



Review article

## Mental health conditions and COVID-19 vaccine outcomes: A scoping review

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### ABSTRACT

**Objective:** Research shows that people with a history of mental health conditions were at increased risk of COVID-19 infection, hospitalisation, and mortality. However, the relationship between mental health conditions and COVID-19 vaccine outcomes such as vaccine intention, uptake and vaccine breakthrough is not yet well-understood.

**Methods:** We conducted a systematic search on the topics of COVID-19 vaccine intentions, vaccine uptake, and vaccine breakthrough, in relation to mental health conditions (e.g., depression, schizophrenia), in four databases: PubMed, MEDLINE, SCOPUS, and PsychINFO, and the publication lists of Clinical Practice Research Datalink (CPRD), The Health Improvement Network (THIN), OpenSAFELY, and QResearch. Inclusion criteria focussed on studies reporting any of the aforementioned COVID-19 vaccine outcomes among people with mental health conditions.

**Results:** Of 251 publications initially identified, 32 met our inclusion criteria. Overall, the evidence is inconclusive regarding the levels of intention to accept COVID-19 vaccines among people with mental health conditions. People with mental health conditions were more likely to have lower uptake of COVID-19 vaccines, compared to people without. Common barriers to COVID-19 vaccine uptake included concerns about the safety, effectiveness, and side effects of the vaccines. Limited evidence also suggests that vaccine breakthrough may be a particular risk for those with substance use disorder.

**Conclusions:** Evidence for the association between COVID-19 vaccine intentions and mental health conditions is mixed. Vaccine uptake might be lower in people with mental health conditions compared to people without, yielding interventions to encourage vaccine uptake in this population. Our understanding of COVID-19 vaccine breakthrough in this population also needs enhancing.

### 1. Introduction

The COVID-19 pandemic resulted in >700 million cases and 6 million deaths globally [62]. Vaccines against SARS-CoV-2 were developed to reduce the spread of the virus and morbidity and mortality caused by COVID-19. The UK was the first country to approve a COVID-19 vaccine and started a vaccine roll-out program in December 2020 [6]. By autumn 2022, approximately 151 million vaccinations were given to the UK population [31]. However, while the mass vaccination roll-out was necessary in the pandemic, certain factors determine whether

vaccines can realise their full potential. Arguably, the two most salient of these are vaccine uptake i.e., an individual's willingness to be vaccinated, and vaccine effectiveness i.e., the ability for vaccines to protect against infection and adverse outcomes.

One factor that may influence both the intention to be vaccinated and vaccine uptake is mental health. Pre-pandemic, the evidence suggested that people with mental illness might be less likely to engage in preventive healthcare such as blood pressure monitoring and vaccinations, compared with people without mental illness [30]. A review of the literature during the pandemic, largely limited to studies capturing the

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intention (or not) to be vaccinated, suggested that people with mental health conditions appeared to be less willing to accept COVID-19 vaccines, but that the relationship varied according to the nature of the mental health condition [20]. Evidence on vaccine uptake also shows a mixed picture. For example, a study in early 2021 found higher COVID-19 vaccine uptake (i.e., receiving at least one dose) among people with mood disorders (e.g., major depression and bipolar disorder) in certain areas in the UK, but lower COVID-19 vaccine uptake among individuals with psychotic disorders (e.g., schizophrenia), compared with people without mental illness [23]. Another study, conducted in China in the same year, found that vaccine uptake among people with mental health conditions was lower than that among other residents (11% vs. 40% respectively) in Wuhan area [24]. This evidence suggests that (1) vaccine intention (i.e., behavioural intention) may not be accordant with vaccine uptake (i.e., behavioural response) among people with mental health conditions, and (2) the presence of a mental health condition may be a contributor to both vaccine intention and vaccine uptake. However, to our knowledge, no review to date has sought to synthesise this evidence in the context of COVID-19 vaccines.

There is also potential for mental health to influence the effectiveness of COVID-19 vaccines. Mental health conditions can dysregulate the immune system and thus can impair the immune response to both viral infections and vaccinations [14,41,59]. For example, pre-pandemic, viral and vaccine challenge studies have shown that depression and stress are associated with poorer antibody responses to vaccinations, as well as increased risk of infection and symptomatic illness [14,15,45,59]. Evidence from the pandemic suggests that this relationship between mental health and impaired responses to respiratory infections may also occur in the context of COVID-19. For example, observational data have shown that greater psychological distress was significantly associated with subsequent self-reported SARS-CoV-2 infection, together with an increased number of, and more severe, symptoms [7]. Similarly, Yang and colleagues reported that people with previous mental health conditions were more likely to get SARS-CoV-2 infection, be hospitalised, and to die from COVID-19 [64]. While no previous review has yet considered the relationship between mental health and COVID-19 vaccine effectiveness, a review by Xiao et al. [63] examined the relationship between measures of the immune response in the context of other vaccines. The review included 13 studies in people with mental disorders including major depressive disorder, schizophrenia, eating disorders, sleep disorders, and stress and trauma disorders. A wide range of different vaccines were considered, including measles vaccine, typhoid vaccines, Hepatitis-B vaccines, and influenza vaccines. The authors concluded that the current evidence base is inconclusive and of low-to-moderate quality [63].

Thus, in summary, the emerging evidence suggests that the relationship between mental health and COVID-19 vaccine intentions may vary between different mental health conditions; the relationship with vaccine uptake is less clear and while poorer COVID-19 outcomes have been associated with mental health conditions, the evidence on the relationship with vaccine effectiveness is limited. Indeed, the relationship between mental health conditions and COVID-19 vaccine breakthrough (i.e., evidence of SARS-CoV-2 infection after vaccination) appears to have received limited consideration.

In an effort to bring this literature together, we present here results from a scoping review in which we have examined the evidence exploring the relationship between indices of mental health (past and current) and vaccine intention (i.e., behavioural intentions, or willingness to be vaccinated), vaccine uptake (behavioural response) and vaccine effectiveness (i.e., breakthrough infection: evidence of infection following vaccination). An understanding of this literature will help to inform whether and in what ways people with mental health conditions need to be supported to reduce their risk of COVID-19 infection.

## 2. Methods

### 2.1. Population

The population of interest was people with mental health conditions. Consistent with previous work, mental health conditions included depression, anxiety, stress-related disorder, substance misuse, psychotic disorders, schizophrenia, and bipolar disorder [55,64]. This review primarily focused on psychiatric disorder diagnoses, regardless of whether they were accessed directly through medical records, or self-reported. However, we also included studies where diagnostic categories were given based on self-reported symptoms, using standardised diagnostic tools such as the Physician Health Questionnaire (PHQ-9, [29]), the 7-item Generalized Anxiety Disorder Questionnaire (GAD-7, [53]). We report findings according to which measurement approach was used i.e., diagnoses via medical records; diagnoses based on self-report and diagnoses based on meeting established diagnostic thresholds. We included studies involving people with a history of mental health conditions as well as those arising during the pandemic. No restrictions were made for other characteristics, including age, gender, health conditions etc. Individuals without mental health conditions, regardless of whether this was measured by existence of diagnoses or self-reported symptoms, were included as control or comparison groups.

### 2.2. Outcomes

The outcomes of interest were intention to accept or decline a COVID-19 vaccination when offered, COVID-19 vaccine uptake (receipt of one or more doses), and COVID-19 vaccine breakthrough. A COVID-19 vaccine breakthrough infection was defined according to the Centers for Disease Control and Prevention (CDC) as: “the detection of SARS-CoV-2 RNA or antigen in a respiratory specimen collected from a person  $\geq 14$  days after receipt of all recommended doses of an FDA-authorized COVID-19 vaccine” [10].

### 2.3. Search strategy

Searches for relevant studies were conducted in PubMed, MEDLINE, SCOPUS, and PsychINFO, on 10th November 2022. To include potentially eligible population-based studies, the CPRD, The Health Improvement Network (THIN), OpenSAFELY, and QResearch lists of publications were also searched. To include articles that may be under review, the electronic pre-print service MedRxiv was also searched. The search paradigm was based on the following combination: (*mental, major* [MeSH terms]) AND (*COVID-19 vaccine* [MeSH terms]). To ensure our searches were comprehensive, we conducted additional searches replacing the term *mental* with psychiatric, schizophrenia, psychotic, bipolar disorder, mood disorder, major depressive disorder, anxiety disorder, personality disorder, eating disorder, alcohol abuse, alcohol misuse, substance abuse, and substance misuse. We limited our searches to publications in English language. We did not limit the searches by time period.

### 2.4. Eligibility criteria

Only observational studies were included i.e., we did not include studies in which the effects of any intervention on vaccine intention, uptake or breakthrough were considered. Eligible studies had to report at least one of the following: (1) intentions towards COVID-19 vaccine (i.e., intended willingness to accept or decline a vaccination when offered) among people with mental health conditions, and in comparison with people without mental health conditions where applicable; (2) COVID-19 vaccine uptake rate among people with mental health conditions, and in comparison with people without mental health conditions where applicable; (3) COVID-19 vaccine breakthrough (i.e., evidence of SARS-CoV-2 infection after vaccination) among people with mental health

conditions. For mixed-method studies, only quantitative findings were included. Only articles reporting results from original observational studies were included. Qualitative studies, reviews, protocols, commentary or opinion pieces, editorial letters and posters were excluded.

2.5. Barriers to COVID-19 vaccine uptake

Demographic predictors (e.g., age, gender, ethnicity, education, socioeconomic status, etc) of vaccine uptake in general have been reviewed previously (see [21]). Thus, we sought to extend this literature by summarising findings on psychological predictors of vaccine uptake. Results on psychological barriers to COVID-19 vaccine uptake among people with mental health conditions were also extracted.

3. Results

3.1. Selection of studies

The database search was conducted on 9th November 2022 and returned 251 initial results. Of these, 197 studies were excluded after title and abstract screening and 22 studies were excluded after full-text screening (Fig. 1). The main reasons for exclusion include the article being a comment piece or review of literature or intervention etc. (k = 51, 23%); studies not conducted among people with mental health conditions (k = 43, 20%), and not investigating the outcomes of interest (k = 16, 7%). Therefore, 32 studies were included in this scoping review.

3.2. Overview of study characteristics

The 32 studies included in this review were conducted across 13 countries and regions including North America (e.g., Canada and the United States), Europe (e.g., United Kingdom, Belgium, France,

Denmark), Asia (e.g., Mainland China, Japan, India), and the Middle East (e.g., Israel and Qatar). Of the 32 studies, 21 used survey designs including 6 longitudinal survey studies. Nine studies conducted analysis using data from electronic health or registration records, including one study linking survey and electronic health record data. Two studies examined vaccine outcomes among patients within psychiatric hospitals through healthcare screening and assessment. Populations investigated by these studies included general public or population-representative cohorts, and more specific cohorts for instance veterans, psychiatric patients, adolescents with attention-deficit/hyperactivity disorder (ADHD), and youth who are 2-spirit, lesbian, gay, bisexual, transgender, queer, and questioning (2SLGBTQ+) and experiencing homelessness, etc. The sizes of the included studies ranged from 62 to 57.9 million.

3.3. Measurement of mental health conditions

Twenty of the 32 reviewed studies identified eligible participants or patients with mental health conditions through clinical diagnoses obtained from medical records [8,13,16,17,19,22,23,25,32,35,38,40,46–48,52,54,57,58,60]. The recorded mental health conditions included depressive disorder, bipolar disorder, schizophrenia, ADHD, PTSD, generalized anxiety disorder, and substance use disorder, etc. One study used records of prescription of psychotropic drugs (i.e., anxiolytics, antipsychotics, hypnotics, and antidepressants) as an indication of patients' mental health conditions [36].

Six studies asked participants to self-report whether they have been diagnosed with mental health conditions [2,9,18,24,43,50]. Five other studies measured self-reported anxiety, depression, substance use, and posttraumatic stress disorder (PTSD) through surveys such as the Physician Health Questionnaire (PHQ-9, [29]), the 7-item Generalized Anxiety Disorder Questionnaire (GAD-7, [53]), and the 20-item post-traumatic stress disorder Checklist-5 (PCL-5, [1,11,28,37,39,40,51]). In

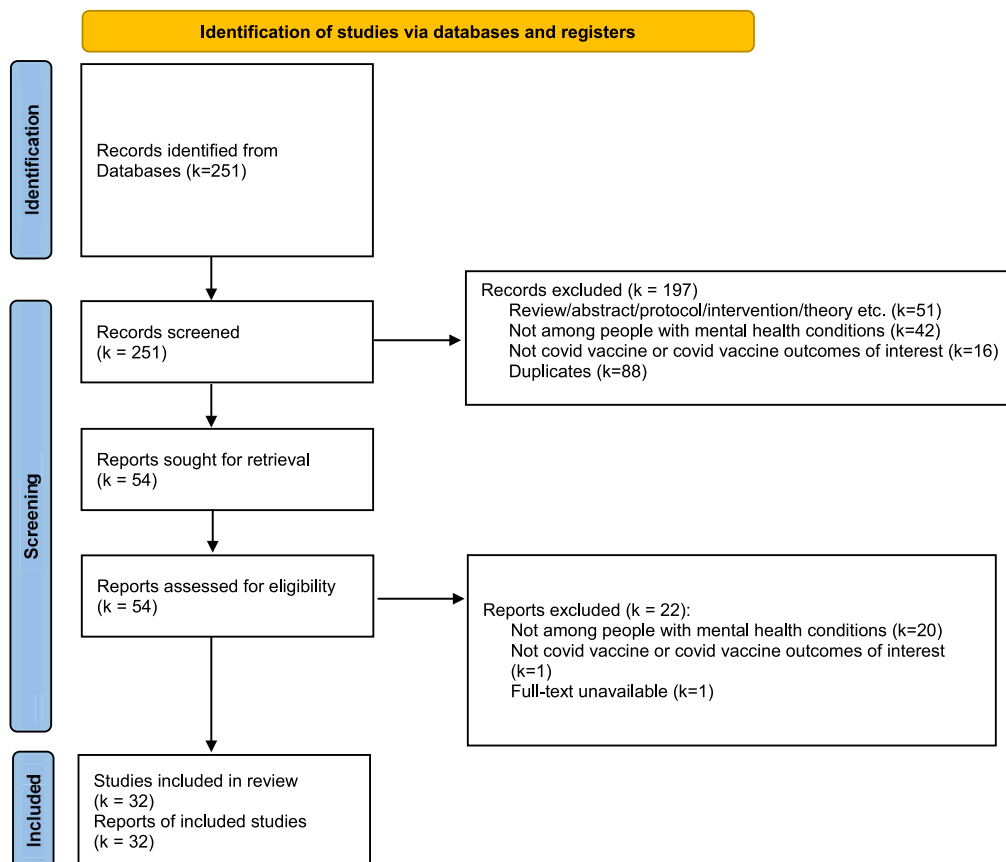


Fig. 1. Flow diagram for the scoping review.

these five studies, individuals were classified as “cases” or equivalent when they met accepted cut-offs for these self-report measures, indicating probable mental health diagnoses.

### 3.4. Mental health conditions and COVID-19 vaccine intentions

Eighteen of the 32 reviewed studies reported on the association between the presence of mental health conditions and intention to accept COVID-19 vaccine or booster vaccine [1,2,8,13,18,19,24,25,28,37,39,43,46–48,50,51,54]. The sizes of the studies range from 92 to 77,104 (see Table 1). 13 of the 18 studies had sample sizes of >500 participants. Participants in these studies were asked to indicate their intentions once the COVID-19 vaccines became available. Seventeen of the 18 studies reported on people with current mental health conditions. In the remaining study, no distinction was made between current and history of mental health conditions [50]. Therefore, we do not distinguish between current and history of mental health conditions in the following reporting. Across the 18 studies, the intended willingness to accept a COVID-19 vaccination was between 41.7% and 93% among people with mental health conditions.

#### 3.4.1. Differences between people with and without mental health conditions

Twelve of the 18 studies compared vaccine intention between people with and without mental health conditions.

**3.4.1.1. Mental health diagnosis from health records.** Of these 12 studies, only three identified patients with mental health conditions through health records [19,25,47]. Two of the three studies reported that people with mental health conditions had less intention to accept the COVID-19 vaccine [19,25]. The proportions intending to accept COVID-19 vaccines were between 70% and 85% in these two studies. Eyllon et al. [19] did not report the proportions of people without mental health conditions intending to be vaccinated, but Jepsen et al. [25] reported 90% of people intending among the general population. Eyllon et al. [19] reported odds ratios of 0.65–1.68 to accept COVID-19 vaccines among people with different mental health conditions compared with those without, adjusting for other factors such as age, gender, and ethnicity. Specifically, patients with substance use disorder had 68% higher odds for not intending ( $p = .002$ ) and patients with bipolar disorder had 35% lower odds for not intending ( $p = .04$ ). Jepsen et al. [25] reported that among mental health patients, the proportion of intended acceptance of COVID-19 vaccine was significantly lower by 4.7% ( $p < .001$ ). The other one of the three studies reported the contrary: among non-vaccinated participants, those with schizophrenia had significantly higher intention to be vaccinated (41.7%) compared to controls (12.5%),  $p = .03$ , [47].

**3.4.1.2. Self-reported mental health diagnosis.** Of the 12 studies, four identified people with mental health conditions through self-reported diagnosis. Among these four studies, three found no differences in vaccine intention between people with and without mental health conditions [2,43,50]. Specifically, one reported that having a mental health condition did not significantly predict intention to accept a COVID-19 booster vaccine, after controlling for other factors such as age and gender [43]. One study found that there were no significant difference in intention to accept COVID-19 vaccines among people with and without mental health conditions [2]. Other factors were not adjusted for in this analysis. One study reported that people with and without mental illness had similar levels of intention to accept COVID-19 vaccines (mean intention score = 4.06 in people with mental illness, mean intention score = 3.93 in people without), but no significance test between these two groups was reported [50]. The other one of the four studies reported that adolescents with ADHD (52%) were significantly less likely to report intent to accept the COVID-19 vaccine, than adolescents without ADHD (66%),  $p = .018$ ,  $d = 0.36$  [18].

**3.4.1.3. Self-reported mental health symptoms.** Of the 12 studies, five measured probable mental health conditions through survey-reported symptoms. Of these, three found no differences in vaccine intention between people with and without mental health conditions [1,28,39]. Abramovich et al. [1] reported that having moderately-severe or severe anxiety or depression did not significantly predict COVID-19 vaccine intentions among 2-spirit, lesbian, gay, bisexual, transgender, queer, and questioning (2SLGBTQ+) young people experiencing homelessness. Khaled et al. [28] reported that although individuals were more likely to report moderate-to-severe depression or anxiety among those who were unwilling or uncertain as to whether to have a COVID-19 vaccine, having moderate-to-severe depression or anxiety did not significantly predict intention to accept COVID-19 vaccines after controlling for other factors such as age and gender. Nishimi, Borsari et al. [39] reported that PTSD symptom clusters did not significantly predict intention to accept COVID-19 vaccines before and after adjusting for other factors. Only one of the five studies reported that people with mental health conditions were less likely to intend to accept the COVID-19 vaccine [51]. They reported that the proportions of participants intending to accept COVID-19 vaccines among people with moderate-to-severe anxiety or depression were between 36% and 49%, while the proportions of intending to accept COVID-19 vaccines among people without anxiety or depression were between 53% and 65%. Sekizawa et al. [51] also reported that people with moderately severe or severe depression at wave 1 and 3 of the study, and people with moderate or severe levels of generalized anxiety at wave 3, were significantly more likely to be undecided about whether to accept COVID-19 vaccines at wave 3 ( $p < .05$ ), after adjusting for other factors such as age, gender, and ethnicity. One of the five studies reported the contrary [37]: individuals with self-reported anxiety or depression were 1.13 times (95% CI: 1.08–1.19) significantly more likely to intend to get a vaccine than those without these conditions.

#### 3.4.2. Differences between different mental health conditions

Only two of the 18 studies reported findings in relation to patients' different diagnoses (accessed through health records) and treatment conditions. Bai et al. [8] investigated vaccine intention in patients with major depressive disorder, bipolar disorder, and schizophrenia. They did not find any significant difference in vaccine intention across these three different diagnoses. However, they reported that community-dwelling psychiatric patients had a higher incidence of being unwilling to accept COVID-19 vaccines (49%) compared to hospitalised patients (31%). Eyllon et al. [19] reported results on the association between vaccine intention and different psychiatric diagnosis namely major depressive disorder, generalized anxiety disorder, other anxiety disorders, PTSD, ADHD, alcohol use disorder, and substance use disorder. They found that, after adjusting for other sociodemographic characteristics and physical comorbidities, patients with substance use disorders had 68% more likely not to intend to (95%CI = 1.21–2.33) accept the COVID-19 vaccine; while bipolar disorder was associated were 35% more likely (95%CI = 0.43–0.98). Other psychiatric diagnoses were not significantly associated with vaccine intention.

Overall, these findings suggest that most studies fail to find evidence of significantly lower vaccine intention in people with mental health conditions, with less than half of the studies reporting significantly lower intention to having COVID-19 vaccines among people with mental health conditions.

### 3.5. Mental health conditions and COVID-19 vaccine uptake

Seventeen of the 32 reviewed studies reported on the association between mental health conditions and uptake of the COVID-19 vaccine or booster vaccine (Table 2, [9,16,17,22–24,32,35–38,46,47,51,52,57,58]). Sizes of the studies ranged from 62 to 57.9 million participants. Nine of the 17 studies measured COVID-19 vaccine uptake using participants' health or medical records

**Table 1**  
Summary of studies investigating the association between mental health conditions and COVID-19 vaccine intention.

Studies reporting less vaccine intention in people with mental health conditions								
Author	Region	Data source (Assessment timing)	Population	Size	Mental health conditions and measure	Confounder	Vaccine intention measure	Results
Dvorsky et al. [18]	US	Survey (ADHD diagnostic evaluations were conducted pre-COVID-19. Data for vaccine outcomes were collected in spring 2020, summer 2020, fall 2020, and spring 2021.)	Adolescents in 11th and 12th grade	196 (male = 87, mean age = 17.5)	Attention-deficit/hyperactivity disorder (ADHD) Self-reported clinical diagnosis	No confounder adjusted.	“If a vaccine that could prevent COVID-19 were made available to you, would you accept it for yourself?” (No/Maybe/Yes/Already vaccinated)	Only 61.8% of adolescents with ADHD reported vaccine acceptance, compared to 81.3% of adolescents without ADHD. Adolescents with ADHD were significantly less likely to report intent to accept the COVID-19 vaccine, than adolescents without ADHD.
Eyllon et al. [19]	US	Survey and electronic health record (Data were collected from February to May 2021)	Patients registered at a group medical practice	14,365 (male = 38%, female = 63%)	Major depressive disorder, generalized anxiety disorder, other anxiety disorders, posttraumatic stress disorder (PTSD), attention deficit and hyperactivity disorder (ADHD), alcohol use disorder (AUD), and substance use disorder (SUD). Clinical diagnosis according to the International Classification of Diseases, Tenth Revision (ICD-10), obtained from medical records	Adjusted for gender, age, race, education, income, and payer type.	Participants were asked if they had received at least one dose of a COVID-19 vaccine. For those who had not yet received a vaccine, they were asked about their intention to be vaccinated (Yes/Unsure/I don't know/Probably would not/Definitely would not)	Vaccine hesitancy was significantly more prevalent among participants with substance use (29.6%), attention deficit and hyperactivity (23.3%), posttraumatic stress (23.1%), bipolar (18.0%), generalized anxiety (16.5%), major depressive (16.1%), and other anxiety (15.5%) disorders, and tobacco use (18.6%). After adjustment for sociodemographic characteristics and physical comorbidities, SUD conferred 68% higher odds for vaccine hesitancy. Bipolar disorder was associated with 35% lower odds for vaccine hesitancy. Nicotine dependence/tobacco use was associated with vaccine hesitancy.
Jefsen et al. [25]	Denmark	Longitudinal survey (The surveys were fielded from 9 February to 22 February 2021 (patient sample) and from 4 February to 21 February 2021 (general population sample).	Randomly selected patients with mental illness from the psychiatric services of the Central Denmark Region and one targeting the general Danish population	Mental illness patients = 992, general Danish population = 2458	Not described Clinical diagnosis obtained from medical records	No confounder adjusted.	“Have you been offered vaccination against coronavirus? (Yes/No/Do not wish to answer). For those answered Yes: “Have you accepted this offer?” (Yes/No/Do not wish to answer). For those answered	Vaccine willingness was high in both groups, but slightly lower among patients with mental illness (84.8%), compared with the general population (89.5%).

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Table 1 (continued)

Studies reporting less vaccine intention in people with mental health conditions								
Author	Region	Data source (Assessment timing)	Population	Size	Mental health conditions and measure	Confounder	Vaccine intention measure	Results
Sekizawa et al. [51]	Japan	Longitudinal survey (Wave 1 was conducted from October 27 to November 6, 2020. Vaccine outcomes were assessed only at Wave 3, between April 23 and May 6, 2021)	Community sample	11,846 (male = 50%, female = 50%) participants.	Depression, anxiety Self-reported survey: Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 scale (GAD-7)	Adjusted for sex, age group, level of education, family members living together, employment, annual household income, bank and saving deposit amount, BMI, pre-existing conditions, and region of residence.	otherwise: "Will you accept vaccination against coronavirus, once it is offered to you?" (Yes/No/Do not wish to answer) "Are you going to receive a vaccine against COVID-19?" (Willing to be vaccinated/ Unwilling to be vaccinated/ Undecided)	After adjusting for other factors, those with moderate-to-severe depression at wave 1 and 3 were more likely to be undecided than those who were not depressed. After adjusting for other factors, those who were mildly depressed at wave 1, moderately depressed at wave 3, and moderate-severely anxious at wave 3 were significantly more likely to be unwilling to be vaccinated.
<b>Studies reporting greater vaccine intention in people with mental health conditions</b>								
Nguyen et al. [37]	US	Longitudinal survey (Data were collected March 17–29, 2021)	Nationally representative sample of the population recruited from the community	77,104 adults (30% had anxiety symptoms, 25% had depression symptoms, 35% had symptoms of either disorder)	Anxiety and depression Self-reported survey: the two-item Patient Health Questionnaire (PHQ-2) and the two-item Generalized Anxiety Disorder (GAD-2) scale	Analysis conducted both unadjusted and adjusted for sex.	"Have you received a COVID-19 vaccine?" (yes/no) For people who answered no, they were asked "Once a vaccine to prevent COVID-19 is available to you, would you... definitely/ probably/ probably not/ or definitely not get a vaccine."	Adults with anxiety or depression were more likely to intend to get a vaccine than those without these conditions.
Raffard et al. [47]	France	Survey (Data were collected between April 2021 and October 2021.)	Patients with diagnosis of schizophrenia	100 patients (female = 38%) and 72 family caregivers (female = 26%)	Schizophrenia Clinical diagnosis obtained from medical records	No confounder adjusted.	"If a vaccine for COVID-19 is available for me, I would get it". (1, strongly disagree – 4, strongly agree)	Among the non-vaccinated participants, the proportion of individuals intending to be vaccinated was significantly higher in patients compared to controls ( $p = .03$ , $\Phi = 0.29$ ).
<b>Studies reporting no difference in vaccine intention in people with and without mental health conditions</b>								
Abramovich et al. [1]	Canada	Survey (Data were collected between January 2021 to June 2021.)	2SLGBTQ+ youth (average age = 20 years) experiencing	92	Anxiety, depression, substance use Self-reported survey	No confounder adjusted.	"Do you plan on receiving the COVID-19 vaccine?" (Yes	Having mild-to-severe depression or anxiety were not significantly

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Table 1 (continued)

Studies reporting less vaccine intention in people with mental health conditions								
Author	Region	Data source (Assessment timing)	Population	Size	Mental health conditions and measure	Confounder	Vaccine intention measure	Results
Afifi et al. [2]	Canada	Longitudinal survey (Vaccine outcomes and current mental health data were collected at wave 3, between November and December 2020)	homelessness. The majority were White 61% (n = 56); identified their gender identity as transgender or gender diverse (n = 53; ~58%); and their sexual orientation as bisexual or pansexual (n = 40; ~ 43%). Young people between the age of 14–17 years (male = 45%, female = 55%).	1000 at baseline (2016–2017), 747 at wave 2 (2019) and 664 in wave 3 (664)	Depression, bipolar disorder, anxiety disorder, obsessive–compulsive disorder, posttraumatic stress disorder, attention-deficit/hyperactivity disorder, eating disorder, alcohol problems, drug problems, oppositional defiant disorder, and conduct disorder Self-reported current mental health conditions “Do you currently have a long-term health condition that is expected to last or has lasted 6 months or more and has been diagnosed by a medical doctor or other health care professional?”	No confounder adjusted.	or have already received it/ No/Unsure) “If a COVID-19 vaccine was available would you get it?” (Yes/No/Maybe/I don’t know)	associated with less vaccine intentions compared to those with minimal depression or anxiety.  Having a mental health conditions were not significantly related to willingness to get a COVID-19 vaccine. Among people reporting having current mental health conditions, willingness to get a COVID-19 vaccine were: 67% yes, 9% no, 25% unsure. Among those without current mental health conditions, willingness were 65% yes, 9% no, 26% unsure.
Khaled et al. [28]	Qatar	Survey (Data were collected from 15 December 2020 through 25 January 2021)	Nationally representative sample of the population recruited from the community	1038 (male = 67%, female = 33%)	Depression and anxiety Self-reported survey: the Physician Health Questionnaire (PHQ-9) and the 7-item Generalized Anxiety Disorder Questionnaire (GAD-7)	Adjusted for age, gender, migrant status/type, ethnicity, education, employment, marital status, living arrangement, chronic disease, and COVID-19 related health conditions and concerns	“I am willing to get coronavirus vaccine if it became available for me” (5-point Likert Scale: 1 = Strongly agree, 2 = Somewhat agree, 3 = Neutral, 4 = Somewhat disagree, 5 = Strongly disagree). Responses were collapsed into three groups: vaccine accepting (strongly agree), vaccine resistant or refusers (strongly disagree) and vaccine hesitant	Having moderate-to-severe depression or anxiety did not significantly predict willingness to access COVID-19 vaccines, after controlling for other factors.

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Table 1 (continued)

Studies reporting less vaccine intention in people with mental health conditions								
Author	Region	Data source (Assessment timing)	Population	Size	Mental health conditions and measure	Confounder	Vaccine intention measure	Results
Nishimi et al. [39,40]	US	Longitudinal survey Baseline data on mental health and COVID-19 experiences were collected in August–September 2020. Follow-up data on mental health and vaccine perceptions and intentions were collected in March–April 2021.)	The sample included community-dwelling US adults with high levels of pre-pandemic trauma and trauma-related distress based on sample recruitment.	544 (male = 21%, female = 77%, other = 3%)	posttraumatic stress disorder (PTSD) Self-reported survey: 20-item posttraumatic stress disorder (PTSD) Checklist-5 (PCL-5)	Adjusted for sexual orientation, race/ethnicity, education, income, political preference, living with children, medical conditions Contra-indicating COVID-19 vaccines, perceived likelihood of contracting COVID-19, perceived severity of COVID-19 if contracted, COVID-19 test, COVID-19 infection in one's household.	(somewhat agree, neutral, somewhat disagree) “Have you received at least one shot of COVID-19 vaccine?” (yes/no) For people who answered no, they were asked “Once a vaccine to prevent COVID-19 is available to you, would you... definitely/probably/not sure/probably not/or definitely not get a vaccine.”	PTSD symptom clusters were not significantly associated with COVID-19 vaccine hesitancy in the full sample.
Paul and Fancourt [43]	UK	Longitudinal survey (Data on intent to receive a COVID-19 booster vaccine were collected 22 November to 6 December 2021. Data on initial intent to receive a first COVID-19 vaccine were collected 2 December 2020 to 31 March 2021. Data on receipt of at least two doses of a COVID-19 vaccine were collected at follow-up.)	Fully vaccinated adults recruited from the community	22,139 adults (weighted: male = 49%, female = 51%)	Depression, anxiety, or other psychiatric diagnosis Self-reported mental health diagnosis (yes/no)	Adjusted for age, gender, ethnicity, education, income, employment, living arrangement, smoking status, key worker status, and physical health	“How likely do you think you are to get a COVID-19 vaccine when one is approved?” (1, very unlikely - 6, very likely) “How likely do you think you are to get a COVID-19 booster vaccine if/when you are offered one?” (1, very unlikely - 6, very likely)	Having a mental health condition was not associated with uncertainty or unwillingness to accept a COVID-19 booster vaccine.
Roberts et al. [50]	US	Survey (Screening for mental health conditions was completed between June 3, 2020 and September 9, 2020. Survey data were collected between July 16, 2020 and September 17, 2020.)	Individuals with mental illness or substance use disorder	332 individuals with mental illness (male = 47%, female = 52%), 328 individuals with no illness (male = 64%, female = 36%)	Not described Self-reported diagnosis of mental illness (yes/no)	No confounder adjusted.	“How willing would you be to receive a vaccine [specify the stage of vaccine approval]” (1–7: 1 = “Not at all willing”; 4 = “Somewhat willing”; 7 = “Extremely willing”)	Participants with mental illness and no illness responded similarly on willingness to accept a COVID-19 vaccine.
Studies reporting general vaccine intention in people with mental health conditions								
Bai et al. [8]	Mainland China	Survey (Data were collected between September 21, 2020 and October 8, 2021.)	Community-dwelling and hospitalised patients with severe mental illness	1853 (27% male)	Major depressive disorder (MDD), bipolar disorder (BD), and schizophrenia (SCZ) Clinical diagnosis according to the	No confounder adjusted.	“Do you intend to be vaccinated against COVID-19 in the future?” (No/Not	The proportion of COVID-19 vaccination hesitancy was 45.3%, with 45.3% in major depressive disorder, 43.6% in

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Table 1 (continued)

Studies reporting less vaccine intention in people with mental health conditions								
Author	Region	Data source (Assessment timing)	Population	Size	Mental health conditions and measure	Confounder	Vaccine intention measure	Results
					International Classification of Diseases, Tenth Revision (ICD-10), obtained from medical records		having vaccination temporarily/ Yes)	bipolar disorder, and 47.4% in schizophrenia subgroups. The proportion of COVID-19 vaccination hesitancy was 49.2% in community-dwelling patients, and 31.3% in hospitalised patients. No significant difference in vaccine hesitancy was found across the three major psychiatric disorders.
Cai et al. [13]	Mainland China	Survey	Patient with depression	1149 (male = 842, female = 307)	Depressive disorder Clinical diagnosis according to the International Classification of Diseases, Tenth Revision (ICD-10), obtained from medical records	NA	“Do you intend to be vaccinated against COVID-19 in the future?” (“I would be vaccinated against COVID-19”/ “I would not accept COVID-19 vaccination temporarily”/ “I would refuse to accept a COVID-19 vaccination”)	A total of 617 depressed patients (53.7%) reported they would accept a future COVID-19 vaccination while 435 patients (37.9%) reported they would not accept COVID-19 vaccination temporarily, and 97 patients (8.4%) stated they would refuse to accept a COVID-19 vaccination.
Huang et al. [24]	Mainland China	Survey	Outpatients and inpatients at a psychiatric speciality hospital	906 (male = 39%, female = 61%)	Psychotic disorders, mood disorders, anxiety disorders, other disorders Self-reported clinical diagnosis	NA	“Are you willing to take a COVID-19 vaccine?” (Yes/No/ Unsure)	Among 906 participated patients, 526 (58.1%) reported that they were willing to take the vaccine, and 282 (31.1%) were hesitant to take the vaccine (17.1% unwilling and 14.0% unsure). 1070 (93%) patients accepted the COVID-19 vaccine they were offered. Logistic regression did not show any effect of diagnosis on vaccination status. This rate was not lower than that in the general population: by July 19, 2021, 88.9% of the adult population in the same area had received their first vaccine dose, and 61.6% were fully vaccinated.
Mazereel et al. [32]	Belgium	Healthcare assessment	Patients at a psychiatric hospital who were offered a COVID vaccine	1151 patients (male = 41%, female = 59%)	Cognitive disorder, psychotic disorder, bipolar disorder, depressive disorder, developmental disorder, anxiety disorder, personality disorder, substance use disorder, eating disorder, adjustment disorder, etc. Clinical diagnosis obtained from medical records	NA	Patients' acceptance of the COVID-19 vaccine when offered.	1070 (93%) patients accepted the COVID-19 vaccine they were offered. Logistic regression did not show any effect of diagnosis on vaccination status. This rate was not lower than that in the general population: by July 19, 2021, 88.9% of the adult population in the same area had received their first vaccine dose, and 61.6% were fully vaccinated.

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Table 1 (continued)

Studies reporting less vaccine intention in people with mental health conditions								
Author	Region	Data source (Assessment timing)	Population	Size	Mental health conditions and measure	Confounder	Vaccine intention measure	Results
Qin et al. [46]	Mainland China	Survey	Psychiatric patients who have previously been diagnosed with bipolar disorders, depressive disorders, anxiety disorders, obsessive compulsive disorders, sleep disorders, schizophrenia, and other mental disorders	1328 patients (male = 34%, female = 66%)	Bipolar disorders, depressive disorders, anxiety disorders, obsessive compulsive disorders, sleep disorders, schizophrenia, and other mental disorders Clinical diagnosis obtained from medical records	NA	Not reported	85.5% of patients were willing to be vaccinated.
Ren et al. [48]	Mainland China	Survey	Psychiatric patients who have previously been diagnosed with schizophrenia, bipolar disorder, major depression disorder, generalized anxiety disorder or other mental disorders.	229 patients and 143 family caregivers	Schizophrenia, bipolar disorder, major depression disorder, generalized anxiety disorder or other mental disorders Clinical diagnosis obtained from medical records	NA	“Would you like to be vaccinated if COVID-19 vaccines become available?” (Yes/No)	77.7% (n = 178) of patients and 100% of the family caregivers said they intended to receive vaccination once the COVID-19 vaccine became available on the market.
Sullivan et al. [54]	US	Survey	People with opioid use disorder (OUD) enrolled in a methadone maintenance program	109 (female = 56%)	Opioid use disorder (OUD) Clinical diagnosis obtained from medical records	NA	Participants were asked to select which best described their COVID-19 vaccination intentions (Willing/Unwilling/Conditionally willing)	32.1% of the participants reported willingness to use a safe and partially effective vaccine against COVID-19. 47.7% endorsed willingness to be vaccinated only if safe and highly effective. 20.1% of the participants were unwilling to be vaccinated in either scenario.

[9,16,17,23,35,36,38,52,57], five of the 17 studies asked participants to self-report their vaccine status [24,37,47,51,58], and two of the 17 studies recorded the number of patients in hospital accepting the COVID-19 vaccine when offered [22,32]. One of the 17 studies did not clearly describe how vaccine uptake was measured [46]. 13 of the 17 studies reported on people with current mental health conditions [9,22,24,32,35–37,46,47,51,52,57,58]. Four of the 17 studies reported on people with either current or history of mental health conditions, but no distinction was made between current and history of mental health conditions [16,17,23,38]. Therefore, we did not distinguish between current and history of mental health conditions in the following reporting.

In the 17 studies, the reported uptake of COVID-19 vaccines (including boosters) ranged from 2% to 93%, among patients with mental health conditions. One study was conducted early in the pandemic when the COVID-19 vaccines were not widely available (October 2020 – May 2021), thus their reported COVID-19 vaccine uptake rates were low (2–3%, [51]). After excluding this study, other

studies reported an uptake of 11–93% among patient with mental health conditions.

### 3.5.1. Differences between people with and without mental health conditions

Thirteen of the 17 studies compared COVID-19 vaccine uptake among people with mental health conditions with uptake among people without these conditions.

**3.5.1.1. Mental health diagnosis from health records.** Of the 13 studies, 11 identified people with mental health conditions through health records or prescription records [16,17,23,32,35,36,38,46,47,52,57]. Of these 11 studies, seven observed that vaccine uptake was between 3 and 21% lower in people with mental health conditions [16,17,36,38,46,47,57]. Among these seven, six reported that the difference in vaccine uptake was statistically significantly lower (all  $p < .05$ ) in people with mental health conditions [17,36,38,46,47,57], among which, four adjusted for other factors such as age and sex [17,36,38,57]. In contrast,

**Table 2**  
Summary of studies investigating the association between mental health conditions and COVID-19 vaccine uptake.

Studies reporting lower vaccine uptake in people with mental health conditions								
Author	Region	Population	Size	Mental health conditions and measure	Vaccine uptake measure (Assessment timing)	Confounder	Barrier to vaccine uptake	Results
Curtis et al. [16,17]	UK	All patients registered with a general practice in England	57.9 million	Severe mental illness Clinical diagnosis (yes/no), obtained from medical records	Electronic health records (Data were collected between 8 December 2020 and 25 May 2021.)	Adjusted for age, sex, ethnicity, socioeconomic status	NA	Presence of a severe mental health condition was associated with lower vaccination rates (71% vs 85% in those without severe mental health conditions) and more declines (5% vs 3% in those without severe mental health conditions) being recorded, and a similar but less divergent pattern was seen in those with a learning disability. Vaccination coverage was substantially lower among those living with severe mental illness (89.5%).
Curtis et al. [16,17]	UK	All patients registered with a general practice in England	57.9 million	Severe mental illness Clinical diagnosis (yes/no), obtained from medical records	Electronic health records (Data were collected between 8 December 2020 and 17 March 2021.)	Adjusted for age, sex, ethnicity, socioeconomic status, and clinical risk groups	NA	After adjusting for sociodemographic, socioeconomic and physical health factors, individuals in receipt of anxiolytics, on antipsychotics and hypnotics were less likely to receive the COVID-19 vaccination. Antidepressant use was not associated with vaccination. A lower proportion of adults with anxiety (39.9%), depression (37.7%), and either disorder (40.2%) received at least 1 dose of the COVID-19 vaccine compared to adults without any symptoms (52.9%). Adults with anxiety or depression were less likely to receive COVID-19 vaccination than those without these conditions.
Murphy et al. [36]	Northern Ireland	Patients registered with the Northern Ireland National Health Authority Information System	1,433,814 individuals (male = 49%, female = 51%). 267,049 (19%) individuals had received psychotropic medication in both 3-month periods before the vaccination programme started.	Recipients of anxiolytics, antipsychotics, hypnotics, and antidepressant. Prescription of psychotropic drugs obtained from medical records	Electronic health records (COVID-19 vaccine data for up to and including 9 September 2021 were included.)	Adjusted for age, gender, household size, socioeconomic and physical health factors,	NA	A lower proportion of adults with anxiety (39.9%), depression (37.7%), and either disorder (40.2%) received at least 1 dose of the COVID-19 vaccine compared to adults without any symptoms (52.9%). Adults with anxiety or depression were less likely to receive COVID-19 vaccination than those without these conditions.
Nguyen et al. [37]	US	Nationally representative sample of the population recruited from the community	77,104 adults (30% had anxiety symptoms, 25% had depression symptoms, 35% had symptoms of either disorder)	Anxiety and depression Self-reported survey: the two-item Patient Health Questionnaire (PHQ-2) and the two-item Generalized Anxiety Disorder (GAD-2) scale	Longitudinal survey (Data were collected March 17–29, 2021)	Analysis conducted both unadjusted and adjusted for sex.	Among those who did not get vaccinated but probably will later, concerns about side effects and uncertainty about whether the vaccine will work were higher among people with anxiety or depressive symptoms than those without any symptoms (56.9% compared to 47.1%, and 19.6% compared to 13.5%, respectively). Among those who did not get vaccinated and probably will not get vaccinated, both a lack of trust in COVID-19	

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Table 2 (continued)

Studies reporting lower vaccine uptake in people with mental health conditions								
Author	Region	Population	Size	Mental health conditions and measure	Vaccine uptake measure (Assessment timing)	Confounder	Barrier to vaccine uptake	Results
Nilsson et al. [38]	Denmark	All Danish residents being alive and living in Denmark on Dec 27, 2020 (i. e. first date of vaccination against SARS-CoV-2 infection in Denmark) and aged at least 15 years on the day of inclusion.	4,935,344 individuals, accounting for 2,560,981 person-years under observation for two doses of vaccines against SARS-CoV-2 infection.	Substance abuse, supported psychiatric housing, psychiatric hospital admission, and severe mental illness (schizophrenia, bipolar disorder, or depressive disorder) Clinical diagnosis obtained from medical records	Electronic health records (Cohort participants were followed from Dec 27, 2020, or from the study participants' 15th birthday, whichever came last, and until they received their second dose of vaccine against SARS-CoV-2 infection, disappeared or left the country, died, or until the end of study on Oct 15, 2021)	Analysis conducted both unadjusted and adjusted for sex.	vaccines and in the government were higher among people with anxiety or depression compared to people without these disorders. Among people who did not get vaccinated and definitely will not get a vaccine, dislike of vaccines was higher among those with anxiety or depression compared to those without either disorder (24.4% compared to 16.2%, respectively). NA	The vaccine uptake for people with psychiatric exposures were lower than in the nonexposed individuals. Among the psychiatric groups, highest cumulative vaccine uptake was found for severe mental illness and lowest uptake for substance abuse.
Qin et al. [46]	Mainland China	Psychiatric patients who have previously been diagnosed with bipolar disorders, depressive disorders, anxiety disorders, obsessive compulsive disorders, sleep disorders, schizophrenia, and other mental disorders	1328 patients (male = 34%, female = 66%)	Bipolar disorders, depressive disorders, anxiety disorders, obsessive compulsive disorders, sleep disorders, schizophrenia, and other mental disorders Clinical diagnosis obtained from medical records	Survey (Data were collected between August 9 and August 24, 2021)	No confounder adjusted.	Patients who were willing to be vaccinated were more likely to get inoculated (77.5%) and patients who were unwilling (20.8%) and uncertain (12.5%) about vaccination were less likely to be inoculated compared to those who were indifferent (43.2%) about vaccines.	69.4% of patients had been vaccinated at the time of the survey, which was lower than their family members (89.8%)
Raffard et al. [47]	France	Patients with diagnosis of schizophrenia	100 patients (female = 38%) and 72 family caregivers (female = 26%)	Schizophrenia Clinical diagnosis obtained from medical records	Survey (Data were collected between April 2021 and October 2021.)	No confounder adjusted.	Non-vaccinated individuals had higher negative attitudes towards vaccine benefit, unforeseen future effects of the	A statistical trend was noted with respect to the proportion of vaccinated participants, showing lower rates

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Table 2 (continued)

Studies reporting lower vaccine uptake in people with mental health conditions								
Author	Region	Population	Size	Mental health conditions and measure	Vaccine uptake measure (Assessment timing)	Confounder	Barrier to vaccine uptake	Results
							vaccine, and commercial profiteering of the vaccine, and had higher preference for natural immunity. Non-vaccinated individuals had lower levels of trust in institutions than did the vaccinated participants.	of vaccination in patients (64%), compared to controls (77.8% of $n = 72$ , $p = .07$ , $\Phi = 0.15$ ).
Tzur Bitan et al. [57]	Israel	Patients with schizophrenia	4797 individuals (male = 60%) with schizophrenia and 34,797 matched controls (male = 60%)	Schizophrenia Clinical diagnosis obtained from medical records	Electronic health records (Data were mined at the end of November 2021.)	Adjusted for demographic and clinical risk factors previously associated with vaccination uptake, including socioeconomic status, sector (ie, population group), marital status, diabetes, hypertension, hyperlipidemia, chronic obstructive pulmonary disease, and ischemic heart disease.	NA	20.7% of individuals with schizophrenia were completely unvaccinated, compared with 14.5% of matched control participants. No significant differences were observed in the uptake of the second vaccine. 74.7% of individuals with schizophrenia completed the booster vaccine, lower than 77.9% in the control group.
Studies reporting greater vaccine uptake in people with mental health conditions								
Balut et al. [9]	US	Veterans experiencing homelessness	83,528 (male = 90%, female = 10%)	Alcohol use disorder, drug use disorder, posttraumatic stress disorder, psychotic disorders, depression, anxiety, schizophrenia, or bipolar disorder Self-reported mental health diagnosis (yes/no)	Electronic health records (The study period was from 14 December 2020 through 1 August 2021)	Both unadjusted and adjusted (for sociodemographic, other health conditions, and healthcare and housing service utilisation variables) results were reported.	NA	Veterans with any mental health conditions (47.2% vs. 38.3%) were more likely to get vaccinated.
Hassan et al. [23]	UK	All patients registered with a general practice in England	1,152,831 adults with and without severe mental illness: exclusive groups of individuals with schizophrenia or related psychotic disorders ( $N = 46,859$ ), bipolar disorder ( $N = 3461$ ), and recurrent major depressive disorder ( $N = 134,661$ ), and a 10% sample of individuals with diagnoses of other	Schizophrenia or related psychotic disorders, bipolar disorder, and recurrent major depressive disorder, and a 10% sample of individuals with diagnoses of other depressive disorders, excluding all previously mentioned diagnoses. Clinical diagnosis obtained from medical records	Electronic health records (Data were mined up to June 30, 2021.)	Analyses controlled for sociodemographic covariates, including age, gender, ethnicity and Index of Multiple Deprivation (IMD) decile.	NA	Compared to matched controls, vaccination rates were highest among people with recurrent major depression (77.1%), followed by bipolar disorder (75.7%), other depressive disorders (75.1%), and psychotic disorders (69.6%). The prevalence of vaccination among all controls was 68.4%. The proportion of individuals recorded as having declined vaccination by June 30, 2021 among all controls was 2.0%.

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Table 2 (continued)

Studies reporting lower vaccine uptake in people with mental health conditions								
Author	Region	Population	Size	Mental health conditions and measure	Vaccine uptake measure (Assessment timing)	Confounder	Barrier to vaccine uptake	Results
			depressive disorders, excluding all previously mentioned diagnoses (N = 45,586).					Rates of having been recorded as declining vaccination were significantly higher across all mental disorders examined, with psychotic disorder diagnoses highest (5.0%), followed by bipolar disorder (3.8%), recurrent major depression (2.9%) and other depressive disorders (2.8%).
Studies reporting similar vaccine uptake in people with and without mental health conditions								
Mazereel et al. [32]	Belgium	Patients at a psychiatric hospital who were offered a COVID vaccine	1151 patients (male = 41%, female = 59%)	Cognitive disorder, psychotic disorder, bipolar disorder, depressive disorder, developmental disorder, anxiety disorder, personality disorder, substance use disorder, eating disorder, adjustment disorder, etc. Clinical diagnosis obtained from medical records	Clinical diagnosis obtained from medical records (Data were collected on July 19, 2021, while administrating COVID-19 vaccines to hospitalised patients.)	No confounder adjusted	NA	1070 (93%) patients accepted the COVID-19 vaccine they were offered. This rate was not lower than that in the general population: by July 19, 2021, 88.9% of the adult population in the same area had received their first vaccine dose, and 61.6% were fully vaccinated. No effect of diagnosis on vaccination status was found.
Moeller et al. [35]	US	Patients at a academic child and adolescent psychiatric hospital	174 (male = 35%, female = 66%)	Attention-deficit/hyperactivity disorder, adjustment disorder, anxiety disorder or trauma-related disorder, autism spectrum disorder, disruptive mood dysregulation disorder, major depressive disorder/suicidal ideations, others Clinical diagnosis obtained from medical records	Healthcare assessment (A 4-week retrospective chart review was performed on all patients admitted from May 27, 2021, to June 23, 2021.)	No confounder adjusted	NA	29.8% of adolescent inpatients with mental illness screened for the COVID-19 vaccine requested and consented to vaccination. 30.5% of adolescent patients have already received one dose of the vaccine before admission. This is comparable to the national average on June 30, 2021, with 30.9% of adolescents aged 12–15 years having at least one dose of the vaccine.
Shkalim Zemer et al. [52]	Israel	Adolescents diagnosed with attention-deficit/hyperactivity disorder (ADHD)	46,511 adolescents aged 12–17 years (n = 8241 with ADHD, 18%)	Attention-deficit/hyperactivity disorder (ADHD) Clinical diagnosis obtained from medical records	Survey (A retrospective chart review was performed on all adolescents aged 12–17 years registered from January 1st 2021 to October 31st 2021. Data cut-off was August 31, 2021.)	Adjusted for age, sex, ethnicity. Censoring was also applied in analysis (i.e. removing from analysis at the time of the event), due to infection prior to vaccination	NA	In total, 52.5% of adolescents with ADHD were vaccinated, compared with 47.8% of adolescents without ADHD. 1.2% of adolescents with ADHD aged 12–15 years received the booster dose, which was comparable to 1.4% of adolescents

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Table 2 (continued)

Studies reporting lower vaccine uptake in people with mental health conditions								
Author	Region	Population	Size	Mental health conditions and measure	Vaccine uptake measure (Assessment timing)	Confounder	Barrier to vaccine uptake	Results
<b>Studies reporting general vaccine uptake in people with mental health conditions</b>								
Gibbon et al. [22]	UK	In-patients within a medical secure psychiatric hospital	85	Not described Clinical diagnosis obtained from medical records	Survey (Not reported)	NA	NA	with non-ADHD aged 16–17 years. A total of 45.8% of adolescents with ADHD aged 16–17 years received the booster dose, higher than 42.5% of adolescents with non-ADHD aged 16–17 years.
Huang et al. [24]	Mainland China	Outpatients and inpatients at a psychiatric speciality hospital	906 (male = 39%, female = 61%)	Psychotic disorders, mood disorders, anxiety disorders, other disorders Self-reported clinical diagnosis	Survey (Between March 24 and April 27, 2021)	NA	Compared to vaccine-hesitant persons, vaccine-recipients were more likely to agree that the preventive effect of vaccines is good, believe that at least half of vaccine-recipients would be immune to COVID-19, believe that vaccines are safe, be not worried about the side effects of vaccines.	98 (10.8%) patients had taken the vaccine at the time of this survey.
Sekizawa et al. [51]	Japan	Community sample	11,846 (male = 50%, female = 50%) participants. 1705 participants reported moderate-to-severe depression symptoms at wave 1, 1751 participants reported at wave 3. 1021 participants reported moderate-to-severe anxiety symptoms at wave 1 and 1057 reported at wave 3.	Depression, anxiety Self-reported survey: Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 scale (GAD-7)	Longitudinal survey (Wave 1 was conducted from October 27 to November 6, 2020. Vaccine outcomes were assessed only at Wave 3, between April 23 and May 6, 2021.)	NA	NA	2% of participants with moderate-to-severe depression symptoms at wave 1 were already vaccinated at wave 3, 3% of participants with moderate-to-severe depression symptoms at wave 3 were already vaccinated at wave 3. 3% of participants with moderate-to-severe anxiety symptoms at wave 1 were already vaccinated at wave 3, 3% of participants with moderate-to-severe anxiety symptoms at wave 3 were already vaccinated at wave 3.
Uvais [58]	India	Patients with severe mental illness	62 patients (male = 69%, female = 31%)	Bipolar affective disorder, schizophrenia, psychosis, obsessive-compulsive disorder, depressive disorder Clinical diagnosis	Survey (Between April 21, 2021, to August 3, 2021)	NA	Respondents in the vaccinated group perceived the vaccine to be more effective in preventing COVID-19 infection than those in the unvaccinated group. Vaccinated respondents were	Only 27.9% of the respondents received the first dose of COVID-19 vaccination, and 59.7% were recommended for vaccination from a healthcare provider.

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Table 2 (continued)

Studies reporting lower vaccine uptake in people with mental health conditions								
Author	Region	Population	Size	Mental health conditions and measure	Vaccine uptake measure (Assessment timing)	Confounder	Barrier to vaccine uptake	Results
				obtained from medical records			also less in agreement with the statement about the risk of COVID-19 vaccine worsening mental illness. Both vaccinated and unvaccinated respondents tended to disagree with the statement about COVID-19 vaccines can cause COVID-19 infection, COVID-19 vaccines can cause mental illness, or it is harmful to take COVID-19 vaccination while taking medications for mental illness. Apart from age, recommendation for vaccination from health care providers was significantly and positively associated with vaccination.	

one of the 13 studies observed that vaccine uptake was up to 1.19 times significantly higher (95% CI: 1.01–1.21, 1.04–1.23) among patients with mental health conditions, compared with people without, after adjusting for other factors such as age, gender, ethnicity, and deprivation [23]. Three of the 13 studies reported similar levels of vaccine uptake among people with and without mental health conditions [32,35,52] but no significance tests were reported in two of them [32,35]. However, significantly higher rates of declining the COVID-19 primary or booster vaccines among people with mental health conditions, compared with people without, were also reported in two of these three studies [23,52]. Two of the 13 studies reported the uptake of booster vaccines. Shkalim Zemer et al. [52] reported significantly higher uptake of the booster vaccine among adolescents with ADHD aged 16–17 (46%) compared with non-ADHD adolescents of the same age (43%), and similar uptake of the booster vaccine among adolescents with ADHD aged 12–15 and non-ADHD adolescents of the same age (1.2% vs 1.4%). Tzur Bitan et al. [57] reported significantly lower uptake of the first vaccine (79%,  $p < .001$ ) and the booster vaccine (75%,  $p < .001$ ) among patients with schizophrenia compared with people without (86% for first vaccine, 78% for booster vaccine). They also reported that, after getting the first vaccine, there was no difference in the uptake of the second COVID-19 vaccine between people with (94%) and without (94%) schizophrenia.

**3.5.1.2. Self-reported mental health diagnosis.** Only one of the 13 studies identified people with mental health conditions using self-reported diagnosis [9]. This study reported that vaccine uptake was significantly higher among patients with mental health conditions (47%), compared with people without mental health conditions (38%). When adjusted for other factors such as age and gender, however, the results

were no longer significant.

**3.5.1.3. Self-reported mental health symptoms.** Only one of the 13 studies measured probable mental health conditions through survey-reported symptoms [37]. This study observed that the uptake of at least 1 dose of the COVID-19 vaccine among people with moderate-to-severe anxiety and/or depression was between 38 and 40%, which was significantly lower than among people without mental health conditions (53%), after adjusting for sex.

### 3.5.2. Differences between different mental health conditions

Two of the 17 studies compared vaccine uptake across different psychiatric diagnoses (accessed through health records) but reported different observations. One reported that 51% of patients with schizophrenia were vaccinated, which was lower (significance levels unreported) than those with other psychiatric disorders: bipolar disorder, 74%; depression disorder, 74%; anxiety disorder, 66%; obsessive-compulsive disorder, 85%; sleep disorder, 80%; other psychiatric disorders, 65% [46]. Another study, however, did not find significant effects of psychiatric diagnosis on vaccine uptake [32].

### 3.5.3. Barriers to COVID-19 vaccine uptake among people with mental health conditions

We also extracted data on barriers to COVID-19 vaccine uptake among people with mental health conditions from these studies. Five of the 17 studies reported results on this [24,37,46,47,58]. Four of the five studies reported that, among people with mental health conditions, unvaccinated individuals were more likely to report greater concerns about the safety, effectiveness, and side effects of the COVID-19 vaccine than vaccinated people [24,37,47,58]. Lack of trust in the vaccine,



development of the vaccine, and the government was reported among some unvaccinated people with mental health conditions in two studies [37,47]. One study reported that the vaccination rate was higher among patients who had the intention to be vaccinated (vaccination rate: 78%), compared with those who did not express this intention (vaccination rate: 21%) or who were uncertain about the vaccination (vaccination rate: 13%, [46]). One study reported that recommendation for vaccination from health care providers was positively associated with vaccine uptake in people with mental health conditions [58].

Overall, the observed uptake of COVID-19 vaccines among people with mental health conditions varied between studies: with 8/13 studies reporting lower vaccine uptake in people with mental health conditions, 2/13 studies reporting higher uptake in people with mental health conditions, and 3/13 reporting no differences. Although with limited evidence, patients with schizophrenia might have lower COVID-19 vaccine uptake, compared with people without mental health conditions and people with other mental health conditions. Among people with mental health conditions, the most common barriers to COVID-19 vaccine uptake include concerns about the safety, effectiveness, and side effects of the COVID-19 vaccine.

### 3.6. Mental health conditions and COVID-19 vaccine breakthrough

Only two out of 32 studies reported outcomes related to breakthrough infection following vaccination in people with mental health conditions (Table 3, [40,60]). Both studies defined a COVID-19 vaccine breakthrough infection as “a positive SARS-CoV-2 test record occurring in the medical records  $\geq 14$  days after their final SARS-CoV-2 vaccine dose”, in line with the CDC definition [10]. Wang et al. [60] included patients with current substance use disorders, while Nishimi, Neylan, et al. [40] included patients who had psychiatric disorder diagnoses within the past five years. Both studies were conducted using data from electronic health records and had very large sample sizes (263,697 in [39,40] and 579,372 in [60]). The observation period was from February 2020 to November 2021 in Nishimi, Neylan, et al. [40], and from December 2020 to August 2021 in Wang et al. [60].

Both studies reported that people with mental health conditions were at increased risk of breakthrough infections for COVID-19. Specifically, Nishimi, Neylan, et al. [40] reported that patients with any psychiatric disorder were 7% more likely to experience a breakthrough infection (95% CI, 1.05–1.09;  $P < .001$ ), compared with patients without psychiatric disorders, after adjusting for potential confounders (e.g., age, ethnicity, vaccine type, time since vaccine, etc.). These patients were still at 3% increased risk of experiencing breakthrough infection (95% CI, 1.01–1.05;  $P < .001$ ), compared with patients without psychiatric disorders, after further adjusting for medical comorbidities (e.g., diabetes, cardiovascular diseases etc.) and smoking status. Nishimi, Neylan, et al. [40] also reported that when considering specific psychiatric disorder the highest relative risks were observed for adjustment disorder (relative risk = 1.13; 95% CI: 1.10–1.16,  $p < .001$ ) and substance use disorders (relative risk = 1.16; 95% CI: 1.12–1.21,  $p < .001$ ), after adjusting for confounders, medical comorbidities, and smoking status, and there was no significant increase for other psychotic disorders (relative risk = 1.05; 95% CI: 0.99–1.11;  $p = .09$ ).

The other study, Wang et al. [60], reported that among patients with substance use disorders, the risks for breakthrough infections were 7% for tobacco use, 7% for opioid use, 7% for alcohol use, 8% for cocaine use, and 8% for cannabis use, all significantly higher than that in matched cohorts without substance use disorder (2–4%,  $p < .001$ ). The modest but higher risks of breakthrough infection among patients with substance use disorder remained significant after controlling for age, gender, ethnicity and vaccine types, for all but tobacco use disorder. However, after controlling for socioeconomic determinants of health (e.g., problems related to education, employment, occupational risk factors, and housing and economic circumstances) and physical comorbidities, the risks for breakthrough infection no longer differed between

patient with substance use disorder and matched cohorts for all but cannabis use disorder. Patients with cannabis use disorder remained at increased risk (hazard ratio = 1.55, 95% CI: 1.22–1.99) compared with matched cohorts without cannabis use disorder. When looking at severe outcomes of vaccine breakthrough infections (i.e., COVID-19 hospitalisation and death) within patients with substance use disorders, the risk of hospitalisation was 22.5% for those who had breakthrough infections and 1.6% for those without breakthrough infections. The risk of death was 1.7% for patients who experienced breakthrough infections and 0.5% respectively. When looking at the type of vaccines patients with substance use received, the risk for breakthrough infection was higher in patients who received the Pfizer than the Moderna vaccine (hazard ratio = 1.49, 95% CI: 1.31–1.69).

Findings from these two studies suggest that patients with mental health conditions, especially those with substance use disorder, might be at a slightly increased risk of experiencing breakthrough infection after being vaccinated against COVID-19.

## 4. Discussion

This review highlights the evidence and gaps in research concerning mental health conditions and three COVID-19 vaccine outcomes: vaccine intentions, vaccine uptake, and breakthrough infection. Overall, the evidence was mixed regarding COVID-19 vaccine intentions among individuals with mental health conditions, compared with those without. When looking at the studies with relatively large sample sizes ( $n > 500$ ) that also adjusted for other confounding factors such as age and gender, three found no significant differences in vaccine intention between people with and without mental health conditions, while two found lower vaccine intentions and one reported higher vaccine intentions among people with mental health conditions. The mixed results may be due to vaccination intentions differing between different mental health conditions. We see some support for this from work revealing that people with substance use disorders being less likely to intend to be vaccinated; while patients with bipolar disorder were more likely to intend to be vaccinated [19]. Although this study was conducted with a relatively large sample size ( $n = 14,365$ ) and it adjusted for other confounding factors (e.g., age, gender, physical comorbidities), the finding should be treated with caution given the current paucity of evidence. Another study included in this review also reported that community-dwelling patients had lower vaccine intention compared to hospitalised patients [8]. Therefore, combining people with different mental health conditions, or combining hospitalised patients and community-dwelling patients together in such investigations might be contributing to seemingly equivocal findings. Future research would benefit from distinguishing patients into subgroups of different mental health conditions or diagnoses to understand the associations between different conditions or diagnoses and vaccine intentions.

### 4.1. Intention versus behaviour

One unique contribution of this review is that we also summarised evidence on the actual uptake of COVID-19 vaccines among people with mental health conditions, and did not rely on data on vaccine intentions alone. One of the reviewed studies reported results on the intention-behaviour association and found that the vaccination rate was higher among patients who were intending to be vaccinated compared with those who were not willing or uncertain [46]. This result offers some support for the development of interventions which change vaccine intentions as the vehicle for promoting vaccine uptake [12,42]. However, although focusing on vaccine intention among people with mental health conditions is important, it might not be sufficient to encourage vaccine uptake in this population. According to the Theory of Planned Behaviour (TPB), attitude towards the behaviour, subjective norm, and perceived behavioural control are three determinants of a behavioural intention, which then lead to a behaviour i.e., intention is an “immediate

**Table 3**  
Summary of studies investigating the association between mental health conditions and COVID-19 vaccine breakthrough.

Author	Region	Data source (Assessment timing)	Population	Size	Mental health conditions and measure	Confounder	Results
Nishimi et al. [39,40]	US	Electronic health records (Data were mined between February 20, 2020, and November 16, 2021)	Patients who accessed Veterans Affairs (VA) health care during the study period, had at least 1 SARS-CoV-2 test recorded in the electronic health record, had no record of SARS-CoV-2 infection prior to vaccination, and had completed a full SARSCoV-2 vaccination regimen 14 days or more prior.	263,697 patients (male = 90.8%)	Depressive, posttraumatic stress, anxiety, adjustment, alcohol use, substance use, bipolar, psychotic, attention-deficit/ hyperactivity, dissociative, and eating disorders. Clinical diagnosis obtained from medical records	Adjusted for sociodemographic factors (ie, age, sex, and race and ethnicity), vaccine type, and time since vaccination (including an interaction term for vaccine type by time since vaccination to account for differential waning effectiveness, medical conditions, obesity, and smoking.	51.4% of the fully vaccinated patients had at least 1 psychiatric disorder diagnosis, and 14.8% developed a breakthrough infection. A diagnosis of any psychiatric disorder was associated with increased incidence of breakthrough infection, both in models adjusted for potential confounders and additionally adjusted for medical comorbidities and smoking. Most specific psychiatric disorder diagnoses were associated with an increased incidence of breakthrough infection, with the highest relative risk observed for adjustment disorder and substance use disorders.
Wang et al. [60]	US	Electronic health records (Data were mined between December 1, 2020 and August 14, 2021)	Fully vaccinated patient with substance use disorders (SUD)	579,372 individuals (30,183 with a diagnosis of SUD and 549,189 without such a diagnosis) who were fully vaccinated between December 2020 and August 2021, and had not contracted COVID-19 infection prior to vaccination	Substance use disorder (SUD) Clinical diagnosis obtained from medical records	Adjusted for demographics (age, gender, ethnicity) and vaccine types for all SUD subtypes, and adverse socioeconomic determinants of health and comorbid medical conditions.	Among SUD patients, the risk for breakthrough infection ranged from 6.8% for tobacco use disorder to 7.8% for cannabis use disorder, all significantly higher than the 3.6% in non-SUD population. Breakthrough infection risk remained significantly higher after controlling for demographics (age, gender, ethnicity) and vaccine types for all SUD subtypes, except for tobacco use disorder, and was highest for cocaine and cannabis use disorders. When matching patients with SUD and non-SUD individuals for lifetime comorbidities and adverse socioeconomic determinants of health, the risk for breakthrough infection no longer differed between these populations, except for patients with cannabis use disorder, who remained at increased risk. The risk for breakthrough infection was higher in SUD patients who received the Pfizer than the Moderna vaccine. In the vaccinated SUD population, individuals with breakthrough infections had higher risk for hospitalisation and death, compared to non-breakthrough infections.

antecedent of behaviour" [3]. Therefore, although intention is a key contributor to behaviour, it might not necessarily translate into a certain behaviour directly. Meta-analyses on the efficacy of TPB examined to what extent behavioural intentions predicted actual behaviours usually report that intentions account for only 25% of the variance in behaviour [5] or 3% - 30% of the variance in health behaviours (e.g., alcohol drinking, physical activity, diet) in particular [33,34]. This intention-behaviour discordance has been reported in previous literature and in other contexts. For example, a meta-analysis focusing on physical activity found that 36% of people who intended to engage in physical activity failed to do so [49]. In a more recent study where TPB was used as the theoretical model to explore the associations between intention and receiving Human papillomavirus (HPV) vaccines using TPB, intention accounted only for 9.6% of the variance in behaviour, while moral norm (i.e., the perceived moral correctness of a behaviour) and intention together accounted for 14.1% of the variances in behaviour [27]. Therefore, interventions targeting other aspects of vaccine delivery should also be considered, for example, making vaccines available at psychiatric clinics, providing psychiatrists with sufficient information about the vaccines, providing more support for patients with mental health conditions to receive vaccines at GPs, having engagement campaigns and activities tailoring to people with mental health conditions and their carers, etc. [32,44,56].

When looking at vaccine uptake, although the reported uptake of the COVID-19 vaccine varied across studies, depending on the timings, settings, and populations under investigation, most of the studies suggested that people with mental health conditions were likely to have a lower rate of vaccine uptake. Especially when looking at studies ( $n = 8$  of 17) using electronic health records with large sample sizes ( $n > 4000$ ), the reported rate of COVID-19 vaccine uptake among people with mental health conditions ranged from 47% to 90% compared with 38% to 95% in people without mental health conditions [9,16,17,23,36,38,52,57]. Five out of these eight studies reported that people with mental health conditions had significantly lower uptake of the COVID-19 vaccine, compared with people without mental health conditions [16,17,36,38,52,57], while three reported significantly greater or similar uptake among people with mental health conditions compared to those without [9,23,52].

#### 4.2. Vaccine breakthrough in people with mental health conditions

Another contribution of this review is the summary on the association between mental health conditions and COVID-19 vaccine breakthrough. Only two published studies were identified and they both suggested that vaccine breakthrough may be a particular risk for those with substance use disorder [40,60]. Both studies were population-based cohort study conducted using electronic health records. The significant higher risks for breakthrough infection for people with substance use disorders remained after controlling for other factors such as age and gender. Wang et al. [60] further reported that these patients were also at risk of more adverse outcomes, including hospitalisation and death, following a breakthrough infection, compared with non-breakthrough infections. These results suggest that having substance use disorders may influence the vulnerability to COVID-19 and thus the effectiveness of COVID-19 vaccines. A previous review on vulnerabilities and complications of substance use disorder in the COVID-19 pandemic has summarised the potential pathways where substance use disorders may contribute to increased vulnerability to COVID-19 [61]. Some potential pathways include: people with some substance use disorders (e.g., smoking of tobacco and marijuana) might have impaired respiratory system, which is a primary target of the SARS-CoV-2 virus; many substance use disorders impair the interactions between the brain and immune responses, resulting in greater vulnerability to infections; stigma and limited access to healthcare among many patients with substance use disorders also contributes to the risks [61]. The latter is also a factor contributing to lower vaccine intentions in this population [4].

However, both studies [40,60] were conducted in the US and so the generalisability of these findings to other countries and populations is unclear.

#### 4.3. Limitations

This scoping review did not assess the quality of the studies or quantitatively estimate the relationships between mental health and COVID-19 vaccine outcomes using meta-analysis. For studies concerning COVID-19 vaccine intention, settings (e.g., in hospital or in community) and populations varied between studies which may limit the generalisability of the findings. In addition, 90% of these studies measured vaccine intention using different self-reported item(s) where self-report biases may be present [26]. Some studies concerning COVID-19 vaccine uptake and breakthrough, did not distinguish between people who were experiencing current mental health conditions and who had previous mental health diagnosis. It is unclear whether current or previous mental health conditions would have any impact on vaccine uptake or breakthrough. Only two studies reported results concerning COVID-19 vaccine breakthrough among people with mental health conditions, suggesting that evidence on this topic is currently limited.

#### 4.4. Future directions

Urgent research effort is needed to investigate the risks of COVID-19 vaccine breakthrough and severe COVID-19 outcomes among people with mental health conditions, and associated risk factors. Future studies should also be encouraged to distinguish between the different mental health conditions and also the impact of current or previous mental health conditions on COVID-19 vaccine outcomes. The nature of barriers to vaccine uptake, and the intention-behaviour gap in vaccinations also need further investigation.

### 5. Conclusions

This is the first review, to our knowledge, focusing on the three COVID-19 vaccine outcomes (i.e., intention, uptake, and vaccine breakthrough) among people with mental health conditions. We found that the evidence regarding the level of vaccine intentions in this population was inconclusive. However, the majority of evidence seemed to suggest that vaccine uptake among people with mental health conditions was lower than people without. Limited evidence seemed to also suggest that people with mental health conditions may be at increased risk of COVID-19 vaccine breakthrough. Future work may also investigate the scale of this issue, and possible consequences.

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## CRedit authorship contribution statement

**Ru Jia:** Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Carol Coupland:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Funding acquisition, Conceptualization. **Yana Vinogradova:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Funding acquisition, Conceptualization. **Nadeem Qureshi:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization. **Emma Turner:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Funding acquisition, Conceptualization. **Kavita Vedhara:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Funding acquisition, Conceptualization.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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