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MENTAL DISORDERS IN PATIENTS WITH NEW CORONAVIRUS INFECTION IN A MULTIDISCIPLINARY HOSPITALSETTING

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DISSERTATION

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CONTENTS

INTRODUCTION

Relevance of the study: The spread of COVID-19 has led to significant changes in the daily lives of most of the world's population [51]. It has been established that patients with COVID-19 may experience numerous mental health issues, including depression, anxiety disorders, stress, panic attacks, irrational anger, impulsivity, somatization disorder, sleep disturbances, post-traumatic stress symptoms, and suicidal behavior. Additionally, several factors have been identified that are associated with mental health issues during COVID-19, including age, gender, marital status, education, occupation, income, and others [139].

The COVID-19 pandemic presents a neuropsychological and psycho-emotional burden. The former is manifested by damage to the central and peripheral nervous systems, neuropsychiatric and cerebrovascular complications, and mental status changes due to the neurotoxic effects of the SARS-CoV-2 virus. The latter is expressed in somatic reactions to the stressful situation [38]. It is assumed that patients affected by COVID-19 may develop psychopathological symptoms for several reasons: worsening of the underlying disease, side effects of medications, fear of death, fear of transmitting the virus to others, social isolation, uncertainty, physical discomfort, and overwhelming negative news coverage in the media [239].

Psychiatric symptoms are common in patients hospitalized for COVID-19 infection. Their identification, diagnosis, and treatment are key to determining the prognosis of the disease and functional recovery. Depression, anxiety, stress, and adjustment disorders, as well as delirium, are widespread among hospitalized patients [94]. Research results by M.A. Samushia et al. [28,29] confirm the heterogeneity of the structure of mental disorders in the acute phase of coronavirus infection, revealing connections between the clinical picture and laboratory indicators of immune response to systemic inflammation.

Degree of study development: However, despite the long-observed link between physical symptoms and mental health issues, this relationship has not been properly studied in the context of COVID-19. Our understanding of the broader patterns of risk factors and vulnerabilities for mental health also remains limited [263]. During the COVID-19 pandemic, the greatest attention was paid to general medical complications, while only a few studies [177] considered the potential direct impact of SARS-CoV-2 on mental health and its neurotropic potential. Furthermore, the indirect consequences of the pandemic for general mental health are of growing concern, especially considering that the SARS-CoV-1 (2002-2003) epidemic was associated with psychiatric complications [252].

Until recently, more attention has been paid to the mental health issues of the general population, healthcare workers, or COVID-19 survivors than to critically ill patients hospitalized with severe conditions. Some studies on multidisciplinary hospitals during the pandemic do not provide any data on patients with mental disorders [18]. Within the hospital setting, the role of psychiatric departments became particularly crucial, presenting challenges for proper clinical management of COVID-19-related psychopathological conditions, especially anxiety and depressive disorders, insomnia, and delirium. These psychiatric complications require rapid and effective treatment using various; factors. Furthermore, the pandemic has influenced the course of already diagnosed mental illnesses. However, existing data on the course of mental disorders during the pandemic are contradictory, and there are few studies dedicated to the direct impact of COVID-19 on the clinical picture of psychiatric conditions [32].

Purpose of the study: to determine the structure and characteristics of mental disorders associated with COVID-19 in the context of organizing consultative psychiatric care in a multidisciplinary hospital.

Research objectives:

1. To determine the structure of mental disorders in patients admitted to a multidisciplinary hospital for treatment of the novel coronavirus infection.

2. To identify comorbid mental disorders that developed concurrently with COVID-19 infection and study their clinical presentation and dynamics.

3. To establish the likelihood of fatal outcomes in patients with mental disorders admitted to a multidisciplinary hospital for treatment of the novel coronavirus infection.

4. To substantiate a framework for providing psychiatric care to patients admitted to a multidisciplinary hospital for treatment of the novel coronavirus infection.

Scientific Novelty:

The novelty of this study lies in the examination of patients during the epidemic surge of COVID-19, which began in major metropolitan areas of Russia and, by April 2020, had confirmed cases in all regions of the Russian Federation. Against this backdrop:

1. For the first time, the structure of mental disorders diagnosed in patients prior to admission to a multidisciplinary hospital was studied.

2. A comprehensive quantitative assessment of delirium in patients with COVID-19 was conducted.

3. A novel combination of delirium components with indicators of physical condition, serving as predictors of disease outcomes, was identified.

4. The reversibility of neurocognitive deficit symptoms by the end of hospital stays was established.

5. A clear relationship between final physical condition indicators, depression, and anxiety was discovered.

6. Based on the findings, a novel framework for providing consultative psychiatric care to patients with COVID-19 and mental disorders admitted to multidisciplinary hospitals was developed.

Theoretical and practical significance: The prevalence and structure of mental disorders during COVID-19 in a multidisciplinary hospital were demonstrated. The relationship between physical and psychiatric symptoms of delirium, neurocognitive deficit syndrome, depression, and anxiety arising in the context of COVID-19 was studied. An important finding was the identification of three patient groups: those with mental disorders combined with COVID-19, those with concerns about COVID-19 but without confirmed infection, and those with mental disorders without concerns about

COVID-19, with suspected but unconfirmed infection. Analyzing incoming patient flows is essential for making timely decisions regarding the deployment of appropriate resources to provide quality psychiatric care. This study highlights the need for psychiatric services at all stages of treatment, determining the sequence and scope of psychiatric consultation activities.

The results helped establish discharge conditions for outpatient follow-up and criteria for transfer to a psychiatric hospital. These data may serve as the basis for initiatives to improve the efficiency of psychiatric care for individuals with mental disorders related to COVID-19 and to strengthen connections between multidisciplinary hospitals with infectious disease wards and outpatient psychiatric and psychotherapeutic services.

Methodology and research methods: The methodology used in the study is based on the fundamental principles of both domestic and international psychiatry. The theoretical foundation of the study is the biopsychosocial model concept by G. L. Engel [103]. The primary research method was the clinical-psychopathological method (categorical model), supplemented by the operational model. Additionally, the clinical-statistical method was employed. The study adhered to the principles of evidence-based medicine.

Research reliability and validation: The reliability of the study is ensured by the representativeness of the sample, the use of valid methods appropriate to the study's objectives, and the application of modern statistical data processing methods. The study's findings have been published in 11 papers, including 4 in peer-reviewed journals listed by the Higher Attestation Commission (HAC) of the Russian Federation and 2 indexed in the Scopus abstract database. The research materials have been presented at international, national, and regional scientific conferences.

Conference Presentations:

1. Sivashova, M.S. Features of the Course of Coronavirus Infection in Patients with Mental Disorders in a Multidisciplinary Hospital / M.S. Sivashova // Personalized Approach in Psychiatry and Addiction. Materials of the VII Scientific-

Practical Conference "Psychotherapy and Psychosocial Work in Psychiatry" and the VI School for Young Psychiatrists of St. Petersburg. – St. Petersburg, 2021. – P. 116-117.

2. Sivashova, M.S. Prognostic Significance of Delirium in COVID-19 in the Elderly / M.S. Sivashova // Psychosomatic Disorders. Materials of the All-Russian Conference-Competition for Young Scientists "Psychiatry of the 21st Century: First Steps into Science and Practice." – Moscow, 2021. – P. 55-56.

3. Sivashova, M.S. Organizational Aspects of Psychiatric Care for Patients with Coronavirus Infection in a Multidisciplinary Hospital / M.S. Sivashova // COVID-19 Section. Materials of the VII All-Russian Scientific Conference of Young Specialists, Postgraduates, and Residents "Innovative Technologies in Medicine: The View of a Young Specialist" edited by R.E. Kalinin. – Ryazan, 2021. – P. 46-48.

4. Sivashova, M.S. Mental Disorders in Patients with Coronavirus Infection in a Multidisciplinary Hospital // Report at the All-Russian Conference for Young Scientists in Memory of Academician A.V. Snezhnevsky. – Moscow, 2023.

5. Sivashova, M.S., Prokopovich, G.A., Pashkovsky, V.E. Structure of Mental Disorders in COVID-19 in a Multidisciplinary Hospital. Clinical and Organizational Aspects / M.S. Sivashova, G.A. Prokopovich, V.E. Pashkovsky // All-Russian Congress with International Participation "Psychoneurology: 19th Century – 21st Century," dedicated to the 115th anniversary of the V.M. Bekhterev National Medical Research Center for Psychiatry and Neurology of the Ministry of Health of Russia and the 165th anniversary of the birth of V.M. Bekhterev. Abstracts of the Conference. – St. Petersburg, May 12-13, 2022. – P. 369-370.

6. Sivashova, M.S., Prokopovich, G.A., Pashkovsky, V.E. Coronavirus Infection and the Course of Schizophrenia / M.S. Sivashova, G.A. Prokopovich, V.E. Pashkovsky // Materials of the Russian Scientific Conference "Psychiatry – Prose and Poetry." – Rostov-on-Don, September 25, 2021. – P. 152-156.

Publications:

1. Prokopovich, G.A. Experience of Psychiatric and Psychotherapeutic Services in an Infectious Disease Hospital During the COVID-19 Pandemic / G.A. Prokopovich, T.V. Vladykina, M.S. Sivashova, O.N. Zueva // V.M. Bekhterev Review

of Psychiatry and Medical Psychology. – 2021. - No.1. – P. 67-76. DOI: 10.31363/2313-7053-2021-1-67-76 [26].

2. Petrova, N.N. Impact of Mental Disorders on COVID-19 Outcomes / N.N. Petrova, V.E. Pashkovsky, M.S. Sivashova et al. // Neurology, Neuropsychiatry, Psychosomatics. – 2021. - Vol.13. - No.5. – P. 40-47. DOI: 10.14412/2074-2711-2021-5-40-47 [24].

3. Pashkovsky, V.E. Features of Cognitive Functioning in Elderly People with COVID-19 / V.E. Pashkovsky, N.N. Petrova, M.S. Sivashova, G.A. Prokopovich // V.M. Bekhterev Review of Psychiatry and Medical Psychology. – 2023, Vol.57, No.1. – P. 61-70. DOI:10.31363/2313-7053-2023-698 [21].

4. Pashkovsky, V.E. Psychiatric Care for COVID-19 Patients in a Multidisciplinary Hospital: Organizational Aspects / V.E. Pashkovsky, N.N. Petrova, M.S. Sivashova, G.A. Prokopovich // Healthcare in the Russian Federation. – 2023. - Vol.67. - No.1. – P. 25-31. DOI: 10.47470/0044-197X-2023-67-1-29-35 [22].

5. Pashkovsky, V.E. Dimensional Approach to Assessing Delirium in COVID-19 in the Elderly / V.E. Pashkovsky, N.N. Petrova, M.S. Sivashova, A.Ya. Vuks, G.A. Prokopovich // V.M. Bekhterev Review of Psychiatry and Medical Psychology. – 2023. - Vol.57. - No.3. – P. 59-69. DOI:10.31363/2313-7053-2023-738 [23].

6. Pashkovsky, V.E. Neurocognitive Syndromes in COVID-19: Clinical Cases / V.E. Pashkovsky, N.N. Petrova, M.S. Sivashova, G.A. Prokopovich // Psychiatry. – 2022. - Vol.20. - No.1. – P. 26-34. DOI: 10.30629/2618-6667-2022-20-1-26-34 [20].

Volume and Structure of the Work

The material is presented in 183 pages of typed text. The work consists of an introduction, 3 chapters, a conclusion, findings, practical recommendations, a list of references, a list of abbreviations, and appendices. The illustrative part includes 31 tables and 3 figures. The list of references contains 271 sources, of which 39 are domestic and 232 are foreign.

Author's Contribution to the Results Presented in the Dissertation

The author independently conducted a review of Russian and foreign literature on the diagnosis, structure, and course of mental disorders during COVID-19. The examination of patients was carried out by the author while working in the "red zone," taking into account the high viral load and significant risk of infection to the medical staff. The author conducted initial clinical-psychological assessments of patients, evaluated their physical condition using the NEWS2 scale for COVID-19, and monitored their condition over time, considering the progression of coronavirus infection. The study design was developed, and the author performed an independent analysis of inpatient records from the infectious disease hospital, as well as analyzed clinical, scale-based, instrumental, and laboratory data. The interpretation, presentation of the findings, formulation of conclusions, defense statements, and practical recommendations were also directly conducted by the author.

Scientific Results

1. The impact of mental disorders on COVID-19 outcomes, [24, 42-45] (the author's personal contribution is no less than 80%).

2. Delirium in COVID-19 patients in a multidisciplinary hospital setting, [23, 61-67] (the author's personal contribution is no less than 80%).

3. Neurocognitive deficits in COVID-19 patients in a multidisciplinary hospital setting, [20, 27-28, 21, 65-67] (the author's personal contribution is no less than 80%).

4. Organizational aspects of providing psychiatric care to patients with COVID-19 and mental disorders in a multidisciplinary hospital setting, [22, 31-34] (the author's personal contribution is no less than 80%).

5. The structure of mental disorders in COVID-19 patients in a multidisciplinary hospital setting, [26, 69-71] (the author's personal contribution is no less than 80%).

Propositions for Defense:

1. Among all inpatients with COVID-19 admitted to a multidisciplinary hospital, mental disorders were diagnosed in 7.1% of cases, with the highest prevalence being organic mental disorders.

2. Correlational relationships were identified between specific symptoms of delirium and physical condition indicators. A comparison of symptoms between patients with clinical stabilization and those with fatal outcomes revealed significant differences only in the variables "sleep-wake cycle" and "motor agitation." Variables such as "respiratory rate" (RR-1), "heart rate," and the total score (TS-2) can be considered predictors of disease outcomes.

3. Comparative analysis of MMSE scale measurements at the beginning and end of hospitalization showed positive dynamics in cognitive performance among patients with neurocognitive deficit syndrome. Improvements were noted in orientation, immediate memory, attention and calculation, word recall, language, and the total score.

4. The highest levels of depression and anxiety were observed in the initial days of hospitalization, but they declined relatively quickly. Correlation analysis revealed a clear relationship between the final NEWS2 physical condition scale scores and the final depression and anxiety scale scores.

5. The framework for consultative psychiatric care for COVID-19 patients with mental disorders involves the work of psychiatrists and psychotherapists in all departments of the multidisciplinary hospital, including the red zone. Psychiatric consultations play a crucial role in determining the prognosis of the primary disease and in functional recovery.

CHAPTER 1.

THE PROBLEM OF NEUROPSYCHIATRIC PATHOLOGY IN THE CONTEXT OF THE NOVEL CORONAVIRUS INFECTION

1.1. Characteristics of Neuropsychiatric Disorders in COVID-19

On March 11, 2020, the World Health Organization (WHO) declared the outbreak of the 2019 coronavirus disease (COVID-19) a pandemic [255]. According to WHO, as of 18:15 Central European Time on November 8, 2023, there were 771,820,937 confirmed cases of COVID-19 globally, including 6,978,175 deaths.

The pandemic significantly disrupted the existing socio-economic order in most countries, including labor market mechanisms, traditional forms, structures, and employment conditions, leading to profound social distortions that affected established sociocultural connections, lifestyles, the configuration of social inequality, and forms and methods of governmental regulation of societal processes [5].

The pandemic inevitably impacted the mental health of the population. Several factors associated with mental health issues during COVID-19 have been identified, including age, gender, marital status, education, occupation, income, place of residence, close contact with individuals infected with COVID-19, pre-existing physical and mental health issues, exposure to news and social media related to COVID-19, coping styles, stigma, psychosocial support, health communication, confidence in healthcare services, individual protective measures, risk of COVID-19 infection, and perceived survival probability. Moreover, the epidemiological distribution of mental health problems and related factors varied across the general population, COVID-19 patients, and healthcare workers [139, 210].

Specific stressors emerged, negatively impacting mental health, and vulnerable groups in terms of psychological stress and pathological psychological defense mechanisms were identified. There was a sharp increase in cases of heterogeneous mental disorders (such as depressive, anxiety, post-traumatic stress disorder, and others) among the population and healthcare workers in infection hotspots [14, 126].

Therefore, underestimating the importance of mental health, which was affected by the viral infection leading to isolation, limited social activity, disrupted sleep, quarantine, and unreliable news, resulted in stress, anxiety, and episodes of depressive reactions. Not only the epidemic but also the “infodemic” created serious public health problems that could further increase the risk of mental illness [154].

The challenges faced by mental health professionals during the pandemic extend beyond disaster psychiatry and include crisis counseling skills, public health knowledge, organizational behavior, psychopharmacology, and providing mental health support to non-psychiatric healthcare workers. Psychiatrists often serve as the primary point of contact with the broader healthcare system for their patients with severe mental illnesses, making them the first responders to the COVID-19 pandemic for many of these individuals. Mental health clinicians need training to recognize the signs and symptoms of this disease and to acquire knowledge of basic strategies to mitigate the disease's spread, both for their patients and for themselves [99, 119].

Initial outbreaks in China were accompanied by 13.8% of cases with severe progression and 6.1% with critical progression [256]. The pandemic of the novel coronavirus infection prompted the need to study the molecular and cellular mechanisms of pathogen-host interaction. The manifestation of neurological symptoms in some COVID-19 patients presents a challenge for neurobiologists due to the insufficiently studied pathomorphogenesis of the disease. A distinctive feature of the pathogenesis of COVID-19 is the cytokine storm, characterized by elevated levels of interleukin-6 (IL-6), IL-1β, tumor necrosis factor-alpha (TNF-α), chemokine ligand 2 (CCL2), and granulocyte-macrophage colony-stimulating factor (GM-CSF). It has been established that virus-induced neuronal death is caused not only by direct cytotoxic effects but also by the dysregulation of the brain's renin-angiotensin system and the release of large amounts of inflammatory cytokines, as part of the cytokine storm. The involvement of neuroglial cells in initiating and sustaining neuroinflammatory and neurodegenerative processes through the activation of their pro-inflammatory phenotype has been demonstrated [1, 152, 163, 188].

Despite significant progress in clinical research that has helped better understand SARS-CoV-2, outbreaks of this viral disease continue to occur in many countries. These outbreaks are primarily attributed to the emergence of mutant variants of the virus. Like other RNA viruses, SARS-CoV-2 adapts through genetic evolution and developing mutations. This leads to the appearance of mutant variants that may have characteristics different from their ancestral strains [68].

There is an increasing amount of relevant data in the literature regarding neuropsychiatric pathology in COVID-19 [165]. Many COVID-19 patients experience neurological complications such as headaches, dizziness, nausea, vomiting, neck muscle tension, olfactory and gustatory disturbances, chronic fatigue, as well as psychological and mental disorders [37, 214, 270]. SARS-CoV-2 infection is associated with a wide range of neurological syndromes affecting the entire nervous system, including the brain's vascular network. A high frequency of acute disseminated encephalomyelitis, particularly with hemorrhagic changes, has been observed [206], with special attention given to common forms of CNS involvement such as encephalitis, cerebrovascular pathology, and headaches. Acute hemorrhagic necrotizing encephalopathy is highlighted as a rare but fatal condition. O.V. Kurushina et al. [12], A. Filatov et al. [107], and L. Mao et al. [177] identified neurological manifestations in patients with more severe infections, including acute cerebrovascular diseases, impaired consciousness, and skeletal muscle damage. Although stroke is a rare complication of COVID-19, it often leads to significant deterioration and mortality. In COVID-19 patients, stroke was correlated with older age, comorbidities, and severe disease progression. Timely assessment and intensive treatment are key to minimizing mortality in patients with acute stroke [53, 136, 232].

Age plays a significant role in the course of the novel coronavirus infection. Studies have shown that this virus leads to worse outcomes and higher mortality rates in elderly individuals and those with comorbidities such as hypertension, cardiovascular disease, diabetes, chronic respiratory diseases, and chronic kidney disease (CKD) [51, 55, 228]. There is limited data on the frequency and evolution of neuropsychiatric manifestations in children with a history of COVID-19. Abnormal

movements, anxiety, and emotional dysregulation have been observed several weeks or months after the resolution of acute infection [227].

Mental disorders also emerge against the backdrop of the novel coronavirus infection [220]. A study conducted by M. Taquet et al. [241] showed that in patients without a prior psychiatric history, a COVID-19 diagnosis was associated with an increased incidence of first psychiatric diagnoses in the following 14-90 days compared to six other health events. The incidence of any psychiatric diagnosis 14 to 90 days after a COVID-19 diagnosis was 18.1% (95% CI 17.6-18.6), with 5.08% (5.2-6.4) being a first diagnosis. The authors conclude that COVID-19 survivors appear to be at increased risk of psychiatric complications, and a psychiatric diagnosis may be an independent risk factor for COVID-19.

According to A. Varatharaj et al. [250], changes in mental status were the second most frequent manifestation, after encephalopathy or encephalitis. Newly diagnosed psychoses, neurocognitive (dementia-like) syndromes, and affective disorders were observed. M.A. Ellul et al. [102] suggest that the proportion of infections leading to neurological diseases is likely to remain small. However, these patients may suffer from significant neurological consequences.

An increasing body of evidence suggests that SARS-CoV-2 infection causes neurological deficits in a significant portion of affected patients. While neurological symptoms manifest acutely during the course of the infection, less is known about the potential long-term consequences for the brain. It is hypothesized that all these symptoms contribute to a decline in cognitive abilities [135, 168]. The combination of physical and mental symptoms may either persist or emerge later, forming a multisystem and disabling syndrome [197]. This syndrome varies from patient to patient and changes over time. It is referred to as "long COVID-19", "post-acute COVID-19 sequelae", "chronic COVID-19" or the most recent term, "post-acute COVID-19 syndrome". While there is no universal consensus on the onset period of the syndrome, the latest NICE guidelines on the matter suggest a 4-week and 12-week timeframe for ongoing symptomatic COVID-19 and post-COVID syndrome, respectively [171].

According to the literature, the most common mental disorders in post-COVID syndrome include asthenia, cognitive impairments, anxiety, depression, insomnia, and stress disorders, which are often combined and form a specific clinical asthenoneurotic syndrome accompanied by depression and cognitive dysfunction [17, 42, 66, 241]. M.S. Alkodaymi et al. [45] note that the existing studies on post-acute COVID-19 syndrome are highly heterogeneous. Future research should include appropriate comparison groups, standardized symptom definitions and measurements, and longer follow-up periods.

1.2. Psychotic Disorders in COVID-19

Previous pandemics have demonstrated that various types of neuropsychiatric symptoms, such as encephalopathy, mood changes, psychoses, neuromuscular dysfunction, or demyelinating processes, can accompany acute viral infections or appear weeks, months, or even longer after recovery. It is hypothesized that the prevalence of schizophrenia spectrum disorders will increase following pandemics [89, 245]. The hypothesis linking infectious epidemics with acute psychosis dates back to the last century. Recently, concerns have been raised about COVID-19 and the risk of first-episode psychosis. The search for potential neurobiological and environmental factors reveals several challenges in establishing a causal relationship between SARS-CoV-2 infection and the onset of psychosis [187]. Some studies point to the risk of mental illness either directly due to virus-induced inflammation or indirectly due to related psychosocial stress, leading to the development of both anxiety-depressive and psychotic symptoms [46, 104, 172, 253]. Others indicate that coronavirus-related psychosis has been identified in various countries, but it is difficult to conclude whether the novel coronavirus is biologically linked to psychosis or exacerbates psychotic symptoms. Therefore, to identify causal links between COVID-19 and psychosis, researchers, according to M. Tariku et al. [242], should conduct prospective studies on the direct biological impact of COVID-19 on the onset of psychosis. Clinicians should also be attentive to psychotic symptoms in treatment centers and quarantine facilities to reduce complications caused by the novel coronavirus.

The onset of delirium is largely explained by a recently proposed theory of systemic integration failure, which unites the most significant previously described hypotheses by describing the varying contributions of each to a complex network of pathways. It highlights areas of overlap and similarity and explains how the variable contribution of these factors can lead to the development of the different cognitive and behavioral dysfunctions characteristic of delirium. The specific cognitive and behavioral manifestations of delirium are the result of a combination of neurotransmitter function and availability, variability in sensory information integration and processing, motor responses to both external and internal signals, and the degree of disruption in neural network connectivity, hence the term "acute brain failure" [176].

Organic changes in the form of systemic inflammation, as well as neuroinflammatory alterations associated with a massive increase in pro-inflammatory molecules in the brain, neuroglial reactivity, changes in the neurochemical landscape, and pathological remodeling of neural networks, in combination with environmental stress, contribute to the development of neuropsychiatric disorders. These disorders include major depressive disorder, bipolar disorder, various psychoses, obsessive-compulsive disorder, and post-traumatic stress disorder [232].

Patients with severe mental illnesses such as schizophrenia, schizoaffective disorder, and bipolar disorder are at increased risk of severe outcomes when infected with coronavirus disease 2019 (COVID-19). However, the question of whether these patients are at a higher risk of contracting COVID-19 remains insufficiently studied. The prevalence of SARS-CoV-2 among patients with severe mental illness was significantly lower than among blood donors, and these differences in prevalence remained significant after adjusting for sex and age [226]. According to S.R. Beach et al. [57], delirium should be considered a potential sign of SARS-CoV-2 infection and may even be the only presenting symptom. Based on the high rates of delirium demonstrated in previous studies, changes in mental status should be considered upon hospital admission. Further research is needed to determine whether delirium in COVID-19 represents primary encephalopathy, indicating viral invasion of the CNS, or secondary encephalopathy related to a systemic inflammatory response or other factors.

Other authors emphasize the role of contributing factors in the emergence of psychosis. According to a single-center retrospective and observational study, nine patients developed psychotic symptoms at least two weeks after the initial somatic manifestations of COVID-19, and they received pharmacological treatment. Delusions and confusion were the most frequent clinical manifestations [205].

The role of iatrogenic factors in the development of psychosis is also discussed in the literature. D.T. Lee et al. [164] observed that a number of patients with severe acute respiratory syndrome (SARS) developed affective psychosis during the acute phase of their illness. After analyzing all psychiatric consultations related to SARS in Hong Kong and investigating the risk factors for psychosis in SARS patients in a comparable case-control study, the authors noted that patients with SARS-associated psychosis received higher cumulative doses of steroids and had a higher incidence of mental illness in their family histories. The study results indicated that steroid toxicity, personal vulnerability, and possibly psychosocial stressors collectively contributed to the development of psychosis in SARS patients. Thus, the use of high doses of corticosteroids was identified as a significant associated factor in psychotic manifestations [105].

The structure of COVID-19-associated psychoses has been represented by various psychopathological syndromes, ranging from mild delusional states to hallucinatory-paranoid experiences [108, 109, 204, 219]. Several studies describe psychoses in patients who had no prior history of mental illness before contracting coronavirus. For instance, a 36-year-old previously healthy woman with no personal or family history of psychiatric disorders developed psychosis for the first time after being diagnosed with symptomatic COVID-19. Her delusions were primarily directed at her partner and focused on the safety of her children and her personal finances. She believed that her partner was attempting to kidnap her children and steal her money [233]. Systematized delusions, affective symptoms, and self-harm ideation requiring long-term treatment and patient care are discussed in the work of T. Maiti et al. [175].

The paper describes acute psychoses with religious delusions. In a patient observed by L. Alba, et al. [43], two weeks after the onset of infection and following

the resolution of fever, there was a sudden onset of disorganized behavior and speech, death delusions, and mystical visual hallucinations in the form of angels and demons. In a case described by A.F. Correa-Palacio et al. [73], religious delusions developed against a manic background: the patient's speech was loud, repetitive, and logorrheic, accompanied by grandiosity, a belief in "direct communication with God," and ideas of persecution by medical staff and the police. The patient experienced visual and auditory hallucinations, as well as eight days of insomnia. The psychosis of a patient observed by R. Noone et al. [200] included disorientation, transformation into the devil, auditory hallucinations, paramnesias, insomnia, episodes of crying, hopelessness, sadness, guilt, and passive suicidal thoughts. In patients described by A. D'Agostino et al. [80], religious delusions were attenuated after treatment with relatively low doses of antipsychotics (olanzapine equivalents = 10.1 ± 5.1 mg).

Alongside patients whose psychoses developed against the backdrop of a coronavirus infection, there were reactive states in those who did not test positive for the virus. One patient was convinced that the end of the world was near and attempted suicide. According to M.J. Valdés-Florido et al. [247], this type of psychosis is associated with a high risk of suicidal behavior and, although short-lived, is characterized by frequent psychotic relapses and low diagnostic stability over time. A patient described by J. Huarcaya-Victoria et al. [144] followed auditory instructions in her head that told her she needed to get tested for the virus. She went to a medical center, where the examination revealed she did not have COVID-19. Nevertheless, the voice continued to issue commands. As a result, she visited two more medical centers to get tested. Over time, the auditory hallucinations intensified, increasing her anxiety. At night, she began to feel a "malevolent demonic force that would take her soul to possess it."

In some cultures, the inability to perform religious rituals and family traditions due to quarantine acted as a psychogenic factor. For example, a patient described by P.S. Chandra et al. [70] lost sleep and obsessively watched news about the spread and deaths caused by COVID-19. She became convinced that her family deity would curse her with COVID-19 for not performing an annual ritual, and if she tested positive for

the virus, the police would take her away from her family.Thus, the physiological changes caused by a coronavirus infection may trigger the manifestation of mental disorders, including those of a psychotic level.

1.3. Neurocognitive Deficit in COVID-19

A serious complication of coronavirus infection is cognitive impairment, which can develop at various times after the onset of the disease and may persist for an indeterminate period. It is unknown whether these impairments will be short-term or long-lasting. It also remains unclear how quickly the damaged brain matter can recover and what consequences the human immune system might face after a new coronavirus infection [25]. To date, the exact pathogenesis and mechanisms underlying cognitive dysfunction in COVID-19 remain unclear, hindering the development of appropriate management strategies. However, proposed mechanisms, suggested by various studies, include direct damage to the blood-brain barrier, systemic inflammation, prolonged hypoxia, and as a complicating factor, long-term hospitalization in intensive care units. Nevertheless, there are no clear management guidelines for patients [231].

Several studies have focused on the impact of age on neurocognitive functioning in COVID-19. Cognitive impairments in children are reflected in only a few studies. In children who recovered from COVID-19 and were examined at Children's Hospital No. 8 in Yekaterinburg, significant differences were found compared to the results of neuropsychological tests conducted on children in the control group. These findings revealed impairments in memory, attention, visual gnosis, visuospatial function, kinesthetic and dynamic praxis, and both verbal and non-verbal components of thinking. According to A.R. Luria's theory [13], these impairments affect the temporo-parieto-occipital, mediobasal, fronto-temporal regions of the brain, the reticular formation, and limbic structures [244].

Elderly individuals are at high risk of developing severe forms of COVID-19 due to age-related factors and the higher prevalence of comorbid conditions, making them more vulnerable to potential long-term neuropsychiatric and cognitive impairments [48]. Furthermore, olfactory and severe taste dysfunctions have been identified as

independent predictors of cognitive impairments in a nationally representative sample of elderly individuals [71]. Among elderly patients, those already diagnosed with dementia were the most vulnerable. The monthly decline in MMSE (Mini-Mental State Examination) scores before the quarantine was 0.2 ± 0.1 points, while during quarantine, it was 0.53 ± 0.3 points, which was statistically significant ($p = 0.001$). Memory was the most affected cognitive domain, with an average decline of 1.5 ± 0.8 points, indicating a rapid decrease in cognitive functions in patients with dementia during the quarantine period [146]. A positive correlation between age and performance in almost all evaluated tasks was noted, indicating milder cognitive impairments with increasing age. When comparing patients by age, it was found that older patients generally maintained cognitive functions, with only minor impairments in attention and processing speed, whereas younger patients exhibited more pronounced and heterogeneous cognitive impairments [92, 137].

The results of C. Solaro et al. [234] also indicate a significant and unexpected frequency of cognitive disorders in young COVID-19 patients during the subacute phase at the time of hospital discharge. Other studies have shown that patients with severe functional impairments experienced significant cognitive and emotional deficits, which may have been influenced by mechanical ventilation, although authors suggest that these deficits were primarily associated with aging, regardless of functional independence measures. These findings should be considered to ensure appropriate neuropsychological care for COVID-19 patients in the subacute phase of the disease, for long-term psychological support and treatment after COVID-19 [44].

Mild cases of COVID-19 do not always correlate with milder cognitive impairments [87]. R.R. Reeves et al. [217] describe a 51-year-old woman who had been functioning normally before the illness and experienced mild symptoms of coronavirus infection, yet developed cognitive impairments to the extent that she was unable to care for herself. According to F. Boesl et al. [64], 89% of patients who sought care at a neurological outpatient clinic initially had mild COVID-19 and were not hospitalized. Most of the patients were women (67% versus 33% men). The most frequently reported symptom was cognitive impairment (72%). Additionally, 30% of patients reported

cognitive deficits and scored below 26 points on the Montreal Cognitive Assessment. Other commonly reported symptoms included fatigue (67%), headaches (36%), and persistent hyposmia (36%). Signs of severe depression were observed in 5.5% of all patients. It has been suggested that olfactory dysfunction serves as a clinical biomarker for both neurological damage and cognitive impairment in mild cases of COVID-19 [211]. Conversely, Y.H. Liu et al. [170] reported that patients with severe COVID-19 exhibited a higher proportion of ongoing cognitive impairments and long-term cognitive decline compared to those with mild COVID-19. Severe COVID-19, delirium, and COPD were identified as risk factors for ongoing cognitive impairments, while low education level, severe COVID-19, delirium, hypertension, and COPD were risk factors for long-term cognitive decline. Diarrhea and oxygen therapy were associated with neurocognitive impairments. Cognitive complaints were also linked to anxiety and depression [47].

During the acute phase, patients requiring intensive care unit (ICU) treatment exhibited greater breadth and severity of impairments compared to those needing less intensive care. The most commonly affected areas were data processing speed (35%), verbal fluency (26-32%), learning ability (27%), and memory (27%). Among all patients, 35% had moderate symptoms of depression (23%), anxiety (15%), or functional decline (15%); 25% of ICU patients reported trauma-related distress [249]. In severe cases during the acute phase, frequently detected cognitive impairments included executive functioning, attention, and memory [63, 254].

A significant proportion of individuals experience persistent fatigue and/or cognitive impairments after the resolution of acute COVID-19. The frequency and debilitating nature of these symptoms have driven efforts to characterize their underlying neurobiological substrates and to determine the best approaches to treatment [69]. Hospitalized COVID-19 patients who reported cognitive symptoms demonstrated declines in cognitive performance, particularly in attention and executive functioning, episodic memory, and visuospatial processing [58, 88, 183, 208].

Cognitive impairments following the acute phase of COVID-19 are commonly observed in patients across various age groups. Since the risk of progression from mild

cognitive impairments to moderate and severe forms is higher than average in such patients, clinicians must be aware of the need for early detection [11].

Accumulating clinical data shows that a large population of COVID-19 survivors may experience long-term dysfunction in one or more organs, a phenomenon widely known as post-COVID or long COVID. Regarding neurocognitive deficits, as reported by J. Khieukhajee et al. [155], multivariate analysis did not reveal any statistical differences in cognitive outcomes between patients who had recovered from acute COVID-19 and a healthy control group. However, most studies indicate that fatigue and cognitive dysfunctions, such as issues with concentration, short-term memory deficits, general memory loss, specific attention decline, impairments in speech and praxis abilities, reduced fluency in encoding and verbal speech, and deficits in executive functions and psychomotor coordination, are among the most common and debilitating features of neuropsychiatric symptoms in post-COVID syndrome [7, 8, 62, 129, 185, 264, 267].

Literature also tracks neurocognitive symptoms based on recovery timelines. Patients in A. Jaywant et al. [150] were assessed, on average, 43.2 days (SD = 19.2) after their initial hospitalization. A total of 50 patients (88%) had documented hypoxemic respiratory failure, and 44 (77%) required intubation. Forty-six patients (81%) had cognitive impairments ranging from mild to severe. These impairments were primarily associated with working memory, cognitive flexibility, divided attention, and processing speed. Executive dysfunction was not significantly correlated with the duration of intubation, time from extubation to assessment, psychiatric diagnosis, or pre-existing cardiovascular/metabolic conditions. Three to four months after discharge, K.W. Miskowiak et al. [186] examined the frequency, nature, and severity of cognitive impairments, as well as their relationship with subjective cognitive complaints, quality of life, and other variables. The percentage of patients with clinically significant cognitive impairments ranged from 59% to 65%, depending on the threshold for clinical significance. Verbal learning and executive functions were the most affected. Six months post-infection, the most frequent symptoms were fatigue, malaise following physical exertion, and cognitive dysfunction [78, 84, 106, 113].

On average, 11 months (range 8-13) after a positive PCR test, cognitive performance in areas such as short-term memory, visuospatial processing, learning, and attention was below normal. One-third of COVID-19 survivors exhibited objective cognitive impairments with frontal-subcortical dysfunction 12 months after discharge from the intensive care unit. Emotional disturbances and perceived cognitive deficits were common. Female gender and PTSD symptoms were predictive factors for perceived cognitive decline, while cognitive reserve was a protective factor for objective cognitive functioning [118, 237].

Thus, COVID-19 can lead to prolonged systemic inflammation, predisposing patients to persistent depression and associated neurocognitive dysfunction. The blood-brain barrier serves as a physiological interface where numerous mechanisms of cognitive impairments converge. The link between inflammation, depression, and neurocognitive impairments in COVID-19 patients should be explored in long-term longitudinal studies to better personalize treatment options for COVID-19 survivors [180, 225].

1.4. Neurotic, Stress-Related and Somatoform Disorders in COVID-19

During epidemics, the number of people whose mental health is affected typically exceeds the number of those directly impacted by the infection. Past crises have shown that the mental health consequences can last longer and have a broader prevalence than the epidemic itself, with psychosocial and economic impacts that may be incalculable when considering their ripple effects in various contexts [74, 202].

Several countries have conducted population surveys on mental health during the COVID-19 pandemic. In Switzerland, an observational cohort study involved 1,547 adults from the general population infected with SARS-CoV-2. The prevalence of individuals reporting symptoms of depression and anxiety was assessed before, during, and after isolation using the DASS-21 scale. The proportion of participants suffering from depression increased from 10.0% to 17.1%, and those with anxiety rose from 9.1% to 17.6% during isolation [97].

In Russia, the severity of anxiety among the population was studied using the C.D. Spielberger method [235], adapted by Y.L. Khanin [34]. It was found that 50.5% of respondents exhibited moderate situational anxiety, 31.0% had high levels, and 18.5% had low levels. Regarding trait anxiety, 44.5% showed a moderate type, 41.5% had high levels, and 14.0% had low levels [39].

C. Zhu et al. [271] reported that, according to contemporary literature, the overall prevalence of depression and anxiety during the pandemic reached 45% and 47%, respectively, significantly higher than in non-epidemic periods. The “COVID-19 Mental Disorders Collaborators” research group [75] concluded that in 2020, the pandemic led to a 27.6% increase in cases of major depressive disorders and a 25.6% increase in anxiety disorders worldwide.

However, M. Daly [82] argued that these figures were obtained during the early stages of the pandemic when symptoms of anxiety and depression were most pronounced, likely representing an acute reaction to an unexpected and unfamiliar emerging crisis.

Data on gender preference in the development of neurotic symptoms during COVID-19 are contradictory. J. Deng et al. [91] found no significant differences in the prevalence of depression, anxiety, and sleep disorders between men and women. On the other hand, other authors suggest that women and individuals with low income are particularly vulnerable. Results showed that gender has a moderate and statistically significant effect on fear and anxiety related to COVID-19, with women being more affected. Women perceive COVID-19 as a greater threat to personal health and the population than men [156, 179, 184]. A meta-analysis revealed an overall prevalence of OCD during the COVID-19 pandemic of 41.2%, with 47.1% in women and 39.1% in men. However, the difference between the sexes was not statistically significant. Overall, it seems that women are at greater risk of OCD during the COVID-19 pandemic. In specific groups, female gender may act as a risk factor: students under 18 years, hospital staff, and participants in Middle Eastern studies. In none of the categories was male gender clearly identified as a risk factor [147].

Research on the age aspect shows that the COVID-19 pandemic has had a range of adverse effects on the mental health of young people [41, 59, 131, 181]. In a review by K. Walsh et al. [252], consisting of 461 records and analyzing 68 selected articles, it was found that the prevalence of anxiety among children during the COVID-19 pandemic ranged from 18.9% to 23.87%, while among adolescents, it ranged from 15.4% to 39.9%. Female gender was the most studied risk factor, and physical activity was the most documented preventive factor.

The combined estimates obtained in the first year of the COVID-19 pandemic suggest that 1 in 4 young people worldwide experience clinically elevated symptoms of depression, while 1 in 5 young people experience clinically elevated symptoms of anxiety. These combined estimates, which increased over time, are twice as high as pre-pandemic estimates. A surge in the population seeking psychiatric care is expected, and allocating resources to address children's and adolescents' mental health issues is crucial [215]. Studies conducted in China showed that mental health problems, particularly emotional disorders, are widespread among adolescents [174]. Stressful events have a significant impact on the epidemiology of emotional disorders. An online survey of 8,079 people revealed that the prevalence of depressive symptoms, anxiety symptoms, and a combination of depression and anxiety symptoms among Chinese high school students during the COVID-19 outbreak was 43.7%, 37.4%, and 31.3%, respectively [269].

The three most common symptoms according to S. Tang et al., [239] (2020) were: anxiety (24.9%), depression (19.7%), and stress (15.2%). Young people reported significantly higher prevalence of generalized anxiety disorder and depressive symptoms compared to older adults [143]. A cross-sectional study of 584 young people, conducted two weeks after the onset of COVID-19 in China, showed that nearly 40.4% of the young people included in the sample were prone to psychological problems, and 14.4% of the sample had symptoms of post-traumatic stress disorder (PTSD). Univariate logistic regression showed that mental health in young people was strongly associated with education level, employment, PTSD symptoms, and the use of negative coping styles [166].

Since its discovery in December 2019, the coronavirus disease 2019 (COVID-19) has had economic, social, physical, and psychological impacts on older adults. In a descriptive review by D.A. Bafail [54], it is reported that older adults during the pandemic experience loneliness, stress, depression, anxiety, sleep disturbances, and suicidal thoughts. A study by K. Fujita et al. [114] shows that adults under 75 years of age, who are generally considered relatively healthy, are at high risk for developing depressive mood and apathy. A survey was conducted among older adults with an average age of 69, who had been diagnosed with major depression before the pandemic. It turned out that they were more concerned about the risk of virus infection than the risks of isolation, showed resilience to stress and physical distancing, and most of them were not socially isolated, maintaining virtual contacts with friends and family. Their quality of life deteriorated, and they worried that their mental health would suffer due to the ongoing physical distancing. They were upset by the inadequate government response to the pandemic [128].

A characteristic feature of anxiety in older age is concern about physical health. There is a high prevalence of post-traumatic stress symptoms, anxiety, depression, and insomnia. Correlational analysis showed that both health anxiety and age discrimination (ageism) were positively associated with anxiety symptoms. Moreover, the relationship between health anxiety and anxiety symptoms was stronger among older adults experiencing age discrimination [61, 122].

A number of studies have reflected the impact of COVID-19 on individuals with comorbidities [261]. The level of distress among patients with severe mental illnesses, caused by the COVID-19 pandemic and widespread quarantine, was undoubtedly higher than in the general population [116, 145]. Approximately a quarter of cancer patients experienced high and persistent PTSD during the first year of the COVID-19 pandemic [56, 209]. During the pandemic, there were reports of increased stress, anxiety symptoms, depression, and sleep problems among individuals with cardiovascular diseases [201].

The 2019 coronavirus disease (COVID-19) has had various impacts on patients with obsessive-compulsive disorder (OCD). It remains a complex task to determine the

extent to which OCD has worsened due to the pandemic [169]. OCD symptoms began to emerge in individuals who had not previously experienced them before the quarantine [79, 83]. The results of the study by M. Dehghani et al. [86] showed that a moderate level of fear of COVID-19 was observed in the study population. Additionally, a relatively high proportion of participants exhibited mild OCD symptoms. It seems that two years after the start of the COVID-19 pandemic, people had adapted to the conditions, and their fear of the disease had decreased. OCD-like symptoms were observed in most individuals recovering from mild and moderate COVID-19. Furthermore, the prevalence, severity, and significance of symptoms varied depending on socio-demographic inequalities and overall health status [229]. During the pandemic, there was a significant increase in the frequency of obsessive thoughts about contamination and compulsive washing/cleaning behaviors. Obsession scores on the CY-BOCS scale, the compulsions subscale ($p<0.001$), total scores, and CGI-S scores ($p<0.001$) during the pandemic were statistically higher than before the pandemic [240]. Most studies showed that OCD symptoms worsened in the early stages of the pandemic, especially in individuals with contamination-related OCD, although other symptoms were also found to worsen. Many patients and individuals in the general population exhibited new OCD symptoms related to COVID-19. The frequency of symptom exacerbations, as reported by patients themselves, and symptoms related to COVID-19 were consistently lower in studies that recruited patients from specialized clinics (compared to online samples). The COVID-19 pandemic was a huge stressor for individuals with OCD, especially for those with symptoms of infection. Despite this, there is strong evidence to suggest that "gold standard" approaches to treating OCD maintained their high efficacy. In patients with OCD (including those with contamination-related obsessions), who received prevention of exposure and response prevention combined with pharmacological treatment, no symptom exacerbation was observed during COVID-19 at both 2- and 6-month follow-ups. The dissemination and effective implementation of evidence-based OCD treatments is an urgent public health priority [67, 124].The stress caused by the pandemic affects not only individuals infected with the new coronavirus but also their surrounding environment [98, 230].

The COVID-19 pandemic has deeply changed the social and work environment for several reasons. Social distancing policies, mandatory quarantines, periods of isolation, fear of illness, as well as the suspension of production activities, loss of income, and fear for the future collectively impact the mental health of citizens and workers [117]. Families of critically ill COVID-19 patients may be at particularly high risk of developing anxiety, depression, and post-traumatic stress disorder [224]. After the loss of a loved one, people who have experienced a significant loss typically undergo acute grief reactions, including distress from separation (such as longing for the deceased), as well as emotional (such as feelings of sadness), cognitive (such as thoughts of self-blame), and behavioral (such as avoidance of places, objects, or thoughts related to the loss) symptoms [218].

The COVID-19 pandemic exacerbated mental health issues among healthcare workers [258]. Post-traumatic stress disorder was the most common mental health disorder reported by medical staff during the COVID-19 pandemic, followed by anxiety, depression, and distress. Their fear of COVID-19 was linked to physical anxiety scales, depression, and sensitivity to anxiety [151, 223]. Compared to non-medical workers, healthcare professionals had a higher prevalence of insomnia, anxiety, depression, somatization, and obsessive-compulsive symptoms [265].

Thus, the neurological and neuropsychiatric manifestations of COVID-19 are numerous. The clinical features of damage to both the central and peripheral nervous systems are evident. Most psychological consequences are secondary to the normative, socio-economic, and psychosocial changes related to the pandemic [222].

1.5. Organization of Care for Patients with Mental Disorders Associated with COVID-19 in a Multispecialty Hospital

The coronavirus pandemic and associated social distancing measures have led to significant changes in people's lives [148]. Analyzing 656 urgent psychiatric consultations in 2019 and 811 in 2020, requested by 425 patients in 2019 and 488 in 2020, researchers observed an increase in the overall and daily number of consultations, which were more frequently required by patients undergoing treatment in local

outpatient services compared to the previous period. Throughout 2020, an increasing number of consultations were conducted remotely, which allowed for the avoidance of hospitalization as much as possible. During the coronavirus pandemic, mental health centers had to face an increased demand for clinical services, especially from the most clinically and socially vulnerable patients, who more often required consultations in outpatient psychiatric services [96,158]. Numerous neuropsychiatric complications related to COVID-19 have been described [141], but large-scale studies providing a broader picture of these complications and their relative frequency are lacking. C. Delorme et al. [90] described a range of neurological and psychiatric complications in patients with COVID-19 observed in a multidisciplinary hospital over six months. A total of 249 COVID-19 patients with de novo neurological or psychiatric symptoms were included in the database, and 245 were included in the final analysis. 114 patients (47%) were hospitalized in the intensive care unit, and 10 (4%) died. The most commonly diagnosed neuropsychiatric complications were encephalopathies (43%), polyneuropathy and myopathy in critical conditions (26%), isolated mental disorders (18%), and cerebrovascular disorders (16%). No patient had cerebrospinal fluid evidence of SARS-CoV-2. Encephalopathy correlated with advanced age and a higher risk of death. Neurological manifestations were widespread among hospitalized COVID-19 patients, with more than half of them presenting some form of neurological symptoms. Neuro-myopathy in critical conditions was associated with prolonged stays in the intensive care unit. Most of these neuro-psychiatric complications could be attributed to critical illness, intensive care, and systemic inflammation, contrasting with the rarity of complications directly related to SARS-CoV-2 or post-infectious disorders [221].

The cross-sectional study included all patients hospitalized with COVID-19 and referred for psychiatric consultation at a large COVID-19 center in Tehran. Of the 1791 hospitalized patients with COVID-19, 132 patients (7.3%) were referred for psychiatric consultation. The most common reasons for referral were anxiety and aggression (23.5%). Meanwhile, 92.4% of patients were diagnosed with at least one mental disorder, including insomnia (64%), delusions (30.3%), anxiety due to hypoxia

(15.3%), and generalized anxiety disorder (10.6%). According to the authors of the study, requests for psychiatric consultations and consideration of mental health issues remain surprisingly low. The most common disorders were insomnia, delusions, and anxiety. The frequency of emotional disorders in hospitalized patients was reported by the COMEBAC Study Group, M.A. Samushiya et al., and Z.M. Nakamura et al. A noticeable pathology among hospitalized patients was cognitive decline. Cognitive impairments seem to be linearly associated with the duration of stay in the intensive care unit (ICU). The longer patients spend in the ICU, the lower their MMSE scores, indicating poorer global cognitive functioning.

Psychiatric disorders caused by psychogenic factors were particularly significant. Hospitalized patients found visiting restrictions difficult, with many reporting that the pandemic made them feel unsafe, affected their sleep, and caused fears of virus transmission from other patients. Among the staff, nearly half feared contracting the virus, most feared bringing it home and infecting their families, and a third were concerned that the pandemic jeopardized the treatment provided to patients [93,175].An important issue of mental pathology in COVID-19 is delirium [49, 85, 111, 177]. Delirium (acute brain dysfunction) is a potentially life-threatening disturbance of brain function that often occurs in critically ill patients. While this type of brain dysfunction develops rapidly in intensive care units, striking limitations in the use of delirium-related terminology at the international level hinder cross-disciplinary discussions and collaborative research. In the English-language literature, synonyms for delirium such as intensive care unit syndrome, acute brain dysfunction, acute brain failure, psychosis, confusion, and encephalopathy are widely used. This often leads to scientific "confusion" regarding the published data and methodology within research, which is further exacerbated by organizational, cultural, and language barriers [191]. Delirium, a dangerous adverse prognostic phenomenon, serves as a barometer of systemic damage in critical conditions. Early reports from China on 25% of encephalopathy cases are likely significantly underestimated, as we know this happens whenever delirium is not controlled using reliable tools. Indeed, patients with COVID-19 are at increased risk of developing delirium due to at least seven factors, including (1) direct CNS damage, (2)

induction of inflammatory mediators in the CNS, (3) secondary effects of organ failure, (4) effects of sedative strategies, (5) prolonged mechanical ventilation, (6) immobilization, and (7) other necessary but harmful environmental factors, including social isolation and quarantine without family. Given the early understanding of the virus's pathobiology and the new interventions used to treat critically ill patients, delirium prevention and management will be extremely challenging, especially in the intensive care unit (ICU) [157].Delirium was a common phenomenon in emergency departments, predominantly of the hypoactive type. Although delirium monitoring is recommended in numerous evidence-based guidelines as part of routine clinical care, it is still widely and consistently not conducted at the patient's bedside in various healthcare settings. According to pre-pandemic data, delirium was not recognized by emergency physicians in 76% of cases [130]. The use of delirium risk assessment could potentially improve delirium screening effectiveness in emergency department settings [178]. Several detection methods have been developed for use in intensive care unit (ICU) patients [101]. When using the Confusion Assessment Method for the ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC), it was found that CAM-ICU showed superior sensitivity and negative predictive value (64% and 83%) compared to ICDSC (43% and 75%). ICDSC showed higher specificity and positive predictive value (95% and 82% versus 88% and 72%) [236,248]. The modified Confusion Assessment Method for the Emergency Department (mCAM-ED) was used in the study by F.F. Grossmann et al. [121]. The authors concluded that the method had sufficient sensitivity.

Psychotic symptoms are observed in patients infected with SARS-CoV-2 without a prior psychiatric history and are more common in patients discharged from intensive care units. These psychotic episodes are accompanied by symptoms of confusion, develop rapidly, and resolve with low doses of antipsychotics [205].

Pharmacological treatments used against COVID-19 may be associated with newly onset psychotic manifestations. When conducting psychopharmacological therapy for patients with coronavirus respiratory syndrome, the potential risks of side effects and complications, primarily related to respiratory function, including adverse

drug interactions, should be assessed [16,153].In not all cases did the use of antipsychotic medications have a beneficial effect. According to J. Helms et al. [133,134], delirium combined with cognitive impairments developed in 118 patients (84.3%). Unexpected agitation was observed in 88 patients (69.3%), despite the high frequency of sedative and antipsychotic infusions, and 89 patients (63.6%) exhibited signs of corticospinal tract dysfunction. In contrast, in the study by C. Diez-Quevedo [94], delirium during hospitalization and mood disorders in the medical history were independently associated with a higher risk of mortality (hazard ratios of 1.39 and 1.52, respectively), while treatment with anxiolytics/sedatives and antidepressants in the previous year was independently associated with a lower risk of mortality (hazard ratios of 0.47 and 0.43, respectively). Specific knowledge about COVID-19 remains insufficient today, but in this context, we must recommend caution in the use of psychotropic drugs to avoid worsening the mental state of patients with mental disorders, who are potentially vulnerable in the context of an epidemic, iatrogenic risk, or loss of efficacy [149].

Immediately after discharge from a multidisciplinary hospital, psychotic symptoms sometimes worsened. A patient described by N. Kozato et al. [159], after being discharged from the intensive care unit, was unable to sleep, became increasingly agitated, and was noted to be banging his head against the walls, causing hematomas. He remained very anxious, developed paranoid delusions, auditory and tactile hallucinations, and required hospitalization in a psychiatric department. Antipsychotic treatment gradually improved his symptoms over several weeks. Six months after acute COVID-19 infection, survivors were primarily affected by fatigue or muscle weakness, sleep problems, anxiety, or depression [142]. One year after treatment in the intensive care unit for COVID-19, 182 of 245 patients (74.3% [95% CI, 68.3% to 79.6%]) reported physical symptoms, 64 of 244 patients (26.2% [95% CI, 20.8% to 32.2%]) reported psychiatric symptoms, and 39 of 241 patients (16.2% [95% CI, 11.8% to 21.5%]) reported cognitive symptoms [132].Healthcare systems around the world have faced the challenge of increasing demand for healthcare services for people with COVID-19. This issue is compounded by fear, stigma, misinformation, and travel

restrictions, which hinder the provision of medical care in any setting. When healthcare systems are overwhelmed and people lack access to necessary medical care, both direct mortality from disease outbreaks and indirect mortality from preventable and treatable conditions rise sharply [2,72].

One of the most serious issues in providing psychiatric care is burnout among healthcare workers. The recent COVID-19 pandemic has had a significant impact on the mental health of nurses caring for elderly patients in facilities. Care in this environment can be challenging, with higher levels of burnout and compassion fatigue [207]. According to surveys conducted in hospitals in Italy, staff directly caring for patients with the new coronavirus infection reported higher levels of stress, emotional exhaustion, and depersonalization ($p < 0.001$) compared to colleagues working in departments not directly caring for COVID-19 patients. Mature defensive functioning was associated with resilience and personal achievements ($r = 0.320$; $p < 0.001$), while neurotic and immature defense mechanisms were linked to stress and burnout. Stress and emotional burnout were predicted by younger age, female gender, greater exposure to COVID-19, lower resilience, and immature defense mechanisms among healthcare workers ($R2 = 463$; $p < 0.001$) [95].

In the study by S.A. Elghazally et al. [100], 201 physicians were included, and the Maslach Burnout Inventory (MBI) scale was used to assess three aspects of burnout syndrome: emotional exhaustion, depersonalization, and reduced personal achievement. It was found that about one-third had high emotional exhaustion, about two-thirds had a high degree of depersonalization, and about one-quarter had a reduction in personal achievement.

The work of psychiatric hospitals in providing care for individuals with mental disorders has evolved with the accumulated experience of combating the coronavirus infection. The experience of China, as the country where the pandemic began, holds significant value. Based on the experience of Wuhan, psychiatric communities in different countries proposed a list of practical recommendations aimed at reducing the risks of infection spread and optimizing psychiatric care. All hospitals should have a reserve bed capacity, which, in normal times, can be used for the rehabilitation and

socialization of patients. Hospitals must be provided with sufficient testing, medications, and personal protective equipment. Faced with an increase in infections and considering that 80% of cases were mild or moderate, local authorities transformed stadiums and exhibition centers into Fangcang shelter hospitals in Wuhan [36,122]. On February 18, 2020, the National Health Commission of China reported that 323 patients with severe mental disorders had been diagnosed with COVID-19 [2]. In order to limit the transmission of COVID-19 and provide urgent treatment for critically ill patients, central and regional authorities implemented a series of effective measures, such as the establishment of infectious disease emergency hospitals and quarantine facilities, as well as the isolation of suspected and diagnosed patients and their close contacts.

To effectively treat millions of patients with severe mental disorders living in the community, a national community-based model was launched in 2004, known as the "Program for the Management and Treatment of Severe Mental Illnesses with Central Government Subsidies," or the "686 Program." This program integrates the resources of hospital services, community-based care, district committees, and the police to provide comprehensive services for monitoring, treatment, rehabilitation, and prevention. The program prioritizes patients with mental disorders and a relatively high risk of aggressive behavior, specifically those with schizophrenia, schizoaffective disorder, paranoid psychosis, bipolar disorder, epilepsy, and intellectual disability [259,260].In 2022, Italy reached second place in the world in terms of coronavirus infections, with China remaining in first place. The experience of organizing psychiatric care for COVID-19 patients is reflected in the work of A. D'Agostino et al. [80]. The authors provide the following recommendations: (1) limit the number of psychiatric staff working together to preserve material and human resources, if necessary, for other medical departments during the epidemic; (2) ensure continuous education for hospitalized patients with acute symptoms, particularly in hygiene standards and social distancing (such patients may generally behave disorganized, and frequent repetition of norms should be considered to minimize the risk of infection); (3) maintain constant and active vigilance when suspecting COVID-19 symptoms to minimize the risk of an outbreak in the department; (4) continuously review the patient

discharge mechanism to minimize the risk of contact with newly admitted patients for those who can safely return home; (5) suspend all group activities, including the use of common dining areas, which should only be allowed for patients who require direct supervision during meals (if unavoidable, a minimum recommended distance of 1-2 meters should be maintained between patients); (6) develop and review isolation procedures in the department based on local architectural and functional conditions, considering the likelihood of asymptomatic or mildly symptomatic patients with a positive result for SARS-CoV-2 and severe acute mental disorders that cannot be treated outside a psychiatric department; and (7) depending on local availability, implement online video conferences for all activities conducted by the staff (this should also be considered when visiting patients and communicating with relatives, whose access to the department should be significantly restricted).

Thus, to ensure that people seek medical help in a timely manner and follow public health recommendations, it is crucial to maintain the trust of the population in the healthcare system, which must be capable of safely meeting basic needs and controlling the risk of infection spread in medical facilities.

CHAPTER 2.
MATERIALS AND METHODS

2.1. Study Design. Patients

The study was conducted during the first wave of the COVID-19 pandemic in St. Petersburg from April 1 to June 30, 2020. During this period, 7,842 patients were admitted for treatment at the St. Petersburg State Budgetary Healthcare Institution "Hospital for War Veterans." A total of 557 (7.1%) patients, diagnosed with mental disorders, were consulted. Among them were 266 men and 291 women. The average age of the patients was 62.36 ± 18.65 years. From this group, a cohort of 97 patients was selected for further study based on the following **inclusion criteria:**

1) A laboratory-confirmed diagnosis of "novel coronavirus infection" (PCR+);

2) The presence of a mental disorder meeting the diagnostic criteria of ICD-10;

3) No history of mental disorders prior to the onset of the novel coronavirus infection.

Exclusion criteria:

1) Mental disorders present before the onset of the novel coronavirus infection;

2) Age under 18 years;

3) Lack of laboratory confirmation of the diagnosis of "novel coronavirus infection" (PCR+).

The socio-demographic data of the patients are presented in Table 2.1.1.

Table 2.1.1. Socio-demographic data of patients

Characteristics	Abs	%
Gender		
Male	43	44.3
Female	54	55.7

		end of table 2.1.1.
Age		
20-30	1	1.0
31-40	8	8.2
41-50	16	16.5
51-60	20	20.7
61-70	25	25.9
71-80	11	11.3
81-90	15	15.4
91-100	1	1.0
Total	97	100
Education		
Higher education	49	50.5
Incomplete higher	4	4.1
Secondary vocational	35	36.2
Secondary education	5	5.1
Incomplete secondary	4	4.1
Total	97	100
Employment		
Full-time employment (pre-retirement age)	26	26.8
Working pensioner	6	6.2
Pensioner	40	41.2
Part-time employment	25	25.8
Total	97	100
Marital status		
Married	37	38.1
Divorced	12	12.5
Single	24	24.7
Widowed	24	24.7
Total	97	100

All patients were divided into groups according to the primary psychiatric diagnosis.

Patients were grouped based on their primary psychiatric diagnosis as follows:

A) Group with the diagnosis: F05.86 "Other delirium due to other viral and bacterial neuroinfections." This group consisted of 30 patients (median age Med. 70.5, interquartile range [IQR] 62-83), including 13 men and 17 women.

B) Group with the diagnosis: F06.76 "Mild cognitive disorder due to other viral and bacterial neuroinfections. Neurocognitive deficit syndrome." A total of 35 patients were examined (median age Med. 61.0, IQR 50.0-69.0), including 15 men and 20 women.

C) Group with the diagnosis: F43.22 "Mixed anxiety and depressive reaction due to adjustment disorder." This group included 32 patients: 11 men and 21 women (median age Med. 52.5, IQR 41.5-57.5). Diagnoses within this group were F06.366 (8 patients, 25.0%) and F06.46 (24 patients, 75.0%).

2.2. Research Methods

2.2.1. Clinical-Psychopathological Method (Categorical Model)

All patients were examined using the clinical-psychopathological method, based on the categorical model, which is traditional for Russian psychiatry. This model follows a descriptive approach, implying clear boundaries between normal and pathological states and between different nosological categories. In this study, patient history was gathered from both patients and their relatives, and medical documentation was reviewed, accompanied by clinical observation.

2.2.2. Psychometric Method

The clinical-psychopathological method was supplemented by operational diagnostics, where concepts are constructed through the description of experimentally measurable operations [10]. In our study, the operational principle of psychiatric diagnosis was applied using the International Classification of Diseases, 10th Revision (ICD-10) [27], along with clinical scales.

1. **COVID-19 Patient Research Card**: For the study of each patient group, a card containing 34 variables was used.
2. **National Early Warning Score (NEWS2) for COVID-19** [193]: NEWS2 assesses seven physiological parameters crucial for identifying patients at risk of early clinical deterioration (respiratory rate, oxygen saturation, need for oxygen therapy, systolic blood pressure, heart rate, body temperature, and consciousness disturbances). The risk is considered low with 1-4 points, requiring physician review every six hours; moderate at 5-6 points or 3 points in any one parameter, requiring reassessment every

two hours; and high with 7 or more points, requiring continuous observation. This system is referenced in the Ministry of Health's temporary clinical guidelines for COVID-19 treatment [4].

3. **Delirium Rating Scale-Revised-98 (DRS-R-98):** Developed by P.T. Trzepacz et al. [246], this scale is used for the initial and repeated assessment of delirium severity. It includes 13 evaluation items across two sections, assessing aspects such as sleep-wake cycle disturbances, perceptual disruptions, delusions, affective lability, speech, thought disorders, motor agitation or retardation, orientation, and memory. Each criterion is rated from 0 (normal) to 3 (severe), and the total delirium severity score is calculated.

4. **Mini Mental State Examination (MMSE):** Developed by M.F. Folstein et al. [112], MMSE consists of 11 tasks that assess orientation, word repetition, calculation, memory, naming, sentence repetition, command comprehension, reading, writing, and drawing. Cognitive impairment is classified as follows: no impairment (24-30 points), mild (19-23 points), moderate (10-18 points), and severe (≤9 points). MMSE is favored for rapid cognitive screening in clinical settings, including intensive care units, over the Montreal Cognitive Assessment (MoCA), though MoCA better differentiates between normal and mild cognitive impairment.

5. **Covi Anxiety Scale:** Developed by L. Covi, R. Lipman, and D.M. McNair [76], this scale measures anxiety intensity based on three parameters: patient complaints, behavior, and somatic manifestations. Each parameter is rated from 1 to 5, and the total score reflects the severity of the anxiety disorder. Interpretation: 0-3 points indicate no anxiety; 3-6 points indicate anxiety symptoms; 6 points or more suggest an anxiety disorder.

6. **Hamilton Anxiety Rating Scale (HARS):** Each parameter is rated on a 5-point scale, from 0 (absent) to 4 (severe). Scores of 6 or below indicate no anxiety, 7-13 suggest possible anxiety disorders, 14-20 indicate anxiety, 21-28 reflect symptomatic anxiety, and scores above 29 signify severe anxiety.

7. **Montgomery-Asberg Depression Rating Scale (MADRS):** Each item is rated from 0 to 6, and the total score ranges from 0 to 60. Scores are interpreted as

follows: 0-15 points indicate no depression, 16-25 points indicate a minor depressive episode, 26-30 points indicate a moderate depressive episode, and over 30 points indicate a major depressive episode. The interpretation of scores does not fully align with ICD-10 depression classification.

8. **Clinical Global Impression Scale (CGI)**

Developed by W. Guy [123], the Clinical Global Impression (CGI) rating scales are used to assess symptom severity, treatment response, and the effectiveness of therapeutic methods in studies involving patients with mental disorders. This is a brief, 3-item observer-rated scale that can be utilized both in clinical practice and research to monitor changes in symptoms.

The scale was developed by researchers from the Early Clinical Drug Evaluation Unit (ECDEU) program under the direction of the National Institute of Mental Health (NIMH). Its purpose was to provide clinical judgment-based assessments of symptom severity and treatment progress. The CGI scale was designed to evaluate patient functioning before and after initiating medication in clinical trials, a crucial aspect of the research process.

The CGI evaluates three key items:

1. Severity of illness (CGI-S)
2. Global improvement (CGI-I)
3. Efficacy index (CGI-E), which reflects the treatment effect and side effects specific to the prescribed medications.

While many researchers acknowledge the scale's validity, it is often considered subjective because it requires clinicians to compare patients to typical cases from their professional experience. The CGI-S assesses the severity of a disorder using the following scale:

0: Not assessable

1: Normal, not at all ill

2: Borderline ill

3: Mildly ill

4: Moderately ill

5: Markedly ill

6: Severely ill

7: Among the most extremely ill patients

The CGI-I evaluates changes in the patient's condition over time:

0: Not assessable

1: Very much improved

2: Much improved

3: Minimally improved

4: No change

5: Minimally worse

6: Much worse

7: Very much worse

2.2.3. Clinical-Archive Method

This method involved studying archived medical histories using a specially designed card, which allowed for the identification of psychiatric disorders in patients admitted to the St. Petersburg Veterans Hospital in 2020, and the creation of a research plan based on the findings.

2.2.4. Clinical-Statistical Method

Descriptive statistics, such as means and medians, were used to describe variable distributions. Statistical significance tests were applied depending on whether the variable followed a normal distribution. For patients with delirium, normally distributed quantitative features were compared using the Student's t-test. Qualitative, ordinal, distribution-independent features were compared using the Mann-Whitney and Wald-Wolfowitz tests, and dependent variables were compared using the Wilcoxon test. Fisher’s exact test was used for nominal variables. Correlations were assessed using Kendall’s tau (Ƭ). A significance level of $p<0.05$ was adopted. For patients with neurocognitive deficits, Fisher's exact test and the Wilcoxon test were used, with

Kendall's tau assessing correlations. Nonparametric statistics were used to present clinical scale results for patients with affective disorders.

Statistical analysis was performed using the STATISTICA 12 package, designed for small sample methods [19]. Logistic regression [110] and Cox proportional hazards regression [77,190,243] were used to model outcome dependence on the studied variables. Odds ratios (OR) and hazard ratios (HR) with 95% confidence intervals (CI) were calculated. Modeling followed a two-step process, involving the inclusion of all predictors and the minimization of Akaike's Information Criterion (AIC) through a stepwise method [213]. Significance levels were adjusted for multiple hypothesis testing using the Benjamini-Hochberg correction [60].

2.2.5. Ethical Considerations

The study was approved by the local ethics committee of the St. Petersburg Veterans Hospital (Protocol No. 26, 06.04.2020). Confidentiality of patient data was maintained by using secured, password-protected computers and databases, with no personal identifiers (names) included in any documents.

2.2.6 Summary

The validity and reliability of the data were ensured by adherence to the ICD-10 diagnostic criteria for mental and behavioral disorders, the representativeness of the sample (557 patient histories reviewed, 97 patients personally examined), the use of well-defined inclusion and exclusion criteria, the application of clinical scales, and statistical processing of the results. Patient assessments were conducted in the COVID-19 "red zone."

CHAPTER 3.

RESULTS OF ORIGINAL RESEARCH

3.1. Consultative Psychiatric Care for COVID-19 Patients in a Multispecialty Hospital: Organizational Aspects

The study was conducted at the St. Petersburg Veterans' Hospital during the period from April 1 to June 30, 2020. Before the COVID-19 pandemic, the hospital provided specialized medical care to veterans and participants of the Great Patriotic War, survivors of the Leningrad blockade, residents of besieged Leningrad, combat veterans, as well as other individuals eligible for similar benefits and other categories of citizens.

Due to the pandemic, the hospital was repurposed as an infectious disease hospital, admitting patients suffering from or suspected of having the new coronavirus infection (COVID-19). From April to June 2020, 7842 patients were admitted to the hospital, compared to 9441 during the same period in 2019. The average age of patients hospitalized in 2019 was 82.74±10.53 years, and in 2020 it was 62.36±18.65 years. The difference is statistically significant ($p=0.0001$). The number of patients who received psychiatric consultations in 2019 was 647 (6.8%), compared to 557 (7.1%) in 2020.

During the study period, psychiatric care was provided by a psychiatrist and a psychotherapist. Since they acted as consultants, the workload was calculated based on outpatient service metrics. A psychiatrist’s consultative appointment assumes 26.2 minutes per visit, plus 30% of the time for completing documentation [33]. According to the Ministry of Health of Russia’s Order No. 438 of September 16, 2003, “On Psychotherapeutic Care,” no specific time is regulated for psychotherapist consultations.

Delirium associated with COVID-19 — 20%;

Agitation — 45%;

Aggression (behavioral disturbances) — 15%;

Suicidal thoughts — 5%;

Complaints of low mood, anxiety, and depression — 35%;

Complaints of fatigue — 50%;

Complaints of tearfulness — 45%;

Complaints of memory impairment ("difficulty thinking") —35%;

Sleep disturbances — 50%.

Patient characteristics are presented in Table 3.1.1.

Table 3.1.1. Patient Characteristics and the Volume of Psychiatric Care Provided from April to June 2020 Compared to the Same Period in 2019

Indicators	2019		2020		*p*
	Abs.	%	Abs.	%	
Consulted by psychiatrist/psychotherapist	647	6,85	557	7,10	.5406
Men	224	34,62	266	47,76	.0000*
Women	423	65,36	291	52,24	.0000*
Urgently requiring psychiatric care	423	65,36	291	52,24	.0675
Requiring psychiatric observation in the hospital	418	64.61	308	55.30	.0012*
Requiring psychiatric observation in outpatient settings	175	27.05	191	34.30	.0078*

*Statistically significant differences

As shown in Table 3.3.1, the proportion of male patients and all patients who were consulted and recommended for outpatient follow-up was significantly higher in 2020, while the proportion of female patients and those requiring ongoing observation was significantly lower. When comparing the proportions of all patients consulted by a psychiatrist/psychotherapist and those urgently requiring psychiatric care in 2019 and 2020, no significant differences were found. A distinctive feature of morbidity in 2020 was the changes in the prevalence of mental disorders (see Table 3.1.2).

As shown in Table 3.1.2, in 2020, the proportions of patients with diagnoses from groups (F10 - F19), (F30 - F39), and (F40 - F48) were significantly higher, while the proportions of patients from groups (F01-F03) and (F05.0 - F06.9) were significantly lower. Patients with diagnoses from groups (F20 - F29) and (F60 - F69) were diagnosed in the hospital only in 2020. Most patients with chronic mental disorders, such as dementia or schizophrenia, were admitted to the hospital from social care institutions (Psycho-Neurological Institutions) due to COVID-19. A small number of them were hospitalized from home or transferred from psychiatric hospitals due to the severe course of the viral infection.

Table 3.1.2.* Prevalence of Mental Disorders and Behavioral Disorders in Hospital Patients from April 1 to July 31, 2019, and 2020

ICD-10 Diagnostic Categories	2019		2020		*p*
	Abs.	%	Abs.	%	
Dementia (F01-F03)	238	36.78	108	19.39	.0000*
Other organic mental disorders (F05.0-F06.9)	303	46.84	190	34.11	.0000*
Mental and behavioral disorders related to psychoactive substance use (F10-F19)	6	0.93	27	4.86	.0001*
Schizophrenia, schizotypal and delusional disorders (F20-F29)	0	0	74	13.29	.0000*
Mood disorders (affective disorders) (F30-F39)	26	4.01	38	6.82	.0420*
Neurotic, stress-related, and somatoform disorders (F40-F48)	74	11.44	117	21.02	.0000*
Personality and behavioral disorders in adulthood (F60-F69)	0	0	3	0.51	.1973
Total	647	100	557	100	

*Significant differences

Patients who had not previously been diagnosed with mental disorders could be brought in from home by emergency medical services due to suspected infection with the novel coronavirus, although this diagnosis was not always confirmed. In such cases, the clinical picture of the mental disorder often prominently featured ideas of infection or active somatic complaints despite an objectively satisfactory condition.

Clinical analysis allowed the categorization of patients into three groups: 1) mental disorders combined with bacteriologically confirmed COVID-19; 2) mental disorders where COVID-19 was clinically or epidemiologically diagnosed but not confirmed by laboratory tests (COVID-associated); 3) mental disorders with overvalued ideas about COVID, but without clinically or bacteriologically confirmed infection (not related to COVID) (see Table 3.1.3).

Table 3.1.3. Distribution of patients in need of psychiatric and psychotherapeutic care based on the association of mental disorders with the novel coronavirus infection (COVID-19) who were treated at the Veterans Hospital from April 1 to June 30, 2020.

ICD-10 Diagnostic Categories	COVID		COVID-associated		Not related to COVID		Total	
	Abs.	%	Abs.	%	Abs.	%	Abs.	%
Dementias (F01-F03)	82	14,72	0	0	26	4,67	108	19,39
Other organic mental disorders (F05.0 - F06.9)	176	31,60	8	1,44	6	1,08	190	34,11
Mental and behavioral disorders due to psychoactive substance use	22	3,95	2	0,36	3	0,54	27	4,85
Schizophrenia, schizotypal, and delusional disorders (F20 - F29)	71	12,75	3	0,54	0	0	74	13,28
Mood (affective) disorders (F30 - F39)	24	4,31	12	2,15	2	0,36	38	6,82
Neurotic, stress-related, and somatoform disorders (F40 - F48)	93	16,70	16	2,87	8	1,44	117	21,01
Disorders of adult personality and behavior (F60 - F69)	1	0,18	2	0,36	0	0	3	0,54
Total	469	84,21	43	7,72	45	8,07	557	10

As shown in Table 3.1.3., in most nosological groups, mental disorders combined with COVID-19 had the highest prevalence. Among mental disorders related to COVID-19 but with unconfirmed infection, a significant proportion consisted of mood disorders (affective disorders) (F30-F39) and neurotic, stress-related, and somatoform disorders (F40-F48). Regardless of nosological classification, more than a third of the examined patients—37.34% (208 individuals)—had affective disorders, and more than half of those requiring psychiatric or psychotherapeutic care—53.50% (298 individuals)—complained of sleep disturbances. In 69.47% (387 individuals) of cases, mental disorders arose against the background of pronounced asthenia. There were 97 (17.41%) patients with laboratory-confirmed COVID-19 who had no previously diagnosed mental disorders before the infection.

A consultation with a psychiatrist or psychotherapist could be necessary at any stage of providing care to COVID-19 patients (see Figure 3.1.1). As illustrated in the scheme in Figure 3.1.1, the first contact with patients occurred in the emergency department.

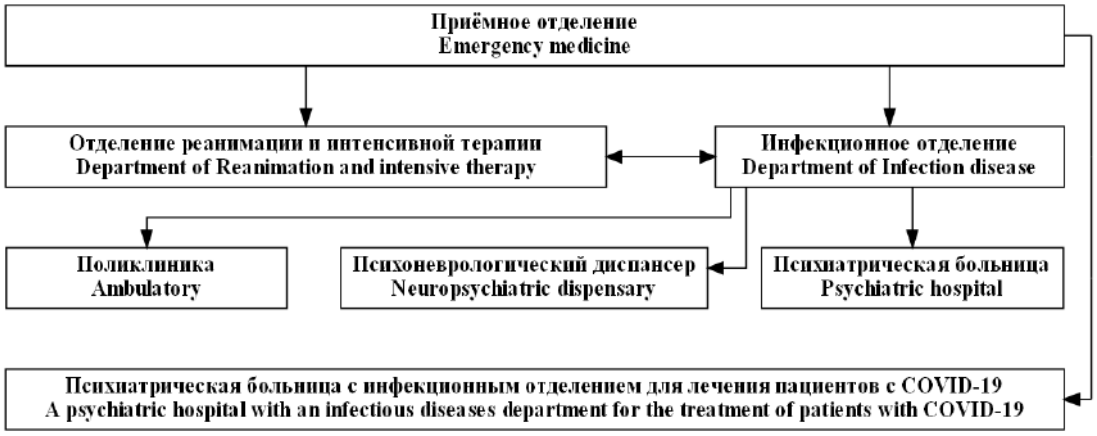

Figure 3.1.1: Patient Routing Scheme for Individuals Admitted to the Hospital with COVID-19.

At this stage, the infectious disease specialist could request a psychiatric evaluation in emergency situations (as indicated) or schedule a planned consultation with a psychiatrist or psychotherapist. If necessary, patients were transferred from the emergency department to a psychiatric hospital ward that also managed COVID-19

treatment. Subsequently, after an initial assessment according to the Temporary Guidelines (Ministry of Health of the Russian Federation, 2020) (including a consultation with a general practitioner, blood and urine biochemical tests, an electrocardiogram, and a CT scan of the lungs), the patient was transferred to the intensive care unit (ICU) or the infectious disease department based on the severity of their physical condition.

Mental health status could deteriorate in either department, and patients were evaluated by a specialist in both settings. As previously noted, mental disorders often accompanied a worsening of the patient's physical condition. Prior to discharge, patients under the care of a psychiatrist or psychotherapist received recommendations regarding future follow-up care. If necessary, patients with mental and behavioral disorders were transferred to a psychiatric hospital. Upon de-escalation of acute symptoms and with the patient's consent to continue treatment, follow-up with a psychiatrist at a neuropsychiatric hospital or outpatient psychotherapy was recommended.

The indications for a psychiatric consultation in the hospital’s emergency department included psychomotor agitation, altered consciousness, depressed mood, agitation, or a history of being under the care of a neuropsychiatric dispensary and/or receiving psychotropic therapy. A joint consultation between the psychiatrist and infectious disease specialist determined whether the patient required urgent transfer to a psychiatric hospital or could remain in the general medical department of the hospital. The patient was examined in an isolated room following sanitary and hygienic regulations. An interdisciplinary assessment of both the mental and physical condition allowed for an evaluation of the connection between the mental disorder and the infectious process.

Since psychotropic medications are administered to somatically weakened patients in cases of coronavirus infection, it is important to consider the somatotropic effects of psychopharmacotherapy, which determine the risk of certain side effects and complications. The development of these effects is linked to the ability of

psychopharmacological agents to influence neurotransmitter metabolism and block synaptic transmission, disrupting neurotransmission [16].

In patients with schizophrenia combined with the novel coronavirus infection, the previously prescribed therapy was continued with dose adjustments based on the patient's current physical condition and potential drug interactions, including haloperidol, risperidone, zuclopenthixol, quetiapine, sulpiride, and clozapine. Psychomotor agitation, in the absence of pneumonia and with stable vital signs, was managed with chlorpromazine or zuclopenthixol, while regularly monitoring somatic changes to adjust the dosages as needed. For anxiety and agitation, a single injection of bromdihydrochlorphenylbenzodiazepine was administered, and supportive therapy included hydroxyzine and low doses of quetiapine. In cases of delirium with psychomotor agitation, attempts to leave the department, or resistance to medical staff, intramuscular injections of haloperidol were prescribed. For less pronounced motor agitation, haloperidol in tablet form, quetiapine, or chlorprothixene were administered, depending on concurrent somatic therapy and the risk of adverse drug interactions.

In cases of seizures, including twilight states, hallucinations, and disturbances of consciousness, previously prescribed anticonvulsant therapies were maintained, such as carbamazepine, valproic acid, lamotrigine, and suxilep. For anxiety, depression, and sleep disturbances, sertraline, hydroxyzine, and quetiapine were prescribed.

Patients' mental disorders could be categorized into two groups based on their clinical course. The first group was heterogeneous and included acute psychotic disorders. Most patients in this group were diagnosed with "F05.86, Other delirium associated with other viral and bacterial neuroinfections." This condition developed against a backdrop of hyperthermia, hypoxia, and severe COVID-19. Patients with pronounced psychomotor agitation were transferred to the intensive care unit (ICU). In the absence of severe agitation or progressive respiratory failure, patients remained in the infectious disease department. If psychosis developed while in the infectious disease department and the patient’s physical condition allowed for transfer to a psychiatric hospital, the attending or on-duty physician prepared a transfer summary, which included information about the patient's transportability and lack of need for

surgical or specialized therapeutic care (cardiology, gastroenterology, etc.), except for COVID-19 treatment. Psychiatric monitoring of patients with psychosis in the hospital was conducted routinely until psychotic symptoms resolved. Only six patients were transferred to psychiatric hospitals with infectious disease departments on an emergency basis (1.08% of those requiring psychiatric care).

The second group consisted of patients with chronic mental disorders, where the scope and nature of psychiatric care depended on both the severity of the somatic condition and the extent of the mental disorders. Due to subfebrile or febrile fever, pronounced asthenia, the need for humidified oxygen insufflation, and somatotropic therapy with a risk of drug interactions with psychotropic medications, 70% of patients required either discontinuation or reduction of psychopharmacotherapy. Full psychotropic treatment was maintained in 15% of patients, as their COVID-19 course was not severe. The remaining 15% required dose increases or changes in psychotropic therapy due to exacerbations of mental disorders, particularly schizophrenia spectrum disorders, in the context of the infection. Patients with affective disorders and obsessive-compulsive disorder received the necessary therapy in full. Somatically stable patients from neuropsychiatric boarding homes and psychiatric hospitals received psychopharmacotherapy as usual, with dose adjustments made using drugs available in the hospital according to their chlorpromazine equivalents.

It should be noted that exacerbations of mental disorders were more common in patients with severe psychiatric conditions and mild COVID-19 (30.2%). If the patient's somatic condition was of moderate severity or satisfactory, and their mental state prevented them from remaining in a general infectious disease department, they were transferred to psychiatric hospitals with infectious disease wards for COVID-19 treatment.

A special group included patients with fear of contracting COVID-19. This group was dominated by anxiety-phobic and somatoform disorders. In two cases, psychotic disorders with delusions of persecution were identified. These patients claimed they could not breathe in or out, despite oxygen saturation levels of 97–98%. Some complained of "cerebral blood supply interruptions," insisting they were experiencing a

stroke, despite the absence of neurological symptoms. In cases of delusional disorders, patients reported that they had been intentionally infected with COVID-19. When COVID-19 tests were negative, these patients were transferred to a psychiatric hospital.

Thus, in patients with positive COVID-19 tests, indications for transfer to a psychiatric hospital with an infectious disease department for COVID-19 treatment included psychotic symptoms after somatic stabilization, severe depression, aggressive or self-harm tendencies, and cognitive impairments that prevented self-care or compliance with infection control protocols. Exacerbations of chronic mental disorders also warranted transfer.

In cases where discharge from the infectious disease department was not possible, but mental disorders did not require immediate hospitalization in a psychiatric facility and there were no somatic contraindications, necessary psychopharmacotherapy was administered within the hospital. Under the current epidemic situation, psychotherapy included short-term, rational individual therapy aimed at reducing anxiety, tapping into internal resources, and exploring coping strategies for stress. The duration of hospitalization was determined by the course of COVID-19.

Patients with chronic mental disorders posed challenges for management due to poor compliance, necessitating increased supervision over medication intake. After somatic stabilization, 40% of patients with chronic mental disorders were transferred back to neuropsychiatric boarding homes. In 20% of cases, due to exacerbation of chronic mental disorders, patients were sent to psychiatric hospitals. Upon discharge, 30% of patients—diagnosed with schizophrenia, post-COVID neurocognitive syndrome, affective and anxiety-phobic disorders, or dementia—were advised to seek care at a neuropsychiatric dispensary. Ten percent of patients whose mental condition stabilized after physical recovery were discharged home under the care of their primary care physician, with no continuation of psychiatric treatment.

Summary

Thus, patients hospitalized in multidisciplinary facilities with confirmed or suspected COVID-19 received multimodal care. Psychiatric and psychotherapeutic care was provided based on the severity of the somatic condition. Approximately 7.1% of all hospitalized patients received specialized care, typically within the hospital. A third of patients required psychiatric care in an outpatient setting after discharge. Based on the experience of consultative work, a model was developed, consisting of the following stages: 1) consultative psychiatric care in the emergency department, 2) consultative psychiatric care in the ICU, and 3) consultative psychiatric care in the infectious disease department. The experience of the psychiatric service in a multidisciplinary hospital highlights the necessity of psychiatric intervention in the treatment of COVID-19 patients.

3.2. Clinical Features of Delirium in Patients in a Multispecialty Hospital

The socio-demographic characteristics of a cohort of patients diagnosed with F05.86, "Other delirium associated with other viral and bacterial neuroinfections," were studied. This cohort consisted of 30 individuals, 16 of whom had a fatal outcome.

Table 3.2.1. Socio-demographic Data of Patients

Items	Abs	%
Gender		
Male	13	43,3
Female	17	56,7
Age		
30-40	2	6,7
41-50	2	6,7
51-60	2	6,7
61-70	9	30,0
71-80	6	20,0
81-90	8	26,6
91-100	1	3,3
Total	30	100
Education		
Higher education	18	60,0
Secondary vocational education	10	33,3
Secondary education	2	6,7
Total	30	100
Employment		
Full-time employment (pre-retirement age)	5	16,7
Working retiree	1	3,3
Retiree	21	70,0
Part-time employment	3	10,0
Total	30	100

		end of table 3. 2. 1.
Married		
Married	14	46,7
Divorced	3	10,0
Single	2	6,7
Widowed	11	36,6
Total	30	100

As shown in table 3.2.1., the cohort included more women than men, although the difference was not statistically significant (p = .4386). Most patients were aged 61-70 years, had higher education, were retired and not employed, and were married. The characteristics of the structure of delirium with the identification of the most frequently occurring symptoms, identified in ½ or more patients, are presented in Table 3.2.2. As seen in Table 3.2.2, all patients exhibited moderate to severe disruptions in the "wakefulness-sleep" cycle. High-ranking symptoms also included severe impairments in perception and long-term memory. The progression of the syndrome varied. An acute change in behavior occurred over a period of several days to a week in 11 patients (36.6%), while a sudden change in behavior occurred within a period of several hours to one day in 19 patients (63.3%).

Table 3.2.2. Structure of delirium according to the DRS-R-98 scale

Items	Degree*	Content	n**	%***
Sleep-wake cycle disturbance	2	Moderate disorganization of sleep-wake cycle (e.g., falling asleep during conversations, napping during the day or several brief awakenings during the night with confusion/behavioral changes or very little nighttime sleep)	15	50,0
Sleep-wake cycle disturbance	3	Severe disruption of sleep-wake cycle (e.g., day-night reversal of sleep-wake cycle or severe circadian fragmentation with multiple periods of sleep and wakefulness or severe sleeplessness.)	15	50,0

end of table 3.2.2.

Perceptual disturbances and hallucinations	3	Hallucinations present	23	76,6
Lability of affect	2	Affect is often inappropriate to the situation and intermittently changes over the course of minutes; emotions are not consistently under self-control, though they respond to redirection by others	15	50,0
Thought process abnormalities	2	Associations loosely connected occasionally, but largely comprehensible	16	53,3
Orientation	2	Disoriented to time and place	17	56,6
Attention	2	Moderate inattention with difficulty focusing and sustaining attention. On formal testing, makes numerous errors and either requires prodding to focus or finish the task	15	50,0
Short-term memory	2	Recalls 1/3 items; may be able to recall other items after category cueing	15	50,0
Long-term memory	3	Recalls 0/3 items and/or has severe difficulty recalling other long-term information	22	73,3
Visuospatial ability	2	Moderate impairment with distorted appreciation of overall design and/or several errors of details or pieces; and/or needing repeated redirection to keep from getting lost in a newer environment despite, trouble locating familiar objects in immediate environment	16	53,3

Note. * gradation according to the DRS-R-98 scale: 0 - no disorders, 1 - mild disorders, 2 - moderate disorders, 3 - severe disorders; **n - absolute number of patients in whom this symptom was detected; *** (%) - percentage of patients in whom this symptom was detected.

The severity of symptoms also fluctuated differently. In 17 patients (56.6%), the severity of symptoms changed over the course of hours, in 2 patients (6.6%) within a few minutes, and in 11 patients (36.6%) no fluctuations in symptoms were noted. The overall score was 26.6 ± 4.6 points. According to the temporal guidelines [3], all patients' disease progression was classified based on physical condition. Mild progression was noted in 4 patients (13.3%), moderate in 7 (23.3%), severe in 9 (30.1%), and extremely severe in 10 (33.3%). Data on the monitoring of patients'

physical condition during the onset of delirium (1st measurement) and on the third day of its progression (2nd measurement) are presented in Table 3.2.3.

A significant deterioration in oxygen insufflation requirements and systolic blood pressure, along with a trend toward a notable increase in the overall score over three days, indicates a worsening of patients' physical condition during this period.

Table 3.2.3. Monitoring physical condition using the NEWS2 scale

Items	First dimension		Second dimension		P****
	Score* (*Med*)**	Score(*IQR*)***	Score (*Med*)	Score (*IQR*)	
Respiratory Rate (per minute)	0,0	0,0 -2,0	0,00	0,0-2,0	.2488
Oxygen saturation (%)	1,0	1,0 -2,0	1,0	0,0-2,0	.7439
Air or Oxygen	1,0	0,0-1,0	1,0	1,0-1,0	.0179
Température (°C)	0,0	0,0-0,0	0,0	0,0-0,0	.4008
Systolic Blood Pressure (mmHg)	0,0	0,0-0,0	0,0	0,0-1,0	.0250
Heart rate (perminute)	0,0	0,0-1,0	1,0	0,0-1,0	.2367
Awareness	3,0	3,0-3,0	3,0	3,0-3,0	1,0000
RESULT	5,5	4,0-7,0	7,5	5,0-9,0	.0680

Notes. * In the NEWS2 scale, the following gradation is applied: 1–4 points (low score) requires an assessment of the patient's condition for determining the appropriate clinical pathway; 5–6 points (medium score) or a single parameter with 3 points requires consultation with an intensive care unit physician to evaluate vital functions and determine the patient's clinical pathway; ⩾7 points (high score) generally requires transferring the patient to the intensive care unit. **Med - median; *** IQR (interquartile range) - the range between the 25th and 75th percentiles; ****p - statistical significance of the differences.

Correlations were found between the overall severity of the disease and symptoms of delirium (Table 3.2.4.).

Table 3.2.4. Relationship between somatic severity of the disease and delirium symptoms

Items	τ*	p**
Sleep-wake cycle disturbance	0,400016835	.0019
Perceptual disturbances and hallucinations	0,0753342525	.5587
Delusions	-0,131825953	.3062
Lability of affect	0,315496644	.0143
Language	0,201112227	.1185
Thought process abnormalities	0,275733469	.0323
Motor agitation	0,319538986	.0131
Motor retardation	-0,0767272082	.5515
Orientation	0,25017198	.0521
Attention	0,199403192	.1217
Short-term memory	0,374364554	.0036
Long-term memory	0,195022426	.1301
Visuospatial ability	0,125054101	.3317

Notes: τ* is the Kendall rank correlation coefficient, p** is the significance of differences.

A significant correlation has been identified between the severity of physical condition and disruptions in the sleep-wake cycle, affective lability, formal thought disorders, motor agitation, short-term memory and disorientation. In addition, correlations were found between delirium symptoms and physical condition indicators according to the NEWS2 scale.

Table 3.2.5. Correlation links between delirium symptoms and physical condition indicators according to the NEWS2 scale

DRS-R-98*	NEWS2**	τ***	*p* ****
1st dimension			
Sleep-wake cycle disturbance	Respiratory Rate (per minute)	-0,264906	.0397
	Oxygen saturation (%)	-0,267261	.0380
Perceptual disturbances and hallucinations	Air or Oxygen	0,381190	.0030
Delusions	Température (°C)	0,264008	.0404
Lability of affect	Systolic Blood Pressure (mmHg)	-0,255879	.0470
Motor agitation	Oxygen saturation (%)	0,332295	.0099
	Heart rate (perminute)	0,252724	.0498
Orientation	Température (°C)	-0,334415	.0094
Attention	Awareness	0,348337	.0068
Short-term memory	Température (°C)	-0,363469	.0047
	Awareness	0,254786	.0480
Long-term memory	Température (°C)	-0,439298	.0006
	Awareness	0,307941	.0168
2d dimension			
Sleep-wake cycle disturbance	Air orOxygen	0,333333	.0096
Perceptual disturbances and hallucinations	Température (°C)	0,266100	.0389
	Heart rate (perminute)	0,260648	.0430
Delusions	Air orOxygen	-0,274397	.0332
Lability of affect	Awareness	0,294373	.0223
Language	Température (°C)	-0,343415	.0076
Thought process abnormalities	Awareness	0,317608	.0137
Motor agitation	Air or Oxygen	0,300359	.0197
Short-termmemory	Awareness	0,254786	.0480
Long-termmemory	Air or Oxygen	0,263822	.0406
	Awareness	0,307941	.0168
Visuospatial ability	Respiratory Rate (per minute)	0,260680	.0430

Notes: *NEWS2 - National Early Warning System, **DRS-R-98 - Delirium Severity Rating Scale, τ*** - Kendall's rank correlation coefficient, p** - significance of differences.

Table 3.2.5. shows the disappearance of previous correlations from the first measurement and the emergence of new ones in the second measurement. For example, the correlation between the DRS-R-98 "Sleep-wake cycle disturbance" indicator and the NEWS2 " Systolic Blood Pressure (mmHg)" disappears, but a new correlation with "Air or Oxygen" emerges. Other correlations that disappear include: between " Perceptual disturbances and hallucinations and "Awareness " between "delusions" and "systolic blood pressure," between "affective lability" and "systolic blood pressure," between "motor agitation" and "Oxygen saturation (%) and Heart rate (per minute)," and between "short-term memory" and "Température (°C)," as well as between " Long-term memory " and "Température (°C)."

At the same time, new correlations appear: between "Perceptual disturbances and hallucinations " and "Température (°C), Heart rate (per minute)," between " Delusions" and "the need for oxygen insufflation," between "affective lability" and "changes in consciousness," between "motor agitation" and " Air or Oxygen," and between " Long-term memory " and " Air or Oxygen." However, the established correlations do not provide direct evidence of causal relationships between the indicators.

Therefore, we conducted a comparison between the groups at the stage of clinical stabilization and completion of risk stratification for adverse outcomes (CS) (n=14) and patients with fatal outcomes (FO) (n=16). All measurements were performed during the patients' lifetime. No statistically significant differences in socio-demographic characteristics (gender, age, education, employment, marital status, disability due to general illness) were found between the comparison groups ($p>0.05$). The CS and FO groups did not differ in the frequency of comorbid somatic diseases. The FO group had significantly more cases of acute respiratory syndrome (15 vs 5, $p=0.0011$) and extremely severe COVID-19 (10 vs 1, $p=0.0003$). Patients with moderate COVID-19 were significantly more frequently identified in the CS group (7 vs 1, $p=0.0099$). Differences in symptoms, as assessed by the DRS-R-98 scale, were found only in the indicators of "sleep-wake cycle" and "motor agitation." In both cases, more pronounced

disturbances were recorded in the FO group: "sleep-wake cycle" (Med. 3.0, IQR 2.0-3.0 vs Med. 2.0, IQR 2.0-3.0, p=0.0327); "motor agitation" (Med. 2.0, IQR 1.0-2.5 vs Med. 1.0, IQR 0.0-2.0, p=0.441).

During the first measurement using the NEWS 2 scale (Table 3.2.6), no significant intergroup differences were identified. During the second measurement, differences were observed only in the overall score. In the FO group, the score indicated the need for routing to the intensive care unit, while in the CS group, it required a consultation with an intensive care physician to assess vital functions.

Table 3.2.6. Monitoring of physical condition using the NEWS2 scale

Item	KS Group			FO Group			*P***
	*Med**	IQR**		*Med*	IQR		
		25%	75%		25%	75%	
1st dimension							
Respiratory Rate (per minute)	0,00	0,00	2,00	0,00	0,00	2,00	.7710
Oxygen saturation (%)	1,00	1,00	1,00	1,00	1,00	2,00	1,000
Air or Oxygen	1,00	0,00	1,00	1,00	0,00	1,00	.9834
Systolic Blood Pressure (mmHg)	0,00	0,00	0,00	0,00	0,00	0,00	.5193
Heart rate per minute	0,00	0,00	1,00	1,00	0,00	1,00	.4175
Température (°C)	0,00	0,00	0,00	0,00	0,00	1,00	.9668
Awareness	3,00	3,00	3,00	3,00	3,00	3,00	.7870
RESULT	5,50	4,00	9,00	8,00	6,50	9,50	.9172
2d dimension							
Respiratory Rate (per minute)	0,00	0,00	2,00	2,00	0,00	2,00	.2048
Oxygen saturation (%)	1,00	0,00	1,00	2,00	0,50	2,00	.0473
Air or Oxygen	1,00	0,00	1,00	1,00	1,00	1,00	.1766
Systolic Blood Pressure (mmHg)	0,00	0,00	1,00	0,00	0,00	0,00	.5605
Heart rate per minute	0,00	0,00	1,00	1,00	0,00	1,00	.1049
Température (°C)	0,00	0,00	0,00	0,00	0,00	1,00	.2706
Awareness	3,00	3,00	3,00	3,00	3,00	3,00	.7552
RESULT	5,50	3,00	8,00	8,00	6,50	9,50	.0344

Notes. The NEWS2 scale uses the following grading: 1–4 points (low score) requires an assessment of the patient's condition for routing; 5–6 points (medium score) or one parameter scoring 3 points requires a consultation with an intensive care physician to assess vital functions and determine the patient's routing; ⩾7 points (high score) usually requires routing the patient to the

intensive care unit. *Med - median; **IQR (interquartile range) - the range between the 25th and 75th percentiles; ***p - significance of differences.

In each group, the NEWS2 scale scores were compared between the 1st and 2nd measurements. Differences were determined using the Wilcoxon test. An improvement in the " Oxygen saturation (%)" indicator at the level of a trend (p=0.0629) was noted in the CS group. In the FO group, on the 3rd day of psychosis, there was a tendency for the respiratory rate per minute to worsen (p=0.0678), and the need for oxygenation was significantly higher (p=0.0277).

To develop a prognostic rule, binary logistic regression algorithms were used [77]. This method allows for calculating the probabilities of one of two possible outcomes of a random variable, depending on several predictor variables that determine it. The equation for estimating the probability of an observation belonging to one of the two groups is:

$$p = \frac{1}{1 + e^{-z}}$$

where e=2.718e = 2.718e=2.718 is the base of the natural logarithms, and z=b0+b1x1+⋯+bnxnz = b_0 + b_1x_1 + \dots + b_nx_nz=b0+b1x1+⋯+bnxn is the regression equation, with coefficients that need to be determined. Thus, the formula for outcome probability takes the form:

$$\mathrm{p} = \frac{1}{1+e^{-B_0-B_1x_1-\ldots-B_nx_n}}$$

In our study, the dependent variable is the outcome, classified as: lethal (0) or non-lethal (1). The prediction is made for the non-lethal outcome.

From the initial set of 12 variables, the "Forward Stepwise (Likelihood Ratio)" method was used to select 3 NEWS2 scale predictors for the logistic regression equation: the " Respiratory Rate (per minute)» during the first measurement" (RR-1), the " Heart rate (per minute)» during the second measurement on the third day of illness (HR-2), and the RESULTduring the second measurement on the third day of illness (R-

2). The selected variables explain 74% of the variability in the predicted outcome, as shown in Table 3.2.7.

Table 3.2.7. Summary for the model			
Step	-2Log-plausibility	Cox&SnellR^2	Nagelkerke's R^2
1	25,497a	0,405	0,543
2	20,822b	0,491	0,658
3	16,972c	0,552	0,740

The achieved Hosmer-Lemeshow test level [138] (Table 3.2.8) indicates that the distance between the observed and expected outcome distributions is small, meaning that the model reproduces the observed results with sufficient accuracy.

Table 3.2.8. is titled "Hosmer-Lemeshow Goodness-of-Fit Test"			
Step	(χ^2)	degrees of freedom.	Meaning
1	4,636	6	0,591
2	3,765	8	0,878
3	3,783	8	0,876

It follows from Table 3.2.9. that the variables R-2 and RR-1 have the strongest influence on the outcome. The variable HR-2 has a weaker influence. It follows from the odds ratio that the chance of a non-fatal outcome increases with the increase in the score of the respiratory rate per 1 min on the NEWS 2 scale at the beginning of delirium and decreases with an increase in the score of the heart rate per 1 min and the total score on the third day of the delirium course. Note that the significance of features, in the case of a small number of observations, is more reliably determined in Table 3.2.10 - model estimates when removing a feature.

Table 3.2.9. Regression coefficients and their estimates				
Item	RR-1	HR -2	R-2	Constant
Coefficient	0,6999	-0,1341	-0,9908	4,6938
Standard error	0,3816	0,0760	0,4276	7,8828
WaldChi-Square	3,3643	3,1094	5,3678	0,3546
Degrees of freedom	1	1	1	1
Level of significance	0,067	0,078	0,021	0,552
Oddsratio	2,0136	0,8745	0,3713	109,270

Table 3.2.10. Model with a deleted member				
Item	Log-likelihood of the model	Change in 2-log like lihood	Degree of freedom	Significance of change
RR-1	-10,725	4,478	1	,034
HR-2	-10,411	3,850	1	,050
R-2	-13,190	9,407	1	,002

Using the coefficients from Table 3.2.9, we obtain the regression equation:

$$Z= 4,6938+ 0,6999\ X_1- 0,1341\ X_2 -0,9908\ X_3\ ,$$

where: X1 is the RR-1 item, X2 is the HR-2 item, X3 is the R-2 score. Then the formula for the probability of the outcome takes the form:

$$p = \frac{1}{1+e^{-4,6938- 0,6999\ X1+ 0,1341\ X2+0,9908\ X3}}$$

The results of this regression function are presented in the classification table. Thus, the model shows (table 3.2.11) that the variables: X1 - the item "respiratory rate" (RR-1), X2 - the item "heart rate" (HR-2) and X3 - the final item (R-2) - can be considered as predictors of the disease outcome.

Table 3.2.11. Classification table				
Observable		Predicted		
		alive		% correct decisions
		No	yes	
Alive	No	15	2	88,2
	Yes	1	12	92,3
Total				90,0
cutoff value- 0,500				

The results obtained are illustrated by the following clinical examples.

Clinical Case 1. Patient A, 65 years old.

Diagnosis: COVID-19 coronavirus infection, extremely severe course (PCR+). Community-acquired bilateral polysegmental pneumonia (CT: 4) Respiratory failure1-2. Ischemic heart disease. Atherosclerotic cardiosclerosis. Hypertension stage. Risk of cardiovascular complications 4. Cerebrovascular disease. Cerebral atherosclerosis. Obesity stage 2. Diabetes mellitus type 2, newly diagnosed. Other delirium due to other viral and bacterial neuroinfections, F05.86.

Life history*:* Born in Leningrad, the eldest child in a complete family. Has a younger sister. Grew up and developed normally. Finished 11th grade, studied "excellently", received a higher legal education. For many years he worked in his specialty, at the time of hospitalization in the infectious diseases hospital he had a private practice. He had not previously sought help from a psychiatrist/narcologist. He is married, has an adult son from his marriage. Relations in the family are warm.

Medical history: Acute infectious disease development, within 24 hours after the onset of the disease, he was taken to the emergency medical service with febrile fever and respiratory failure. From the emergency room, due to the severity of his condition, he was sent to the intensive care unit. Saturation upon admission was 65-67%, non-invasive artificial ventilation of the lungs was used. The reason for calling a psychiatrist on the second day of hospitalization was the patient's psychomotor

agitation. The patient became anxious, restless, and tore off his oxygen mask. He was stopped by medical personnel while trying to leave the intensive care unit, actively demanded that his personal belongings be returned, and stated that he needed to hurry because "a taxi was waiting for him." After the personnel attempted to return the patient to the ward and resume oxygen supply, he became aggressive and attempted to use physical aggression against medical personnel.

Mental status on initial examination: Consciousness is delirious. He is correctly oriented toward his own personality; when asked to introduce himself, he gives his last name, first name, patronymic, age, and occupation. He is formally oriented toward time: he correctly states the current year, but makes mistakes in the month and season, and cannot name the exact date. When asked about his current location, he states that he “does not know” where he is now, but that he “was previously in the hospital, and now it’s some kind of living room.” He states that he is going to “immediately return home.” During the conversation, he jumps out of bed, pushing the medical staff away. He suddenly declares that his wife is “dying right now,” and demands that he be “released immediately” so that he can “leave by taxi.” He becomes motorically disinhibited. He easily becomes embittered by explanations, assuring that he will “be back in 20 minutes.” He does not fully comprehend the severity of his condition. His attention is distracted and exhausted. During the conversation, he begins to answer questions other than those asked. His thinking is not purposeful. It is difficult to assess his intelligence and memory at the time of examination due to the patient's agitated state. There is no criticism of his condition. Rapid relief of severe acute psychomotor agitation was performed with haloperidol, at a dose of 5 mg intramuscularly. Dyspnea and the involvement of accessory muscles in the act of breathing are objectively noted. Saturation before resumption of oxygenation is 65%. The score on the DRS-R-98 scale is 32. The total score on the NEWS2 scale was 11 points. Follow-up examination after 3 days: The patient is lethargic and bradypsychic. He is mobile within the bed, but has motor discoordination. He responds to speech by fixating his gaze on the speaker, but is difficult to reach when in contact, and only answers simple questions asked in a loud voice. His answers are

monosyllabic, not always on the essence of the question. Often after multiple repetitions. Consciousness is undulated. He states his name correctly. His orientation in place and time is impaired. He reports that he is "at home". His thinking is not purposeful. There is no criticism of his condition. According to the observations of the medical staff of the intensive care unit, in the evening and at night the patient becomes more active, talks without a visible interlocutor, calls someone. He falls asleep in the morning. Affective instability is noted, the patient's emotions are labile and practically do not correspond to the situation. The patient does not follow the instructions of the medical staff, needs care, because he cannot take care of himself. DRS-R-98 – 32 points. Total score on the NEWS2 scale is 13 points.

Discussion

Delirious clouding of consciousness was caused by the severity of the coronavirus infection, a marked decrease in blood oxygenation and fibril fever. Delirious clouding of consciousness began with psychomotor agitation, affective disorders and allopsychic disorientation, but after 3 days of delirium the patient became inhibited, noticeable disturbances in the sleep-wake cycle, the presence of hallucinatory experiences in the evening and night time were noticeable, and disturbances in active attention worsened. The patient died on the 5th day of delirium.

Clinical Case 2. Patient K, 58 years old.

Diagnosis: COVID-19, moderate severity (PCR+). Community-acquired bilateral polysegmental pneumonia (CT: 2). Respiratory failure 0. Coronary heart disease. Atherosclerotic cardiosclerosis. Hypertension stage 2. Arterial hypertension stage 2. Risk of cardiovascular complications 4. Cerebral atherosclerosis. Stage II dyscirculatory encephalopathy. Status post-strumectomy in 1998 due to diffuse euthyroid goiter (DEG). Euthyroidism on L-thyroxine. Chronic pyelonephritis, latent course. Right kidney cyst. Cholelithiasis. Chronic calculous cholecystitis, in remission. Other delirium due to viral and bacterial neuroinfections, F05.86.

Life history. Born in Leningrad, the only child in a full family. Early development without peculiarities. Started school on time, studied "well" and

"excellently". Received a higher education in economics. For the last 10 years, she worked in managerial positions. Married, has two adult sons. Retired 3 years ago. Lives with her husband in a suburban house.

Medical history (according to the patient's husband): No prior psychiatric consultations. Examined by a polyclinic therapist due to a rise in body temperature to subfebrile levels, marked fatigue and exhaustion, and cough. A PCR test was taken during the visit. Home treatment recommendations were provided. Over the course of 5 days, her condition worsened: she became sluggish, stopped getting out of bed, and ceased responding to her husband's questions. She couldn't sleep at night and would sometimes quietly mumble to herself.

After the husband returned to the clinic, the positive PCR test result was reported. The patient was transported by emergency medical services (EMS) to an infectious disease hospital. Due to poor communication, EMS doctors suspected an acute cerebrovascular accident (CVA). After performing a brain CT scan and ruling out acute vascular pathology, a psychiatrist was consulted. During the initial examination, no oxygen therapy was required, her body temperature was subfebrile, and her somatic condition was stable.

Mental status at initial examination: Consciousness fluctuates. The patient is sluggish and unproductive in communication. Her attention is difficult to engage, requiring constant verbal stimulation. She ignores most of the questions directed at her and answers the rest with brief, often irrelevant responses. She correctly states her name but insists that she is "32 years old." When asked where she is, she remains silent for a long time and then answers, "in a maternity ward, in the delivery room." Periodically, she starts quietly mumbling, speaking to no visible interlocutor. Her thinking is not goal-directed. Memory assessment was difficult at the time of the initial examination. There is no insight into her condition. DRS-R-98 score: 26 points. NEWS2 score: 3 points.

Re-examination 3 days later: The patient is now fully conscious. She is correctly oriented to her own identity, understands that she is in an infectious disease hospital, correctly names the current year and month but is off by 3 days with the date.

She is sleepy and sluggish, falling asleep quickly after the conversation ends. Her speech is somewhat slow, and she has difficulty finding words. She answers questions briefly but appropriately. When short-term memory was assessed, she recalled 2 out of 3 words. When long-term memory was assessed, she could remember only one word. There are moderate disturbances in visual-spatial orientation. She tires quickly. Her attention is distractible, and her memory of recent events is impaired. Her insight is superficial.

Medical staff observations: The patient is sleepy during the day and wakes up periodically at night, mumbling to herself, calling for her husband, and telling the staff that they are "on vacation, and he probably went to the sea." However, she soon falls back asleep. Occasionally, she becomes tearful for no apparent reason but calms down quickly. DRS-R-98 score: 18 points. NEWS2 score: 3 points.

Discussion

The patient was admitted to the hospital with moderate COVID-19 without signs of respiratory failure. After stabilization of her somatic condition, her symptoms of altered consciousness gradually subsided. The patient was examined in dynamics on the 1st, 3rd, 6th, and 9th days of hospitalization. By the 6th day, her sleep-wake cycle had normalized, her affect stabilized, and there were no more nighttime awakenings or signs of hallucinosis. Attention, memory, and spatial orientation disturbances persisted but were fully restored by the 9th day of hospitalization. The patient was discharged on the 15th day of hospitalization.

Summary

Delirium is one of the most common manifestations of acute brain dysfunction and is a serious complication of COVID-19 in hospitalized patients. It is a strong predictor of poor outcomes in elderly patients. A significant correlation has been identified between the severity of the physical condition and disturbances in the sleep-wake cycle, affect lability, formal thought disorder, motor agitation, and disorientation. Moreover, correlations were found between delirium symptoms and physical condition

scores on the NEWS2 scale. The presence of symptoms such as "sleep-wake" disturbances and "motor agitation" on the DRS-R-98 scale can be considered predictors of worse COVID-19 outcomes, along with somatic predictors such as "respiratory rate," "heart rate," and the "total NEWS2 score" on the 3rd day of delirium.

3.3. Neurocognitive Deficit in COVID-19

The socio-demographic characteristics of a cohort of patients diagnosed with F06.76 Mild Cognitive Impairment associated with other viral and bacterial neuroinfections were studied. The neurocognitive deficit syndrome was identified.

Table 3.3.1. Socio-demographic Data of Patients

Items	Abs	%
Gender		
Male	15	42,9
Female	20	57,1
Age		
40-50	10	28,6
51-60	6	17,1
61-70	12	34,3
71-80	3	8,6
81-90	4	11,4
Total	35	100
Education		
Higher education	23	65,7
Secondary vocational education	1	2,9
Secondary education	11	31,4
Total	35	100
Employment		
Full-time employment (pre-retirement age)	15	42,9
Working retiree	13	37,1
Retiree	6	17,1
Part-time employment	1	2,9
Total	35	100
Married		
Married	19	54,3
Divorced	6	17,1
Single	2	5,7
Widowed	8	22,9
Total	30	100

As shown in Table 3.3.1., there are more women than men in the cohort, although the difference is not significant (p = .3390). Most patients were aged 61-70 years, had higher education, were permanently employed, and were married.

To study the phenomenological characteristics of cognitive impairments in patients hospitalized with coronavirus infection (COVID-19), an analysis of their cognitive performance was conducted.

The assessment of patients' orientation using the MMSE scale in the first measurement showed that, during the initial examination, 1 out of 35 patients could not correctly answer what year it was. When asked about the current month, 6 out of 35 patients could not provide the correct answer. 13 individuals were unable to identify the current date and day of the week. Each patient in the sample correctly named the country and city of their location. However, 15 patients were unable to answer the name of the medical institution where they were being treated, even if they understood they were in a hospital. 21 patients could not specify the hospital's address, and 13 out of 35 confused the floor they were on.

Regarding memory recall, where patients were required to repeat objects named by the doctor, only 15 could immediately repeat all 3 simple objects, 19 repeated 2 objects, and 1 person repeated only 1 object. When it came to recalling words previously presented for memorization, 2 patients were unable to recall any words, 24 could recall only 1 word, 8 recalled 2 words, and only 1 patient could recall all 3.

In the assessment of calculation and attention, 3 out of 35 patients could not correctly subtract 7 from 100. 6 patients correctly performed the first subtraction but made mistakes in the second. 11 patients completed 2 subtractions correctly, 13 patients correctly completed 3, and 2 successfully completed 4 subtractions. No one from the sample was able to perform all 5 subtractions correctly during the initial examination.

During the initial speech assessment, all patients in the sample were able to correctly name the clock and pencil shown to them, but none of them were able to accurately repeat the phrase 'no ifs, ands, or buts,' omitting 'and.' None of the patients in the sample were able to write a complete sentence or reproduce a geometric drawing

during the initial examination. No patient completed the task of following a complex instruction (take the paper in the right hand, fold the paper in half, and place it on the lap) without error.

Significantly better results were obtained during the second assessment (Table 3.3.2.). The median score improvement across all items was statistically significant.

Table 3.3.2. Cognitive functioning indicators according to the MMSE scale*

Item	1st dimension			2st dimension			*P*
	Med	25%	75%	*Med*	25%	75%	
A. Orientation	7,0	6,0	8,0	9,0	8,0	10,0	.0000
B. Registration	2,0	2,0	3,0	3,0	3,0	3,0	.0006
C. Attention and calculation	2,0	1,0	3,0	2,0	2,0	4,0	.0000
D. Recall	1,0	1,0	2,0	2,0	2,0	3,0	.0000
E. Language	5,0	4,0	5,0	6,0	6,0	8,0	.0000
Total score	17,0	15,0	20,0	24,0	23,0	27,0	.0000

Note: *MMSE - Mini-Mental State Examination

The results for the orientation point have improved, 16 patients out of 35 answered all questions correctly. Before discharge, a significant portion of patients made mistakes only in the current date and/or day of the week (14 people), however, previously these same patients did not answer a larger number of questions, thus, their dynamics are positive. Significant orientation disorders persisted only in 5 people.

During the repeated examination, improved memorization was revealed: 29 people were able to immediately reproduce all 3 objects, 6 people - 2. 13 people were able to recall all three words again, 14 people - two, and 8 patients - only one. Also, the indicators for counting improved, 16 people from the sample performed 4 subtractions without errors, 10 people from 3 to 8 subtractions. There were no patients who made mistakes in the first two subtractions.

When examining the results of speech, reading and writing, it is evident that before discharge only 3 patients were able to complete all tasks without errors. The

patients made the main errors when following complex instructions, drawing geometric figures and repeating a complex phrase ("no ifs, ands or buts").

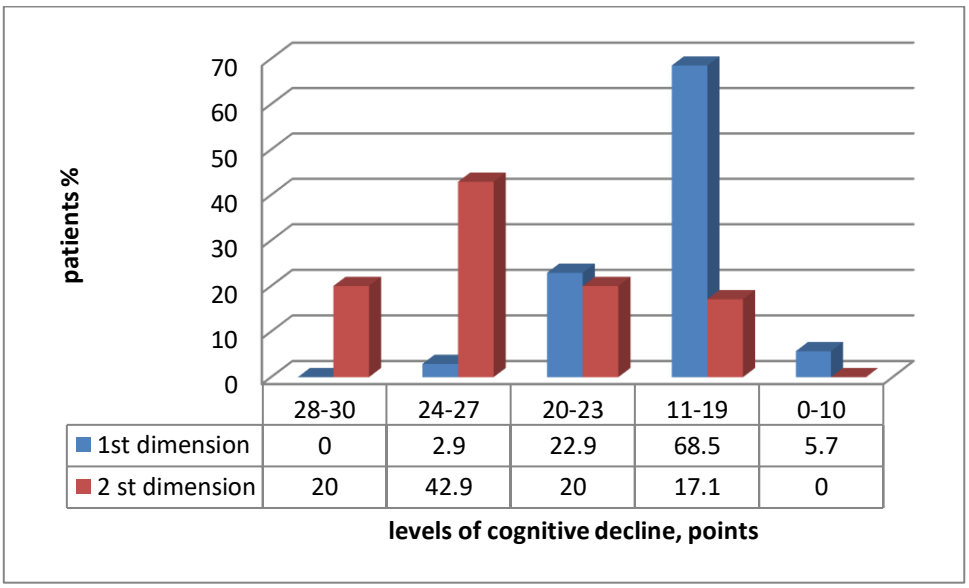

Figure 3.3.1.: Distribution of patients by levels of cognitive impairment according to the MMSE: - 28–30 - No cognitive impairment; 24–27- Mild cognitive iimpairment; 20–23- Mild dementia; 11–19- Moderate dementia; 0–10 - Severe dementia.

From the graph in Figure 3.3.1., it is evident that during the first measurement, the largest proportion of patients had moderate dementia (68.5%), while during the second measurement, at the point of recovery, the largest proportion had mild cognitive impairment (42.9%). In the first measurement, there were no patients who scored more than 23 points (indicating no neurocognitive deficit), and in the second measurement, no patients demonstrated severe neurocognitive impairment (scores >9 points). During the second measurement, 7 patients (20%) who did not show significant cognitive decline on the MMSE scale still reported subjective complaints, including feelings of distraction, difficulties in word retrieval during conversation, and feelings of frustration or anxiety due to forgetfulness.

In accordance with the temporal guidelines [3], the disease progression type was determined for all patients based on their physical condition. Mild progression was observed in 1 patient (2.9%), moderate in 27 (77.1%), severe in 5 (14.3%), and extremely severe in 2 (5.7%). Data on the monitoring of patients' physical conditions at

the 1st and 2nd measurements are presented in Table 3.3.2. As seen in Table 3.3.3, the median NEWS2 total score during the first measurement indicated the need for consultation with an intensive care unit physician, while during the second measurement, it indicated the need for a routine assessment by the attending physician.

Table 3.3.3. Monitoring of physical condition using the NEWS2 scale

Item	*1st dimension*			*2d dimension*			*P***
	*Med**	IQR**		*Med*	IQR		
		25%	75%		25%	75%	
Respiratory Rate (per minute)	0,00	0,00	0,00	0,00	0,00	0,00	.7670
Oxygen saturation (%)	2,000000	1,000000	2,000000	0,00	0,00	0,00	.0000
Air or Oxygen	1,000000	0,00	1,000000	0,00	0,00	0,00	.0056
Température (°C)	0,00	0,00	0,00	0,00	0,00	0,00	.5286
Systolic Blood Pressure (mmHg)	0,00	0,00	0,00	0,00	0,00	0,00	1,000000
Heart rate (perminute)	0,00	0,00	0,00	0,00	0,00	0,00	.1088
Awareness	0,00	0,00	0,00	0,00	0,00	0,00	-
RESULT	3,000000	1,000000	3,000000	0,00	0,00	0,00	.0023

Notes. NEWS2 - National Early Warning Score scale, the following grading is adopted in the NEWS2 scale: 1 – 4 points (low score) requires assessment of the patient's condition for routing; 5 – 6 points (medium score) or one of the parameters at 3 points requires consultation with an intensive care unit physician to assess vital functions and determine the need for patient routing; ⩾7 points (high score) generally requires routing the patient to the intensive care unit; *Med - median; **IQR (interquartile range) - the range between the 25th and 75th percentiles; ***p - significance of differences.

The decrease in the overall score was due to a statistically significant decrease in saturation and oxygenation requirements.

When interpreting correlation relationships, it is important to consider the opposite directionality of the scale indicators. For instance, in the MMSE (Mini-Mental State Examination), improvement is reflected by moving from lower to higher scores

(<10-30), while in the NEWS2 (National Early Warning Score), improvement is shown by moving from higher to lower scores (>7-1).

Table 3.3.4. Correlation relationships between the overall severity score of the patient's condition on the NEWS2 scale and MMSE items

Item	*1st dimension*		*2d dimension*	
	τ***	*p* ****	τ***	*p* ****
A. Orientation	-0,1254	.2891	-0,4972	.0000
B. Registration	-0,1385	.2418	-0,5996	.0000
C. Attention and calculation	-0,1308	.2689	-0,5027	.0000
D. Recall	-0,3343	.0047	-0,5113	.0000
E. Language	-0,0299	.8004	-0,5359	.0000
Total score	-0,1283	.2782	-0,5234	.0000

Notes: *MMSE - Mini-Mental State Examination, **NEWS2 - National Early Warning Scale, τ*** - Kendall rank correlation coefficient, p** - significance of differences.

Thus, a correlation coefficient between the total NEWS2 score and the word recall indicator of -0.3343, p = .0047, is interpreted as a decrease in the number of recalled words as the overall condition worsens (i.e., as the total NEWS2 score increases).

As shown in Table 3.3.4., at the first measurement, a negative correlation was found only between the overall severity of the patient's condition, as measured by NEWS2, and the "word recall" indicator in the MMSE. The correlations with "orientation," "immediate memory (recall)," "attention and calculation," "language," and "total score" were statistically insignificant. Upon recovery, negative correlations were found across all items.

Additionally, a change in the structure of correlations between MMSE and NEWS2 over time (1st and 2nd measurements) was observed.Table 3.3.5. demonstrates an expansion of statistically significant relationships between NEWS2 parameters and MMSE parameters in the second dimension compared to the first by 5.7 times.

Table 3.3.5. Correlation relationships between the MMSE items and the patient's condition on the NEWS2 scale			
MMSE (I)*	NEWS2 (I)**	τ***	*p* ****
1st dimension			
Registration	Respiratory Rate (per minute)	-0,281567	.0173
	Systolic Blood Pressure (mmHg)	-0,297117	.0120
Recall	Oxygen saturation (%)	-0,310838	.0086
	Air or Oxygen	-0,289642	.0143
	Systolic Blood Pressure (mmHg)	-0,302715	.0105
	RESULT	-0,334390	.0047
2d dimension			
Orientation	Respiratory Rate (per minute)	-0,521572	.0000
	Oxygen saturation (%)	-0,4109356	.0005
	Air or Oxygen	-0,506279	.0000
	Systolic Blood Pressure (mmHg)	-0,4563147	.0001
	RESULT	-0,497250	.0000
Registration	Respiratory Rate (per minute)	-0,680882	.0000
	Oxygen saturation (%)	-0,464238	.0000
	Air or Oxygen	-0,597701	.0000
	Systolic Blood Pressure (mmHg)	-0,551441	.0000
	Heart rate (perminute)	-0,377036	.0014
	RESULT	-0,5996303	.0000
Attention and calculation	Respiratory Rate (per minute)	-0,456592	.0001
	Oxygen saturation (%)	-0,456592	.0001
	Air or Oxygen	-0,523236	.0000
	Systolic Blood Pressure (mmHg)	-0,384556	.0011
	RESULT	-0,502759	.0000
Recall	Respiratory Rate (per minute)	-0,462478	.0000
	Oxygen saturation (%)	--0,462478	.0000
	Air or Oxygen	-0,532000	.0000
	Systolic Blood Pressure (mmHg)	-0,387120	.0010
	Heart rate (perminute)	-0,232104	.0498
	RESULT	-0,511342	.0000
Language	Respiratory Rate (per minute)	-0,493900	.0000
	Oxygen saturation (%)	-0,475049	.0000
	Air or Oxygen	-0,553090	.0000
	Systolic Blood Pressure (mmHg)	-0,402230	.0006
	Heart rate (per minute)	-0,269248	.0228
	RESULT	0,739132	.0000

			end of table 3.3.5.
Total score	Respiratory Rate (per minute)	-0,501060	.0000
	Oxygen saturation (%)	-0,462517	.0000
	Air or Oxygen	-0,536796	.0000
	Systolic Blood Pressure (mmHg)	-0,4239180	.0003
	Respiratory Rate (per minute)	-0,242870	.0401
	Heart rate (per minute)	-0,523429	.0000

Notes: *MMSE - Mini-Mental State Examination, **NEWS2 - National Early Warning Scale, τ*** - Kendall rank correlation coefficient, p** - significance of differences.

Thus, as cognitive functioning improves, the mutual influence of physical and cognitive indicators expands. The correlation links between the final MMSE scores at the first and second measurements and a number of anamnestic data were also analyzed (Table 3.3.6.)

Table 3.3.6. Correlation relationships between the final MMSE scores at 1 and 2 measurements and anamnestic data of patients with Covid19

Item	*1st dimension*		*2d dimension*	
	*τ**	*p***	*τ**	*p***
Gender	-0,139190	.239541	-0,178391	.1317
Age	-0,442569	.000184	-0,473988	.0000
Severity of thedisease	-0,130231	.271144	-0,387973	.0010
Tumors	0,129503	.273832	-0,056939	.6304
Endocrine, metabolic diseases	-0,040125	.734572	0,005428	.9634
Diseases of the nervous system	-0,460806	.000099	-0,335806	.0045
Cardiovascular diseases	-0,468272	.000076	-0,401553	.0006
Respiratory diseases	0,031237	.791818	-0,163753	.1664
Diseases of the digestive system	-0,387653	.001054	-0,251219	.0337
Diseases of the genitourinary system	-0,171200	.148005	-0,016285	.8905

Notes: *- Kendall's rank correlation coefficient, p**- significance of differences

Significant negative correlations were found with age, disease severity (only at the 2nd measurement), diseases of the nervous, cardiovascular and digestive systems. Statistically significant correlations with gender, disease severity at the first measurement, tumors, diseases of the endocrine, respiratory and genitourinary systems were not obtained.

The obtained results are illustrated by the following clinical examples.

Clinical cases

Case 1. Patient O., 57 years old.

Diagnosis: Coronavirus infection caused by the COVID-19 virus, mild course. Diabetes mellitus type II. Ischemic heart disease. Atherosclerotic cardiosclerosis Hypertension stage II. Chronic gastritis outside of exacerbation. Chronic pyelonephritis, latent course. Neurocognitive syndrome.

Life History: Born in Leningrad as the first child of two in a complete family, with a younger sister. There is no history of psychiatric disorders in the family. His early development, according to reports, was unremarkable. He grew up as an active and sociable child. He performed well in school and graduated from the Baltic State Technical University "Voenmech", specializing as a mechanical engineer, and is currently working in his field. He denies the use of alcohol and psychoactive substances. He is married and has a son. According to his wife, he managed his work well, led an active lifestyle, monitored his health, and regularly took antihypertensive therapy.

Medical History: The patient was diagnosed with a coronavirus infection by the outpatient clinic. He was treated at home. On the 5th day of illness, his condition worsened. He experienced significant weakness, fatigue, concentration difficulties, and episodes of "poor orientation." Upon admission to the hospital, he complained of "slowed thinking" and "inability to think."

Mental Status: Upon admission, his consciousness was clear. He correctly identified the current month and year but was off by three days regarding the date. He understood that he was in a hospital, but could not name the institution or its address. He appeared somewhat tense and confused. His gaze was not well-focused. His facial expressions and gestures were minimal. He was emotionally flat and exhibited psychomotor retardation. His speech was quiet and slow. He complained of memory and attention issues, stating: "My head feels like it's not mine," "I can't gather my thoughts," "I don't know if it's day or night… what floor are we on? I can't figure it out. I know I'm not at home, they took me to the hospital, but which one?" He was distressed by the hospitalization and fixated on his physical condition, frequently

asking stereotypical questions about test results. He had difficulty processing complex questions, often pausing before answering, requiring repeated verbal prompting. When questions were simplified, he provided brief but relevant responses. His interaction was formal. His memory for recent events was impaired. Tests of speech and praxis showed significant deficits. He was asthenic and easily fatigued. He did not express delusional ideas or perceptual disturbances. His attention was difficult to shift, and his thinking was concrete and impoverished in content. His insight into his condition was superficial. On the MMSE (Mini-Mental State Examination) upon admission, he scored 19 points, with deficits in attention, counting, word recall, speech, and praxis.

During COVID-19 Therapy: The patient was apathetic and lacked initiative. He had difficulties remembering the daily schedule of the ward and frequently needed reminders to complete diagnostic procedures (he would forget that CT scans or ECGs were scheduled for that day). He also asked the medical staff for assistance in charging his phone, and his family expressed concern that he was not calling them.

Before Discharge: The patient was correctly oriented in place, time, and self. His mood was stable, and he appeared relaxed and friendly. His speech was at a normal pace. However, he remained apathetic and uninterested in his surroundings. He answered simple questions appropriately but briefly and had difficulty understanding complex questions. He fatigued quickly during conversations. No psychotic symptoms were observed. His attention was easily distracted, and his thinking was concrete and rigid. Subjectively, he reported memory and attention difficulties, which caused him distress. Upon repeated examination (immediately before discharge), there was noted improvement in orientation and memory with the stabilization of his physical condition. Minor errors persisted in tasks related to counting, speech, praxis, and attention. His MMSE score was 27 points.

Discussion:

Despite the mild course of the coronavirus infection, the patient, a middle-aged individual with comorbid somatic conditions, developed cognitive impairments reaching the level of dementia. As his physical condition improved, there was a

positive trend in cognitive function: by the time of discharge, the cognitive impairments were no longer severe, but full recovery of cognitive function had not yet occurred.

Case 2: Patient E_2, 48 years old.

Diagnosis: COVID-19 infection, moderate severity. Bilateral polysegmental viral pneumonia, CT_3 (60%). Respiratory failure, grade 0-1. Obesity, grade 3. Neurocognitive syndrome.

Life History: There is no family history of psychiatric disorders. He is an only child. Early development was unremarkable. From childhood, he was an active, energetic, and restless child. He played football, enjoyed physical activities, and performed satisfactorily in school. He completed 8 years of school and graduated from a vocational school as a mechanic. Initially, he worked in his profession, but later became a plumber. He had good relations with his colleagues. He lives with his wife and daughter in a separate apartment.

Medical History: Ten days before hospitalization, he complained of weakness, fatigue, drowsiness, fever up to 38°C, cough, and increasing shortness of breath. According to his wife, he became distracted, "lost," and sluggish, frequently distracted and unable to focus. To get his attention, she had to speak loudly and repeat his name frequently. He answered questions briefly and often not in line with what was asked. He was admitted to the hospital due to hyperthermia and worsening shortness of breath.

Mental Status: Upon admission, the patient was not fully oriented to himself; he could not state his exact age. He was also imprecise in time orientation, correctly identifying the current month and year but was six days off on the date. He could not recall how many days he had been in the hospital, guessing "about a week." He understood that he was in a medical facility but could not name the reason for his hospitalization: "probably something with my heart." When informed of his viral pneumonia confirmed by CT, he stated, "I've had pneumonia before, but this doesn’t feel like pneumonia." Based on his symptoms, he concluded that he had a cardiac condition. His mood was elevated, he was talkative, and his sense of personal boundaries was diminished, addressing the medical staff informally. His judgment was superficial. He relayed his medical history inconsistently, did not fully understand

questions, and sometimes answered off-topic. He responded appropriately to straightforward questions. His memory for recent events was impaired; for instance, he remembered that he worked as a plumber but could not recall the last time he went to work or whether he needed a medical leave form. He complained of a "foggy head" and that he "couldn't think straight." When asked to memorize three simple words, he could immediately recall two and one after three minutes. He showed distractibility, quickly fatigued during conversations, and had no delusions or hallucinations. He lacked insight into his condition. His MMSE score upon admission was 15 points, indicating significant impairments in attention, counting, word recall, speech, and praxis.

In the Ward: The patient repeatedly removed his oxygen cannula, stating that oxygen made him feel "cold" and "uncomfortable." He believed oxygen support was unnecessary despite his shortness of breath and did not understand the severity of his condition. His critical and prognostic abilities were reduced. He had difficulty navigating the ward, often unable to find the bathroom or his room, and occasionally lay in other patients' beds, disrupting the ward routine. He displayed fixation amnesia, distractibility, attention fatigue, and impoverished thinking. The patient required supervision from the medical staff.

After the improvement of the patient's physical condition, he became better oriented within the ward and followed the regimen. He understood that he was hospitalized due to a coronavirus infection, but he categorically denied having pneumonia, despite the CT scan results. He believed that "people don't get pneumonia without a cough" and did not comprehend the explanations. He became irritable, expressing dissatisfaction with the hospitalization, the need for intravenous medications, and diagnostic procedures. Fatigue persisted; due to severe weakness, he spent most of his time in bed, and his sleep was shallow. He refused food, stating it was "tasteless." He correctly identified the current month and year but not the day. He complained that he couldn't understand what he read. His memory improved, and he began to consistently report his medical history, remembered the names of his attending physician, psychiatrist, and several nurses (with whom he had the most contact), and his roommates. His thinking was concrete and somewhat slowed. His critical thinking

was partial ("I am sick, but I don't have pneumonia; I don't need such intense treatment; I have COVID, but it can also be treated at home"). There were noted impairments in memory, attention, calculation, speech, and praxis.

Before discharge, his mental state was characterized by full orientation to place, time, and self. He realized he had recovered from a life-threatening illness and acknowledged the necessity of the treatment, including oxygen therapy. His mood was somewhat depressed, which the patient explained by saying, "I only now realize that I could have died." His activity level increased; he read and communicated with his family via phone messaging, but noted increased fatigue and reduced concentration: "My eyes quickly start to hurt from both the phone and reading, and when I read, I can completely forget what I just read." He experienced anxiety about his family and work colleagues due to the risk of infecting others. He reported not feeling rested after sleep and had difficulty recalling dates of past events or remembering the doctor's instructions upon discharge. He displayed adequate critical thinking regarding his condition, the illness he had endured, the need for two weeks of self-isolation after discharge, and returning to work only after clearance from the outpatient service. His MMSE score before discharge was 28 points, with some remaining impairments in memory, attention, and calculation.

Discussion:

The structure of the neurocognitive syndrome in a moderately severe case of COVID-19 in a patient with comorbid physical conditions was characterized by impairments in memory, attention, calculation, speech, and praxis, as well as a reduced capacity for critical evaluation, which led to disruptions in treatment adherence and complicated patient management. During the course of therapy for the coronavirus infection, there was improvement in cognitive functioning, with a positive dynamic in the MMSE score, from dementia at admission to moderate cognitive impairment as the patient's physical condition improved, and by the time of discharge, to mild cognitive impairment.

Case 3. Patient V., 82 years old.

Diagnosis: Coronavirus infection caused by the COVID-19 virus, extremely severe course. Community-acquired pneumonia CT1 (10%) upon admission. Cerebral atherosclerosis. Stage III dyscirculatory encephalopathy. Coronary heart disease. Atherosclerotic cardiosclerosis. Stage III hypertension. Risk stage IV. Stage II obesity. Neurocognitive syndrome. Death occurred on the 30th day of hospitalization.

Life history: The patient grew and developed according to her age, showing no behavioral differences from her peers. She completed 8 years of school and a vocational training program in sewing. She worked in her field and retired at 60 but continued to take private orders. A widow, she had two adult daughters who lived separately. The patient lived independently, led an active lifestyle, took frequent walks, read, maintained an interest in life, communicated with acquaintances, watched television, and visited theaters and museums.

Medical history: According to the patient's daughter, 5 days before hospitalization, she became lethargic, apathetic, and distracted. She stopped cooking and refused to eat. The day before hospitalization, she stopped answering phone calls. She recognized her daughters but did not respond appropriately to questions, became withdrawn, and stopped sleeping. She was hospitalized due to hyperthermia, weakness, and difficulty breathing. Upon admission, a CT scan revealed community-acquired, multi-segmental pneumonia CT-1 (10%).

Mental status: Upon admission, consciousness was not impaired. The patient was correctly oriented in terms of personal identity. Orientation in time and place was partial: she correctly named the current month and year but did not know the date, address, or hospital name. She was fairly critical of her condition, understanding that she was in the hospital: "They said pneumonia... one of my daughters is locked up at home because of the virus... maybe I have it too?" She also mentioned, "I'm not usually like this," and "my head feels off." During conversation, she gave short answers that were not always relevant but provided accurate responses when questions were simplified. She was confused about dates and events in her biography. She followed simple verbal instructions but made mistakes when reading written instructions.

Although she recognized her errors, she refused to try again. She was fatigued and apathetic. She could not recall three words given to her for memory testing but later remembered one. Her ability to count was impaired, and she made significant mistakes in writing and drawing pentagons. She did not express delusional ideas or experience perceptual disturbances. Her attention was distractible and easily fatigued. Her thinking was concrete, slow-paced, and lacking in content. At the time of examination, her MMSE score was 17 points.

The patient's physical condition deteriorated, as evidenced by increasing levels of CRP, D-dimer, and fibrinogen in her blood tests, decreased hemoglobin and total protein in her complete blood count, a drop in oxygen saturation, and worsening respiratory failure. This was accompanied by anxiety and refusals to undergo treatment and diagnostic procedures. When her vital signs stabilized, she became more organized and followed the medical staff’s instructions. Her MMSE score showed no changes during the hospitalization.

Discussion.

Despite her advanced age and comorbid physical conditions, the patient's cognitive functioning prior to the coronavirus infection did not exceed typical age-related changes. Although her orientation and immediate memory were relatively preserved, she exhibited significant impairments in attention, counting, immediate recall of new information, and praxis. Throughout the observation period, there were no changes in her cognitive performance.

Summary

A comparative analysis of MMSE scores at the beginning and end of hospitalization revealed positive dynamics in the cognitive indicators of patients with neurocognitive deficit syndrome by the time of discharge. There was an improvement in orientation, immediate memory, attention and counting, word recall, speech, and the total MMSE score. Over time, significant negative correlations were found between the overall severity score of the patient's condition (as measured by the NEWS2 scale) and MMSE subscales, including immediate memory, attention and counting, word recall,

speech, and the total score. A correlation was identified between the final MMSE score and the patient's age, the severity of COVID-19, and a history of nervous, cardiovascular, and digestive system diseases.

Currently, data on the relationship between COVID-19 and persistent cognitive impairments are accumulating. Therefore, data on the dynamics of cognitive indicators during treatment may serve as a guide for assessing neuropsychological status. Further studies are needed to confirm this relationship, determine whether cognitive impairments are related to the acute phase's clinical signs or the recovery phase at the time of assessment, and quantify the rate of recovery. In particular, assessing the baseline cognitive level at admission, as well as assessments at discharge and during follow-up visits, is essential for gaining knowledge about the potential long-term neuropsychological and psychological consequences of COVID-19. These assessments are necessary for developing rehabilitation programs post-hospitalization. Objective neurocognitive measurements can provide valuable information for neuropsychiatric triage and should be included as endpoints in clinical studies.

3.4. Anxiety and Depressive Symptoms within the Structure of COVID-19

The socio-demographic characteristics of a cohort of patients diagnosed with F43.22 mixed anxiety and depressive reaction due to adaptation disorder were studied.

Table 3.4.1. Socio-demographic Data of Patients		
Items	Abs	%
Gender		
Male	11	34,4
Female	21	65,6
Age		
40-50	8	25,0
51-60	12	37,6
61-70	4	12,6
71-80	1	2,9
Total	32	100
Education		
Higher education	23	71,9
Secondary vocational education	2	6,2
Secondary education	7	21,9
Total	32	100
Employment		
Full-time employment (pre-retirement age)	21	65,7
Part-time employment	11	34,3
Total	32	100
Married		
Married	15	46,9
Divorced	6	18,7
Single	5	15,7
Widowed	6	18,7
Total	32	100

As shown in Table 3.4.1., there were more women than men in the cohort, with a significant difference ($p = .0245$). Most patients were between 51 and 60 years old, held higher education degrees, had stable employment, and were married. Among patients hospitalized with COVID-19 infection, there was a high prevalence of clinically significant symptoms of anxiety and depression. The polymorphism of the clinical presentation of anxiety-depressive disorders in patients diagnosed with COVID-19 highlighted the need to study their clinical indicators over time.

At admission, 11 patients (34.4%) had a mild course of COVID-19 infection, 14 (43.7%) had a moderate course, 3 (9.4%) had a severe course, and 4 (12.5%) had a critical course. The results of physical condition monitoring are presented in Table 3.4.2.

Table 3.4.2. Data on monitoring the physical condition of patients with coronavirus infection COVID19 using the NEWS2 scale*

item	1st dimension		2d dimension		p-value
	Med	*IQR*	*Med*	*IQR*	
Respiratory Rate (per minute)	0,0	0,0-2,0	0,0	0,0-0,0	.003
Oxygen saturation (%)	1,0	0,0-1,0	0,0	0,0-0,0	.001
Air or Oxygen	0,0	0,0-0,0	0,0	0,0-0,0	.043
Température (°C)	0,0	0,0-0,0	0,0	0,0-0,0	.715
Systolic Blood Pressure (mmHg)	0,0	0,0-1,0	0,0	0,0-0,0	.005
Heart rate (per minute)	0,0	0,0-0,0	0,0	0,0-0,0	.043
Awareness	0,0	0,0-0,0	0,0	0,0-0,0	-
RESULT	1,5	0,0-4,0	0,0	0,0-0,0	.000

Note: *NEWS2 - National Early Warning Scale. Med-median, IQR- interquartile range, p-value - parameter differences, significant - $p < 0.05$

Data from the first measurement indicated that, in the initial days of hospitalization, 11 patients (34.4%) presented with a mild form of the illness. Fourteen patients (43.7%) required assessment to determine the need for further care, 3 patients (9.4%) required consultation with an intensive care unit (ICU) physician to assess vital functions, and 4 patients (12.5%) required ICU admission. By the second measurement, significant improvement was observed in 29 patients (90.6%), while moderate symptoms of the primary illness persisted in 1 patient (3.1%), and 2 patients (6.3%) remained in a severe condition.

Upon admission, 14 patients (43.7%) with moderate illness (stable condition not requiring oxygen therapy) reported symptoms of severe anxiety, peaking in the morning and causing early awakening, tension, “internal tremors” throughout the day, increased irritability, a sensation of suffocation, and associated fear of death. These

patients noted that their anxiety and fear for their health and lives intensified gradually with news of the COVID-19 spread. When clinical symptoms of illness appeared, respiratory issues quickly followed, often prompting them to open windows to "get fresh air," though this provided no relief. In the hospital, these patients appeared tense, often exhibited excessive motor activity, looked visibly anxious, and were fixated on their physical condition. They frequently sought attention from the medical staff, asking persistent questions about their health, requesting additional diagnostics, or asking to change their therapy.

Behavioral issues were more common in these patients: during periods of high anxiety, they attempted to leave the room or department, insisted that windows be opened (disregarding safety protocols), and often clashed with roommates and nursing staff.

Five patients (15.6%) could not articulate complaints about their physical condition but expressed fear about the lethality of the infection, appearing restless and seeking extra attention. Due to heightened sensitivity and irritability, they struggled to tolerate the noise from oxygen concentrators in their rooms and either attempted to turn them off or requested to be moved to a different room, which was not feasible due to high occupancy. Emotional lability and diminished critical and prognostic abilities were also noted. Some patients from out of town—3 patients (9.4%) at the peak of their anxiety disorder—refused transfer to a rehabilitation unit, fearing they would be taken to a psychiatric hospital. As a result, they attempted to leave the hospital on their own, despite having no family or acquaintances in the city.

Table 3.4.3. Anxiety indicators in patients with coronavirus infection COVID 19 according to the Covy scale

Item	1st dimension		2st dimension		p-value
	Med	*IQR*	*Med*	*IQR*	
Complaints	3,0	2,0-3,0	1,0	1,0-2,0	.000
Behavior	2,0	2,0-3,0	1,0	0,0-1,0	.000
Somatic symptoms of anxiety	2,0	1,5-3,0	1,0	0,0-1,0	.000
Score: NaN	7,0	6,0-9,0	3,0	1,0-4,0	.000

Note: Med-median, IQR- interquartile range, p-value - parameter differences, significant - $p < 0.05$

As shown in Table 3.4.3., the overall median Covy scale score [76] decreased from 7 to 3 points during the treatment, indicating a 57.1% reduction. According to the results of the first Covi scale assessment (Table 3.4.3), no anxiety was noted in 1 patient (3.1%), mild anxiety symptoms were present in 12 patients (37.5%), and 19 patients (59.4%) exhibited an anxious state. By the end of hospitalization, anxiety symptoms were absent in 23 patients (71.9%). Symptoms persisted in 5 patients (15.6%), and 4 patients (12.5%) continued to exhibit an anxious state. Patients in severe somatic condition also experienced intense fear of death, were restless, and showed motor discoordination within the confines of their beds. They reported insomnia ("afraid to sleep and never wake up again") and autonomic symptoms. These patients described episodes of paroxysmal anxiety that developed immediately after ICU staff left to attend to other patients. They demanded constant attention, engaging staff in conversation despite respiratory insufficiency and extensive oxygen therapy, and were preoccupied with thoughts of imminent death. More detailed data on anxiety symptoms are provided in table 3.4.4.

As seen in Table 3.4.4., the median scores from the first and second assessments differed significantly, except for gastrointestinal symptoms. The overall score decreased from 21.0 to 8.0 (61.9%). According to the results of the first assessment using the Hamilton scale [127], 4 patients (12.5%) were identified as "possibly having anxiety disorders," 10 patients (31.2%) had "anxiety disorders," 6 patients (18.7%) had "symptomatic anxiety," and 12 patients (37.6%) exhibited "severe anxiety." By the end of treatment, no anxiety was noted in 13 patients (40.6%), while the categories "possibly having anxiety disorders," "symptomatic anxiety," and "severe anxiety" were observed in 16 patients (50.0%), 1 patient (3.1%), and 2 patients (6.3%), respectively.

Table 3.4.4. Anxiety scores in patients with COVID-19 coronavirus infection according to the Hamilton scale [127]					
Item	1st dimension		2st dimension		p-value
	Med	*IQR*	*Med*	*IQR*	
Anxious mood	3,0	3,0-3,0	1,0	1,0-2,0	.0000
Tension	2,0	2,0-3,0	1,0	1,0-1,0	.0000
Fears	2,0	0,5-2,5	0,0	0,0-1-0	.0002
Insomnia	2,0	2,0-3,0	1,0	1,0-1,0	.0000
Intellectual	2,0	1,0-3,0	1,0	0,0-1,0	.0000
Depressed mood	3,0	2,0-4,0	1,0	0,0-1,0	.0000
Somatic complaints: Muscular	1,0	0,0-2,0	0,0	0,0-0,0	.0004
Somatic complaints: Sensory	2,0	1,0-2,0	0,5	0,0-1,0	.0001
Cardiovascular symptoms	0,0	0,0-2,0	0,0	0,0-0,0	.0087
Respiratory symptoms	2,0	0,0-3,0	0,0	0,0-2,0	.0008
Gastrointestinal symptoms	0,0	0,0-1,0	0,0	0,0-0,0	.1823
Genitourinary symptoms	0,0	0,0-1,5	0,0	0,0-0,0	.0125
Autonomic symptoms	2,0	1,0-2,0	1,0	0,0-1,0	.0000
Behavior at interview	1,0	1,0-2,0	0,0	0,0-1,0	.0000
Total score	21,0	18,0-32,5	8,0	4,5-11.5	.0000

Note: Med-median, IQR- interquartile range, p-value - parameter differences, significant - $p < 0.05$

Patients who lost relatives during hospitalization exhibited predominant depressive symptoms. These patients, often elderly, expressed thoughts of not wanting to live and a hope for “reunion” with the deceased. Their anxiety was frequently related less to their somatic condition and more to the need to arrange funerals, although the severity of their illness prevented their discharge for handling these matters. In younger patients, the news of a family member's death (often a parent) triggered an acute grief reaction with weeping and psychomotor agitation. One patient, who had spent an extended period in the ICU, experienced high anxiety levels, sleep disturbances, obsessive anticipation of a worsening condition, and intrusive memories of her time in the ICU, which intermittently seemed “real” to her. During intense anxiety episodes, she “heard” ICU equipment sounds and feared death, as she perceived her somatic deterioration as inevitable.

In addition to anxiety, depressive symptoms were observed in the studied patients (Table 3.4.5.).

Table 3.4.5. Depression rates in patients with coronavirus infection COVID-19 according to the Montgomery-Asberg scale [189]

Item	1st dimension		2st dimension		p-value
	Med	*IQR*	*Med*	*IQR*	
Apparent Sadness	3,0	2,5-4,0	1,0	1,0-2,0	.0000
Reported sadness	3,0	2,0-4,0	1,0	1,0-2,0	.0000
Innertension	3,0	2,0-4,0	1,0	1,0-2,0	.0000
Reduced sleep	3,0	2,0-4,0	1,0	1,0-2,0	.0000
Reduced appetite	3,0	2,0-4,0	1,0	1,0-1,0	.0000
Concentration Difficulties	2,0	2,0-3,0	1,0	1,0-1,5	.0000
Lassitude	3,0	2,0-3,0	1,0	1,0-2,0	.0000
Inability to feel	2,0	2,0-3,0	1,0	0,0-1,0	.0000
Pessimistic thoughts	3,0	2,0-3,0	0,0	0,0-1,0	.0000
Suicidal thoughts	0,0	0,0-0,0	0,0	0,0-0,0	.5001
Scoring	26,0	19,5-31,0	8,0	6,5-12,0	.0000

Note: Med-median, IQR- interquartile range, p-value - differences in parameters, significant - $p < 0.05$/Note: Med-median, IQR- inter

The median scores from the first and second measurements, except for the "suicidal thoughts" indicator, differed significantly. The overall score in the second measurement decreased from 26.0 to 8.0 (69.2%). According to the first measurement, 12 patients (37.5%) showed a “mild depressive episode,” 9 patients (28.1%) a “major depressive episode,” 8 patients (25.0%) a “moderate episode,” and 3 patients (9.4%) had “no depressive episode.” By the end of the hospital stay, “no depressive episode” was observed in 26 patients (81.2%), a “mild depressive episode” in 3 patients (9.4%), and a “major episode” in 3 patients (9.4%).

According to the Clinical Global Impression scale at admission, 17 patients (53.1%) had moderately expressed mental disturbances, 12 patients (37.5%) had significantly expressed disturbances, and 3 patients (9.4%) were in severe mental condition. During treatment, significant improvement was observed in 12 patients (37.5%), substantial improvement in 16 patients (50.0%), and slight improvement in 4 patients (12.5%).

A correlation between the final scores on the physical condition scales and the depression and anxiety scales was studied, with results shown in Table 3.4.6. As seen in Table 3.4.6, the correlation coefficient was statistically insignificant only between the final scores of the NEWS2 physical condition scale and the Montgomery–Asberg Depression Scale [189] in the first measurement.

Table 3.4.6. Correlation between the final scores of the physical condition scales and the depression and anxiety scales

Scales	Scale NEWS -2, 1st dimension		Scale NEWS -2, 2st dimension	
	rank correlation coefficient. R	p-value	rank correlation coefficient R	p-value
Montgomery—Asberg Depression Rating Scale, MADRS	0,266654	0,140140	0,514642	.0025
The Hamilton Anxiety Rating Scale (HAM-A)	0,384652	0,029723	0,512796	.0026
Covy anxiety Scale	0,419655	0,016801	0,509016	.0029

Note: *NEWS2 - National Early Warning Scale

In all other cases, a clear correlation was demonstrated between the final scores of the physical condition scales and the depression and anxiety scales.

Treatment included short-term therapy and medication, with the latter adjusted based on the severity of the primary illness. Anxiety, a pronounced symptom during the acute phase of viral infection, was not managed with early-generation drugs (barbiturate derivatives and medium- or long-acting benzodiazepines) due to their muscle-relaxant effects and the potential risk of respiratory depression. Among anxiolytics, hydroxyzine was preferred, while sertraline was chosen as an antidepressant. Certain selective serotonin reuptake inhibitors (such as fluvoxamine, paroxetine, and sertraline) may potentially offer cytoprotective effects due to their secondary action in reducing sphingomyelinase activity. A similar effect has been suggested for the anxiolytic hydroxyzine [4]. By the end of hospitalization, 40.5% of

patients no longer displayed anxiety symptoms, and depressive symptoms were absent in 81.2%.

The findings are illustrated by the following clinical cases:

Clinical Case 1.**Patient E., 59 years old.**

Diagnosis: Moderate COVID-19 infection (PCR+). Community-acquired bilateral polysegmental viral pneumonia (CT1 – 25%). Respiratory failure 0 stage. Organic anxiety disorder associated with other viral and bacterial neuroinfections.

Life history: Born in Leningrad, only child in a complete family. Early development was unremarkable. Completed medical studies at the First Pavlov State Medical University of St. Petersburg. Works as a department head. Married, with one adult son, and lives with his wife in a separate apartment. In April 2020, he was exposed to a COVID-19 positive patient at work, subsequently experiencing fever, severe weakness, and cough. After a bilateral polysegmental pneumonia was observed in a CT scan, he was hospitalized. COVID-19 was confirmed in the hospital, but his physical condition remained stable, and he did not require oxygen supplementation. Psychiatric consultation was prompted by marked anxiety, agitation, and motor restlessness.

Initial Psychiatric Evaluation: The patient was fully conscious and oriented. He was anxious, tense, and restless, with a loud, fast-paced voice. He was constantly active in the hospital room, stating that "it is hard to stay still, and movement distracts me from constant thoughts about death." He was preoccupied with thoughts of sudden death, though he acknowledged that "rationally, I know my condition is stable, with normal vital signs." He would only sit or lie down when he was too tired to stand. Night sleep was disrupted as he could not remain still for long. He reported sleeping for only about two hours a night, along with sensations of chest heaviness and an intense fear of a sudden physical deterioration, "scared that I won’t be able to breathe or exhale." He also reported palpitations, sweating, and diarrhea, attributing his condition to the "grim mortality statistics for COVID-19." No psychotic symptoms were noted, and cognitive function was intact.

During the initial assessment, his Hamilton Anxiety Scale score was 48, and his Covi Anxiety Scale score was 12. Due to motor agitation and significant circadian rhythm disruptions, and with his stable physical condition (NEWS2 score of 1 due to tachycardia), he was given a short course of intramuscular phenazepam injections, followed by hydroxyzine, along with short-term psychotherapy to reduce anxiety levels.

Before Discharge: The patient was fully oriented, calm, and organized in behavior, with normal speech tempo and volume. He reported: "Anxiety has decreased, and sleep has returned, but there's still a sense of heaviness in the chest, and occasionally I worry that my condition might worsen and that I'll lose control again." However, he found it easier to distract himself from these thoughts with external stimuli. He was preoccupied with somatic sensations, and unusual bodily perceptions triggered brief episodes of anxiety. His insight into his condition was intact. Sleep and appetite were adequate.

Summary

At the follow-up assessment, he scored 13 on the Hamilton Anxiety Scale, 4 on the Covi Anxiety Scale, and 0 on the NEWS2 scale. Despite initial high scores on the Covi and Hamilton anxiety scales, significant reductions were observed following treatment with phenazepam and hydroxyzine, although moderate anxiety persisted. Upon discharge, outpatient psychiatric follow-up was recommended.

Clinical Case 2. Patient P., 34 years old.

Diagnosis: Mild COVID-19 infection (PCR+). Varicose veins of the lower limbs. Non-psychotic depressive disorder associated with other viral and bacterial neuroinfections.

Life history: Born in Leningrad, only child in a complete family. Holds a higher degree in law and works in her field. Single, childless, and living with her parents in a separate apartment. She was exposed to a feverish colleague later confirmed to have COVID-19. She tested positive for COVID-19 shortly after and developed mild

symptoms. Her parents, who lived with her, also tested positive and required hospitalization due to severe somatic conditions.

The patient was admitted to the hospital to care for her parents, feeling increasingly distressed, anxious, and guilty, believing she "infected her family." Sleep and appetite were disrupted, and her condition worsened after her mother was transferred to the ICU. Shortly afterward, her father passed away in the general ward. The patient was evaluated by a psychotherapist upon admission and by a psychiatrist after her father's death.

Initial Psychiatric Evaluation: The patient was conscious and oriented. Her mood was low, and affect was unstable, fluctuating between irritability and anxiety. She had a flattened expression and minimal gesticulation, with a quiet, monotone voice and a slow conversational pace. She expressed self-blame, believing she "infected the whole family, causing their death." After her father's death, she believed her mother would soon die in the ICU. She refused medical help, saying, "I deserve whatever happens next, whether pneumonia or death." She denied active suicidal intentions, holding onto a slight hope that her mother might survive.

During the assessment, her Montgomery-Asberg Depression Rating Scale score was 44, her Hamilton Anxiety Scale score was 28, and her Covi Anxiety Scale score was 8, with a NEWS2 score of 0. She was prescribed sertraline, hydroxyzine, and brief psychotherapy. Following her mother's transfer from the ICU to the general ward, her anxiety scores decreased from 28 to 14 on the Hamilton Scale and from 8 to 4 on the Covi Scale, though her depression score remained unchanged.

Before Discharge: She was conscious and oriented, with a persistently low mood but showing improved energy and activity. She effectively cared for her mother, and her emotional instability had diminished. She reported early morning awakenings and low mood in the mornings but did not voice self-blame spontaneously, though she felt "guilty" about her father. Her improvement correlated with her mother's transfer to the general ward, giving her "a reason to live and care for her." She denied any delusions or hallucinations, had no risky behavior, and continued to have disrupted sleep and reduced appetite.

Montgomery-Asberg score before discharge was 26, Hamilton Anxiety Scale score 7, and Covi Anxiety Scale score 3, with a NEWS2 score of 0. At discharge, she was referred for outpatient psychiatric follow-up.

Summary

Among patients hospitalized with COVID-19, clinically significant anxiety and depression symptoms were highly prevalent. The variability in the clinical presentation of anxiety-depressive disorders in COVID-19 patients necessitated tracking these indicators over time. Physical and mental symptoms were assessed using the Hamilton and Covi anxiety scales, the Montgomery-Asberg depression scale, and the NEWS2 physical health scale. Treatment involved short-term psychotherapy and pharmacotherapy, coordinated with a clinical pharmacologist. Data indicated that anxiety and depression symptoms were most intense in the initial days of hospitalization but rapidly decreased. By discharge, anxiety symptoms were resolved in 40.6% of patients and depressive symptoms in 81.2%. Correlation measures revealed a clear relationship between NEWS2 physical health scores and the final scores on the depression and anxiety scales.

3.5. Impact of Mental Disorders on COVID-19 Outcomes

An analysis of the clinical and dynamic indicators of COVID-19 patients with mental disorders was conducted to identify predictors of adverse outcomes related to the mental state. A total of 97 patients were examined. Their socio-demographic data are presented in Table 3.2.1 (Chapter 2).

At the time of the examination, the patients had mental disorders classified under the following ICD-10 categories [27]: F05.86 Other delirium, due to other viral and bacterial neuroinfections – 30.9%, F06.76 Mild cognitive disorder due to other viral and bacterial neuroinfections. Neurocognitive deficit syndrome – 36.1%, F43.22 Mixed anxiety and depressive reaction, due to an adaptation disorder – 33.0%.

The sample included patients whose mental disorders developed in the context of COVID-19 infection (delirium, neurocognitive disorders, neurotic, stress-related, and somatoform disorders). These data were taken into account during statistical analysis.

The study was prospective in nature. During the observation period, 24 (24.7%) patients (Group 1) died, while 73 (75.3%) patients (Group 2) were discharged after recovering from the primary illness.

Statistical analysis revealed no gender differences between patients in Groups 1 and 2. However, the age of patients was significantly higher in Group 1 (68.3±17.1 vs 60.0±14.0, $p = .0168$). The age range in Group 1 was from 36 to 92 years, while in Group 2 it was from 20 to 85 years. The average length of hospitalization for patients with a favorable outcome (Group 2) was Md 21.0 (IQR 12.0–28.0) days, while for those with an unfavorable outcome, it was Md 11.5 (IQR 6.0–16.5) days, with the difference being statistically significant ($p = .0020$). Socio-demographic variables differed only in employment status: there were significantly more retirees in Group 1 (65.4% vs 32.9%, $p = .0071$). No significant intergroup differences were found in terms of education level, marital status, or disability.

Table 3.5.1. Clinical and anamnestic characteristics of the study groups				
Variable	Parameter	1st group (N=24)	2nd group (N=73)	*P*
Gender	Male	13 (54,2%)	30 (41,1 %)	.3781
	Female	11 (45,8%)	43 (58,9%)	.3781
	Total	24 (100%)	71 (100%)	
The ICD-10 for Mental and Behavioural disorders Total	F05.8Otherdelirium	16 (66,7%)	14 (19,2%)	.0000*
	F06.7Mild cognitivedisorder	6 (25,0%)	29 (39,7%)	.0000*
	F43.22 Mixed anxiety and depressive reaction	2 (8,3%)	30 (41,1%)	.0000*
	Total	24 (100)	73 (100)	97 (100)
Severity of mental disorder at initial examination	0 – impossibletoestimate	-	-	
	1 – Normal—not at all ill, symptoms of disorder not present past seven days	-	-	-
	2 – Borderline mentally ill—subtle or suspected pathology	-	-	-
	3 – Mildly ill—clearly established symptoms with minimal, if any, distress or difficulty in social and occupational function	-	-	-
	4 – Moderately ill—overt symptoms causing noticeable, but modest, functional impairment or distress; symptom level may warrant medication	-	3(4,1)	.7419
	5 – Markedly ill—intrusive symptoms that distinctly impair social/occupational function or cause intrusive levels of distress	14 (58,3)	58(79,5)	. 0746
	6 – Severely ill—disruptive pathology, behavior and function are frequently influenced by symptoms, may require assistance from others	9(37,5)	12(16,4)	.0591
	7 – Among the most extremely ill patients—pathology drastically interferes in many life functions; may be hospitalized	1(4,2)	-	.5563
	Total	24 (100)	73 (100)	-

end of table 3.5.1

Dynamics of mental state	0 – impossible to estimate	-	-	-
	1 – Very much improved—nearly all better; good level of functioning; minimal symptoms; represents a very substantial change	-	38(52,1)	.0000*
	2 – Much improved—notably better with significant reduction of symptoms; increase in the level of functioning but some symptoms remain	2(8,3)	16 (21,9)	.2370
	3 – Minimally improved—slightly better with little or no clinically meaningful reduction of symptoms. Represents very little change in basic clinical status, level of care, or functional capacity	20 (83,3)	9(12,3)	.0000*
	4 – No change—symptoms remain essentially unchanged	1(4,2)	10 (13,7)	.3647
	5 – Minimally worse—slightly worse but may not be clinically meaningful; may represent very little change in basic clinical status or functional capacity	-	-	
	6 – Much worse—clinically significant increase in symptoms and diminished functioning	1 (4,2)	-	.5563
	7 – Very much worse—severe exacerbation of symptoms and loss of functioning	-	-	
	Total	24 (100)	73 (100)	
Severity of coronavirus infection	1. Asymptomatic course	1 (4,1%)	2(2,8%)	.7419
	2. Mild course		8 (10,9%)	.2057
	3. Moderate course		55 (75,4)	.0000*
	4. Severe course	8 (33,3%)	8 (10,9%)	.0248*
	5. Extremely severe course	15 (62,6%)		.0000*
	Total	24 (100%)	73(100%)	

*the difference is statistically significant.

As seen from the data presented in Table 3.5.1., patients with an unfavorable outcome (Group 1) had a significantly higher prevalence of delirium cases (F05.8), whereas those with a favorable outcome (Group 2) showed a significantly higher proportion of cases involving mixed anxiety and depressive reactions associated with adjustment disorder. Severe and critically severe cases of COVID-19 were predominant in Group 1, while moderate cases were more common in Group 2.

On the Clinical Global Impression scale during the initial examination, severe mental conditions were more frequently observed in Group 1, with a trend toward statistical significance (p = .0591). The dynamic characteristics of the disease varied significantly between the groups: cases of significant improvement were more common in Group 2, while cases of minor improvement were more frequent in Group 1.

Table 3.5.2. Concomitant somatic pathology in patients with coronavirus infection*

Diseases	1st group (N=26)	2d group(N=71)	*P*
Diseases of the eye and its appendages		1(1,4%)	0,599
Diseases of the skin and subcutaneous tissue		1 (1,4%)	0,599
Diseases of the genitourinary system	17 (65,4%)	37 (52,1%)	0,350
Diseases of the nervous system	20 (76,9%)	34 (47,9%)	0,020**
Diseases of the digestive system	21 (80,8%)	39 (54,9%)	0,037*
Diseases of the cardiovascular system	25 (96,2%)	51 (71,8%)	0,021*
Diseases of the ear and mastoid process	1 (3,8%)	2 (2,8%)	0,687
Substance abuse		2 (2,8%)	0,954
Tumors	6 (23,1%)	3 (4,2%)	0,015*
Exogenies (injuries, burns)	1 (3,8%)	6 (8,5%)	0,738
Endocrine, metabolic diseases, eating disorders	12 (46,2%)	22 (31,0%)	0,252

* total percentage < 100%, since some patients had multiple pathologies, ** difference is statistically significant.

It is worth noting that Table 3.5.2 includes only somatic diseases not directly associated with COVID-19. In Group 1, there was a statistically significant predominance of diseases of the nervous, digestive, and cardiovascular systems, as well as oncological conditions. In addition to comparing the groups, predictive models for disease outcomes were developed. At the first stage, a logistic regression model was constructed, incorporating the following factors: gender, age, comorbidities, severity of mental state at initial examination, dynamics of mental disorders, and severity of COVID-19 (Table 3.5.3.).

Table 3.5.3. Logistic model for predicting outcomes

Parameter	*Basic model1.1*			*Reducedmodel1.2*		
	OR	95%CI	*P*	P	95%CI	*P*
Intercept	0,06	0,00–160 000,00	0,688	0,02	0,00- 0,27	0,025
Female	1,17	0,05- 33,77	0,920			
Age	0,94	0,83–1,03	0,232			
Tumors	7,69	0,16–1232,76	0,353			
Endocrine, metabolic diseases, nutritional disorders	5,71	0,27–530,21	0,314			
Diseases of the nervous system	1,88	0,04–110,48	0,728			
Diseases of the cardiovascular system	7,22	0,02–19 115,10	0,571			
Diseases of the respiratory system	0,77	0,00–3408,61	0,961			
Diseases of the genitourinary system	0,49	0,01–20,08	0,703			
Other diseases	0,37	0,00–22 843,62	0,843			
Exogenia	0,19	0,00–1387,00	0,788			
Severity of mental disorder at initial examination	2,18	0,06–123,67	0,661			
Minor improvement in mental state	5,58	0,06–1317,57	0,464	3,77	0,10- 159,86	0,449
Significant improvement in mental state	0,01	0,00–1,73	0,141	0,04	0,00 - 0,95	0,075
Severe course of coronavirus infection	583,12	30,26–160 000,00	0,001	328,02	32,70 - 12100,18	<0,001
AIC	53,77			33,17		
R^2Tjur	0,88			0,86		

Notes: OR – odds ratio; CI – confidence interval; Intercept – model constant; AIC – Akaike information criterion; R2 Tjur – pseudo-coefficient of determination.odds ratio confidence interval

During the optimization process, the lowest AIC for the model was achieved with the combination of the following variables: severity of COVID-19 ($p < 0.001$) and dynamics of mental state—at least significant improvement ($p = 0.075$).

The subsequent model (Table 3.5.4) assessed the risk of fatal outcomes, taking into account the duration of patient follow-up. In the logistic model, the dynamics of mental state were not excluded despite not meeting the traditional level of statistical significance; therefore, this parameter was retained in the model. Since the dynamics of mental state are potentially associated with the initial mental disorder and anamnesis, the assessment of the initial mental state and exogenous factors (substance use and traumatic brain injury) were included in the model. Gender and age, although excluded from the logistic model, were also incorporated as covariates. The results of the predictive analysis are visually presented in Figure 5.3.1.

Table 3.5.4. Cox proportional hazards model [77] for predicting outcomes

Parameter	*Basic model 1.1*			*Reduced model 1.2*		
	HR	95%CI	*P*	HR	95%CI	*P*
Female gender	0,84	0,31 - 2,26	0,731			
Age	1,03	1,00 - 1,06	0,073	1,03	1,00 - 1,06	0,037
Exogenia	0,63	0,07 - 5,74	0,679			
Severe or extremely severe mental state at initial examination	4,34	1,44 - 13,03	0,009	4,55	1,66 - 12,48	0,003
Slight improvement in mental state	0,99	0,18 - 5,54	0,993	0,87	0,17 - 4,37	0,861
Significant improvement in mental state	0,10,	0,01 - 0,97	0,047	0,09	0,01 - 0,76	0,027
Severe course of coronavirus infection	32,87	4,00 - 270,18	0,001	33,17	4,01 - 274,65	0,001
Concordance (std. er.)	0,93 (0,02)			0,93 (0,02)		
AIC	137,05			133,35		
R^2Nagelkerke	0,64			0,64		

Notes: HR – hazard ratio; CI – confidence interval; Concordance (std. Er) – coefficient of concordance (standard error); AIC – Akaike information criterion; R2 Nagelkerke – pseudo-coefficient of determination.

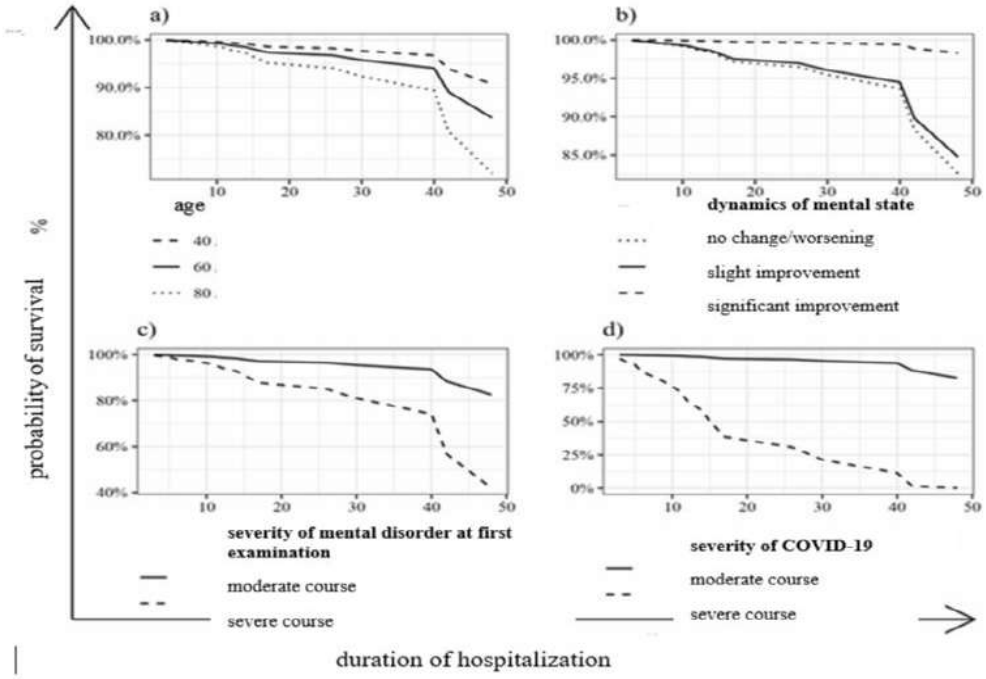

Figure 5.3.1. Patient survival curves according to the reduced Cox proportional hazards model 2.2.

The graphs (Figure 5.3.1) demonstrate that the likelihood of a non-fatal outcome decreases with age. Moreover, after forty days of hospitalization, the prognosis significantly worsens for individuals over 80 years old. It is shown that a favorable prognosis is achievable only with substantial improvement in mental state during psychotropic therapy.

The study results indicate that severe mental conditions, such as delirium, are predictors of low patient survival, particularly during prolonged hospitalizations. It was established that the most significant factor contributing to an unfavorable outcome is the severity of COVID-19; in such cases, the risk of death persists throughout the entire hospitalization period.

A comparative analysis of data from deceased and surviving COVID-19 patients revealed statistically significant differences in variables related to specific mental disorders, their severity, and progression, as well as the severity of COVID-19. The likelihood of a fatal outcome increased with age and the severity of the current mental disorder, while it decreased following the resolution of acute psychotic symptoms

during psychotropic therapy. The findings highlight the particular prognostic significance of delirium within the spectrum of mental disorders associated with COVID-19.

CONCLUSION

This study began in 2020, at a time when understanding of mental disorders in relation to the novel coronavirus was just beginning to take shape. In the interim clinical guidelines [3], Section 5.7 "Special Patient Groups" did not include information on patients with mental disorders, which appeared later [4]. The literature noted a near absence of studies on the direct impact of COVID-19 on the clinical presentation of mental illnesses [32]. This gap informed the formulation of the study's objective: "To determine the structure and characteristics of mental disorders associated with COVID-19 in the context of organizing consultative psychiatric care in a multidisciplinary hospital."

To achieve this objective, the first task was to identify the structure of mental disorders in patients admitted for treatment at the Veterans' Hospital (St. Petersburg) due to COVID-19. A retrospective analysis established that from April to June 2020, 557 patients were admitted to the hospital with the following diagnoses: dementia (F01-F03); other organic mental disorders (F05.0-F06.9); mental and behavioral disorders due to the use of psychoactive substances (F10-F19); schizophrenia, schizotypal, and delusional disorders (F20-F29); mood (affective) disorders (F30-F39); neurotic, stress-related, and somatoform disorders (F40-F48); and personality and behavioral disorders in adulthood (F60-F69).

It was established that patients with mental health conditions can be categorized into three groups: those with chronic mental disorders diagnosed prior to COVID-19 infection; those with newly onset mental disorders caused by COVID-19; and those with anxiety-phobic disorders related to COVID-19 but without a verified COVID-19 infection.

This classification facilitated the further management of patients, both within the COVID-19 hospital and during transfers to psychiatric hospitals. The coronavirus is one of the primary viruses that primarily affects the human respiratory system but also has neuroinvasive properties, enabling it to spread from the respiratory tract to the central nervous system [52].

The analysis conducted in this study confirms the significance of mental disorders in the course of COVID-19 and aids in defining approaches for providing psychiatric and psychotherapeutic care in a multidisciplinary hospital for this pathology.

In addressing the second objective, we prospectively studied mental disorders that developed concurrently with COVID-19 infection. During the pandemic, identifying delirium as a potential manifestation of COVID-19 became particularly important [35]. However, delirium is traditionally viewed as a syndrome of altered consciousness without a comprehensive assessment of its complex structure [216].

Among studies on psychoses associated with COVID-19, some authors consider only confusion as part of delirium, while depressive mood, anxiety, memory impairment, and insomnia are classified under other syndromes [212]. Others have noted an increased prevalence of myoclonus, rigidity, alogia, and abulia in cases of COVID-19-related delirium [40]. Furthermore, the clinical presentation of delirium in COVID-19 is heterogeneous. According to T.E. Poloni et al. [212], in the acute phase, 52.4% of patients exhibited hypoactive delirium, while 47.6% showed hyperactive delirium.

In our study, the use of the DRS-R-98 scale allowed for a comprehensive quantitative assessment of delirium in older adults with COVID-19. It was shown that all examined patients had moderate to severe disruptions in the sleep-wake cycle, which differed from the characteristics of delirium reported by other researchers. The results of this study indicate that delirium associated with COVID-19 is also characterized by severe impairments in perception and long-term memory. These findings are generally consistent with the results of J. Helms et al. [134], who reported cognitive dysfunction in patients with delirium.

Unlike delirium observed in patients in respiratory intensive care units, which was consistently characterized by attention and thought process impairments [216], our study found that sleep-wake cycle disturbances were predominant. A parallelism was established between the severity of COVID-19 and delirium symptoms.

The use of the DRS-R-98 scale enabled a deeper understanding of the structure of delirium; however, its use was limited by difficulties in performing repeated serial assessments and the lack of differential evaluation of hyperactivity and hypoactivity [157]. Unfortunately, there are no data on the use of the DRS-R-98 scale in other infectious psychoses. However, when comparing our findings with those obtained in the evaluation of intoxication delirium (delirium syndrome caused by 1,4-butanediol poisoning) [30], similarities in the final DRS-R-98 scores were found. This suggests a resemblance in certain manifestations of organic delirium syndromes, despite their differing etiologies.

Thus, it was identified that specific features such as "sleep-wake cycle" and "motor agitation" assessed via the DRS-R-98 scale can be considered predictors of worse outcomes in COVID-19, alongside somatic outcome predictors such as "respiratory rate," "heart rate," and the "total NEWS2 score" on the third day of delirium.

The study of cognitive impairments associated with COVID-19 remains in the initial phase of synthesizing phenomenological data. Research has often been conducted under conditions of mass patient admissions and overburdened healthcare staff. While the manifestations of the acute phase are not yet fully understood, post-COVID impairments are beginning to take precedence. It remains unclear whether cognitive deficits are reversible or represent the early stages of a neurodegenerative process triggered by the coronavirus infection.

These cognitive impairments can potentially be interpreted as manifestations of a reversible syndrome commonly seen in infectious, inflammatory, or toxic conditions without a specific nosological classification [161]. Other authors have referred to this as a "neurocognitive (dementia-like) syndrome" [182,254]. Given that the ICD-10 does not include a direct term for "neurocognitive syndrome," this study applies the term "F06.76 Mild cognitive impairment associated with other viral and bacterial neuroinfections: Neurocognitive deficit syndrome."

It is believed that, unlike the MMSE, the Montreal Cognitive Assessment (MoCA) [198] is better at distinguishing between normal cognitive abilities and mild cognitive impairments. The advantage of using the MMSE for the studied cohort lies in its long-standing use as a screening tool for cognitive disorders over 40 years. It requires no special training and is convenient for rapid testing, even in intensive care settings. Furthermore, according to A.J. Larner [162], combining MoCA with MMSE—whether sequentially or in parallel—did not improve diagnostic utility compared to either test alone.

In our study, we observed the dynamics of cognitive variables in COVID-19 patients at admission (first measurement) and discharge (second measurement). During the first measurement, a decline in median scores across all MMSE items was identified. These findings align with contemporary literature. For instance, according to F. Alemanno [44], 80% of 87 patients (mean age 67.23 ± 12.89 years) exhibited neuropsychological impairments detected using MoCA and MMSE. In another study [199], general cognitive decline was observed in 33.3% of patients with pathological MMSE scores, with specific deficits in attention, memory, language, and praxis.

The authors concluded that cognitive impairment appears to be linearly associated with the duration of stay in the intensive care unit (ICU). The longer the ICU stay, the lower the MMSE score, indicating reduced global cognitive functioning. In our study, significantly better results were obtained during the second measurement (prior to discharge). At this stage, orientation and immediate memory scores improved, though language scores remained low. The statistically significant increase in median scores reflected an improvement in correct responses across all MMSE items.

Our findings partially align with those of S. Bonizzato [65], where 58.3% of patients scored below the MMSE threshold at baseline, but improvement was observed before discharge. Improved cognitive functioning at the second measurement was significantly correlated with MMSE total scores, saturation levels, oxygenation needs, and overall NEWS2 somatic scale scores.

Significant correlations were also identified between MMSE total scores and age, disease severity (second measurement), and comorbid conditions affecting the nervous,

cardiovascular, and digestive systems. Similar findings have been reported in studies by K. Krupp [160], D.M. Whiteside [254], and F. Alemanno [44], showing that neurocognitive symptoms correlate with severe disease, advanced age, male sex, and comorbidities such as hypertension, kidney failure, neoplastic diseases, hyperlipidemia, delirium, and hypoxemia during hospitalization.

The primary causes of cognitive decline remain unclear, but current hypotheses include hypoxic-ischemic brain damage, immunopathological mechanisms, and the neurotropism of SARS-CoV-2 infection [254].

Among patients hospitalized with the new coronavirus infection COVID-19, there is a high prevalence of clinically significant symptoms of anxiety and depression. The polymorphism of the clinical picture of anxiety-depressive disorders in patients with identified COVID-19 prompted the need to study their clinical indicators over time.

As in several studies [6, 125], our research also revealed a high co-occurrence of COVID-19 symptoms with anxiety and depression scores on the Montgomery-Åsberg, Hamilton, and Covi scales. Unlike the study by S.Z. Eshimbetova et al. [6], we were unable to trace the development of astheno-psychogenic, asthenic, and dysphoric depressive states. This may be related to the insufficient observation period. Given the complexity of the etiopathogenesis of the new coronavirus infection, it is reasonable to agree that affective symptoms are shaped by both exogenous and psychogenic factors. However, it seems unlikely that it is possible to determine the contribution of each of these factors at this stage.

Nevertheless, the data we obtained—except for one instance (the lack of statistical significance of the correlation coefficient between the depression score and the final physical condition score at the onset of the disease)—indicates a relationship between physical condition indicators and anxiety at the onset of the disease, and depression and anxiety at the end. The values of affective symptomatology decreased as physical symptoms alleviated: by 57.1% on the Covi scale [76], by 61.9% on the Hamilton scale [127], and by 69.2% on the Montgomery-Åsberg scale [189]. This partially corresponds with the results of C. Parker et al. [204], which showed that a

significant number of patients hospitalized with COVID-19 exhibited symptoms of depression and anxiety. While the anxiety level decreased during treatment, the depression level remained fairly stable. Our findings are also supported by the results of E. Argüder et al. [50], who observed the onset of anxiety in 50% of patients at the beginning of the illness, with symptoms disappearing in 40.6% of them as a result of treatment.

The third task of this study was to investigate the impact of mental disorders on the outcome of COVID-19. It was found that delirium is associated with high mortality in COVID-19 patients, which correlates with the data from F.B. Garcez et al. [115] about the association between delirium and prolonged hospitalization, treatment in intensive care units, and the use of mechanical ventilation. Our results confirm the prognostic significance of delirium developed in the context of COVID-19, with the duration of hospitalization serving as an intermediary factor in the relationship between delirium and mortality. International literature discusses potential risk factors for poor COVID-19 outcomes, including advanced age [266]. Our data partially align with the conclusions of G. Grasselli et al. [120], who link the likelihood of death not only to age but also to male sex. According to our data, age is an independent risk factor for death in COVID-19: based on prognostic models, the risk of death increased by 1.03 times for each additional year of age.

It is believed that the prognosis for COVID-19 is worse in patients with comorbidities, including mental disorders [262]. However, our study did not confirm a worsened prognosis for COVID-19 in patients with chronic psychiatric disorders of the schizophrenic or affective spectrum, nor was there a link to an increased risk of death. On the other hand, the infection may not be related to the debut of a mental disorder but may simply coincide with it in terms of clinical manifestation. A definitive diagnostic conclusion will be possible through subsequent follow-up observations of patients [31]. When infected with the SARS-CoV-2 virus, there is a high likelihood not only of developing mental disorders but also of worsening the mental condition in patients with pre-existing mental disorders, as noted in 20.9% of cases [268]. In our study, there was no exacerbation of chronic mental disorders against the backdrop of COVID-19

infection requiring hospitalization, as long as supportive psychotropic therapy was maintained. A comparative analysis of deceased and surviving patients with COVID-19 revealed statistically significant differences between variables related to specific mental disorders, their severity and dynamics, and the severity of COVID-19 infection. The patients' age had a significant impact on the prognosis of COVID-19. The results reflect the special prognostic significance of delirium within the structure of mental disorders developed during COVID-19 infection.

Finally, as part of the fourth task, a scheme for providing psychiatric care to patients hospitalized for treatment of COVID-19 at the Veterans Hospital in St. Petersburg was developed. Our task did not include, nor was it feasible, to create a comprehensive multi-level model of care for patients with mental disorders and COVID-19, involving a network of inpatient, outpatient, and social institutions. We focused on developing a scheme for organizing consultative psychiatric care, which is provided within a single healthcare facility—a multidisciplinary hospital for veterans. Based on the experience of consultative work, a scheme was developed with the following components: 1) consultative psychiatric care in the emergency department, 2) consultative psychiatric care in the intensive care unit, and 3) consultative psychiatric care in the infectious disease department. Depending on the severity of the somatic condition, patients with acute psychotic symptoms either received treatment in the intensive care unit or were transferred to the psychiatric hospital’s infectious disease unit. Patients with negative COVID-19 tests and in need of psychiatric care were transferred to a psychiatric hospital operating in the standard mode. The study helped clarify therapeutic tactics for different patient groups. For patients with chronic mental disorders, psychopharmacotherapy had to be significantly reduced in cases of severe infectious illness. In cases of mild COVID-19 progression, psychotropic therapy was carried out in full. Overall, our results align with the data from I.S. Kitsul et al. [9], which indicates that the severity of the condition and its proven relationship with age are partially determined by the presence of comorbid conditions. Notably, it is worth mentioning that exacerbations of mental disorders were more common in patients with severe mental impairments, even with mild COVID-19 progression. Given the

epidemic situation, psychotherapy involved short-term individual rational therapy aimed at reducing anxiety levels, focusing on internal resources, and exploring coping strategies for the stressful situation.

The experience of the psychiatric service in a multidisciplinary hospital underscores the necessity of the psychiatric unit's involvement in treating COVID-19 patients.

FINDINGS

1. Among patients in the multidisciplinary hospital who were admitted during the early period of the COVID-19 pandemic, mental disorders were most commonly represented by F01-F03 dementias (19.4%), F05.0-F06.9 other organic mental disorders (34.1%), and F40-F48 neurotic, stress-related, and somatoform disorders (21.0%).

2. The use of the DRS-R-98 scale enabled a comprehensive quantitative assessment of delirium in patients with COVID-19. It was shown that all the patients studied had moderate to severe impairments in the "wake-sleep" cycle, perception, long-term memory, short-term memory and visuospatial orientation. The most pronounced delirium symptoms were correlated with the most severe physical symptoms. The logistic regression model demonstrated that the variables "respiratory rate," "heart rate," and the final NEWS2 scale score can be considered predictors of disease outcome.

3. A comparative analysis of the initial and final scores of patients with neurocognitive deficits on the MMSE scale showed improvement in orientation, immediate memory, attention and calculation, word recall, and speech, indicating their reversibility. Their dynamics were influenced by age, the severity of COVID-19, and the presence of comorbidities in the medical history.

4. The presence of emotional disorders in the structure of the psychopathological picture is a characteristic feature of the mental pathology associated with COVID-19. Positive dynamics in emotional symptoms were related to a clear correlation between the final physical condition scores and the depression and anxiety scales.

5. Patients hospitalized in a multidisciplinary hospital with COVID-19 or suspected of having it received multimodal care. Based on the experience of consultative work, a scheme was developed, consisting of the following components: 1) consultative psychiatric care in the emergency department, 2) consultative psychiatric care in the intensive care unit, 3) consultative psychiatric care in the infectious disease department. The decision on the duration of treatment in the multidisciplinary hospital can be made at any stage based on the assessment of the severity of the somatic and mental state and the prognosis for the duration of psychiatric treatment.

PRACTICAL RECOMMENDATIONS

1. When providing care for patients with COVID-19 and mental disorders, it is essential to obtain information about any pre-existing mental disorders prior to the onset of symptoms of the new coronavirus infection. The source of this information may include primary medical documentation (ambulance referral), conversations with relatives and accompanying individuals, as well as the patient themselves, if their condition allows for an interview. If necessary, this information can be quickly obtained through a request to the local psychiatric and neurological dispensary.

2. Considering the high risk of developing exogenous psychopathological symptoms in infected patients, special attention should be given to the appearance of such psychoneurological symptoms as anosmia, ageusia, and parageusia, dizziness, rapidly worsening headache, attention disturbances, inattention, and escalating anxiety. These symptoms may indicate a change in the severity of the course of COVID-19 or the development of neurological complications, necessitating further examination by somatic specialists and adjustment of the treatment plan.

3. In patients with delirium developed in the course of COVID-19, the deterioration of physical condition statistically significantly leads to changes in parameters of the delirium severity scale (DRS-R-98), such as disturbances in the sleep-wake cycle, increased affective lability, formal thought disorders, motor agitation, and disturbances in temporal and spatial orientation. If these symptoms worsen, the patient requires reassessment of their somatic condition.

4. Significant changes in parameters such as disturbances in the sleep-wake cycle and motor agitation, as measured on the DRS-R-98 scale, were statistically more common in patients with a fatal outcome. Therefore, if these symptoms develop, it is advisable to assess the patient’s somatic condition (NEWS2) and consider their transfer to the intensive care unit.

5. When further directing patients, all aspects of the patient’s condition must be considered. After recovery from the primary illness, if no current psychotic symptoms are present and there are non-psychotic mental disorders, the patient should

be discharged from the hospital with recommendations to visit the local psychiatric and neurological dispensary. Transfer to a psychiatric hospital is indicated for all patients with persistent psychotic symptoms and lack of insight.

LIST OF ABBREVIATIONS

AP – arterial pressure

CAS – Covey Anxiety Scale

CNS – central nervous system

CKD – chronic kidney disease

Covid-19 – acute respiratory infection caused by coronavirusSARS-CoV-2 (2019-nCoV)

COPD – chronic obstructive pulmonary disease

CCL2 – chemokine ligand 2

CY-BOCS -Yale – Brownobsessive-compulsivescale

CGI-S -ClinicalGlobalImpressionScale

DASS-21-DepressionAnxietyandStressScale

DRS-R-98- Delirium Rating Scale-Revised-98

GM-CSF – granulocyte-macrophage colony-stimulating factor

GVV – hospital for war veterans

HARS- HamiltonAnxietyRatingScale

ICU - Intensive Care Unit and Resuscitation DepartmentIL-6 – interleukin-6

IL-1β – interleukin 1 beta

MMSE - MiniMentalStateExamination

NEWS2 - TheNationalEarlyWarningScore 2

OCD - obsessive-compulsive disorder

PCR - polymerase chain reaction

PTSD - post-traumatic stress disorder

SARS-CoV-2 -severeacuterespiratorysyndromecoronavirus 2

TNF-α – tumor necrosis factor-alpha

CNS – central nervous system

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APPENDICES

Appendix 1

Patient card associated with Covid-19

General data

Last name, first name, patronymic _____

Case history No _____

Date of admission _____

Address (district, street, house, apartment)_____

Diagnosis somatic _____

Diagnosis psychiatric _____

1. Gender M_____1 F_____2

2. Age in y. (abs) _____

3. Education

Higher	*1*
Incomplete higher	*2*
Secondary special	*3*
Среднее	*4*
Incomplete secondary	*5*

4 Employment

Employed	1.
WorkingRetiree	2.
Retiree	3.
Other	4.

5. Marriage

Married	1
Divorced	2
Single	3
Widower (widow)	4

6. Disability

Group 1 Disability	1
Group 2 Disability	2
Group 3 Disability	3
None	4

InfectiousandParasiticDiseases

№	**Name**	No	Yes
7	COVID-19	1	2
8	OtherInfections	1	2

9. **If COVID-19 is present, its severity is as follows:**

Asymptomaticcourse	1
Mildcourse	2
Moderatecourse	3
Severecourse	4
Extremelyseverecourse	5

Comorbidities

Code	Name	No	Yes
10	Tumors	1	2
11	Endocrine, metabolic diseases, and nutritional disorders	1	2
12	Nervoussystem diseases	1	2
13	Eye diseases and their appendages	1	2
14	Ear and mastoid process diseases	1	2
15	Cardiovascular diseases	1	2
16	Respiratory diseases	1	2
17	Digestivesystem diseases	1	2
18	Skin and subcutaneous tissue diseases	1	2
19	Genitourinary system diseases	1	2
20	Exogenous factors (injuries, burns)	1	2
21	Substance abuse	1	2
22	Mental disorders (before COVID-19)	1	2
23	Others	1	2

24. **Pathologies Subjectto Investigation**

ICD-10	**Name**	**No.**
F05	Delirium not induced by alcohol or other psychoactive substances	1
F06.7	Mildcognitive disorder	2
F20-F29	Schizophrenia	3
F32	Depressive episode	4
F42	Obsessive-compulsive disorder	5
F43	Reactions to severe stress and adjustment disorders	6

TREATMENT

№	Name	No	Yes
25	Phenazepam (tablets 0.5 mg; 0.1% solution for intramuscular and intravenous injections; the medication is started with a dose of 1–2 mg. If necessary, administration is repeated every 1.5 hours at 1 mg until symptoms are fully relieved)	1	2
26	Diazepam (tablets 5 mg; 0.5% solution for intramuscular and intravenous injections. Administration starts with a dose of 5–10 mg, repeated if necessary every 3–4 hours)	1	2
27	Hydroxyzine (12.5 mg – 100 mg per day), alimemazine (5 mg – 15 mg up to 3–4 times per day), chlorprothixene (15 mg – 30 mg up to 3–4 times per day)	1	2
28	Aminazine solution (excluding individuals over 65 years old; 2.5% solution for intramuscular injections, 25 mg – 100 mg per day)	1	2
29	Droperidol solution (0.25% solution for intramuscular injections; single doses of 2.5 mg – 5 mg, up to 2–3 times per day)	1	2
30	Haloperidol solution (0.5% solution for intramuscular and intravenous injections; for intramuscular injections in adults, the initial dose is 5 mg, up to 2 times per day, with a maximum daily dose not exceeding 30 mg; for individuals over 65 years old: 0.5–2 mg up to 2–3 times per day)	1	2
31	Other	1	2

32. OUTCOME

Name	№
Recovery	*1*
Discharged under the supervision of a psychiatrist at the place of residence	*2*
Transferred to a psychiatric hospital at the place of residence	*3*
Deceased	*4*

33. date of receipt

34. date of disposal

Appendix 2

National Early Warning Score (NEWS)

Purpose: Prediction of risks of clinical deterioration of patients' condition, bedside monitoring of the effectiveness of the therapy used, optimization of in-hospital routing.

Source: National Early Warning Score (NEWS) 2. https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news-2.

Adaptation: Popova K.N., Zhukov A.A., Zykina I.L., Troschanskiy D.V., Tyurin I.N., Protsenko D.N. NEWS2 score in the practice of infectious diseases hospital in COVID-19 patients. Implementation and results. Messenger of Anesthesiology and Resuscitation, 2021, Vol. 18, no. 1, P. 7-16. (In Russ.) DOI: 10.21292/2078-5658-2021-18-1-7-16

Here is the translated and formatted table in English:

Parameter	**Scoring Criteria**	**Patient Score**
Respiratory Rate (breaths/min)		
⩽8	3	
9-11	1	
12-20	0	
21-24	2	
⩾25	3	
Oxygen Saturation (SpO_2, %)		
⩽91	3	
92-93	2	
94-95	1	
⩾96	0	
Insufflation		
да	1	
нет	0	
Body Temperature (°C)		
⩽35,0	3	
35,1-36,0	1	
36,1-38,0	0	
38,1-39,0	1	
⩾39,1	2	
Systolic Blood Pressure (mmHg)		
⩽90	3	
91-100	2	
101-110	1	
111-219	0	
⩾220	3	
Heart Rate (beats/min)		
⩽40	3	
41-50	1	

51-90	0	
91-110	1	
111-130	2	
⩾131	3	
Change in Consciousness		
нет	0	
есть	3	
COVID-19 Status		
ConfirmedPositive	0	
Suspected	0	
Unlikely	0	
ConfirmedNegative	0	
TOTAL	TOTAL _____ Points (SpecifyResult)	

Appendix 3

DELIRIUM RATING SCALE-R-98 (DRS-R-98)

Purpose: The scale is used for initial assessment and repeated measurements of the severity of delirium symptoms.

Source: Trzepacz PT, Franco JG, Meagher DJ, Lee Y, Kim JL, Kishi Y, Furlanetto LM, Negreiros D, Huang MC, Chen CH, Kean J, Leonard M. Phenotype of subsyndromal delirium using pooled multicultural Delirium Rating Scale--Revised-98 data. J Psychosom Res. 2012 Jul;73(1):10-7. doi: 10.1016/j.jpsychores.2012.04.010. Epub 2012 May 30. PMID: 22691554.

Validation: Almuhairi ES, Badejo M, Peer A, Pitkanen M, McKenzie CA. The Validity and Applicability of the Revised Delirium Rating Scale (DRS-R98) for Delirium Severity Assessment in a Critical Care Setting. J Intensive Care Med. 2024 Mar;39(3):240-249. doi: 10.1177/08850666231199986. Epub 2023 Sep 5. PMID: 37670545; PMCID: PMC10845842.

This is a revision of the Delirium Rating Scale (Trzepacz et al. 1988). It is used for initial assessment and repeated measurements of delirium symptom severity. The sum of the 13 item scores provides a severity score. All available sources of information are used to rate the items (nurses, family, chart) in addition to examination of the patient. For serial repeated ratings of delirium severity, reasonable time frames should be chosen between ratings to document meaningful changes because delirium symptom severity can fluctuate without interventions.

DRS-R-98 SEVERITY SCALE

1. **Sleep-wake cycle disturbance**

Rate sleep-wake pattern using all sources of information, including from family, caregivers,

nurses' reports, and patient. Try to distinguish sleep from resting with eyes closed.

0. Not present

1. Mild sleep continuity disturbance at night or occasional drowsiness during the day

2. Moderate disorganization of sleep-wake cycle (e.g., falling asleep during conversations, napping during the day or several brief awakenings during the night with confusion/behavioral changes or very little nighttime sleep)

3. Severe disruption of sleep-wake cycle (e.g., day-night reversal of sleep-wake cycle or severe circadian fragmentation with multiple periods of sleep and wakefulness or severe sleeplessness.)

2. **Perceptual disturbances and hallucinations**

Illusions and hallucinations can be of any sensory modality. Misperceptions are “simple” if they are uncomplicated, such as a sound, noise, color, spot, or flashes and ‘‘complex’’ if they are multidimensional, such as voices, music, people,animals, or scenes. Rate if reported by patient or caregiver, or inferred by observation.

0. Not present

1. Mild perceptual disturbances (e.g., feelings of derealization or depersonalization; or patient may not be able to discriminate dreams from reality)

2. Illusions present

3. Hallucinations present

3. **Delusions**

Delusions can be of any type, but are most often persecutory. Rate if reported by patient, family or caregiver. Rate as delusional if ideas are unlikely to be true yet are believed by the patient who cannot be dissuaded by logic. Delusional ideas cannot be explained otherwise by the patient’s usual cultural or religious background.

0. Not present

1. Mildly suspicious, hypervigilant, or preoccupied

2. Unusual or overvalued ideation that does not reach delusional proportions or could be plausible

3. Delusional

4. **Lability of affect**

Rate the patient's affect as the outward presentation of emotions and not as a description of what the patient feels.

0. Not present

1. Affect somewhat altered or incongruent to situation; changes over the course of hours; emotions are mostly under self-control

2. Affect is often inappropriate to the situation and intermittently changes over the course of minutes; emotions are not consistently under self-control, though they respond to redirection by others

3. Severe and consistent disinhibition of emotions; affect changes rapidly, is inappropriate to context, and does not respond to redirection by others

5. **Language**

Rate abnormalities of spoken, written or sign language that cannot be otherwise attributed to dialect or stuttering. Assess fluency, grammar, comprehension, semantic content and naming. Test comprehension and naming nonverbally if necessary by having patient follow commands or point.

0. Normal language

1. Mild impairment including word-finding difficulty or problems with naming or fluency

2. Moderate impairment including comprehension difficulties or deficits in meaningful communication (semantic content)

3. Severe impairment including nonsensical semantic content, word salad, muteness, or severely reduced comprehension

6. **Thought process abnormalities**

Rate abnormalities of thinking processes based on verbal or written output. If a patient does not speak or write, do not rate this item.

0. Normal thought processes

1. Tangential or circumstantial

2. Associations loosely connected occasionally, but largely comprehensible

3. Associations loosely connected most of the time

7. **Motor agitation**

Rate by observation, including from other sources of observation such as by visitors, family and clinical staff. Do not include dyskinesia, tics, or chorea.

0. No restlessness or agitation

1. Mild restlessness of gross motor movements or mild fidgetiness

2. Moderate motor agitation including dramatic movements of the extremities, pacing, fidgeting, removing intravenous lines, etc.

3. Severe motor agitation, such as combativeness or a need for restraints or seclusion

8**. Motor retardation.**

Rate movements by direct observation or from other sources of observation such as family, visitors, or clinical staff. Do not rate components of retardation that are caused by parkinsonian symptoms. Do not rate drowsiness or sleep.

0. No slowness of voluntary movements

1. Mildly reduced frequency, spontaneity or speed of motor movements, to the degree that may interfere somewhat with the assessment.

2. Moderately reduced frequency, spontaneity or speed of motor movements to the degree that it interferes with participation in activities or self-care

3. Severe motor retardation with few spontaneous movements.

9**. Orientation**

Patients who cannot speak can be given a visual or auditory presentation of multiple choice answers. Allow patient to be wrong by up to 7 days instead of 2 days for patients hospitalized more than 3 weeks. Disorientation to person means not recognizing familiar persons and may be intact even if the person has naming difficulty but recognizes the person. Disorientation to person is most severe when one doesn’t know one’s own identity and is rare. Disorientation to person usually occurs after disorientation to time and/or place.

0. Oriented to person, place and time

1. Disoriented to time (e.g., by more than 2 days or wrong month or wrong year) or to place (e.g., name of

building, city, state), but not both

2. Disoriented to time and place

3. Disoriented to person

10**. Attention**

Patients with sensory deficits or who are intubated or whose hand movements are constrained should be tested using an alternate modality besides writing. Attention can be assessed during the interview (e.g., verbal perseverations, distractibility, and difficulty with set shifting) and/or through use of specific tests, e.g., digit span.

0. Alert and attentive

1. Mildly distractible or mild difficulty sustaining attention, but able to refocus with cueing. On formal testing makes only minor errors and is not significantly slow in responses

2. Moderate inattention with difficulty focusing and sustaining attention. On formal testing, makes numerous errors and either requires prodding to focus or finish the task

3. Severe difficulty focusing and/or sustaining attention, with many incorrect or incomplete responses or inability to follow instructions. Distractible by other noises or events in the environment

11. **Short-term memory**

Defined as recall of information (e.g., 3 items presented either verbally or visually) after a delay of about 2 to 3 minutes. When formally tested, information must be registered adequately before recall is tested. The number of trials to register as well as effect of cueing can be noted on scoresheet. Patient should not be allowed to rehearse during the delay period and should be distracted during that time. Patient may speak or nonverbally communicate to the examiner the identity of the correct items. Short-term deficits noticed during the course of the interview can be used also.

0. Short-term memory intact

1. Recalls 2/3 items; may be able to recall third item after category cueing

2. Recalls 1/3 items; may be able to recall other items after category cueing

3. Recalls 0/3 items

12. **Long-term memory**

Can be assessed formally or through interviewing for recall of past personal (e.g., past medical history or information or experiences that can be corroborated from another source) or general information that is culturally relevant. When formally tested, use a verbal and/or visual modality for 3 items that are adequately registered and recalled after at least 5 minutes. The patient should not be allowed to rehearse during the delay period during formal testing. Make allowances for patients with less than 8 years of education or who are mentally retarded regarding general information questions. Rating of the severity of deficits may involve a judgment about all the ways long-term memory is assessed, including recent and/or remote long-term memory ability informally tested during the interview as well as any formal testing of recent long-term memory using 3 items.

0. No significant long-term memory deficits

1. Recalls 2/3 items and/or has minor difficulty recalling details of other long-term information

2. Recalls 1/3 items and/or has moderate difficulty recalling other long-term information

3. Recalls 0/3 items and/or has severe difficulty recalling other long-term information

13. **Visuospatial ability**

Assess informally and formally. Consider patient’s difficulty navigating one’s way around living areas or environment (e.g., getting lost). Test formally by drawing or copying a design, by arranging puzzle pieces, or by drawing a map and identifying major cities, etc. Take into account any visual impairments that may affect performance.

0. No impairment

1. Mild impairment such that overall design and most details or pieces are correct; and/or little difficultynavigating in his/her surroundings

2. Moderate impairment with distorted appreciation of overall design and/or several errors of details or pieces;

and/or needing repeated redirection to keep from getting lost in a newer environment despite, trouble locating

familiar objects in immediate environment

3. Severe impairment on formal testing; and/or repeated wandering or getting lost in environment

ADDITIONAL DIAGNOSTIC CRITERIA DRS-R-98

These three criteria may be of additional assistance in differentiating delirium from other disorders for diagnostic or research purposes. They are not included in the overall severity rating.

XIV Acuity of Onset

Rate the acuity of onset of the initial symptoms of the most recent disorder or episode, not the entire illness from onset. Distinguish the new delirious symptoms from the symptoms of the preexisting mental disorder. For example, if a patient with severe depression develops delirium due to drug overdose, rate the acuity of onset of delirium symptoms, not depression symptoms.

0 No significant difference from usual or long-term baseline behavior.

1 Symptoms developed gradually over a period of weeks to a month.

2 Acute change in behavior or personality occurred over a period of days to a week.

3 Abrupt change in behavior occurred over a period of hours to 1 day.

XV Symptom Severity Fluctuations

Assess the waxing and waning of one or more symptoms over a period of time. Typically, cognitive, affective, hallucination, thought disorder, and speech impairment are assessed. Note that perceptual disturbances are usually intermittent; however, as delirium worsens, they become continuous, although the severity of other symptoms continues to fluctuate.

0 No fluctuations in symptom severity.

1 Symptom severity fluctuates over hours.

2 Symptom severity fluctuates over minutes.

XVI. Somatic Pathology

Assess the possibility that a physiological, somatic, or drug problem is the cause of the delirious symptoms being assessed. Many patients have such problems, but they may not see a causal relationship between this problem and the symptoms that have arisen.

0 None or currently cannot be the cause.

1 There is any somatic disease that could affect the mental state.

2 Drugs, infections, metabolic disorders, CNS damage or other health problems that could definitely be the cause of behavioral disorders or mental disorder.

Interpretation. The assessment of the severity of delirium is the sum of points on 13 scale points. When choosing an answer option, in addition to the data from a direct examination of the patient, it is necessary to take into account information from all available sources (medical staff, family, medical records). It is important to remember that the symptoms of delirium increase and decrease without any external intervention, therefore, for repeated sequential assessments of their severity, measurements should be made at reasonable intervals, reflecting only significant changes in the condition in the documentation.

Appendix 4

MINI MENTAL STATE EXAMINATION

Purpose: The Mini-Mental State Examination (MMSE) was originally developed as a brief screening tool to provide a quantitative evaluation of cognitive impairment and to record cognitive changes over time.

Origin: Folstein, M. F., Folstein, S. E., McHugh, P. R. (1975). "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res, 12(3), 189-198.

Mini-Mental State Examination (MMSE)

Patient's Name: Date:

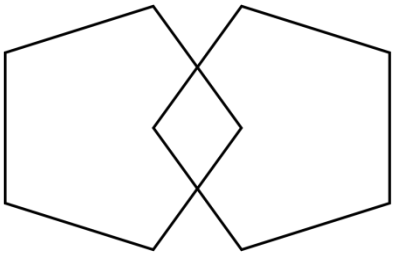
Instructions: Score one point for each correct response within each question or activity.

Standardised Mini-Mental State Examination (SMMSE)

Please see accompanying guidelines for administration and scoring instructions

Say: I am going to ask you some questions and give you some problems to solve. Please try to answer asbest you can.

1	**Allow ten seconds for each reply. Say:**	
	a) What year is this? (accept exact answer only)	/1
	b) What season is this? (during the last week of the old season or first week of a new season, accept either)	/1
	c) What month is this? (on the first day of a new month or the last day of the previous month, accept either)	/1
	d) What is today's date? (accept previous or next date)	/1
	e) What day of the week is this? (accept exact answer only)	/1
2	**Allow ten seconds for each reply. Say:**	
	a) What country are we in? (accept exact answer only)	/1
	b) What state are we in? (accept exact answer only)	/1
	c) What city/town are we in? (accept exact answer only)	/1
	d) <At home> What is the street address of this house? (accept street name and house	
	number or equivalent in rural areas) What is the name of this building? (accept exact name of institution only)	/1
	e) <At home> What room are we in? (accept exact answer only) <In facility> What floor of the building are we on? (accept exact answer only)	/1
3	Say: I am going to name three objects. When I am finished, I want you to repeat them. Remember what they are because I am going to ask you to name them again in a few minutes (say slowly at approximately one-second intervals). Ball Car Man For repeated use: Bell, jar, fan; bill, tar, can; bull, bar, pan Say: Please repeat the three items for me (score one point for each correct reply on the first attempt) /3	/3

	Allow 20 seconds for reply; if the person did not repeat all three, repeat until they are learned or up to a maximum of five times (but only score first attempt)	
4.	Say: Spell the word WORLD (you may help the person to spell the word correctly). Say: Now spell it backwards please (allow 30 seconds; if the person cannot spell world even with assistance, score zero). Refer to accompanying guide for scoring instructions (score on reverse of this sheet)	/5
5.	**Say: Now what were the three objects I asked you to remember? (score one point for each correct answer regardless of order; allow ten seconds)**	**/3**
6.	**Show wristwatch. Ask: What is this called? (score one point for correct response; accept 'wristwatch' or 'watch'; do not accept 'clock' or 'time', etc.; allow ten seconds)**	**/1**
7.	Show pencil. Ask: What is this called? (score one point for correct response; accept 'pencil' only; score zero for pen; allow ten seconds for reply)	/1
8	Say: I would like you to repeat a phrase after me: No ifs, ands, or buts (allow ten seconds for response. Score one point for a correct repetition. Must be exact, e.g. no ifs or buts, score zero)	/1
9.	**Say: Read the words on this page and then do what it says Then, hand the person the sheet with CLOSE YOUR EYES (score on reverse of this sheet) on it. If the subject just reads and does not close eyes, you may repeat: Read the words on this page and then do what it says, a maximum of three times. See point number three in Directions for Administration section of accompanying guidelines. Allow ten seconds; score one point only if the person closes their eyes. The person does not have to read aloud.**	**/1**
10.	Hand the person a pencil and paper. Say: Write any complete sentence on that piece of paper (allow 30 seconds. Score one point. The sentence must make sense. Ignore spelling errors).	/1
11.	Place design (see page 3), pencil, eraser and paper in front of the person. Say: Copy this design please. Allow multiple tries. Wait until the person is finished and hands it back. Score one point for a correctly copied diagram. The person must have drawn a four-sided figure between two five-sided figures. Maximum time: one minute	/1
12.	Ask the person if he is right or left handed. Take a piece of paper, hold it up in front of the person and say the following: Take this paper in your right/left hand (whichever is non-dominant), fold the paper in half once with both hands and put the paper down on the floor.	
	Takes paper in correct hand 	/1

	Folds it in half	/1
	Puts it on the floor_	/1
	TOTAL TEST SCORE:	30
	ADJUSTED SCORE:	/

Interpretations

Any score of 24 or more (out of 30) indicates a normal cognition. Below this, scores can indicate severe (≤9 points), moderate (10–18 points) or mild (19–23 points) cognitive impairment. The raw score may also need to be corrected for educational attainment and age. Even a maximum score of 30 points can never rule out dementia and there is no strong evidence to support this examination as a stand-alone one-time test for identifying high risk individuals who are likely to develop Alzheimer's. Low to very low scores may correlate closely with the presence of dementia, although other mental disorders can also lead to abnormal findings on MMSE testing. The presence of purely physical problems can also interfere with interpretation if not properly noted; for example, a patient may be physically unable to hear or read instructions properly or may have a motor deficit that affects writing and drawing skills.

In order to maximize the benefits of the MMSE the following recommendations from Tombaugh and McIntyre (1992) should be employed:

1. The MMSE should be used as a screening device for cognitive impairment or a diagnostic adjunct in which a low score indicates the need for further evaluation. It should not serve as the sole criterion for diagnosing dementia or to differentiate between various forms of dementia. However, the MMSE scores may be used to classify the severity of cognitive impairment or to document serial change in dementia patients.
2. The following four cut-off levels should be employed to classify the severity of cognitive impairment: no cognitive impairment 24–30; mild cognitive impairment 19–23; moderate cognitive impairment 10–18; and severe cognitive impairment ≤9.

3. The MMSE should not be used clinically unless the person has at least a grade-eight educationand is fluent in English. While this recommendation does not discount the possibility that future research may show that number of years of education constitutes a risk factor for dementia, it does acknowledge the weight of evidence showing that low educational levels substantially increase the likelihood of misclassifying normal subjects as cognitively impaired.

4. Serial sevens and WORLD should not be considered equivalent items. Both items should be administered and the higher of the two should be used. In scoring serial sevens, each number must be independently compared to the prior number to ensure that a single mistake is not unduly penalized. WORLD should be spelled forward (and corrected) prior to spelling it backward.

5. The words "apple", "penny", and "table" should be used for registration and recall. If necessary, the words may be administered up to three times in order to obtain perfect registration, but the score is based on the first trial.

6. The "county" and "where are you" orientation to place questions should be modified: the name of the county where a person lives should be asked rather than the county of the testing site, and the name of the street where the individual lives should be asked rather than the name of the floor where the testing is taking place.

The MMSE may help differentiate different types of dementias. People with Alzheimer's disease may score significantly lower on orientation to time and place as well as recall, compared to those who have dementia with Lewy bodies, vascular dementia, or Parkinson's disease dementia.

Appendix 5

Covy anxiety Scale

Purpose: The Covy anxiety scale is a screening scale used in clinical trials for the preliminary assessment of anxiety disorders.

Origin: Covi L, Lipman R., McNair D.M., Crezlinsky T. Symptomatic volunteers in multicenter drug trials. Prog Neuropsychopharmacol. 1979; 3: 521.

Complaints (feels nervous, trembling, panicking, sudden unreasonable fear, fright, excitement, difficulty concentrating on any task)	
does not experience	1
Slightly	2
Moderately	3
Significantly	4
Strongly	5
Behavior (looks scared, trembling, restless, flinching, panicking)	
No	1
Slightly	2
Moderately	3
Significantly	4
very strongly	5
Somatic symptoms of anxiety (unreasonable sweating, trembling, rapid heartbeat, shortness of breath, increased urination, restless sleep, discomfort in the epigastric region, lump in the throat)	
No	1
Slightly	2
Moderately	3
Significantly	4
very strongly	5
Score: NaN	

Interpretation:

0-3 points - no anxiety

3-6 points - symptoms of anxiety

6 points and above - anxiety

Appendix 6

The Hamilton Anxiety Rating Scale - (HARS)

Purpose The Hamilton Anxiety Rating Scale (HARS) is designed to assess the condition of patients with an established diagnosis of anxiety disorder and to assess anxiety in patients suffering from other disorders, most often depressive disorders.

Origin:(official website of the developers, publication with validation): Hamilton M. The assessment of anxiety states by rating. BrJMedPsychol. 1959; 32: 50 - 55.

- Interpretation of Score
- 0-17: Mild anxiety
- 18-24: Mild to moderate anxiety
- 25-30: Moderate to severe anxiety
- 31-56: Severe anxiety

The Hamilton Anxiety Rating Scale - (HARS)

	PARAMETERS	SYMPTOMS	SEVERITY				
			0	1	2	3	4
1	ANXIOUS MOOD	Worries Anticipation of the worst Fearful anticipation Irritability					
2	TENSION	Feelings of tension Fatigability Startles response Easily moved to tears Trembling Feelings of restlessness Inability to relax					
3	FEARS	Fear of dark Fear of strangers Fear of being left alone Fear of animals Fear of traffic Fear of crowds					
4	INSOMNIA	Difficulty in falling asleep or staying asleep Broken sleep Night-terrors Unsatisfying sleep and fatigue on					

		waking Dreams Nightmares					
5	INTELLECTUAL	Difficulty in concentration Poor memory					
6	DEPRESSED MOOD	Loss of interest in activities Lack of pleasure in hobbies Depression Early waking Diurnal swing					
7	SOMATIC COMPLAINTS: MUSCULAR	Pains and aches Twitching, stiffness Myoclonic jerks Grinding of teeth (Bruxism) Unsteady voice Increased muscular tone					
8	SOMATIC COMPLAINTS: SENSORY	Tinnitus Blurring of vision Hot and cold flushes Feelings of weakness Pricking sensation					
9	CARDIOVASCULAR SYMPTOMS	Tachycardia Palpitations Chest Pain Throbbing of vessels Fainting feelings Missing beat Sensation of feeling faint					
10	RESPIRATORY SYMPTOMS	Chest pressure or constriction Choking feelings Sighing Dyspnea Shortness of Breath					
11	GASTROINTESTINAL SYMPTOMS	Difficulty in swallowing Wind, abdominal pain Burning sensations Abdominal fullness Nausea or Vomiting Borborygmi Looseness of bowels Loss of weight Constipation Dysphagia					
12	GENITOURINARY SYMPTOMS	Frequency of micturition Urgency of micturition Amenorrhea Menorrhagia Development of frigidity Premature ejaculation Loss of libido Impotence					

13	AUTONOMIC SYMPTOMS	Dry mouth Flushing Pallor Tendency to sweat Giddiness Tension headache Raising of hair					
14	BEHAVIOR AT INTERVIEW	Fidgeting Restlessness or pacing Tremor of hands Furrowed brow Strained face Sighing or rapid respiration Facial pallor Swallowing Belching Brisk Tendon Jerks Dilated Pupils Exophthalmos					
	Add up results for each column						
Total Score							

The scale consists of 14 items, each representing a distinct symptom of anxiety. Each item is scored on a scale ranging from 0 (not present) to 4 (severe). Total Score: The total score ranges from 0 to 56, with higher scores indicating more severe anxiety.

A clinician typically administers the Hamilton Anxiety Rating Scale. The clinician conducts a semi-structured interview with the patient, asking questions that correspond to the 14 items on the scale. The clinician then rates the severity of each symptom based on the patient's responses and their clinical judgment.

Administration Process:

Introduction: The clinician explains the purpose of the assessment to the patient.

Interview: The clinician asks questions related to each of the 14 items.

Scoring: The clinician rates each item from 0 to 4 based on the severity of the symptom.Total Score Calculation: The clinician sums the scores for all 14 items to obtain the total HAM-A score.

Appendix 7

Montgomery–Åsberg Depression Rating Scale (MADRS)

Purpose The Montgomery Asberg Depression Rating Scale (MADRS) is used by clinicians to assess the severity of depression among patients with a diagnosis of depression. It is designed to be sensitive to change resulting from antidepressant therapy.
Origin:(official website of the developers, publication with validation):Montgomery SA, Asberg M (April 1979). "A new depression scale designed to be sensitive to change". British Journal of Psychiatry. 134 (4): 382–89. doi:10.1192/bjp.134.4.382. PMID 444788. S2CID 22246215

Montgomery and Asberg Depression Rating Scale (MADRS)
The rating should be based on a clinical interview moving from broadly phrased questions about symptoms to more detailed ones which allow a precise rating of severity. The rater must decide whether the rating lieson the defined scale steps (0, 2, 4, 6) or between them (1,3,5).It is important to remember that it is only on rare occasions that a depressed patient is encountered who cannot be rated on the items in the scale. If definite answers cannot be elicited from the patient all relevant clues as well as information from other sources should be used as a basis for the rating in line with customary clinical practice. The scale may be used for any time interval between ratings, be it weekly or otherwise but this must be recorded.

1. Apparent Sadness
Representing despondency, gloom and despair, (more than just ordinary transient low spirits)
reflected in speech, facial expression, and posture. Rate by depth and inability to brighten up.
0 No sadness.
1

2 Looks dispirited but does brighten up
without difficulty.
3
4 Appears sad and unhappy most of the time.
5
6 Looks miserable all the time. Extremely
despondent.

2. Reported sadness

Representing reports of depressed mood, regardless of whether it is reflected in appearance or not.

Includes low spirits, despondency or the feeling of being beyond help and without hope.

Rate according to intensity, duration and the extent to which the mood is reported to be influenced by
events.

0 Occasional sadness in keeping with the
circumstances.
1
2 Sad or low but brightens up without difficulty.
3
4 Pervasive feelings of sadness or gloominess.
The mood is still influenced by external
circumstances.
5
6 Continuous or unvarying sadness, misery or despondency.

3.

Inner tension

Representing feelings of ill-defined discomfort, edginess, inner turmoil, mental tension mounting to either panic, dread or anguish. Rate according to intensity, frequency, duration and the extent of reassurance called for.

0 Placid. Only fleeting inner tension.

1

2 Occasional feelings of edginess and ill defined discomfort.

3

4 Continuous feelings of inner tension or intermittent panic which the patient can only master with some difficulty.

5

6 Unrelenting dread or anguish. Overwhelming panic

4. **Reduced sleep**

Representing the experience of reduced duration or depth of sleep compared to the subject's own normal pattern when well.

0 Sleeps as usual.

1

2 Slight difficulty dropping off to sleep or slightly reduced, light or fitful sleep.

3

4 Sleep reduced or broken by at least two hours.

5

6 Less than two or three hours sleep

5. **Reduced appetite**

Representing the feeling of a loss of appetite compared with when well. Rate by loss of desire for food or the need to force oneself to eat.

0 Normal or increased appetite.

1

2 Slightly reduced appetite.

3

4 No appetite. Food is tasteless.

5

6 Needs persuasion to eat at all.

6. Concentration Difficulties

Representing difficulties in collecting one's thoughts mounting to incapacitating lack of concentration.

Rate according to intensity, frequency, and degree of incapacity produced.

0 No difficulties in concentrating.

1

2 Occasional difficulties in collecting one's thoughts.

3

4 Difficulties in concentrating and sustaining thought which reduces ability to read or hold a conversation.

5

6 Unable to read or converse without great difficulty.

7. Lassitude

Representing a difficulty getting started or slowness initiating and performing everyday activities.

0 Hardly any difficulty in getting started. No sluggishness.

1

2 Difficulties in starting activities.

3

4 Difficulties in starting simple routine activities

which are carried out with effort.

5

6 Complete lassitude. Unable to do anything without help.

8. **Inability to feel**

Representing the subjective experience of reduced interest in the surroundings, or activities that normally give pleasure. The ability to react with adequate emotion to circumstances or people is reduced.

0 Normal interest in the surroundings and in

other people.

1

2 Reduced ability to enjoy usual interests.

3

4 Loss of interest in the surroundings. Loss of feelings or friends

and acquaintances.

5

6 The experience of being emotionally paralysed, inability to feel anger, grief or pleasure and a complete or even painful failure to feel for close relatives and friends.

9. Pessimistic thoughts

Representing thoughts of guilt, inferiority, self-reproach, sinfulness, remorse and ruin.

0 No pessimistic thoughts.

1

2 Fluctuating ideas of failure, self-reproach or self depreciation.

3

4 Persistent self-accusations, or definite but still rational ideas of guilt or sin. Increasingly

pessimistic about the future.

5

6 Delusions of ruin, remorse or unredeemable sin. Self-accusations which are absurd and unshakable.

10. Suicidal thoughts

Representing the feeling that life is not worth living, that a natural death would be welcome, suicidal

thoughts, and preparations for suicide. Suicidal attempts should not in themselves influence the rating.

0 Enjoys life or takes it as it comes.

1

2 Weary of life. Only fleeting suicidal thoughts.

3

4 Probably better off dead. Suicidal thoughts are common, and suicide is considered as a possible solution, but without specific plansor intention.

5

6 Explicit plans for suicide when there is an opportunity. Active preparation for suicide.

Scoring:

Each item has a severity scale from 0 to 6, with higher scores reflecting more severe symptoms. Ratings can be added to form an overall score (from 0 to 60). Snaith, Harrop, Newby, and Teale (1986) proposed the following cut-offs: scores of 0-6 indicate an absence of symptoms; 7-19 represent mild depression; 20-34 moderate; 35-60 indicate severe depression.

Appendix 8

The Clinical Global Impressions Scale

Purpose: The scale is designed to assess symptom severity, response to treatment, and effectiveness of treatment methods in studies of patients with mental disorders.

Origin: Guy W, editor. *ECDEU Assessment Manual for Psychopharmacology*. Rockville, MD: US Department of Heath, Education, and Welfare Public Health Service Alcohol, Drug Abuse, and Mental Health Administration; 1976.

Validation: Huber CG, Lambert M, Naber D, Schacht A, Hundemer HP, Wagner TT, Schimmelmann BG. Validation of a Clinical Global Impression Scale for Aggression (CGI-A) in a sample of 558 psychiatric patients. Schizophr Res. 2008 Mar;100(1-3):342-8. doi: 10.1016/j.schres.2007.12.480. Epub 2008 Feb 5. PMID: 18255271.

Adapted from Kay SR. Positive and negative symptoms in schizophrenia: Assessment and research. Clin Exp Psychiatry Monograph No 5. Brunner/Mazel, 1991.

CGI-S guidelines

Given your overall clinical experience with this particular category of patients, how severe would you rate the severity of this patient's mental disorder at this time?

1 = Normal—not at all ill, symptoms of disorder not present past seven days
2 = Borderline mentally ill—subtle or suspected pathology
3 = Mildly ill—clearly established symptoms with minimal, if any, distress or difficulty in social and occupational function
4 = Moderately ill—overt symptoms causing noticeable, but modest, functional impairment or distress; symptom level may warrant medication
5 = Markedly ill—intrusive symptoms that distinctly impair social/occupational function or cause intrusive levels of distress

6 = Severely ill—disruptive pathology, behavior and function are frequently influenced by symptoms, may require assistance from others

7 = Among the most extremely ill patients—pathology drastically interferes in many life functions; may be hospitalized

CGI-I guidelines

Assess the overall improvement in the patient's condition, whether or not you think it is solely due to the drug treatment. Assess how much it has changed compared to his or her initial condition.

1 = Very much improved—nearly all better; good level of functioning; minimal symptoms; represents a very substantial change

2 = Much improved—notably better with significant reduction of symptoms; increase in the level of functioning but some symptoms remain

3 = Minimally improved—slightly better with little or no clinically meaningful reduction of symptoms. Represents very little change in basic clinical status, level of care, or functional capacity

4 = No change—symptoms remain essentially unchanged

5 = Minimally worse—slightly worse but may not be clinically meaningful; may represent very little change in basic clinical status or functional capacity

6 = Much worse—clinically significant increase in symptoms and diminished functioning

7 = Very much worse—severe exacerbation of symptoms and loss of functioning

Efficacy index

Effectiveness Index: Rate this item based on the drug effect alone. Select the terms that best describe the degree of therapeutic effect and side effects, and write a number in the box where the two intersect.

Example: The therapeutic effect is rated as "moderate" and the side effects are rated as "do not significantly affect the patient's functional status".

Therapeuticeffect		Side effects			
		No	Do not significantly interfere with patient's functioning	Significantly interfere with patient's functioning	Outweightherapeutic effect
Marked	Vast improvement. Complete or nearly complete remission of all symptoms	**1**	**2**	**3**	**4**
Moderate	Decided improvement. Partial remission of symptoms	**5**	**6**	**7**	**8**
Minimal patient	Slight improvement which doesn't alter status of care of patient	**9**	**10**	**11**	**12**
Unchangedorworse		**1**	**14**	**15**	**16**

Interpretation of results:

The CGI is rated on a 7-point scale, with the severity of illness scale using a response range from 1 (Healthy) to 7 (Very much worse). The CGI-C (Clinical Global Improvement or Change) score ranges from 1 (Very much improved) to 7 (Very much worse). The assessment of treatment response should take into account both therapeutic efficacy and treatment-related adverse events and ranges from 0 (Much improved and

no adverse effects) to 4 (No change or worsening and adverse effects outweighing therapeutic effect). Each CGI item is rated separately; the scale does not produce a total score.