Diploma Thesis

Vaccines in individuals with severe mental disorders

Prevalence rates, effects, and side effects as well as COVID-19 vaccination willingness

submitted by

Nina Bonkat

for the academic degree

Doctor of Medical Science

(Dr. med. univ.)

at the

Medical University of Graz

Department of Psychiatry and Psychotherapeutic Medicine

under the supervision of

Dr.in Frederike Fellendorf

Univ. Prof.in PDin Dr. in Eva Reininghaus, MBA

Graz, 10.02.2022

Statutory Declaration

I herewith formally declare that I have written the submitted dissertation independently. I did not use any outside support except for the quoted literature and other sources mentioned in the paper. I clearly marked and separately listed all of the literature and all of the other sources which I employed when producing this academic work, either literally or in content.

Graz, 10.02.2022 *Nina Bonkat eh.*

Danksagung

Ich möchte mich bei meiner Betreuerin, Frau Dr.in Frederike Fellendorf, für die umfangreiche Hilfe und Unterstützung während der Erstellung meiner Diplomarbeit bedanken. Vielen Dank für die vielen Hinweise und Tipps zur wissenschaftlichen Arbeit, sowie auch die hilfreichen Kommentare und Korrekturen meiner vielen Entwürfe der Diplomarbeit.

Vielen Dank auch an meine Betreuerin, Frau Univ. Prof.in PDin Dr.in Eva Reininghaus, MBA, die es mir ermöglichte, meine Diplomarbeit am Institut für Psychiatrie und Psychotherapeutische Medizin zu schreiben, sowie an mehreren wissenschaftlichen Projekten mitzuarbeiten. Ich möchte mich auch für das Durchlesen meiner Diplomarbeit und das Feedback dazu bedanken.

Ich möchte mich bei meinen Eltern für die durchgehende Unterstützung während meiner gesamten Studienzeit bedanken.

Contents

List of Abbreviations

ACE2	Angiotensin Converting Enzyme 2
aOR	adjusted Odds Ratio
AD	Affective Disorder
BBB	Blood Brain Barrier
BD	Bipolar Disorder
BDI	Beck Depression Inventory
BMI	Body Mass Index
CDC	Center of Disease Control
cMDD	current Major Depressive Disorder
CMV	Cytomegalovirus
COPD	Chronic Obstructive Pulmonary Disease
COVID-19	Coronavirus Disease 2019
CRP	C-Reactive Protein
DM	Diabetes Mellitus
DTap-IPV	Diphteria/Tetanus/Pertusis/Polio
EMA	European Medicines Agency
GDS	Geriatric Depression Scale
HBs	Hepatitis B surface
HBV	Hepatitis B Virus
HC	Healthy Controls
HIV	Human Immunodeficiency Virus
HPA	Hypothalamic-Pituitary-Adrenal
HPV	Human Papillomavirus
ICD	International Statistical Classification of Diseases and Related Health Problems
IFN- y	Interferon-gamma
IL-6	Interleukin-6
KMO	Kaiser-Meyer-Olkin
MDD	Major Depressive Disorder
MIF	Macrophage Migration Inhibitory Factor
MMR	Mumps/Measles/Rubella
OR	Odds Ratio

PPD	Primary Psychotic Disorder
PTSS	Posttraumatic Stress Symptoms
rMDD	remitted Major Depressive Disorder
RR	Relative Risk
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SMI	Severe Mental Illness
SNS	Sympathetic Nervous System
SPMI	Severe and Persistent Mental Illness
SPSS	Statistical Package for Social Sciences
SSRIs	Selective Serotonin Reuptake Inhibitors
SZ	Schizophrenia
TNFα	Tumor Necrosis Factor α
TSST	Trier Social Stress Test
VLPs	Virus Like Particles
VZV	Varicella Zoster Virus
VZV-RCF	Varicella Zoster Virus- Specific Responder Cell Frequency
WHO	World Health Organization

List of Figures

List of Tables

Zusammenfassung

Hintergrund: Menschen mit schweren psychischen Störungen haben ein höheres Risiko, sich mit der Coronavirus Krankheit-2019 (COVID-19) zu infizieren. Zusätzlich haben sie auch ein höheres Risiko, im Falle einer Infektion, einen schweren Verlauf der Krankheit zu erleiden. Es ist deshalb besonders wichtig, Menschen in dieser Hochrisikogruppe mit einer Impfung vor einer Infektion zu schützen.

Methoden: Es wurde eine Literaturrecherche der Datenbank Pubmed im Januar 2021 durchgeführt, um Daten zu Impfungen im Allgemeinen in Menschen mit schweren psychischen Störungen zu finden. Dazu wurden die Schlagwörter "vaccin* AND (depress* OR schizophrenia OR bipolar OR mania)" verwendet. Englisch- oder deutschsprachige Studien, die die Impfprävalenz, die Wirkungen, Nebenwirkungen und Interaktionen mit Psychopharmaka von Impfungen in Menschen mit psychischen Störungen analysierten, wurden inkludiert. Zusätzlich wurde eine online-Fragebogenstudie an der Universitätsklinik für Psychiatrie und Psychotherapeutische Medizin der Medizinischen Universität Graz von April bis Mai 2021 durchgeführt, um die COVID-19 Impfbereitschaft, sowie Gründe für und gegen eine Impfung bei Menschen mit affektiven Störungen (AD), zu analysieren.

Ergebnisse: Die Literaturrecherche fand 42 relevante Studien, von denen 23 Studien die Impfprävalenzen oder Impfbereitschaftsdaten erforschten und 17 Studien die Immunogenität oder Nebenwirkungen von Impfungen erkundeten. Die Ergebnisse dieser Studien waren inkonsistent. Weitere zwei Studien begutachteten die Interaktionen zwischen dem Antipsychotikum Clozapin und mehreren Impfungen. Daten der online-Fragebogenstudie von 118 Teilnehmern, von denen die Hälfte an einer AD litten und die andere Hälfte gesunde Kontrollen (HC) waren, zeigte, dass es keinen signifikanten Unterschied in der COVID-19 Impfbereitschaft gab.

Diskussion: Die Studien variierten nicht nur in den Ergebnissen, sondern auch in ihrem Studiendesign und den Teilnehmergruppen, sowie in der Art der Impfung und eingeschlossenen psychischen Erkrankungen. Die meisten Studien analysierten die Grippeimpfung bei Menschen mit Depression. Weitere Forschung zu diesem wichtigen Thema ist deshalb erforderlich. Glücklicherweise war die COVID-19 Impfbereitschaft bei Menschen mit AD genauso hoch, wie bei HC. Spezielle Impfprogramme könnten Menschen mit psychischen Erkrankungen helfen, weitere Schwierigkeiten in Bezug auf die

Impfung zu überwinden und dadurch eine ausreichende Durchimpfungsrate in dieser Hochrisikogruppe zu erreichen.

Abstract

Background: Individuals with severe mental disorders (SMI) are at an increased risk of an infection with the coronavirus disease 2019 (COVID-19), as well as a more severe illness course. It is important that these individuals are protected against the infection with a vaccination.

Methods: As little information on the COVID-19 vaccine in individuals with SMI existed at the time of researching in January 2021, a literature review of the database Pubmed using the keywords "vaccin* AND (depress* OR schizophrenia OR bipolar OR mania)" was conducted to find data on vaccines in general in these individuals. Studies in English or German language investigating the prevalence rates, effects, or side effects of vaccines in individuals with SMI or interactions between psychopharmaceuticals and vaccines were included. Additionally, an online survey was conducted from April to May 2021 at the Medical University of Graz, Department of Psychiatry and Psychotherapeutic Medicine, to investigate the willingness of individuals with affective disorders (AD) to receive the COVID-19 vaccination.

Results: The literature review found 42 relevant articles, of which 23 studies investigated vaccine prevalence rates or willingness to be vaccinated and 17 studies reported data on immunogenicity and side effects of vaccines in individuals with SMI. The results of these studies were inconsistent. Additionally, two studies investigating the interactions between the antipsychotic clozapine and different vaccines were found. Data from 118 participants of the survey study, half suffering from AD and half being healthy controls (HC), showed that there was no significant difference between the two groups in the willingness to get vaccinated against COVID-19.

Discussion: The studies differed in the study design and population, as well as the vaccine types and psychiatric disorders they investigated. Most studies investigated the influenza vaccine in individuals with depression or depressive symptoms. Further research on this topic is necessary. Fortunately, the survey study found that individuals with AD were as willing as HC to receive a COVID-19 vaccine. Special vaccination programs might be beneficial in helping individuals with mental disorders, overcome further barriers that prevent them from getting a vaccination and, therefore, achieve a sufficient vaccine coverage in this high-risk group.

1. Introduction

The coronavirus disease 19 (COVID-19) pandemic has changed life as we know it. Mask wearing, social distancing, frequent hand washing, quarantining in case of sickness or suspected infection, and multiple lockdowns have become the norm. Even though all those measures were put in place to stop or minimize the spread of the virus, the pandemic still has claimed the lives of millions of people since its start almost two years ago. In 2020 the best hope to end the pandemic became a vaccine and numerous research teams all over the world started working on one. In December 2020, the first vaccine against COVID-19 by BioNTech/ Pfizer was approved, followed by more in the subsequent months. Vaccine rollout was slower than expected in many countries, including Austria, though. There was much debate of who should be prioritized in receiving a vaccine, based on the risk of an infection or severity of illness. The group that I am focusing on in this thesis is the population of the severe mentally ill. These individuals are potentially at a higher risk for infection and severity of COVID-19 and demands were made, that they too should be prioritized in the vaccine rollout. Little is known on the topic of their views on the COVID-19 vaccine and their willingness to receive it, once offered, as well as potential (side) effects of the vaccine in these people. In the introduction, I will discuss current knowledge on the COVID-19 infection in individuals with severe mental illness (SMI), as well as general aspects of vaccines. Furthermore, I carried out a literature search in January 2021 to gather information on vaccinations in general in individuals with SMI. I focused on the vaccination prevalence of various vaccines in the population of the mentally ill, the antibody production and maintenance, as well as side effects after vaccination, and possible interaction between psychopharmaceuticals and vaccines. To investigate the willingness of these people to receive the COVID-19 vaccination, as well as their concerns and worries about the vaccines, an online survey study was conducted at the department for Psychiatry and Psychotherapeutic Medicine at the Medical University Graz. Two publications, which presented the results of the literature search and one publication, which discussed the findings of the online survey study have been accepted or are currently in revision in different journals.

1.1. COVID-19

The first case of COVID-19, which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was identified in Wuhan, China in December 2019. The World Health Organization (WHO) declared COVID-19 a pandemic on March 11, 2020. (1) Since the beginning of the outbreak up to February 2022 over 376,229,000 cases have been confirmed all over the world and over 5,681,000 people have died from or with the infection. (2)

The Centers for Disease Control and Prevention (CDC) has identified certain individuals, who have a higher risk of a severe outcome, complications, and death due to a COVID-19 infection. These risk factors are cancer, chronic kidney disease, chronic obstructive pulmonary disease (COPD), obesity (body mass index (BMI) over 30 kg/m^2), Down syndrome, certain heart conditions like cardiovascular disease or cardiomyopathies, solid organ transplant leading to an immunocompromised state, pregnancy, sickle cell disease, smoking, and type 2 diabetes mellitus (DM). (3) Furthermore, asthma, cerebrovascular disease, hypertension, dementia, liver disease, pulmonary fibrosis, thalassemia, being overweight (BMI between 25 and 30 kg/m^2), type 1 DM, and an immunocompromised state from causes other than solid organ transplant, such as the human immunodeficiency virus (HIV) or the use of corticosteroids, could potentially increase the risk for a severe illness when infected with COVID-19. (3)

A systematic review (4) assessed 17 studies to find factors associated with the severity of the illness or death due to COVID-19. This review found seven risk factors, which with a high consistency lead to severe outcomes when infected with COVID-19. These are high age, high values of C-reactive protein (CRP), D-dimer, body temperature, and sequential organ failure score, as well as lower albumin and DM. Some of the medium consistency risk factors identified by the review are elevated Interleukin-6 (IL-6) levels, which is a proinflammatory cytokine, higher white blood cell and neutrophile counts, as well as decreased lymphocyte counts.

1.2 Severe mental illness

SMIs are mental, behavioral, or emotional disorders, characterized by serious disability, which impairs one or more important functions of daily live. (5) SMI include major depressive disorder (MDD), schizophrenia (SZ), and bipolar disorder (BD). MDD and BD are mood disorders, also known as affective disorders (AD). Table 1 describes the symptoms of these mental disorders in more detail. (6,7)

Table 1: Symptoms of select mental disorders

MDD	BD	SZ
Prolonged hopelessness Low mood Fatigue Lethargy Suicidal thoughts	Extreme shifts in mood: <u>Depression:</u> • Hopelessness • Low mood • Fatigue • Lethargy • Suicidal thoughts <u>Mania:</u> • Impulsiveness • Exaggerated self confidence • Aggression • Irritability	Loss of touch with reality Hallucinations Delusions Paranoia Disordered thinking Disordered speaking Reduced ability to: • initiate plans • speak • express emotions

Note: MDD = major depressive disorder; BD= bipolar disorder, SZ= schizophrenia

There is evidence (8-10), that people with SMI have higher rates of medical comorbidities. A study (8) analyzing medical comorbidities in patients with SZ and AD found that these individuals have higher odds of having asthma, chronic bronchitis, emphysema, liver problems, kidney disease, and DM. A literature review by De Hert and colleagues (9) identified a significant association between obesity and SMI, that differed based on diagnosis. Patients with SZ, for example, have a 2.8 to 3.5 higher likelihood of being obese, while patients with mood disorders have a 1.2 to 1.5 increased risk of being obese. One of the factors that could lead to weight gain in these patients is the medication often prescribed to them. Antipsychotics, especially of the second generation, such as clozapine, quetiapine, and olanzapine, that are commonly used to treat SZ and BD, can cause obesity as well as type 2 DM. (11) Other psychotropic medications like antidepressants, especially tricyclic antidepressants (12), and mood stabilizers like lithium (10) have also been linked to weight gain. However, there is evidence that in drug-naïve patients with BD overweight is more prevalent than in healthy controls, as well as than in drug-naïve patients with obsessive-compulsive disorder. (13) Therefore, besides side-effects of psychotropic drugs, factors like lifestyle choices, such as lack of exercise and poor diet, and components

related to the mental illness like depressive symptoms and anhedonia could lead to obesity in individuals with SMI. (9,13)

The review by De Hert (9) also identified a higher prevalence of DM, cardiovascular disease, and COPD in this group. In addition to having a higher number of chronic physical diseases than the general population, the rate of unhealthy lifestyle choices like smoking (14,15) and substance use (16) is also higher in individuals with SMI. A prospective cohort study (14), which studied smoking habits in people with SZ, BD, and controls from 1999 to 2011 found a 64% prevalence rate of smokers in the SZ group and a 44% prevalence rate in the bipolar group. Compared to that only 19% of the control group were smokers. Another study (15) found a 2.7 odds ratio (OR) for both current and lifetime smoking in people with past-month mental illness compared to individuals with no mental illness. A Danish study (16) identified a three to eight times higher ratio of substance use disorder in patients with SMI, depending on the type of psychiatric disorder.

SMI are associated with an altered immune system. MDD leads to a proinflammatory state with proinflammatory cytokines like IL-6 and Tumor Necrosis Factor-alpha (TNF-α) being elevated. (17) The adaptive immune system is also altered due to a decrease in the number of natural killer cells and an elevation of regulatory T-cells, which act as a suppressor to the immune system. (18) Sleep problems, which are often associated with MDD (19), lead to further reduction of natural killer cells and the cellular immune system. (18,20) In people with BD many proinflammatory cytokines, like IL-6, IL-1 beta, and TNF-alpha, as well as acute phase proteins like CRP are elevated, especially during acute mood phases. (21) Additionally, a study (22) has found elevated levels of neutrophil counts in individuals with BD compared to healthy controls. Proinflammatory cytokines are also elevated in SZ patients. Oxidative stress and altered numbers of circulating lymphocytes are associated with SZ. (23) Furthermore, lower lymphocyte numbers were identified in both SZ and BD patients compared to controls. (24) Due to these higher rates of physical comorbidities, lifestyle factors like smoking and substance use, impaired immune systems, and possibly other factors, people with SMI are associated with an up to three times higher mortality than the general population and a 13-30 years reduced life-expectancy. (9, 25-27)

1.3 Severe mental illnesses and infectious diseases

Individuals with SMI are at a higher risk for contracting infectious diseases. A retrospective study (28) done in England, which analyzed the occurrence of pneumococcal disease in patients hospitalized for depression, SZ, BD, or anxiety compared with individuals with no record of hospitalization for a psychiatric disease, found that

individuals hospitalized for a mental disorder had a twofold risk increase for pneumococcal disease compared to the controls. When only analyzing people under 60 years old, there was an almost threefold risk for the individuals with mental disorders. The study (28) also found a twofold risk for severe outcomes like pneumococcal septicaemia and meningitis in the individuals with mental disorders compared to people without mental disorders. Another study (9) also found a higher prevalence of infectious diseases[7], especially respiratory tract diseases, like tuberculosis and pneumonia and viral infections like HIV and hepatitis C. People with mental disorders have a five to eleven times increased risk of infection with hepatitis B (HBV) and C and a higher prevalence of tuberculosis compared to the general population. (9) Furthermore, they have higher hospitalization rates and mortality from influenza infections. (29) There have been multiple reports of outbreaks of infectious diseases in psychiatric facilities, especially of respiratory infections. (30) Influenza outbreaks led to a high infection prevalence in psychiatric departments, as eight of 26 patients in one unit became symptomatic after one outbreak (31), in addition to a high mortality rate, as 13 out of 26 infected patients died in a geriatric psychiatry department (32). As individuals with mental illness suffer from both higher infection rates and worse outcomes from many viral and bacterial infectious diseases, it can be hypothesized that mental illness will also be associated with higher infection rates, more severe outcomes, and higher death rates of COVID-19.

1.4 Severe mental illnesses and COVID-19

1.4.1 Increased infection risk

There are conflicting results regarding the risk for a COVID-19 infection of individuals with mental illness. On one hand, multiple studies have identified an increased risk for a COVID-19 infection in individuals with mental illness. A case control study (33) using data from health records across all 50 states of the United States found a significantly increased risk, with individuals with depression and SZ being affected the most. Depressed patients had an OR of 7.64 and SZ patients an OR of 7.34 for COVID-19 infection. Women and African Americans with mental disorders had higher odds for being infected than men and Caucasians respectively. This study group also analyzed the risk for individuals with substance use disorder and found a fully adjusted odds ratio (aOR) of 8.7 for these individuals to contract COVID-19. (34) As substance use is significantly greater in the population of the mentally ill than the general population, this risk is relevant for individuals with SMI, who also have a substance use disorder. Another study (35) from the United States, a retrospective cohort study, which gained access to the data of 69.8 million

patients, found an increased risk of 65% of contracting COVID-19 for patients 18 years or older that had a mental illness diagnosis in the year prior to the pandemic. The cohorts were matched for physical risk factors. Additionally, a study (36) analyzing data from the UK Biobank of individuals in England who had a prepandemic diagnosis of a psychiatric disorder vs. controls without a diagnosis of a psychiatric disorder, found an OR of 1.44 for a COVID-19 infection in individuals with any psychiatric disorder. The risk was highest in individuals with depression (OR=1.62), anxiety (OR=1.60), and psychotic disorder (OR=1.60).

On the other hand, a few studies (37,38) have found no difference between the infection rates in the mentally ill population versus the general population. A cohort study (37), conducted from January to May of 2020 in South Korea, found no correlation between mental illness and COVID-19 infections. Similarly, a longitudinal population-based register study (38) conducted in Sweden observed no statistical difference between the SMI group and the control group.

These conflicting results could be the result of a possible underrepresentation due to a lack of proper diagnosis of the COVID-19 cases in the mentally ill patients. Individuals with SMI can experience depression and anhedonia, which might impair them from getting a COVID-19 test and they would, as a result, not be registered as a COVID-19 case. There could also be cultural differences leading to the different results of the studies, as both the American studies and the English study found an increased risk, while the South Korean and the Swedish one did not. Nevertheless, there was a significantly increased risk for a COVID-19 infection in individuals with mental disorders identified by multiple studies.

1.4.1.1 Factors associated with the increased risk for infection

One aspect possibly leading to the greater susceptibility for infectious diseases in individuals with SMI is their impaired immune system. In addition, this risk could be due to socioeconomic factors. Socioeconomic deprivation is strongly associated with mental illness. (39) Many of these individuals live in institutions, where they are more likely to come in close contact with other individuals. This can make it difficult for them to practice social distancing and increase the transmission of the virus. Individuals with SMI often have jobs with poorer working conditions, where the risk for transmission of COVID-19 is high. Due to their socioeconomic deprivation, they are also more likely to be homeless or live in overcrowded conditions, where it is easier for the virus to spread.

Furthermore, cognitive defects, which can result from a severe chronic mental disorder, could lead to incomprehension of COVID-19 guidelines to stop the spread. (7,40)

Symptoms of SMI, like hallucinations and delusions in SZ patients, mania in BP patients, as well as lethargy in MDD and BD patients could also result in these individuals not following the suggested guidelines and, therefore, have a higher risk of infection. (7,40) People with SMI frequently have a lower educational gain (41) and lower health literacy (42) than the general population. This might lead to them not understanding the rules, like social distancing, mask-wearing, or quarantining, set in place to limit the spread of the virus. Furthermore, symptoms of apathy, anhedonia, or hopelessness, especially in patients with MDD, might cause them not to follow the guidelines to protect themselves from getting infected, even if they are aware of the rules. A study (43) using cross-sectional telephone surveys in South India to research the impact of COVID-19 on patients with SMI one month after the first lockdown in March 2020 found that of 132 patients, eleven patients were not aware the pandemic was going on and twelve did not know of the need to quarantine. Additionally, only 28% knew three or more symptoms of the disease and only 38% knew of precautions to prevent infection. Furthermore, 73.5% were not worried about contracting COVID-19, meaning that they were probably less inclined to follow the guidelines. In the general population 96% or more acknowledged the need for frequent handwashing, social distancing, and quarantining if symptomatic. These factors lead to the increased risk of individuals with SMI to become infected with COVID-19, identified by multiple studies.

1.4.2. Course and mortality

Other than the worse outcomes observed in individuals with SMI from other infectious diseases (28,29,32), these individuals also have multiple of the risk factors associated with severe COVID-19 outcomes. Many of the comorbidities and life-style choices, like smoking, that were proven to be higher in individuals with SMI (8-10,14,15), are risk factors for a worse COVID-19 outcome, further strengthening the hypothesis, that the severity and mortality rate of COVID-19 would be higher in this group of people. However, neither the CDC, nor the systematic review by Rod and colleagues (4) listed SMI as a risk factor for a severe outcome or death due to a COVID-19 infection, even though many studies (33,36-38,44,45) have found both an increase in mortality and an increase in severe outcomes and complications due to COVID-19 infections in people with SMI. The previously mentioned case control study (33), which analyzed health records from across the United States, found a mortality rate of 8.5% for COVID-19 patients, which had a recent diagnosis of a mental disorder, compared to only a 4.7% mortality rate among COVID-19 patients without mental disorders. The hospitalization rate was also

significantly higher with 27.4% in patients with mental disorders vs. 18.6% in patients with no mental disorder. The South Korean cohort study (37) identified an aOR of 1.29 for a severe outcome from COVID-19 and an aOR of 1.38 for death from a COVID-19 infection in patients with mental illnesses. The risk for a severe outcome was even higher in patients hospitalized in a psychiatric ward (OR=2.22) and when stratified by the severity of the mental illness (OR=3.94). The UK Biobank study (36) found an OR of 1.55 for hospitalization due to a COVID-19 infection in the cases with psychiatric disorders. The risk was higher for patients with depression or anxiety (OR of 1.70 for both) than for patients with psychotic disorder (OR of 1.47). The OR for death was 2.03 for patients with psychiatric disorder overall. Patients with psychotic disorder had a higher risk (OR=3.50), than patients with depression (OR=2.68) or anxiety (OR=1.89) of dying due to a COVID infection. Additionally, the Swedish study (38) found a twofold increased risk of death due to COVID-19 in the SMI group compared to the control group. When only the individuals over 60 years were analyzed, the SMI group had an over four times increased risk of dying compared to the control group. Interestingly, when the analysis was done on individuals who had neither hypertension, cardiovascular disease, DM, or chronic respiratory disease, a threefold increase of COVID-19 associated death was found in the individuals with SMI, which was higher than the overall risk found in this study. This shows that these medical comorbidities did not lead to the increased mortality rate in this group.

In the previously mentioned South Korean study (37), the ORs were also adjusted for clinical characteristics, meaning that any increased rates of comorbidities in the mentally ill group was not the sole reason for the higher rates of severe outcome and death. In the English study (36), after adjusting for somatic comorbidities, the ORs of the mentally ill population for being hospitalized or dying from COVID-19 decreased a little from the aforementioned ratios, but the risk was still significantly higher than that of the general population. A cohort study (44) executed in New Haven, USA between February and April 2020 identified an unadjusted hazard ratio (HR) of 2.3 for the patients with psychiatric disorders of dying from COVID-19. After adjusting for both demographic characteristics and physical comorbidities, the HR was 1.5, remaining significant. Another retrospective cohort study (45) conducted at the New York University between March and May 2020, however, found that only SZ was associated with a significant increase in COVID-19 related mortality, but did not find a correlation between mortality and mood disorders or anxiety after fully adjusting for demographic and medical risk factors. Overall, these studies have shown that mental disorders are associated with a higher risk for a severe

outcome, hospitalization, and death due to COVID-19. This risk remained significant even after adjusting for physical comorbidities, of which some have been identified as risk factors for a severe outcome, and for demographic characteristics, like age, sex, and income. Other factors than the increased physical diseases in individuals with SMI, therefore, must play a role in the elevated risk of this group.

1.4.2.1. Factors that amplify the risk of severe outcome/death

Individuals with SMI are more often socially isolated due to stigmatization, negative symptoms of their disorders like depressive states and positive symptoms like hallucinations, which might lead to alienation from other people. (46) This social isolation might result in these individuals receiving either delayed or no care when their condition from a COVID-19 infection worsens and as a result could lead to an increased mortality rate. Stigmatization towards people with SMI also leads to an undertreatment of physical diseases in this group, as their symptoms are often not taken seriously, which could lead to delayed care in the infected and a worsening of their illness. (47) Another important factor that increases the risk for a severe outcome or death due to a COVID-19 infection in people with SMI is their impaired immune system. The previously mentioned literature review about factors that influence the severity of a COVID-19 infection by Rod and colleagues (4) identified heightened CRP, IL-6, and neutrophile count, as well as lower lymphocyte counts as risk factors. All of these occur in patients with SMI due to their altered immune systems. (17-24)

A severe COVID-19 infection is characterized by a “cytokine storm”, which is a release of high levels of cytokines into the circulation, with the ability to cause damage in multiple organs. It is believed to be triggered by an “imbalance in immune-system regulation”. (48) Heightened CRP levels have also been identified as a biomarker to predict a “cytokine storm”. (48) The altered levels of many immune cells and heightened numbers of cytokines in individuals with SMI (17-24) demonstrate that an imbalance in the immune systems of these individuals exists. As CRP levels are also elevated in these individuals (21), a “cytokine storm” could be provoked and worsen the outcome in case of a COVID-19 infection. This shows that SMI by itself is an important risk factor for severe outcomes and mortality in COVID-19 patients.

Some of the medication that are prescribed to individuals with SMI can also influence immune system function and potentially lead to a worsening state in the COVID-19 infected. A study (49) done on mice found a deregulation of both the acute and adaptive immune responses in mice treated with Risperidon, an antipsychotic used in the treatment

of SZ, BD, and depression. Clozapine, another antipsychotic, can cause blood dyscrasia, most importantly agranulocytosis. (50,51) Tricyclic antidepressants can also, in rare cases, lead to agranulocytosis. (50) Interestingly, another class of antidepressants, selective serotonin reuptake inhibitors (SSRIs), have been proposed as a possible treatment for the coronavirus disease. (52) This is due to the fact, that SSRIs prevent the elevation of inflammatory cytokines and could help in averting a "cytokine storm". The mood stabilizers Lithium and Carbamazepine also effect the immune system. Lithium generally stimulates the production of white blood cells, while Carbamazepine leads to a reduction in their number. (50) A case-control study (53) found that benzodiazepines were associated with an increased risk for pneumonia and death from community acquired pneumonia perhaps due to their activation of the $GABA_A$ receptor in immune cells. It is possible that they could also lead to an increase in death from COVID-19. Therefore, it is important to evaluate the current medication in mentally ill COVID-19 patients.

Smokers are more prevalent among the group of mentally ill individuals than the general population. (14,15) Smoking is listed as a risk factor for a severe outcome of a COVID-19 infection. (4) SARS-CoV-2 uses the angiotensin-converting enzyme 2 (ACE2) to enter the cells and cause infection. (54) It has been shown that the expression of ACE2 is increased in bronchial epithelial cells in current smokers. (54) This makes it easier for the virus to enter the cells in current smokers. In addition, smoking is associated with the promotion of lung inflammation with increasing number of proinflammatory cytokines (54), which might also increase the risk for a "cytokine storm" in a COVID-19 infection. All these factors could accumulate to result in the heightened mortality and increased number of severe outcomes in individuals with SMI, even after having adjusted for medical comorbidities.

1.4.3. Increased risk for psychiatric symptoms

Not only do SMIs increase the risk for COVID-19, an infection with COVID-19 heightens the risk for psychiatric symptoms as well. There has been a large number of cases, in which psychiatric symptoms were observed during and after a COVID-19 infection in patients. (35,55-60) These include symptoms of depression, anxiety, somatization, insomnia, as well as posttraumatic stress symptoms (PTSS) and obsessive-compulsive symptoms. A smaller, but still significant percentage of people with no prior psychiatric disorder, were even diagnosed with anxiety or depressive disorder in a span of 90 days following infection with SARS-COV2. (35,58)

There have been multiple mechanisms proposed of how the coronavirus can cause neuropsychiatric symptoms. The virus could reach the brain either retrogradely through the olfactory nerve or systemically through the blood brain barrier (BBB). (61) However, in only a few individuals with neuropsychiatric symptoms, the virus has been detected in the cerebral spinal fluid. (62) Other mechanisms are hyperinflammation and immune cell reactions induced by the virus. (58,61) During a "cytokine storm", the proinflammatory cytokines, especially IL-6, could lead to a dysfunction of the BBB (61) and result in infiltration of the brain with immune cells (58) which could cause psychiatric symptoms. The coronavirus also leads to a hypercoagulable state, which could affect the cerebrovascular system and lead to a stroke. (61) In fact, a stroke is the most common neurological display related to a COVID-19 infection seen in hospitalized patients. (61) As stroke is a risk factor for depression (63), this could also lead to the psychiatric manifestations, especially depressive symptoms, in COVID-19 patients. Most patients studied, who had psychiatric symptoms following a COVID-19 infection, had no previous mental illness or it was not specified. However, a COVID-19 infection could also lead to these symptoms in individuals with previous psychiatric diagnosis and, therefore, result in a worsening or exacerbation of their state. (64)

A study (65) conducted in China during the first lockdown in February 2020, found that psychiatric patients were significantly more likely to experience a greater number of depressive symptoms, anxiety, stress, insomnia, and PTSS compared to healthy controls. Additionally, a recent literature review (66) showed that individuals with SMI, especially with AD, experienced more symptoms of depression, anxiety, and stress during the pandemic than HC. Therefore, not only an infection, but also the lockdown measures put in place due to the pandemic put mentally ill individuals at risk for an increase in their psychiatric symptoms**.**

1.5. Vaccinations

A successful prevention against many infectious pathogens is a vaccine. Diseases, like smallpox and polio have been successfully eliminated and childhood illnesses like haemophilus influence have seen a large reduction in morbidity after the implementation of vaccines against them. (67) One study (68) found the risk of dying from pneumonia cut almost in half (aOR=0.599) in elderly individuals, who received the pneumococcal 13-valent conjugated vaccine. After implementation of the national vaccination program for HBV in Korea, the prevalence of the disease decreased from 6-8% to 2-3% in Korean children. (69) The influenza vaccination led to a significant reduction in hospitalization

due to pneumonia and influenza in elderly individuals (70,71) and a significant decrease in influenza illness and influenza related hospitalization and death in nursing home residents. (72) Vaccinations, therefore, might reduce this increased risk for infection of many illnesses in the mentally ill population.

In December 2020, the first vaccines against COVID-19 were approved. In March 2021, the European Medicines Agency (EMA) authorized the fourth COVID-19 vaccine Janssen, developed by Johnson and Johnson, to be used in the European Union. This vaccine follows the already approved Biontech/Pfizer, Moderna, and AstraZeneca COVID-19 vaccines.

Vaccines are substances meant to stimulate one's immune system and to prepare it in case of infection with a harmful pathogen. The vaccine contains antigens of the specific kind of pathogen it protects against, which initiate the adaptive immune response, without causing the actual infection. T-lymphocytes, which are highly specific to that antigen, and B-lymphocytes, which turn into plasma cells to produce highly specific antibodies, are activated by the vaccine. After the immune stimulus is gone, a few of these cells remain as memory cells, which can rapidly reactivate and mount a successful immune response in case of an infection with the same pathogen. (73)

There are many different types of vaccines for many different pathogens. Live-attenuated vaccines are produced from pathogens, more often viruses than bacteria, that have been weakened or altered, so that they cannot cause the actual disease. They are highly effective and often require only one or two doses to reach long-term immunity. However, they can cause symptoms of the disease after vaccination, although these are usually much milder than of the actual infection. Some examples of live-attenuated vaccines are the measles, mumps, and rubella (MMR) vaccines, as well as the varicella vaccine. Some intranasal influenza vaccines are also live-attenuated.

Another type of vaccine is the inactivated vaccine, which are made by inactivating the pathogens, so that they cannot cause any symptoms of the disease and are safer than the live-attenuated vaccines. The hepatitis A, pertussis, rabies, and inactivated polio vaccines are all inactivated vaccines. Subunit vaccines, on the other hand, are made of only parts of the pathogen, like proteins, polysaccharides, virus-like particles (VLPs) or of toxins made by the pathogen. They, therefore, cause even less adverse reactions than the inactivated vaccine, however, they do not stimulate the immune system and provide immunity as strongly as the two previous types of vaccines.

Protein vaccines, like seasonal influenza vaccines and the hepatitis B vaccine, toxoid vaccines, like the diphtheria and tetanus vaccine, VLPs, like the human papillomavirus (HPV) vaccine, and polysaccharide vaccines, such as the pneumococcal and haemophilus influenza vaccine, are all examples of different subunit vaccines. (73)

A very new form of vaccine is a mRNA vaccine, in which the mRNA codes for proteins of the pathogen. The mRNA is then translated into the protein and an immune response can be mounted. (74) The COVID-19 vaccines by Pfizer/ BioNTech and Moderna are both mRNA vaccines. (75)

Viral vector vaccines, a combination of both live-attenuated and subunit vaccines, are another new vaccine form. Using a modified form of a virus, like retroviruses and adenoviruses, they deliver the genetic code for an antigen of the pathogen, into body cells. This antigen can then trigger an immune response, when manufactured by the cell into a protein. (73,76) The Oxford/ AstraZeneca and Johnson & Johnson's Janssen COVID-19 vaccines are both viral vector vaccines. (76)

These vaccine types are illustrated further in figure 1, which is a graphic from the Open University. (77)

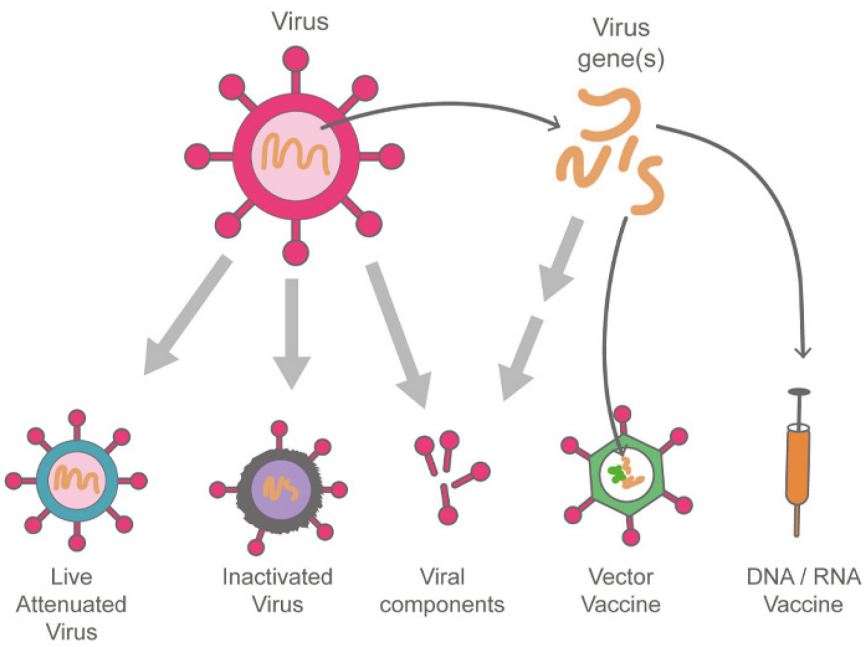

Figure 1: Five different strategies for producing an anti-viral vaccine (77)

1.5.1 Vaccine response

Many of today's vaccines protect against diseases by stimulating the formation of antibodies, known as humoral immunity, but some also stimulate the cell-mediated immunity, resulting in a T-cell response. (78) Antibody titers, which measure the number of antibodies to a specific antigen present in a person's blood, are correlates of protection of the vaccines and are therefore an easy way to determine if a person is immune to a disease. (79) For example, a Hepatitis A antibody titer of 10 mIU/mL protects against the hepatitis A virus in almost all cases. (80) It is not guaranteed, though, that an individual will reach immunity after receiving the recommended doses of a vaccine.

There are many factors that can influence a vaccine response and the maintenance of protective antibody levels in a person. One important intrinsic factor is age. Both newborns and the elderly generally have lower antibody responses after vaccinations. (81) Furthermore, the antibody levels decrease at a faster rate in older individuals. Sex has also been shown to have an effect, as females generally have higher antibody responses to many vaccines than males. (81) Genetics can also influence one's ability to mount antibody responses to vaccines. (81) Comorbidities, like celiac disease and DM in children and chronic kidney and liver disease in adults, have been associated with a lower antibody response. (81) Behavioral factors, like chronic psychological stress, less sleep, and smoking have been shown to have mostly negative associations with antibody formation after vaccination. (81) Acute stress, on the other hand, has been shown to have enhancing effects on both the innate and adaptive immune system and lead to long lasting immunity after vaccination. (82)

1.5.1.1 Stress and vaccine response

Social stressors can upregulate immune response genes, which when activated lead to a release of proinflammatory cytokines. (83) In addition, stress activates the sympathetic nervous system (SNS) and the hypothalamic-pituitary-adrenal (HPA) axis, which leads to the release of glucocorticoids, like cortisol. (84) Glucocorticoids normally work as a negative feedback and suppress the immune response genes, stopping the release of the proinflammatory cytokines and therefore, having an anti-inflammatory effect. The constantly elevated cortisol in chronic stress, however, can lead to glucocorticoid insensitivity, eliminating the anti-inflammatory effect of glucocorticoids, and leading to a persistent proinflammatory state. (83,85) This excessive inflammation leads to an aging of the immune system or "immunosenescence" and the immune system starts to lose the ability to "reshape" to deal with the stressors. (86) Chronic stress and cortisol are also

associated with a reduction in the number of B-lymphocytes in the blood stream. (87,88) Both the chronic proinflammatory state, as well as the changes in B-lymphocytes could alter and impair the immune response to vaccines and result in lower antibody titers in individuals experiencing chronic stress. (78) As previously stated, the mental disorders MDD, SZ, and BD are also characterized by an increase in pro-inflammatory cytokines, most notably IL-6 and TNFa, and an impaired adaptive immune system. Additionally, mental disorders, especially MDD, are associated with an activation and dysregulation of the HPA axis, with cortisol being elevated. (89-91)

Stress has even been linked to the development, progression, and worsening of MDD. (83,85,92) Proinflammatory cytokines have been shown to induce "sickness behavior", which is characterized by lethargy, anhedonia, sleep disruption, and loss of appetite as response to an infection. (93,94) These symptoms are very similar to the symptoms, individuals with MDD experience, suggesting that proinflammatory cytokines, which are elevated in stress, are involved somehow in the development of depression. (85) Furthermore, these cytokines activate the kynurenine pathway, which results in a serotonin reduction and could lead to depression. (85)

The chronic inflammatory state in mental disorders and chronic stress has also been related to dysfunctions in many bodily systems. The excessive inflammation correlates with cardiovascular disease, insulin resistance and DM type 2, obesity, and osteoarthritis (92), providing another explanation for the increased rate of comorbidities in people with SMI. Due to the immune profiles being very similar in individuals with chronic stress and individuals with SMI, it can be hypothesized that just like chronic stress, mental disorders can impair the immune response to vaccines and result in lower antibody titers than in healthy individuals.

1.5.2 Vaccine side effects

Vaccine adverse events can range from mild local symptoms, like pain or swelling at the injection site, to moderate systemic symptoms, like fever or drowsiness, to severe reactions, like febrile seizures, immune thrombocytopenic purpura, intussusception, or serious allergic reactions. (95) Although, mild reactions to vaccines are common, severe side effects are very rare. (95)

Vaccines are an inflammatory stressor and lead to an increase in proinflammatory cytokines. (96) These cytokines can lead to "sickness behavior" and subjective side effects after vaccination, like pain, swelling, headache, or fever. (93,94,97) It has been shown that local reactions were heightened in women who had a greater increase in TNF-a and

macrophage migration inhibitory factor (MIF) after influenza vaccination. (98) MIF has proinflammatory properties and functions in both the innate and adaptive immune system. (99) Additionally, systemic symptoms were increased in women who had marginally higher IL-6 before vaccination and higher MIF post-vaccination. (98) As individuals with mental disorders already have increased proinflammatory cytokines and will possibly see greater inflammation after vaccination, they might experience more side effects.

1.6 Research aims

At the beginning of the vaccination process in early 2021, supplies of the COVID-19 vaccines were limited and, as a result, groups with heightened risk for severe outcomes in case of an infection were being prioritized in the vaccination process. As individuals with SMI have an increased risk, they too should have been prioritized, which has also been argued by DeHert and colleagues. (100) However, up to February 2021 only eight out of 20 countries in Europe specifically mentioned mental illness in their vaccine strategies for COVID-19. (101) Of those, only Germany, the Netherlands, Denmark, and the UK prioritized outpatients with SMI in the vaccination process. (101) It is not enough to prioritize these individuals, though.

Individuals with SMI have been shown to have greater difficulties in accessing health care than healthy individuals. One study (102) reports two to seven times increased odds for experiencing barriers to the access of health care for individuals with MDD, BD, or SZ. The individuals with BD and SZ were also significantly less likely to have a primary health care physician than controls. (102) Barriers that these individuals experience are stigmatization and discrimination, cognitive deficits or symptoms of the SMI that could prevent them from seeking care, tendency of physicians to focus on mental health rather than physical health, poor communication between the patient and physician, inadequacies in being able to handle both behavioral and emotional problems in people with SMI, financial barriers, and lack of health insurance. (103) These barriers could also hinder people with mental disorders in receiving preventative care including vaccinations and, as a result, the vaccination prevalence in this group might be lower. In order for these people to receive a COVID-19 vaccination, they need to be reached and barriers that might prevent them from getting vaccinated need to be overcome.

It is also questionable, if their altered immune systems will be able to mount a sufficient antibody response after vaccination, that provides enough protection from a COVID-19 infection. Furthermore, possible interactions between psychotropic drugs and the COVID-19 vaccinations are of concern.

As there was limited data available at the time of research in January 2021, regarding the COVID-19 vaccine specifically, a literature search was conducted to find data on general prevalence rates of vaccinations, antibody production, and side effects after vaccinations and interactions with psychopharmaceuticals in people with mental disorders.
In addition, individuals with SMI need to be willing to receive the vaccine. Therefore, an online survey study was conducted at the institute for Psychiatry and Psychotherapeutic Medicine of the Medical University Graz in April to May 2021 to receive data on the willingness to be vaccinated, COVID-19 vaccination rate, view on the vaccine, and side-effects that occurred after vaccination in patients with mental disorders. We hypothesized that the willingness and the vaccination rate would be lower in people with SMI, as well as them experiencing more subjective side effects.

1.7 Publications

The findings of the literature review were presented in two reviews. The paper “Outcomes associated with different vaccines in individuals with bipolar disorder and impact on the current COVID-19 pandemic- a systematic review” by Reininghaus et al. (104) has been accepted and published in the European Neuropsychopharmacology. This paper discussed the articles found in the literature review, which focused on effects of vaccines in people with bipolar disorder. My part in this publication was the literature search, as well as reviewing and giving feedback on the manuscript. The second paper "Severe mental disorders and vaccinations – a systematic literature search" by Bonkat, Fellendorf et al. (105) has been accepted and published in the World Journal of Biological Psychiatry. In this paper we focused on all the relevant articles discovered in the literature search and, therefore, on vaccination prevalence rates, effects of vaccines, and interactions with psychopharmaceuticals in individuals with mental disorders. In addition to the research, I took part in the writing process for this review as a shared first author.
The findings of the survey study were discussed in the paper “Willingness to be vaccinated against COVID-19 is equal in individuals with affective disorders and healthy controls” by Fellendorf et al. (106), which is currently in major revision in the Journal Vaccine: X. For this paper, I helped with the construction of the questionnaire, as well as the data gathering process and reviewing of the manuscript.

2. Methods

2.1 Literature review- Vaccinations in individuals with severe mental illness

The database Pubmed was systematically screened for relevant papers by two researchers (Bonkat N. and Fellendorf F.) with the search terms “Vaccin*” AND (“Depress*” OR “Schizophrenia” OR “Bipolar” OR “Mania” OR “Manic”) in January 2021. With the additional [tw] all publications where the keywords were cited in title, abstract, MeSH terms, and MeSH subheadings were shown and searched. To identify potentially missed studies, the bibliographies of found studies and reviews were screened. Studies in English or German language that focused on vaccination rates, efficacy, antibody production, or seroprevalence after vaccination, side effects and psychiatric outcomes after vaccination, and interactions with psychotropic medications in individuals with the mental disorders SZ, depression, or BD were included, as well as studies focusing on the vaccination rates of mothers with mental disorders. Studies that focused on maternal infection in pregnancy, prenatal infections, studies on animals, and preclinical studies were excluded. The reviews were searched for additional studies, but the review itself was not included.

2.2. Survey on COVID-19 vaccination willingness of individuals with affective disorder

2.2.1. Procedure and Participants

The online survey was conducted at the Medical University of Graz, Department of Psychiatry and Psychotherapeutic Medicine. It was sent out via email using the software limesurvey from April 28th to May 20th, 2021. Participants were either former or current inpatients with a diagnosed affective disorder according to the International Statistical Classification of Diseases and Related Health Problems (ICD)-10 or healthy controls (HC) recruited via written invitation or word of mouth. HC included medical students, clinical staff, and circle of acquaintances. The participation in the study was voluntary and survey answers were anonymous. All participants were of legal age and gave their informed consent online before participation. The study has been approved by the local ethics committee (Medical University of Graz, Austria; EK-number: 33-229 ex 20/21) in compliance with the current revision of the Declaration of Helsinki, ICH guideline for Good Clinical Practice and current regulations. See the annex for the full survey. In total, 165 individuals completed the survey and 181 individuals started or opened the survey but did not complete it. Of these, we included 59 patients with AD and 59 HC who were matched for age and sex in the investigation. Individuals with the psychiatric diagnoses’ psychotic disorders, personality

disorders, and addictive disorders were excluded due to the number of individuals with these disorders being too small. Of the individuals with AD, 26 were diagnosed with MDD and 33 with BD. Each group included 41 females and 18 males.

Inclusion criteria were psychiatric patients with current severe, moderate, or light symptoms, as well as remitted patients, who retained the power of judgement and critic. Individuals without psychiatric illness were included for controls. The participants were at least 18 years of age.

Exclusion criteria were refusal to give informed consent, other current severe brain organic diseases like delirium or brain tumor, past severe traumatic brain injury, as well as moderate to severe dementia.

2.2.2. Materials

The self-constructed questionnaire, which can be viewed in the annex, was in German language and collected data on sociodemographic variables, like age, sex, profession, and education status, as well as medical history like current or former psychiatric or somatic illnesses and whether they smoked.

Further, individuals were asked whether they had been tested positive for COVID-19 in the past or were currently infected, how they would subjectively rate their knowledge about the COVID-19 vaccines, their COVID-19 vaccination status (vaccinated?, reason for receiving vaccine? which vaccine?, any side effects), and whether they had an opportunity to get vaccinated in the past, but refused. The variable of the survey willingness to vaccinate in general was calculated by taking the mean of eight items using a five-point likert scale (0 = disagree, 1 = rather disagree, 2 = neutral, 3 = rather agree, 4 = agree). Of these eight items, four reflected a high willingness to vaccinate when answered with a higher number. These were: “the benefit of vaccinations clearly outweighs the risk”; “vaccinations offer good protection for the general population”; “I get vaccinated against tick-borne encephalitis regularly”; “I get vaccinated against influenza regularly”. For the other four statements, which were “the risk of immediate side effects from vaccinations clearly outweighs the benefits”; “the risk of long-term side effects of vaccinations clearly outweighs the benefits”; I see little benefit for the general population”; “I am concerned that vaccinations interact with other medication that I take”, a higher number reflected a lower willingness to get vaccinated. These were therefore recoded. Internal consistency was given for the items of this scale, shown with a Cronbachs alpha of .85.

The same method was used to contruct the main variable willingness to be vaccinated against COVID-19. The mean of nine items, which had a five-point likert scale option (0 = disagree,

1 = rather disagree, 2 = neutral, 3 = rather agree, 4 = agree) was calculated. These nine items were : “the benefit of the COVID-19 vaccination clearly outweighs the risk”; “the risk of the vaccination clearly outweighs the benefits” (recoded); “I want to prevent a personally serious COVID-19 course with a vaccination”; I might want to help protect others with my own vaccination”; “I am concerned that the vaccination will interact with other medication that I take” (recoded); “It takes little effort for me to get vaccinated”; “I generally do not see any benefit in vaccinations” (recoded); “I will mainly get vaccinated because relatives advise me to do so”; “I will mainly get vaccinated because doctors advise me to do so”. The final two statements which assessed whether the individual would get vaccinated if they receive advise or a recommendation from someone else, implied extrinsic motivated willingness to get vaccinated, while the rest implied internal motivated willingness. Individuals could also share other reasons for or against getting vaccinated in a free text. Again, internal consistency was given for the items on the scale (Crohnbach’s alpha=.86).

To determine the hesitancy of participants towards getting vaccinated, the following questions were asked: “How likely is it that you will be vaccinated against COVID-19 as soon as you get the chance?”; “How likely is it that you will be vaccinated against COVID-19 within the next year?”; “How likely is it that you will be vaccinated against COVID-19 within five years?”. These questions could be answered using a scale from 0 to 100%. Additionally, individuals were asked, if they liked to wait to get vaccinated and when answered with yes, the following statements were asked with a five-point Likert scale option (0 = disagree, 1 = rather disagree, 2 = neutral, 3 = rather agree, 4 = agree): “I am worried about immediate side effects”; “I am worried about long-term side effects”; “I currently see no personal benefit as I have already had COVID-19”; “I do not see personal benefit as I am not expecting a severe COVID-19 course”; “I currently do not see a personal benefit as I generally do not see any benefits in vaccinations”; “I fear that the vaccination will not be effective against infection but only against severe COVID-19 courses and I personally do not expect this”; “It is too difficult to get the vaccination”; “Vaccine development was faster than other vaccine approvals”; “In my opinion the vaccines have not been tested enough”; “other reasons”.

2.2.3. Statistical analyses

The statistical analysis was conducted using the IBM Statistical Package for Social Sciences (SPSS) version 25. Differences between the two groups AD and HC were assessed using the Chi-square test for nominal data. For metric data, the differences, or lack thereof, were tested for using t-tests. This pertained mainly to the willingness to be vaccinated in general and

against COVID-19. To assess the underlying structure of the willingness to be vaccinated against COVID-19 items, an exploratory principal axis factor analysis was used. Two factors were obtained which were the intrinsic and extrinsic motivated willingness. For both factors, t-tests were used to assess the differences between the AD and HC group. Error probabilities below .05 were accepted.

Values of the item analysis including item difficulty and item discrimination values for the variable *willingness to be vaccinated against Covid-19* can be found in Table 2.

Table 2: Item analysis of the variable *willingness to be vaccinated against COVID-19*

Variable	Item Difficulties	Item Discrimination
Item 1: *Benefit outweighs risk*	84.50	.66
Item 2: *Risk outweighs benefit (recoded)*	66.36	.47
Item 3: *Prevention of a serious COVID-19 course*	80.75	.72
Item 4: *Help protect others with own vaccination*	84.00	.74
Item 5: *Concerned of interaction with other medication (recoded)*	81.97	.38
Item 6: *Little effort to get vaccinated*	84.50	.63
Item 7: *Mainly because relatives advise*	20.50	.22
Item 8: *Mainly because doctors advise*	30.50	.36
Item 9: *Generally no benefit in vaccinations (recoded)*	90.59	.65

Note. N = 118. Item coding from 0 to 4.

The suitability of the data for the exploratory principal axis factor analysis across all items of the *willingness to be vaccinated against COVID-19* variable, was assessed in advance. The Kaiser-Meyer-Olkin (KMO) criterion verified an adequate sample for carrying out the analysis (KMO = .83), and all KMO values for the single items were greater than .53, thereby above the acceptable threshold-value of .50. Bartlett's test of sphericity indicated that correlations between all items were adequate for factor analysis ($\chi^2(36) = 514.37$, $p < .001$). An initial analysis was administered to obtain eigenvalues for each factor. Kaiser's eigenvalue extraction criterion and the scree plot suggested the extraction of two factors (intrinsic and extrinsic motivated willingness to be vaccinated against COVID-19), which explained 56.09 % of the total variance. Table 3 shows the unrotated factor loadings. Normal

distribution was not given for the factor of internal and external motivated willingness, so the following analyses regarding this factor were calculated with 95%-BCa Bootstrapping confidence intervals.

Table 3: Unrotated factor loadings for *willingness to be vaccinated against COVID-19* items

Variable	Factor loading	
	Factor Internal Motivation	Factor External Motivation
Item 1: *Benefit outweighs risk*	.81	-.10
Item 2: *Risk outweighs benefit (recoded)*	.58	-.17
Item 3: *Prevention of a serious COVID-19 course*	.86	-.01
Item 4: *Help protect others with own vaccination*	.82	-.02
Item 5: *Concerned of interaction with other medication (recoded)*	.50	-.21
Item 6: *Little effort to get vaccinated*	.75	-.06
Item 7: *Mainly because relatives advise*	.16	.74
Item 8: *Mainly because doctors advise*	.33	.71
Item 9: *Generally no benefit in vaccinations (recoded)*	.75	-.11

Note: Extraction method = Principal axis factoring

3. Results

3.1. Literature review- Vaccinations in individuals with severe mental illness

The literature search found 44 results, which met the inclusion criteria. Two of those were excluded due to them being reviews. 19 studies focused on vaccination prevalence rates, four studies on vaccination rates of children of mothers with mental disorders, one study on the willingness of SZ patients to be vaccinated, 16 studies on effects of vaccines in individuals with mental disorders, and two studies on interactions between vaccinations and the psychotropic medication clozapine. See figure 2 for more details on the screening process.

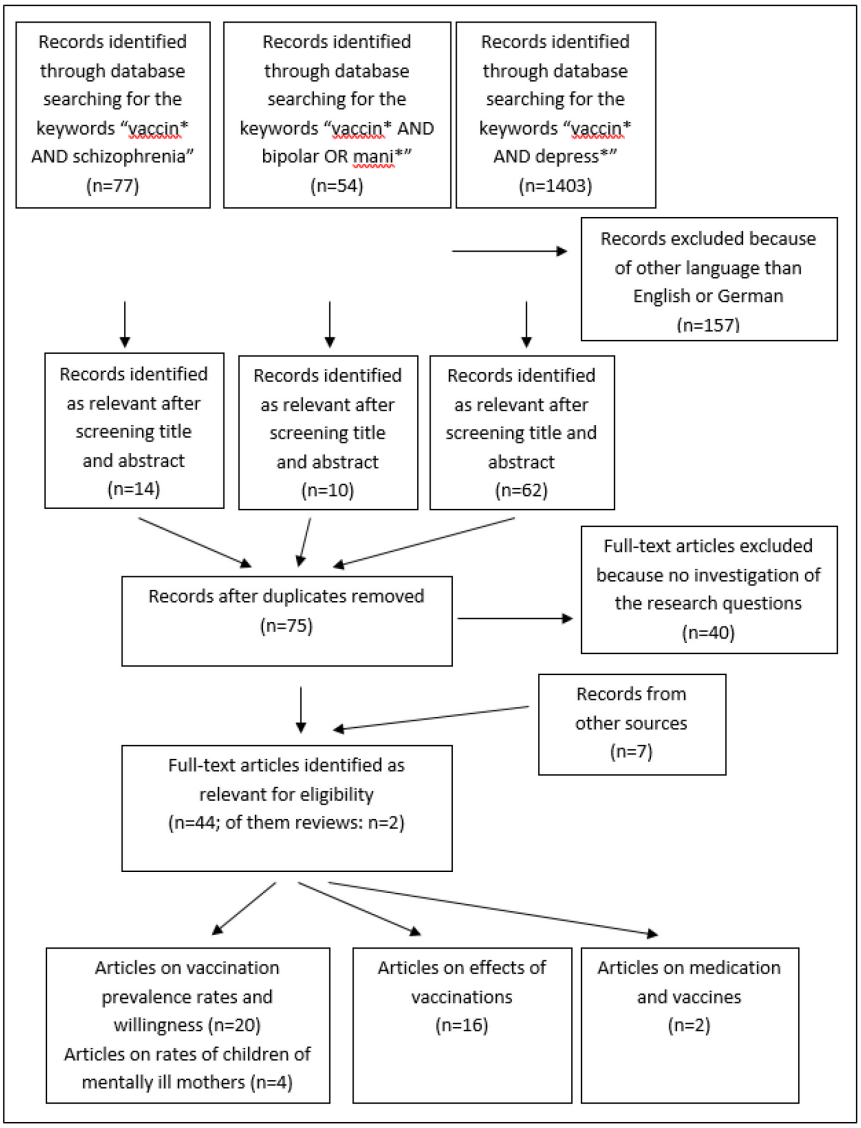

Figure 2: Screening process for literature search

3.1.1. Prevalence rates

There was one study found, which investigated the willingness to vaccinate in SZ patients, as well as 19 studies which researched the prevalence rates of different vaccinations in people with mental disorders. Additionally, four studies looked at vaccination rates in children of mothers with mental illnesses.

3.1.1.1 Lower willingness to vaccinate in schizophrenic patients compared to controls

A cross-sectional questionnaire study (107) conducted in Australia investigated the views of patients with SZ on protective measures against the swine flu compared to controls. 74.2% of the SZ patients were at least moderately willing to be vaccinated, compared to 80.1% of controls, resulting in a significantly reduced OR of 0.41 for willingness to be vaccinated when having SZ. Barriers to vaccination, which were reported significantly more often by subjects with SZ than controls, were concerns about side effects, cost of the vaccine, and difficulties with transportation to the clinic.

3.1.1.2 Lower vaccination rates in people with mental disorders compared to controls

A total of eight studies, of which six were conducted in the US, one in South Korea, and one in Great Britain, reported lower vaccination rates in people with mental disorders. A cross-sectional survey study (108) conducted via face-to-face interviews in the Los Angeles area on African Americans who were at least 65 years of age, found an OR=0.92 for people having a higher number of depressive symptoms to have received an influenza vaccination in the past year. Additionally, a survey study (109) carried out in the US used data from the National Behavior Risk Factor Surveillance System, found an OR of 0.81 for participants aged 18 or older with poor mental health to receive an influenza vaccination. Contrarily, when comparing depressed and nondepressed individuals, they calculated an OR of 1.29 for depressed participants to receive the influenza vaccination. Another survey study (110) from the US, that used data from the 1999 National Health Interview Service, determined an OR of 1.24 for depressed patients to have failed to receive the influenza vaccination. The odds for depressed individuals who were not treated was even higher (OR=1.51). Interestingly, the odds decreased for patients receiving specialty treatment (OR=1.11). Patients with primary care treatment were less likely than nondepressed to have failed to receive the vaccination (OR=0.95). Another American study (111) used data from 1998 to 1999 of veterans who had medical diagnoses like COPD or DM and made at least three outpatient visits to a general or specialty medical clinic in the past year. This

study found an OR of 0.95 and an OR of 0.90 for individuals with psychiatric disorders to receive the pneumococcal and the influenza vaccine respectively. Furthermore, an OR of 0.70 to receive the influenza vaccination for individuals with psychological distress was found by Thorpe and colleagues (112), who analyzed data from the Medical Expenditure Panel survey in the US of individuals aged 65 years or older. Psychological distress includes depressive symptoms and individuals were characterized with high psychological distress if they had a score below 42 on the Mental Component Summary score of the SF-12. A cross-sectional study (113) conducted in an outpatient psychiatric clinic for severely mentally ill patients in Alabama, measured an influenza vaccination rate of 28.4% in this group, compared with a rate of 40.9% in the general population. The odds of the psychiatric patients to receive a flu shot was increased significantly, however, when having a recommendation from their healthcare provider (OR=4.12).

The South Korean study (114) found an inverse association between depressive mood and influenza vaccination receipt in adolescents with asthma (OR=0.77). Finally, the British study (115), which analyzed data from the UK Medical Research Council of people aged 74 years and older between 1995 and 2000, found a significant negative association between depressive symptoms in women and influenza vaccination. 61.2% of women with a score over 5 on the Geriatric Depression Scale (GDS), 59.2% with a GDS of 4-5, and 66.6% with a lower GDS lower than 4 were vaccinated (p=0.034). This study, however, did not detect a statistically significant association between the GDS score in men and their influenza vaccine receipt, even though there was a negative trend between the scores and the vaccination rates. One study (116) reported both lower and higher vaccination rates for specific vaccinations. This study measured lower rates of the pertussis, Hepatitis A, Hepatitis B, and MMR vaccines in 392 individuals with severe and persistent mental illness (SPMI) in the US compared to the general population, but higher vaccination rates of the influenza and pneumococcal vaccine in this group.

Additionally, three studies found lower odds for children of mothers with mental disorders to be vaccinated. Turner and colleagues (117) observed an OR of 4.92 for mothers with poor depression to be late-starters or non-initiators for their children's vaccinations in a cohort of 157 mothers recruited in 1997 in Australia. A population-based cohort study (118), which included 850,243 born between January 1., 2000 to August 31., 2013 and 517,107 mothers in Denmark determined the relative risk (RR) for children of mothers with past or recent depression to have not received the MMR and diphteria/tetanus/pertussis/polio (DTap-IPV) vaccinations. They detected a RR of 1.06 and

1.12 for children to have not received the MMR vaccination of mothers with past and recent depression respectively. Additionally, they calculated a slightly lower, but still significant, RR of 1.03 and 1.07 for children to have not received the DTap-IPV vaccination of mothers with past and recent depression respectively. Lastly, a retrospective cohort study (119) from the UK followed 479,949 mothers and their children born between 1993 and 2015 for a two-year period. They observed an aOR of 0.86 for children of mothers with mental illness to have received all vaccinations at the two-year interval. The aOR was even lower at 0.71 for children of mothers with psychotic disorder. Conversely, one study did not find a relationship between depressive symptoms of mothers and the vaccination rate of their children. This cross-sectional study (120) investigated 582 randomly selected low-income Brazilian children between January and December 2002.

3.1.1.3 Equal or higher vaccination rates in people with mental disorders compared to controls

Many studies, however, did not report lower vaccination rates in the group of the mentally ill than the general population. The literature search found four studies, which found no association between mental health and vaccination receipt, three studies which found both the same or higher vaccination rates in the mentally ill group, as well as two studies which reported solely higher vaccination rates in the group with mental disorders compared to controls. A survey study (121), which included questionnaires from ten countries in Europe including Austria and Germany, did not find an association between depressive symptoms and influenza vaccination receipt in the 15,380 individuals over the age of 50 years, who answered the questionnaire about preventive services. Additionally, a nonsignificant OR of 0.94 (p=0.94), for individuals with frequent depressive mood to receive the influenza vaccination, was observed by Kwon and colleagues (122), who examined data from 3567 individuals aged 65 years or older in South Korea from 2007 to 2009. Green and Pope (123) did not find a significant association between depressive symptoms and influenza and pneumonia vaccination receipt in 2369 males and 3472 members of the Kaiser Permanente Northwest in 1995 in the US either. A questionnaire study (124) using data from 120 COPD patients in Magdeburg, Germany from 2015 to 2017 reviewed the influenza vaccine receipt in this group. 10% of the vaccinated individuals and 5% of the nonvaccinated individuals were depressed, which was not a significant difference. Investigating the influenza and pertussis vaccination receipts in pregnant women, a prospective cohort study (125) in Adelaide Australia, on one hand, determined a non-significant OR of 0.99 for women with high depressive scores to receive the influenza

vaccine. On the other hand, they observed significantly higher odds for pregnant women with high depressive scores to receive the pertussis vaccination (OR=1.14). A cross-sectional study (126) of adults in Germany analyzed the correlation between depression and preventative service use. They found increased odds for women with diagnosed depression (aOR=1.3, $p<0.001$) and not quite significant higher odds (aOR=1.2, $p=0.051$) for men with diagnosed depression to receive the influenza vaccine, but no significant association between the receipt of the pertussis and tetanus vaccine and diagnosed depression in men and women. Furthermore, a retrospective cohort study (127) conducted in the US using data from 4,102 participants aged 65 to 80 years in the US detected an aOR of 1.47 for individuals with any mental health diagnoses to be vaccinated against influenza, with an even higher aOR of 1.77 in a subset with physical comorbidities. Interestingly, individuals with depression and anxiety without physical comorbidities had a non-significant aOR of 0.88. Antidepressant recipients had an aOR of 1.94. The two studies that reported solely higher vaccination rates in the mentally ill population were a retrospective study (128) of 550 Native Americans in the Seattle Area and a cross-sectional survey study (129) in 3,384 American veterans with either spinal cord injury or disorder. In the first study (128) 15% of the 51% of individuals who had never received the influenza vaccine had depression, while a much higher percentage (37%) of the 49% that had received it, were depressed. Similarly, 37% of the 21% that had received the pneumococcal vaccine had depression and only 23% of the 79% that had not received it, were depressed. The second study (129) observed an OR of 1.29 for the veterans with depression to receive the influenza vaccine.

Finally, one study was found, which compared the influenza vaccine prevalence among different mental disorders. This interview study (130) conducted in Sacramento, California on 221 adult participants with either primary psychotic disorder (PPD), BD, or MDD from January 2005 to May 2007, found that individuals with PPD had a slightly higher vaccination rate (32%), than people with MDD (22%) or BD (17%).

3.1.2. Immunogenicity of vaccines

The literature search found ten studies that investigated antibody titers in people with the mental disorders depression, SZ, BD, or anxiety. These studies presented conflicting results.

3.1.2.1 Lower antibody titers in people with mental disorders compared to controls

On one hand, some studies found significantly lower seroconversion rates, meaning the development of antibodies in the blood after being presented with an antigen (131), as well as lower peak antibody titers in the mentally ill population. One interventional study (132), in which 288 haemodialysis patients were vaccinated against Hepatitis B, measured the depressive mood using the Beck Depression Inventory (BDI) in the patients and compared the 37 individuals who did not seroconvert, meaning they had an anti-HBs titer of less than 10 mIU/mL, to the 151 individuals who did seroconvert. The BDI measures depressive symptoms, by asking patients to self-report on 21 items. It ranges from 0 to 63 points, with 63 being the highest level of depression (133). This study (132) found that the BDI was negatively associated with the antibody titers with an OR of 0.903. The average BDI score in the seroconversion group was 17.9+ 9.0 and the BDI score in non-seroconversion group was 22.2+ 10.4, with a p-value of 0.014. A slightly older interventional study (134) from 1994, measured antibody titers after Hepatitis vaccination in 100 institutionalized psychiatric patients. 73 of these patients did not seroconvert. The geometric mean of the antibody titers two months after the third dose of vaccine was 3.69 (2.56-5.31) mIU/mL, so lower than the protective level of 10 mIU/mL. The non-responder rate of 73% in these psychiatric patients was much higher than the ones reported in the general population ranging from about 10-20%. (135-138) The majority of these patients had SZ, while seven suffered from mania, and 15 from depression.

An even older study (139) from 1949 compared the maximum serum titers of 22 institutionalized male SZ patients with a slightly younger group of 17 healthy controls after pertussis vaccination, with the SZ patients developing significantly lower antibody titers. A randomized double blind, placebo controlled study (140) from 2013 compared 40 MDD patients with 52 healthy controls. 12 medicated MDD patients, who received antidepressant medication, 12 unmedicated MDD patients and 30 controls were injected with the shingles vaccine, the rest received a placebo. The immunity against the varizella zoster virus (VZV) was determined by measuring the VZV-specific responder cell frequency (VZV-RCF), which was measured before and after vaccination. The VZV causes chickenpox after first exposure and remains dormant in the sensory nerve roots, where it can reactivate later in life, when immunity against it declines, and cause shingles. (141) A significant increase of 69.7% (31.4% to 119.2%) from baseline in VZV-RCF was found in the controls and an even larger increase of 288.1% (90.9% to 689.0%) in MDD

patients being treated with antidepressants. Even though they had the lowest baseline levels to start with, the VZV-RCF levels in MDD subjects not receiving treatment, saw a -32.9% (-65.5% to 29.7%) change, which was not statistically significant. Contradictory to these results, a cross-sectional study (142), which observed whether 176 participants with mood disorders, either BD, current or remitted MDD, and 175 non-depressed controls were seropositive (antibody titer immunoglobulin (Ig) G≥10IU/L) for measles, found an aOR=0.39 (0.18-0.85) for medicated MDD individuals to be seropositive compared to unmedicated MDD individuals (p=0.018). The study also found lower rates of seropositivity in the remitted MDD (rMDD) individuals (aOR=0.50 (0.26-0.97), p=0.038) and the current MDD (cMDD) individuals (aOR=0.47 (0.24-0.90), p=0.021) compared to controls. Individuals with BD had a lower percentage of individuals seropositive for measles, but a higher one than MDD individuals. These differences were not statistically significant, though. Overall, individuals with mood disorder had lower odds (aOR=0.53 (0.31-0.88), p=0.015) for being seropositive than controls.

3.1.2.2 Higher antibody titers in people with mental disorders compared to controls

On the other hand, a few studies found higher antibody titers in SZ patients and people with depressive symptoms. A study (143), in which 10 SZ patients after an acute psychiatric episode, 22 depressed patients, and seven healthy controls were vaccinated against cholera, observed significantly higher titers after vaccination in SZ patients than in both depressed patients and controls, who did not significantly differ in antibody titers. Another study (144), investigating antibody titers in 85 healthy medical students with different levels of depressive symptoms after Hepatitis B vaccination, found that individuals with higher levels of depression had higher peak antibody titers (r=0.26, p=0.009).

3.1.2.3 Equal antibody titers in people with mental disorders compared to controls

Some studies did not find any differences in antibody responses in individuals with depression and SZ compared to controls. A cross-sectional study (145) measuring Hepatitis B surface (HBs) antibody levels in 415 vaccinated SZ patients and 3,038 controls did not find a significant difference in these groups. They did find higher Hbs antigen levels in the SZ group, though, suggesting the rate of HBV infection is higher in the SZ group. (146) This means that even though these individuals were routinely immunized, they still had a higher chance of contracting HBV than individuals without SZ. Moynihan and colleagues

(147), who studied factors associated with antibody responses after influenza vaccination in 37 nursing home residents over the age of 65, did not find an association between depression in these individuals and their response to the vaccine. Another study (148) conducted by Glaser and colleagues measured the response to influenza vaccination in 119 older adults with the mean age of 71 years. Between the 48 individuals who responded with a fourfold antibody titer increase after vaccination, meaning they seroconverted, and the 71 who did not seroconvert, there was no difference in depressive symptoms (p=0.94).

3.1.3 Inflammatory response and side effects of vaccines

3.1.3.1 Higher inflammatory response to vaccines in people with depression compared to controls

The search found three studies, that investigated inflammation in individuals with depression or depressive symptoms after influenza vaccination. A study (99) measuring MIF in the serum of 22 pregnant women before and one week after influenza vaccination, found that women with high depressive symptoms had significantly higher MIF than women with no or only minimal depressive symptoms. The depressed subjects had an average pre-vaccination concentration of 0.31 log ng/ml MIF and a post-vaccination concentration of 0.47 log ng/ml MIF, while the nondepressed subjects had concentrations of 0.24 log ng/ml MIF at both points, so unchanged by the vaccine. The study by Glaser and colleagues (148) also investigated IL-6 titers in the individuals prior to and after vaccination. In the depressed group, 3% saw no change in IL-6 after vaccination, 38% had lower IL-6 levels after vaccination, and 59% had higher IL-6 levels after vaccination, so there was a significant increase in inflammation in this group (p=0.02). The nondepressed group, on the other hand saw no significant increase in IL-6 as 46% had lower and 54% had higher IL-6 levels after vaccination (p=0.86). IL-6, Cortisol, adrenocorticotropic hormone (ACTH), and TNFa levels were measured before and one and six months after influenza vaccination in 10 individuals with minor depression or MDD and 10 controls in another study. (149) TNF-a was found to be elevated one month after vaccination in the depressed patients. Additionally, significantly higher IL-6 levels were found in depressed patients, as well as higher cortisol and lower ACTH levels at all three points. This provides further evidence for an activated and dysregulated HPA-axis in depression. The depressed subjects had a significantly higher rate of being positive for anti-cytomegalovirus (CMV) IgG than the controls. After controlling for CMV titers, most of the inflammatory differences between the two groups disappeared, suggesting that the depressed subjects had higher inflammatory markers due to the chronic CMV infections. All these studies found

greater inflammation at base line, as well as a greater inflammatory response to influenza vaccination in depressed patients.

3.1.3.2 Side effects after vaccination in people with depression

Furthermore, four studies researched side effects or changes in mood in subjects with depression. A randomized placebo-controlled study (150) investigated the association between depression and perceived side-effects after influenza vaccination. The 33 individuals with depression were significantly more likely than the 662 individuals without depression to complain of one or more side effects ($p<0.01$). A research group trying to identify risk factors associated with paresthesia after administration of the 2009 flu pandemic vaccine in Canada, found an increased OR of 1.90 for individuals having a medical history of depression and an OR of 2.11 for individuals with current depressive symptoms. (151) A single-blind placebo controlled randomized cross-over study (152) investigated the effect of typhus vaccination and/ or the Trier Social Stress Test (TSST) on mood and biomarkers of inflammation in 21 women with rMDD and 18 healthy controls. They found a significant reduction in mood in the women with rMDD after vaccination without TSST (p=0.008), as well as a significant increase in the proinflammatory cytokine Interferon-gamma (IFN-y) after vaccination with TSST. Furthermore, a pilot investigation (153) in Australia studied whether individuals with depression or anxiety would have greater "sickness behavior" after influenza vaccination. They determined positive and negative affect in 83 healthy subjects and 29 subjects with depression and/or anxiety before and after vaccination. The depressed subjects had a more pronounced reduction in positive affect scores after vaccination than the controls, however there was a decrease in both groups. Low positive affect is anhedonia, which is a "sickness behavior".

3.1.4. Vaccinations and psychopharmaceuticals

In the search, two studies were found that investigated interactions between the antipsychotic clozapine and vaccines. An open label study (154) investigated the effect the influenza vaccination has on serum clozapine and CRP levels in 16 subjects with SZ taking clozapine. There was no significant change seen in the concentrations of clozapine and CRP at any point after vaccination. However, two patients were excluded from analysis due to abdominal pain and pharyngitis, who experienced an increase in both the clozapine and CRP serum concentrations, but that was likely due to the infections. Furthermore, a cross-sectional case control study (155) researched the effect clozapine has on antibody levels for haemophilus influenzae type b, tetanus, and pneumococcal polysaccharide in 123 SZ patients taking clozapine and 113 SZ clozapine naïve patients. Although, a large

number of subjects had IgG antibody levels for all those pathogens below a protective level, there was not a significant difference seen between those two groups. Clozapine treated patients, however, did on average have 28 IU/ml lower levels of pneumococcal-specific IgA and 26 IU/ml lower pneumococcal-specific IgM than the clozapine-naïve patients (p<0.001).

3.2. Survey on COVID-19 vaccination willingness of individuals with affective disorder

3.2.1. Cohort description

The two groups AD and HC, which each consisted of 59 individuals, were matched for sex and age. As shown by figure 3, the majority of the individuals in both groups were between 30 and 60 years of age. Table 4 displays sociodemographic and clinical data of the participants. The two groups differed in their current occupation, as shown by a p-value less than .001. In the AD group, less individuals were employed or currently in training than in the HC group. Additionally, a larger percentage of people with AD were unemployed, retired, or in rehabilitation than HC. There were no significant differences between current somatic disorders between the two groups. The only exception was endocrine diseases, of which five individuals from the AD group suffered, but none from the HC group (p=.022). However, endocrine diseases are not seen as a risk factor for a more severe course of COVID-19 infections, like the other somatic disorders. Surprisingly, there was no significant difference between the number of smokers in the group, even though smoking is generally more prevalent in the population of the mentally ill. (14,15) A little more than half of the AD group suffered from BD and the rest from unipolar depression.

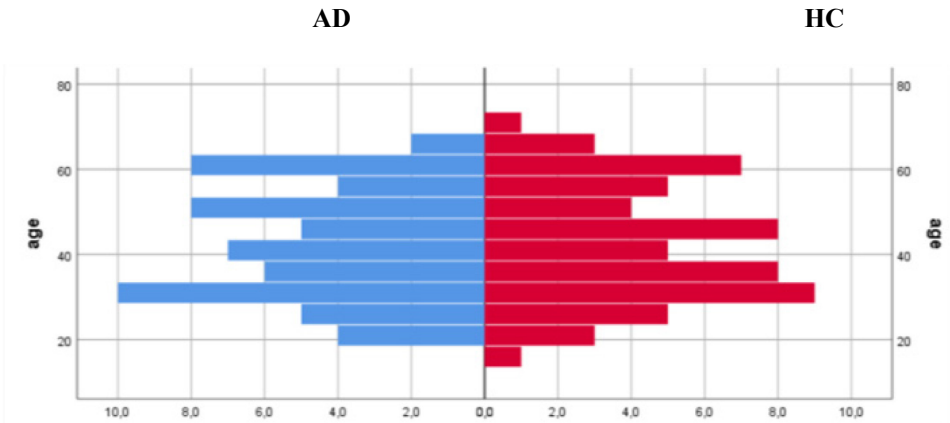

Figure 3: Age of participants with affective disorders (AD) and healthy controls (HC)

Table 4: Sociodemographic and clinical data of participants with AD and HC

	AD ***n* = 59**	**HC** ***n* = 59**	***statistics***	***p***
Sex *n (%)*			$X^2(1) = 0.00$	1.000
- Female	41 (69.5)	41 (69.5)		
- Male	18 (30.5)	18 (30.5)		
Age *M (SD)*	42.15 (13.41)	42.66 (13.78)	$T(116) = 0.20$	.839
Highest education *%*			$X^2(4) = 6.37$	.383
- Compulsory school	3.4	1.7		
- Completed apprenticeship	11.9	5.1		
- Vocational school	8.5	8.5		
- High school/baccalaureate	28.8	30.5		
- University	47.4	54.3		
Current occupation *%*			**$X^2(6) = 27.71$**	**<.001**
- Unemployed	13.6	3.4		
- employed	32.2	62.7		
- Self-employed	5.1	10.2		
- In training/ school	3.4	11.9		
- Retirement	28.8	8.5		
- Rehabilitation period	13.6	0.0		
- Grace period	3.4	3.4		
Somatic disorder				
- Hypertension	13.6	10.2	$X^2(1) = 0.32$	.569
- Asthma	3.4	3.4	$X^2(1) = 0.00$	1.000
- COPD	0.0	1.7	$X^2(1) = 1.01$	.315
- Acute airway/lung disease	1.7	0.0	$X^2(1) = 1.01$	.315
- Diabetes mellitus	6.8	1.7	$X^2(1) = 1.88$	.170
- Coronary heart disease	3.4	0.0	$X^2(1) = 2.03$	.154
- Immunosuppressive treatment	0.0	3.4	$X^2(1) = 2.03$	.154
- Endocrine disease	8.5	0.0	**$X^2(1) = 5.22$**	**.022**
Smoking *%*	30.5	23.7	$X^2(1) = 0.69$	.408
Principal psychiatric disorder *%*				
- Unipolar depressive disorder	44.1			
- Bipolar disorder	55.9			
Psychiatric comorbidity *%*				
- Anxiety disorder	27.1			
- Eating disorder	8.5			
- Substance abuse disorder	6.8			

- Personality disorder	15.3

Note: AD = affective disorders; HC = healthy controls; M = mean; SD = standard deviation; COPD = chronic obstructive pulmonal disease

3.2.2. Differences between groups

In the AD group two and in the HC group five individuals were infected with COVID-19 in the past (p=.275). At the time of the study, no one was infected in either group. Table 5 shows details to the willingness to get vaccinated, as well as the COVID-19 vaccination status of the participants. There was a significant difference in the willingness to get vaccinated in general between the two groups, with a slightly higher willingness in the HC group. The subjective knowledge of the individuals in the two groups about the COVID-19 vaccines did not differ significantly, with most people in both groups rating their knowledge as rather high or very high. Only two people in the AD group and none in the HC group rated their knowledge as very low.

In the AD group, six people and in the HC group nine people had the option to receive a vaccination in the past, but refused, which was not a significant difference. Unlike the willingness to receive vaccinations in general, the willingness to receive a COVID-19 vaccine did not differ between the two groups. However, the means of the willingness to receive the COVID-19 vaccine in both groups were slightly lower than the means of the willingness to get vaccinated in general. In addition, the individuals who were not yet vaccinated, displayed a high desire to get vaccinated as soon as possible, with the mean being 78.13% and 76.00% (measured on a scale from 0 to 100%) in the AD and HC group respectively. This desire increased only slightly when asked about the next year and the next five years.

Significantly more individuals in the HC group were already vaccinated against COVID-19 than in the AD group. More details to the already vaccinated individuals can be found in table 6. About the same percentage of individuals in both groups were vaccinated with the Biontech/ Pfizer vaccine, while more of the HC group were vaccinated with AstraZeneca and more of the AD group with Moderna. A large amount of the HC group was vaccinated because of working in health care and very few in both groups were vaccinated because of an increased risk of a severe illness course. More specifically, only 6.8% of the AD group, but 32.2% of the HC group were prioritized in the vaccination process because of working in health care. Other reasons for prioritization were risk of severe illness course (AD 3.4% vs HC 1.7%), age (AD 1.7% vs HC 3.4%), pedagogical work (AD 5.1% vs HC 3.4%), and no specific reason (AD 10.2% vs HC 3.4%). There was

no difference in the side effects the individuals suffered from the vaccine between the two groups.

Table 5: Differences between AD and HC in COVID-19 vaccination status and willingness to get vaccinated

	AD ***n* = 59**	**HC** ***n* = 59**	***statistics***	***p***
Subjective knowledge about COVID-19 vaccination *%*			$X^2(4) = 2.70$	.610
- Very low	3.4	0.0		
- Rather low	8.5	6.8		
- Neither high nor low	20.3	23.7		
- Rather high	49.2	45.8		
- Very high	18.6	23.7		
Already vaccinated *%*	25.4	44.1	**$X^2(1) = 6.03$**	**.014**
Option for a vaccination in the past and refusal *%*	10.2	15.3	$X^2(1) = 0.69$	.407
Willingness for vaccination in general *M (SD)* [a]	2.71 (0.94)	3.07 (0.85)	**T(116)=2.20**	**.030**
Willingness for vaccination against COVID-19 *M (SD)* [b]	2.69 (0.76)	2.88 (0.76)	$T(116) = 1.41$	.161
Internal motivated willingness to get vaccinated *M (SD)*	-0.12 (0.96)	0.08 (1.03)	$T(114) = 1.10$	.273
External motivated willingness to get vaccinated *M (SD)*	0.07 (0.94)	-0.01 (0.86)	$T(114) = -.48$	.635
Either already vaccinated or willing to get vaccinated as soon as possible *M (SD)* [b]	82.14 (33.84)	86.41 (30.22)	$T(116) = 0.72$	.471
Willingness for vaccination of the currently not vaccinated participants[c]				
- As soon as possible	78.13 (36.87)	76.00 (35.80)	$T(59) = -.22$	.826
- Within the next year	80.71 (35.09)	79.70 (34.83)	$T(59) = -.11$	.913
- Within the next five years	83.66 (34.28)	82.91 (30.73)	$T(59) = -.09$	.932

Note: AD = affective disorders; HC = healthy controls; [a]=mean of five-point likert scale: "the benefit of vaccinations clearly outweighs the risk", "vaccinations offer good protection for the general population", "I get vaccinated against tick-borne encephalitis regularly", "I get vaccinated against influenza regularly", "the risk of immediate side effects from vaccinations clearly outweighs the benefits" (recoded), "the risk of long-term side effects of vaccinations clearly outweighs the benefits" (recoded), I see little benefit for the general population" (recoded), "I am concerned that vaccinations interact with other medication that I take" (recoded); [b] = mean of five-point likert scale: "the benefit of the COVID-19 vaccination clearly outweighs the risk", "the risk of the vaccination clearly outweighs the benefits" (recoded), "I want to counteract a personally serious COVID-19 course with a vaccination", I might want to help protect others with my own vaccination", "I am concerned that the vaccination interact with other medication that I take" (recoded), "It takes little effort for

me to get vaccinated", "I will mainly get vaccinated because relatives advise me to do so", "I will mainly get vaccinated because doctors advise me to do so", "I generally do not see any benefit in vaccinations" (recoded); [c] = response scale 0-100%

Table 6: Details to already vaccinated individuals

	AD ***n* = 15**	**HC** ***n* = 26**	***statistics***	***p***
Which COVID-19 vaccine? %			$X^2(2)= 4.62$	.100
- Moderna	26.7	3.8		
- Biontech/ Pfizer	40.0	46.2		
- Astrazeneca	33.3	50.0		
Side effects after vaccine *%*			$X^2(6) = 4.87$	.561
- None	20.0	26.9		
- Very mild symptoms (fatigue) for a couple hours	6.7	15.4		
- Mild symptoms for one to two days	20.0	7.7		
- Moderate symptoms with restriction in daily routine up to two days	20.0	11.5		
- Moderate symptoms for more than two days	6.7	11.5		
- Severe symptoms (fever, reduced performance) up to two days	6.7	19.2		
- Severe symptoms for more than two days	20.0	7.7		

Note: AD = affective disorders; HC = healthy controls

3.2.3. Reasons against vaccination

Table 7 and the figure 4 show reasons why individuals would rather wait to receive a COVID-19 vaccination. Many in both groups, but more in the AD group, stated that fears of both acute and long-term side effects, as well as the fast development of the vaccine with too little testing as the main reasons. Only very few agreed with the statement, that they see no benefit in vaccines in general or that they wouldn't get vaccinated because they already had COVID-19 in the past. Reasons that were given in the free text by individuals in the AD group were "low risk of infection because of little social contact", "trust in immune system", and "intervention in human genetics". The HC group gave the following free text answers: "completely new drug approval in short time", "severe COVID-19 courses are rare and expected more in elderly; therefore, no need to risk side effects for the

whole population", "would like to choose the vaccine", and "not sufficiently informed about consequences of vaccination in terms of fertility and genetic defects".

Table 7: Reasons for waiting to get vaccinated against COVID-19 of individuals with AD and HC

	AD ***n* = 13**	**HC** ***n* = 10**	***statistics***	***p***
Fears of acute side effects *M (SD)*	3.23 (0.832)	2.60 (1.174)	*T*=-1.510	.146
Fears of long-term side effects *M (SD)*	3.85 (0.376)	3.00 (1.414)	*T*=-2.077	.050
COVID-19 in the past *M (SD)*	0.54 (1.198)	1.50 (1.581)	*T*=1.662	.111
Expectation of a mild COVID-19 course *M (SD)*	2.31 (1.548)	2.40 (1.350))	*T*=0.150	.882
There is no benefit to vaccines in general *M (SD)*	1.00 (1.528)	0.90 (1.101)	*T* =-0.175	.863
Effect only against severe course not against infection *M (SD)*	2.23 (1.363)	2.60 (1.647)	*T* = 0.589	.562
expense *M (SD)*	1.31 (0.947)	1.70 (1.337)	*T*=0.825	.419
Much faster development of the vaccines *M (SD)*	3.69 (0.630)	3.20 (0.789)	*T*=-1.666	.111
Too little testing of the vaccines *M (SD)*	3.69 (0.480)	2.90 (1.101)	***T*=-2.335**	**.030**
other *M (SD)*	1.92 (1.441)	2.60 (0.843)	*T*=1.318	.202

Note: AD = affective disorders; HC = healthy controls; M = mean; SD = standard deviation; [a]=mean of a five point likert scale: (0=disagree, 1=rather disagree, 2= neither disagree nor agree, 3=rather agree, 4=agree)

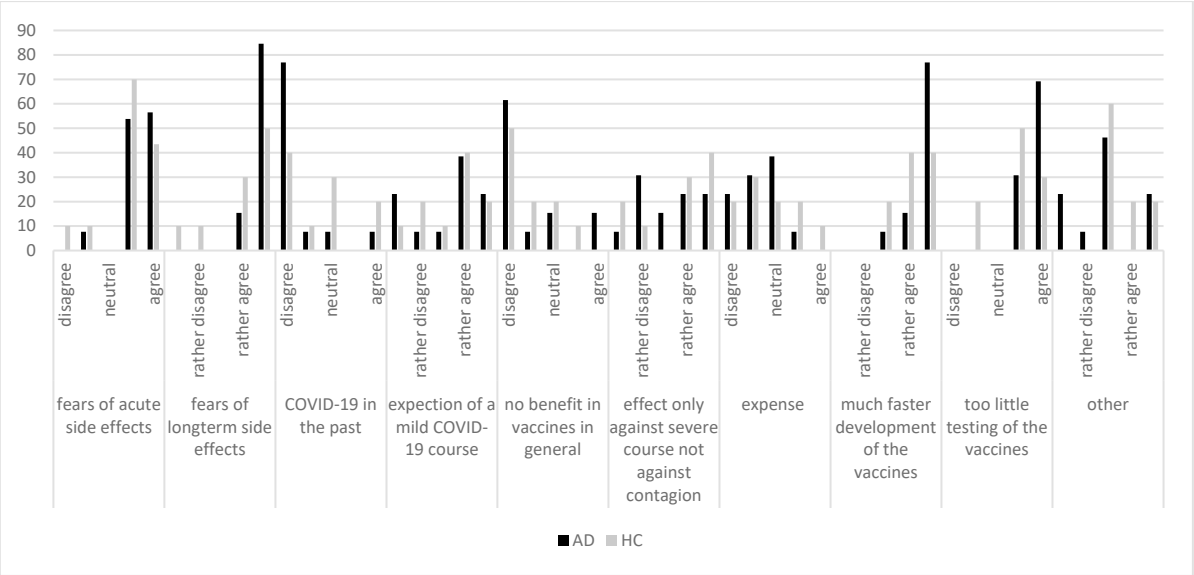

Figure 4: Reasons for waiting to get vaccinated against Covid-19 of individuals with affective disorders (AD) and healthy controls (HC)

4. Discussion

The aim of the literature review on vaccines in individuals with psychiatric disorders was to identify and analyze existing data on prevalence rates, effects, and side effects of vaccines in these individuals, as well as possible interactions of vaccines with psychopharmaceuticals. Additionally, the main aim of the online survey study was to assess the willingness of people with AD to get vaccinated against COVID-19 compared to HC and discover possible reasons for a vaccine hesitancy.

We detected 42 relevant studies in the literature search on vaccinations in general in individuals with SMI. Of these studies, 19 evaluated the prevalence rates of different vaccines in the population of the mentally ill and four inspected the vaccine prevalence rates in children of mentally ill mothers. One study investigated the willingness of patients with SZ to get the influenza vaccine. The effects, as well as side effects of vaccinations were studied by 16 papers. Two studies focused on the interaction between the psychopharmaceutical clozapine and different vaccines. Overall, these studies presented different results, with some finding higher and some finding lower prevalence rates of vaccines in the population of mentally ill individuals compared to mentally healthy individuals. Several did not find any differences between the two groups. The results also varied in the effects, meaning the antibody production or maintenance after a vaccination, the side effects after vaccinations in individuals with mental disorders, and the interactions between clozapine and vaccines. Not only the results, but also the study designs, the study population, the vaccines that were investigated, what mental illness was looked at, and the way the mental illness was defined differed across these studies.

Our online questionnaire study did not determine a difference in the willingness of individuals to receive the COVID-19 vaccination between the AD and the HC group. There was a slight difference in the willingness to get vaccinated in general between the groups, though, with the HC being slightly more willing. At the time of the study, there was a significantly higher COVID-19 vaccination coverage in the HC group than in the AD group.

4.1. Literature review

4.1.1. Prevalence rates

The studies presented contradictory results, as many found lower vaccination rates in people with mental disorders, but just as many found the same or even higher vaccination rates in this group. These studies worked with heterogeneous samples and many differed in age, race, and sex of their study populations. Also, only three studies worked with subjects

with diagnosed psychiatric disorders, while the others determined mental illness by using various surveys, scales, and questionnaires. In the group of individuals with mental disorders, differences in vaccination rates existed among individuals with varying demographic characteristics. Differences in vaccine uptake between men and women, especially, exist, as highlighted by two studies. (115,125)

Some of the studies showed that for individuals with frequent access to health care, the vaccination coverage was higher, even if they had a mental disorder. The study (110) of the 1999 National Health Interview service found that depressed individuals, who had specialty treatment, were more likely to be vaccinated than the ones without treatment. The ones with primary care treatment had even higher odds of being vaccinated. Also, one study (127) found that mentally ill individuals with physical comorbidities and individuals with antidepressant treatment were more likely to be vaccinated than people without comorbidities and treatment. A possible explanation for this phenomenon is that people with comorbidities have more frequent contact with the health care system and, therefore, have higher vaccination rates. Additionally, the antidepressant recipient group might represent a population of people who are more compliant and accepting of treatment and, as a result, are more likely to follow doctors' recommendations to get vaccinated. In addition, in the study of the Native Americans (128), the more health problems the individuals had and the more medication they used, the higher was the vaccine uptake. The veterans with spinal cord injury might also represent a population that have more frequent contact with the health care system due to their disability and might, therefore, be more likely to get vaccinated. (129) A systematic review (156) identifying factors that influence the influenza vaccination behavior in older adults, determined that recommendation, advice, and reminders by a health care provider was strongly associated with vaccination uptake. In the study by Lorenz et al. (113), the majority of individuals with SMI, who received recommendations, were in the vaccinated group. They calculated an OR of 4.12 for getting the flu shot, when having received a recommendation from their healthcare provider, showing that advice by physicians increases the vaccine uptake in the mentally ill as well.

However, the study (111) of the American veterans goes against this theory, as the individuals with mental disorders made 1.3 times more medical visits in the past year as people without mental illness, but still had lower vaccination rates. Also, in the study by Thorpe and colleagues (112) the distressed group had more outpatient visits, but lower vaccination rates. This might be due to physicians focusing more on the mental health

issues of the individuals and less on any somatic complaints and preventive services. Recommendations by health care providers cannot overcome all barriers that exist, which lead to the lower vaccination rates in some mentally ill groups. The study by Maguire and colleagues (107) showed that individuals with SZ were slightly less willing to get vaccinated than healthy controls, so even if they would receive a recommendation by their physicians to get vaccinated, they might still hesitate out of concern for side effects and mistrust in the vaccine, cost of the vaccine, transportation issues, and other reasons. Interestingly, many of the studies that reported lower vaccination coverage in the mentally ill population were conducted in the US, while many of the ones who reported the same or higher coverage in individuals with mental disorders compared to controls were done in Europe. (121,124,126) In the study by Lorenz et al. (113), 78.8% of the unvaccinated group did not have insurance. In other American studies, Medicare insurance predicted higher immunization rates (128) and individuals with health insurance had a higher usage of preventive care than those without. (130) In the United States, a significant amount of people is uninsured, while the entire population of Australia, South Korea, and many European countries including Germany, Italy, and the UK is covered by health insurance. (157) Individuals with SMI or serious psychological distress are significantly less likely to have health insurance in the US than individuals without mental illness. (158,159) Lack of health insurance, which is a more notable issue in the US than elsewhere, therefore presents a significant barrier for these individuals to receive treatment and use preventive services, like vaccinations. Another obstacle for vaccination that is more prominent in the US, is the cost barrier. A study (160) comparing health care barriers for the mentally ill in the US, Netherlands, and Ontario, Canada identified the financial barrier in low-income individuals greater for the ones in the US, than in the two other countries (aOR=2.43). These two challenges that individuals with mental illnesses face in the US, might explain the more prominent lower vaccination rates seen there in the mentally ill, compared to other countries.

Another worry is children of mothers with mental disorders not receiving all their necessary vaccinations, as pointed out by three of the four found studies on this topic. (117-119) It is important to get through to these individuals, not only to increase the vaccination rates in them, but also in their children. Special vaccination programs might be necessary to reach individuals with SMI and provide vaccinations. Miles and colleagues (116), who implemented such a program by creating mobile vaccination clinics that could overcome the financial and transportation barriers and provide vaccinations to adults with

SPMI, were successful in increasing the vaccination rate 25% above baseline for the Hepatitis A and B, MMR, and tetanus/diphteria/pertussis vaccine, and a slightly lower, but still significant increase in the Influenza and Pneumovac vaccination rates. In the UK, it has been recommended that primary care physicians set up clinics specifically for people with mental disorders to meet their physical health care needs. (161) Such clinics could also be used to apply needed vaccinations. A systematic review (162) has identified provider reminder systems as a strong factor in improving vaccination rates. Therefore, for the mentally ill individuals with frequent medical visits, doctors' recommendations, as well as reminders can be an important tool in increasing the vaccine uptake in this group. All these approaches could potentially help in reaching individuals with mental disorders, that still lack vaccinations.

4.1.2. Immunogenicity of vaccines

Overall, the studies presented contradictory results, but most studies, which focused on individuals with chronic severe mental disorders, found lower antibody titers after vaccination. The two studies, which reported higher antibody titers were conducted on otherwise healthy medical students, who had symptoms of depression (144), and SZ patients right after an acute psychiatric episode. (143) It was not mentioned that the students were suffering from chronic depression, so it can be assumed that these symptoms were acute. Acute stress right before influenza vaccination has been shown to enhance the antibody response in women. (163) The depressive symptoms in the healthy medical students might have acted as acute stressors on the immune system, enhancing the antibody response. The acute psychiatric episodes in the SZ patients, who had higher antibody titers after cholera vaccination might also have provided a similar enhancing effect on the immune system as acute stress.

Another explanation for these results is that even though vaccine immunogenicity, which is the ability of the vaccine to cause antibody formation, was higher in these individuals, the vaccine efficacy, or the ability of the antibodies to protect the individual from an infection from the pathogen, might be lower. (144) In other words, these individuals have more antibodies, but these antibodies might not necessarily be functioning to protect them from infection. This is evident in the study by Wang et al. (145), in which SZ patients had similar immunogenicity to hepatitis B, as healthy individuals, but were less protected as shown by the higher infection rate of hepatitis B in the population of individuals with SZ. The studies by Moynihan et al. (147) and Glaser et al. (148) did not identify an association between depressive symptoms and antibody response to the influenza vaccine. They

studied individuals with different levels of depressive symptoms with most of them being mild, but no individuals with diagnosed severe mood disorders, like MDD or BD. Most studies that found a lower antibody response in people with mental disorders, were conducted on individuals with diagnosis of the severe mental disorders MDD and SZ and/ or chronic conditions of mental illness. Chronic conditions of mental illness, just like chronic stress, leads to a constant proinflammatory state and an impaired immune system that might be a factor in the lower response rates after vaccination in these individuals. Having depressive symptoms on the other hand is not necessarily the same as being diagnosed with a severe mental disorder like MDD and might only be a transient state, that does not affect the immune system as much as a chronic SMI does, especially when the symptoms are mild. It can therefore be concluded that the length and severity of the mental disorder affects the amount of antibody formation after vaccination. The study by Vaughan and colleagues (139) provides further evidence for this, as it observed a slight negative correlation between antibody titers and length of hospitalization due to the mental illness. Factors like physical comorbidities, smoking, and sleep problems, which are common in individuals with mental illness (8-10,14,15,19), and can reduce the antibody response to vaccines (81), could also be an explanation for the lower antibody titers in these individuals found by many of the studies.

Psychotropic medications could influence the response to vaccinations as well. In the shingles vaccination study (140), antidepressant drugs normalized the response to the shingles vaccine and the MDD patients treated with these medications had an even higher increase in VZV-RCF than controls. Antidepressants have been shown to have anti-inflammatory effects and lead to a reduction of IL-6 in the serum of treated patients. (164) Furthermore, SSRIs lead to the reduction of IL-1b, another proinflammatory cytokine. (164) It can therefore be assumed that inflammation plays an important role in reducing the antibody response to vaccines and treating this inflammation can help in normalizing the antibody formation. However, in the study measuring antibodies for measles, medicated MDD patients were less likely to be seropositive for measles. These individuals had on average lived with depression significantly longer than the unmedicated subjects, though. (142) These lower seropositivity rates are likely due to the longer and more severe courses of depression in this group compared to the unmedicated group, rather than the medications influencing the antibody maintenance in these individuals. The medicated patients have lived with a chronic proinflammatory state and altered immune system longer, which might have led to the faster degradation of the measle antibodies. Another

medication that might affect the antibody formation or maintenance after vaccination is lithium. It is used to treat BD and, in some cases, unipolar depression. (165) As it can stimulate IgG antibody production (166), lithium has been proposed as an oral adjuvant for viral vaccines like the influenza and rubella vaccines. (167) To potentially increase the immunogenicity of vaccines in BD and MDD patients, they could be treated with lithium prior to vaccination.

4.1.3. Inflammatory and side effects of vaccines

The studies found greater inflammatory responses, as well as more side effects in individuals with mental illness. The increased inflammatory response to the immune stimulus of vaccines might at least in part explain the greater risk of side effects after vaccination for individuals with depression. This could be damaging in the attempt to motivate individuals with mental disorders to get vaccinated. Concerns about side effects as well as "catching the flu" from the vaccines could discourage these individuals from getting a vaccination. Side effects like fever, headache, and fatigue from an influenza vaccine can resemble symptoms of the flu, but it has been shown that these systemic side effects don't differ in people receiving the vaccine or a placebo. (168) In the study (107) investigating views of SZ patients on protective measures against influenza, 71.8% were concerned of catching the flu virus from the vaccine compared to only 50.2% of controls. This could be due to an incomprehension of how vaccines work or due to them experiencing side effects after a previous influenza vaccination and falsely believing them to be symptoms of an influenza infection they received from the vaccine. It is important for health professionals to educate these patients on vaccine safety and possible side effects that might occur, as well as to clarify, that although they might experience mild symptoms resembling the flu, the vaccine cannot infect them with influenza. Individuals with certain mental illnesses might be more at risk of suffering from specific side effects from a vaccine, like paresthesia from the 2009 pandemic vaccine (151), than individuals without mental illness. Although several studies did find increased side effects in depressed patients, they were mild to moderate reactions and no study reported an increased rate of severe reactions to vaccination in subjects with mental disorders. It can therefore be concluded that vaccines are generally as safe in these individuals as in the general population.

One worrisome aspect, though, is that vaccines might worsen symptoms of a mental disorders. As vaccines are inflammatory stressors, they might lead to exacerbation or relapse in individuals with psychiatric illnesses. Not only did studies report a greater

decrease in positive affect after vaccination from baseline in patients with depression and anxiety (153), but they also reported a greater reduction in mood after vaccination in women with remitted depression than controls. (152) Positive affect is a positive mood state like joy, pleasure, pride, and enthusiasm. (169) A loss in positive affect is strongly associated with depression and a loss of pleasure is a symptom of the disorder (170). Thus, by leading to a decline in positive affect, the influenza vaccination led to depressive symptoms in psychiatric patients in the study by Harper and colleagues and, therefore, could have led to a worsening or exacerbation of these patients' depression. (153) Remitted patients are also more strongly affected by vaccine than controls, as a greater reduction in mood as a result to the vaccination was seen in these individuals. (152) The vaccine could potentially result in a relapse in these patients. No studies were found investigating side effects and inflammation in patients with psychotic disorder, like SZ, but these individuals might also be at risk of exacerbation of their illness due to a vaccination. It might be important to closely monitor individuals with SMI after vaccination to administer treatment in case of a worsening in their state.

4.1.4. Vaccinations and psychotropic drugs

The two studies found no or only partial interactions between vaccinations and clozapine. The influenza vaccination has been shown to depress the theophylline metabolism (theophylline is metabolized mainly by CYP1A2), suggesting that the vaccine has an inhibitory effect on the cytochrome. (171,172) It has been proposed that vaccines and other immune-modulating factors achieve this by raising the levels of cytokines. (173) CYP1A2 is also involved in breaking down clozapine into its metabolites and help with its elimination. (174) Even though the open label study (154) identified no effect of the influenza vaccination on clozapine levels, if a vaccine raises cytokine levels enough to suppress CYP1A2, it could affect the serum levels of substances like clozapine and its metabolites. (154) However, as in the two patients with infections clozapine levels were raised, infections probably influence clozapine levels to a much greater extent than vaccinations. The cross-sectional study (155) is another example of SZ patients having low antibody maintenance after many vaccinations. In addition, it shows that clozapine might have an effect on certain antibody levels after vaccination, especially IgA and IgM.

There is some evidence that other psychotropic drugs have interactions with vaccines too. It was already mentioned that lithium influences some vaccinations, in that it can increase the immunogenicity of the vaccines. (166,167) Conversely, the pertussis vaccine has been shown to have an effect on lithium levels in a study (175) conducted on rats. The injection

of the vaccine was associated with an elevation of lithium levels in the serum and tissues of the rats. The researchers hypothesized that multiple mechanisms added together to impair the excretion of the drugs in the kidney. However, it is not clear what effect the vaccine would have in humans treated with lithium. Antidepressants might be able to influence the antibody formation after vaccination as well, as already discussed. (140)

4.2. COVID-19 vaccination willingness of individuals with affective disorder

The results of the online questionnaire study showed that there was no difference in the willingness to be vaccinated against COVID-19 between individuals with AD and HC. However, at the time of the study, significantly more HC were already vaccinated against COVID-19 than individuals with AD. Only a small percentage of individuals were hesitant against receiving the vaccination. Some of the reasons, these participants wished to wait to get vaccinated, were fear of acute and long-term side effects, the much faster development of the vaccines compared to others, and too little testing of the vaccines.

In the HC group, a significantly larger percentage was already vaccinated against COVID-19 at the time of the study late April to May, than in the AD group. At the end of the survey on May 20th, 41.22% of the vaccine eligible population in Austria had been at least partially immunized and 15.44% were already fully immunized. (176) The HC group, therefore, had a similar vaccination prevalence as the general population, as 44.1% were already vaccinated, while the AD group, in which 25.4% had been vaccinated, a much lower one. This could be explained by the fact, that the number of people employed in the HC group was double the amount employed in the AD group. A lot more people were unemployed or retired in the AD group.

Additionally, there was no difference in the somatic comorbidities considered risk factors for COVID-19 like DM, COPD, asthma, or coronary heart disease and may warrant prioritization in the vaccine process, between the two groups. Since the two groups were matched by age and sex, there was also no difference in age. Up until the end of the study, individuals with risk factors for a severe course, older individuals, and individuals with employment especially in health care and education, were prioritized in Austria. As many individuals in the HC group worked in health care, which 32.2% of the 59 participants also listed as a reason they received the vaccination, it explains the above average vaccination rate in that group. Only 6.8% of the AD group listed working in health care as the reason for their vaccination. The below average vaccination prevalence in the AD group could be

due to the unemployment rate of 13.6%, which is higher than the Austrian unemployment rate of 7.7% in May 2021. (177)

Unlike the study by Allsup and Gosney (150), in which individuals with depression perceived more side effects after the influenza vaccination than HC, in our study the participants in the two groups did not differ in the reported side effects after the COVID-19 vaccine. Although it is too early to see any long-term side effects that may appear years after the vaccination, the results of this study show that, fortunately, individuals with AD are not at a higher risk for immediate side effects than individuals without a mental disorder.

However, fear of side effects was still a main reason for individuals in both groups to wish to wait with the vaccination. Especially the individuals with AD listed fear of long-term side effects as a reason they would not get vaccinated right away. This was a rather small percentage of both groups though, as only 13 individuals with AD and 10 HC out of the 59 in each group were hesitant and wished to wait with the vaccination. Also, six individuals with AD and nine HC had the option to be vaccinated against COVID-19 in the past but refused. In the study by Maguire (107), individuals with SZ were less willing to get vaccinated against influenza than HC and listed fear of side effects as a reason. In addition, many participants of the study were concerned of "catching the flu" from the vaccine, showing that their knowledge of the influenza vaccination was limited. Contrarily, in this study, very few participants in either group rated their knowledge of the COVID-19 vaccination as very low or rather low and the majority rated it as rather high. This, of course, is only subjective and cannot measure the actual knowledge of the individuals. However, it shows that the individuals with AD in this study were at least subjectively similarly informed about the vaccine as HC. Misinformation, like the belief that the influenza vaccine can cause flu disease, can discourage individuals from being vaccinated. In fact, a survey study (178) conducted in the UK and USA detected that misinformation decreased the number of people who would take the COVID-19 vaccine.

As the vaccine hesitancy in our study did not differ between individuals with AD and HC, it can be inferred, that participants from one group did not possess more misinformation than people in the other group. Hopefully this means, that the barrier of misinformation and lack of knowledge, which could hinder individuals from getting vaccinated, will not be as prominent for individuals with mental disorders and avert them from getting the vaccination against COVID-19.

Other than the fear of side effects, participants listed the fast development and too little testing of the vaccines as main reasons, they would rather wait to get a COVID-19 vaccine. These concerns were more prominent in the AD group, however only the worry of too little testing was significantly more pronounced in the AD group than the HC group. Fortunately, individuals in both groups disagreed with the statement, that there is no benefit to vaccines in general. Hopefully, as more and more people receive the COVID-19 vaccinations without serious side effects, these worries about the safety of the vaccines will diminish and the individuals will reconsider and be less hesitant towards receiving the vaccine.

The main finding of the online questionnaire study was that there was no difference between the HC and the AD group in their willingness to be vaccinated against COVID-19. The means of 2.69 and 2.88 for the AD and the HC group respectively both displayed a rather high willingness, as this was measured on five-point likert scale ranging from 0 to 4. The higher the number, the higher the willingness to vaccinate was. In addition, the currently not vaccinated individuals were rather eager to get vaccinated as soon as possible in both groups, as the willingness on a scale from 0 to 100 was 78.13 in the AD group and 76.00 in the HC group. Another survey study (179), which investigated the willingness for a COVID-19 vaccination in the general population in different European countries in September 2020, found that 73.9% of participants in Denmark, Germany, France, Italy, Portugal, the Netherlands, and the UK were willing to be vaccinated. The percentage found is about the same as the willingness measured in our study. A study by Schernhammer et al. (180), which investigated COVID-19 vaccine hesitancy and reasons associated with it, conducted from November to December 2020 in Austria, determined a 41.1% intermediate or severe vaccine hesitancy in participants. This was higher than the hesitancy in our study which was between 17% and 22%, as 13 and 10 people, in the AD and the HC groups respectively, wished to wait. In the Austrian study (180), good perceived health, higher education level, being over 55 years of age, male gender, and living in more densely populated areas all correlated with a lower vaccine hesitancy. In our questionnaire study there was no difference in these factors, as the two groups were matched for age and sex and there was no significant difference in education levels and somatic comorbidities. Since there was no difference in the vaccine hesitancy between the two groups, it can be inferred that having an AD does not correlate with a higher or lower vaccine hesitancy or with a higher or lower willingness to receive the COVID-19 vaccination.

Fortunately, the vaccine hesitancy was found to be lower than in the other study (180) conducted on the general population in Austria. On one hand, this could be due to a general decrease in the vaccine hesitancy over time as our study was conducted 5 months after the study by Schernhammer and colleagues. (180) Maybe, since already 27.92% of the Austrian population were at least partially immunized and only very few cases of severe side effects existed at the start of our survey in April (176), people were less hesitant about getting the vaccination than in November when the vaccination process hadn't started yet. On the other hand, the knowledge the participants possessed about the COVID-19 vaccine might also have influenced the vaccine hesitancy and willingness. A study (181), conducted in southern Ethiopia about factors associated with the willingness to receive the COVID-19 vaccine, discovered that lack of knowledge about the COVID-19 vaccines was associated with a lower vaccine willingness. Furthermore, a Vietnamese study (182) determined that knowledge about COVID-19 increased the odds of vaccine acceptance. Participants in our study rated their knowledge of the COVID-19 vaccines as high or rather high, which could have led to the lower vaccine hesitancy compared to the other study. Furthermore, the lower vaccine hesitancy could have been the result of our study being conducted in Graz, while the other study collected data from individuals living all over Austria, including more rural areas and less densely populated areas than Graz, where less information might be known about the vaccines. In addition, about 50% of both groups in our study completed university. Since a higher education status and living in more densely populated areas correlates with lower vaccine hesitancy (180), this might explain the lower vaccine hesitancy in our study group.

Even though, there was not a significant difference in the willingness to vaccinate against COVID-19, there was a significant difference in the willingness to vaccinate in general. The individuals in the HC group were slightly more willing, with the means being 2.71 in the AD group and 3.07 in the HC group. Looking at the numbers, this, albeit being significant, is not a big difference. The willingness of both groups was higher than the willingness to get vaccinated against COVID-19 was, although again only slightly higher. On a five-point likert scale, with which the vaccine willingness was measured, a 3 is a rather high willingness. The means in both groups were close to 3, meaning that the willingness to vaccinate in general and, more importantly against COVID-19, in both groups was rather high.

Even though it was likely due to the differences in occupation that lead to the significant higher COVID-19 coverage in the HC group at the time of the study, other barriers like

stigmatization, symptoms of the AD, like fatigue, lethargy, or hopelessness, and logistical problems, like difficulties reaching the location of vaccination could hinder patients with AD and other mental disorders from getting vaccinated. The participants of our study all had access to the health care system and as a result might receive information about the COVID-19 vaccines and the importance of getting vaccinated, which might have been one factor leading to the high vaccine willingness. However, individuals with SMI, who might not have been diagnosed yet and might not see a physician regularly, potentially will not have such a high vaccine willingness, due to being less informed about COVID-19 and the vaccines. The other barriers could also be more prominent for these individuals, due to them not being treated and therefore having more pronounced symptoms of the mental disorder. Therefore, the vaccine coverage of those individuals might be even lower than that of the AD group in our study. In order to reach the individuals with SMI, special vaccination programs like the ones used in the study by Miles and colleagues (116) might be advantageous. With the use of mobile vaccination clinics, they were able to significantly raise the vaccination rates of many vaccines. Similar programs could be used to raise the COVID-19 vaccination coverage in the population of the mentally ill and, therefore, provide protection against a COVID-19 infection, or at least against a severe course of the illness for these vulnerable individuals.

4.2.1. Limitations

One limitation of the questionnaire study was that the sample size was rather small, as there were only 59 individuals in each group. Due to the few participants in the study, analyses to investigate the role of side effects could not be conducted. Additionally, only individuals with the affective disorders unipolar depression or BD were analyzed, as not enough individuals with psychotic disorder completed the questionnaire. Another limitation was that the questionnaire was only issued to current or former patients at the Department of Psychiatry and Psychotherapeutic Medicine at the Medical University of Graz and not to patients of other psychiatric departments in Graz or the surrounding area. As the survey was online, individuals required access to the internet to complete the survey, so some people were not able to participate. The study also excluded individuals, who were illiterate or had trouble seeing, as they were also not able to fill out the survey. There was no objective rating of the current psychopathological symptoms of the individuals available and therefore not clear how much their symptoms affect them. Finally, the willingness to be vaccinated against COVID-19 and in general was a self-

constructed variable with no reference values and standardization. Therefore, item statistics and factor analysis were conducted.

5. Conclusion

Although, many studies found higher vaccination rates in the mentally ill population than expected, there exists an undervaccination in some groups of people with mental disorders, as well as in their children. It is important to help these individuals overcome the barriers preventing them from getting necessary vaccines. This is imperative, as they suffer more prominently from infectious diseases than the general population, many of which can be protected against with a vaccine. Especially now with the global COVID-19 pandemic going on, these individuals need to be protected due to their higher COVID-19 infection rates and related mortality with one of the vaccines against the virus.

Individuals with severe mental disorders, particularly when they are chronically affected, could see lower antibody responses to certain vaccinations. The antibody maintenance may also be impaired in these individuals and they could, as a result, be below protective levels of these antibodies at a faster rate than individuals without mental illness. It might be necessary to administer booster vaccinations to these individuals more often than to healthy individuals in order to keep them protected against specific infectious diseases. Mentally ill individuals might also be at more risk for mild to moderate side effects from vaccines and from worsening of their symptoms due to a vaccine. Interactions between psychotropic medications and vaccines can occur. Some of them are advantageous like lithium and, potentially, antidepressants being able to increase the antibody formation after vaccination, while others are harmful like clozapine possibly reducing antibody levels. Vaccines could potentially change the serum levels of certain medications these individuals are treated with. It might be necessary to closely monitor these individuals after a vaccination and be aware of side effects, exacerbations of illness, or interactions with medications. Overall, though, the benefit of vaccines, which can prevent many infectious diseases that individuals with SMI are at a greater risk for, outweigh possible risks in these individuals. However, these findings were from studies, which worked with heterogenous samples, as well as data from a long time ago, so it is important that further research is conducted on this important topic to gain more insight on vaccinations in the population of the mentally ill.

The results of our survey showed that there was no difference in the willingness of individuals with AD to be vaccinated against COVID-19 compared to HC. In addition, there were no differences in the side effects, the already vaccinated individuals experienced after their COVID-19 vaccines. As individuals with mental disorders, including AD, are at higher risk for both infection with COVID-19 and severe courses and death due to an infection, it is fortunate that the majority of the individuals with AD were willing to get vaccinated. Furthermore, the vaccines seem to be as safe for individuals with AD as they are for mentally healthy individuals. To increase the vaccination rate and help individuals with mental disorders, special vaccination programs might be helpful. With the assistance of such programs, individuals with mental disorders will hopefully be able to overcome certain barriers, which might prevent them from getting vaccinated and sufficient COVID-19 vaccination coverage will be achieved in this high-risk group.

6. References

1. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. Acta Biomed. 2020 Mar 19;91(1):157-160. doi: 10.23750/abm.v91i1.9397. PMID: 32191675; PMCID: PMC7569573.

2. COVID-19 [Internet]. European Centre for Disease Prevention and Control. 2021 [cited 2022Feb6]. Available from: https://www.ecdc.europa.eu/en/covid-19

3. Certain Medical Conditions and Risk for Severe COVID-19 Illness [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; [cited 2021Mar8]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

4: Rod JE, Oviedo-Trespalacios O, Cortes-Ramirez J. A brief-review of the risk factors for covid-19 severity. Rev Saude Publica. 2020;54:60. doi: 10.11606/s1518-8787.2020054002481. Epub 2020 Jun 1. PMID: 32491116; PMCID: PMC7263798.

5. Mental Illness [Internet]. National Institute of Mental Health. U.S. Department of Health and Human Services; 2021 [cited 2021Apr17]. Available from: https://www.nimh.nih.gov/health/statistics/mental-illness.shtml

6. Ellis ME. Affective disorders [Internet]. healthline. 2020 [cited 2021Apr8]. Available from: https://www.healthline.com/health/affective-disorders

7. Torres F. What Is Schizophrenia? [Internet]. American Psychiatric Association. American Psychiatric Association; 2020 [cited 2021Apr8]. Available from: https://www.psychiatry.org/patients-families/schizophrenia/what-is-schizophrenia

8. Sokal J, Messias E, Dickerson FB, Kreyenbuhl J, Brown CH, Goldberg RW, Dixon LB. Comorbidity of medical illnesses among adults with serious mental illness who are receiving community psychiatric services. J Nerv Ment Dis. 2004 Jun;192(6):421-7. doi: 10.1097/01.nmd.0000130135.78017.96. PMID: 15167405.

9. De Hert M, Correll CU, Bobes J, et al. Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. World Psychiatry 2011; 10: 52–77.

10. Fagiolini A, Chengappa KN, Soreca I, Chang J. Bipolar disorder and the metabolic syndrome: causal factors, psychiatric outcomes and economic burden. CNS Drugs. 2008;22(8):655-69. doi: 10.2165/00023210-200822080-00004. PMID: 18601304.

11. Muench J, Hamer AM. Adverse effects of antipsychotic medications. Am Fam Physician. 2010 Mar 1;81(5):617-22. PMID: 20187598.

12. Fava M. Weight gain and antidepressants. J Clin Psychiatry. 2000;61 Suppl 11:37-41. PMID: 10926053.

13. Maina G, Salvi V, Vitalucci A, D'Ambrosio V, Bogetto F. Prevalence and correlates of overweight in drug-naïve patients with bipolar disorder. J Affect Disord. 2008

Sep;110(1-2):149-55. doi: 10.1016/j.jad.2007.12.233. Epub 2008 Jan 29. PMID: 18234351.

14. Dickerson F, Stallings CR, Origoni AE, Vaughan C, Khushalani S, Schroeder J, Yolken RH. Cigarette smoking among persons with schizophrenia or bipolar disorder in routine clinical settings, 1999-2011. Psychiatr Serv. 2013 Jan;64(1):44-50. doi: 10.1176/appi.ps.201200143. PMID: 23280457.

15. Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness: A population-based prevalence study. JAMA. 2000 Nov 22-29;284(20):2606-10. doi: 10.1001/jama.284.20.2606. PMID: 11086367.

16. Hansen SS, Munk-Jørgensen P, Guldbaek B, Solgård T, Lauszus KS, Albrechtsen N, Borg L, Egander A, Faurholdt K, Gilberg A, Gosden NP, Lorenzen J, Richelsen B, Weischer K, Bertelsen A. Psychoactive substance use diagnoses among psychiatric in-patients. Acta Psychiatr Scand. 2000 Dec;102(6):432-8. doi: 10.1034/j.1600-0447.2000.102006432.x. PMID: 11142432.

17. Dowlati Y, Herrmann N, Swardfager W, Liu H, Sham L, Reim EK, Lanctôt KL. A meta-analysis of cytokines in major depression. Biol Psychiatry. 2010 Mar 1;67(5):446-57. doi: 10.1016/j.biopsych.2009.09.033. Epub 2009 Dec 16. PMID: 20015486

18. Suzuki H, Savitz J, Kent Teague T, Gandhapudi SK, Tan C, Misaki M, McKinney BA, Irwin MR, Drevets WC, Bodurka J. Altered populations of natural killer cells, cytotoxic T lymphocytes, and regulatory T cells in major depressive disorder: Association with sleep disturbance. Brain Behav Immun. 2017 Nov;66:193-200. doi: 10.1016/j.bbi.2017.06.011. Epub 2017 Jun 20. PMID: 28645775; PMCID: PMC5650936.

19. Murphy MJ, Peterson MJ. Sleep Disturbances in Depression. Sleep Med Clin. 2015 Mar;10(1):17-23. doi: 10.1016/j.jsmc.2014.11.009. Epub 2014 Dec 12. PMID: 26055669; PMCID: PMC5678925.

20. Irwin M, McClintick J, Costlow C, Fortner M, White J, Gillin JC. Partial night sleep deprivation reduces natural killer and cellular immune responses in humans. FASEB J. 1996 Apr;10(5):643-53. doi: 10.1096/fasebj.10.5.8621064. PMID: 8621064.

21. Fries GR, Walss-Bass C, Bauer ME, Teixeira AL. Revisiting inflammation in bipolar disorder. Pharmacol Biochem Behav. 2019 Feb;177:12-19. doi: 10.1016/j.pbb.2018.12.006. Epub 2018 Dec 24. PMID: 30586559.

22. Munkholm K, Jacoby AS, Lenskjold T, Bruunsgaard H, Vinberg M, Kessing LV. Leukocytes in peripheral blood in patients with bipolar disorder - Trait and state alterations and association with levels of cytokines and C-reactive protein. Psychiatry Res. 2018 Mar;261:383-390. doi: 10.1016/j.psychres.2018.01.022. Epub 2018 Jan 11. PMID: 29353768.

23. Kirkpatrick B, Miller BJ. Inflammation and schizophrenia. Schizophr Bull. 2013 Nov;39(6):1174-9. doi: 10.1093/schbul/sbt141. Epub 2013 Sep 26. PMID: 24072812; PMCID: PMC3796097.

24.Özdin S, Sarisoy G, Böke Ö. A comparison of the neutrophil-lymphocyte, platelet-lymphocyte and monocyte-lymphocyte ratios in schizophrenia and bipolar disorder patients - a retrospective file review. Nord J Psychiatry. 2017 Oct;71(7):509-512. doi: 10.1080/08039488.2017.1340517. Epub 2017 Jun 23. PMID: 28644753.

25. Harris, C., & Barraclough, B. (1998). Excess mortality of mental disorder. British Journal of Psychiatry, 173(01), 11–53. doi:10.1192/bjp.173.1.11

26.Tidemalm D, Waern M, Stefansson CG, Elofsson S, Runeson B. Excess mortality in persons with severe mental disorder in Sweden: a cohort study of 12 103 individuals with and without contact with psychiatric services. Clin Pract Epidemiol Ment Health. 2008 Oct 14;4:23. doi: 10.1186/1745-0179-4-23. PMID: 18854034; PMCID: PMC2576252.

27. Walker ER, McGee RE, Druss BG. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. JAMA Psychiatry. 2015 Apr;72(4):334-41. doi: 10.1001/jamapsychiatry.2014.2502. Erratum in: JAMA Psychiatry. 2015 Jul;72(7):736. Erratum in: JAMA Psychiatry. 2015 Dec;72(12):1259. PMID: 25671328; PMCID: PMC4461039.

28. Seminog OO, Goldacre MJ. Risk of pneumonia and pneumococcal disease in people with severe mental illness: English record linkage studies. Thorax. 2013 Feb;68(2):171-6. Doi: 10.1136/thoraxjnl-2012-202480. Epub 2012 Dec 15. PMID: 23242947.

29. Lawrence D, Holman DA, Jablensky A. Preventable physical illness in people with mental illness. Crawley, Western Australia: The University of Western Australia, 2001.

30. Fukuta Y, Muder RR. Infections in psychiatric facilities, with an emphasis on outbreaks. Infect Control Hosp Epidemiol. 2013 Jan;34(1):80-8. doi: 10.1086/668774. Epub 2012 Nov 27. PMID: 23221197.

31. Risa KJ, McAndrew JM, Muder RR. Influenza outbreak management on a locked behavioral health unit. Am J Infect Control. 2009 Feb;37(1):76-8. doi: 10.1016/j.ajic.2008.05.008. Epub 2008 Oct 22. PMID: 18945518.

32. Strihavková M, Havlícková M, Tůmová B. Epidemie chripky typu B na gerontopsychiatrickém oddělení psychiatrické lécebny [An epidemic of type B influenza in the geriatric psychiatry department of a psychiatric hospital]. Cas Lek Cesk. 1990 Sep 7;129(36):1129-32. Czech. PMID: 2224975.

33. Wang Q, Xu R, Volkow ND. Increased risk of COVID-19 infection and mortality in people with mental disorders: analysis from electronic health records in the United States. World Psychiatry. 2020 Oct 7:10.1002/wps.20806. doi: 10.1002/wps.20806. Epub ahead of print. PMID: 33026219; PMCID: PMC7675495.

34. Wang QQ, Kaelber DC, Xu R, Volkow ND. COVID-19 risk and outcomes in patients with substance use disorders: analyses from electronic health records in the United States. Mol Psychiatry 2020; published online Sept 14. https://doi.org/10.1038/s41380-020-00880-7.

35. Taquet M, Luciano S, Geddes JR, Harrison PJ. Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA. Lancet Psychiatry. 2021 Feb;8(2):130-140. doi: 10.1016/S2215-0366(20)30462-4. Epub 2020 Nov 9. Erratum in: Lancet Psychiatry. 2021 Jan;8(1):e1. PMID: 33181098; PMCID: PMC7820108.

36. Yang H, Chen W, Hu Y, et al. Pre-pandemic psychiatric disorders and risk of COVID-19: a UK Biobank cohort analysis. Lancet Healthy Longev 2020; 1: e69–79.

37. Lee SW, Yang JM, Moon SY, Yoo IK, Ha EK, Kim SY, Park UM, Choi S, Lee SH, Ahn YM, Kim JM, Koh HY, Yon DK. Association between mental illness and COVID-19 susceptibility and clinical outcomes in South Korea: a nationwide cohort study. Lancet Psychiatry. 2020 Dec;7(12):1025-1031. doi: 10.1016/S2215-0366(20)30421-1. Epub 2020 Sep 17. PMID: 32950066; PMCID: PMC7498216

38. Death associated with coronavirus (COVID-19) infection in individuals with severe mental disorders in Sweden during the early months of the outbreak—a exploratory cross-sectional analysis of a population-based register study. Front Psychiatry 2021; 11: 1538.

39. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet. 2012 Jul 7;380(9836):37-43. doi: 10.1016/S0140-6736(12)60240-2. Epub 2012 May 10. PMID: 22579043.

40. Sheffield JM, Karcher NR, Barch DM. Cognitive Deficits in Psychotic Disorders: A Lifespan Perspective. Neuropsychol Rev. 2018 Dec;28(4):509-533. doi: 10.1007/s11065-018-9388-2. Epub 2018 Oct 20. PMID: 30343458; PMCID: PMC6475621.

41. Sheffield JM, Karcher NR, Barch DM. Cognitive Deficits in Psychotic Disorders: A Lifespan Perspective. Neuropsychol Rev. 2018 Dec;28(4):509-533. doi: 10.1007/s11065-018-9388-2. Epub 2018 Oct 20. PMID: 30343458; PMCID: PMC6475621.

42. Degan TJ, Kelly PJ, Robinson LD, Deane FP, Wolstencroft K, Turut S, Meldrum R. Health literacy in people living with mental illness: A latent profile analysis. Psychiatry Res. 2019 Oct;280:112499. doi: 10.1016/j.psychres.2019.112499. Epub 2019 Jul 29. PMID: 31398576.

43. Muruganandam P, Neelamegam S, Menon V, Alexander J, Chaturvedi SK. COVID-19 and Severe Mental Illness: Impact on patients and its relation with their awareness about COVID-19. Psychiatry Res. 2020 Sep;291:113265. doi: 10.1016/j.psychres.2020.113265. Epub 2020 Jun 29. PMID: 32763536; PMCID: PMC7322460.

44. Li L, Li F, Fortunati F, Krystal JH. Association of a prior psychiatric diagnosis with mortality among hospitalized patients with coronavirus disease 2019 (COVID-19) infection. JAMA Netw Open 2020; 3: e2023282.

45. Nemani K, Li C, Olfson M, et al. Association of psychiatric disorders with mortality among patients with COVID-19. JAMA Psychiatry 2021; published online Jan 27. https//doi.org/10.1001/ jamapsychiatry.2020.4442.

46. Linz SJ, Sturm BA. The phenomenon of social isolation in the severely mentally ill. Perspect Psychiatr Care. 2013 Oct;49(4):243-54. doi: 10.1111/ppc.12010. Epub 2013 Jan 18. PMID: 25187445.

47. Knaak S, Mantler E, Szeto A. Mental illness-related stigma in healthcare: Barriers to access and care and evidence-based solutions. Healthc Manage Forum. 2017 Mar;30(2):111-116. doi: 10.1177/0840470416679413. Epub 2017 Feb 16. PMID: 28929889; PMCID: PMC5347358

48. Wang J, Jiang M, Chen X, Montaner LJ. Cytokine storm and leukocyte changes in mild versus severe SARS-CoV-2 infection: Review of 3939 COVID-19 patients in China and emerging pathogenesis and therapy concepts. J Leukoc Biol. 2020 Jul;108(1):17-41. doi: 10.1002/JLB.3COVR0520-272R. Epub 2020 Jun 13. PMID: 32534467; PMCID: PMC7323250.

49. May M, Slitzky M, Rostama B, Barlow D, Houseknecht KL. Antipsychotic-induced immune dysfunction: A consideration for COVID-19 risk. Brain Behav Immun Health. 2020 Jul;6:100097. Doi: 10.1016/j.bbih.2020.100097. Epub 2020 Jun 23. PMID: 32835296; PMCID: PMC7308744.

50. Oyesanmi O, Kunkel EJ, Monti DA, Field HL. Hematologic side effects of psychotropics. Psychosomatics. 1999 Sep-Oct;40(5):414-21. doi: 10.1016/S0033-3182(99)71206-5. PMID: 10479946.

51. Demler TL, Trigoboff E. Are clozapine patients at risk for blood dyscrasias with concomitant tamiflu use? Psychiatry (Edgmont). 2009 Nov;6(11):29-33. PMID: 20049148; PMCID: PMC2801479.

52. Hamed MGM, Hagag RS. The possible immunoregulatory and anti-inflammatory effects of selective serotonin reuptake inhibitors in coronavirus disease patients. Med Hypotheses. 2020 Nov;144:110140. doi: 10.1016/j.mehy.2020.110140. Epub 2020 Jul 26. PMID: 32768893; PMCID: PMC7382922.

53. Obiora E, Hubbard R, Sanders RD, Myles PR. The impact of benzodiazepines on occurrence of pneumonia and mortality from pneumonia: a nested case-control and

survival analysis in a population-based cohort. Thorax. 2013 Feb;68(2):163-70. doi: 10.1136/thoraxjnl-2012-202374. Epub 2012 Dec 5. PMID: 23220867.

54. Kashyap VK, Dhasmana A, Massey A, Kotnala S, Zafar N, Jaggi M, Yallapu MM, Chauhan SC. Smoking and COVID-19: Adding Fuel to the Flame. Int J Mol Sci. 2020 Sep 9;21(18):6581. doi: 10.3390/ijms21186581. PMID: 32916821; PMCID: PMC7555793

55. Dinakaran D, Manjunatha N, Naveen Kumar C, Suresh BM. Neuropsychiatric aspects of COVID-19 pandemic: A selective review. Asian J Psychiatr. 2020 Oct;53:102188. doi: 10.1016/j.ajp.2020.102188. Epub 2020 May 30. PMID: 32512530; PMCID: PMC7261092.

56. Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: Systematic review of the current evidence. Brain Behav Immun. 2020 Oct;89:531-542. doi: 10.1016/j.bbi.2020.05.048. Epub 2020 May 30. PMID: 32485289; PMCID: PMC7260522.

57. Literature review: Hossain MM, Tasnim S, Sultana A, Faizah F, Mazumder H, Zou L, McKyer ELJ, Ahmed HU, Ma P. Epidemiology of mental health problems in COVID-19: a review. F1000Res. 2020 Jun 23;9:636. doi: 10.12688/f1000research.24457.1. PMID: 33093946; PMCID: PMC7549174.

58. Nakamura ZM, Nash RP, Laughon SL, Rosenstein DL. Neuropsychiatric Complications of COVID-19. Curr Psychiatry Rep. 2021 Mar 16;23(5):25. doi: 10.1007/s11920-021-01237-9. PMID: 33725218; PMCID: PMC7962429.

59. Fellendorf, F. T., Reininghaus, E. Z., Ratzenhofer, M., Lenger, M., Maget, A., Platzer, M., Bengesser, S. A., Birner, A., Queissner, R., Hamm, C., Pilz, R., & Dalkner, N. (2021). COVID-19-related fears and information frequency predict sleep behavior in bipolar disorder. Brain Behavior, 00:e02182.

60. Dalkner N, Wagner-Skacel J, Ratzenhofer M, Fellendorf F, Lenger M, Maget A, Tmava-Berisha A, Pilz R, Queissner R, Hamm C, Bengesser S, Platzer M, Birner A, Reininghaus E. Psychological symptoms during and after Austrian first lockdown in individuals with bipolar disorder? A follow-up control-group investigation. Int J Bipolar Disord. 2021 Jun 1;9(1):16. doi: 10.1186/s40345-021-00222-8. PMID: 34059980; PMCID: PMC8166528.

61. Achar A, Ghosh C. COVID-19-Associated Neurological Disorders: The Potential Route of CNS Invasion and Blood-Brain Relevance. Cells. 2020 Oct 27;9(11):2360. doi: 10.3390/cells9112360. PMID: 33120941; PMCID: PMC7692725.

62. Al Saiegh F, Ghosh R, Leibold A, Avery MB, Schmidt RF, Theofanis T, Mouchtouris N, Philipp L, Peiper SC, Wang ZX, Rincon F, Tjoumakaris SI, Jabbour P, Rosenwasser RH, Gooch MR. Status of SARS-CoV-2 in cerebrospinal fluid of patients with COVID-19 and stroke. J Neurol Neurosurg Psychiatry. 2020 Aug;91(8):846-848. doi: 10.1136/jnnp-2020-323522. Epub 2020 Apr 30. PMID: 32354770.

63. Robinson RG, Jorge RE. Post-Stroke Depression: A Review. Am J Psychiatry. 2016 Mar 1;173(3):221-31. doi: 10.1176/appi.ajp.2015.15030363. Epub 2015 Dec 18. PMID: 26684921.

64. Yang Y, Li W, Zhang Q, Zhang L, Cheung T, Xiang YT. Mental health services for older adults in China during the COVID-19 outbreak. Lancet Psychiatry. 2020 Apr;7(4):e19. doi: 10.1016/S2215-0366(20)30079-1. Epub 2020 Feb 19. PMID: 32085843; PMCID: PMC7128970.

65. Hao F, Tan W, Jiang L, Zhang L, Zhao X, Zou Y, Hu Y, Luo X, Jiang X, McIntyre RS, Tran B, Sun J, Zhang Z, Ho R, Ho C, Tam W. Do psychiatric patients experience more psychiatric symptoms during COVID-19 pandemic and lockdown? A case-control study with service and research implications for immunopsychiatry. Brain Behav Immun. 2020 Jul;87:100-106. doi: 10.1016/j.bbi.2020.04.069. Epub 2020 Apr 27. PMID: 32353518; PMCID: PMC7184991.

66. Fleischmann E, Dalkner N, Fellendorf FT, Reininghaus EZ. Psychological impact of the COVID-19 pandemic on individuals with serious mental disorders: A systematic review of the literature. World J Psychiatry. 2021 Dec 19;11(12):1387-1406. doi: 10.5498/wjp.v11.i12.1387. PMID: 35070784; PMCID: PMC8717042.

67. Impact of Vaccines Universally Recommended for Children—United States, 1900-1998. JAMA. 1999;281(16):1482–1483. doi:10.1001/jama.281.16.1482-JWR0428-2-1

68. Baldo V, Cocchio S, Gallo T, Furlan P, Romor P, Bertoncello C, Buja A, Baldovin T. Pneumococcal Conjugated Vaccine Reduces the High Mortality for Community-Acquired Pneumonia in the Elderly: an Italian Regional Experience. PLoS One. 2016 Nov 15;11(11):e0166637. doi: 10.1371/journal.pone.0166637. PMID: 27846277; PMCID: PMC5112912.

69. Gwack J, Park SK, Lee EH, Park B, Choi Y, Yoo KY. Hepatitis B vaccination and liver cancer mortality reduction in Korean children and adolescents. Asian Pac J Cancer Prev. 2011;12(9):2205-8. PMID: 22296357.

70. Mullooly JP, Bennett MD, Hornbrook MC, Barker WH, Williams WW, Patriarca PA, Rhodes PH. Influenza vaccination programs for elderly persons: cost-effectiveness in a health maintenance organization. Ann Intern Med. 1994 Dec 15;121(12):947-52. doi: 10.7326/0003-4819-121-12-199412150-00008. PMID: 7978721.

71. Nichol KL, Margolis KL, Wuorenma J, Von Sternberg T. The efficacy and cost effectiveness of vaccination against influenza among elderly persons living in the community. N Engl J Med. 1994 Sep 22;331(12):778-84. doi: 10.1056/NEJM199409223311206. PMID: 8065407.

72. Patriarca PA, Weber JA, Parker RA, Hall WN, Kendal AP, Bregman DJ, Schonberger LB. Efficacy of influenza vaccine in nursing homes. Reduction in illness and complications during an influenza A (H3N2) epidemic. JAMA. 1985 Feb 22;253(8):1136-9. PMID: 3968844.

73.Vetter V, Denizer G, Friedland LR, Krishnan J, Shapiro M. Understanding modern-day vaccines: what you need to know. Ann Med. 2018 Mar;50(2):110-120. doi: 10.1080/07853890.2017.1407035. Epub 2017 Nov 27. PMID: 29172780.

74. Pardi N, Hogan MJ, Porter FW, Weissman D. mRNA vaccines - a new era in vaccinology. Nat Rev Drug Discov. 2018 Apr;17(4):261-279. doi: 10.1038/nrd.2017.243. Epub 2018 Jan 12. PMID: 29326426; PMCID: PMC5906799.

75. Meo SA, Bukhari IA, Akram J, Meo AS, Klonoff DC. COVID-19 vaccines: comparison of biological, pharmacological characteristics and adverse effects of Pfizer/BioNTech and Moderna Vaccines. Eur Rev Med Pharmacol Sci. 2021 Feb;25(3):1663-1669. doi: 10.26355/eurrev_202102_24877. PMID: 33629336.

76. Weber R. Explaining Johnson & Johnson's, AstraZeneca's new COVID-19 vaccines [Internet]. The Ohio State University Wexner Medical Center. 2021 [cited 2021Mar18]. Available from: https://wexnermedical.osu.edu/blog/explaining-johnson-johnson-astrazeneca-vaccines

77. Kingsley D. Five different strategies for producing an anti-viral vaccine [image]. Open.edu. 2021 [cited 2021Aug16] Available from: https://www.open.edu/openlearn/science-maths-technology/biology/vaccines-viruses

78. Powell ND, Allen RG, Hufnagle AR, Sheridan JF, Bailey MT. Stressor-induced alterations of adaptive immunity to vaccination and viral pathogens. Immunol Allergy Clin North Am. 2011 Feb;31(1):69-79. doi: 10.1016/j.iac.2010.09.002. PMID: 21094924; PMCID: PMC3339561.

79. Walker B, Feavers I. Adjuvant effects on antibody titre. Methods Mol Biol. 2010;626:187-98. doi: 10.1007/978-1-60761-585-9_13. PMID: 20099129.

80. Plotkin SA. Vaccines: correlates of vaccine-induced immunity. Clin Infect Dis. 2008 Aug 1;47(3):401-9. doi: 10.1086/589862. PMID: 18558875.

81. Zimmermann P, Curtis N. Factors That Influence the Immune Response to Vaccination. Clin Microbiol Rev. 2019 Mar 13;32(2):e00084-18. doi: 10.1128/CMR.00084-18. PMID: 30867162; PMCID: PMC6431125.

82. Dhabhar FS, Viswanathan K. Short-term stress experienced at time of immunization induces a long-lasting increase in immunologic memory. Am J Physiol Regul Integr Comp Physiol. 2005 Sep;289(3):R738-44. doi: 10.1152/ajpregu.00145.2005. Epub 2005 May 12. PMID: 15890793.

83.Slavich GM, Irwin MR. From stress to inflammation and major depressive disorder: a social signal transduction theory of depression. Psychol Bull. 2014 May;140(3):774-815. doi: 10.1037/a0035302. Epub 2014 Jan 13. PMID: 24417575; PMCID: PMC4006295.

84. Chu B, Marwaha K, Sanvictores T, et al. Physiology, Stress Reaction. [Updated 2020 Oct 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK541120/

85. Liu YZ, Wang YX, Jiang CL. Inflammation: The Common Pathway of Stress-Related Diseases. Front Hum Neurosci. 2017 Jun 20;11:316. doi: 10.3389/fnhum.2017.00316. PMID: 28676747; PMCID: PMC5476783.

86. Franceschi C, Bonafè M, Valensin S, Olivieri F, De Luca M, Ottaviani E, De Benedictis G. Inflamm-aging. An evolutionary perspective on immunosenescence. Ann N Y Acad Sci. 2000 Jun;908:244-54. doi: 10.1111/j.1749-6632.2000.tb06651.x. PMID: 10911963.

87. McGregor BA, Murphy KM, Albano DL, Ceballos RM. Stress, cortisol, and B lymphocytes: a novel approach to understanding academic stress and immune function. Stress. 2016;19(2):185-91. doi: 10.3109/10253890.2015.1127913. PMID: 26644211; PMCID: PMC4837014.

88. McGregor, B.A., Antoni, M.H., Ceballos, R. and Blomberg, B.B. (2008), Very low CD19+ B-lymphocyte percentage is associated with high levels of academic stress among healthy graduate students. Stress and Health, 24: 413-418. https://doi.org/10.1002/smi.1188

89: Varghese FP, Brown ES. The Hypothalamic-Pituitary-Adrenal Axis in Major Depressive Disorder: A Brief Primer for Primary Care Physicians. Prim Care Companion J Clin Psychiatry. 2001 Aug;3(4):151-155. doi: 10.4088/pcc.v03n0401. PMID: 15014598; PMCID: PMC181180.

90: Chan HY, Chang CJ, Chiang SC, Chen JJ, Chen CH, Sun HJ, Hwu HG, Lai MS. A randomised controlled study of risperidone and olanzapine for schizophrenic patients with neuroleptic-induced acute dystonia or parkinsonism. J Psychopharmacol. 2010 Jan;24(1):91-8. doi: 10.1177/0269881108096070. Epub 2008 Sep 18. PMID: 18801830; PMCID: PMC2951595.

91: Belvederi Murri M, Prestia D, Mondelli V, Pariante C, Patti S, Olivieri B, Arzani C, Masotti M, Respino M, Antonioli M, Vassallo L, Serafini G, Perna G, Pompili M, Amore M. The HPA axis in bipolar disorder: Systematic review and meta-analysis. Psychoneuroendocrinology. 2016 Jan;63:327-42. doi: 10.1016/j.psyneuen.2015.10.014. Epub 2015 Oct 21. PMID: 26547798.

92. Bennett JM, Reeves G, Billman GE, Sturmberg JP. Inflammation-Nature's Way to Efficiently Respond to All Types of Challenges: Implications for Understanding and Managing "the Epidemic" of Chronic Diseases. Front Med (Lausanne). 2018 Nov 27;5:316. doi: 10.3389/fmed.2018.00316. PMID: 30538987; PMCID: PMC6277637.

93. Kelley, K. W., Bluthé, R.-M., Dantzer, R., Zhou, J.-H., Shen, W.-H., Johnson, R. W., & Broussard, S. R. (2003). Cytokine-induced sickness behavior. Brain, Behavior, and Immunity, 17(1), 112–118. doi:10.1016/s0889-1591(02)00077-6

94. Harper JA, South C, Trivedi MH, Toups MS. Pilot investigation into the sickness response to influenza vaccination in adults: Effect of depression and anxiety. Gen Hosp Psychiatry. 2017 Sep;48:56-61. doi: 10.1016/j.genhosppsych.2017.07.005. Epub 2017 Jul 25. PMID: 28779589; PMCID: PMC5606200

95. Spencer JP, Trondsen Pawlowski RH, Thomas S. Vaccine Adverse Events: Separating Myth from Reality. Am Fam Physician. 2017 Jun 15;95(12):786-794. PMID: 28671426.

96. Christian LM, Iams JD, Porter K, Glaser R. Inflammatory responses to trivalent influenza virus vaccine among pregnant women. Vaccine. 2011 Nov 8;29(48):8982-7. doi: 10.1016/j.vaccine.2011.09.039. Epub 2011 Sep 22. PMID: 21945263; PMCID: PMC3204610.

97. Dantzer R, Kelley KW. Twenty years of research on cytokine-induced sickness behavior. Brain Behav Immun. 2007 Feb;21(2):153-60. doi: 10.1016/j.bbi.2006.09.006. Epub 2006 Nov 7. PMID: 17088043; PMCID: PMC1850954.

98. Christian LM, Porter K, Karlsson E, Schultz-Cherry S. Proinflammatory cytokine responses correspond with subjective side effects after influenza virus vaccination. Vaccine. 2015 Jun 26;33(29):3360-6. doi: 10.1016/j.vaccine.2015.05.008. Epub 2015 May 28. PMID: 26027906; PMCID: PMC4467994.

99. Christian LM, Franco A, Iams JD, Sheridan J, Glaser R. Depressive symptoms predict exaggerated inflammatory responses to an in vivo immune challenge among pregnant women. Brain Behav Immun. 2010 Jan;24(1):49-53. doi: 10.1016/j.bbi.2009.05.055. Epub 2009 May 21. PMID: 19464358; PMCID: PMC2787729.

100. De Hert M, Mazereel V, Detraux J, Van Assche K. Prioritizing COVID-19 vaccination for people with severe mental illness. World Psychiatry. 2020 Nov 1. doi: 10.1002/wps.20826. Epub ahead of print. PMID: 33131217.

101. De Picker LJ, Dias MC, Benros ME, Vai B, Branchi I, Benedetti F, Borsini A, Leza JC, Kärkkäinen H, Männikkö M, Pariante CM, Güngör ES, Szczegielniak A, Tamouza R, van der Markt A, Fusar-Poli P, Beezhold J, Leboyer M. Severe mental illness and European COVID-19 vaccination strategies. Lancet Psychiatry. 2021 Feb 17:S2215-0366(21)00046-8. doi: 10.1016/S2215-0366(21)00046-8. Epub ahead of print. Erratum in: Lancet Psychiatry. 2021 Feb 25;: PMID: 33609450; PMCID: PMC7906735.

102. Bradford DW, Kim MM, Braxton LE, Marx CE, Butterfield M, Elbogen EB. Access to medical care among persons with psychotic and major affective disorders. Psychiatr Serv. 2008 Aug;59(8):847-52. doi: 10.1176/ps.2008.59.8.847. PMID: 18678680.

103. De Hert M, Cohen D, Bobes J, Cetkovich-Bakmas M, Leucht S, Ndetei DM, Newcomer JW, Uwakwe R, Asai I, Möller HJ, Gautam S, Detraux J, Correll CU. Physical illness in patients with severe mental disorders. II. Barriers to care, monitoring and treatment guidelines, plus recommendations at the system and individual level. World Psychiatry. 2011 Jun;10(2):138-51. doi: 10.1002/j.2051-5545.2011.tb00036.x. PMID: 21633691; PMCID: PMC3104888.

104. Reininghaus EZ, Manchia M, Dalkner N, Bonkat N, Squassina A, Hodl I, Vieta E, Reif A, Hajek T, Landén M, Correll CU, Scott J, Etain B, Rietschel M, Bergink V, Martinez-Cengotitabengoa M, Kessing LV, Fagiolini A, Bauer M, Goodwin G, Gonzalez-Pinto A, Kupka RW, Schulze TG, Lagerberg TV, Yildiz A, Henry C, Morken G, Ritter P, Nieslen RE, Licht RW, Bechdolf A, Andreassen OA, Fellendorf FT. Outcomes associated with different vaccines in individuals with bipolar disorder and impact on the current COVID-19 pandemic- a systematic review. Eur Neuropsychopharmacol. 2021 Sep 10:S0924-977X(21)00743-4. doi: 10.1016/j.euroneuro.2021.09.001. Epub ahead of print. PMID: 34607722; PMCID: PMC8429356.

105. Bonkat N, Fellendorf FT, Dalkner N, Reininghaus EZ. Severe mental disorders and vaccinations - a systematic review. World J Biol Psychiatry. 2022 Jan 11:1-16. doi: 10.1080/15622975.2021.2013095. Epub ahead of print. PMID: 35014937.

106. Fellendorf FT, Bonkat N, Schönthaler E, Ratzenhofer M, Bengesser SA, Dalkner N, Reininghaus EZ. Willingness to be vaccinated against COVID-19 is equal in individuals with affective disorders and healthy controls. Vaccine: X, forthcoming.

107. Maguire PA, Reay RE, Looi JC. Nothing to sneeze at - uptake of protective measures against an influenza pandemic by people with schizophrenia: willingness and perceived barriers. Australas Psychiatry. 2019 Apr;27(2):171-178. doi: 10.1177/1039856218815748. Epub 2018 Dec 3. PMID: 30501496; PMCID: PMC7227129.

108. Bazargan M, Wisseh C, Adinkrah E, Ameli H, Santana D, Cobb S, Assari S. Influenza Vaccination among Underserved African-American Older Adults. Biomed Res Int. 2020 Nov 5;2020:2160894. Doi: 10.1155/2020/2160894. PMID: 33224975; PMCID: PMC7671800

109. Davis RE, Geneus CJ. Impact of Health-Related Quality of Life and Social Determinants on Yearly Influenza Immunization in the United States. Value in Health. 2016;19(3).

110. Druss BG, Rask K, Katon WJ. Major depression, depression treatment and quality of primary medical care. Gen Hosp Psychiatry. 2008 Jan-Feb;30(1):20-5. doi: 10.1016/j.genhosppsych.2007.08.015. PMID: 18164936; PMCID: PMC2246043.

111. Druss BG, Rosenheck RA, Desai MM, Perlin JB. Quality of preventive medical care for patients with mental disorders. Med Care. 2002 Feb;40(2):129-36. doi: 10.1097/00005650-200202000-00007. PMID: 11802085.

112. Thorpe JM, Kalinowski CT, Patterson ME, Sleath BL. Psychological distress as a barrier to preventive care in community-dwelling elderly in the United States. Med Care. 2006 Feb;44(2):187-91. doi: 10.1097/01.mlr.0000196965.54871.d5. PMID: 16434919.

113. Lorenz RA, Norris MM, Norton LC, Westrick SC. Factors associated with influenza vaccination decisions among patients with mental illness. Int J Psychiatry Med. 2013;46(1):1-13. doi: 10.2190/PM.46.1.a. PMID: 24547606.

114. Kyung Y, Choi MH, Lee JS, Lee JH, Jo SH, Kim SH. Influencing Factors for Influenza Vaccination among South Korean Adolescents with Asthma Based on a Nationwide Cross-Sectional Study. Int Arch Allergy Immunol. 2020;181(6):434-445. doi: 10.1159/000506336. Epub 2020 Mar 6. PMID: 32146467.

115. Mangtani P, Breeze E, Kovats S, Ng ES, Roberts JA, Fletcher A. Inequalities in influenza vaccine uptake among people aged over 74 years in Britain. Prev Med. 2005 Aug;41(2):545-53. doi: 10.1016/j.ypmed.2005.02.001. PMID: 15917051.

116. Miles LW, Williams N, Luthy KE, Eden L. Adult Vaccination Rates in the Mentally Ill Population: An Outpatient Improvement Project. J Am Psychiatr Nurses Assoc. 2020 Mar/Apr;26(2):172-180. doi: 10.1177/1078390319831763. Epub 2019 Mar 13. PMID: 30866701.

117. Turner C, Boyle F, O'Rourke P. Mothers' health post-partum and their patterns of seeking vaccination for their infants. Int J Nurs Pract. 2003 Apr;9(2):120-6. Doi: 10.1046/j.1322-7114.2003.00410.x. PMID: 12694481.

118. Lyngsøe BK, Vestergaard CH, Rytter D, Vestergaard M, Munk-Olsen T, Bech BH. Attendance of routine childcare visits in primary care for children of mothers with depression: a nationwide population-based cohort study. Br J Gen Pract. 2018 Feb;68(667):e97-e104. Doi: 10.3399/bjgp18X694565. Epub 2018 Jan 15. PMID: 29335326; PMCID: PMC5774969.

119. Osam CS, Pierce M, Hope H, Ashcroft DM, Abel KM. The influence of maternal mental illness on vaccination uptake in children: a UK population-based cohort study. Eur J Epidemiol. 2020 Sep;35(9):879-889. doi: 10.1007/s10654-020-00632-5. Epub 2020 Apr 24. PMID: 32328992; PMCID: PMC7524844.

120. Surkan PJ, Kiihl SF, Kozuki N, Vieira LM. Social support of low-income Brazilian mothers related to time to completion of childhood vaccinations. Hum Vaccin Immunother. 2012 May;8(5):596-603. doi: 10.4161/hv.19203. Epub 2012 May 1. PMID: 22634449.

121. Peytremann-Bridevaux I, Voellinger R, Santos-Eggimann B. Healthcare and preventive services utilization of elderly Europeans with depressive symptoms. J Affect Disord. 2008 Jan;105(1-3):247-52. doi: 10.1016/j.jad.2007.04.011. Epub 2007 May 16. PMID: 17509695.

122. Kwon DS, Kim K, Park SM. Factors associated with influenza vaccination coverage among the elderly in South Korea: the Fourth Korean National Health and Nutrition Examination Survey (KNHANES IV). BMJ Open. 2016 Dec 28;6(12):e012618. doi: 10.1136/bmjopen-2016-012618. PMID: 28031209; PMCID: PMC5223688.

123. Green CA, Pope CR. Depressive symptoms, health promotion, and health risk behaviors. Am J Health Promot. 2000 Sep-Oct;15(1):29-34. doi: 10.4278/0890-1171-15.1.29. PMID: 11184116.

124. Fischer BC, Schulz KT, Wiemann M, Lücke E, Schreiber J. Untersuchungen zu Einflussfaktoren auf die Influenza-Impfraten bei Patienten mit chronisch obstruktiver

Lungenerkrankung [Studies on Factors Influencing Influenza Vaccination Rates in Patients with Chronic Obstructive Pulmonary Disease]. Pneumologie. 2020 Sep 14. German. doi: 10.1055/a-1180-0111. Epub ahead of print. PMID: 32927490

125. Mohammed H, Roberts CT, Grzeskowiak LE, Giles L, Leemaqz S, Dalton J, Dekker G, Marshall HS. Psychosocial determinants of pertussis and influenza vaccine uptake in pregnant women: A prospective study. Vaccine. 2020 Apr 9;38(17):3358-3368. Doi: 10.1016/j.vaccine.2020.02.020. Epub 2020 Feb 16. PMID: 32070678.

126. Maske UE, Jaedtke M, Luppa M, Riedel-Heller S, Kleiber D, Busch MA. Diagnostizierte Depression und Inanspruchnahme von medizinischen Versorgungs- und Vorsorgeleistungen bei Erwachsenen in Deutschland [Diagnosed Depression and Utilization of Health Care Services and Preventive Measures in the General Adult Population in Germany - Results from a Nationwide Cross-Sectional Telephone Survey]. Psychiatr Prax. 2019 Mar;46(2):73-81. German. doi: 10.1055/s-0042-122327. Epub 2017 Apr 3. PMID: 28371950.

127. Lawrence T, Zubatsky M, Meyer D. The association between mental health diagnoses and influenza vaccine receipt among older primary care patients. Psychol Health Med. 2020 Oct;25(9):1083-1093. Doi: 10.1080/13548506.2020.1717557. Epub 2020 Jan 20. PMID: 31958989.

128. Buchwald D, Sheffield J, Furman R, Hartman S, Dudden M, Manson S. Influenza and pneumococcal vaccination among Native American elders in a primary care practice. Arch Intern Med. 2000 May 22;160(10):1443-8. Doi: 10.1001/archinte.160.10.1443. PMID: 10826456

129. Lavela SL, Goldstein B, Etingen B, Miskevics S, Weaver FM. Factors Associated With H1N1 Influenza Vaccine Receipt in a High-Risk Population During the 2009-2010 H1N1 Influenza Pandemic. Top Spinal Cord Inj Rehabil. 2012 Fall;18(4):306-14. Doi: 10.1310/sci1804-306. PMID: 23459437; PMCID: PMC3584783.

130. Xiong GL, Iosif AM, Bermudes RA, McCarron RM, Hales RE. Preventive medical services use among community mental health patients with severe mental illness:the influence of gender and insurance coverage. Prim Care Companion J Clin Psychiatry. 2010;12(5):PCC.09m00927. doi: 10.4088/PCC.09m00927gre. PMID: 21274355; PMCID: PMC3026000

131. Shiel WJC. Definition of Seroconversion [Internet]. MedicineNet. MedicineNet; 2018 [cited 2021Mar20]. Available from: https://www.medicinenet.com/seroconversion/definition.htm

132. Afsar B, Elsurer R, Eyileten T, Yilmaz MI, Caglar K. Antibody response following hepatitis B vaccination in dialysis patients: does depression and life quality matter? Vaccine. 2009 Sep 25;27(42):5865-9. doi: 10.1016/j.vaccine.2009.07.055. Epub 2009 Aug 3. PMID: 19654067.

133. Beck AT,Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4(June):561–71.

134. Russo R, Ciminale M, Ditommaso S, Siliquini R, Zotti C, Ruggenini AM. Hepatitis B vaccination in psychiatric patients. Lancet. 1994 Feb 5;343(8893):356. Doi: 10.1016/s0140-6736(94)91193-2. PMID: 7905164

135. Roome AJ, Walsh SJ, Catter ML, Haddle JL: Hepatitis B vaccine responsiveness in Connecticut public safety personnel. JAMA. 1993, 270: 2931-34.

136. Louther J, Feldman J, Rivera P, Villa N, DeHovitz J, Sepkowitz KA: Hepatitis B vaccination program at a New York City hospital: Seroprevalence, seroconversion, and declination. Am J Infect Control. 1998, 26 (4): 423-7.

137. Platkov E, Shlyakhov E, Glick Y, Khalemsky S, Fischbein A: Immunologic evaluation of hepatitis B vaccine application in hospital staff. Int J Occup Med Environ Health. 2003, 16 (3): 249-53.

138. Luiz AS, et al: Hepatitis B in Health Care workers: Prevalence, vaccination and relation to occupational factor. The Brazilian journal of infectious disease. 2005, 9 (5): 384-389.

139. Vaughan WT Jr, Sullivan JC, Elmadjian F. Immunity and schizophrenia; a survey of the ability of schizophrenic patients to develop an active immunity following the injection of pertussis vaccine. Psychosom Med. 1949 Nov-Dec;11(6):327-33. Doi: 10.1097/00006842-194911000-00001. PMID: 15406182

140. Irwin MR, Levin MJ, Laudenslager ML, Olmstead R, Lucko A, Lang N, Carrillo C, Stanley HA, Caulfield MJ, Weinberg A, Chan IS, Clair J, Smith JG, Marchese RD, Williams HM, Beck DJ, McCook PT, Zhang JH, Johnson G, Oxman MN. Varicella zoster virus-specific immune responses to a herpes zoster vaccine in elderly recipients with major depression and the impact of antidepressant medications. Clin Infect Dis. 2013 Apr;56(8):1085-93. doi: 10.1093/cid/cis1208. Epub 2013 Feb 13. PMID: 23413415; PMCID: PMC3601721.

141. Anderson WE. Varicella-Zoster Virus (VZV) [Internet]. Practice Essentials, Background, Pathophysiology. Medscape; 2019 [cited 2021Mar20]. Available from: https://emedicine.medscape.com/article/231927-overview#a5

142. Ford BN, Yolken RH, Dickerson FB, Teague TK, Irwin MR, Paulus MP, Savitz J. Reduced immunity to measles in adults with major depressive disorder. Psychol Med. 2019 Jan;49(2):243-249. doi: 10.1017/S0033291718000661. Epub 2018 Mar 19. PMID: 29552990; PMCID: PMC6441972.

143. Friedman SB, Cohen J, Iker H. Antibody response to cholera vaccine. Differences between depressed, schizophrenic, and normal subjects. Arch Gen Psychiatry. 1967 Mar;16(3):312-5. doi: 10.1001/archpsyc.1967.01730210052009. PMID: 6021476.

144. Petry LJ, Weems LB 2nd, Livingstone JN 2nd. Relationship of stress, distress, and the immunologic response to a recombinant hepatitis B vaccine. J Fam Pract. 1991 May;32(5):481-6. PMID: 1827147.

145. Wang Y, Yu L, Zhou H, Zhou Z, Zhu H, Li Y, Zheng Z, Li X, Dong C. Serologic and molecular characteristics of hepatitis B virus infection in vaccinated schizophrenia patients in China. J Infect Dev Ctries. 2016 Apr 28;10(4):427-31. Doi: 10.3855/jidc.7377. PMID: 27131009.

146. Hepatitis B Blood Tests [Internet]. Hepatitis B Foundation | Baruch S. Blumberg Institute. [cited 2021Mar20]. Available from: https://www.hepb.org/prevention-and-diagnosis/diagnosis/hbv-blood-tests/

147. Moynihan JA, Larson MR, Treanor J, Duberstein PR, Power A, Shore B, Ader R. Psychosocial factors and the response to influenza vaccination in older adults. Psychosom Med. 2004 Nov-Dec;66(6):950-3. doi: 10.1097/01.psy.0000140001.49208.2d. PMID: 15564363.

148. Glaser R, Robles TF, Sheridan J, Malarkey WB, Kiecolt-Glaser JK. Mild depressive symptoms are associated with amplified and prolonged inflammatory responses after influenza virus vaccination in older adults. Arch Gen Psychiatry. 2003 Oct;60(10):1009-14. doi: 10.1001/archpsyc.60.10.1009. PMID: 14557146.

149. Trzonkowski P, Myśliwska J, Godlewska B, Szmit E, Łukaszuk K, Wieckiewicz J, Brydak L, Machała M, Landowski J, Myśliwski A. Immune consequences of the spontaneous pro-inflammatory status in depressed elderly patients. Brain Behav Immun. 2004 Mar;18(2):135-48. doi: 10.1016/S0889-1591(03)00111-9. PMID: 14759591

150. Allsup SJ, Gosney MA. Anxiety and depression in an older research population and their impact on clinical outcomes in a randomised controlled trial. Postgrad Med J. 2002 Nov;78(925):674-7. doi: 10.1136/pmj.78.925.674. PMID: 12496325; PMCID: PMC1742575.

151. De Serres G, Rouleau I, Skowronski DM, Ouakki M, Lacroix K, Bédard F, Toth E, Landry M, Dupré N. Paresthesia and sensory disturbances associated with 2009 pandemic vaccine receipt: Clinical features and risk factors. Vaccine. 2015 Aug 26;33(36):4464-71. doi: 10.1016/j.vaccine.2015.07.028. Epub 2015 Jul 22. PMID: 26209839

152. Niemegeers P, De Boer P, Dumont GJH, Van Den Eede F, Fransen E, Claes SJ, Morrens M, Sabbe BGC. Differential Effects of Inflammatory and Psychosocial Stress on Mood, Hypothalamic-Pituitary-Adrenal Axis, and Inflammation in Remitted Depression. Neuropsychobiology. 138.

153. Harper JA, South C, Trivedi MH, Toups MS. Pilot investigation into the sickness response to influenza vaccination in adults: Effect of depression and anxiety. Gen Hosp Psychiatry. 2017 Sep;48:56-61. doi: 10.1016/j.genhosppsych.2017.07.005. Epub 2017 Jul 25. PMID: 28779589; PMCID: PMC5606200.

154. Raaska K, Raitasuo V, Neuvonen PJ. Effect of influenza vaccination on serum clozapine and its main metabolite concentrations in patients with schizophrenia. Eur J Clin Pharmacol. 2001 Dec;57(10):705-8. Doi: 10.1007/s002280100375. PMID: 11829199.

155. Ponsford M, Castle D, Tahir T, Robinson R, Wade W, Steven R, Bramhall K, Moody M, Carne E, Ford C, Farewell D, Williams P, El-Shanawany T, Jolles S. Clozapine is associated with secondary antibody deficiency. Br J Psychiatry. 2018 Sep 27;214(2):1-7. Doi: 10.1192/bjp.2018.152. Epub ahead of print. PMID: 30259827; PMCID: PMC6429246.

156. Kan T, Zhang J. Factors influencing seasonal influenza vaccination behaviour among elderly people: a systematic review. Public Health. 2018 Mar;156:67-78. doi: 10.1016/j.puhe.2017.12.007. Epub 2018 Feb 3. PMID: 29408191; PMCID: PMC7111770.

157. Percent insured [Internet]. Peterson-KFF Health System Tracker. 2020 [cited 2021Apr7]. Available from: https://www.healthsystemtracker.org/indicator/access-affordability/percent-insured/

158. Garfield RL, Zuvekas SH, Lave JR, Donohue JM. The impact of national health care reform on adults with severe mental disorders. Am J Psychiatry. 2011 May;168(5):486-94. doi: 10.1176/appi.ajp.2010.10060792. Epub 2011 Feb 1. PMID: 21285138.

159. Pearson WS, Dhingra SS, Strine TW, Liang YW, Berry JT, Mokdad AH. Relationships between serious psychological distress and the use of health services in the United States: findings from the Behavioral Risk Factor Surveillance System. Int J Public Health. 2009 Jun;54 Suppl 1:23-9. doi: 10.1007/s00038-009-0003-4. PMID: 19347251.

160. Sareen J, Jagdeo A, Cox BJ, Clara I, ten Have M, Belik SL, de Graaf R, Stein MB. Perceived barriers to mental health service utilization in the United States, Ontario, and the Netherlands. Psychiatr Serv. 2007 Mar;58(3):357-64. doi: 10.1176/ps.2007.58.3.357. PMID: 17325109.

161. O'Brien G, Cormac I, Phelan M, Jones G, Walsh M, Murphy M, Osborn D. Physical health in mental health. [Internet] London: Royal College of Psychiatrists; 2009 [cited 2021Apr8]. Available from: https://www.ucl.ac.uk/core-study/sites/core-study/files/18physical_mental.pdf

162. Ndiaye SM, Hopkins DP, Shefer AM, Hinman AR, Briss PA, Rodewald L, Willis B; Task Force on Community Preventive Services. Interventions to improve influenza, pneumococcal polysaccharide, and hepatitis B vaccination coverage among high-risk adults: a systematic review. Am J Prev Med. 2005 Jun;28(5 Suppl):248-79. doi: 10.1016/j.amepre.2005.02.016. PMID: 15894160.

163. Edwards KM, Burns VE, Reynolds T, Carroll D, Drayson M, Ring C. Acute stress exposure prior to influenza vaccination enhances antibody response in women. Brain Behav Immun. 2006 Mar;20(2):159-68. doi: 10.1016/j.bbi.2005.07.001. Epub 2005 Aug 15. PMID: 16102936.

164. Więdłocha, M., Marcinowicz, P., Krupa, R., Janoska-Jaździk, M., Janus, M., Dębowska, W., … Szulc, A. (2018). Effect of antidepressant treatment on peripheral

inflammation markers – A meta-analysis. Progress in Neuro-Psychopharmacology and Biological Psychiatry, 80, 217–226. doi:10.1016/j.pnpbp.2017.04.026

165. Young W. Review of lithium effects on brain and blood. Cell Transplant. 2009;18(9):951 75. doi: 10.3727/096368909X471251. Epub 2009 May 13. PMID: 19523343

166. Weetman AP, McGregor AM, Lazarus JH, Smith BR, Hall R. The enhancement of immunoglobulin synthesis by human lymphocytes with lithium. Clin Immunol Immunopathol. 1982 Mar;22(3):400-7. doi: 10.1016/0090-1229(82)90057-5. PMID: 6286192.

167. Ishizaka S, Yoshikawa M, Kitagami K, Tsujii T. Oral adjuvants for viral vaccines in humans. Vaccine. 1990 Aug;8(4):337-41. doi: 10.1016/0264-410x(90)90091-y. PMID: 2396473.139. Spencer JP, Trondsen Pawlowski RH, Thomas S. Vaccine Adverse Events: Separating Myth from Reality. Am Fam Physician. 2017 Jun 15;95(12):786-794. PMID: 28671426.

168. Nichol KL, Margolis KL, Lind A, Murdoch M, McFadden R, Hauge M, Magnan S, Drake M. Side effects associated with influenza vaccination in healthy working adults. A randomized, placebo-controlled trial. Arch Intern Med. 1996 Jul 22;156(14):1546-50. PMID: 8687262.

169. Ackerman CE. What is Positive and Negative Affect in Psychology? Definitions + Scale [Internet]. PositivePsychology.com. 2021 [cited 2021Mar23]. Available from: https://positivepsychology.com/positive-negative-affect/

170. Watson D, Clark LA, Carey G. Positive and negative affectivity and their relation to anxiety and depressive disorders. J Abnorm Psychol. 1988 Aug;97(3):346-53. doi: 10.1037//0021-843x.97.3.346. PMID: 3192830.

171. Renton KW, Gray JD, Hall RI. Decreased elimination of theophylline after influenza vaccination. Can Med Assoc J. 1980 Aug 23;123(4):288-90. PMID: 7260771; PMCID: PMC1704744.

172. Meredith CG, Christian CD, Johnson RF, Troxell R, Davis GL, Schenker S. Effects of influenza virus vaccine on hepatic drug metabolism. Clin Pharmacol Ther. 1985 Apr;37(4):396-401. doi: 10.1038/clpt.1985.61. PMID: 3979001.

173. Morgan ET. Regulation of cytochrome p450 by inflammatory mediators: why and how? Drug Metab Dispos. 2001 Mar;29(3):207-12. Erratum in: Drug Metab Dispos 2001 Jun;29(6):932. PMID: 11181485.

174. Fang J, Coutts RT, McKenna KF, Baker GB. Elucidation of individual cytochrome P450 enzymes involved in the metabolism of clozapine. Naunyn Schmiedebergs Arch Pharmacol. 1998 Nov;358(5):592-9. doi: 10.1007/pl00005298. PMID: 9840430.

175. Levine S, Saltzman A, Katof B, Meister A, Cooper TB. Pertussis vaccine and pertussis toxin increase lithium levels in rats: possible role of G-proteins. Prog

Neuropsychopharmacol Biol Psychiatry. 2000 Jan;24(1):97-104. doi: 10.1016/s0278-5846(99)00083-4. PMID: 10659986.

176. Bundesministerium Österreich. Coronaschutzimpfung in Österreich [Internet]. 2021 [cited 2021July10]. Available from https://info.gesundheitsministerium.at

177. Mohr M. Österreich - Arbeitslosenquote nach Monaten 2021 [Internet]. Statista. 2021 [cited 2021July10]. Available from: https://de.statista.com/statistik/daten/studie/288887/umfrage/arbeitslosenquote-in-oesterreich-nach-monaten/

178. Loomba S, de Figueiredo A, Piatek SJ, de Graaf K, Larson HJ. Measuring the impact of COVID-19 vaccine misinformation on vaccination intent in the UK and USA. Nat Hum Behav. 2021 Mar;5(3):337-348. doi: 10.1038/s41562-021-01056-1. Epub 2021 Feb 5. Erratum in: Nat Hum Behav. 2021 Mar 8;: Erratum in: Nat Hum Behav. 2021 Jul 8;: PMID: 33547453.

179. Neumann-Böhme S, Varghese NE, Sabat I, Barros PP, Brouwer W, van Exel J, Schreyögg J, Stargardt T. Once we have it, will we use it? A European survey on willingness to be vaccinated against COVID-19. Eur J Health Econ. 2020 Sep;21(7):977-982. doi: 10.1007/s10198-020-01208-6. PMID: 32591957; PMCID: PMC7317261.

180. Schernhammer E, Weitzer J, Laubichler MD, Birmann BM, Bertau M, Zenk L, Caniglia G, Jäger CC, Steiner G. Correlates of COVID-19 vaccine hesitancy in Austria: trust and the government. J Public Health (Oxf). 2021 May 5:fdab122. doi: 10.1093/pubmed/fdab122. Epub ahead of print. PMID: 33948665; PMCID: PMC8135852.

181. Zewude B, Habtegiorgis T. Willingness to Take COVID-19 Vaccine Among People Most at Risk of Exposure in Southern Ethiopia. Pragmat Obs Res. 2021 May 27;12:37-47. doi: 10.2147/POR.S313991. PMID: 34079423; PMCID: PMC8166351.

182. Huynh G, Nguyen TV, Nguyen DD, Lam QM, Pham TN, Nguyen HTN. Knowledge About COVID-19, Beliefs and Vaccination Acceptance Against COVID-19 Among High-Risk People in Ho Chi Minh City, Vietnam. Infect Drug Resist. 2021 May 13;14:1773-1780. doi: 10.2147/IDR.S308446. PMID: 34012276; PMCID: PMC8128504.

7. Annex:

Fragebogen: Erhebung der Einstellung zur COVID-19 Impfung

Demographische Daten:

1. Wie alt sind Sie? (Zahl)

2. Bitte geben Sie ihr biologisches Geschlecht an:
   - Männlich
   - Weiblich

3. Bitte geben Sie Ihren höchsten Ausbildungsabschluss an:
   - Keine formale Ausbildung
   - Pflichtschulabschluss
   - Abgeschlossene Lehrausbildung
   - Berufsbildende mittlere Schule
   - Matura
   - Abgeschlossenes Bachelorstudium
   - Abgeschlossenes Master/Diplomstudium
   - Doktorat/PHD

4. Bitte geben Sie Ihren derzeitigen Beschäftigungsstatus an:
   - Arbeitslos
   - Unselbstständig erwerbstätig (Arbeiter*in; Angestellte*r)
   - Selbstständig
   - In Ausbildung
   - Pensionist*in
   - Reha-Geld/ I-Pension

5. Bitte geben Sie an, welche psychiatrische(n) Erkrankung(en) derzeit bei Ihnen vorliegen (Mehrfachantworten möglich):
   - Keine
   - Depressive Störung
   - Bipolare Störung
   - Panikstörung
   - Generalisierte Angststörung
   - Schizophrenie
   - Essstörung
   - Alkoholkrankheit
   - Andere Suchterkrankung
   - Persönlichkeitsstörungen
   - Andere: (Freitext)

   5.a *(wenn eine Erkrankung vorliegt):* Wie stark beeinflusst Sie Ihre aktuelle psychische Krankheitssymptomatik derzeit im Alltag?

   - Sehr stark
   - Eher stark
   - Manchmal
   - Etwas
   - Wenig
   - Gar nicht

6. Bitte geben Sie an, welche psychiatrische(n) Erkrankung(en) jemals bei Ihnen diagnostiziert wurde (Mehrfachantworten möglich):
   - Keine
   - Depressive Störung
   - Bipolare Störung
   - Panikstörung

- Generalisierte Angststörung
- Schizophrenie
- Essstörung
- Alkoholkrankheit
- Andere Suchterkrankung
- Persönlichkeitsstörungen
- Andere: (Freitext)

7. Bitte geben Sie an, welche körperliche(n) Erkrankung(en) derzeit bei Ihnen vorliegen (Mehrfachantworten möglich):
   - Bluthochdruck
   - Asthma
   - COPD
   - Diabetes
   - Koronare Herzkrankheit
   - Herzinfarkt
   - Schlaganfall
   - Erkrankung, die immunsuppressive Therapie erfordert (wenn ja): Welche (Freitext)
   - Andere: (Freitext)

8. Bitte geben Sie an, welche körperliche(n) Erkrankung(en) jemals bei Ihnen diagnostiziert wurde (Mehrfachantworten möglich):
   - Bluthochdruck
   - Asthma
   - COPD
   - Diabetes
   - Koronare Herzkrankheit
   - Herzinfarkt
   - Schlaganfall
   - Erkrankung, die immunsuppressive Therapie erfordert (wenn ja): Welche (Freitext)
   - Andere: (Freitext)

9. Rauchen Sie Zigaretten?
   - Nein
   - Ja

   9.a (wenn ja): Wieviele pro Tag?

10. Wie würden Sie generell Ihre Einstellung zu Impfungen beschreiben? (Mehrfachantworten möglich)
    - Der Nutzen von Impfungen überwiegt für mich persönlich deutlich gegenüber dem Risiko
    - Das Risiko durch sofortige Nebenwirkungen von Impfungen überwiegt für mich persönlich deutlich gegenüber dem Nutzen
    - Das Risiko durch Langzeitnebenwirkungen von Impfungen überwiegt für mich persönlich deutlich gegenüber dem Nutzen
    - Großflächige Impfungen bieten einen guten Schutz für die Gesamtbevölkerung
    - Ich sehe generell wenig Nutzen durch Impfungen für die Gesamtbevölkerung
    - Ich habe die Befürchtung Impfungen haben Wechselwirkungen mit anderen Medikamenten, die ich einnehme
    - Ich habe keine Impfungen, die über verpflichtende Vorgaben hinausgehen erhalten
    - Ich habe auch Impfungen, die über verpflichtende Vorgaben hinausgehen erhalten
    - Ich werde regelmäßig gegen FSME geimpft
    - Ich werde regelmäßig gegen Influenza geimpft

Coronavirus Status:

11. Hatten Sie in der Vergangenheit oder haben Sie aktuell COVID-19 bzw. wurden positiv darauf getestet?
    - Ja
    - Nein

Impfung gegen COVID-19:

12. Wie hoch schätzen Sie ihr Wissen über die COVID-19 Impfungen ein?
    - Sehr hoch
    - Eher hoch
    - Weder noch
    - Eher wenig
    - Sehr wenig

13. Hatten Sie bereits die Möglichkeit sich impfen zu lassen und haben diese abgelehnt?
    - Ja
    - Nein

14. Haben Sie bereits eine COVID-19 Impfung erhalten?

    14.aa (*wenn Ja)*: Mit welchem Impfstoff wurden Sie geimpft?

    - Biontech/ Pfizer
    - Moderna
    - AstraZeneca
    - Weiß nicht
    - Andere

    14.ab *(wenn ja):* Haben Sie Nebenwirkungen verspürt?

    - Nein
    - Ja, aber nur wenige Stunden sehr leichte Symptome (wie Müdigkeit, Erschöpfung)
    - Ja, 1-2 Tage leichte Symptome (wie Müdigkeit, Erschöpfung)
    - Ja, 1-2 Tage moderate Symptome (wie eingeschränkte Leistungsfähigkeit, die Auswirkungen auf die Alltagsführung hatte)
    - Ja, 1-2 Tage schwere Symptome (wie Fieber; deutlich eingeschränkte Leistungsfähigkeit)
    - Ja, länger als 2 Tage moderate Symptome (wie eingeschränkte Leistungsfähigkeit, die Auswirkungen auf die Alltagsführung hatte)
    - Ja, länger als 2 Tage schwere Symptome (wie Fieber; deutlich eingeschränkte Leistungsfähigkeit)
      13aba: Wenn ja, bitte beschreiben Sie Ihre Beschwerden etwas näher: (Freitext)

    14.ac *(wenn ja)* Aus welchen Gründen wurden Sie bereits geimpft? (Mehrfachantwort möglich)
    - Erhöhtes Risiko für einen schweren COVID-19 Verlauf
    - Arbeit im Gesundheitswesen
    - Wohnhaft in einer Pflegeeinrichtung
    - Alter
    - Pädagogisches Personal
    - Weiß nicht
    - Andere Gründe

15. Wie sehr treffen die folgenden Aussagen auf Sie zu?
    - Ich denke der Nutzen der COVID-19 Impfung überwiegt deutlich dem Risiko von Nebenwirkungen.
      Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
    - Ich denke das Risiko der Impfung überwiegt deutlich dem Nutzen.
      Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
    - Ich möchte durch eine Impfung einem persönlich schwerwiegenden COVID-19 Verlauf entgegenwirken.
      Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
    - Ich möchte durch meine Impfung möglicherweise zum Schutz von Anderen beitragen
      Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
    - Ich habe die Befürchtung die Impfung hat Wechselwirkungen mit anderen Medikamenten, die ich einnehme

Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu

- Es wird für mich ein geringer Aufwand sein mich impfen zu lassen.
  Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
- Ich werde mich hauptsächlich impfen lassen, da Angehörige mir dazu raten
  Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
- Ich werde mich hauptsächlich impfen lassen, da Ärzte/Ärztinnen mir dazu raten
  Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
- Ich sehe generell keinen Nutzen in Impfungen.
  Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
- Andere Bemerkungen: (Freitext)

(wenn14 ja)→ Ende

Haben Sie vor sich gegen COVID-19 impfen zu lassen?

16. Wie wahrscheinlich ist es, dass Sie sich gegen Covid-19 sobald Sie die Möglichkeit impfen lassen?
    0-100 %

    Wie wahrscheinlich ist es, dass Sie sich gegen Covid-19 innerhalb eines Jahres impfen lassen?
    0-100%

    Wie wahrscheinlich ist es, dass Sie sich gegen Covid-19 innerhalb von fünf Jahren impfen lassen?
    0-100%

17. Wollen Sie mit der Impfung noch abwarten?
    - Nein
    - Ja

(*wenn: ja*) Aus welchem Grund möchten Sie noch abwarten bzw sich nicht impfen lassen?

- Ich habe Sorgen um direkt eintretenden Nebenwirkungen
  Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
- Ich habe Sorgen um Langzeit Nebenwirkungen
  Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
- Ich sehe derzeit keinen persönlichen Nutzen in der Impfung, da ich bereits COVID-19 hatte
  Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
- Ich sehe derzeit keinen persönlichen Nutzen in der Impfung, da ich keinen schweren COVID-19 Verlauf erwarte
  Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
- Ich sehe derzeit keinen persönlichen Nutzen in der Impfung, da ich generell keinen Nutzen in Impfungen sehe
  Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
- Ich befürchte, dass die Impfung nicht gegen eine Ansteckung wirksam sein wird, sondern nur gegen schwere COVID-19 Verläufe und diesen erwarte ich persönlich nicht
  Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
- Es ist zu schwer die Impfung zu erhalten
  Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
- Impfstoffentwicklung verlief schneller als andere Impfzulassungen

Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu

- Die Impfstoffe wurde meines Erachtens zu wenig getestet
  Ratingskala 0-4 trifft vollkommen zu, trifft einigermaßen zu, weder noch, trifft eher nicht zu, trifft überhaupt nicht zu
- Anderes: (Freitext)