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Review Article

COVID-19 Incidence and Post-COVID Syndrome in Mental Health Disorders: A Systematic Review with Meta-Analyses

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Abstract

Unveiling the connection between mental health and COVID-19, this study delves into pre-existing disorders' impact on susceptibility and post-COVID syndrome. By meticulously reviewing 29 publications, including 52 effect-size estimates from renowned databases, intriguing insights emerge. Surprisingly, individuals with mental health disorders don't exhibit a higher risk of COVID-19 infection. However, the study unveils a compelling revelation - they face a heightened likelihood of post-COVID syndrome. While SARS-CoV-2 infection risk isn't elevated in this group, vulnerability to post-COVID complications prevails. With a profound grasp of limitations and strengths, the findings ripple with implications, urging greater support and care for this resilient population. By recognizing their unique needs, we can pave the way for better health outcomes in a post-pandemic world.

Keywords: covid-19 infection; post-covid syndrome; mental health disorders; long covid; covid-19

I-Introduction:

The Coronavirus disease 2019 (COVID-19) epidemic crisis rapidly escalated into a global pandemic, with more than 767 million individuals infected and 6.9 million deaths as of June 2023 (World Health Organization [WHO], 2023). The pandemic resulted in a burden of potential years of life lost over a decade and has indeed influenced our lives in one way or another. When the pandemic escalated quickly, researchers started investigating factors that may cause some individuals to be more vulnerable (Solis et al., 2020). Literature on past pandemics and natural disasters suggests that numerous factors could make it more likely for people with mental illnesses to contract COVID-19. These vulnerability factors include insomnia, higher prevalence of somatic comorbidities, impaired immune system, chronic stress exposure, poor health behavior, difficulties in evaluating health information and adhering to preventive behaviors, limitations in access to health care, homelessness, or living in areas where the risk of contagion is higher. All of these are related to infection risk and disease course and are frequently present in people who have poor mental health (Chireh et al., 2019; Chrousos, 2009; Shinn & Viron, 2020). Some researchers (e.g., Shinn & Viron, 2020; Wang et al., 2021b) have expressed their concerns that people with a pre-existing mental health disorder may be at a higher risk of COVID-19 infection and that the outcomes of the disease may be worse. Although, before the COVID-19 pandemic, it was estimated that 20-25% of adults are suffering from mental health disorders (450 million globally, 84 million, i.e., 1 out of 6, in the EU (European Union) countries; OECD, 2018), research on the potential effects of (pre-existing) mental health disorders on COVID-19 infection risk, and outcomes of the infection are not yet fully understood. Existing literature on the relationship between COVID-19 susceptibility and various types of mental health disorders is scarce and provides inconsistent findings. A South Korean population-based study found no significant differences in COVID-19 infection rates between psychiatric patients and the general population (Lee et al., 2020); in contrast, a US cohort found that having a psychiatric diagnosis may be a unique risk factor for infection (Taquet et al., 2020). This is in line with three other studies reporting an elevated risk of testing positive for COVID-19 (Liu et al., 2021; Wang et al., 2021b; Yang et al., 2020). Nevertheless, Goldenberg et al. (2022) found a lower infection rate among people with a history of psychiatric hospitalization, particularly those with a history of drug or alcohol abuse. Similar results were found in a large-scale cohort study in Israel (Tzur-Bitan et al., 2022), a large cohort study in the USA (Egede et al., 2021), and a population-based study conducted in the UK (van der Meer et al., 2020). It is also controversial whether individuals with different mental health disorders have various susceptibility risks to a COVID-19 infection. Studies seem to differ in their findings. It was hypothesized that people with schizophrenia might be more susceptible to transmissions of COVID-19 (Fonseca et al., 2020; Kozloff et al., 2020; Moreno et al., 2020; Wang et al., 2021b) for several reasons. For example, patients with schizophrenia have a dysregulated immune system (Rodrigues-Amorim et al., 2018), cognitive impairments, lower risk awareness, and barriers to adequate housing (Yao et al., 2020a) and timely access to preventative

health care (Knaak et al., 2017), poverty (Burns et al., 2014) and difficulties adopting and adhering to the protective measures (Maguire et al., 2019) due to impairments in insight and decision-making capacity (Larkin & Hutton, 2017). However, Tzur-Bitan et al. (2021) and Texeria et al. (2021) reported contradicting results. They showed that individuals with schizophrenia were less likely to be tested positive for COVID-19, while Merzon et al. (2021) found no significant association. Similar to the relationship between schizophrenia and COVID-19 infection, the relationship between mood disorders, anxiety disorder, neurodevelopmental disorders, substance use disorder, and COVID-19 risk is also unclear. For example, some studies showed increased susceptibility to COVID-19 in people with mood and anxiety disorders (Neelam et al., 2021; Wang et al., 2021b), substance abuse disorders (SUD) such as tobacco use disorder, alcohol use disorder, cannabis use disorder, injected drug use disorder, cocaine use disorder, and opioid use disorder (Wang et al., 2021a), and attention-deficit/hyperactive disorder (ADHD; Breaux et al., 2021; Cohen et al., 2022; Merzon et al., 2021, Neelam et al., 2021; Wang et al., 2021b). On the contrary, other studies reported lower rates of COVID-19 infection in people with mood disorders (Texeria et al., 2021) and drug or alcohol abuse (Goldberger et al., 2022). In addition, some studies did not find a significant positive relationship between the COVID-19 infection rate and mental health disorders; for example, people with depression or anxiety (Ceban et al., 2021), or autism spectrum disorder (ASD; Merzon et al., 2021). In a nutshell, the existing literature on the effects of (pre-existing) various mental health disorders in COVID-19 susceptibility is not only scarce but also inconsistent. To better understand how different mental health disorders are affected by the virus, a systematic review is needed.

Pre-Existing Mental Health Disorders and Post-COVID Syndrome

After 2.5 years, the coronavirus disease (COVID-19) pandemic remains a worldwide health problem. Illness severity and its outcomes vary from person to person. Yet, recent studies demonstrated that an increasing number of patients experience prolonged symptoms of the COVID-19 virus (Our World in Data, 2022; Petersen et al., 2021). Post-COVID syndrome, also known as a long-COVID condition, is a complicated and increasingly recognized illness. It is characterized by prolonged diverse symptoms in which some infected patients do not recover for several weeks or months after the onset of COVID-19 infection (Nabavi, 2020; WHO, 2022). Post-COVID syndrome has recently been reported to cause a variety of neurological and mental symptoms such as fatigue, chest pain, breathlessness, body aches, cognitive impairment, insomnia, headaches, anxiety, and depression (Carfi et al., 2020; Chopra et al., 2021; Huang et al., 2021). In addition to these symptoms, those with post-COVID syndrome reported a diminished quality of life, employment problems, issues with their physical and cognitive abilities, and difficulties participating in society (Aiyegbusi et al., 2021; Tobacof et al., 2022). According to Carfi et al. (2021)'s underestimated calculations, at least 10% of COVID-19 survivors suffer from persistent COVID-19 symptoms, which means approximately 6 million people are at risk of post-COVID syndrome globally. Further, according to the U.K.'s Office for National Statistics (2022), post-COVID syndrome symptoms negatively impacted 1.6 million people (73% of those with self-reported long COVID). Among them, 333,000 people reported that their capacity to carry out daily activities had been restricted a lot. The research on post-COVID syndrome has increased, yet the patient profile, associated problems, long-term effects, and the timeline of the disease remain unknown (d'Ettorre et al., 2022). According to limited observational data, patients who require intensive care unit (ICU) admission and/or ventilatory support appear to be at an increased risk of developing post-COVID syndrome (Halpin et al., 2021), even though sequelae are also seen in individuals with mild to moderate symptoms (Davis et al., 2021; Lemhöfer et al., 2021). It is also known that comorbidities such as cancer, diabetes, heart disease, chronic arterial hypertension, chronic obstructive pulmonary disease, chronic kidney disease, and alcohol and tobacco addiction are correlated with the severity and mortality of COVID-19 (de Miranda et al., 2022; Panda et al., 2022; Sargin Altunok et al., 2022; Zhu et al., 2022). Although the prognosis of the novel post-COVID syndrome is unknown, it is likely to be determined by the comorbid conditions, the severity of clinical symptoms, and treatment response. Recently, de Miranda et al. (2022) showed that the symptoms mentioned earlier were correlated with the severity of the disease, and the severity of acute infection mainly determined the duration of symptoms in post-COVID drome. Thus far, the attempts to identify mutual characteristics of patients with post-COVID syndrome have yielded somewhat inconsistent findings. For instance, Sudre et al. (2021) followed more than 4000 COVID patients. They identified a number of factors that anticipated post-COVID syndrome, such as being over 70 years old, being female, having more than five symptoms during the first week of illness, and having comorbidities. However, Cirulli et al. (2020) revealed that the post-COVID syndrome risk factor was having more than five symptoms during the disease course, not sex or comorbidities. Similarly, Stavem et al. (2021) conducted a four-month follow-up study with 434 COVID-19 patients and found that the presence of at least 10 symptoms during acute COVID-19 was found to be a risk factor for post-COVID syndrome. Although some studies concluded that having comorbid disorders is a risk factor for post-COVID syndrome, studies that investigated mental health disorders as comorbid disorders are scarce. Townsend et al. (2020) demonstrated that COVID-19 patients who experienced persistent fatigue 10 weeks after discharge were more likely to be females and have a history of being diagnosed with anxiety or depression or taking antidepressants. Similarly, Poyraz et al. (2020) found that female sex and history of psychiatric illness were risk factors for experiencing persistent COVID-19 symptoms. The lack of information on why some people suffer from post-COVID syndrome and how the human body recovers from post-COVID syndrome is still an ongoing challenge for science, with inconsistent data thus far.

Research Objectives and Implications

Given the complex interactions between COVID-19 infection and mental disorders, a thorough, meticulous meta-analysis is required to evaluate the overall and type-specific risk of mental health disorders for COVID-19 infection and clinical outcomes. Furthermore, there is a need for studies to review several types of mental disorders to understand better who is affected by the virus most and how the COVID-19 pandemic is impacting vulnerable populations. The pandemic has clearly given rise to a new wave of chronic, disabling problems that require considerable attention from the scientific and medical communities, and the absence of knowledge regarding why and how the human body is affected by the virus is a critical gap in the literature. The existing literature on post-COVID syndrome is limited, especially when it comes to who is affected and to what extent. However, its significant effects, from raised healthcare expenses to productivity losses on people, societies, and countries, are clear. Given the swiftly increased number of people presenting with COVID-19 sequelae, the acquisition of the most correct knowledge about the illness is a necessary step for humans to survive this pandemic. Nonetheless, to the best of my knowledge, no meta-analysis systematically investigated the relationship between pre-existing mental disorders subtypes (e.g., psychotic disorders, neurodevelopmental disorders, mood disorders, anxiety, and substance abuse disorders) and COVID-19 infection rate and associated post-COVID syndrome. The aim of this study is to assess whether preexisting mental health disorders are

associated with a higher risk of COVID-19 susceptibility and post-COVID syndrome. Therefore, I conducted a meta-analysis to assess the relationship between mental health disorders and the risk of COVID-19 infection and disease outcomes for general and type-specific mental health disorders. I have two main objectives: (1) I calculate the pooled overall estimates of the association between mental and neurological disorders and COVID-19 susceptibility, (2) I evaluate the relationship between specific mental health disorders and the risk of developing persistent covid outcomes.

Hypotheses

(1) People with pre-existing mental disorders are more prone to be infected with the COVID-19 virus relative to people without pre-existing existing mental health disorders.

(2) It is expected that people with pre-existing mental health disorders are more likely to suffer from post-COVID syndrome relative to people without pre-existing mental health disorders.

Methods

Registration and Protocol

This systematic review with meta-analyses is a sub-project of a larger research project, and the protocol for the project has been preregistered in PROSPERO (ID: CRD42021269432) and the Open Science Foundation (https://osf.io/35jhm/registrations). This meta-analysis complied with MOOSE (Stroup et al., 2000) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009).

Search Strategy and Study Selection

This systematic review and meta-analysis were conducted using searches in PubMed, Web of Science, and the preprint server Biorxiv.org, which was supplemented with a non-systematic search in Google Scholar. According to Bramer et al. (2017), this is the optimal database combination for a systematic literature search. Keywords such as ("COVID 19" OR COVID-19 OR COVID19 OR "SARS CoV-2" OR "Severe Acute Respiratory Syndrome Coronavirus 2" OR coronavirus OR SARS-CoV OR SARS-CoV-2) AND (psychiatry OR mental OR "clinical psychology" OR substance use OR alcohol OR "illegal drugs" OR addiction OR dependence OR depress* OR mood OR "adjustment disorder" OR Bipolar OR mania OR schizophrenia OR psychosis OR psychotic OR anxi* OR PTSD OR "post-traumatic stress disorder" OR "adjustment disorder" OR "somatic symptom disorder" OR "eating disorders" OR "Binge eating" OR anorexia OR ADHD OR "attention deficit hyperactivity disorder" OR "conduct disorder") were used to filter the intended studies from inception up to August 11, 2022. Papers written in English, Dutch, Spanish, German, or French were included in the search. Additionally, reference lists of reviews and meta-analyses that might meet the inclusion criteria were hand-searched from the found eligible articles for more potential articles. Duplicate articles were removed using EndNote 20. The articles have independently assessed for their eligibility for inclusion. The first decision on eligibility was based on titles and abstracts of the potential articles and the second (final) decision was based on full texts. Then the inclusion and exclusion decisions were cross-checked, and any discrepancy was solved by discussion.

Inclusion and Exclusion Criteria

The articles were included if they (1) reported SARS-CoV-2 infection rate and/or course of COVID-19 for patients with preexisting mental disorders vs. controls, (2) were written in English, German, French, Spanish, Arabic, or Dutch, and (3) patients were diagnosed with mental disorders according to DSM or ICD. The articles were excluded if (1) the full text could not be retrieved or (2) no relevant outcome data could be extracted, even after the corresponding authors of the article were contacted, (3) no original data were reported (e.g., opinion papers, reviews) or if (4) the mental health disorder diagnoses were based on self-report questionnaires. If the articles reported overlapping data sets, only the most comprehensive information in line with this study's purpose was included to avoid data duplication.

The exposure of interest was pre-existing mental health disorders assessed according to diagnostic systems such as ICD 9 or 10 (World Health Organization, 1979, 1993) or DSM-4 or 5 (American Psychiatric Association, 1992, 2013). The outcomes of interests were (1) a relative infection rate in people with mental health disorders that were presented as the percentage of SARS-CoV-2 positive tests, and (2) a COVID-19 outcome variable, defined by a post-COVID syndrome, in other words, long COVID.

Data Extraction and Quality Assessment

The extraction included basic study information such as first author, year of publication, which country the study was conducted in, total sample size, number of participants with mental disorders, number of participants who developed the outcome of interest both in control and focus groups, psychiatric disorders, comorbidities, mean or median age, gender distribution, study design, the outcome of interests, outcome data as raw numbers or effect-size estimates, and corresponding 95% Confidence Intervals (95% CI), and adjusted or unadjusted values.

The data extraction and methodological quality assessment of selected studies were independently conducted by the author and the supervisor by using The Quality Assessment Tool for Cross-Sectional Studies, which is a recommended and updated tool by the United States National Institute of Health (2021).

Statistical Analyses

The analyses were performed in JASP version 14.1, and summary tables on the characteristics of eligible papers were created. The relationship between preexisting (both current and lifetime) mental disorders and SARS-CoV-2 infection rates and the post-COVID syndrome was assessed by pooling data by means of Random-effects meta-analyses. Both classical meta-analyses and Bayesian meta-analyses were used to analyze the data.

Pooled data, accompanied by the 95% confidence interval (95% CIs), were analyzed. A p-value of $< .05$ was set as a statistical significance point. Cochran's Q2 heterogeneity test and I2 statistic were used to assess statistical heterogeneity. Kendall's Tau (Sterne et al., 2001) rank correlation test and Egger test were used to assess publication bias, and funnel plot asymmetry was used for visual inspection. When heterogeneity in outcome was detected, meta-regression and subgroup analyses were performed to explore study characteristics that could explain the heterogeneity.

Results

Study Selection and Characteristics

The initial database search yielded 67901 studies, and 42175 remained after removing duplicates. After screening titles and abstracts, 220 studies were found to be eligible. Among these eligible studies, 181 were further excluded after the full-text screening. Finally, 29 articles were eligible and included in this analysis (total sample size N = 85.064.921, average n per study = 2.933.273, with a range from 96 to 73.099.850; see Figure

1). Table A1 in the appendix lists all the articles included for full-text assessment and reasons for inclusion and exclusion. The flow chart (see Figure 1) summarizes the identification, screening, and inclusion of studies. Out of the previously mentioned 29 included articles, 25 examined the effect of pre-existing mental health disorders on the COVID-19 infection rate, and 4 assessed the effect of pre-existing mental health disorders on the post-COVID syndrome. The selection of articles for inclusion in the study was constrained by limited availability. Nonetheless, Cheung and Vijayakumar (2016) have posited the feasibility of employing a minimum of two studies when conducting a meta-analysis. Their examination of the requisite number of studies for such analyses revealed a spectrum spanning from three to 526 studies.

Table 1 provides demographic and clinical information on the samples of the studies included. Table 2 provides further information on the assessment of predictor variables, outcome variables, and study characteristics. The sample size ranged from 96 to 73099850 for the articles on infection risk, and from 646 to 5017431 for the articles on the post-COVID syndrome. The median sample size for infection risk was 48449, and 533821 for the post-COVID syndrome. The average age of the included samples ranged between 9 and 81 years. The percentage of females per sample ranged from 16 to 64%. The country of assessment varied, with the US being the most significant source of research.

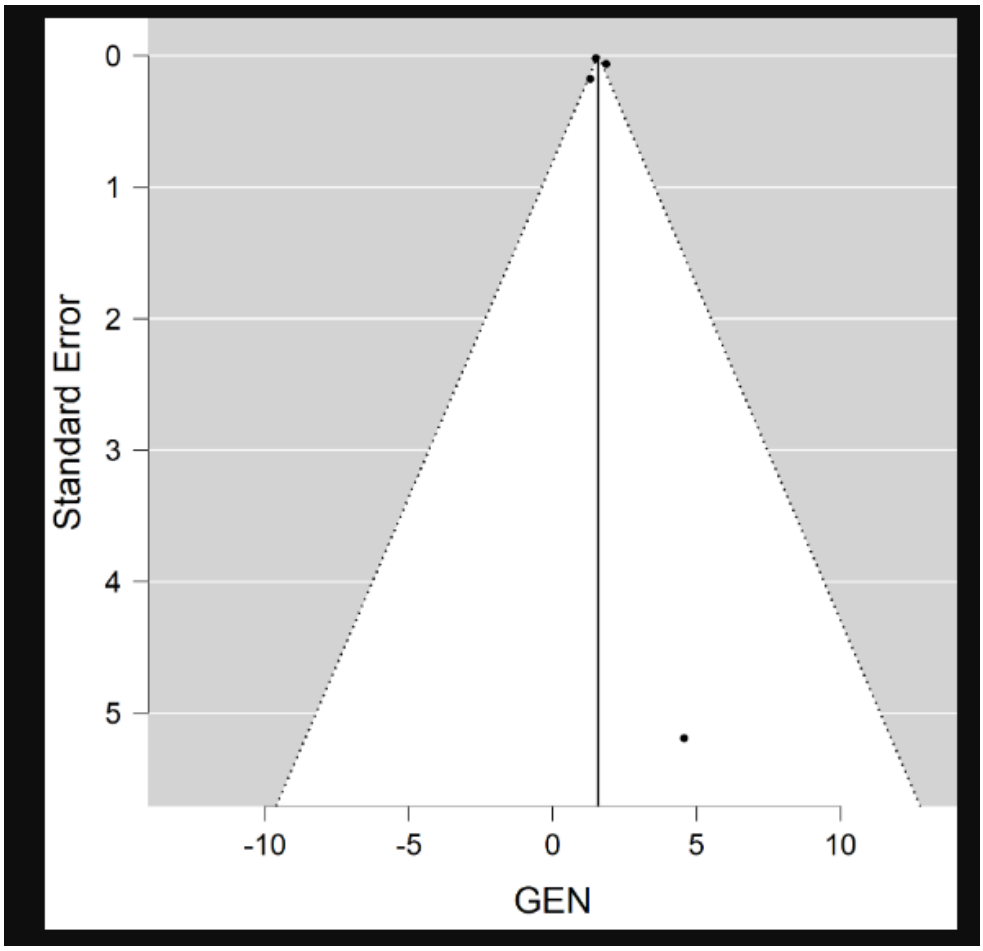

Figure 1: Flowchart on identification, screening, and inclusion of eligible publications

Articles	*N*	Age	% Female	Predictors	Country
COVID-19 infection rate					
Allen et al. 2020	188653	50 MED.	57	SUD	USA
Amin et al. 2022	96	26 MED.	38	Schizophrenia	Indonesia
Azar et al. 2020	14036	51 AV.	61	Depression	USA
Bailey et al. 2021	135794	9 AV.	47	Mental disorders	USA
Canal-Rivero et al. 2021	558274	48 AV.	36	Severe disorders	Spain
Cohen et al. 2022	64409	12 AV.	48	ADHD	Israel
Dai et al. 2022	473958	68 AV.	55	Mental disorders	UK
De Vito et al. 2021	382	81 AV.	63	Mental disorders	Italy
Egede et al. 2021	30976	60 MED.	53	Several categories	USA
Goldberger et al. 2022	125273	N.P.	N.P.	Psychiatric disorders	Israel

Articles	*N*	Age	% Female	Predictors	Country
Haimovich et al. 2020	2182	65 AV.	48	Several categories	USA
Lebin et al. 2020	5419	52 AV.	16	AUD	USA
Lee et al. 2021	48449	60 AV.	55	Several categories	South Korea
Merzon et al. 2021	14022	39 AV.	48	Several categories	Israel
Nemani et al. 2021	26540	47 MED.	54	Several categories	USA
Nemani et al. 2022	1958	51 AV.	26	Schizophrenia	USA
Nilsson et al. 2021	4412382	48 AV.	51	Several categories	Denmark
Orlando et al. 2021	20855	60 MED.	44	Several categories	Italy
Taquet et al. 2021	1729837	50 MED.	55	Several categories	USA
Tang et al. 2020	1970	73 AV.	55	Depression	USA
Teixeira et al. 2021	2535098	44 AV.	62	Several categories	USA
Tzur Bitan et al. 2021	51078	51 AV.	61	Schizophrenia	Israel
Varela-Rodríguez et al. 2021	188	60 AV.	29	AUD	Spain
Wang et al. 2021 [a]	73099850	2 MED.	54	SUD	USA
Yang et al. 2020	421014	8 AV.	55	Several categories	UK
Post-COVID syndrome					
Al-Aly et al. 2022	33940	71 AV.	5	Several categories	USA
De Miranda et al. 2022	646	50 AV.	54	Depression	Brazil
Jones et al. 2021	3151	52 AV.	64	Mental disorders	UK
Thompson et al., 2022	1064491	N.P.	N.P.	Mental disorders	UK

Table 1: Demographic and Clinical Information of the studies included

Notes. Abbreviations: AUD = alcohol use disorder; SUD = substance use disorder; AV = average; MED = median; N.P = not presented; Mental disorders; the study groups and reports on several mental health disorders as 1 group; Several categories, the study reports separate associations on several categories of mental health disorders

Quality Assessment

Most of the studies included had high methodological quality. Methodological quality scores of the studies included ranged between 0 and 13 (M = 7.03, SD = 3.17, see Table A3).

Meta-Analyses

COVID-19 Infection Risk

For the first hypothesis of the current meta-analysis, a total of 25 studies (k = 51) were entered into analyses. Pre-existing mental health disorders were divided into six groups, and two analyses were run for each group. The results of the Classical Meta-Analyses are presented in Table 3. Bayesian Meta-Analyses were also conducted to analyze the relationship. In Table 4, posterior estimates per model and model probabilities of Bayesian Meta-Analyses are presented. The results based on the random-effects model revealed that pre-existing anxiety disorder, mood disorders (i.e., depressive disorder and bipolar disorder), neurodevelopmental disorders, schizophrenia spectrum disorder, substance use disorder, or a mixed category of mental disorders (i.e., several disorders together, severe mental health disorders, personality disorders, and eating disorders) were not associated with an increase in SARS-CoV-2 susceptibility. Forest plots on these estimates are presented in Figures 2 to 7. From left to right figures shows study names, forest plot of observed outcomes, and statistics for each study (i.e., standard differences in means and lower and upper limit of 95% CI).

Article	Predictor [Method]	Outcome	Type of study	Statistical control
Al-Aly et al. 2022	Time frame not known, any mental health conditions [ICD 10]	Persistent Covid-19 symptoms	Retrospective cohort, e-records	Comorbidities
Allen et al. 2020	Lifetime SUD [ICD 10]	Test positivity	Retrospective cohort, e-records	Age, gender, comorbidities
Amin et al. 2022	Time frame not known, schizophrenia, age [ICD 10]	Test positivity	Cross-sectional design	Age, gender, schizophrenia
Azar et al. 2020	Timeframe not known, mood disorder [ICD 10]	Test positivity	Retrospective cohort, e-records	No control

Article	Predictor [Method]	Outcome	Type of study	Statistical control
Bailey et al. 2021	Lifetime, any mental health conditions [ICD-10]	Test positivity	Retrospective cohort, e-records	No control
Canal-Rivero et al. 2021	Current severe mental disorders (psychotic spectrum, affective spectrum, personality disorders, other disorders) [ICD 10]	Test positivity	Retrospective cohort, e-records	No control
Cohen et al. 2022	ADHD (medication treatment yes vs no) vs non-ADHD	Test positivity	Retrospective cohort, e-records	Non-ADHD vs ADHD (medically treated vs untreated), adjusted for age and sector
Dai et al. 2022	Between March 2006 and December 2010, mental health disorders [ICD 10]	Enhanced risk of COVID- 19 infection.	Prospective population-based cohort, e-records	Adjusted for age, sex, education, ethnicity, BMI, overall health rating, usual walking pace, mental health, and comorbidities
De Miranda et al. 2022	From March 2020 to November 2021, infection severity, comorbidities	Persistent COVID-19 symptoms	Longitudinal study	No control
De Vito et al. 2021	Diagnosed mental illness, exact method is unknown	Test positivity	Retrospective cohort	Analyses controlled for covariates. Selection of covariates is based on analyses and is not further specified in the article
Egede et al. 2021	Current bipolar, psychotic-, internalizing-, externalizing- disorders [ICD 9 and 10]	Test positivity	Retrospective cohort, e-records	Analyses were controlled for age, BMI, ethnicity, SES, gender
Goldberger et al. 2022	Between 1 March 2020 and 31 March 2021, [ICD 10], age, psychiatric disorders	Rates of COVID-19 testing, infection rate,	Nation-wide cohort, e-records	Analyses were adjusted for age, sex, vaccination status, reported diseases, and conditions.
Haimovich et al. 2020	Lifetime psychosis, depression [ICD 9 and 10]	Test positivity	Retrospective cohort, e-records	Analyses controlled for covariates, but these are not specified.
Jones et al. 2021	Timeline not known, diagnosed before January 2020, depression and anxiety, comorbidities	Persistent Covid-19 symptoms	Observational study, e-records	Adjusted for demographics, hospital visits for COVID-19, frailty, chronic comorbid conditions
Lebin et al. 2020	Lifetime AUD – exact method is unknown	Test positivity	Retrospective cohort, e-records	No control
Lee et al. 2020	Past year anxiety and stress related disorders, mood disorders, SUD, personality disorders, eating disorders [ICD 10]	Test positivity	Retrospective cohort, e-records	Analyses were controlled for age, SES indicators, ethnicity, SES, gender, comorbidities
Merzon et al. 2021	Lifetime autism spectrum disorder, depression and anxiety, schizophrenia, ADHD [ICD 9 and 10]	Test positivity	Retrospective cohort, e-records	Analyses were controlled for demographic variables and comorbidities
Nemani et al. 2021	Current anxiety disorder, mood disorder, schizophrenia spectrum disorder [ICD 10R CM]	Test positivity	Retrospective cohort, e-records	Analyses were controlled for demographic variables (race, ethnicity, age, insurance type), psychiatric diagnosis, medical comorbidities (BMI, smoking status)
Nemani et al. 2022	Between March 8 and December 1, 2020, affective or nonaffective psychoses (based on admission decission), use of medication	Test positivity	Retrospective cohort, e-records	Analyses were adjusted for age, sex and other covariates.
Nilsson et al. 2022	Prior to 27 February 2020, a low educational level, /or experiences of homelessness, imprisonment, substance abuse, supported psychiatric housing, psychiatric admission, severe mental illness [ICD 8 and 10], and chronic medical condition.	Test positivity	Retrospective cohort, e-records	Propensity matching
Orlando et al. 2021	Lifetime psychosis, depression, anxiety (ICD-9)	Test positivity	Retrospective cohort, e-records	Analyses were controlled for demographic variables and comorbidities

Article	Predictor [Method]	Outcome	Type of study	Statistical control
Tang et al. 2020	Depression, time frame not known [ICD 10R CM]	Test positivity	Retrospective cohort, e-records	No control
Taquet et al. 2021	Current any psychiatric illness [ICD 10]	Test positivity	Retrospective cohort, e-records	Analyses were controlled for demographic variables and comorbidities
Teixeira et al. 2021	Time frame not known, schizophrenia, mood disorders, anxiety disorders [ICD 9 and 10]	Likelihood of testing positive for COVID-19.	Cross-sectional study, e-records	Analyses were controlled for multiple confounding factors such as age, race and ethnicity, and comorbid medical conditions
Thompson et al. 2022	Time frame not known, psychosis, schizophrenia, bipolar disorder, or depression	Persistent covid-19 symptoms	Population-based cohort study, e-records	Adjusted for age, sex, and ethnicity
Tzur Bitan et al. 2021	Lifetime schizophrenia [ICD 9 and 10]	Test positivity	Retrospective cohort, e-records	Matched
Varela-Rodríguez et al. 2021	Lifetime AUD [ICD 10, DSM 5]	Test positivity	Retrospective cohort, e-records	Analyses were controlled for demographic gender, age and comorbidities
Wang et al. 2021 a	Current, any SUD, SNOMED concept codes	Test positivity,	Retrospective cohort, e-records	Analyses were controlled for age, gender race, and insurance type
Yang et al. 2020	Current/recent depression, anxiety, stress-related disorders, SUD, psychotic disorder [ICD 9 and ICD 10)	Test positivity	Retrospective cohort, e-records	Analyses were controlled for age, SES indicators, ethnicity, SES, gender, comorbidities

Abbreviations. DSM, Diagnostic and Statistical Manual of Mental Disorders; ICD, International Classification of Disease, ICU, Intensive Care Unit

Table 2: Characteristics of included studies and samples by outcome

Mental health disorders	OR (95% *CI*)	*k*	*N*	I^2	Tau	Egger's *t*	*Q*
Anxiety disorder	1.17 (0.80-1.55)	4	3060903	96.06*	0.10*	0 .40	21.73***
Mix/other [a]	1.11 (0.74-1.47)	9	7219157	98.62*	0.51*	0.43	654.19***
Mood disorders	0.86 (0.69-1.04)	9	12905361	97.32*	0.25*	1.25	224.10***
Neurodevelopmental disorders	1.28 (0.83-1.73)	4	566411	73.05*	0.34	0.70	13.19**
Schizophrenia spectrum disorder [a]	0.98 (0.61-1.36)	7	15738625	99.74*	0.44	2.92***	140.34***
Substance use disorder [a]	1.23 (0.78-1.69)	5	78012001	99.45*	0.42*	1.14	1203.97***

Note. Classical Meta-Analysis random effects model

[a] Estimates come from analyses including nationwide data, at the expense of local data.

* $p < .05$, ** $p < .01$, *** $p < .001$

Table 3: Mental health disorders and SARS-CoV-2 infection risk

Mental health disorders	*Mean* (95% *CI*)	BF_{10}	*SD*	H_0
Anxiety disorder	0.11 (-0.19-0.36)	.27	0.14	0.79
Mix/other [a]	0.07 (-0.30-0.43)	.21	0.18	0.83
Mood disorders	-0.17 (-0.39-0.06)	.44	0.11	0.70
Neurodevelopmental disorders	0.21 (-0.15-0.59)	.46	0.19	0.68
Schizophrenia spectrum disorder [a]	0.07 (-0.42-0.59)	.26	0.25	0.80
Substance use disorder [a]	0.21 (-0.25-0.69)	.41	0.23	0.71

Note. Bayesian Meta-Analysis random effects model

[a] Estimates come from analyses including nationwide data at the expense of local data.

Table 4: Mental health disorders and SARS-CoV-2 infection risk posterior estimates and model probabilities

Figure 2

Forest plot illustrating the relationship between COVID-19 infection rate and anxiety.

---insert Figure 2 here---

Figure 3

Forest plot illustrating the relationship between COVID-19 infection rate and mental health disorders (mix).

---insert Figure 3 here---

Figure 4

Forest plot illustrating the relationship between COVID-19 infection rate and mood disorders.

---insert Figure 4 here---

Figure 5

Forest plot illustrating the relationship between COVID-19 infection rate and neurodevelopmental disorders.

---insert Figure 5 here---

Figure 6

Forest plot illustrating the relationship between COVID-19 infection rate and schizophrenia spectrum disorders.

---insert Figure 6 here---

Figure 7

Forest plot illustrating the relationship between COVID-19 infection rate and substance use disorder.

---insert Figure 7 here---

Between study heterogeneity in outcomes were high and significant in all analyses. Detailed results of the investigations can be seen in Table 3. Only the analysis with schizophrenia spectrum disorder data indicated evidence for publication bias (z = 2.92, p = 0,003). Figure A5 shows an asymmetrical funnel plot, with most studies gathered on the tip of the triangle and half of the studies falling outside the triangle. Funnel plots for all mental health disorders' assessment on publication bias can be found in Appendix Figures A1–A6.

Post-COVID Syndrome

Four studies reporting the relationship between pre-existing mental health disorders and the post-COVID syndrome were analyzed using Bayesian Meta-Analysis and Classical Meta-Analysis. The results demonstrated that people with pre-existing mental health disorders are more likely to suffer from post-COVID syndrome relative to people without pre-existing existing mental disorders (Posterior probabilities of Random H_0 = 0.27 and Random H_1 = 0.73). The pooled posterior estimate based on the Bayesian random-effects model was BF_{10} = 2.72 (k = 4, 95% CI = 0.05 to 0.37, N = 5127677). The classical meta-analysis results showed that the odds of suffering from post-COVID syndrome were higher for people with pre-existing mental health disorders (k = 4, OR = 1.58, 95% CI = 1.28-1.89, z =10.16, p <.001). Forest plots on these estimates are presented in Figure 8.

Figure 8

Forest plot of prevalence estimates of the post-COVID-19 syndrome in people with pre-existing mental health disorders.

---insert Figure 8 here---

Assessment of the heterogeneity of the selected studies revealed high levels of between-study heterogeneity in outcomes (Q = 30.85, p < 0.001, Tau^2 = 0.06, I^2 = 91.39%). Publication bias was assessed through Begg's funnel plot (Begg, 1994; see Figure A7), which indicated no asymmetry, and Egger's test statistic (Egger et al., 1997). Neither the regression test nor the rank correlation test indicated any funnel plot asymmetry (z = 0.31, p = 0.761, and *Kendal's T* = 0.33 p = 0.750, respectively). Moderator analyses were not conducted due to the low level of observations in the dataset.

Discussion

The present meta-analysis aimed to examine the relationship between pre-existing mental health disorders and (1) COVID-19 susceptibility, and (2) post-COVID syndrome. To investigate this, the current literature was systematically reviewed.

Susceptibility for COVID-19 Infection and Mental Health Disorders

The first hypothesis states that people with pre-existing mental disorders are more prone to be infected with the COVID-19 virus. To investigate this, the relationship between the COVID-19 infection rate and different mental disorders was examined. Even though some research has shown that having pre-existing mental health disorders puts individuals at a higher risk of getting infected by the COVID-19 virus (Breaux et al., 2021; Cohen et al., 2022; Fonseca et al., 2020; Kozloff et al., 2020; Merzon et al., 2021; Moreno et al., 2020; Neelam et al., 2021; Wang et al., 2021b), the results of the current study did not support these findings.

Post-COVID Syndrome and Mental Health Disorders

The second hypothesis states that people with pre-existing mental health disorders are more likely to suffer from post-COVID syndrome relative to people without pre-existing mental health disorders. In line with the hypothesis, the results showed that people with pre-existing mental health disorders are more likely to suffer from post-COVID syndrome. Similar results were seen in previous studies that examined the relationship between pandemics (Zhang et al., 2020) or chronic illnesses resulting from viral or non-viral viruses (Hickie et al., 2006) and mental health disorders. For example, both Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS) cause some persisting symptoms after infection. One of the long-lasting effects of SARS includes chronic fatigue syndrome, which has previously been found to have increased incidence in people with mental health disorders (Hickie et al., 2006; Zhang et al., 2020). Given the shared symptoms of these diseases, it is possible to see similar effects in COVID-19 survivors.

Alternatively, previous studies indicate that with some mental health disorders, such as mood disorders and substance abuse disorders, there is a heightened prevalence of somatic comorbidities, including diabetes, obesity, and cardiovascular disease (Barton et al., 2020; Coello et al., 2019; Dalack & Roose, 1990; Goldstein et al., 2020; Mansur et al., 2019). These somatic comorbidities are known to be associated with more severe COVID-19 manifestations (Sargin Altinok et al., 2022; Zaman et al., 2020; Zhu et al., 2021). Also, the recent study by de Miranda et al. (2022) illustrated that the severity of the disease was the main determinant of the duration of the post-COVID syndrome. Although the exact mechanisms that explain the relationship between mental health disorders and post-COVID syndrome are not yet known, above mentioned associations may explain the underlying association between mental health disorders and post-COVID syndrome.

Implications, Future Research, and Recommendations

The results of this study have several implications. From a research perspective, this systematic review and meta-analysis provided a valuable contribution to the literature by combining multiple studies and analyzing the above-mentioned associations. As mentioned earlier, there seems to be a discourse on the relationship between pre-existing mental health disorders and COVID-19 susceptibility, with some articles increasing but other research stating it is decreasing, and other literature concluding that there is no significant relation between the two. Combining, summarizing, and analyzing multiple individual pieces of research enabled us to have more representative and reliable results. The actual relationship between pre-existing mental health disorders and COVID-19 susceptibility has been better identified. Additionally, this study revealed that individuals with pre-existing mental health disorders are more prone to suffer from the prolonged effects of COVID-19. This study, therefore, provides a more comprehensive picture of the effects of pre-existing mental health

disorders on COVID-19 susceptibility and on post-COVID syndrome. These findings have not been reported broadly elsewhere in the literature and could serve as a starting point for further research on the post-COVID syndrome. Future research, on the other hand, should focus on the effects of individual mental health disorders, and whether and how they play a role in these relationships. This meta-analysis included articles from December 2019 to August 11, 2022. The relevant research on the topics would increase in the following years, adding even larger sample sizes and more diverse data to be explored. Although large samples with well-powered studies were included, due to the limited published data, it was not possible to run moderator and sub-group analyses. Therefore, future studies should consider including more studies to further explore potential relationships.

From a preventive perspective, patients with mental health disorders should be considered at high risk for post-COVID syndrome. Policymakers should consider these results in new healthcare plans, insurance, vaccination policies, and health education campaigns, specifically in areas with limited importance and/or access to care for this vulnerable group. Governments and healthcare providers should work on interventions to decrease stigma related to mental health disorders and infections, and provide routine check-ups, especially during pandemics and epidemics. Previous research on disasters demonstrated that up to 40% of affected people seeking mental health support during or after a disaster have pre-existing mental health disorders (North & Pfefferbaum, 2013). It is also shown that the COVID-19 pandemic caused further adverse effects on mental health among people with pre-existing mental health disorders (Pan et al., 2020; Rheenen et al., 2020). Healthcare workers should be more aware of risk among high-risk groups and inform these patients about the effects of persistent symptoms of COVID-19, and better guide them on medical and mental aftercare. Although previous research (Chit et al., 2009) pointed out that the SARS virus could cause significant prolonged symptoms among people with and without a history of mental health disorders, we also witnessed how most countries poorly managed one of the biggest pandemics of humankind. New infectious epidemics will rise due to globalization (Wong, & Yuen, 2006), which means this pandemic is not the last one. Some precautions should be taken to better protect people with mental health disorders. While more research on pandemics is being conducted, current knowledge of disaster response management should be improved and applied when necessary.

From a mental health treatment perspective, the results are relevant to the treatment of several mental health disorders. Considering people with mental health disorders are more prone to suffer from post-COVID syndrome and physical symptoms of this syndrome make it harder for individuals to travel, modern ways of digital communication allow them to receive the necessary support, treatment, intervention, and education in their homes (Salawu et al., 2020; Zhang, & Ho, 2017). Additionally, during the high peak season, many governments restricted face-to-face interactions and set social distancing and quarantining requirements. Therefore, during the COVID-19 pandemic, online consultations and smartphone telehealth apps (telerehabilitation and telepsychiatry) have rapidly increased (Li et al., 2020; Yao et al., 2020b). Cognitive behavioral therapy (CBT) is recommended for many mental health disorders, such as mood and anxiety disorders and chronic fatigue syndrome (Castell et al., 2011; Cuijpers et al., 2016). Studies also showed that online CBT is an effective and efficient treatment tool with reduced travel time and cost and increased accessibility (Prvu Bettger & Resnik, 2020; Soh et al., 2020; Vugts et al., 2018). Thus, considering restrictive physical health consequences of post-COVID syndrome (e.g., tiredness and fatigue, and chronic fatigue syndrome), online treatment tools should be encouraged to treat people with post-COVID syndrome,

Strengths and Limitations

To my knowledge, this is the first comprehensive systematic review and meta-analysis to provide a quantitative estimate between the type-specific mental health disorders and COVID-19 susceptibility, as well as post-COVID syndrome risk in COVID-19 patients. The results of this meta-analysis were in line with a previous meta-analysis (Ceban et al., 2021). However, this study has a more robust analytical approach. First, the presented results were stratified by mental health disorder categories when possible. Second, this study has a strong methodological design in accordance with The Quality Assessment Tool for Cross-Sectional Studies (United States National Institute of Health, 2021). Third, overall heterogeneity and the sample size were high. Lastly, this study endeavored to avoid including overlapping datasets.

The limitations of this systematic review and meta-analysis should be acknowledged. First, it is important to consider the limited number of studies included for the post-COVID syndrome. Hence the interpretation of the results does not provide a complete picture of stratified mental health disorders. Second, mental health disorders were defined according to ICD or DSM codes in insurance or government data. Although these are widely used, for better insurance benefits, some patients could be misdiagnosed, or there could be wrongly entered data in patient records. These administrative data may have high specificity but varied sensitivity (Wilchesky et al., 2004). Third, some studies have inadequately differentiated mental health disorders (i.e., they only stated mood disorders but not major depressive disorders or bipolar disorders), which could impact the result as they could show different characteristics. Although some studies had better distinctions than others, they were all grouped into the most appropriate category. Even though this study has high heterogeneity and sample size, heterogeneity could not always be explained with moderator and sub-group analyses. At last, the samples consisted of an unequal gender ratio and varying ages, and one study had no data on age and gender. This could cause limitations for the current study, while gender and age differences could result in experiencing the disease differently, because they may play a role in smoking behaviors and the prevalence of comorbidities (Mukherjee & Pahan, 2021; Ya'qoub et al., 2021).

Summary and Conclusion

This study consists of two meta-analyses investigating the relationship between pre-existing mental health disorders and susceptibility to COVID-19 (N = 83.962.693), and post-COVID syndrome (N = 1.102.228). The results of this study can be described as partially unexpected. The first analysis revealed that the infection rate for SARS-CoV-2 infection was not significantly different among people with and without pre-existing mental health disorders. However, the second analysis revealed that people with pre-existing mental health disorders are more likely to suffer from the post-COVID syndrome. These results suggest that although people with pre-existing mental health disorders are not statistically more at risk in terms of susceptibility to SARS-coV-19 infection, they are statistically more prone to suffer from persistent COVID-19 symptoms. Therefore, they should be categorized as an at-risk group based on pre-existing mental illness conditions, similar to people with pre-existing somatic conditions (e.g., cardiovascular disease, obesity). It is essential to note the increased prevalence of mental health disorders due to the COVID-19 pandemic (Taquet et al., 2021), as well as the emergence of the post-COVID syndrome, which can also cause mental health symptoms. In all, the results point out that public health authorities should consider close monitoring and adequate aftercare in patients with mental health disorders who got COVID-19. Future research should address how different mental health disorders interact with the post-COVID syndrome and how the COVID-19 infection influences the trajectory of the current mental health disorders.

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293. Appendices

Table A1

Articles submitted to full-text assessment for in- vs exclusion.

Decision	Study	Reason
No	Abbasi-Oshaghi et al. 2022	Opinion paper (1 page review)
No	Abdalbary et al. 2022	No mental health □ risk
No	Adamuz et al. 2021	No mental health □ risk; poster

Decision	Study	Reason
No	Ahmadi et al. 2020	No mental health risk; poster
No	Ahmadi et al. 2021	No mental health risk
Yes	Al-Aly et al. 2022	Mental health persistent covid symptoms
No	Alizadehsani et al. 2020	No mental health risk
No	Alizadehsani et al. 2021	No mental health risk
Yes	Allen et al. 2020	Mental health risk
Yes	Amin et al. 2022	Mental health risk
No	Ao et al. 2022	Mental health risk
No	Arbel et al. 2020	No mental health risk
No	Arbel et al. 2021	Mental health risk
No	Arbello et al. 2020	No mental health risk
No	Attalla et al. 2021	No mental health risk data
No	Ayana et al. 2021	No mental health risk data
Yes	Azar al. 2020	Mental health risk
Yes	Bailey al. 2021	Mental health risk and course
No	Bain et al. 2021	No mental health risk/outcome data
No	Bajaj et al. 2020	No mental health risk/outcome data
No	Batty et al. 2020	Exclude; double data
No	Becker et al. 2021	No mental health outcome
No	Beckwith et al. 2022	Mental health risk
No	Bhargava et al. 2021	No mental health risk/outcome data
No	Breslau et al. 2021	No mental health risk/outcome data
No	Brinkman et al. 2022	No mental health risk/outcome data
No	Bruggmann et al. 2022	No Mental health risk/outcome
No	Buonsenso et al. 2022	No mental health risk/outcome data

Decision	Study	Reason
No	Burgaña et al. 2021	No mental health □ risk/outcome data
No	Buttiron et al. 2021	No mental health □ risk/outcome data
No	Buttiron et al. 2021	No mental health □ risk/outcome data
Yes	Canal-Rivero et al. 2021	Mental health □ risk and course
No	Cao et al. 2020 PLoS ONE	No mental health □ risk/outcome data
No	Carrat et al. 2021	No mental health □ risk/outcome data
No	Caspersen et al. 2022	No mental health □ risk/outcome data
No	Ceban et al. 2021	Meta-analysis
No	Chaudhary et al. 2022	No mental health □ risk/outcome data
No	Chung et al. 2021	No mental health □ risk/outcome data
Yes	Cohen et al. 2022	Mental health □ risk/outcome
No	Cosco et al. 2021	No mental health □ risk/outcome data
No	Crook et al. 2021	Review
Yes	Dai et al. 2022	Mental health □ risk
No	Dang et al. 2022	No mental health □ risk
No	Das et al. 2021	No mental health □ risk
No	de Leon et al. 2020	Opinion paper
Yes	de Miranda et al. 2022	Mental health □ persistent covid symptoms
No	de Picker et al. 2021	No mental health □ risk
Yes	de Vito et al. 2021 [MEDRXIV]	Mental health □ risk and course
No	Diaz et al. 2021	No mental health □ risk
No	Diminich et al. 2022	Only poster abstract is available
No	Djuric et al. 2021	No mental health □ risk
Yes	Egede et al. 2021	Mental health □ risk and course

Decision	Study	Reason
No	Englett et al. 2021	Case report / opinion
No	Essau et al. 2021	No mental health □ risk
No	Fabelo-Roche et al. 2021	No mental health □ risk
No	Fares-Otero et al. 2021	No mental health □ risk
No	Fitzgerald et al. 2021	No mental health □ risk data
No	Fuld et al. 2022	No preexisting mental health □ risk
No	Fumagalli et al. 2022	No mental health □ risk
No	Gabunia et al. 2022	No mental health □ risk
No	Gang et al. 2022	No mental health □ risk
No	Gao et al. 2020	No mental health □ risk
No	Gasnier et al. 2022	No pre-existing mental health □ risk- no aimed association
No	Gayam et al. 2020	No mental health □ risk
No	Gilley et al. 2022	No mental health □ risk
Yes	Goldberger et al. 2022	Mental health □ risk
No	Gorji et al. 2022	No mental health □ risk- anorexia
No	Govind et al. 2021	Mental health □ risk but only patients
No	Gu et al. 2020	No mental health □ risk
No	Guliani et al. 2022	No mental health □ risk
No	Guo et al. 2021	No mental health □ risk
No	Guzek et al. 2022	No mental health □ risk
No	Günal et al. 2020	Exclusion based on language
Yes	Haimovich et al. 2020	Mental health □ risk
No	Harrison et al. 2021	No mental health □ risk
No	Heald et al. 2022	No mental health □ risk

Decision	Study	Reason
No	Heesakkers et al. 2022	No mental health □ risk
No	Hirakawa et al. 2021	No mental health □ risk
No	Hölzle et al. 2020	No mental health □ risk
No	Huang et al. 2021a	Meta-analysis mechanisms □ risk
No	Huang et al. 2021b [MEDRXIV]	No mental health □ risk
No	Iqbal et al. 2020	No mental health □ risk
No	Jalodia et al. 2022	No mental health □ risk
No	Jang et al. 2020	No mental health □ risk
No	Jemberi et al. 2020	No mental health □ risk
No	Ji et al. 2020	Double data South Korea nation wide
Yes	Jones et al. 2021	Mental health □ persistent covid symptoms
No	Karaoulanis et al. 2021	Review
No	Karthaka et al. 2021	No mental health □ risk
No	Khalaf et al. 2022	No mental health □ risk
No	Kianersi et al. 2021	No mental health □ risk
No	Kolin et al. 2021	Overlap in data
No	Kondakov et al. 2021	No mental health □ risk
No	Kozloff et al. 2020	No mental health □ risk
No	Landén et al. 2021	No mental health □ risk
No	Landes et al. 2021	No mental health □ risk
No	Lassen et al. 2020	No mental health □ risk
Yes	Lebin et al. 2020	Mental health □ risk
Yes	Lee et al. 2020	Mental health □ risk
No	Li et al. 2022	No usable mental health □ risk
No	Liu et al. 2020	No mental health □ risk

Decision	Study	Reason
No	Livingston et al. 2020	No mental health □ risk
No	Luykx et al. 2021	No mental health □ risk
No	Ma et al. 2021	No mental health □ risk
No	Maguire and Looi, 2020	Not available
No	Mahmoud et al. 2021	No mental health □ risk, ptsd
No	Martín-Rodríguez et al. 2021	No mental health □ risk
No	Marel et al. 2021	Opinion paper
No	Meinlschmidt et al. 2022	No mental health disorder diagnosis □ risk
No	McKeigue et al. 2020	No mental health □ risk
No	McKetta et al. 2021	No mental health □ risk
No	Mena et al. 2021	No mental health □ risk
Yes	Merzon et al. 2020	Mental health □ risk
No	Moayed et al. 2021	No mental health □ risk
No	Moni et al. 2021	No mental health □ risk
No	Morlock et al. 2021	No mental health □ risk
No	Mousavi 2020	Opinion paper
No	Munblit et al. 2021	No mental health □ risk
No	Murga et al. 2021	No mental health □ risk
No	Muruganandam et al. 2020	No mental health □ risk
No	Murphy et al. 2022	No full-text access
No	Musheyev et al. 2021	No usable mental health □ risk
No	Narayan et al. 2021	No mental health □ risk
No	Nehme et al. 2022	No usable mental health □ risk – self-report
Yes	Nemani et al. 2021	Mental health □ risk– research letter
Yes	Nemani et al. 2021	Mental health □ risk

Decision	Study	Reason
No	Neuman Podczaska et al. 2020	No mental health □ risk
No	Neville et al. 2022	No mental health □ risk
No	Nguyen et al. 2020	No mental health □ risk
Yes	Nilsson et al. 2022	Mental health □ risk
Yes	Nishimi et al. 2021	Mental health □ risk
No	Ocsovszky et al. 2022	No usable mental health □ risk
No	Ohlis et al. 2022	Mental health □ risk/outcome / no mentally healthy control group
No	Okubo et al. 2021	No mental health □ risk
Yes	Orlando et al. 2021	Mental health □ risk
No	Park and Rhim, 2021	No mental health □ risk
No	Peckham et al. 2021	No mental health □ risk
No	Pérez-Segura et al. 2021	No usable mental health □ risk
No	Pizzonia et al. 2021	No mental health □ risk
Yes	Rajkumar 2021	Mental health □ risk
Yes	Rajkumar 2022	Mental health □ risk
No	Rauchman et al. 2021	No mental health □ risk
No	Rebora et al. 2021	No mental health □ risk
No	Righi et al. 2022	No mental health □ risk
No	Rivera-Izquierdo et al. 2022	No mental health disorder diagnosis □ risk
No	Rodriguez et al. 2021	No mental health □ risk
No	Romero-Duarte et al. 2022	No mental health disorder diagnosis □risk
No	Rosoff et al. 2021	No mental health □ risk
No	Rubin 2020	Opinion paper
No	Said et al. 2021	No mental health □ risk
No	Saldi et al. 2021	No mental health □ risk

Decision	Study	Reason
No	Salim 2021	Opinion paper
No	Salinas-Botrán et al. 2021	No mental health disorder diagnosis risk
No	Saurabh et al. 2021	No mental health risk
No	Segaloff et al. 2021	No mental health risk
No	Shafran et al. 2021	No mental health risk
No	Shang et al. 2020	No mental health risk
No	Shi et al. 2020	No mental health risk
No	Shrivastava et al. 2020	Opinion paper
No	Slaunwhite et al. 2020	No mental health risk
No	Spagnolo et al. 2020	Opinion paper
No	Stahlman et al. 2021	Mental health risk, No full-text access
No	Stanton et al. 2020	No mental health risk
No	Susanto et al. 2022	No mental health risk
No	Swendson 2020	Opinion paper
No	Tamburin et al. 2021	No mental health risk
Yes	Tang et al. 2020	Mental health risk
No	Taquet et al. 2021 a	No mental health risk
Yes	Taquet et al. 2021 b	Mental health risk
Yes	Teixeira et al. 2021	Mental health risk
No	Testino 2020	Opinion paper
No	Testino et al. 2022	No mental health risk
Yes	Thompson et al. 2022	Mental health persistent covid symptoms
No	Tobolowsky et al. 2021	No mental health risk
No	Tzur Bitan et al. 2021	Mental health risk
No	Tzur et al. 2022	Mental health booster vaccination rate

Decision	Study	Reason
No	Vadukapuram et al. 2022	Review article
No	Valente et al. 2021	No mental health □ risk
No	van der Meer et al. 2020	Exclude; double data
No	van der Valk et al. 2021	No mental health □ risk
No	van Laar et al. 2020	No mental health □ risk
No	Vedhara et al. 2022	No mental health □ risk
No	Veldhuis et al. 2021	No mental health □ risk
No	Vena et al. 2020	No mental health □ risk
No	Vidot et al. 2021	No mental health □ risk
No	Vissink et al. 2021	No mental health □ risk
No	Volpatto et al. 2021	Review article
No	Vukotic et al. 2021	No mental health □ risk
Yes	Wang et al. 2021a	Mental health □ risk
No	Wang et al. 2021b	Mental health □ risk
No	Wen et al. 2021	No mental health □ risk
No	Williams et al. 2020	No mental health □ risk
No	Wisnivesky et al. 2022	No mental health □ risk
No	Woodruff et al. 2021	No mental health □ risk
No	Xiang et al. 2021 [MEDRXIV]	Genetic correlation data
No	Xie et al. 2020	No mental health □ risk
No	Xu et al. 2021	No mental health □ risk
No	Yaksi et al. 2022	No mental health □ risk
Yes	Yang et al. 2022	Mental health □ risk-anorexia
No	Yang et al. 2022	No usable mental health □ risk, anorexia
No	Yolken 2021	Opinion paper

Decision	Study	Reason
No	Yoshida et al. 2021	No mental health □ risk
No	Zhang et al. 2020	No mental health □ risk
No	Zhang et al. 2021	No mental health □ risk
No	Zhang et al. 2021	Mental health □ no risk, anorexia
No	Zheng et al. 2020	No mental health □ risk
No	Zhu et al. 2020 J Psychiatric Res	No mental health □ risk
No	Zhu et al. 2020 PLoS ONE	No mental health □ risk
No	Zielinska-Turek et al. 2021	No mental health □ risk
No	Zijlmans et al. 2021	Mental health □ no risk
No	Zimmermann et al. 2021	No mental health, review paper

Note: In- and excluded articles are indicated in yes and no respectively, no in the first column: exclusion, yes: inclusion. The final column provides the reason for the decision.

Table A2

Overlap in data set and action taken per analysis

Infection risk	[*k*] effect-sizes included	Action
Anxiety disorders	[4] Lee et al. (2020), Orlando et al. (2021), Teixeria et al. (2021), Yang et al. (2021)	No potential overlap
Mix/other	[11] Bailey et al. (2021), Canal-Rivero et al. (2021), De Vito et al. (2021), Egede et al. (2021), Lee et al. (2020), Merzon et al. (2021), Nilsson et al. (2022), Taquet et al. (2021), Taquet et al. (2021), Yang et al. (2021)	Taquet et al. report nationwide data form the US. Hence the analyses were once run with this study excluded and once with the other studies from the US excluded: Bailey et al. (2020), Egede et al. (2021)
Mood disorders	[11] Azar et al. (2020), Dai et al. (2022), Egede et al. (2021), Goldberger et al. (2022), Haimovich et al. (2021), Lee et al. (2020), Orlando et al. (2021), Tang et al. (2021), Teixeria et al. (2021), Yang et al. (2020)	Dai et al. (2022) and Yang et al. (2020) both report nationwide data from the UK. Thus, the analyses were once run with one of them, once with the other one. UK excluded: Yang et al. (2020) Teixeria et al (2021) reported nationwide data from 2021. Hence the analyses were once run with this study excluded and once with the other studies from the US excluded: Egede et al. (2021), Azar et al.

Infection risk	[*k*] effect-sizes included	Action
		(2020), Haimovich et al. (2021), Tang et al. (2021) US excluded: Teixeria et al (2021)
Neuro-dev. disorders	[4] Cohen et al. (2022), Merzon et al. (2021), Dai et al. (2022)	No potential overlap Both Cohen et al. (2022) and Merzon et al. (2021) from Isreal but they use data from different health services
Psychosis spectrum	[12] Amin et al. (2022), Dai et al. (2022), Egede et al. (2021), Goldberger et al. (2022), Haimovich et al. (2021), Merzon et al. (2021), Nemani et al. (2022), Orlando et al. (2021), Teixeria et al. (2021), Tzur Bitan et al. (2021), Yang et al. (2021)	Goldberger et al. (2022), Merzon et al. (2021) and Tzur Bitan et al. (2021) report on nationwide data from Israel. Hence the analyses were once run with this study excluded and once with the other studies. Israel excluded: Merzon et al. (2021) and Tzur-Bitan et al. (2021) Teixeria et al. (2021) report nationwide data from the US. Hence the analyses were once run with the other studies from the US excluded. US excluded: Egede et al. (2021),Haimovich et al. (2021) and Nemani et al. (2022)
SUD	[9] Allen et al. (2020), Egede et al. (2021), Lebin et al. (2021), Lee et al. (2020), Salvatore et al. (2021), Varela-Rodriguez et al. (2021), Wang et al. (2021), Yang et al. (2021)	Wang et al. (2021) report nationwide data form the US. Hence the analyses were once run with the other studies from the US excluded. US excluded: Allen et al. (2020), Egede et al. (2021), Lebin et al. (2021) Dai et al. (2022) and Yang et al. (2021) report UK Biobank data. Yang et al (2021) is excluded
Post-COVID syndrome	**[*k*] effect-sizes included**	**Action**
Mix	[4] Al-Aly et al. 2022, de Miranda et al.2022, Jones et al 2021, Thompson et al 2022	No potential overlap

294.

295. Table A6

296. Quality assessment of included studies

Article	Quality assessment of systematic reviews and meta-analyses criteria
Al-Aly et al. 2022	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 5

Article	Quality assessment of systematic reviews and meta-analyses criteria
Allen et al. 2020	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 9
Amin et al. 2022	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 9
Azar al. 2020	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 4
Bailey et al. 2021	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 3
Canal-Rivero et al. 2021	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 3
Cohen et al. 2022	1□; 2□; 3□; 4a□ 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 11
Dai et al. 2022	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 11
De Miranda et al. 2022	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 7
De Vito et al. 2021	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 5
Egede et al. 2021	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 9
Goldberger et al. 2022	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 9
Haimovich et al. 2020	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 0
Jones et al. 2021	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 5
Lebin et al. 2020	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 6
Lee et al. 2020	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 13
Merzon et al. 2021	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 7
Nemani et al. 2021	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 9
Nemani et al. 2022	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 9
Nilsson et al. 2022	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 11
Orlando et al. 2021	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 7
Rajkumar et al. 2021	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 3
Rajkumar et al. 2022	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 1
Tang et al. 2020	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 6
Taquet et al. 2021	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 9
Teixeira et al. 2021	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 11
Thompson et al. 2022	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 9
Tzur Bitan et al. 2021	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 7
Wang et al. 2021 a	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 11

Article	Quality assessment of systematic reviews and meta-analyses criteria
Yang et al. 2020	1□; 2□; 3□; 4a□; 4b□; 5□; 6□; 7□; 8□; 9□; 10□; 11□; 12□; 13□; 14□: T = 8

297. Notes. □ = yes; □ = neutral / don't know; □ = no

298.

299. -- insert Figure A1 here—

300. Funnel plot illustrating the relationship between COVID-19 infection rate and pre-existing anxiety disorders.

301. --insert Figure A2 here—

302. Funnel plot illustrating the relationship between COVID-19 infection rate and mental health disorders (mix).

303. **-- insert Figure A3 here—**

304. Funnel plot illustrating the relationship between COVID-19 infection rate and mood disorders.

305. -- insert Figure A4 here—

306. Funnel plot illustrating the relationship between COVID-19 infection rate and neurodevelopmental disorders

307. -- insert Figure A5 here—

308. Funnel plot illustrating the relationship between COVID-19 infection rate and schizophrenia spectrum disorders.

309. -- insert Figure A6 here—

310. Funnel plot illustrating the relationship between COVID-19 infection rate and substance use disorder.

311. -- insert Figure A7 here—

312. Funnel plot of prevalence estimates of the post-COVID-19 syndrome in people with pre-existing mental health disorders

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