           | 36                  | 58             | 13.9 (11.5–16.3)                 | 2.3 (1.5–3.1)  | 352                 | 1.7 (1.5–1.9)   |
| Affective disorders              | 13,245             | 762                         | 6.0 (5.5–6.5)  | 142                           | 42                  | 61             | 11.9 (9.5–14.3)                  | 2.3 (1.5–3.1)  | 329                 | 1.3 (1.1–1.5)   |
| Bipolar disorder                 | 5437              | 340                         | 6.5 (5.7–7.3)  | 44                            | 10                  | 19             | 10.9 (7.1–14.6)                  | 1.6 (0.5–2.7)  | 83                  | 1.0 (0.8–1.2)   |
| Any SMI                          | 55,092             | 3344                        | 6.3 (6.1–6.6)  | 590                           | 120                 | 179            | 13.8 (12.6–15.0)                 | 2.1 (1.7–2.5)  | 1131                | 1.5 (1.4–1.6)   |
| Total population                 | 3,144,188          | 282,672                     | 9.1 (9.1–9.1) | 17,877                        | 2698                | 3729           | 8.0 (7.8–8.1)                   | 1.4 (1.3–1.4)  | 1.9 (1.8–2.0)       | 1.9 (1.8–2.0)   |

\(a\) Adjusted to the average population of Israel in 2019 as standard population.

\(b\) Deaths officially attributed to COVID-19 until end of April 2021.

\(c\) All deaths until end of April 2021.
psychiatric disorder compared to the total population, finding that individuals with a history of hospitalization for a psychiatric disorder, particularly those with non-affective psychotic disorders, were less likely to be tested for COVID-19 and had fewer confirmed COVID-19 infections. Those infected were more likely to be hospitalized and to die. Individuals with a history of hospitalization for a psychiatric disorder, particularly those with non-affective psychotic disorders, had lower rates of vaccination compared with the total population.

Testing for COVID-19
Compared to the total population (62%), the percentage of individuals with a history of hospitalization for a psychiatric disorder that were tested for COVID-19 at least once was lower (51%), particularly persons with non-affective psychotic disorders (49%). This finding might be caused by lack of initiative in mentally ill persons, particularly males with non-affective psychotic disorders, who typically have higher levels of negative symptoms [17], are less active socially and have less contact with verified cases, hence are less often referred to testing. This result differs from a previous study of Tzur Bitan in Israel [2], which reported more testing for COVID-19 in persons with schizophrenia (30.2% vs. 22.1% in the control group). That study was based on data from the largest HMO in the country, providing health care to approximately half of the population, but used data until October 2020, covering the first wave of COVID-19 in Israel, during which testing was relatively limited. The data in this current study includes the next two, larger waves, when massive testing was done in Israel, which might explain the higher rate of testing in the total population. Data on testing in the UK-Biobank also found higher rates of testing for COVID-19 in psychiatric patients, but those data are from the beginning of the pandemic (April 2020) and are not population-based. In addition, the Biobank study and the previous Israeli study included individuals who had been hospitalized, but also included data from primary care physicians on individuals who have never been hospitalized for a psychiatric disorder and might be presumed to be less severely ill, hence more aware of the importance of being tested. The higher probability of testing in those with more psychiatric hospitalizations may reflect the policy of testing all individuals before admission to psychiatric facilities, and repeat testing in hospitalized individuals in cases of suspected exposure to individuals with COVID-19.

Fig. 2  Outcomes of confirmed COVID-19 infection by age, with 95% CI. A COVID-19 hospitalization rate. B COVID-19 deaths. C All deaths.

Table 2. Odds ratios for hospitalization and death in persons infected with COVID-19 with SMI, compared to those infected in the total population without SMI, from logistic regression models.

| Psychiatric diagnosis/Outcome | Odds ratio and 95% CI for persons infected with COVID-19 with SMI compared those without SMI |
|------------------------------|-----------------------------------------------|
|                              | Hospitalization | COVID-19 deaths<sup>a</sup> | All deaths<sup>b</sup> |
| Model 1                      |                 |                             |                          |
| Non-affective psychotic disorders | 2.35 (2.14–2.59) | 1.84 (1.52–2.22) | 2.26 (1.92–2.65) |
| Schizophrenia                | 2.43 (2.16–2.73) | 1.96 (1.56–2.44) | 2.42 (2.00–2.94) |
| Affective disorders          | 1.77 (1.52–2.07) | 1.82 (1.41–2.36) | 2.02 (1.60–2.54) |
| Bipolar disorder             | 1.69 (1.32–2.16) | 1.94 (1.26–2.99) | 2.43 (1.68–3.54) |
| Any SMI                      | 2.10 (1.96–2.25) | 1.76 (1.54–2.01) | 2.02 (1.80–2.28) |
| Model 2                      |                 |                             |                          |
| Non-affective psychotic disorders | 2.44 (2.21–2.68) | 2.05 (1.69–2.48) | 2.49 (2.11–2.93) |
| Schizophrenia                | 2.52 (2.24–2.84) | 2.22 (1.77–2.78) | 2.69 (2.21–3.27) |
| Affective disorders          | 1.77 (1.51–2.07) | 1.81 (1.38–2.36) | 2.00 (1.57–2.55) |
| Bipolar disorder             | 1.72 (1.34–2.20) | 1.92 (1.22–3.04) | 2.45 (1.65–3.64) |
| Any SMI                      | 2.13 (1.99–2.28) | 1.84 (1.61–2.11) | 2.11 (1.87–2.38) |

<sup>a</sup>Deaths officially attributed to COVID-19 until end of April 2021.
<sup>b</sup>All deaths until end of April 2021.
Rates of confirmed COVID-19 infection

Previous authors have hypothesized that persons with mental illness live socially isolated lives [11, 18], thus having less contact and less exposure to infection. The results of the current study, comparing rates of confirmed infection with COVID-19 in individuals with a history of hospitalization for a psychiatric disorder with the total population, were in accord with this hypothesis, finding lower rates of infection among individuals with a history of hospitalization for a psychiatric disorder, especially in patients who reported abusing drugs or alcohol. Similar findings were reported in the UK population-based study [1] and in the study on the large HMO in Israel [2]. A population-based study from South Korea reported no difference in rates of confirmed COVID-19 infection between psychiatric patients and the general population, while a large study from the US found that people with mental disorders had higher rates of confirmed COVID-19 infection [3, 7]. However, the latter two studies included persons with no hospitalization in psychiatric facilities, many of whom presumably had less severe psychopathology.

Hospitalization and mortality

Among persons with confirmed infection with COVID-19, individuals with a history of hospitalization for a psychiatric disorder were twice as likely to be hospitalized or to die from any cause, compared with the total population. The adjusted mortality risk was highest in persons with non-affective psychotic or bipolar disorders. This is similar to the twofold higher mortality in individuals with a history of hospitalization for a psychiatric disorder unrelated to COVID-19, reported all over the world, and in Israel [19–21]. The risk for COVID-19 attributed deaths was also increased, but somewhat less than for all-cause mortality, presumably reflecting the high risk of mortality from COVID-19 in all persons infected, with or without a history of hospitalization for a psychiatric disorder. In persons over age 75, there was no significant difference in mortality between persons with confirmed infection with COVID-19 with or without a history of hospitalization for a psychiatric disorder. This may be due to the high excess mortality during the COVID-19 pandemic found in this age group [22], which appears to overshadow the increased risk for mortality in individuals with a history of hospitalization for a psychiatric disorder.

Similar findings have been reported in several studies on schizophrenia and affective disorders, and confirmed in meta-analyses [10–12]. Those papers compared rates of mortality in persons with a psychiatric disorder with a confirmed infection with COVID-19, with persons without these diagnoses, controlling for potential confounders, and found, as we did, an approximately twofold increased risk of death. Our data expands on those findings, and add greater precision by directly comparing mortality in individuals with a history of hospitalization for a psychiatric disorder who did or did not have a confirmed infection with COVID-19, finding rates of mortality in those with a confirmed infection with COVID-19 to be over double those of the non-infected.

The data reported here cannot explain these high mortality rates in individuals with a history of hospitalization for a psychiatric disorder infected with COVID-19. Possible mechanisms that have been suggested include barriers to care, which are probably not the case, as universal insurance coverage ensures equal access to medical care and hospitalization to all citizens in Israel. These findings are not due to anti-psychotic treatment, which has recently been shown not to cause mortality in patients with a psychiatric disorder infected with COVID-19 [23]. These data cannot relate to other proposed mechanisms, such as social determinants of health, and immunological disturbances [10, 18].

Vaccinations

To the best of our knowledge, this is the first report on vaccinations for COVID-19 in individuals with a history of hospitalization for a psychiatric disorder from an entire population, showing considerably lower rates, 60% compared to 75% in the total population, with the lowest rates in persons with non-affective psychotic disorders, 57%. There are little data published

| Effect | Odds ratio with 95% CI | COVID-19 test | Infection | Vaccination |
|--------|----------------------|--------------|-----------|-------------|
| Males vs females | 0.83 (0.81–0.85) | 0.93 (0.88–0.97) | 0.93 (0.91–0.95) |
| Age at beginning of study: 25–34 vs 18–24 | 0.76 (0.72–0.80) | 0.79 (0.71–0.87) | 1.02 (0.96–1.07) |
| 35–44 vs 15–24 | 0.58 (0.55–0.61) | 0.65 (0.59–0.72) | 1.21 (1.15–1.27) |
| 45–54 vs 15–24 | 0.50 (0.47–0.53) | 0.59 (0.53–0.65) | 1.47 (1.39–1.55) |
| 55–64 vs 15–24 | 0.43 (0.41–0.46) | 0.56 (0.50–0.62) | 1.69 (1.61–1.78) |
| 65–74 vs 15–24 | 0.42 (0.39–0.44) | 0.61 (0.55–0.67) | 1.93 (1.83–2.05) |
| 75–84 vs 15–24 | 0.46 (0.43–0.49) | 0.82 (0.73–0.92) | 1.78 (1.66–1.91) |
| 85+ vs 15–24 | 0.36 (0.33–0.39) | 0.71 (0.60–0.83) | 0.65 (0.60–0.71) |
| Psychiatric diagnosis at last hospitalization: Non affective psychotic disorders vs Other | 0.70 (0.68–0.72) | 0.99 (0.93–1.05) | 0.85 (0.83–0.87) |
| Affective disorders vs Other | 1.01 (0.98–1.05) | 0.98 (0.92–1.05) | 1.31 (1.27–1.36) |
| Substance abuse any hospitalization vs no recorded abuse | 1.01 (0.97–1.04) | 0.55 (0.51–0.61) | 0.87 (0.84–0.91) |
| Alcohol abuse any hospitalization vs no recorded abuse | 1.00 (0.96–1.05) | 0.70 (0.62–0.78) | 0.84 (0.80–0.88) |
| Previous suicide attempt2 vs no recorded attempt | 1.01 (0.98–1.04) | 0.91 (0.86–0.97) | 1.08 (1.04–1.11) |
| Involuntary hospitalization ever vs voluntary | 0.90 (0.87–0.92) | 0.99 (0.94–1.05) | 0.69 (0.68–0.71) |
| Number of hospitalizations: 2–3 vs 1 | 1.27 (1.24–1.31) | 1.10 (1.04–1.17) | 2.18 (2.07–2.29) |
| 4–6 vs 1 | 1.71 (1.65–1.78) | 1.15 (1.07–1.25) | 1.33 (1.30–1.37) |
| 7–9 vs 1 | 2.17 (2.06–2.29) | 1.31 (1.18–1.46) | 1.66 (1.59–1.72) |
| 10+ vs 1 | 3.82 (3.64–4.01) | 1.56 (1.42–1.72) | 1.92 (1.81–2.03) |

All results are significant with p ≤ 0.001 except those italicized.
on vaccination for COVID-19 of persons with psychiatric disorders. One study from the UK described trends and variations in vaccine coverage, and mentioned that persons with a psychiatric disorder were less likely to be vaccinated compared to the general population (89.5% vs. 94.7%) [24]. The study conducted in the largest HMO in Israel focused on vaccination rates for persons with schizophrenia and also reported lower rates of vaccination [15], while a study from Belgium on psychiatric inpatients reported rates of vaccine acceptance [16] similar to the general population.

Risk for non-vaccination was particularly increased in individuals with a history of hospitalization for a psychiatric disorder aged 85 and older, particularly those with non-affective psychotic disorders, of whom only 37% were vaccinated, compared with 80% in persons that age in the total population. The reasons for these particularly low rates of vaccination in elderly individuals with a history of hospitalization for a psychiatric disorder are not clear. Other risk factors for non-vaccination in individuals with a history of hospitalization for a psychiatric disorder include use of alcohol or drugs, and a history of involuntary admission, perhaps indicating that the more severely ill persons are less likely to be vaccinated. On the other hand, as the number of hospitalizations increased, so did the chances of being vaccinated. This is probably because in January 2021 all patients hospitalized in psychiatric hospitals were vaccinated, including persons chronically hospitalized, many of whom had large numbers of previous hospitalizations compared to the majority of persons with a psychiatric disorder who live in the community.

It is important to mention that Israel was the first country in the world to vaccinate on a large scale, and there was much uncertainty both regarding the effectiveness and potential side-effects of the vaccine, factors which greatly impacted vaccine acceptance in the general population [25], and probably caused hesitancy in the individuals with a history of hospitalization for a psychiatric disorder reported here. The vaccine hesitancy reported here might be attributed to lack of awareness related to cognitive impairment, lack of motivation and low levels of activity. In a minority of patients, paranoia might be a factor [26, 27]. The lower vaccination rate for COVID-19 in individuals with a history of hospitalization for a psychiatric disorder is consistent with the literature regarding other preventive vaccines. For example, rates of vaccination for influenza in persons with mental illness are as low as 25% [28, 29].

It is important to understand these findings in the context of the Israeli health and mental health system. Based on the National Health Insurance Law, all citizens receive free medical and psychiatric care, with nominal payment for clinical visits and medication and no hospitalization charge. Those services are administered by four official health insurance organizations that compete and receive payment from the government for each patient. These disparities in treatment and morbidity disparities in a country that allows full access to medical treatment for individuals with a psychiatric disorder raise significant concerns regarding even greater disparities in countries with less accessible health systems.

The strengths of this study are the large nationwide database including all individuals with a history of hospitalization for a psychiatric disorder, which was merged with nationwide databases on all COVID-19 tests, confirmed infection, hospitalization, mortality and vaccinations in the entire country, enabling direct comparison of these variables between individuals with a history of hospitalization for a psychiatric disorder and the total population. Study limitations include the fact that individuals with a psychiatric disorder were identified based on having been hospitalized at least once during their lifetime in a psychiatric facility, hence does not include information about outpatients who have never been hospitalized, including the majority of individuals with affective disorders, drug and alcohol abuse, anxiety and personality disorders. However, at least for schizophrenia, a previous study [30] found that 93% of all persons with schizophrenia will be hospitalized at some point of their lives. Furthermore, the diagnoses in the hospitalization registry are clinician-based and are not research diagnoses. However, a study comparing the clinical diagnoses in the registry with research diagnoses reported agreement in 87–89% of the cases [31]. We also did not have medical data for the total population to enable adjustment for these factors. When analyzing outcomes of infected persons we adjusted for medical comorbidity but those data were based on self-report and not on medical records, and therefore may not be complete or accurate. Lastly, we reported on testing and risk of confirmed infection with COVID-19 but do not have data on infected individuals who are asymptomatic and are not tested. This might be more common in individuals with a history of hospitalization for a psychiatric disorder, who might be less aware of their symptoms or less likely to come in to be tested when symptomatic.

**CONCLUSIONS**

Despite these limitations, this study highlights the need to increase testing for COVID-19 in individuals with a history of hospitalization for a psychiatric disorder, and closely monitor those found positive for potential medical complications. Efforts must be made to reach-out to vaccinate persons with individuals with a history of hospitalization for a psychiatric disorder, particularly older males with schizophrenia who are both least likely to be vaccinated, and are at highest risk for mortality.

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**AUTHOR CONTRIBUTIONS**

NG Analyzed the data. TBL contributed to writing the protocol obtaining regulatory approval, and commented on the paper. ZH contributed to writing the protocol obtaining regulatory approval, and commented on the paper. RY contributed to writing the protocol obtaining regulatory approval, and commented on the paper. MD Commented on the final manuscript. ES contributed to writing the protocol obtaining regulatory approval, and commented on the paper. LL commented on the final manuscript. TE brought in the first draft of the paper and commented on the final manuscript. MW conceived the study, obtained IRP approval, commented on the manuscript, and takes full responsibility for the entire project.

**COMPETING INTERESTS**

The authors declare no competing interests.

**ADDITIONAL INFORMATION**

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