ST. PETERSBURG INSTITUTE OF STOMATOLOGY
POSTGRADUATE EDUCATION

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SCIENTIFIC SUBSTANTIATION OF THE SYSTEM OF PROPHYLACTIC MEASURES TO PREVENT THE SPREAD OF A NEW CORONAVIRUS INFECTION (COVID-19) AMONG HOSPITAL MEDICAL STAFF

Scientific specialty 3.2.3. Public health, healthcare organization and sociology, medical and social expertise

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INTRODUCTION

Relevance of the research

The pandemic of a new coronavirus infection (COVID-19) has become one of the urgent problems of the XXI century. The rapid spread of this disease, high infectiousness and mortality rates have led to an enormous burden on health care systems in all countries of the world and required the rapid organization of activities aimed at preserving public health. While much research and efforts are being made worldwide to prevent infectious disease outbreaks, the strong, collaborative and coordinated efforts of the world's health systems have helped to reduce the spread of COVID-19.

All populations have been exposed to the disease. The risk groups for a severe course of COVID-19 are persons with chronic diseases, persons over 60 years of age, as well as professional risk groups: employees of medical and educational organizations, social service organizations.

Vaccination of the population as the most effective measure in the fight against various infectious diseases, including diseases with airborne transmission mechanism (measles, influenza, meningococcal infection, etc.) has historically proved itself. However, when a previously unknown virus is identified, the creation of an effective vaccine in a short period of time in order to create collective immunity is an urgent task.

Collective immunity is an indirect indicator of protection against COVID-19 disease and is composed of the immunity of individuals within a defined group. Epidemiologic observation of the structure, peculiarities of formation and dynamics of collective immunity will allow competent and timely adjustment of approaches to anti-epidemic measures both in individual risk groups, in particular among health workers, and in society as a whole. The current epidemic has entered a low-level epidemic phase, when a significant number of people have developed immunity as a result of the transferred disease or artificially - through immunization.

The present work deals with organizational issues of planning aspects of infectious disease departments, separation and isolation of patients, timely and effective disinfection activities, timely diagnosis of COVID-19, protective measures for personnel, and issues of formation of collective immunity to SARS-CoV-2 virus. The study of the level of humoral and cellular immunity to COVID-19 in medical workers is important from the point of view of both planning anti-epidemic measures and predicting the effectiveness of the response to vaccination to SARS-CoV-2.

The emergence of a COVID-19 pandemic exacerbates the ongoing challenges posed by infectious diseases and highlights the need for research and preparedness, even during inter-epidemic periods.

The degree of elaboration of the research topic

Given the speed of spread of this virus and its impact on every sphere of society worldwide, the issues of epidemiology and dynamics of the epidemic process have been studied by many domestic and foreign authors (V. G. Akimkin, A. Yu. Popova, A. A. Kuzin, G. G. Onishchenko, E. B. Ezhlova, S. Huang, Y. Wang, Q. X. Long, B. Z. Liu, etc.). Organization of work and reprofiling under infectious hospitals, the system of diagnostics and protection of patients and employees in their works are described by V. V. Kutyrev, A. Yu. Kutyrev, A. Yu. Popova, L. Geng, Y. Fan, Y. Lai et al. The mechanisms of formation of collective immunity to COVID-19 and its necessary levels to prevent infection of the population and individual professional groups have been discussed in the scientific community since the beginning of the pandemic. Organizational measures developed in the course of the study will contribute to reducing the risks of COVID-19 spread in health care organizations. The high relevance of this problem and its significance for public health and public health care determined the purpose and objectives of this study.

The aim of the research

To develop and substantiate a set of preventive measures to prevent the spread of COVID-19 among different groups of medical workers in hospitals, depending on their profile and the phase of development of the epidemic process.

Object of the research

General hospital and «covid hospital» health care workers providing care during the pre-vaccination, early and late post-vaccination periods of active spread of COVID-19.

Subject of the research

Evaluation of the effectiveness of a set of preventive measures to prevent the spread of COVID-19 among medical personnel of hospitals of different profiles.

The main objectives of the research

1. To give a comparative characterization of the dynamics of COVID-19 morbidity in the population of St. Petersburg and in the medical personnel of a «covid» hospital and a general hospital, taking into account gender and age differences in the pre-vaccination period.
2. To evaluate the dynamics of the vaccination process of medical personnel in hospitals and the state of their humoral immunity in the early and late postvaccinal periods.
3. To determine the structure of collective immunity in a «covid» hospital and a general hospital at different phases of the epidemic process development.
4. To establish the time interval and to estimate the relationship between the occurrence of the disease in medical personnel taking into account the previously transferred disease and the vaccination period in order to identify the degree of immunity tension by mathematical modeling.

5. To evaluate the relationship between the occurrence of recurrent disease and the level of humoral immunity after vaccination and transferred disease in the prevaccinal, early and late postvaccinal periods by mathematical testing of statistical hypotheses.
6. To evaluate significant levels of humoral and cellular immunity and their impact on cases of recurrent disease by mathematical modeling.
7. To substantiate the model of organizational measures to prevent the spread of COVID-19 in medical personnel of «covid» hospitals and general hospitals.

Scientific novelty of the study

1. A comparative characterization and assessment of the dynamics of the course of the COVID-19 epidemic process among medical workers of a «covid» hospital and a general hospital in St. Petersburg is given.
2. The effectiveness of vaccine prophylaxis as the main anti-epidemic measure was studied on the basis of evaluation of the structure and mechanisms of formation of humoral and cellular link of collective immunity in COVID-19 among medical workers.
3. The time interval was determined and the relationship between the occurrence of recurrent disease in medical personnel was evaluated, taking into account the previously transferred disease and the period of vaccination; the dependence of the occurrence of recurrent disease and the level of humoral immunity after vaccination and transferred disease in the prevaccinal, early and late postvaccinal periods was assessed.
4. Models of prophylactic measures to prevent the spread of COVID-19 in medical personnel in a «covid» hospital and a general hospital were substantiated.
5. For the first time the methodology of statistical and mathematical analysis of databases was applied to assess the effectiveness of organizational and anti-epidemic measures in various hospitals during the period of active spread of COVID-19.

Theoretical and practical significance of the research

The complex of preventive measures developed as a result of this work allows to reduce the risk of spread of airborne viral infections, including COVID-19, in medical organizations, new methodical approaches to the management of collective immunity of personnel contribute to the stabilization of anti-epidemic situation in hospitals.

Research methodology and methods

Empirical data were collected and processed taking into account modern approaches to statistical analysis. In order to evaluate organizational measures and mechanisms of collective immunity formation, as a result of the analysis of the created databases, statistical hypotheses were selectively put forward and tested using mathematical tests.

Primary data were collected and processed using Microsoft Office Excel 2020 software. Statistical analysis was performed using the statistical programming language R (version 4.1.2).

Basic provisions for the thesis defense

1. In the pre-vaccinal period of COVID-19 spreading the morbidity of medical workers of «covid» hospital and general hospital does not have reliable differences, but is significantly higher than the city-wide morbidity rates in the population, significant changes towards predominance appear in the late post-vaccinal period in the «covid» hospital.
2. The dynamics of recurrent disease in medical personnel of the «covid» hospital and general hospital is associated with vaccination, after which the average waiting period for the disease increases in the «covid» hospital, while the disease rate in the group «overdosed and vaccinated» is significantly lower than in the only vaccinated, which is associated with the presence of cellular immunity and does not depend on gender and age characteristics.
3. Humoral and cellular immunity in both studied groups of inpatients in persons of the group «over-vaccinated and vaccinated» have reliable differences in levels and structure, respectively, in contrast to only vaccinated, and IgG indices vary over time towards reduction, determining the need for optimal revaccination period and the probability of disease onset in certain time intervals.
4. Organizational measures to protect medical personnel and patients from the spread of COVID-19 in hospitals should be carried out in an integrated manner and include sanitary and anti-epidemic measures, isolation, vaccination of more than 77.5% of employees of «covid» hospital and more than 67.6% of general hospitals.

The degree of reliability and approbation of the research results

The reliability of the study is ensured by the correct application of modern methods of collection and processing of initial information, the use of approved mathematical apparatus, direct participation of the author in the analysis of initial data and research results and is confirmed by verification, discussion of research results at scientific conferences, publications of research results in peer-reviewed scientific publications.

Personal contribution of the author

The author plays a leading role in the choice of research direction, development of the research program, conducting research, analysis and generalization of the results obtained. In the works performed in co-authorship, the author personally carried out the formation of scientific hypotheses, process modeling, analysis of circulation data, generalization of the obtained results, their analytical and statistical processing. The author's contribution is decisive and consists in direct participation in all stages of the research: from the formulation of tasks, their theoretical and practical realization to the discussion of the results in scientific publications and reports and their implementation in practice.

Main scientific results

Data from literature sources on the pathogenesis and clinical course of COVID-19 have been studied [3, p. 126]. A comparative epidemiological analysis of Russian and foreign vaccines against COVID-19 in terms of their mechanism of action, peculiarities of vaccination and immune response formation was carried out on the basis of literature data and current regulatory framework [32, pp. 144-145]. The author's personal participation in obtaining these results: collection of material, generalization of literature data, writing the section of the article.

On the basis of literature data the ways of creation of collective immunity against COVID-19 and its structure, peculiarities of immune response formation after the transferred disease and vaccination, including generalized scientific experience of estimation of IgG preservation duration and their level over time [109, pp. 214-216]. The author's personal participation in obtaining these results: collection of material, analysis of literature data, interpretation of results, statistical processing of data, writing the article.

The dynamics of morbidity, taking into account gender and age differences and the structure of collective immunity against COVID-19 in medical workers at the prevaccinal [32, p. 147], early and late vaccination stages [52, p. 7] were analyzed. A comparative characterization of the dynamics of COVID-19 morbidity in medical workers of St. Petersburg hospitals in comparison with the city-wide data is given [52, pp. 6-7]. The author's personal participation in obtaining these results: collection of material, analysis of literature data, interpretation of results, statistical processing of data, writing the article.

When studying the levels of humoral and cellular immunity to COVID-19 in health care workers.

Workers by the method of mathematical analysis of statistical hypotheses the level of repeated diseases was estimated, the dynamics of Ig G levels was determined. The period of re-infection with COVID-19 in medical workers was determined [95, pp. 50-51]. The author's personal participation in obtaining these results: collection of material, analysis of literature data, interpretation of results, statistical processing of data, writing the article.

A system of basic organizational measures aimed at preventing the spread of COVID-19 in a «covid» hospital and a general hospital is proposed, depending on the profile of the medical organization and the type of medical care provided, the phase of the course of the epidemic process and the structure of collective immunity [52, pp.7-8]. The author's personal participation in obtaining these results: collection of material, analysis of literature data, interpretation of results, statistical processing of data, writing the article.

The set of organizational measures proposed based on the results of the work was implemented in the practical activities of public and commercial medical organizations of St. Petersburg.

The main results of the scientific work are presented:

1. Justification of the system of preventive measures in medical organizations aimed at preventing the spread of a new coronavirus infection (COVID-19) / O. V. Mironenko, N. M. Batyukov, M. G. Stupin, A. A. Tovanova // Institute of Stomatology. - 2024. - № 1(102). - C. 6-8.

2. COVID-19 and amyotrophic lateral sclerosis: epidemiologic, pathophysiologic and clinical aspects / O. I. Kopytenkova, O. V. Mironenko, E. F. Turovinina [et al] // Medical Science and Education of the Urals. - 2024. - T. 25, № 1(117). - C. 126-131.

3. Application of mathematical modeling method to assess the state of collective immunity of hospital staff during the spread of COVID-19 / O. V. Mironenko, A. N. Marchenko, A.A. Tovanova [et al] // Medical Science and Education of the Urals. - 2023. - T. 24, № 4 (116). - C. 48-52.

4. Results of dynamic observation of the state of collective immunity in the medical staff of a multidisciplinary hospital during the spread of COVID-19 / V. A. Volchkov, O. V. Mironenko, A. N. Marchenko [et al.] // Medical Science and Education of the Urals. - 2022. - T. 23, № 3 (111). - C. 72-78.

5. Study of the state of collective immunity of medical personnel of a multidisciplinary hospital in the initial period of spread of a new coronavirus infection (COVID-19)/ O. V. Mironenko, A. N. Marchenko, A. A. Tovanova [et al.] // Medical Science and Education of the Urals. - 2022. - T. 23, № 2 (110). - C. 142-149.

6. Possibilities of creating collective immunity in the vaccine prophylaxis of professional risk groups / O. V. Mironenko, L. A. Soprun, A. A. Tovanova, Kh. K. Magomedov // Interdisciplinary aspects of internal diseases: a collection of scientific papers; ed. by I. A. Gorbacheva. A. Gorbacheva. - SPb.: RIC PSPbSMU, 2022.

7. Mironenko, O.V. Dynamics of morbidity of medical personnel of a multidisciplinary hospital with a new coronavirus infection during the spread of COVID-19 / O.V. Mironenko, A.A. Tovanova. Tovanova // Developing century-old traditions, providing "Sanitary shield" of the country: Proceedings of the XIII All-Russian Congress of hygienists, toxicologists and sanitary doctors with international participation, dedicated to the 100th anniversary of the founding of the State Sanitary and Epidemiological Service of Russia, Moscow, October 26-28, 2022 - Mytishchi: Federal Scientific Center of Hygiene named after F.F. Erisman, Russia. F.F. Erisman, 2022. - C. 87-90.

8. Mironenko, O. V. Regularities of the formation of collective immunity of medical workers of a multidisciplinary hospital during the spread of COVID-19 / O. V. Mironenko, A. A. Tovanova, E. A. Fedorova // Proceedings of the XII Congress of the All-Russian Scientific and Practical Society of Epidemiologists, Microbiologists and Parasitologists, Moscow, October 26-28, 2022; edited by A. Y. Popova, V. G. Akimkin. - Moscow: Federal Budgetary Institution of Science

"Central Research Institute of Epidemiology" of the Federal Service for Supervision of Consumer Rights Protection and Human Welfare, 2022. - C. 433.

9. Tovanova, A. A. Creating collective immunity as the main preventive measure in the spread of a new coronavirus infection (COVID-19)/ A. A. Tovanova // Bulletin of St. Petersburg University. Medicine. - 2022. - T. 17, № 3. - C. 212-220.

The obtained results of the study are used in the educational process in the training of students, undergraduates, residents, postgraduates and advanced training of doctors and nurses of the Department of Hygiene, Ecology and Epidemiology of Tyumen State Medical University of the Ministry of Health of the Russian Federation, the Department of Municipal Hygiene of I.I. Mechnikov Federal State Budgetary Educational Institution of Higher Professional Education "I.I. Mechnikov Northwestern State Medical University", the Department of Epidemiology, Parasitology and Disinfectology of I.I. Mechnikov Northwestern State Medical University.

Methodical recommendations for cycles of additional training of doctors-specialists were published:

1. Organization of work of radiology departments and algorithms of examination during the period of spread of acute respiratory viral infections, influenza and new coronavirus infection (COVID-19). Methodical recommendations / O. V. Mironenko, T. N. Trofimova, O. V. Lukina, P. V. Gavrilova, V. A. Ratnikov, A. K. Ratnikova, V. A. Kashchenko, E. A. Fedorova, A. A. Tovanova, D. A. Obukhov, M. G. Stupin. - SPb.: Izd-vo FGBOU VO "SZSMU named after I.I. Mechnikov", 2022. - 60 c.

2. Individual protection means in professional activity of medical workers of stomatological profile: educational and methodical manual / O.V. Mironenko, A. S. Nekhoroshev, O. I. Kopytenkova, S. N. Noskov, Kh. K. Magomedov, A. A. Tovanova, E. A. Fedorova, A. A. Kulieva. - SPb.: Izd-vo FGBOU VO "I.I. Mechnikov NWGMU", 2024. -79 c.

The main provisions of the dissertation research were reported and discussed at 9 scientific-practical conferences, including the XXV Anniversary International Medical and Biological Scientific Conference of Young Researchers «Fundamental Science and Clinical Medicine. Man and his health» (St. Petersburg, 2022), All-Russian scientific-practical conference with international participation «Topical issues of prevention of infectious and non-infectious diseases: epidemiological, organizational and hygienic aspects» (Moscow, 2023), All-Russian scientific-practical conference with international participation «Preventive medicine – 2023» (St. Petersburg, 2023), XVIII All-Russian Congress «Health - the basis of human potential: problems and solutions» (St. Petersburg, 2023).

Compliance with the declared specialty

The thesis corresponds to the passport of specialty 3.2.3 Public health, organization and sociology of health care, medical and social expertise.

Publications

Nine scientific papers have been published on the research materials, including three articles in peer-reviewed journals included in the List of the Higher Attestation Commission of the Ministry of Science and Higher Education of the Russian Federation.

Scope and structure of the thesis

The volume of the work is 138 pages of typewritten text (In Russian), including 17 tables, 32 figures, 190 bibliographic sources (73 foreign). Structure of the work: introduction, literature review, presentation of the program and methods of research, results of own research, conclusion.

Chapter 1 LITERATURE REVIEW

1.1 Peculiarities of spread and course of epidemic process COVID-19

COVID-19 was one of the most significant events in modern history. Conducting research allows us to better understand the causes and consequences of the pandemic and to identify effective strategies and organizational models for managing such events in the future [1, 51].

The COVID-19 pandemic began in late December 2019 as an outbreak of pneumonia cases caused by an unknown pathogen in Wuhan, China, and spread from there to the rest of the world. On 07.01.2020, Chinese experts identified the virus that caused the pneumonia. It turned out to be a new, previously unknown virus of the coronavirus family [131].

The COVID-19 pathogen was given the provisional name 2019-nCov until the final virological status and other characteristics were established. After identification of the virus and its genome by the International Committee on Taxonomy of Viruses on 11.02.2020, it was given the name SARS-CoV-2, which denotes a link to the previously known SARS (severe respiratory syndrome) virus and describes it as a new coronavirus [5, 50, 124].

The rapid spread of the virus led to an epidemic in China, followed by a worldwide pandemic. On 11.03.2020, the World Health Organization declared the second pandemic of the 21st century after swine flu, as the disease had already spread globally and covered all continents [26, 38, 190].

The first case of COVID-19 in Russia was registered on 31.01.2020. The patient was a woman who arrived from China to Tyumen. In St. Petersburg, the first registered COVID-19 patient was a man who returned from Italy on 03.03.2020.

The acute viral disease known as COVID-19 is characterized by predominant upper respiratory tract involvement and is caused by a single-stranded RNA-containing virus of the genus Betacoronavirus of the family Coronaviridae, line Beta-CoV B. The epidemiology and course of the COVID-19 epidemic are presented in Annex 1.

Until 2002, coronaviruses were considered as agents causing upper respiratory tract diseases of mostly mild severity (with extremely rare fatalities): laryngitis, tracheitis, etc. Four seasonal coronaviruses (HCoV-229E, -OC43, -NL63 and -HKU1) were circulating in human populations

In late 2002, the SARS-CoV coronavirus was discovered to cause severe acute respiratory syndrome in humans. This virus belongs to the genus Betacoronavirus. The natural reservoirs of SARS-CoV are bats and the intermediate hosts are camels and Himalayan civets. During the epidemic, more than 8000 cases were reported in 37 countries, of which 774 were fatal. No new cases of SARS-CoV have been reported since 2004.

In 2012, a new coronavirus, MERS-CoV, causing Middle East respiratory syndrome and also belonging to the genus Betacoronavirus, was identified. The main natural reservoirs of MERS-CoV are bats and one-humped camels (dromedaries). Since this year, 2519 cases of coronavirus infection caused by MERS-CoV have been reported, of which 866 have been fatal. All cases are geographically associated with the Arabian Peninsula (82% of cases reported in Saudi Arabia). MERS-CoV continues to circulate and cause new cases [157].

The most pathogenic for humans, from the clinical point of view, in the group are MERS-CoV, SARS-CoV, SARS-CoV2, for this reason they are assigned to group II of pathogenicity [3, 38], and COVID-19 disease is included in the list of diseases that pose a danger to others (Decree of the Government of Russia from 31.01.2020 № 66).

The SARS-CoV-2 coronavirus is suspected to be a recombinant virus between a bat coronavirus and a coronavirus of unknown origin. The genetic sequence of SARS-CoV-2 is at least 79% like that of SARS-CoV [150].

Peculiarities of the development of the epidemic process

COVID-19 is ubiquitous on all continents and in virtually all countries. However, the epidemiologic situation is highly heterogeneous. As of July 2023, there are 692196067 COVID-19 survivors worldwide. Among all regions of the world, the Americas region is the leader in the number of cases and deaths detected. The largest number of cases is currently registered in the USA (87 331 566 people), followed by India, Brazil, France, Germany. Russia ranks 7th in the world ranking (18 379 583 cases of infection, of which 380 076 were fatal) [108, 132].

It should be noted that official statistics are based on the definition of a confirmed case, which is a case «with laboratory confirmation of COVID-19 infection regardless of clinical manifestations and symptoms of disease» (World Health Organization 2020).Thus, the data may not take into account individuals who are not covered by testing or who have not sought medical care [1299, 1333].

The incidence of disease depends on the isolation and containment measures used in countries. High levels of disease prevalence and mortality are observed when control measures are incomplete or delayed, as observed in Italy, Spain, the United States and the United Kingdom. Conversely, the timely and comprehensive implementation of strict quarantine measures ensures low COVID-19 disease prevalence and mortality. Also, the heterogeneity of the epidemic situation in different countries is due to the different approaches to conducting diagnostic methods of investigation and the subsequent application of mathematical and statistical analysis techniques [26, 44].

The rapid collection of data on illnesses and deaths and their openness undoubtedly provide significant advantages in controlling the epidemic, forecasting its development and planning measures to contain the infection. An important aspect of analyzing the COVID-19 epidemic is the comparison of countries and territories in terms of morbidity, mortality and morbidity rates [25, 26].

Statistics and forecasting the course of a pandemic

Health care professionals making administrative decisions attempt to provide a plausible perspective of events for at least the medium term. For this purpose, different techniques are used: mathematical modeling of the epidemic; orientation on epidemics of this infectious agent of the past years; orientation on epidemics caused by pathogens close in biological properties, virulence, pathogenicity and transmission routes in the historically available period; qualitative consideration of known factors and creation of an empirical model of the epidemic taking into account regional peculiarities and common sense. It should be noted that mathematical modeling in recent years has proved its worth in predicting the development of a number of diseases, e.g. HIV infection, viral hepatitis [28, 100].

In the context of the COVID-19 pandemic, health care workers have proven to be one of the most vulnerable populations. Hospital staff in various types of hospitals are at increased risk of COVID-19 infection due to close contact with patients and the possibility of contact with surfaces around patients. Other risk factors include ignorance of infection safety issues, lack of pre-admission training, and improper use of personal protective equipment. The incidence of COVID-19 in health care workers was significantly higher at all stages of infection compared with other categories and occupational groups [2, 30, 46, 136, 146, 167, 169].

The epidemiology, pathogenesis and diagnosis of respiratory viral infections are well enough studied, and basic anti-epidemic measures, if properly applied, are effective, but the spread of COVID-19 indicates the need for their differentiated application, especially with regard to the care of infectious patients directly in the health facility.

Various measures have been introduced to prevent the spread of COVID-19 globally, which included:

1. Quarantine measures such as restriction of public events, closure of educational institutions and businesses, and restriction of population movement.
2. The imposition of restrictions on international and internal movements, including restrictions on entry and exit, as well as restrictions on movement within the country.
3. Mandatory use of personal protective equipment (wearing masks, gloves) and observance of social distancing.
4. Strengthening disinfection and hygiene measures such as frequent hand washing and disinfection of surfaces.
5. Strengthen monitoring and control of disease, including testing of presumptive diagnosed persons and surveillance and screening of contacts.

Operational changesin legislation allowed to regulate the dynamics of COVID-19 spread based on the levels of infection in the population and the burden on the country's health care system.

1.2 Analysis of regulations for 2020-2021.

One of the first normative acts in the beginning of COVID-19 distribution were informational letters of the Federal Service for Supervision of Consumer Rights Protection and Human Welfare.

The letter dated 23.01.2020 № 02/770-2020-32 «On instructions for disinfection measures for the prevention of diseases caused by coronaviruses» provides information on the epidemiology of coronaviruses, as well as groups of disinfectants recommended for use.

Measures to prevent the importation and spread of 2019-nCoV on the territory of the Russian Federation are regulated by the Decree of the Chief State Sanitary Doctor of the Russian Federation from 24.01.2020 № 2 «On measures to prevent the spread of a new coronavirus infection caused by 2019-nCoV».

29.01.2020 The Ministry of Health of the Russian Federation and the Federal Service for Supervision of Consumer Rights Protection and Human Welfare approved the Temporary Methodological Recommendations «Prevention, Diagnosis and Treatment of New Coronavirus Infection (2019-nCoV)», version 1. This document was a complete guide for medical organizations and included etiology and pathogenesis of the disease, epidemiological characteristics. The standard COVID-19 2019-nCoV case definition includes the criterion of having visited epidemiologically 2019-nCoV-unfavorable countries and regions (mainly Wuhan) in the past 14 days before the onset of symptoms. The diagnosis of coronavirus infection, clinical features and basic principles of treatment are described. At the beginning of the active spread of COVID-19, recommendations for etiotropic therapy from the perspective of evidence-based medicine for the treatment of 2019-nCoV infection and specific prophylaxis were lacking. To carry out nonspecific prophylaxis of coronavirus infection, standard measures of influence on the links of the epidemic process were applied, as for airborne infection. With regard to the first link (source of infection): isolation of patients, use of masks, use of disposable instruments. Measures aimed at the mechanism of pathogen transmission included: control of hand hygiene, use personal protective equipment, thorough disinfection of surfaces, air and instruments, treatment of medical waste generated by contact with patients and suspected of COVID-19 disease as class B medical waste. For the susceptible contingent, the key factor of prevention is timely application to medical institutions for medical assistance in case of symptoms of acute respiratory infection. Recommendations are given to tourists traveling outside the Russian Federation, especially to Asian regions.

The routing procedure in these Temporary Medical Recommendations regulates the provision of medical care to patients with new coronavirus infection caused by 2019-nCoV in medical organizations. Medical care is provided in accordance with the already developed and approved orders of the Ministry of Health and Social Development of Russia from 31.01.2012 № 69n «On approval of the Procedure for the provision of medical care to adult patients with infectious diseases» and from

05.05.2012 № 521n «On approval of the Procedure for the provision of medical care to children with infectious diseases».

All medical organizations in order to be ready to take measures in case of importation or emergence of COVID-19 should have an operational plan of primary anti-epidemic measures in case of detection of a patient suspected of this disease, be guided by sanitary legislation, including the regional Plan of organizational sanitary and epidemiological measures to prevent the importation and spread of COVID-19, caused by 2019-nCoV, approved by the authorized executive authority of the subject of the Russian Federation.

In the letter dated 31.01.2020 №02/1297-2020-32 of the Rospotrebnadzor Directorate, even before the first cases were registered in Russia, a temporary procedure of actions in case of final laboratory confirmation of a COVID-19 case is presented. This procedure, in addition to the measures described in the first version of the Temporary Medical Recommendations, includes isolation and examination of contact persons on the 1st day of hospitalization and on the 10th day of hospitalization; final disinfection at the place of residence (stay) of the nCoV patient; control over the anti-epidemic regime in the medical organization where the nCoV patient and contact persons were hospitalized.

In order to organize preventive measures among employees of organizations of all forms of ownership, explanations were given in the letter dated 10.03.2020 № 02/3853-2020-27 «On measures to prevent a new coronavirus infection (COVID-19)».

In connection with the ongoing global spread, the threat of importation and spread of COVID-19 on the territory of the Russian Federation, the Decree of the Chief State Sanitary Doctor of the Russian Federation dated 18.03.2020 No. 7 «On ensuring the isolation regime to prevent the spread of COVID-2019» was published. Within three calendar days, all those arriving on the territory of the Russian Federation had to fill out a questionnaire and undergo laboratory testing for COVID-19 by PCR method with subsequent posting of the result on the Unified Portal of Public Services.

On 19.03.2020 the main Order of the Ministry of Health of the Russian Federation No. 198n «On temporary order of organization of work of medical organizations in order to implement measures to prevent and reduce the risks of spread of new coronavirus infection COVID-19» came into force, describing the basic principles of organization of medical care for patients with new coronavirus infection COVID-19 in medical organizations and their structural subdivisions, as well as measures taken by medical workers to prevent nosocomial spread of COVID-19.

In view of the active increase in the number of COVID-19 patients, the Ministry of Health of the Russian Federation is taking measures to repurpose medical organizations (Letter of the Ministry of Health of the Russian Federation from 24.03.2020 № 30-1/10/2-24 «On the minimum requirements for buildings and premises where it is planned to organize additional infectious beds»).

With the emergence of new operational data, the Ministry of Health amends Order No. 198n, the main ones being PPE requirements (Order of the Ministry of Health of the Russian Federation of 27.03.2020 No. 246n), minimum requirements for the implementation of medical activities aimed at prevention, diagnosis and treatment of COVID-19 (Order of the Ministry of Health of the Russian Federation of 2.04.2020 No. 264n).

Methodological recommendations MR 3.1.0170-20 «Epidemiology and prevention of COVID-19» (approved by the head of the Federal Service for Supervision of Consumer Rights Protection and Human Welfare 30.03.2020) became the main document for the organization of anti-epidemic measures in medical institutions.

In connection with the shortage of medical personnel, an important decision was to involve in the provision of medical care to prevent the spread of COVID-19 persons studying at higher and secondary professional medical and pharmaceutical education (Letter of the Ministry of Health of the Russian Federation from 29.03.2020 № 16-0/10/2-39; Order of the Ministry of Health of the Russian Federation from 14.04.2020 № 327N), the extension of valid certificates of specialists, as well as admission to work without a valid certificate.

For employers, there is an extensive list of regulations governing the use of PPE by employees, transfer to remote work to minimize contacts [34, 61, 71, 75, 78, 79].

On 8.04.2020 the document regulating all aspects of medical activity during COVID-19 distribution - Temporary Methodological Recommendations «Prevention, Diagnosis and Treatment of New Coronavirus Infection» came into force (COVID-19) [23].

Throughout 2020, Russia adopted a number of new laws and made significant changes to existing regulations in connection with COVID-19. These changes addressed various aspects, including medical care, quarantine measures, social support and other aspects of pandemic control. Among them is the letter of the Federal Service for Supervision of Consumer Rights Protection and Human Welfare dated 09.04.2020, which gives recommendations to prevent the spread of COVID-19 in medical organizations providing medical care in hospital settings, clarifications on the use of PPE (letter dated 11.04.2020 №02/6673-2020-32 «On sending recommendations on the use of personal protective equipment for different categories of citizens at risk of COVID-19 infection»). In addition, a large number of regulatory acts on accreditation were published [64].

The first prerequisites for mass immunization were in the Order of the Ministry of Health of the Russian Federation from 4.12.2020 № 1288n, in order to help medical organizations and competent information of the population about the need for vaccination. Orders of the Ministry of Health of Russia from 09.12.2020 № 1307n and from 03.02.2021 № 47n in the calendar of preventive vaccinations for epidemic indications included prophylactic vaccination against infection COVID-19, caused by the virus SARS-CoV-2. Thus, since the end of 2020, all types of organizational and preventive measures have been widely used in medical [8, 9, 39, 48, 58, 59, 70, 75, 81, 82, 83, 85, 87, 102].

The epidemiology, pathogenesis and diagnosis of respiratory viral infections are well enough studied, and the basic anti-epidemic measures are effective if properly applied, but the spread of COVID-19 indicates the need for their differentiated application, especially with regard to the care of infectious patients directly in the health facility.

1.3 Non-specific prevention COVID-19

Nonspecific prevention are measures aimed at preventing the spread of infection and are carried out with respect to the source of infection (sick person and asymptomatic carrier), the mechanism of transmission of the infectious agent, and the susceptible population (protection of persons who are and/or have been in contact with a sick person) [10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 41, 70, 76 77, 101, 144].

Measures in relation to the source of infection: diagnostic (early diagnosis and active detection of infected persons); treatment; isolation, including hospitalization for clinical and epidemiological indications, with the use of special transport and compliance with routing to medical organizations [23, 67, 78, 79, 80, 84].

Measures aimed at the mechanism of transmission of the infectious agent: focal disinfection: current and final; observance of personal hygiene rules (hand washing, use of antiseptics, medical masks, gloves); use of personal protective equipment for medical workers; decontamination and disposal of medical waste of class B [23, 39, 69, 80, 101,103, 123, 142, 152, 185].

Measures aimed at the susceptible contingent: emergency prophylaxis; regime-limiting measures, including clinical observation and quarantine, observance of self-isolation regime and use of social separation measures (temporary cessation of work of public catering enterprises, retail trade (except for trade in essential goods), transition to a remote mode of work, transfer to distance learning educational organizations; examination for SARS-CoV-2 at the appearance of clinical signs of infection [23, 33, 42, 65, 66, 72, 74].

1.4 Specific prophylaxis. Collective immunity

At the current stage of the COVID-19 epidemiologic process, countries around the world have adopted various strategies to contain and mitigate COVID-19. The use of vaccination is the main tool in the fight against this disease and the main opportunity to resume the activities of health care organizations in a regular mode. In order to increase the effectiveness of this anti-epidemic measure, it is first of all necessary to increase vaccination coverage of the most vulnerable groups with a high risk of transmission (young people, occupational risk groups) [1, 30, 96, 138].

In the calendar of preventive vaccinations for epidemic indications, categories of citizens are defined taking into account the priority of receiving vaccine against COVID-19. Since 18.01.2021, mass vaccination of the population against COVID-19 has been carried out in the Russian Federation. The following vaccines are registered in the Russian Federation:

• Combined vector vaccine («Gam-COVID-Vac», solution for intramuscular injection), date of registration 11.08.2020;

• Combined vector vaccine («Gam-COVID-Vac-Lio»), registration date 25.08.2020;

• vaccine based on peptide antigens («EpiVacCorona»), registration date 13.10.2020;

• Coronavirus inactivated whole-virion concentrated purified vaccine («CoviVac»), registration date 19.02.2021;

• COVID-19 prophylactic vaccine (Sputnik Light), registration date 06.05.2021;

• vaccine based on peptide antigens («AVRORA-CoV»), date of registration 26.08.2021, date of re-registration 12.04.2022;

• Combined vector vaccine («Gam-COVID-Vac-M»), registration date 24.11.2021;

• Subunit recombinant vaccine («Convasel»), date of registration 18.03.2022;

• Combined vector vaccine («Gam-COVID-Vac», nasal drops), date of registration 31.03.2022;

• Combined vector vaccine («Salnavak»), registration date 04.07.2022.

More than 80% of virus-neutralizing antibodies are directed to the receptor-binding domain (RBD) S-protein of SARS-CoV-2. Thus, the detection of antibodies to the receptor-binding domain (anti-RBD antibodies) is recommended when assessing the intensity of postvaccinal protective immunity by immunochemical methods. Methods using flow cytometry or a commercial ELISpot immunoassay are used to identify SARS-CoV-2-specific B cells that produce antibodies that confer immunity. Therefore, tests for SARS-CoV-2-specific antibodies and measurement of B-cell levels are necessary to characterize specific humoral immunity in COVID-19 patients [119, 125, 145, 166].

At the beginning of the pandemic, the target antigens for serologic assays were nucleocapsid protein (N) and spike protein (S). The presence of immunoglobulin G to SARS-CoV-2 virus indicated that an individual had been infected and had developed an immune response either to the virus from current or prior infection or to the development of postvaccine immunity. After positive PCR results (laboratory-confirmed diagnosis of COVID-19), seroprevalence is reported to be between 88 and 100%. It is noted that IgG seroconversion takes longer among asymptomatic or mildly asymptomatic individuals, as the level of humoral immunity formed as a result of the disease is lower [111, 113, 120, 155, 161, 168, 171, 175].

Serologic antibody testing based on the humoral immune response can guide public health measures and strategies for control, monitoring the prevalence and spread of the virus [73, 130, 147, 175].

According to the authors, SARS-CoV-2-specific T cells are detected up to eight months post-disease in COVID-19 patients. However, this issue is insufficiently studied, in particular among the preservation of protective antibody titer in risk groups, which include health care workers [27, 127, 140, 155, 172, 177177, 183].

According to the researchers, the presence of IgG antibodies against adhesions or nucleocapsid is associated with a significant reduction in the risk of SARS-CoV-2 re-infection over the next six months. The IgG antibody response wanes over time, with the strength and duration of the antibody response indicating whether individuals can be protected from re-infection, which may have diagnostic value and would be a vector for adjusting organizational interventions [128, 149, 153, 170, 187].

Collective immunity

The formation of specific protection of the population (its individual groups) or «collective immunity» begins at the beginning of the epidemic, when the pathogen enters a population that previously had no immunity to it. The incidence rate then begins to decline due to a reduction in the proportion of susceptible populations and organizational protective measures such as social distancing and the use of personal protective equipment. It is assumed that the population reaches collective immunity at the peak of the epidemic naturally. In this case, the threshold is equivalent to the level of vaccination that must be maintained in the population. When this threshold is reached, the rate of spread of infection and the number of people who become ill are reduced [109, 112, 122].

Collective, or population immunity, is one of the most effective means of preventing infectious diseases. It is created by spreading the disease among the population. This creates a reservoir of individuals who are immune to re-infection: passively, naturally, and actively, artificially (through population immunization). According to the researchers, there is no difference in how the necessary threshold is reached: naturally (COVID-19 survivors) or artificially (vaccinated individuals) [104, 115, 116].

Collective immunity, in turn, protects indirectly. It reduces the incidence of disease and the likelihood of exposure to the pathogen, but susceptible people remain at risk of infection. The presence of a broad immune layer in the population can be an effective factor in reducing the spread of the pathogen. Thus, maintaining collective immunity artificially, i.e. through vaccination, is particularly important for the elderly, persons with chronic diseases and health care workers [36, 73, 109, 110].

According to literature sources, the level of collective immunity, at which the population will effectively resist the spread of infection if there is a significant proportion of persons with developed defense mechanisms, should be between 50 and 72%. Resolutions of the chief state sanitary doctors of the regions of the Russian Federation set the threshold of vaccination at 80% of the total number of employees of organizations [54, 111, 112, 122, 147, 159].

Taking into account the recommendations of the World Health Organization, today in Russia before reaching the level of collective immunity of the population according to epidemic indications it is necessary to carry out vaccination against COVID-19 six months after the disease (including in previously vaccinated persons) or six months after the previous vaccination (so-called emergency vaccination). Therefore, the main share in the structure of collective immunity should come from the artificial way of its formation, that is to say active immunization [8, 117].

Natural immunity to SARS-CoV-2 develops after the disease has been transmitted. This results in a rapid and effective immune response that will subsequently protect the human body. However, the presence and duration of immune memory cells specific for SARS-CoV-2, which provide reliable protective immunity in individuals with transferred infection, remains poorly understood. According to the authors, natural immunity can persist for more than 12 months [6, 121].

Several publications have shown that the T-cell response to human coronaviruses, including SARS-CoV-1, MERS and SARS-CoV-2, can be strong and long-lasting. Assessment of T-cell immunity to SARS-CoV-2 is important not only for risk stratification and identification of potentially protected populations with immunity acquired through infection, but also for determining the immunogenicity and potential efficacy of vaccines under development. The principle of test systems for determining the level of cellular immune response is to determine the number of T cells secreting gamma interferon in vitro [30, 56].

1.5 Organization of measures to prevent infectious diseases in health care facilities

Organizational measures in medical institutions during the rise in the incidence of airborne infections are based mainly on the mechanism of transmission of the causative agent. They include:

- drawing up annual preventive and treatment plans, including drawing up a plan for repurposing beds in somatic wards for infectious disease beds during the period of an upswing in the incidence of acute respiratory viral infections and influenza;
- creating a stockpile of antiviral drugs for the treatment of patients with acute respiratory infection;
- isolation of patients with suspected acute respiratory infection to separate rooms or units (wards, boxes, departments, sections);
- restriction of visits;

- organization of active early detection of cases of acute respiratory infections among patients and employees in the hospital;
- restriction of movement of medical workers in hospital wards during the period of disease outbreak;
- provision of personal protective equipment (respiratory protection - masks, special clothing, gloves) to medical personnel providing medical care to patients suspected of acute respiratory infection, preventing the reuse of disposable personal protective equipment;
- strengthening of precautionary measures in patient care with the organization and creation of conditions for hand hygiene after contact with patients;
- compliance with the rules of collection and destruction of masks, tissues, handkerchiefs and other hygiene products infected with respiratory secretions;
- ensuring timely laboratory diagnostics of patients;
- creating a stock of consumables and transport medium for taking material from patients and ensuring temporary storage of transport medium in refrigerators for no more than 7 days [23,35, 40, 43, 57, 60, 62, 63, 68, 75, 88, 89, 90, 91, 92, 93, 101, 103].

These measures are nonspecific and require adjustment depending on the activities of the medical organization and the specific nosology.

1.6 Organization of health facilities in a pandemic

The following measures were taken to create such conditions for health workers to work safely during the COVID-19 pandemic. Activities of medical organizations during the pandemic period were carried out in compliance with the requirements of a strict anti-epidemic regime, separation of flows and work in the «red zone», where there were also patients actively releasing the virus into the external environment SARS-CoV-2 [40, 60, 62].

The use of personal protective equipment is necessary because of the direct threat of contamination and has been used in the same manner as in any biological contamination hotspot, where working without protective equipment and respirators is prohibited. The United States Centers for Disease Control and Prevention (CDC) also encourages the use of gloves when caring for people with COVID-19 [7, 142, 152, 158].

In conditions of high probability of admission of a patient with a new coronavirus infection (possibility of hospital-acquired infection foci), it is necessary to implement the following measures:

- prohibition of visits of relatives and other persons to patients in inpatient medical organizations;
- prohibition of visits to inpatient medical organizations by persons who are not employees of the organization;

• stopping and postponing planned hospitalization;

• performing twice daily physical examinations and thermometry on all patients and recording the results in the observation sheet;

• training and instruction of medical staff on prevention of COVID-19 spread, implementation of anti-epidemic measures, use of personal protective equipment and personal prevention measures;

• developing a procedure to follow when a patient with a suspected infection caused by a novel coronavirus is identified.

Hospitalization of patients (persons with suspected disease) is carried out in boxes, boxed wards or, in their absence, in wards with an airlock and a sanitary unit in compliance with the principle of one-stage (cyclical) filling of wards and taking into account the severity of the condition of patients.

Patients with suspected and confirmed infection should be separated (kept in different wards). If new patients with suspected infection are identified, they may be placed on the ward with other patients with suspected infection. If during hospitalization a patient with suspected or confirmed infection will require intensive care or oxygen support, if possible, an intensive care unit should be organized in the ward to which the patient is isolated.

According to Sanitary Regulations 3.1.3597-20 «Prevention of new coronavirus infection (COVID-19)», medical waste, including biological excretions of patients (sputum, urine, feces, etc.), are classified as extremely epidemiologically hazardous waste of class B and are subject to mandatory disinfection or decontamination by physical methods (thermal, microwave, radiation, etc.). For this purpose, the hospital should have a specialized facility operating using such methods. Disposal of class B non-disinfected waste outside the territory of the medical organization is not allowed. After hardware disinfection with the use of physical methods and change of appearance, class B waste can be accumulated, temporarily stored, transported, destroyed and buried together with class A waste. n this case, according to the requirements of Sanitary rules and regulations 2.1.3684-21 «Sanitary and Epidemiological Requirements for the maintenance of urban and rural settlements, water bodies, drinking water and drinking water supply, air, soil, living quarters, operation of industrial and public premises, organization and conduct of sanitary and anti-epidemic (preventive) measures», the use of chemical disinfection methods is possible only for disinfection of food waste and excretions of patients, as well as in the organization of anti-epidemic (preventive) measures [45].

In order to prevent healthcare-associated infections in COVID-19 patients, it is necessary to implement a full range of measures to ensure epidemiological safety of medical care, including hand treatment with alcohol antiseptics, use of a third pair of sterile/non-sterile gloves according to standard indications, performance of all invasive manipulations in compliance with standard operating procedures, monitoring of invasive procedures, and timely examination [33, 40, 42, 60].

It is necessary to strengthen microbiological monitoring of circulating strains of actual infectious agents, including Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Staphylococcus spp. (MRSA) and others, by examining patients and objects of the hospital environment to determine the resistance of microorganisms to antimicrobials. It is required to strengthen control over the epidemiological safety of medical care and prevention of infections associated with the provision of medical care using checklists and the use of various forms of surveillance, including video surveillance [35].

In order to limit unreasonable consumption of personal protective equipment, it is recommended to determine the need for it in medical organizations, as well as to ensure its proper use. In order to rationalize the need for personal protective equipment while ensuring the safety of health care workers, it is recommended to:

• Limit, through technical and administrative measures, the number of persons working in high-risk areas who require the use of personal protective equipment.

• Determine the required number of health care workers in contact with patients.

• Adjust the required number of ward entrances.

• Provide for remote counseling for patients and persons with suspected COVID-19.

• Introduce extended respirator use (wearing the same respirator when working with multiple patients without removing the respirator).

• Application of the maximum possible modes of natural ventilation (constant maximum possible ventilation) allows to achieve a sharp decrease in the concentration of infectious aerosol in the air of the premises and, accordingly, sharply reduce the risk of spread of infections through the air. An effective way of disinfection of indoor air is the use of ultraviolet bactericidal units with a dose of ultraviolet bactericidal radiation not less than 25 mJ/cm^2, built into the central systems of supply and exhaust ventilation. Such supply and exhaust ventilation in the presence of people must operate continuously during the entire working time [35, 60, 88, 101].

• In areas at high risk of COVID-19 spread, the use of room air conditioners (split systems) should be avoided as they actually increase the risk of infection by maintaining high concentrations of infectious aerosol with blocked natural ventilation. The use of closed-type irradiators (recirculators) with a source of ultraviolet bactericidal radiation inside is an effective measure to reduce the risk of airborne infections, including COVID-19, only if sufficient UV doses (at least 25 mJ/cm2) and the necessary air exchange rate (ensuring recirculation of the entire volume of air in the room at least 4 times in 1 hour) are provided. Closed irradiators in the presence of people shall operate continuously during the entire working time [11, 41, 88, 101].

Due to the rapid spread of the disease and its epidemic potential, the development of a set of organizational and preventive measures is an urgent task to prevent the spread of COVID-19 in medical institutions. The above-mentioned urgent directions to prevent the spread of not only COVID-19, but also any airborne infection prone to global course, require complex organizational measures to reduce the risk of spread of infections in medical organizations, whose activities during pandemics determine the effectiveness of the country's health care system.

Chapter 2 MATERIALS AND METHODS OF RESEARCH

2.1 Structural and logical scheme of the study (design)

To achieve the set goal and formulated objectives, theoretical foundations and approaches to this work are developed on the basis of literature analysis. The obtained information is processed with the help of statistical and mathematical methods with the subsequent substantiation of models of organizational measures to prevent the spread of COVID-19 in medical personnel of «covid» hospitals and general hospitals.

The dynamic surveillance was constructed based on the development of the COVID-19 epidemic process and divided into two phases:

1) from the start of COVID-19 dissemination (pre-vaccination period) and the start of vaccination prophylaxis (March 2020 to August 2021) - early post-vaccination period.

2) late postvaccination period after 10 months from the start of vaccination (September through December 2021).

The study was conducted according to a standardized stage scheme:

1. Analysis of literary sources and regulatory documents.

2. Design development, definition of the aim and objectives of the research, selection of its objects.

3.Collection of data on morbidity, vaccination, humoral and cellular immunity levels in health care workers according to selected criteria and facilities.

4. Processing of the obtained material with its subsequent description and the advancement of scientific hypotheses.

5.Statistical and mathematical analysis, formulation of conclusions, development of practical proposals and recommendations.

To achieve the goal of the study and solve the set tasks, we developed a structural and logistic scheme (design) of the study, clearly illustrating its stages (Table 1)

Table 1– Structural and logistical research design

Scientific research stage	Evidence
1 stage Preparatory (determining the relevance of the study, the purpose and objectives of the study, planning the study)	
Theoretical analysis of data on the epidemiology of COVID-19, information on humoral and cellular immunity according to the domestic and foreign literature. Analysis of data on organizational measures in medical organizations to prevent the spread of COVID-19.	Analytical Monographic
Stage 2 Writing the research program	
Selection of research methodologies. Primary data collection. Selection of observation units and comparison groups, preliminary analytical analysis of data and tabular presentation of data	
Stage 3 Organization and conduct of the research. Proposing scientific hypotheses.	
Analysis of COVID-19 morbidity in medical personnel of hospitals and population of St. Petersburg	Grouping and comparison method; Analytical Statistical Mathematical modeling and creation of regression models Laboratory-diagnostic
Analysis of the dynamics of vaccination of medical personnel in hospitals, study of the structure of collective immunity of employees	
Analysis of the occurrence of recurrent disease in medical personnel, taking into account previous disease and vaccination period	
Analysis of the relationship between the occurrence of recurrent disease and the level of humoral immunity	
Analysis of significant levels of humoral and cellular immunity	
Stage 4 Synthesis of obtained data, preparation of scientific hypotheses, mathematical modeling, statistical processing of data	
Formulation of conclusions, development of practical proposals	Synthetic

2.2 Research materials

In the course of the study, we developed a system of data collection on morbidity, vaccination and the level of humoral and cellular immunity among medical workers of «covid» and general hospital in St. Petersburg for the period 2020-2021, on the basis of which databases on observation groups were formed (Annex 2). Three observation groups were identified:

1) medical workers of multidisciplinary hospital No. 1 (1334 persons), reassigned to provide medical care to patients with new coronavirus infection in the periods 28.03.2020 - 27.07.2020, 10.11.2020 - 22.02.2021, 26.06.2021 - 24.07.2021, 16.10.21 - 31.12.2021;

2) medical workers of multidisciplinary hospital No. 2 (1307 people), which worked in a planned mode throughout the epidemic COVID-19 morbidity upsurge;

3) patients at a private medical clinic undergoing humoral and cellular immunity studies, vaccinated and re-infected with COVID-19 (67 patients).

The total number of observation units was 2708 (Table 2).

Table 2 - Characterization of observation groups

	Inpatient No. 1	Inpatient No. 2	Private medical center
Number of employees, persons.	1383 (49 – maternity)	1307	Patients– 67
Actual number of employees, persons.	1334	1307	-
Men, persons.	266 (19,9%)	254 (19,5%)	38 (56,7%)
Women, persons.	1068 (80,1%)	1053 (80,5%)	29 (43,3%)
Age of employees	18–85 y.	18–81 y.	23–84 y.
Junior medical staff, persons.	320	287	-
Nursing staff, people.	617	640	-
Senior medical staff, persons.	397	380	-
Numberofcompartments	67	45	-

Table 3 - Materials and methods of research

Monitoring period	A set of preventive and organizational measures	The structure of collective immunity	Statistical testing of mathematical hypotheses (mathematical modeling)	Objects
Commencement of COVID-19 dissemination (March-November 2020)	Architectural and planning Disinfection Isolation Application of personal protective equipment Modern methods of laboratory diagnostics (PCR)	1. People who've had the disease 2. Uninfected	Descriptive analysis of the studied data for asymmetry of their distribution Wilcoxon test Descriptive analysis of data Testing the distribution for normality t-test of mean Construction of confidence interval for the true mean Bootstrapping	Incidence COVID-19

Continuation of Table 3

Vaccination start period, early post-vaccination period (December 2020 - August 2021).	Architectural and planning Disinfection Isolation Vaccination (double vaccination) Application of personal protective equipment Modern laboratory diagnostic methods (PCR, ELISA)	1.Those who have been ill 2.Those who have been immunized and those who have been ill 3. Vaccinated and not infected 4. Not infected and not immunized	Descriptive analysis of data, Equality of proportions test	Structure of collective immunity Baseline indicator - number of vaccinated persons
Late post-vaccination period (September - December 2021)	Architectural and planning Disinfection Isolation Vaccination (double vaccination, single vaccination) Application of personal protective equipment	1.Vaccinated 2.Those who have been ill (not more than six months ago), unvaccinated 3. Not infected and not immunized 4. Not infected and unvaccinated, with medical contraindications	Contiguity tables, Pearson's chi-square test, Equality of proportions test, Logit regression Bootstrapping Analysis of antibody distribution plots Formal test for the presence of distribution curvature Wilcoxon test Descriptive analysis of the data under study for asymmetry of distribution. Wilcoxon test Mann-Whitney test	Recurrent morbidity after vaccination Levels of humoral and cellular immunity

COVID-19 «incidence» in health care workers in this study was considered, based on the standard COVID-19 case definition, to be «a positive laboratory result for SARS-CoV-2 RNA using nucleic acid amplification techniques, regardless of clinical manifestations».

Medical workers were examined to determine the level of specific IgG against SARS-CoV-2 by enzyme immunoassay using the Abbott ARCHITECT SARS-CoV-2 IgG II Quant test system, Ireland.

For laboratory determination of T-cells specifically responding to SARS-CoV-2 virus antigens and evaluation of T-cell immune response, the TigerTest® SARS-CoV-2 kit, JSC «Generium», Russia, was used.

2.3 Methods of research and data processing

Empirical data were collected and processed taking into account modern approaches to statistical analysis. The empirical data were collected using the sampling method of observation.

In order to evaluate the organizational measures and mechanisms of collective immunity formation, as a result of the analysis of the databases created by us, statistical hypotheses were selectively put forward and tested using statistical tests (Table 4).

Table 4 - Methodology for evaluating statistical hypotheses

Hypothesis to be tested	Statistical tests	Confirmed hypothesis
The morbidity of medical workers in a general hospital is lower than the morbidity of workers in a «covid» hospital	Descriptive analysis of the studied data for asymmetry of their distribution. Wilcoxontest	The morbidity of medical workers in a general hospital in the median is significantly lower than the morbidity of workers in a «covid» hospital

Continuation of Table 4

The morbidity of medical workers in hospitals is higher than the citywide level of the general population, but with a similar trend in the course of the epidemic in St. Petersburg	Descriptive analysis of the studied data for asymmetry of their distribution. Wilcoxon test	Morbidity of medical workers in hospitals in the median value is significantly higher than the city-wide morbidity rate of the population as a whole (for the period 2020-2021).
The period during which a recurrence of illness occurs after the disease has passed (6-12 months).	Descriptive analysis of data Testing the distribution for normality t-test of mean Constructing a confidence interval for the true mean Bootstrapping	The period during which recurrent disease occurs prior to vaccination after a first illness is on average 8 months (with a confidence range of 6 to 10 months)
The number of immunized health care workers in both hospitals is equal	Descriptive analysis of data Equality of proportions test	The number of immunized health care workers in both hospitals was significantly equal in percentage terms.
The majority of health care workers at both hospitals are vaccinated with Sputnik V (double vaccination)	Equal Proportion Test	The majority of health care workers at both hospitals are vaccinated with Sputnik V (double vaccination)
Recurrent morbidity is lower in those who have been re-infected and vaccinated than in those who have been vaccinated alone (due to cellular immunity)	Contiguity tables Pearson's chi-square test Equality of proportions test Logit regression	Recurrent morbidity in the over-vaccinated and vaccinated was significantly lower than in the vaccinated alone at both hospitals.
The number of recurrent illnesses in vaccinated individuals is lower than in unvaccinated individuals.	Equal Proportion Test	The number of recurrent illnesses after vaccination in vaccinated individuals was significantly lower as a percentage of vaccinated than unvaccinated individuals at both hospitalizations.

Continuation of Table 4

The number of recurrent illnesses after vaccination in the covid inpatient unit was significantly greater as a percentage than the number of recurrent illnesses in vaccinated general inpatient employees	Equality of proportions test Bootstrapping (robustness test)	The number of recurrent illnesses after vaccination in the covid hospital was significantly lower as a percentage than recurrent illnesses in vaccinated general hospital employees
The period during which the disease occurs after vaccination ranges from 5 to 6 months, most commonly after 5.5 months	Descriptive analysis of data Test for normality of distribution t-test of mean Construction of confidence intervals for the true mean Bootstrapping Mediancomparisontest	The period during which the disease occurs after vaccination is: In a «covid» hospital from 6.9 to 8 months, most often after 7.5 months In a general hospital between 5.46 and 6.34 months, most often after 5.9 months.
The antibody titer is higher in persons who have been over-vaccinated and vaccinated with Companion V than in persons who were not over-vaccinated before vaccination	Analysis of antibody distribution plots Formal test for the presence of distribution curvature Wilcoxontest	The antibody titer after Sputnik V vaccination is median higher in persons who had an illness before vaccination than in persons who did not have an illness before vaccination
The median value of antibody titers in those vaccinated with Sputnik V, reaches a maximum value between 60 and 90 days after vaccination	Descriptivedataanalysis Bootstrapping	(a) The median value of antibody titers in Companion V vaccinees reaches a maximum value between 60 and 90 days after vaccination (from the first dose) and is 1144.3 BAU/ml (with 95% confidence interval [498.25; 1886.0]); it then decreases 7-fold over 180 days from the start of vaccination to 164.35 BAU/ml (95% confidence interval [208.5; 761.05]);

Continuation of Table 4

		(b) The median value of antibody titers in Companion V vaccines, between 0 and 60 days post vaccination is 892.7 BAU/ml (with 95% confidence interval [428.9; 1359.9]); between 30 and 90 days post-vaccination is 1077.5 BAU/ml (with 95% confidence interval [577.6; 1288.0]); between 90 and 180 days is 268.53 BAU/ml (with 95% confidence interval [171.3; 455.6]).
The probability of morbidity after vaccination with SputnikV 6 months from the date of the first dose is X%, and the antibody level is Y BAU/ml	Estimation of the probability of «success», determination of CI limits Calculation of median titers Wilcoxon test	The probability of morbidity after vaccination with «Sputnik V» 5 months after the date of the first dose is 3.53% (in the range from 2.29 to 4.79%) - statistically significantly less than 5%, while the median value of antibody titers in non-diseased persons is 330.8 BAU/ml. The probability of morbidity after vaccination with SputnikV 6 months after the first dose is 5.41% (in the range from 3.89% to 6.92%) - statistically significantly less than 10%, while the median value of antibody titers in non-diseased persons is 274.05 BAU/ml.

End of Table 4

In individuals who had been re-infected and vaccinated with Companion V, 6 months after vaccination, the value of the median level of cellular immunity NMO is higher than the median level of cellular immunity S	Descriptive analysis of the studied data for asymmetry of their distribution. Wilcoxon test Mann-Whitney test	In individuals who have been re-infected and vaccinated with Companion V, 6 months after vaccination, the value of the median level of cellular immunity NMO is significantly higher than the median level of cellular immunity S, and this result persists regardless of the sex of the individual

2.4 Statistical processing of the study results

The reliability of the results of the dissertation research is determined by the methods of data collection and analysis, which are adequate to the objectives set forth.

The study materials are subjected to statistical processing using methods of parametric and nonparametric analysis. Accumulation, correction, systematization of the initial information and visualization of the obtained results are carried out in Microsoft Office Excel 2020 spreadsheets. Statistical analysis is carried out using the statistical programming language R (version 4.1.2).

The degree of reliability of the study results is determined by the representativeness of the sample, sufficient volume of observations, use of modern statistical tools in accordance with the objectives. The level of reliability of negation of the «null» hypothesis was accepted at the level of at least 95% ($p > 0.05$).

When assessing the morbidity of the personnel of medical institutions, due to the need to formally verify that the empirical distributions of the studied indicators are indeed not symmetric, which further confirms the application of the Wilcoxon test for equality of medians of distributions as a more robust to curvature alternative to the classical t-test for comparing the mean values of distributions, the test for statistical significance of distribution curvature is applied. The test is performed at the traditional 5% significance level. Based on the observations, two hypotheses are put forward: null and alternative hypotheses.

H_0: the true curvature of the morbidity distribution is zero (the distribution is symmetric);

H_1: the true curvature of the morbidity distribution is different from zero (asymmetric distribution).

Under the conditions of fairness of the null hypothesis (H_0) the value of the test statistic (T) has an asymptotically standard normal distribution. Accordingly, the p-value obtained within the test is compared with the chosen 5% significance level, and a conclusion is made about rejection/non-rejection of the null hypothesis of the test [180].

The use of the Wilcoxon test in the follow-up is due to the fact that this test is more robust to distributional skewness than the standard t-test for comparing averages. It is used to compare differences in median values between two independent samples when:

- the sampling distribution differs from the normal distribution;
- sample sizes are small ($n < 30$);
- формы распределений двух групп примерно совпадают.

Thus, when comparing the median values of morbidity in two hospitals, the following hypotheses were hypothesized:

H_0: the true median values of the morbidity rates of the two hospitals under consideration do not differ from each other;

H_1: the true median value of morbidity in a general hospital is lower than the same indicator in a «covid» hospital.

Under conditions of fairness of the null hypothesis, the value of the test statistic W was calculated. The p-value obtained within the test (based on specialized tables) is compared with the selected 5% significance level, and a conclusion is made about rejection/non-rejection of the null hypothesis of the test [189].

The application of normality testing (normality of distribution test) is a prerequisite for a number of other tests (t-test, F-test, etc.) and is mandatory when the sample size is small (less than 30-40 observations).

In this case, the Shapiro-Wilk procedure as one of the modern, powerful and reliable small-sample tests is used to conduct the normality test. Similarly to those described above, this test is conducted at the traditional 5% significance level.

H_0: the distribution of the tested indicator does not differ from normal;

H_1: the distribution of the tested indicator differs from normal.

Under the conditions of validity of the null hypothesis, the value of the test statistic W has a distribution specific to the test. The p-value obtained within the test is compared with the chosen 5% significance level, and the conclusion is made about rejection/non-rejection of the null hypothesis of the test [181].

In determining the period during which recurrent disease occurs in the pre-vaccination period following a primary disease, a test comparing the mean to a given number was chosen. The eight-month interval chosen in the initial data analysis was used as the «set» number. This statistical procedure allows us to test the equality of the true mean value of some indicator to some number and, accordingly, to conclude whether the calculated mean of this indicator differs (statistically significantly) from the tested number. In a small sample size the test is valid provided that the distribution of the tested indicator is normal. Under the conditions of fairness of the null hypothesis, the value of the test statistic T has Student's distribution. The p-value obtained by the test is compared with the selected 5% significance level, and the conclusion is made about rejection/non-rejection of the null hypothesis of the test [188].

In the case when the distribution of the studied statistic could not be obtained analytically, but nevertheless it is necessary to calculate confidence interval limits, variance, etc. for these data, the bootstrapping technique, proposed in the work of B. Efron in 1979, was used. Bootstrapping is a method of calculating descriptive statistics of probability distributions based on repeated generation of pseudo-samples (of the same size as the original sample) by Monte Carlo method on the basis of the existing original sample. The essence of the method is to generate (with repetitions) samples of values from the existing original sample. For each such (pseudo) sample, the value of the statistic under study is calculated. As a result, an empirical distribution (histogram) of the obtained set of values of the investigated statistic is constructed, which is then used for the above-mentioned purposes [126].

When analyzing the structure of collective immunity of medical workers of two hospitals, the test for comparison of proportions is carried out using the procedure proposed by K. Pearson. The equality of the proportions of «successes» is investigated in two data sets. The null hypothesis is the fact that the proportions of «successes» in the two data sets coincide. Under the conditions of fairness of the null hypothesis, the value of the test statistic X has a chi-square distribution. The p-value obtained within the test is compared with the selected 5% significance level [165].

Pearson's x-square test is used to test whether or not there is a relationship between discrete (binary) variables, since in this case the classical Pearson's correlation test used for continuous variables is not applicable. The test is based on the conjugacy table that is constructed for the discrete (binary) variables under study. This procedure was a pretest for the construction of logit regression. Hypotheses of this test:

H_0: there is no relationship between the variables under consideration (it is equal to zero);

H_1: there is a relationship between the variables under consideration (it is not equal to zero).

Under the conditions of fairness of the null hypothesis, the value of the test statistic X has a chi-square distribution. The p-value obtained within the test is compared with the selected 5% significance level [118].

In further analysis, we chose logistic (logit) regression, which is an econometric analysis tool that allows us to empirically describe the impact of a selected set of factors on the dependent variable Y, which has a binary character, i.e. can take only two values - 0 or 1.

The logit regression specification has the following general form (Formula 1):

$$P(Y = 1) = \Lambda(\beta_0 + \beta_1 \cdot X_1 + \beta_2 \cdot X_2 + .. + \beta_m \cdot X_m + \varepsilon) \qquad (1)$$

Where $P()$ – probability function;

$\Lambda(x) = \frac{1}{1+e^{-x}}$ – distribution function of the logistic law;

β_j – regression coefficient;

$X_1 .. X_m$ – set of explanatory variables (factors).

Thus, a logit regression always describes the probability for Y to take the value 1, and this probability is explained by a linear combination of a selected set of factors through a nonlinear transformation of the logistic law distribution function. The parameters of this regression are estimated using the maximum likelihood method.

The test for individual statistical significance of logit regression coefficients was performed at the traditional 5% significance level according to the following scheme. Test Hypotheses:

H_0: the true value of the coefficient is zero;

H_1: the true value of the coefficient is not equal to zero.

Under the conditions of fairness of the null hypothesis, the value of the test statistic z has an asymptotically normal distribution. The p-value obtained by the test is compared with the selected 5% significance level, and the conclusion is made about the rejection/non-rejection of the null hypothesis of the test, and, accordingly, about the statistical significance or insignificance of the calculated estimate of the angular coefficient [151].

When assessing the «probability of success», the most relevant was the use of the binomial probability law and its properties, since, on the one hand, we are talking about independent tests (employees of different departments, different gender and age), but at the same time taken from a single general population (all employees are employees of the same hospital and, therefore, are subjected to similar risk conditions).

The binomial distribution is a discrete probability distribution whose probability density is described by the following formula (Formula 2):

$$P(X = k) = C_n^k \cdot p^k \cdot (1 - p)^{n-k} \qquad (2)$$

where:

- X – random variable distributed according to the binomial law;
- k – the number of «successes» in a series of Bernoulli trials of length n trials;
- p – probability of «success» in the Bernoulli test.

The meaning of the binomial law is to determine the probability of occurrence of exactly «k» successes in a series of Bernoulli trials of length «n» with a given probability of «success» in each such trial equal to «p».

However, from the empirical point of view, we face the opposite task: to make a reliable estimate of the unknown parameter «p» (probability of success) based on the observed number of «successes» in a series of independent but «typical» tests. In this situation, the estimation is based on the maximum likelihood principle. To justify the relevance of applying the maximum likelihood principle for solving the problem, we proceed from the fact that for a large sample the estimates obtained by the maximum likelihood principle are consistent, efficient and asymptotically normal [160].

Estimation of the unknown parameter of the probability of success «p» with application of the maximum likelihood principle for some series of tests, part of values in which is equal to 1 («success») and part to 0 («failure»), was as follows (Formula 3):

Where k is the number of «successes» (value 1)in a series of «n» trials.

Тогда:

$$P(p) = C_n^k \cdot p^k (1-p)^{n-k} \quad (3)$$

According to the maximum likelihood principle procedure, the logarithm of the likelihood function has the form (Formula 4):

$$LL(p) = log\, log\, [P(p)] = log(C_n^k) + k \cdot log\, log\, (p) + (n-k) \cdot log(1-p) \quad (4)$$

Taking the first derivative of this function at «p» and equating it to zero yields:

$$LL'(p) = \frac{k}{p} - \frac{n-k}{1-p} = 0.$$

From the above relation we obtain, $\hat{p}_{\text{ММП}} = \frac{k}{n}$. This means that an estimate of the probability of «success» in a series of «n» Bernoulli trials is the fraction of «successes» that fall out. In our case $\hat{p} = 0{,}0353$.

Once the MMP estimate of the probability of success is obtained$\hat{p} = \frac{k}{n}$, for it, taking into account the properties of asymptotic normality and the following formal requirements [160]:

- $n \cdot p > 5$;
- $n \cdot (1-p) > 5$;

The boundaries of the standard 95% confidence interval were calculated using the following formula:

$$CI = p \pm z_{\alpha/2} \cdot \sqrt{\frac{p \cdot (1-p)}{n}}$$

Where $z_{\alpha/2}$ – the corresponding critical value for the significance level (equal to 5%) from the standard normal law. In this case $z_{\alpha/2} = 1{,}96$.

Accordingly, having obtained the boundaries of the 95% confidence interval for the probability, we can estimate whether the value of the probability being tested (the probability of COVID-19 disease) falls within the boundaries of this interval [160].

Thus, to test statistical hypotheses, we applied parametric and nonparametric methods of analysis suitable for specific metrics and sample size, taking into account all factors that could affect the results of the study. Synthesis of the obtained data was performed at stage 4 of the study, thanks to which the main statements, conclusions and justification of the main organizational measures for the formation of collective immunity in different types of hospitals in order to prevent the spread of COVID-19 were proved.

Chapter 3 CHARACTERISTICS OF COVID-19 MORBIDITY AMONG MEDICAL PERSONNEL OF HOSPITALS IN THE PRE-VACCINE PERIOD, ORGANIZATIONAL ANTI-EPIDEMIC MEASURES

3.1 Dynamics of COVID-19 morbidity in the population of St. Petersburg and in medical personnel of hospitals in the pre-vaccination period

Epidemic rise of morbidity on the territory of the Russian Federation began with megacities (Moscow, St. Petersburg), where the most intensive spread of SARS CoV-2 virus was also registered (V. G. Akimkin, A. Y. Popova et al.). V. G. Akimkini coauthors in studying the manifestations of the epidemic process COVID-19 for 2020-2021 distinguish four periods of morbidity rise. In I epidemic rise the peak of morbidity occurred on 04.05.2020 - 11.05.2020, in II - on 24.12.2020, in III - on 12.07.2021 - 18.07.2021, in IV rise - on 01.11.2021 - 07.11.2021. In the St. Petersburg hospitals we studied, there are three pronounced peaks of morbidity during the above period: May 2020 (the incidence rate in the «covid» hospital was 102.4 per 1000 people, in the general hospital - 84.9 per 1000 people), December 2020 (96.0 per 1000 people and 19.9 per 1000 people, respectively) and June-July 2021 (34.5 per 1000 people and 6.9 per 1000 people) (Figure 1).

The course of the COVID-19 epidemic process in hospitals is certainly related to morbidity in the general population and administrative management measures in the general population [32].

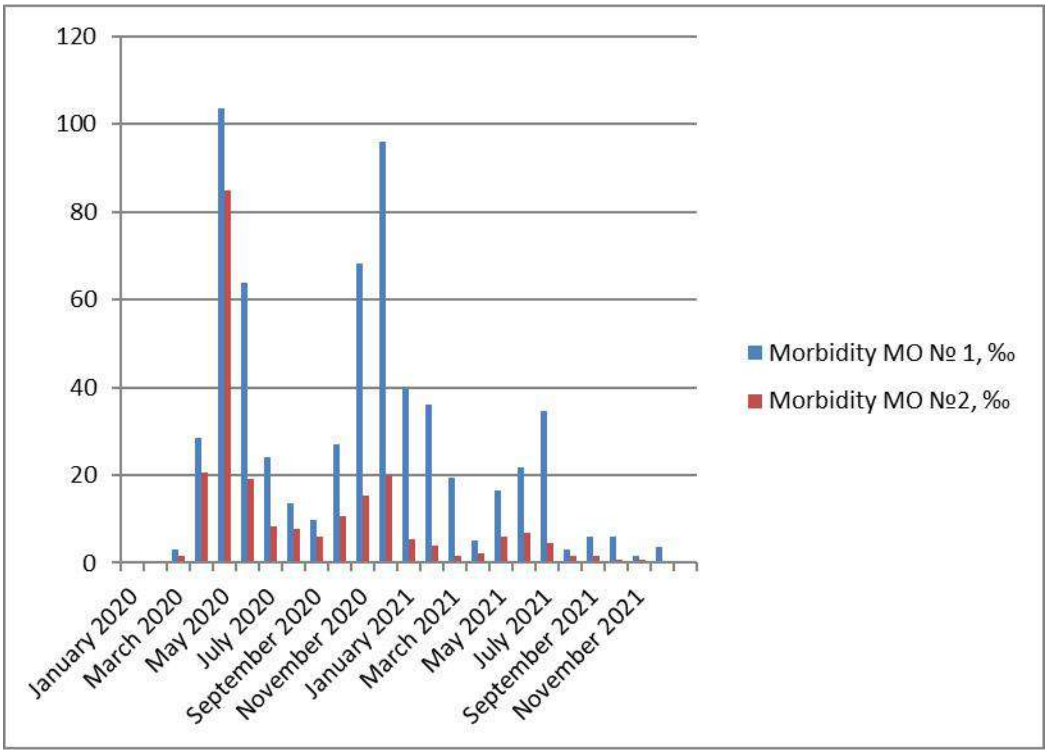


Figure 1 - Dynamics of morbidity of medical workers in 2020-2021.

Since the beginning of the pandemic, health care workers have become the primary risk group for COVID-19 infection. This fact is associated with a high number of contacts with patients with a confirmed diagnosis of COVID-19, as well as with asymptomatic patients in the course of their work; prolonged viral load, non-compliance with the requirements of sanitary and anti-epidemic regime in medical organizations or neglect of them; lack of personal protective equipment and their improper use; lack of specific prophylaxis measures during the period of the beginning of growth and active spread of COVID-19.

In the «covid» hospital (observation group No. 1) after re-profiling as an infectious disease hospital from 11.11.2020, 25 infectious disease departments with 660 beds, including 41 intensive care beds, 45 beds in three intensive care units were deployed.

Among the organizational and re-planning measures in the pre-vaccination period in order to prevent the spread of COVID-19 among the staff and patients, various organizational measures were applied in this hospital: re-planning measures, creation of a «red» zone, staff training, use of personal protective equipment, enhanced disinfection regime.

In the conditions of COVID-19 spread (pre-vaccination period) the hospital was twice reassigned to receive patients with COVID-19 in 2020. From 29.03.2020 to 24.07.2020 and from 11.11.2020 by the Order of the Health Care Committee from 05.11.2020 № 802-r the hospital was reassigned to receive and provide medical care to COVID-19 patients and persons with suspected COVID-19.

During re-profiling, mandatory training for all groups of medical workers was conducted, including using educational modules posted on the Portal of Continuing Medical and Pharmaceutical Education of the Ministry of Health of Russia, introductory and ongoing briefings for employees on the prevention of COVID-19 spread, hand hygiene, anti-epidemic measures, use of personal protective equipment and personal prophylaxis measures, with credits signed by each employee..

Systematic control of compliance with sanitary and epidemic regime, hand hygiene rules and use of personal protective equipment within the framework of production control was carried out.

Medical and service personnel are provided with working clothes and use personal protective equipment when providing medical care: suits, shoe covers, gloves, masks, respirators. The hospital has a minimum three-week supply of personal protective equipment, antiseptics and disinfectants.

The institution organized daily thermometry at the entrance to the institution and at the end of the working day in the departments, interviewing staff before starting work. Staff with symptoms of acute respiratory infections (fever, cough, runny nose) were not allowed to work.

One of the most important measures at the admission of patients to the hospital is triage in the admission department, with the allocation of separate flows of patients with a confirmed diagnosis of COVID-19 and patients with acute respiratory viral infections, influenza and nosocomial pneumonia, taking into account the severity of the clinical course of the disease and the need for intensive care and resuscitation:

- Extremely severe and critically ill patients on ventilator are immediately escorted to intensive care units.

- Severe patients are evaluated in conjunction with the anesthesiologist/resuscitator on duty to determine further tactics.

- Patients of moderate severity are seen in the exam rooms of the emergency room.

- Patients in satisfactory condition after examination and additional examination are referred to outpatient treatment.

The maximum utilization of the emergency room was 10 people if all sanitary and anti-epidemic norms were observed. Throughput capacity of the reception department was 5 - 7 patients per hour:

- processing time of medical record of an inpatient – 5 - 10 minutes;

- time for examination of one patient and parallel blood collection for tests, smears (if indicated) – 20 - 30 minutes;

- clinical blood test turnaround time - 20 minutes;

- time for chest radiography - 20 minutes.

After completion of all necessary therapeutic and diagnostic measures in the emergency room and registration of medical documentation, patients are transported to inpatient units.

In inpatient wards, a one-stage ward occupancy principle is followed whenever possible, with patients divided according to the presence or absence of a positive sample for COVID-19.

In the emergency room, patients arriving without a positive smear are sampled for PCR in 100% of cases. Sampling for bacteriological studies for etiological interpretation of pathogens of out-of-hospital pneumonia is carried out in the following departments.

Patients who are negative for COVID-19 or diagnosed with community-acquired pneumonia should have a sputum or pharyngeal swab submitted within 24 hours for microbiologic culture followed by antibiotic sensitivity testing. Stuart's transport medium (for sputum and deep pharyngeal swabs for suspected community-acquired pneumonia) is available 24 hours a day in the emergency laboratory, and material in this medium can be stored at room temperature for 72 hours. Bronchoalveolar lavage examination was performed only when indicated because it is an invasive procedure that increases the risk of nosocomial infections. Pharyngeal swab seeding is recommended in patients with difficult sputum discharge, as forced cough is prohibited in suspected COVID-19 and in elderly patients, as it can lead to thromboembolism of small and large branches of the pulmonary artery.

Current disinfection was performed daily in all rooms of the hospital by specially allocated teams of medical personnel not involved in the treatment of patients. Current disinfection was carried out twice a day by irrigation with disinfectant solution in all common rooms. Indicator test strips were used to control the concentration of the applied disinfectant working solution, disinfectant solution was prepared centrally for all departments of the hospital.

After vacating the premises, final disinfection is carried out. For final disinfection, aerosol generators «Ultrasprayers» with consumable disinfectant «Desargent» (ready-made solution containing 6% hydrogen peroxide and silver salts as an active ingredient) are used

Every day the premises of risk groups (admission department, intensive care units, intensive care rooms of X-ray and CT examinations) are treated with the help of pulsed ultraviolet units of «Alpha» series, designed for prompt disinfection of air and surfaces of premises from all types of hospital microflora, including pathogens of viral diseases.

Laboratory quality control of final disinfection in the premises during the reprofiling of the hospital after treatment of patients with confirmed diagnosis of COVID-19 was carried out by specialists of the Center for Hygiene and Epidemiology in St. Petersburg. Microbiological studies of environmental objects for conditionally pathogenic microflora in intensive care units were also conducted. The isolated microflora is tested for sensitivity to antibiotics, as well as to disinfectants according to epidemiological indications.

If strains of microorganisms resistant to disinfectants used in the hospital are identified, they are rotated to disinfectants based on other groups of active ingredients. For example, in December 2020, a study of the effectiveness of disinfectant «Dismozone R Plus» against nosocomial pathogens Acinetobacter baumannii and Klebsiella pneumonia was conducted. As a result, an effective concentration of disinfectant was selected.

Changes have also affected the system of waste management, which is generated in the hospital. Since the active dissemination of COVID-19 and the re-profiling of the hospital, all wastes of the institution began to be divided into two groups, the group «class B wastes» disappeared:

- Class A waste is waste from the «green zone» - administration departments, technical services building, items prepared for write-off (furniture, rags, out-of-date equipment, transportation containers of storage facilities, etc.).

- Class B waste is waste from departments involved in the treatment and diagnosis of patients with COVID-19.

According to the main provisions of sanitary and epidemiological rules SR 3.1.3597-20 «Prevention of new coronavirus infection (COVID-19)» SARS-CoV-2 virus is classified as pathogenicity group II. In this regard, the waste generated in medical institutions as a result of medical activities in the provision of medical care to patients infected with SARS-CoV-2 refers to medical waste of class B, including in departments of radial diagnostics. This type of medical waste is subject to mandatory thermal disinfection using equipment with all necessary documentation confirming the possibility of handling class B medical waste. This type of waste without hardware disinfection with the use of physical methods is prohibited for removal from the medical organization (Sanitary Regulations 2.1.3684-21 «Sanitary and Epidemiological Requirements for the maintenance of urban and rural settlements, water bodies, drinking water and drinking water supply, air, soil, living quarters, operation of industrial and public premises, organization and conduct of sanitary and anti-epidemic (preventive) measures»). For removal from the medical organization, disposable containers (bags, tanks) are marked with the inscription «Waste. Class B» with the name of the organization, subdivision, date of disinfection and name of the person responsible for waste collection and disinfection, as well as the date of final packaging of medical wastes.

For this class of waste, primary thermal decontamination with shredding is carried out at two units - NEWSTER10 (waste from «red zone» departments), MEDISTER160 (bacteriological and PCR laboratories) with transfer of this waste to a specialized organization for further autoclaving.

Continuous control of personnel morbidity was established. Laboratory examination of personnel to detect SARS-CoV-2 virus in the presence of medical indications in accordance with the established procedure, further - once every seven days.

Observation group No. 2 (general hospital) operated as an emergency hospital during the period of active spread. The institution has 1038 beds, a total of 31 treatment and 17 auxiliary departments. The hospital has the following main structural subdivisions: outpatient consultation department, admission department, anesthesiology and reanimation department, operating rooms for emergency and planned care; cardiology departments №1, 2, 3, cardiac reanimation department; intensive care department for patients with acute cerebral circulatory failure, department of surgical treatment of complex heart rhythm disorders and electrocardiostimulation; surgical departments №1, 2, 3, 4; neurosurgical departments №1, 2; department of neurosurgery №1, 2; department of cardiac surgery №1, 2; department of surgical treatment of complex heart rhythm disorders and electrocardiostimulation; medical rehabilitation department, emergency department. In the conditions of the COVID-19 pandemic, the hospital was not reprofiled to receive patients with COVID-19 and continued to provide specialized medical care in all profiles to residents of all districts of the city. As a result of the fact that almost all other hospitals did not accept general medical patients, the load on the hospital was high.

A strict selection of patients was carried out at the admission department. To ensure detailed collection of epidemiologic anamnesis from persons admitted to the institution, reflecting information about the citizen's stay outside the Russian Federation or contact with patients with symptoms not excluding COVID-19, an epidemiologic anamnesis form was developed and is mandatory for filling out.

To exclude COVID-19 entry, thermometry, CT examination, and COVID-19 swabbing were performed for suspected pneumonia and other acute respiratory infections. Patients with out-of-hospital pneumonia suspected of COVID-19 were transferred to other hospitals immediately from the emergency room. However, in many patients, manifestations of this infection were detected only after a certain period of time in departments.

The most frequent admissions with COVID-19 were neurological patients with acute cerebral circulatory failure, cardiologic patients with acute myocardial infarction and patients with other urgent pathology. Every day 200 - 400 patients were admitted to the hospital.

The results of PCR tests for COVID-19 were performed daily in the laboratories of the city. The results of the tests were reported around the clock and immediately sent to the heads of the departments in order to transfer the patient to the infectious disease hospital as soon as possible. This was extremely important for the hospital because of the shortage of inpatient beds, so great efforts were made to transfer the patients.

As of April 2021, a PCR laboratory was opened in the general hospital and thus patient screening became timely.

Isolation rooms were designated in each ward for short-term stay of COVID-19 patients before transfer to an infectious disease hospital.

Emphasis on controlling the health status of medical personnel was carried out by examining staff: in addition to PCR for COVID-19, staff were tested for antibodies to SOVID-19. Laboratory examination of personnel for SARS-CoV-2 virus detection was performed in the presence of medical indications in accordance with the established procedure, further - once every seven days, except for persons with IgG-antibodies to the RBD-fragment of S-protein S-protein of SARS-CoV-2 virus as a result of immunization or a transferred disease.

In order to ensure safe operations and prevent the spread of COVID-19 in the general hospital, in accordance with the current documents of higher organizations of the Federal Service for Supervision of Consumer Rights Protection and Human Welfare bodies, each department has all current orders and regulations, including the following:

1. Standard for safe operation of medical organizations to counter the spread of COVID-19 in St. Petersburg.

2. All versions of the «Interim Guidelines» with signatures in the staff familiarization sheets are kept in the departments, as well as with the doctor-epidemiologist.

3.Orders for the agency have been prepared for all orders, decrees, and directives from higher authorities and are available in the offices for ongoing staff training.

Mandatory staff training was conducted for all groups of medical workers, including using educational modules posted on the Portal of Continuing Medical and Pharmaceutical Education of the Ministry of Health of the Russian Federation, introductory and ongoing briefings for staff on prevention, spread of COVID-19, hand hygiene, anti-epidemic measures, use of personal protective equipment and personal prophylaxis measures, with credits signed by each employee. Systematic control of compliance with the sanitary and epidemic regime, hand hygiene rules and use of personal protective equipment is carried out within the framework of production control.

Medical and service personnel are provided with working clothes and use personal protective equipment when providing medical care. There is a stock of personal protective equipment, antiseptics and disinfectants in the hospital.

The hospital organizes daily thermometry at the entrance to the institution and at the end of the working day in the departments, and interviews with staff before starting work. Personnel with symptoms of acute respiratory infections (fever, cough, runny nose) are not allowed to work and are notified of the need to go to a medical institution. Resumption of admission to work is carried out only in the presence of a certificate of recovery from a medical institution.

The departments have created conditions for staff, visitors and patients to follow the rules of hand hygiene in the departments, with the use of elbow (non-kiste) operated faucets, soap dispensers and skin antiseptics. There are stocks of soap, skin antiseptics for staff and visitors in the amount not less than the estimated need for one month of work.

In order to control the implementation of isolation and disinfection measures in COVID-19-positive patients, a card of anti-epidemic measures has been developed. If several COVID-19 patients are detected in one department, an order is issued to suspend hospitalization in that department.

After the last patient is discharged from the ward, final disinfection is carried out by the disinfection station team. Contact patients and staff are examined, if necessary, and work in the ward resumes. The inpatient unit management purchased equipment for quality disinfection.

In addition to monitoring compliance with the entire set of anti-epidemic measures, when analyzing the incidence of infectious diseases, timely reorganization measures were carried out to organize the treatment and diagnostic process in the hospital in a complex epidemiological situation, optimize the use of bed capacity, reduce the duration of hospitalization (reducing the average bed-day). Temporary unification of clinical departments in the fields of traumatology, cardiology, neurology, therapy, neurosurgery was carried out.

Analysis of the incidence of COVID-19 in medical personnel in the studied hospitals showed that zero case of the disease was recorded in March 2020. This was a 43-year-old woman, an employee of the intensive care ward of the thoracic surgery department of the «covid» hospital. A case in this study was considered to be a laboratory-confirmed diagnosis of U07.1 Coronavirus infection COVID-19 (virus identified by real-time PCR).

In the covid hospital, 821 health facility staff members were overdosed between January 2020 and December 2021, representing 22.70% of the total. The incidence among males and females was at the same level (62.20% of males overdosed, 61.40% of females overdosed, x-square = 0.56, $p>0.05$).

When analyzing the morbidity of employees depending on the level of position, it was found that among senior medical staff (doctors), 61.20% of employees were overdosed, middle medical staff - 67.90% of employees, and among junior medical staff - 49.60% of employees.

In the general hospital, 297 staff members had COVID-19 during the above period, which is 63.20% of the total number. The incidence among males and females is at the same level (24.8% of males, 22.20% of females, x-square = 0.77, $p>0.05$).

In order to assess the COVID-19 morbidity levels of hospital medical workers, descriptive analysis of the studied data was performed, first of all, for the asymmetry of their distribution. The asymmetry (curvature) of the distribution was substantiated using the statistical test.

From the basic analysis of descriptive statistics, it can be seen that the median incidence values in the two study samples (20.60 and 5.75) are different (Table 5).

Table 5 – Descriptive morbidity statistics

	Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
Observation group No. 1	1,50	6,00	20,60	28,65	35,62	103,40
Observation group No. 2	0,00	1,50	5,75	10,43	10,12	84,90

When plotting the graphs, we can clearly see that the morbidity distributions for the two hospitals have a right-handed curvature (Figures 2, 3).

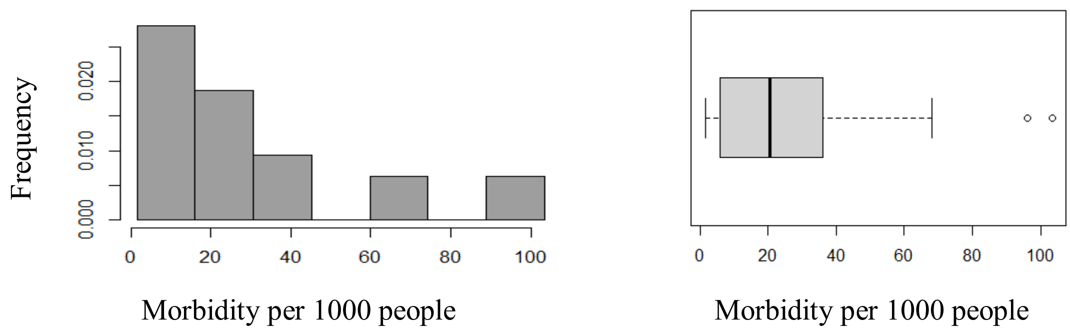


Figure 2 - Distribution plots of the baseline incidence of COVID-19 in the «covid» hospital per 1,000 people

Both graphs clearly show that the distribution of morbidity really has a rightward curvature. To confirm this conclusion, we conducted a formal test for the significance of the curvature of the distribution, which showed that the distribution under consideration is asymmetric, in this case it does have a positive (right-handed) curvature (T = 1.351, p = 0.004).

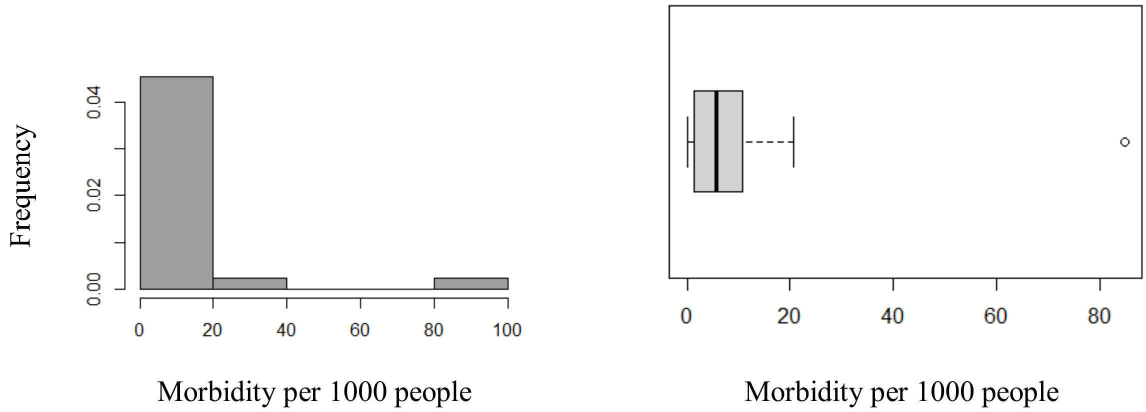


Figure 3 - Distribution plots of baseline COVID-19 incidence in general hospitalization per 1000 people

Both graphs similarly indicate that the distribution of morbidity does have a rightward curvature. This fact was confirmed by conducting a formal test for the significance of the curvature of the distribution (T = 3.506, p-value < 2.2e-16).

The calculated values of the slope (curvature) of the two distributions (1.35 for the «covid» hospital and 3.50 for the general hospital) are moderate, which means that the Wilcoxon test is justified in this case.

The Wilcoxon test is conducted at the traditional 5% significance level. The alternative hypothesis was that the true median value of morbidity in the general hospital is lower than the same indicator in the «covid» hospital. Indeed, the median values of morbidity in the two hospitals under consideration are statistically significantly different (W = 120.00, p = 0.002)

Thus, the morbidity of medical workers in the general hospital in the median value is significantly lower than the morbidity of workers in the «covid» hospital in the pre-vaccination period. This fact is probably due to the fact that medical workers of the «covid» hospital primarily provided care to patients with confirmed/presumptive diagnosis of COVID-19, which increased the significant level of viral load on the staff.

When compared with the city-wide incidence rate for St. Petersburg in the pre-vaccine period (2020-2021), the basic analysis of descriptive statistics shows that the median value of the incidence rate in the population was 1.75, in the covid hospital - 20.60 and in the general hospital - 5.75. Thus, the median values are different in the three samples studied. The distribution of citywide morbidity data has a right-handed curvature (Figure 4).

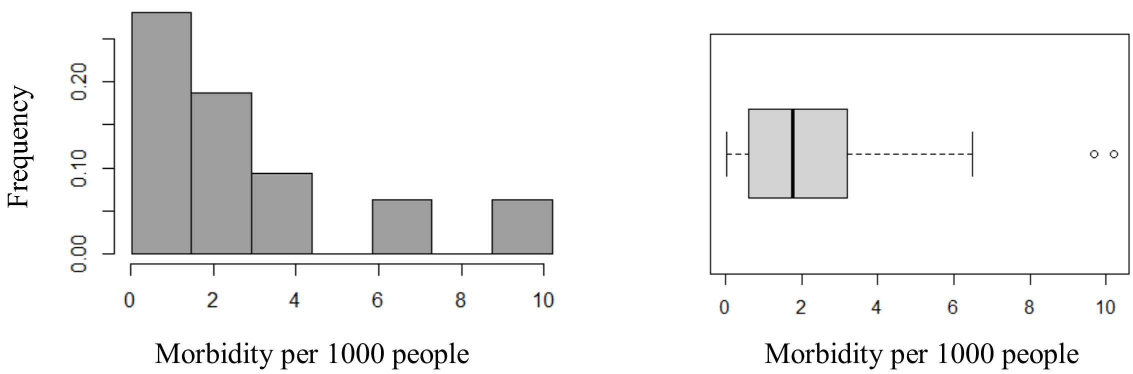


Figure 4 - Distribution plots of baseline citywide incidence rates in 2020-2021 per 10,000 people.

When conducting a formal test for the significance of the curvature of the distribution at the 5% significance level (T = 1.451, p-value = 0.002), we found that the distribution under consideration is asymmetric, in this case it does have positive (right-handed) curvature. The calculated value of the curvature of the distribution of citywide data (1.45) is moderate, and thus justifies the need to apply the Wilcoxon test.

When the Wilcoxon test was applied to compare the median values of morbidity in the «covid» hospital and citywide (W = 439.50, p-value = 1.872e-06) the median value of morbidity of the covid hospital is significantly higher than the similar value of the citywide indicator. When this index is analyzed with the median value of general hospital (W = 346.50, p-value = 0.007), it is proved that the median value of morbidity of general hospital is significantly higher than the similar value of citywide index (Figure 5).

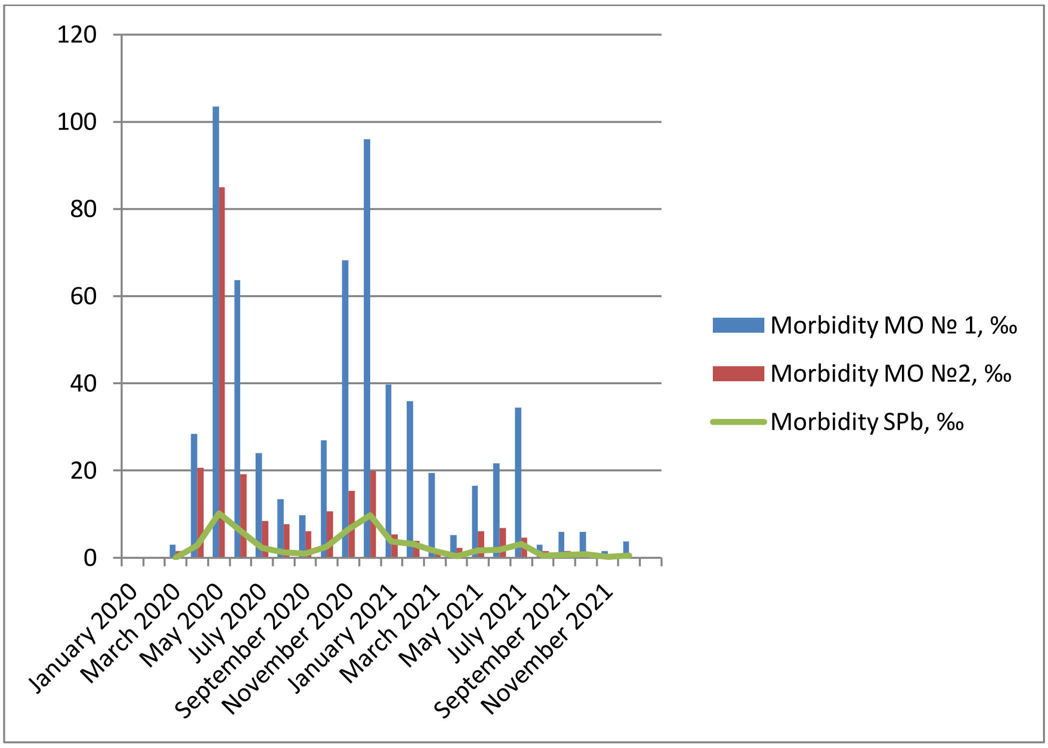


Figure 5 - Dynamics of morbidity among medical workers in hospitals and residents of St. Petersburg

Thus, the morbidity of health workers in multidisciplinary hospitals in the median value is significantly higher than the city-wide morbidity rate of the general population in the pre-vaccinal period (2020-2021), however, in the «covid» hospital the level of staff morbidity is higher than in the general hospital (Me = 20.60; Me = 5.75) and is respectively 62.20% (men), 61.40% (women) - x-square = 0.56, $p > 0.05$; and 24.80% (men) - 22.20% (women) - x-square = 0.77, $p > 0.05$). At the same time, the dynamics of morbidity has similar trends: peaks of morbidity were observed in May 2020, December 2020, and June - July 2021.

3.2 Dynamics of the process of vaccination of medical personnel in hospitals and the structure of collective immunity of employees at different phases of the epidemic process development

The active spread of COVID-19 and the multiplied burden on health care systems worldwide required the rapid development and implementation of effective anti-epidemic measures. Creation of collective immunity of the population through immunization is considered by scientists as the most effective, safe and economically feasible measure of COVID-19 prevention and a way to prevent further spread of the disease. The development of effective vaccines in a short period of time has become an urgent task.

On 11.08.2020, the world's first vaccine «Gam-KOVID-Vac» - a combined vector vaccine for the prevention of coronavirus infection caused by SARS-CoV-2 virus («Sputnik V») was registered by

N.F. Gamaleya Research Center for Ecological Medicine of the Ministry of Health of Russia. Ministry of Health of Russia. This vaccine is two-component, the active substance of the first component - adenovirus particles of 26 serotype, containing the gene of protein S of SARS-CoV-2 virus, the second - adenovirus particles of 5 serotype, containing the gene of protein S of SARS-CoV-2 virus. The recommended interval between administration of the second component is 21 days. This drug is the most widely used and actively used in all regions of the Russian Federation [94].

One of the first contingents of mass vaccination, according to Sanitary Regulations 3.1.3597-20 «Prevention of new coronavirus infection (COVID-19)», were certain professional groups, where medical workers were of particular importance, in order to strengthen collective immunity. In the studied hospitals, employees started to be vaccinated from November 2020 (Figure 6).

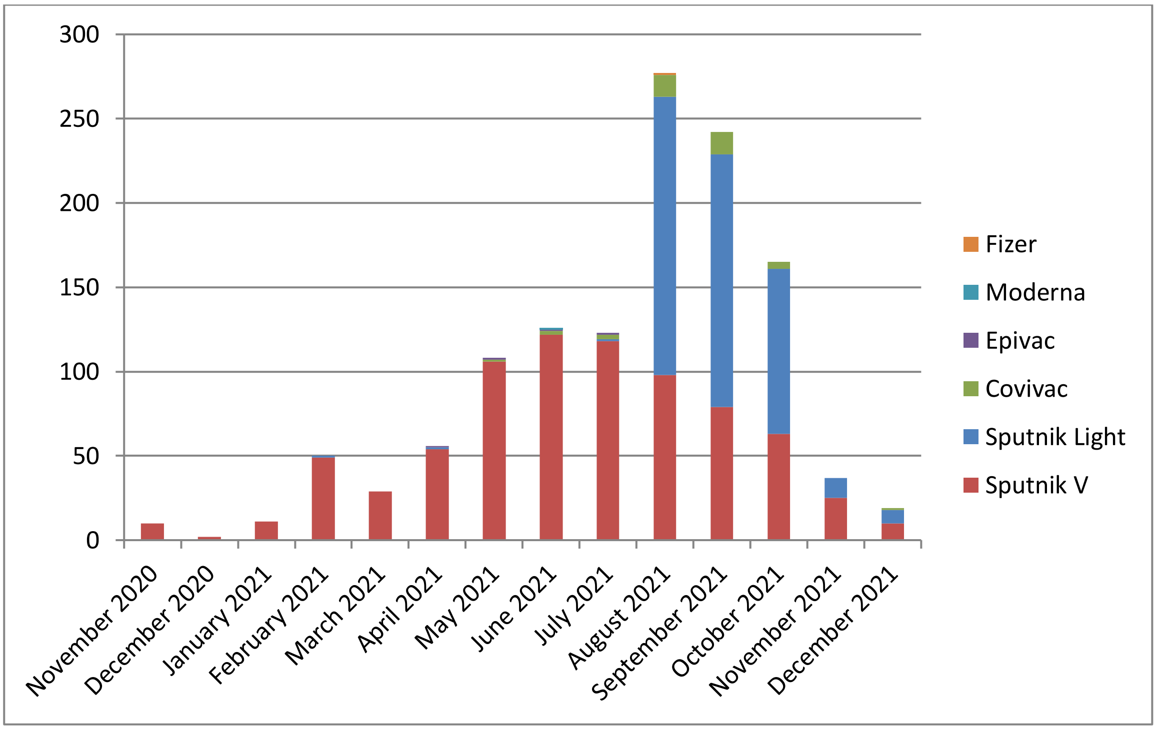


Figure 6 - Vaccination dynamics of the employees of the «covid» hospital and general hospital from November 2020 to December 2021 (sheet 1 of 2)

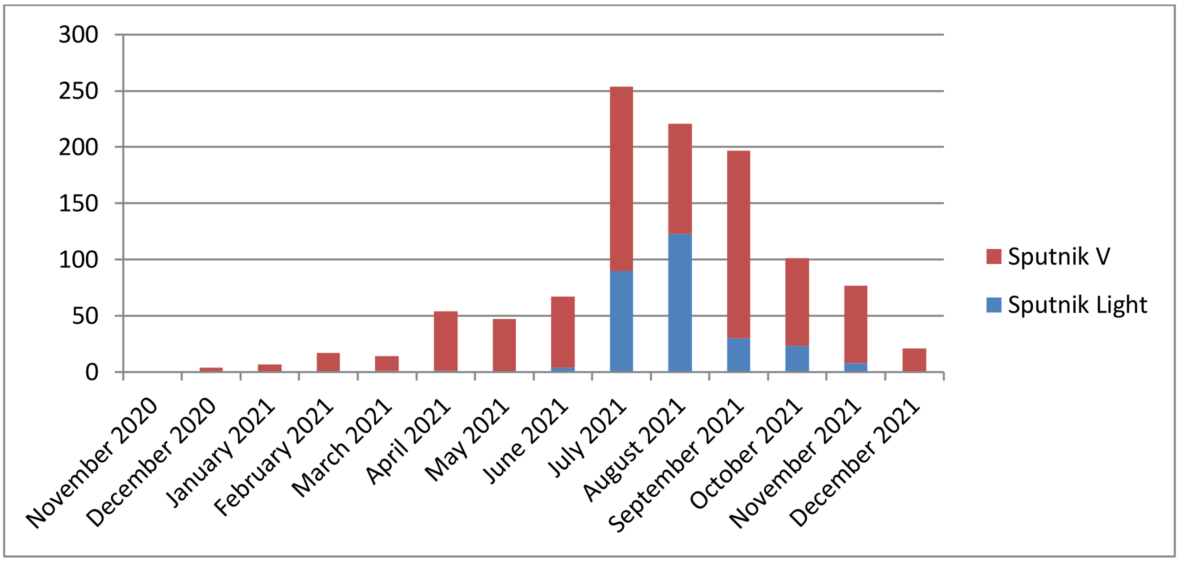


Figure 6 (sheet 1 of 2)

From 18.01.2021 in the Russian Federation is carried out mass vaccination of the population against COVID-19. According to the Order of the Ministry of Health of the Russian Federation from 06.12.2021 № 1122n «On approval of the national calendar of preventive vaccinations, the calendar of preventive vaccinations for epidemic indications and the order of preventive vaccinations» vaccination against COVID-19 is included in the national calendar of preventive vaccinations for epidemic indications. It also defines categories of citizens with priority in receiving COVID-19 vaccine, including employees of medical institutions.

For the period November 2020 through December 2021, the estimated average proportion vaccinated in the «covid» inpatient population was 0.94. 94.08% of the total workforce at this hospital is vaccinated. The calculated mean value of the proportion immunized in the general hospital was 0.82. 82.71% of the total number of employees in this hospital are immunized (Table 6).

Table 6 - Number of vaccinated health workers as of December 2021, persons.

	Observation group No. 1, number of people	Observation group No. 2, number of people
Gam-Covid-Wak	776	801
Sputnik Light	436	280
Covivvac	37	-
Moderna/Fizer/EpiVac	6	-
Medical withdrawal	4	44
Not immunized	75	182

The estimated proportion of employees vaccinated with Sputnik V among all those vaccinated in the covid hospital was 61.83%. The calculated value of the proportion of staff vaccinated with other vaccines among all vaccinated in the covid hospital was 38.17%. Based on a test of equality of proportions.

(X-squared = 139.63, df = 1.00, p-value < 2.2e-16) the calculated proportion vaccinated with two-component Sputnik V in the covid hospital is statistically significantly higher than the calculated proportion vaccinated with other immunobiological medicines.

A similar test was performed on the data of general hospital. The calculated value of the share of medical workers vaccinated with two-component Sputnik V ("Gam-Covid-Vac") among all vaccinated in the general hospital is 74.10%. The estimated value of the share of employees vaccinated with other vaccines among all those vaccinated in the «covid» hospital is 25.90%.

The calculated proportion vaccinated with the two-component SputnikV, in the general hospital was statistically significantly greater than the calculated proportion vaccinated in this hospital (X-squared = 500.28, df = 1.00, p-value< 2.2e-16).

Thus, the majority of health care workers in both hospitals were vaccinated with Sputnik V (double vaccination) (Figure 7).

Observation group No. 1

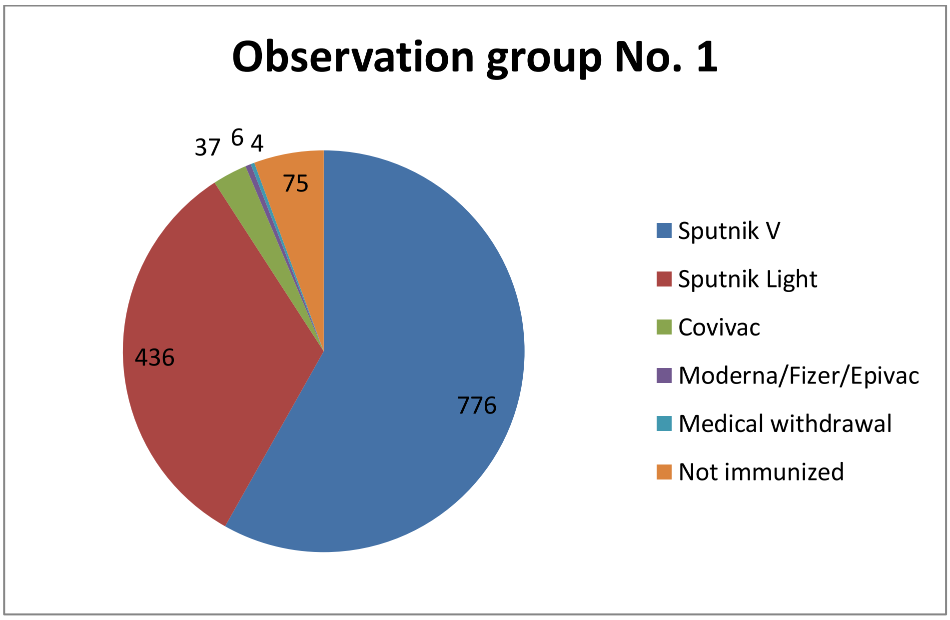


Figure 7 - Number of medical staff vaccinated with different immunobiological medicines against COVID-19, persons (sheet 1 of 2)

Observation group No. 2

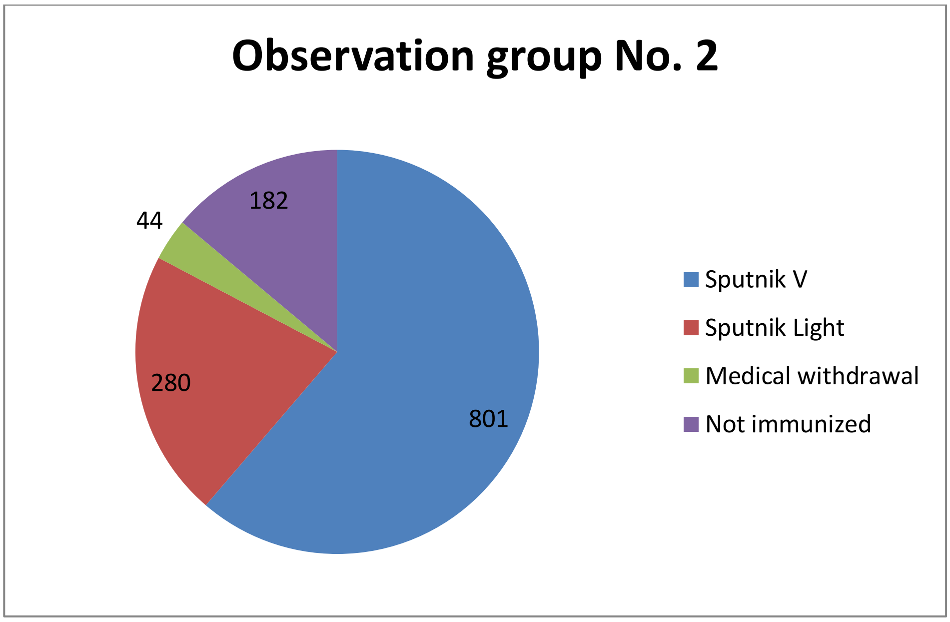


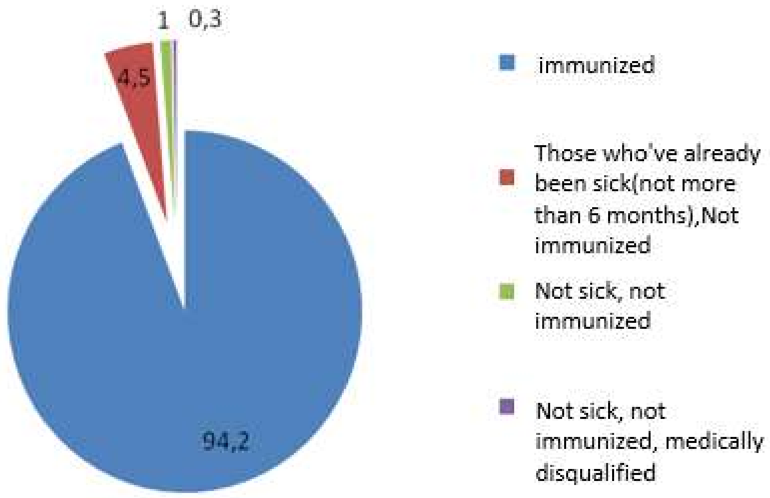
Figure 7 (sheet 2 of 2)

To compare the number of vaccinated individuals in the two hospitals, we performed a test of equality of proportions at the 5% level of significance (X-squared = 82.433, df = 1.00, p-value < 2.2e-16). The calculated proportion vaccinated in the «covid» hospital was statistically significantly greater than the calculated proportion vaccinated in the general hospital, which explains the differences in the structure of collective immunity in these institutions.

By December 2021, the structure of collective immunity against COVID-19 among employees of multidisciplinary hospitals consisted of the following groups: 1) those who were not sick and unvaccinated; 2) those who were overexposed and unvaccinated (no more than six months had passed since the disease); 3) those who were not sick and unvaccinated and had a permanent medical withdrawal; 4) those who were vaccinated.

The structure of collective immunity in both hospitals had similar trends when formed at different stages of the epidemic process. During the period of active spread of COVID-19 and the beginning of vaccination in both hospitals, the groups of overvaccinated people prevailed. In the late postvaccination period, the structure of collective immunity had the following structure (Figure 8).

Observation group No. 1



Observation group No. 2

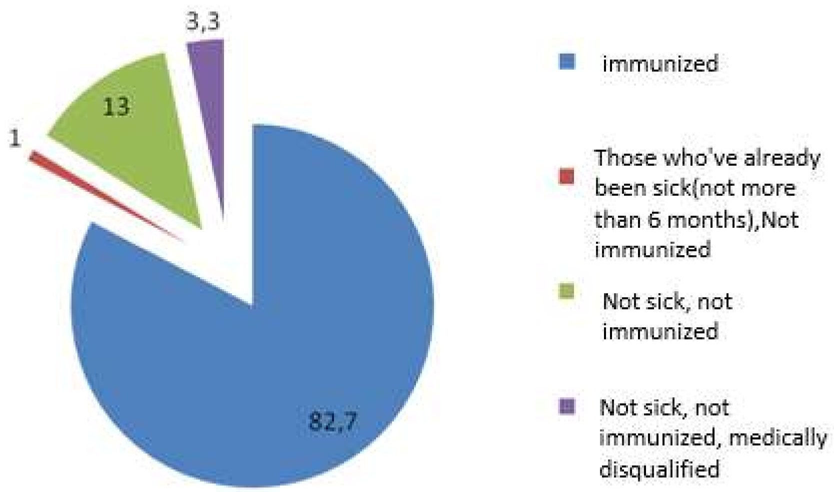


Figure 8 - Structure of collective immunity of employees of «covid» hospital and general hospital, %

Collective immunity is one of the effective means of containing the spread of COVID-19. It is created by spreading the disease among the population. This creates a reservoir of individuals who are immune to re-infection (passive, natural way) and immunizes the population (active, artificial way). According to researchers, there is no difference in the way the necessary threshold is reached: naturally (COVID-19 survivors) or artificially (vaccinated individuals) [190]. Collective immunity, in turn, has the character of indirect protection. It reduces the incidence of disease and the probability of contact with the pathogen, but susceptible individuals remain at risk of infection. The presence of a broad immune layer among health workers can serve as an effective factor in reducing the rate of spread of the pathogen, so it seems relevant to consider the issues of the duration of preservation of the levels of humoral and cellular immunity and the immunity of personnel to subsequent disease [47].

The number of vaccinated staff in the «covid» hospital was statistically significantly higher than in the general hospital and was (94.20%) vs (82.70%) respectively (X-squared = 82.43, p-value < 2.2e-16), which defines the collective immunity profile of the studied groups.

3.3. Analysis of the relationship between the occurrence of recurrent illness in health care personnel, previous illness and vaccination period

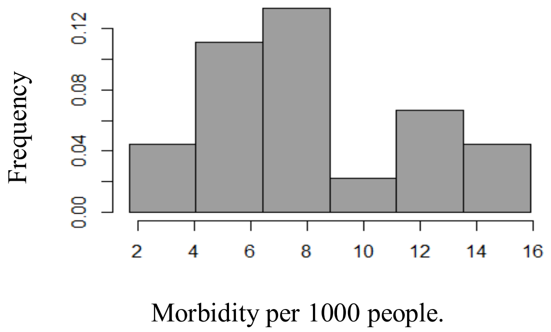
Since the onset of the COVID-19 pandemic, caused by a new infectious agent, the question of immune reconstitution after the disease and, consequently, the possibility of re-infection has been an issue. As early as 2020, reports of patients who tested positive again for SARS-CoV-2 after recovery began to appear. Recurrent positivity and re-infection with SARS-CoV-2 was a major concern. Although the infection induces the production of neutralizing antibodies in more than 90% of cases, it was unclear whether and for how long they provide protection [121, 154].

To assess the association between the occurrence of recurrent illness in the staff of medical organizations, we performed statistical analysis. In the pre-vaccination period, the staff of the «covid» hospital carried the disease from 1 to 3 times. Repeated morbidity before the beginning of immunization of the personnel we recorded only in the «covid» hospital: 19 persons became ill twice during this period, and 1 person - twice. In order to estimate the duration of the period during which the recurrent disease occurs, a descriptive analysis of the data was carried out (Table 7).

Table 7 - Descriptive statistics of recurrent morbidity in the pre-vaccination period

	Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
Observation group No. 1	1,70	5,05	8,10	8,20	11,50	15,90

The estimated mean time to recurrence at this stage of the COVID-19 epidemic is 8.2 months (Figure 9).



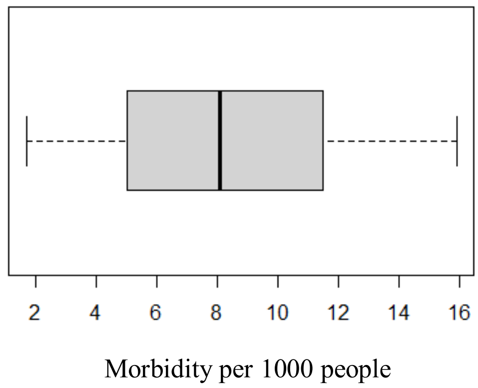


Figure 9 - Analysis of the distribution of recurrent morbidity in a «covid» hospital per 1,000 people

The histogram and "box" diagram show that the distribution is quite symmetrical, without obvious outliers, so we tested the distribution for normality (Shapiro-Wilk test, W = 0.958, p-value = 0.539). The probability value (p-value = 0.53) is greater than the chosen significance level of 0.05, so the null hypothesis of the test is not rejected. The distribution under consideration does not differ from the normal distribution. This gives formal grounds for conducting the subsequent test of the mean value.

In conducting the mean comparison test, we hypothesized that:

H_0: the true average occurrence of recurrent morbidity (in months) is 8;

H_1: the true average occurrence of recurrent morbidity (in months) is not equal to 8.

The calculated mean of the occurrence of recurrent morbidity was not statistically significantly different from 8 (t = 0.227, p-value = 0.822). The test also yielded a confidence interval for the true mean by t-distribution (from 6.30 to 10.10).

Since the data on re-vaccination incidence before vaccination in our sample of 19 individuals, we apply the bootstrapping technique to determine bootstrapped confidence interval bounds for the mean, which in this case is more reliable (Figure 10). The resulting confidence interval - 6.52 to 9.97.

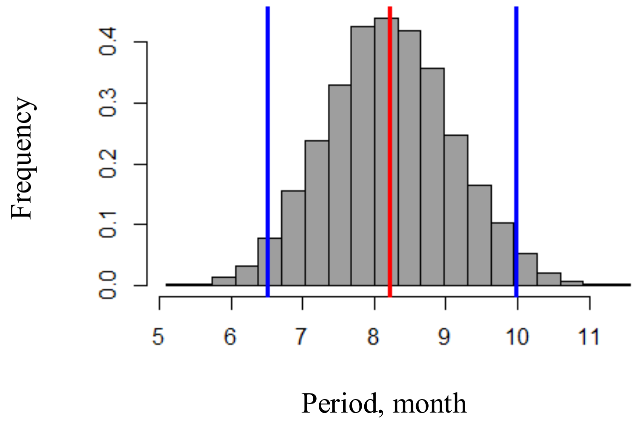


Figure 10 - Bootstrapped confidence interval bounds for the mean value of recurrent morbidity of covid hospital employees

Thus, the period during which recurrent disease occurs in the pre-vaccine period after primary illness is on average 8 months (with a confidence range of 6 to 10 months).

COVID-19 is known to elicit strong T-cell immune responses. Following natural COVID-19 infection, there is a rapid activation of T-cell responses that play a key role in controlling disease progression. T-cell responses, which play a key role in controlling disease progression [162, 163, 179].

According to scientists, due to the high mortality rate of COVID-19, acquiring immunity only after the disease is an insufficient protective measure, other measures such as mass immunization are required [163]. Therefore, it is important to assess the relationship between morbidity and vaccination.

In the postvaccine period, cases of COVID-19 have been reported in both pre-vaccinated and subsequently vaccinated individuals and in vaccinated individuals not previously infected with COVID-19. The incidence rates in these two groups were also estimated by us in both hospitals using contiguity tables, Pearson's chi-square test, test for (non) equality of proportions, and logit regression.

In the statistical treatment of the hypothesis of recrudescence in the «covid» hospitalization, the entire sample was divided into two groups: 1) those who were re-infected and vaccinated; 2) those who were vaccinated and did not get sick before vaccination.

At the first stage, we applied contingency tables, where the fact of disease before vaccination was labeled as 1, absence of disease in the anamnesis - 0 (Table 8).

Table 8 - Number of cases of illnesses of medical workers in the post-vaccination period

Observation group No. 1		The fact of transferred disease after vaccination, people.	
		0	1
Disease before vaccination, persons.	0	412	75 (15,4%)
	1	711	57 (7,42%)

Pearson's x-square test was conducted at the traditional 5% significance level.

H_0: the relationship between binary variables (the fact of illness before vaccination and the fact of illness after vaccination for vaccinated employees of the «covid» hospital) is absent, i.e. equal to zero.;

H_1: the relationship between the binary variables (disease fact before vaccination and disease fact after vaccination for vaccinated covid hospital staff) is present (not equal to zero).

X-squared = 19.318,p-value = 1.106e-05,which is less than the selected significance level of 0.05, so the null hypothesis of the test is rejected. Thus, the relationship between the binary variables is present (statistically significantly different from zero).

From the obtained results we can see that the morbidity rate among the unvaccinated and vaccinated employees of the covid hospital is 15.40%, which is higher than the similar indicator for the diseased and vaccinated, equal to 7.42%. To compare the calculated proportions, we apply the test of (non) equality of proportions (X-squared = 19.318, p-value = 0). The calculated proportion of health workers who were not sick before vaccination but became ill after vaccination is statistically significantly greater than the calculated proportion of those who were sick before vaccination and became ill after vaccination in the covid inpatient facility.

To estimate the recurrent morbidity after vaccination, we applied the simplest logit model. The angular coefficient calculated during data processing is -0.82.To assess the statistical significance of the coefficient, we perform a test at the traditional 5% significance level. The value of the test statistic z = -4.402, p = 1.07e-05, therefore, the null hypothesis was rejected, the calculated angular coefficient -0.82 is statistically significant.

Thus, the fact of having a disease before vaccination does statistically significantly reduce the likelihood of getting sick after vaccination.

Similarly, we estimate information on morbidity in general hospital (Table 9).

Table 9 - Number of cases of illnesses of medical workers in the post-vaccination period

Observation group No. 2		The fact of transferred disease after vaccination, people.	
		0	1
Disease before vaccination, persons.	0	668	146 (17,9%)
	1	239	28 (10,4%)

When assessing the association between the binary variables - sickness fact before vaccination and sickness fact after vaccination for vaccinated general hospital employees (X-squared = 7.718, df = 1.00, p-value = 0.005) - the relationship is present, statistically significant greater than zero. From the results obtained, it can be seen that the incidence of the disease among the unvaccinated before vaccination and vaccinated employees of general hospital is 17.94%, which is greater than the same proportion of 10.49% for those who were sick and vaccinated. The calculated proportion of those who were not sick before vaccination but were sick after vaccination in the general hospital is statistically significantly higher than the calculated proportion of those who were sick before vaccination and those who were sick after vaccination (X-squared = 7.718, p-value = 0).

Similarly, we calculate the angular coefficient and check its statistical significance. Estimate = -0.62, the value of the test statistic z = -2.839, p = 0.004, it is less than the chosen significance level of 0.05, so the null hypothesis of the test is rejected, and the calculated angular coefficient of -0.62 is statistically significant. Thus, the fact of having a disease before vaccination does statistically significantly reduce the probability of getting sick after vaccination.

In both medical organizations, the recurrent morbidity in those who became ill before vaccination and subsequently vaccinated was significantly lower than in those who were vaccinated only, i.e. the fact of illness before vaccination does statistically significantly reduce the probability of becoming ill after immunization. In our opinion, this fact is associated with the presence of cellular immunity in COVID-19 survivors.

The effectiveness of vaccination as an anti-epidemic measure can be assessed by the number of illnesses in the late vaccination period. The number of repeated illnesses after vaccination in vaccinated persons in percentage terms is significantly lower than in unvaccinated persons in both hospitals.

This hypothesis was evaluated by the previously described statistical test of (non)equality of proportions. Information on the number of re-infected patients in both observation groups is presented in Table 10.

Table 10 - Number of diseases in the late vaccination period, persons.

Inpatient hospital	Number of vaccinated/unvaccinated employees	
	0	1
Observation group No. 1	79	1255
Observation group No. 2	226	1081
	Number of recurrent illnesses in unvaccinated employees	
	0	1
Observation group No. 1	35	44
Observation group No. 2	77	149
	Number of recurrent illnesses in vaccinated employees	
	0	1
Observation group No. 1	1123	132
Observation group No. 2	907	174

From the results obtained, it can be seen that the post-vaccination recurrent morbidity among vaccinated covid hospital staff is 10.51%, which is less than the value of the same indicator (recurrent morbidity) for unvaccinated covid hospital staff of 55.69% (Figure 11).

Observation group No. 1

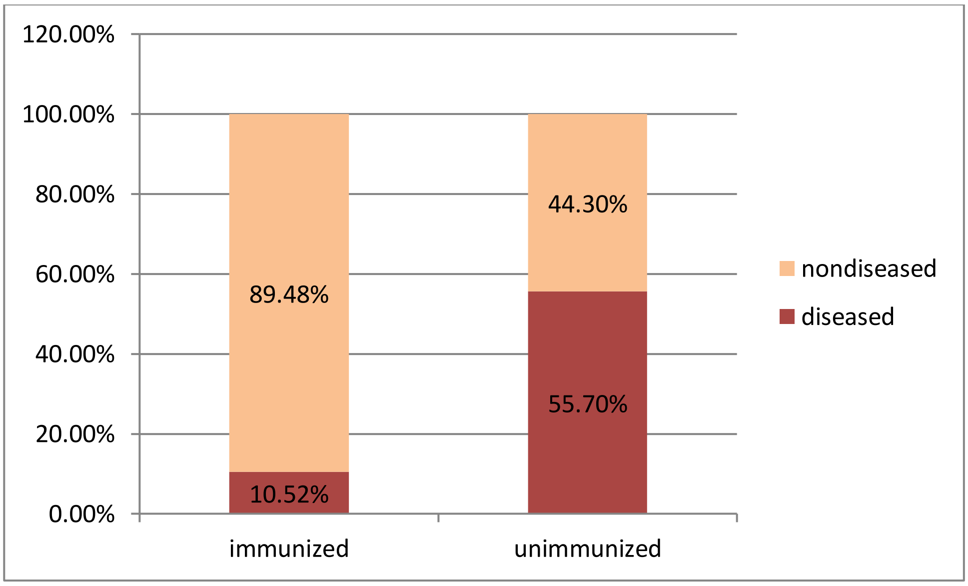


Figure 11 - Morbidity of health care workers in the post-vaccination period (sheet 1 of 2)

Observation group No. 2

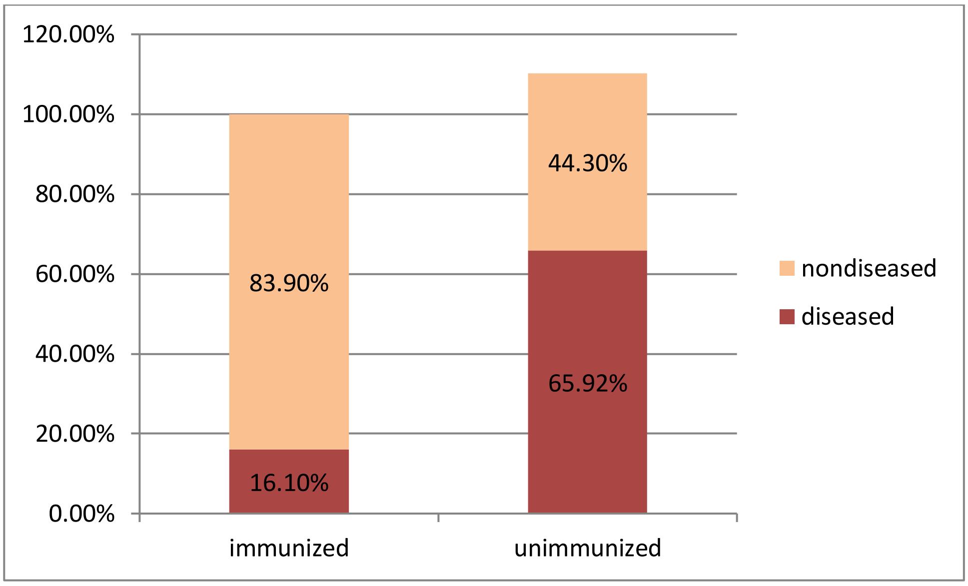


Figure 11 (sheet 2 of 2)

The test of (non)equality of proportions is conducted at the traditional 5% significance level, X-squared = 128.54, p-value < 2.2e-16. The calculated proportion (fraction) of vaccinated covid hospital employees who became re-infected is statistically significantly lower than the calculated proportion (fraction) of unvaccinated covid hospital employees who became re-infected.

Recurrent morbidity after vaccination among vaccinated employees of general hospital is 16.09%, which is less than the value of the same indicator (recurrent morbidity) for unvaccinated employees of this hospital, equal to 65.92%. When the test was performed at the traditional 5% significance level, X-squared = 246.81, df = 1.00, p-value < 2.2e-16. The calculated proportion (fraction) of re-illness in vaccinated general hospital employees who were re-vaccinated was statistically significantly lower than the calculated proportion (fraction)of re-illness in unvaccinated employees at this institution. Recurrent morbidity in the over-vaccinated and vaccinated is significantly lower than in the vaccinated only in both hospitals.

Chapter 4 DYNAMICS OF COLLECTIVE IMMUNITY FORMATION IN EARLY AND LATE POSTVACCINAL PERIODS

4.1Assessment of the relationship between the occurrence of recurrent disease and the level of humoral immunity after vaccination or disease in the prevaccinal, early and late postvaccinal periods

Determining the efficacy and duration of humoral immunity to SARS-CoV-2 is important for management tactics and predicting the course of the COVID-19 pandemic. Evaluation of significant levels of humoral and cellular immunity is a possible way to assess their impact on the incidence of recurrent disease among workers in health care organizations **Error! Reference source not found.**[95].

To assess the results of the organizational and anti-epidemic measures taken, we consider it important to evaluate the hypothesis about the morbidity of health workers in the late vaccine period in two hospitals.

For both inpatient units, those employees who became ill after vaccination were selected. Having calculated the proportions, it is necessary to perform a test of equality of proportions. To confirm the robustness of the obtained results, bootstrapping is performed and the corresponding distribution for the ratio of the proportions is obtained. The bootstrapped confidence interval found is analyzed for inclusion of the value 1.

In the «covid» hospital 132 people out of 1255 vaccinated out of 1255 were re-infected, in the general hospital this ratio is 1081 to 174. From the obtained results we can see that the recurrent morbidity after vaccination among the vaccinated employees of the «covid» hospital is 10.51%, which is less than the value of the similar indicator (recurrent morbidity) for the vaccinated employees of the general hospital, equal to 16.09%. In the test of equality of proportions, the value of test statistic X-squared = 15.38, probability value p-value = 4.374e-05, it is less than the selected significance level of 0.05, so the null hypothesis of the test is rejected. The calculated proportion (proportion) of re-illness of vaccinated employees of covid hospital is statistically significantly less than the calculated proportion (proportion) of re-illness of unvaccinated employees of general hospital.

A bootstrapping technique was applied to check the robustness of the results (Figure 12).

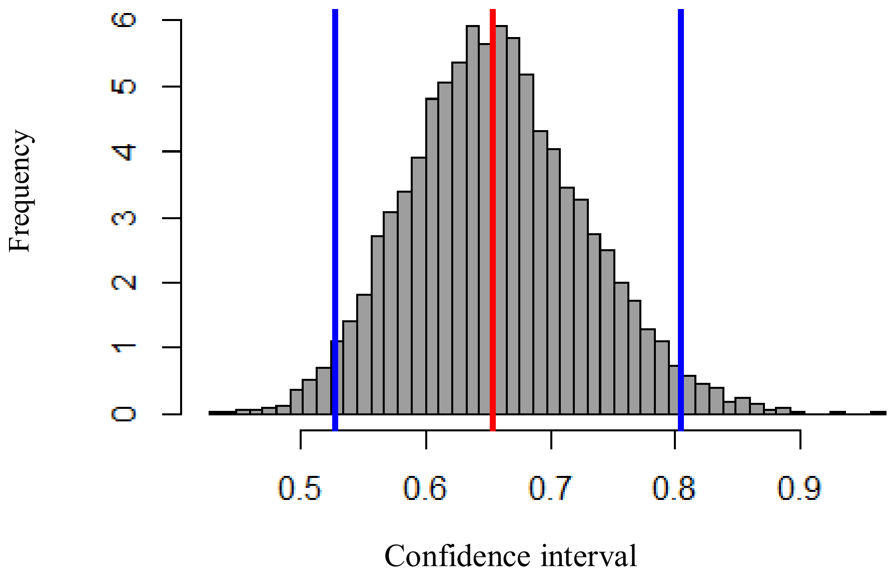


Figure 12 - Bootstrapped 95% confidence interval of recurrent morbidity among vaccinated hospital employees

The 95% confidence interval found using the bootstrapping technique is [0.52; 0.80]. This confidence interval does not contain the value of 1, which means that the recurrent morbidity among vaccinated employees of a «covid» hospital is indeed significantly lower than among vaccinated employees of a general hospital.

Thus, we concluded that the number of recurrent diseases after vaccination in the «covid» hospital in percentage ratio is significantly lower than the number of recurrent diseases in vaccinated employees of the general hospital. This fact may be associated with the application and stricter control of other organizational measures: these are architectural and planning decisions (creation of a «red» zone), the use of personal protective equipment, increased viral load, as well as the attitude to each patient as a «dangerous» patient.

The question of preserving the duration of humoral immunity and determining the period during which the disease does not occur after vaccination is relevant to the evaluation of vaccine prophylaxis as one of the main organizational measures in the hospital during the period of active spread of COVID-19.

To evaluate this hypothesis, we determined the period between the first vaccine administration and recurrent morbidity after vaccination.

We perform descriptive analysis, test the distribution for normality, perform a t-test for the mean, and construct a confidence interval for the true mean. Since the data in the sample has a skewed distribution despite its sufficient volume, we apply the bootstrapping technique to determine bootstrapped confidence interval bounds for the mean and for the median value. We also compared mean and median values for two hospitals.

In a descriptive analysis of COVID-19 incidence data after vaccination in the «covid» hospital, the following descriptive statistics were obtained (Table 11).

Table 11 - Descriptive statistics of COVID-19 incidence after vaccination in the «covid» inpatient setting

	Min.	1st Qu	Median	Mean	3rd Qu.	Max.
Observation group No. 1	0,30	5,00	7,45	7,47	9,35	16,80

Estimated mean time to recurrent illness (before vaccination) after a covid first illness is 7.47 months.

Both graphs (histogram and box plot, Figure 13) show that the distribution is skewed (has right-handed curvature), due to the presence of at least one obvious outlier. This means that it makes sense to formally test for normality.

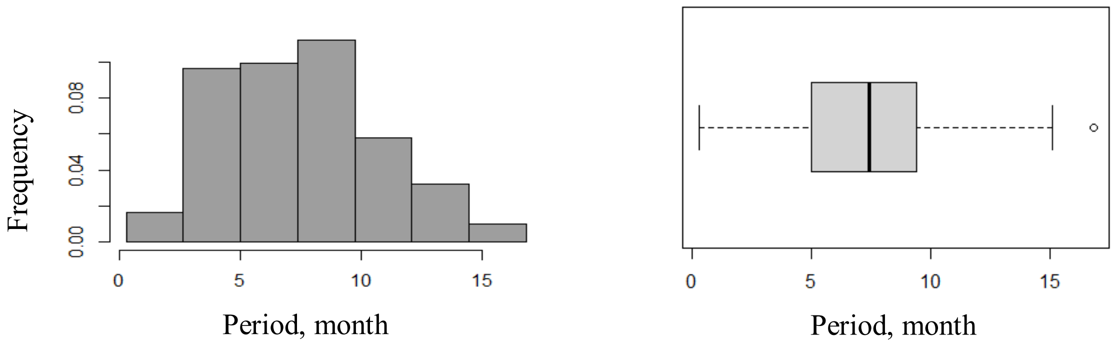


Figure 13 - Distribution graph of baseline morbidity values after vaccination in the «covid» hospital

The normality of distribution is analyzed at the traditional 5% significance level. Hypotheses of the test:

H_0: the distribution of recurrent morbidity does not differ from normal;

H_1: the distribution of recurrent morbidity differs from normal.

The value of the test statistic W = 0.97, the probability value p-value = 0.006, it is less than the chosen significance level of 0.05, so the null hypothesis of the test is rejected. We conclude that the distribution under consideration differs from the normal distribution; accordingly, the results of the t-test of the mean can be valid only asymptotically (i.e., there should be more than 100 observations in the sample - corresponding to our sample).

The test of mean comparison is similarly conducted at the traditional 5% significance level. The value of the test statistic t = -0.09, the probability value is 0.92, it is greater than the selected significance level of 0.05, so the null hypothesis of the test is not rejected. Hence it is concluded that the calculated mean value of occurrence of recurrent morbidity (in months) is not statistically significantly different from 7.5 (months). The test also yielded a confidence interval for the true mean value according to the t-distribution (from 6.92 to 8.02).

We apply the bootstrapping technique to determine bootstrapped confidence interval bounds for the mean and for the median value (Figure 14). When determining the bounds for the mean value, the following data were obtained:

means = 7,46; 2,5% quantile = 6,92; 97,5% quantile = 8,02; medians =7,33, 2,5% quantile = 6,15; 97,5% quantile = 8,2.

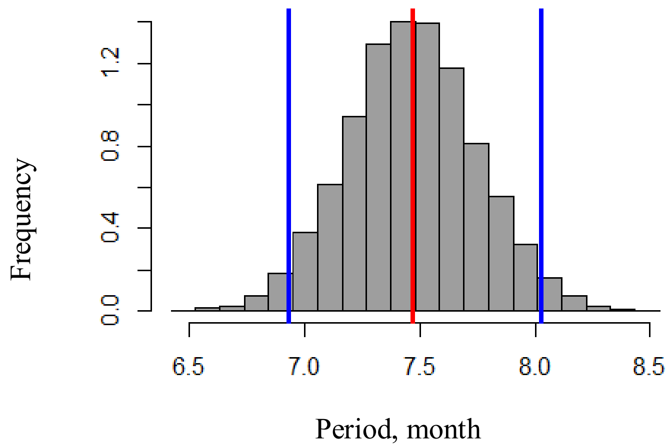


Figure 14 - Bootstrapped confidence interval bounds for mean and median values in the «covid» inpatient setting (sheet 1 of 2)

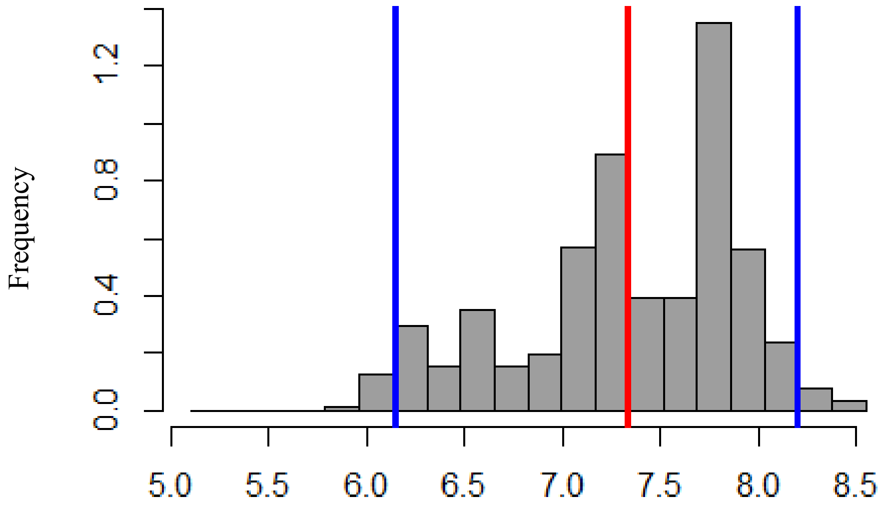


Figure 14 (sheet 2 of 2)

For estimation of morbidity after vaccination in a general hospital, statistical hypothesis testing follows the same algorithm. Descriptive statistics of morbidity in the general hospital during the above period are presented in Table 12.

Table 12 - General descriptive statistics for general hospitalization

	Min.	1st Qu	Median	Mean	3rd Qu.	Max.
Observation group No. 2	0,40	3,80	5,55	5,90	7,47	17,30

Estimated mean time to recurrent illness before vaccination after the first illness is 5.9 months.

Both graphs (histogram and box plot) show that the distribution is skewed, with right-handed curvature due to the presence of at least two obvious outliers (Figure 15). This means that it makes sense to formally test for normality.

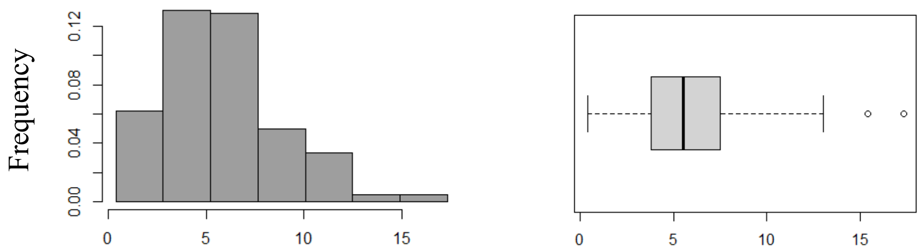


Figure 15 - Distribution graph of baseline morbidity values after vaccination in a general hospital

In order to analyze the normality of the distribution, the Shapiro-Wilk test was performed at the traditional 5% significance level. As a result of the test the following values were obtained: W = 0.95, p-value = 3.004e-05, thus, the distribution under consideration differs from the normal distribution; accordingly, the results of the t-test of the mean can be valid only asymptotically (i.e., there should be more than 100 observations in the sample - similar to the conditions in this hypothesis).

To estimate the true mean, we conduct the mean comparison test. The test is conducted at the traditional 5% significance level. Hypotheses of the test:

: the true average occurrence of recurrent morbidity (in months) is 6;

: the true average occurrence of recurrent morbidity (in months) is not equal to 6.

The value of test statistic t = -0.43,p-value = 0.66. The probability value is greater than the chosen significance level of 0.05, so the null hypothesis of the test is not rejected. We conclude that the calculated mean value of occurrence of recurrent morbidity (in months) is not statistically significantly different from 6.0 (months). The test also yields a confidence interval for the true mean value according to the t-distribution (from 5.45 to 6.34).

To determine bootstrapped confidence interval bounds for the mean and for the median value, we apply the bootstrapping technique (Figure 16). When determining the boundaries of the mean value, the following data were obtained: mean = 5.90, 2.5% quantile = 5.45; 97.5% quantile = 6.35.

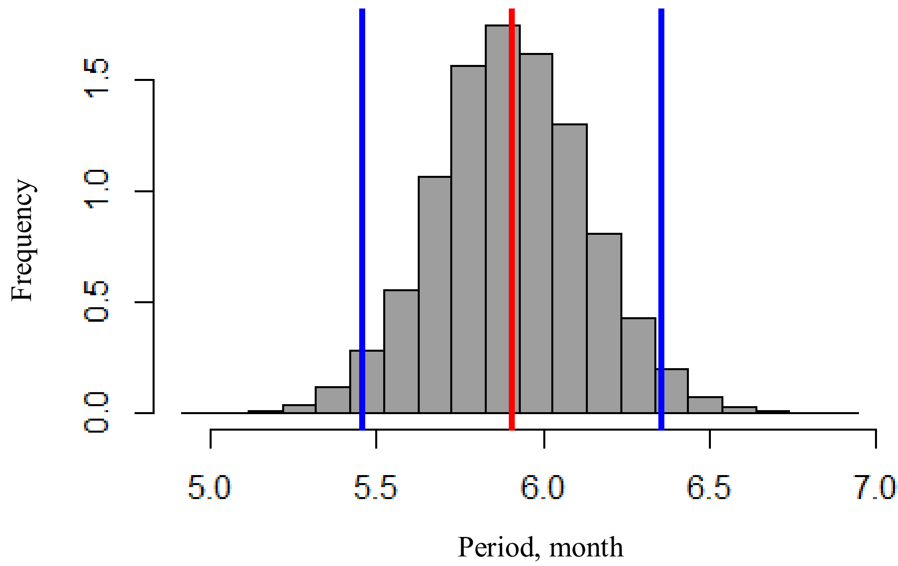


Figure 16 - Bootstrapped confidence interval boundaries
for the mean value in a general hospital

In determining bootstrapped boundaries for medians: medians= 5.51, 2.5% quantile = 5.10; 97.5% quantile = 6.15 (Figure 17).

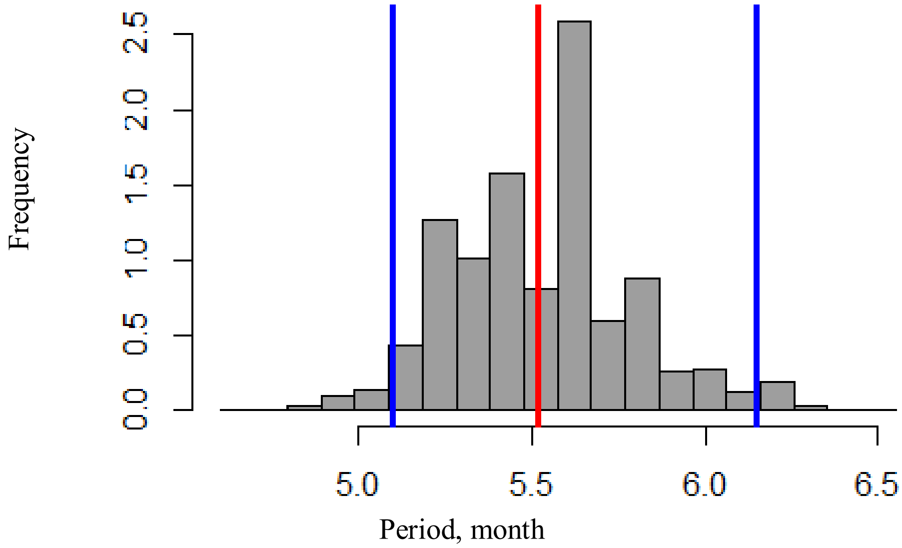


Figure 17 - Bootstrapped confidence interval bounds for the median value in general hospitalization

Since the mean and median values for the two hospitals were different, it seems necessary to conduct formal tests for their comparison. In this case, we applied the test of comparison of averages. The mean value of the period of morbidity after vaccination in the «covid» hospital is 7.4, in the general hospital it is 5.9. These values are obviously different. Nevertheless, it is necessary to conduct a formal test at the traditional 5% significance level. Hypotheses of this test:

H_0: the true mean values of post-vaccination morbidity of the staff of the two hospitals under consideration do not differ from each other;

H_1: the true average value of morbidity in a «covid» hospital is higher than the same indicator in a general hospital.

The value of the test statistic is T = 4.38. If the null hypothesis is valid, this statistic has Student's t-distribution. The probability p-value = 8.247e-06, it is less than the chosen significance level of 0.05, so the null hypothesis of the test is rejected. Thus, the estimated mean values of post-vaccination morbidity of the staff of the two hospitals under consideration differ significantly (statistically significant).

In turn, the median value of the post-vaccination morbidity period in a «covid» hospital is 7.4, while in a general hospital it is 5.5. These values are obviously different. However, it is necessary to conduct a formal test of comparison of medians for the two hospitals - the Wilcoxon test.

The value of test statistic W = 1.48185^{4},probability p-value = 6.807e-06,it is less than the selected significance level of 0.05, so the null hypothesis of the test is rejected. Estimated median values of post-vaccination morbidity of employees of the two hospitals under consideration are significantly (statistically significantly) different.

Thus, mathematical processing of databases established statistically significant differences in the indicator "period of COVID-19 disease onset after vaccination with Companion V", which ranges from 6.9 to 8.0 months in the «covid» hospital (maximum 7.5 months, p-value = 0.92) and from 5.4 to 6.3 months in the general hospital (maximum 5.9 months, p-value = 0.66).

4.2 Assessment of significant levels of humoral and cellular immunity and their impact on cases of recurrent disease

Previous studies of seasonal coronaviruses demonstrate that after SARS-CoV-1 infection, IgG levels remained high enough for 4 - 5 months, while in MERS-CoV infection, with antibodies persisting in recovered patients for more than 2 years [38, 99, 157, 190]. According to the World Health Organization standard, the «protective» level of antibodies is a titer of more than 300 BAU/ml.

o assess the levels of antibody titers after vaccination with Sputnik V in persons who had been over-vaccinated before vaccination and in persons who had not been over-vaccinated before vaccination, we analyzed the antibody distribution plots of both groups, performed a formal test for the presence of distribution curvature, and a Wilcoxon test to compare the medians of the two groups.

Let's consider the distribution of antibody titer in those who were over vaccinated before vaccination with "Sputnik V". There were 106 such employees in the «covid» hospital (Figure 18).

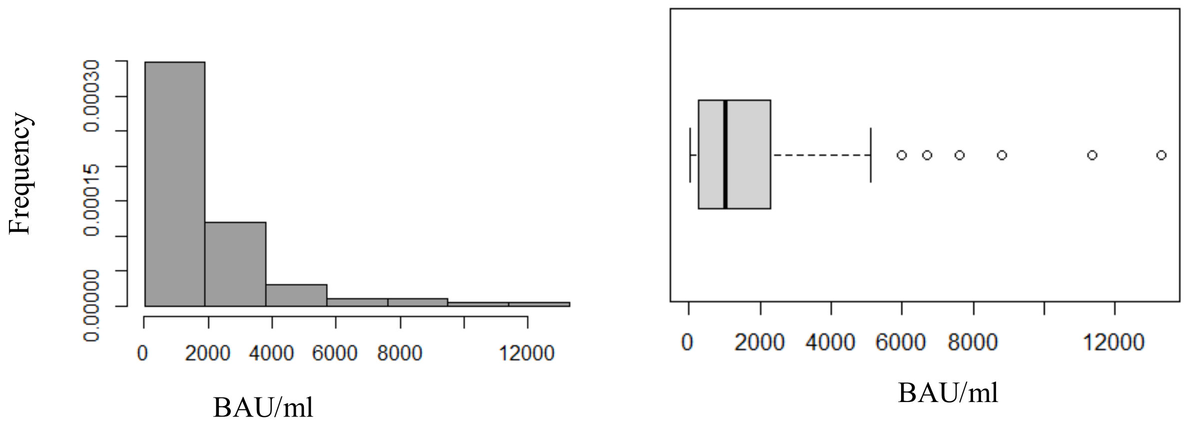


Figure 18 - Distribution of antibody titers in over-vaccinated patients before vaccination with Sputnik V, BAU/ml

The histogram and box plot indicate that the distribution of antibody titer in those who were over-vaccinated before vaccination with Companion V has a pronounced right-handed curvature.

In a formal analysis of the curvature of the antibody distribution, the calculated value of the slope (curvature) of the distribution was 2.67, which is moderate, and therefore, the subsequent use of the Wilcoxon test in this case is justified. The test for distribution curvature is conducted at the traditional 5% significance level. Hypotheses of the test:

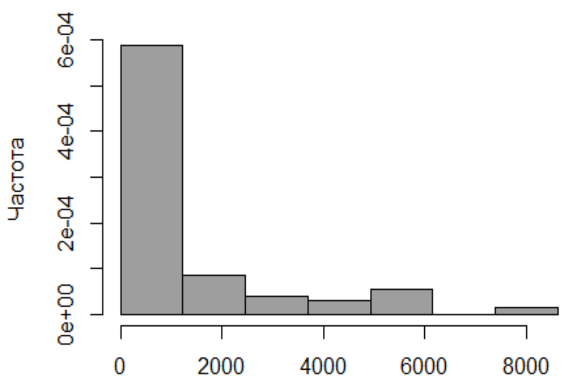
H_0: the true curvature of the distribution of antibody titers is zero (symmetric distribution);

H_1: the true curvature of the distribution of antibody titers is different from zero (asymmetric distribution).

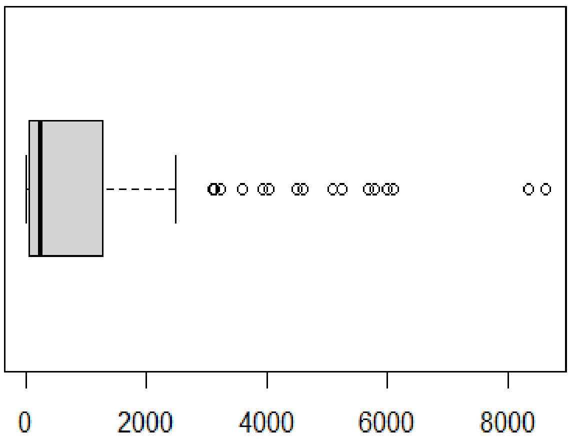
The value of the test statistic T = 2.67, p-value < 2.2e-16, it is less than the chosen significance level of 0.05, so the null hypothesis of the test is rejected. The considered distribution is asymmetric, in this case it really has positive (right-handed) curvature.

When considering the distribution of antibody titer in employees who were not sick before vaccination (105 people), both graphs show that the distribution of antibody titer in those who were not sick before vaccination with Sputnik V, the distribution of antibody titer in those who were overv accinated before vaccination with Sputnik has a pronounced rightward curvature (Figure 19).

Frequency



BAU/ml



BAU/ml

Figure 19 - Distribution of antibody titer in employees who were not sick before vaccination, BAU/ml

The calculated value of distribution curvature of 2.051 is moderate, which means that the subsequent application of the Wilcoxon test in this case is justified. Similarly, we conduct a formal test for the presence of distribution curvature. T = 2.05, p-value < 2.2e-16, therefore, the distribution under consideration is asymmetric, in this case it really has a positive (right-handed) curvature.

Since the necessary prerequisites are met, we perform the Wilcoxon median equality test for the «covid» hospitalization. The test is conducted at the traditional 5% significance level. Hypotheses of the test:

H_0: The true median antibody values of covid in patients who were over vaccinated and unvaccinated before vaccination do not differ from each other;

H_1: The true median antibody value of covid hospital staff who were overexposed before vaccination is higher than that of unvaccinated staff members.

The value of the test statistic W = 7367.50, the probability value is 2.4·10^(-5), it is less than the chosen significance level of 0.05, so the null hypothesis of the test is rejected. The median antibody value of employees who were sick before vaccination (it is equal to 1016.55 BAU/ml) is statistically significantly higher than that of employees who were not sick before vaccination (it is equal to 231,40 BAU/ml).

To predict morbidity after vaccination and to determine the period during which humoral immunity persists in health care workers, we formed categories by month and by month intervals and performed bootstrapping (BS) to determine 95% confidence intervals for the calculated median values (Figure 20).

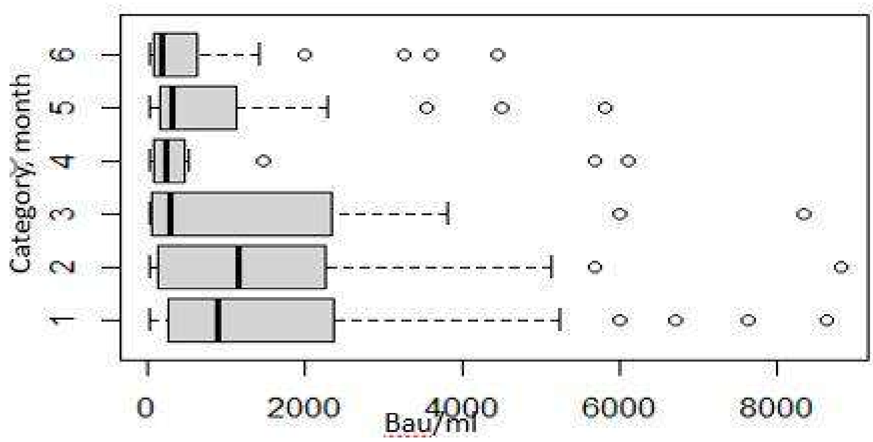
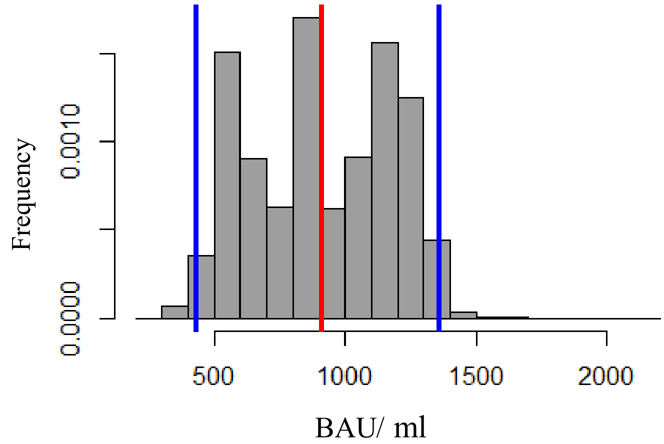
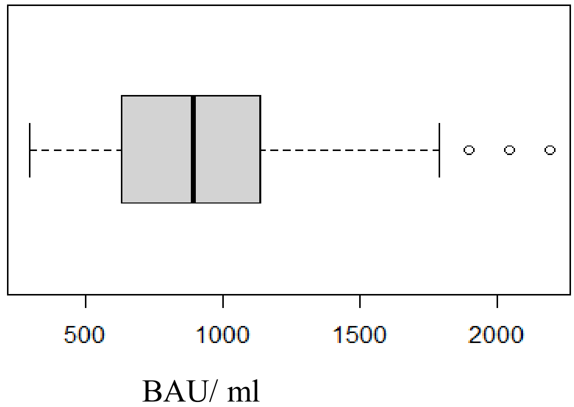


Figure 20 - Distribution of IgG titers after vaccination, BAU/ml

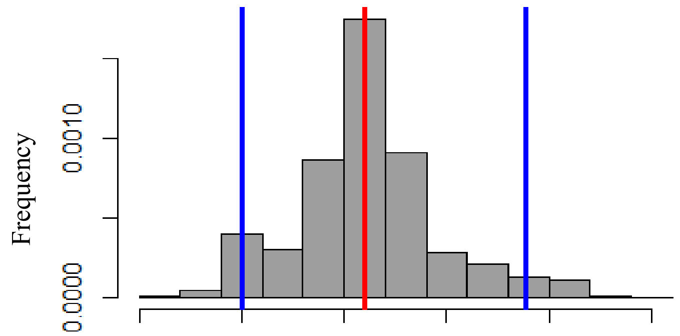
An interval of one month was defined as category 1. When analyzing the interval categories, the following median antibody titers were determined (Figure 21).



Mean median = 910.00; 95% BS CI [428.9; 1359.9]

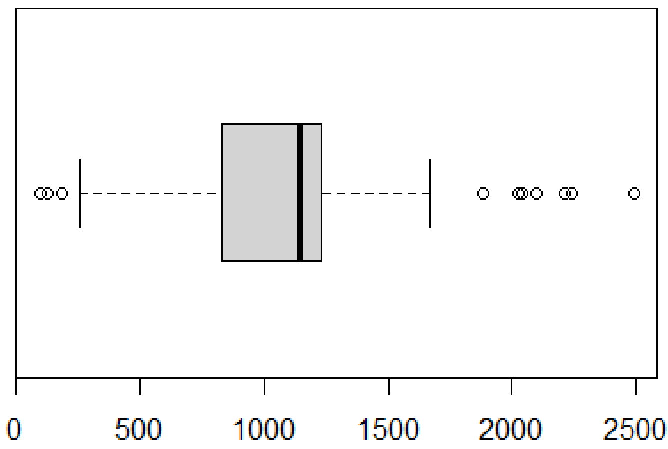


BS IgG medians between 61 and 90 days

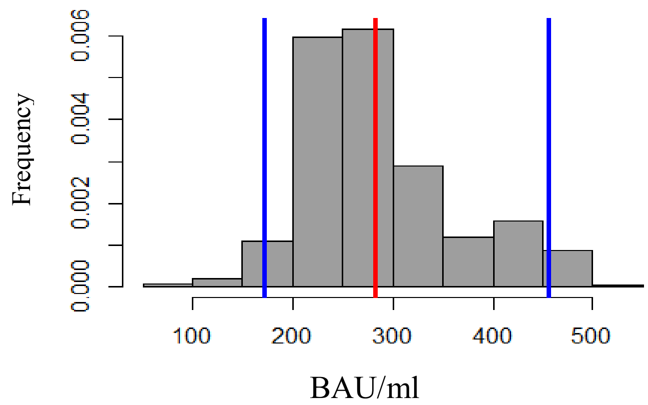


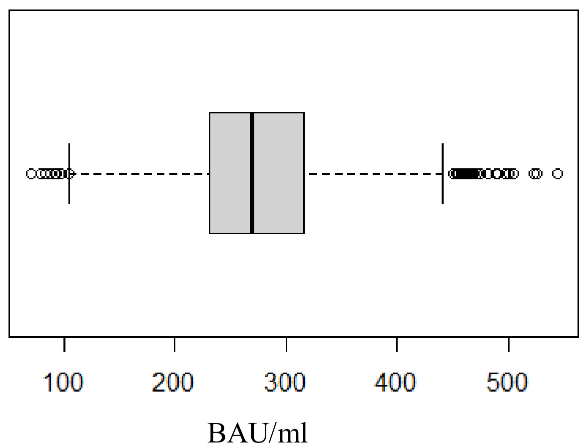
Mean median = 1144.3; 95% BS CI [498.2; 1886.0]

Figure 20 - Median values of antibody titers in different interval categories (sheet 1 of 3)



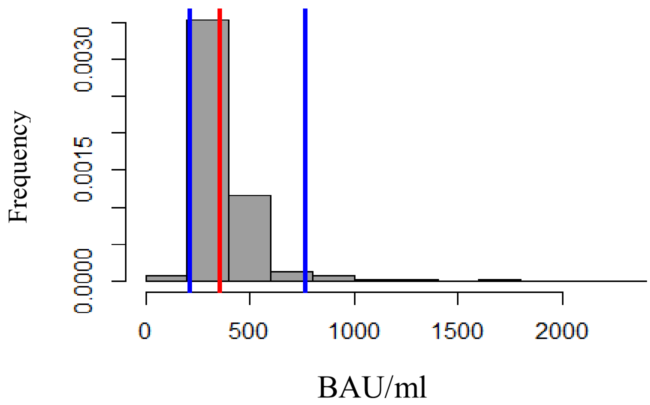
BS IgG medians between 91 and 180 days
Mean median = 282.5; 95% BS CI [171.3; 455.6]





BS median IgG medians between 150 and 180 days

Figure 20 (sheet 2 of 3)



Mean median = 357.3; 95% BS CI [208.5; 701.0]

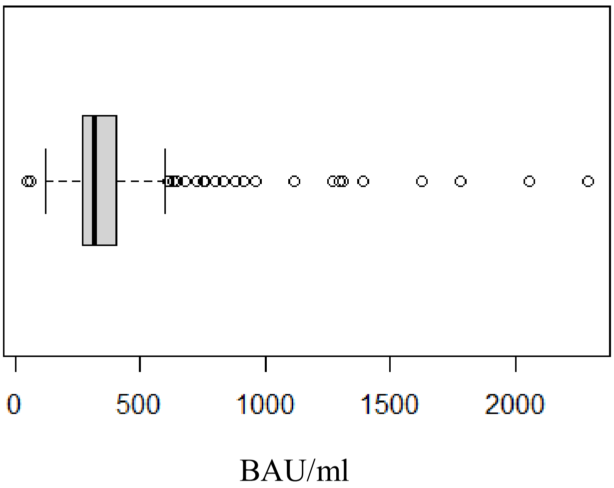


Figure 20 (sheet 3 of 3)

In employees of the study groups vaccinated with Sputnik V, the median IgG level reaches its maximum value between 61 and 90 days after the first dose of the vaccine and is 1144.30 BAU/ml (with 95% confidence interval [498.25; 1886.00]).

Between 0 and 60 days post-vaccination, it is 892.70BAU/ml (with 95% confidence interval [428.9; 1359.9]), and decreases to 268.53 BAU/ml (with 95% confidence interval [171.30; 455.60]) between 91 and 180 days; after 181 days, it reaches a minimum level of 164.35 BAU/ml (with 95% confidence interval [208,50; 761,05]).

4.3 Assessment of significant levels of humoral and cellular immunity and their impact on cases of recurrent disease

The study of the level of humoral and cellular immunity to COVID-19 in health care workers is important from the point of view of both planning anti-epidemic measures and predicting the effectiveness of the response to vaccination against SARS-CoV-2. In the late vaccination period, it became clear that revaccination of health workers was necessary in order to maintain the level of collective immunity. Based on the estimated data on the period of repeated disease, recommendations for vaccination of the Ministry of Health of the Russian Federation, we calculate the probability of morbidity in five and six months after vaccination.

Determine the total number of employees who became ill in the first five months and the first six months after the date of the first vaccination. Then we calculate the proportion of employees who became ill in the first five months and the first six months in the total number of employees considered - this will be the estimate of the probability of "success", and determine the limits of the 95% confidence interval for it. For each of the two cases (five and six months), we calculate the medians of the titers of those who became ill and those who did not become ill, and perform the Wilcoxon test to compare the medians.

The probability of illness after five months was 0.03 (CI 0.02; 0.04). The upper limit of the 95% confidence interval is less than 0.05; this means that the probability of recurrent disease at a horizon of up to five months after vaccination is statistically significantly less than 5%.

The box plots presented clearly demonstrate the fact that the median antibody titer value for those who became ill in the first five months after vaccination is greater than for those who did not become ill during this period (Figure 22).

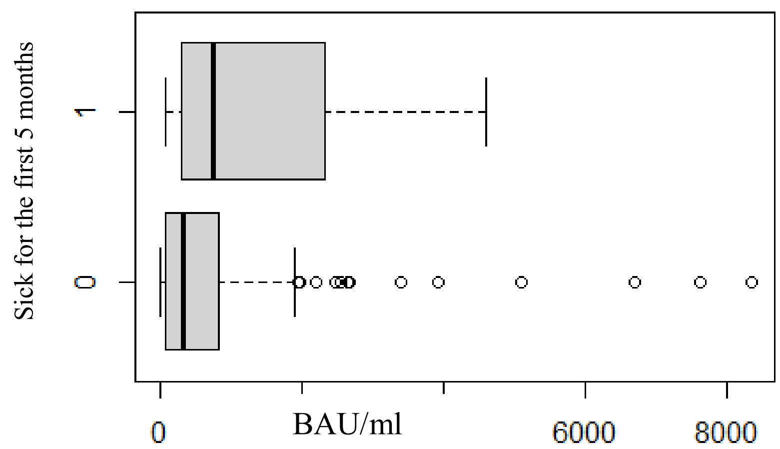


Figure 22 - Median IgG values five months after vaccination

The Wilcoxon test is conducted at the traditional 5% significance level. Hypotheses of the test:

H_0: The true median IgG values for those who became ill in the first five months after vaccination and those who did not become ill during this period do not differ from each other;

H_1: The true median IgG value for those who became ill in the first five months after vaccination is greater than for those who did not become ill during this period.

The value of test statistic W = 511.00, p-value = 0.04, it is less than the selected significance level of 0.05,so the null hypothesis of the test is rejected. Consequently, the median antibody titer value for those who became ill in the first five months after vaccination is greater than that of those who did not become ill during this period (Figure 23).

Using a similar algorithm, we analyze the incidence of disease six months after vaccination. The probability of disease six months after vaccination was 0.05 (CI 0.03; 0.06). The upper limit of the 95% confidence interval is greater than 005, but less than 0.10; this means that the probability of recurrent disease at a horizon of up to six months after vaccination is statistically significantly less than 10%.

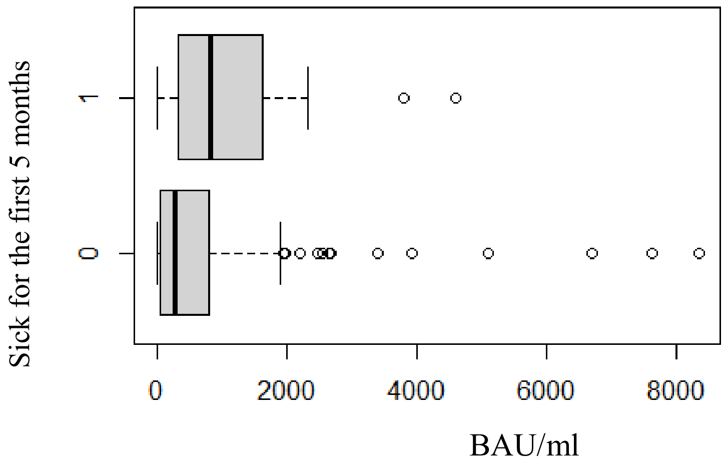


Figure 23 - Median IgG values five months after vaccination, BAU/ml

The box plots presented clearly demonstrate the fact that the median antibody titer value for those who became ill in the first six months after vaccination is greater than for those who did not become ill during this period.

In order to justify the necessity of revaccination after six months, the indicator "probability of morbidity of employees of the study groups after vaccination" was estimated five months after the date of the first dose, which amounted to 3.53% (in the range from 2.29 to 4.79%) - with a median IgG value of 330.80 BAU/ml, and after six months - 5.41% (in the range from 3.89% to 6.92%) with a median IgG value of 274.05 BAU/ml, which can be a reference point of indications for revaccination.

In assessing the recurrent morbidity, we have previously statistically proved the fact that the recurrent morbidity in those who have been re-infected and vaccinated is significantly lower than in those who have only been vaccinated. This finding is most likely due to the presence of cellular immunity and its active function in protecting the body from recurrent disease. To assess the significance of cellular immunity, we analyzed the data of 67 patients who were tested for the state of humoral and cellular immunity in vaccinated and COVID-19 re-infected patients. Of particular importance was the information on the intensity of cellular and humoral immunity in persons after the disease and vaccination. In the persons who had an illness and then vaccinated with Companion V, six months after vaccination, the median level of T-cell response to NMO protein peptides (Me = 26.5): N, M, ORF3a, ORF7a (cellular response as a result of the disease) was significantly higher than the median level of cellular response to S-protein peptides (Me = 51.00) (cellular response to vaccination).

To test this hypothesis, we conducted a descriptive analysis of the studied variables for asymmetry of their distribution. We substantiate the asymmetry (curvature) of the distribution using a statistical test. The presence of curvature in the distribution of the indicator justifies the need to apply the Mann-Whitney test. According to the results of this test we make a statistical conclusion about the difference of centers (medians) of distributions of the studied indicators (Table 13).

Table 13 - General descriptive statistics of cellular immunity levels

	Min.	1st Qu	Median	Mean	3rd Qu.	Max.
Protein S	10,00	20,00	26,50	36,33	45,00	129,00
Proteins NMO	8,00	27,25	51,00	69,41	95,00	245,00

From the basic analysis of descriptive statistics, it is evident that the median values for the two study variables S and NMO (respectively, 26.50 and 51.00) are different.

Both graphs indicate that the distribution of the NMO variable does have right-handed curvature (Figure 24).

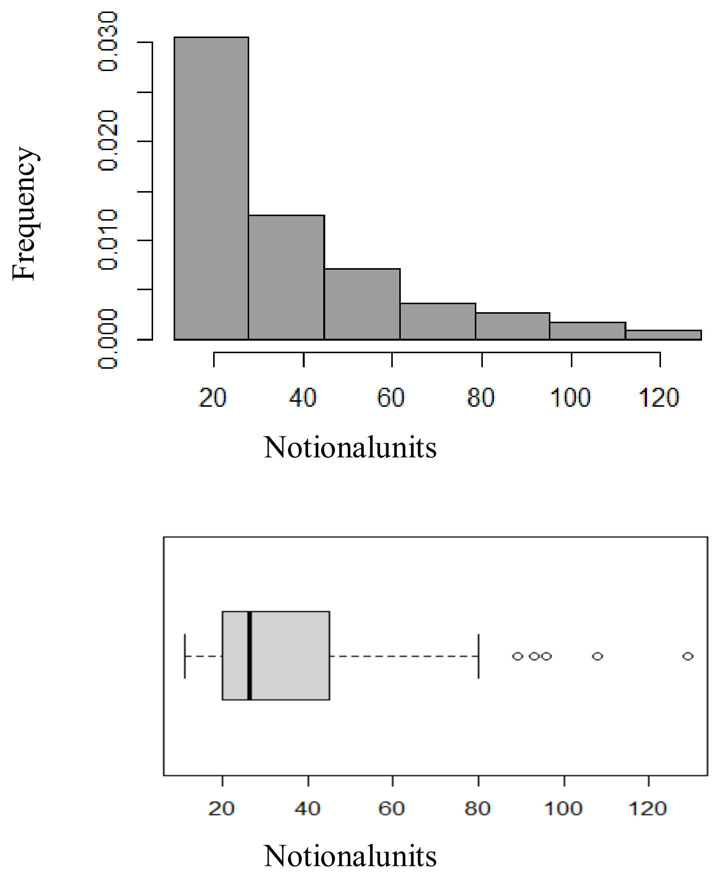
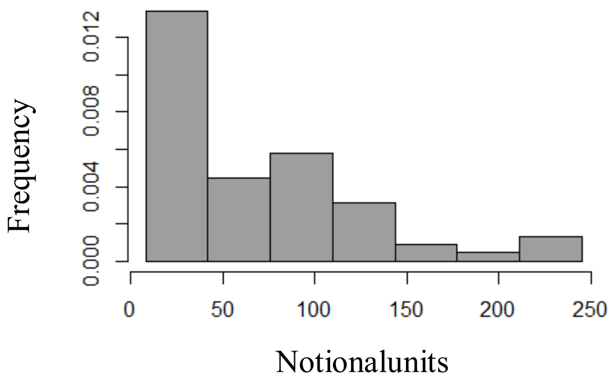


Figure 24 - Distribution plots of protein S levels, units.

In the curvature test, the calculated value of the curvature of the distribution of variable S (1.60) is very moderate, which means that the application of the Wilcoxon test in this case is justified. T = 1.60, p-value < 2.2e-16, hence the distribution under consideration is asymmetric, in this case it does have positive (right-handed) curvature (Figure 25).



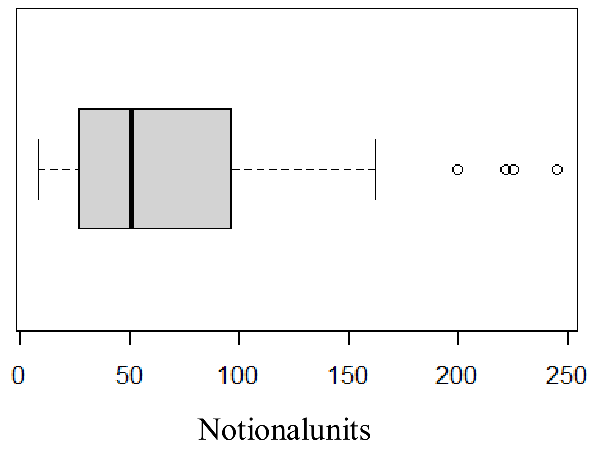


Figure 25 - Distribution plots of NMO protein levels, conditional units

The calculated value of the slope (curvature) of the distribution of the variable NMO (1.33) is very moderate, which means that the application of the Wilcoxon test in this case is justified. T = 1.33, p-value < 2.2e-16, therefore, the distribution under consideration is asymmetric, in this case it really has a positive (right-handed) curvature.

To compare the median values of the variables S and NMO we apply the Mann-Whitney test. Hypotheses of the test:

H_0: the true median values of the variables S and NMO do not differ from each other;

H_1: the true median value of the variable NMO is higher than that of the variable S.

The value of test statistic W = 1996.00, probability value p-value = 6.503e-09, it is less than the selected significance level of 0.05, so the null hypothesis of the test is rejected. Thus, the median value of the variable NMO is significantly higher than the median value of the variable S.

In assessing gender differences in the levels of S and NMO variables, the overall descriptive statistics are presented in Table 14.

Table 14 - General descriptive statistics of cellular immunity levels in women

	Min.	1st Qu	Median	Mean	3rd Qu.	Max.
Protein S	11, 00	19, 00	25, 00	35, 41	53, 00	108, 00
Proteins NMO	13, 00	32, 00	37, 00	65, 79	92, 00	225, 00

From the basic analysis of descriptive statistics, it can be seen that the median values for the two study variables S and NMO (25.00 and 37.00, respectively) differ among women.

The calculated value of the slope of the distribution of variable S (1.34) and variable NMO (1.39) is very moderate, which means that the application of the Wilcoxon test in this case is justified. When conducting a formal curvature test, the distribution in question is asymmetric; in this case, it does have positive (right-handed) curvature (T = 1.34, p-value = 0.0035; T = 1.39, p-value = 0.0045). Moreover, the median value of the variable NMO is significantly higher than the median value of the variable S (V = 415.50, p-value = 9.672e-06) (Figures 26, 27).

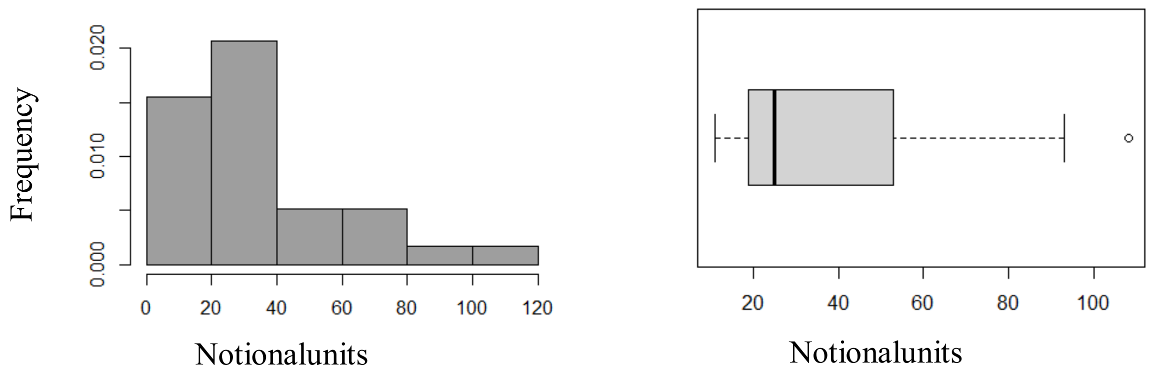


Figure 26 - Distribution plots of protein S levels in women, conditional units

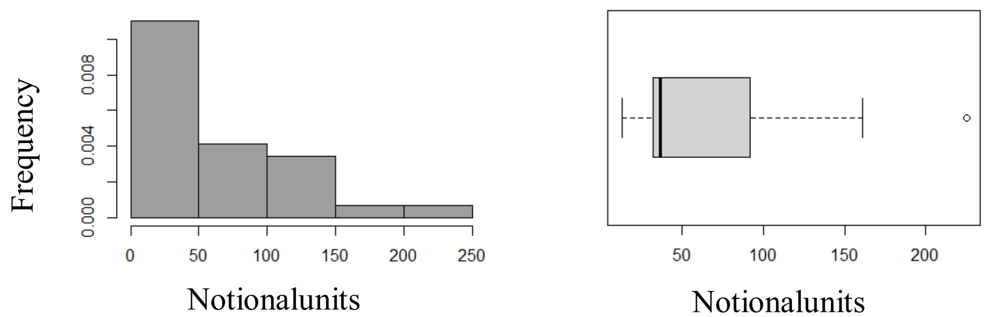


Figure 27 - Distribution plots of protein NMO levels in women, conditional units

From the basic analysis of descriptive statistics, it can be seen that the median values for the two study variables S and NMO (29 and 69, respectively) are different for males (Table 15).

Table 15 - General descriptive statistics of cellular immunity levels in men

	Min.	1st Qu	Median	Mean	3rd Qu.	Max.
Protein S	12,00	21,00	29,00	3,05	45,00	129,00
Proteins NMO	8,00	26,00	69,00	72,24	96,00	245,00

The graphs indicate that the distribution of variable NMO and variable S for men does have a right-handed curvature (Figures 28, 29).

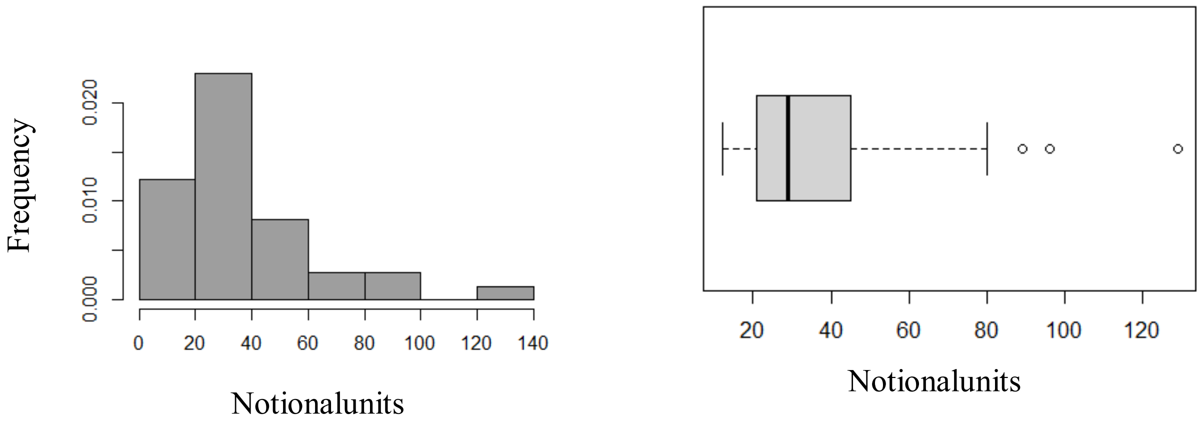


Figure 28 - Distribution plots of protein S levels in men, conditional units.

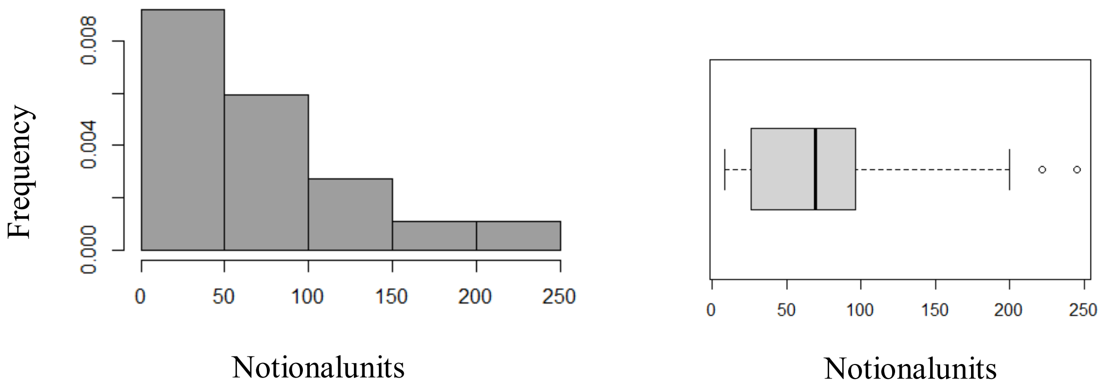


Figure 29 - Distribution plots of NMO protein levels in men, conditional units.

The calculated value of the slope (curvature) of the distribution of variable S (1.79) and variable NMO (1.25) is very moderate, which means that the application of the Wilcoxon test in this case is justified. With the Wilcoxon test ($T = 1.79$, p-value $< 2.2e-16$; $T = 1.25$, p-value $= 0.001$) the distribution under consideration is asymmetric, in this case it does have a positive (right-handed) curvature. The median value of the NMO variable is significantly higher than the median value of the S variable ($V = 610.50$, p-value $= 4.804e-05$).

The recurrent morbidity in the group of employees of the studied hospitals "over-infected and vaccinated" is significantly lower than in the vaccinated only ($z = -4.402, p = 1.07e-05$), which is confirmed by the data on the level of cellular immunity six months after vaccination - the value of the median level of cellular immunity NMO is significantly higher in the group "over-vaccinated and vaccinated" than in the group "vaccinated", and this result has no gender differences ($W = 610.50$, p-value = 4.804e-05).

Chapter 5 JUSTIFICATION OF A COMPLEX OF PREVENTIVE MEASURES IN HOSPITALS OF DIFFERENT PROFILES IN ORDER TO PREVENT THE SPREAD OF COVID-19

Organizational measures in hospitals during the period of active spread of COVID-19 should be carried out in accordance with the data on the routes and mechanisms of transmission of SARS-CoV-2 virus. All measures should be adapted to the specific conditions and profile of the hospital and recommendations of public health authorities and the Federal Service for Supervision of Consumer Rights Protection and Human Welfare in a particular region.

Antiepidemic measures in the hospital are divided into nonspecific and specific. Nonspecific, in turn, can be divided into the main groups: isolation, architectural and planning, disinfection and sterilization, administrative (Figure 30).

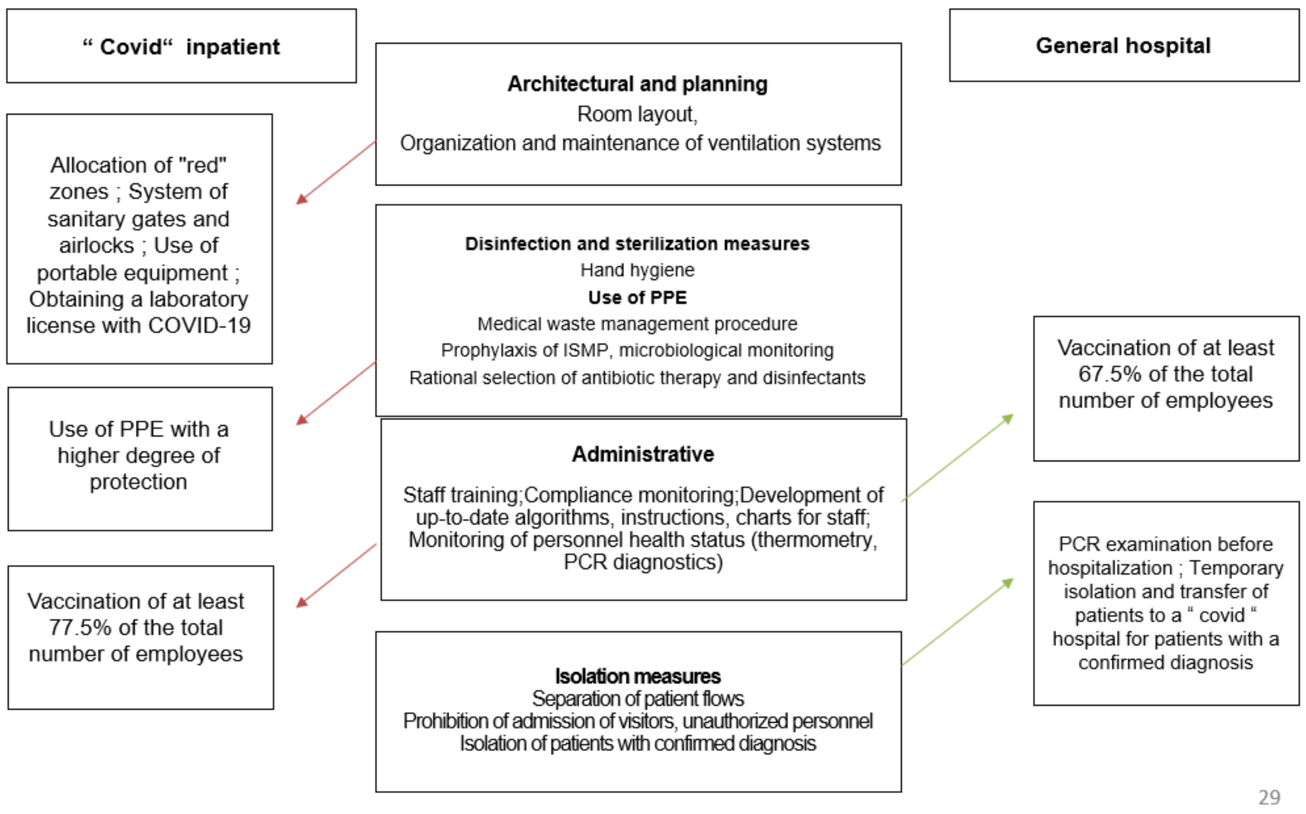


Figure 30 - Complex of organizational and preventive measures in hospitals

Isolation anti-epidemic measures. The primary importance is attached to limiting the access of persons not involved in the functioning of the hospital and relatives of patients to the territory of the medical facility.

Daily thermometry and questioning of employees before the beginning of the working shift should be organized in the institution, personnel with manifestations of acute respiratory infections (fever, cough, runny nose) are not allowed to work, are sent for treatment taking into account the patient routing scheme. In the «covid» hospital, medical personnel who were in close contact with

COVID-19 patients and in case of detection of the above signs are sent under medical observation in self-isolation mode. This approach is part of the anti-epidemic measures planned to prevent further spread of infection and protect the health of staff and patients [88].

It is recommended to hospitalize patients with acute respiratory viral infections, influenza, pneumonia of undetermined etiology (or persons with suspected disease) in boxes, boxed rooms or, in their absence, in rooms with an airlock and a sanitary unit, taking into account the severity of the patients' condition and the principle of one-stage (cyclical) filling of rooms. Persons with suspected infection are recommended to be placed in wards with 1 - 2 beds. Patients with a confirmed diagnosis can be placed in wards with a higher capacity in compliance with hygienic requirements for the area of wards for 1 bed in infectious diseases hospitals (at least 8 square meters. m) and placement of beds at a distance of at least 1.5 m from each other.

Patients must wear medical masks and observe hand hygiene in the presence of staff or other patients. It is forbidden to leave the rooms (boxes). The use of mobile communication devices is allowed (in intensive care units, taking into account the clinical condition) with their disinfection with alcohol-containing agents. For uses in the «red» zone are allocated means of mobile communication, which are subject to current disinfection with alcohol-containing disinfectants, their removal outside the zone is not allowed [45, 49].

In a general hospital it is obligatory to introduce PCR testing of patients on admission, as well as referral of the patient to a specialized institution in case of confirmation of the diagnosis of COVID-19.

Administrative measures. The management of medical organizations ensures staff training, including using educational modules posted on the Portal of Continuing Medical and Pharmaceutical Education of the Ministry of Health of Russia, introductory and ongoing briefings for staff on the prevention of COVID-19, prevention of healthcare-associated infections (HAI), hand hygiene, anti-epidemic measures, use of PPE and personal prophylaxis measures with the adoption of credits, as well as systematic.

Having clear algorithms and instructions for the staff facilitates compliance with the requirements of the sanitary and epidemic regime in the organization. Medical personnel providing care to patients diagnosed with COVID-19 or suspected COVID-19 should not touch eyes, nose, mouth, hands, including gloves. Personnel in protective clothing are not allowed to go outside the "red" zone. In case of contact of patients' biological material with unprotected skin and mucous membranes of the personnel, the algorithm of emergency actions must be followed: open parts of the body are treated with 70% alcohol (alcohol-containing skin antiseptic), mucous membranes of the mouth and throat are rinsed with 70% ethyl alcohol, a 2% solution of boric acid is injected into the nose and eyes [49].

All medical organizations should develop and approve standards for procedures associated with increased risk of infection of the patient (catheterization of vessels, bladder, invasive and non-invasive respiratory support, etc.) and medical staff (intubation, tracheostomy, bronchoscopy, etc.), and ensure control of their implementation, including the use of checklists. All violations should be addressed at general meetings with the staff in order to prevent errors in the algorithms in the [49].

Disinfection and sterilization measures play a key role in hospital safety and hygiene, especially when dealing with infectious diseases such as COVID-19.

Compliance with requirements for disinfection and sterilization of equipment and tools, routine cleaning - at least twice a day; air disinfection and hand hygiene should be performed on a continuous basis.

The hospital organizes the work of the commission on prevention of UTIs, microbiological monitoring, control over the rational use of antimicrobial agents [98].

Regular internal control of hand hygiene compliance in other hospital departments, especially in intensive care units, at least twice a week. In intensive care units, it is possible to use technical means (video cameras) to monitor staff compliance with hand hygiene rules and other measures to prevent healthcare-associated infections [45, 49, 98].

In a «covid» hospital, it is recommended to keep medical records in "red" areas electronically with printing outside the area. Computer keyboards must be disinfected before and after the end of work on the computer. Hand hygiene must be performed before and after working on the computer keyboard. It is recommended to keep paper documents at room temperature in a clean room for a period of time exceeding the survival time of the pathogen (at least 5 days), or disinfect them in a disinfection chamber, in steam-air-formalin, steam and combined disinfection chambers and air disinfection chambers for disinfection of books up to 30 mm thick, contaminated with pathogens of intestinal and droplet infections, as well as dermatophytes (disinfection by steam-air method at 70-75 ° C and exposure time of 180 minutes). A small number of documents can be disinfected in an air sterilizer at 70-75 °C for 30 minutes [49, 88].

A strict anti-epidemic regime is established in the «covid» hospital, provided for infections with aerosol transmission mechanism, current and final disinfection with the use of disinfectants registered and authorized for use in the prescribed manner in regimes that ensure effective disinfection in relation to viral infections. In the premises of the infectious disease hospital is carried out daily current disinfection, after vacating the premises - final disinfection. During the current disinfection, special attention should be paid to all surfaces with which the infected patient came into contact, door handles, chair, table, etc., as well as to all surfaces with which the infected patient came into contact. A clean disposable tissue should be taken to disinfect a new object. In the box, ward after discharge, death or transfer of the patient is carried out final disinfection of surfaces, furniture, equipment, care items, bedding is submitted to the disinfection chamber. Laboratory quality control of final disinfection is carried out selectively (in at least 10% of cases), including determination of the concentration of disinfectants and solutions, express sampling for residual quantity of disinfectants, selection and examination.

A strict anti-epidemic regime with the use of disinfectants in a mode that ensures the death of viruses, as well as increasing the frequency (at least twice a shift) of routine cleaning of all rooms is also established in the general hospital.

Application of personal protective equipment. In accordance with the profile of the institution, the specifics of the department, the level of probable viral load and the nature of the procedures performed, a targeted and rational application of personal protective equipment is carried out to ensure the safety of medical workers and patients.

Medical and service personnel should be provided with working clothes (at least three sets) and use personal protective equipment in accordance with sanitary rules when providing medical care.

If resources are limited, personal protective equipment such as respirators, goggles (face shields), full-face masks with filters, plague suit/jumpsuit/robe, shoe covers, when serving a homogeneous contingent of patients (e.g., several patients with a laboratory-confirmed diagnosis) without going outside the «red» zone may be used during the working shift with the duration of their use not exceeding four hours. In the «clean» zone rooms, staff must wear medical masks.

Use of external gloves subject to hand hygiene regulations:

1) before direct patient contact;

2) before performing manipulations that require aseptic technique;

3) after manipulations that may involve contact with biological fluids, mucous membranes, dressings;

4) after patient contact (including intact patient skin, e.g., when measuring pulse or blood pressure);

5) after contact with medical equipment and other environmental objects surrounding the patient.

Personnel shall be provided with hand hygiene products, including alcohol-containing skin antiseptics in small packs. Skin antiseptics containing ethyl alcohol (not less than 70% by weight), isopropyl alcohol (not less than 60% by weight) or a mixture of alcohols (not less than 60% by weight) shall be used for hand hygiene treatment).

Inpatient planning in COVID-19 is important because it determines the efficient use of space and resources to ensure patient and staff safety and minimize the risk of spread of infection. These decisions include optimizing patient placement, creating areas of varying degrees of protection, ensuring access to necessary equipment and supplies, and organizing workflow to accommodate the likely viral load and the nature of the procedures being performed.

In «covid» hospitals there are «clean» and «red» zones with independent entrances for patients and staff and organization on the border of the zones of sanitary passageway or, if there is no such possibility, rooms equipped with sinks and open-type bactericidal irradiators for putting on, as well as for removal and disinfection of protective clothing. The place for putting on personal protective equipment shall be equipped with furniture for storing clean personal protective equipment and a mirror for self-checking the correctness of putting on. The room for removal and disinfection of personal protective equipment should be equipped with containers for removed personal protective equipment, a table/bench for placing the necessary number of containers with disinfectant solution for current disinfection. To reduce contamination of protective clothing before its removal, it is possible to use disinfection sluices (frames).

The «red» zone includes rooms for receiving patients, wards/boxes/semi-boxes for patients with sanitary facilities and showers, resuscitation wards (halls), nurses' stations, rooms for preparation of infusion systems (procedure rooms), rooms for disinfection and preliminary cleaning of medical instruments and equipment, treatment of ventilators, rooms for temporary storage of biomaterial samples, bodies of the dead, dirty linen, medical waste, «dirty» zone of the sanitary passageway, rooms for working with biomaterial in laboratories, loading zones of laundries and disinfection chamber. The «clean» zone includes dressing rooms and other staff living quarters, residents' rooms, rooms for laboratory staff, sterile zone of the central sterilization department (CSD), «clean» zones of sanitary passages, storage rooms for clean linen and medicines, storage rooms for consumables, instruments, disinfected equipment, refreshment rooms [49].

Non-contact (or non-kiste controlled) dispensers of skin antiseptics, containers with clean gloves and for the discharge of used gloves are provided in front of the entrance to the wards (boxes), to the rooms of the «clean» zone, to the staff's living quarters. In units with high intensity of patient care and with a high load on the staff (intensive care units, etc.) dispensers with skin antiseptics for hand treatment are placed in places convenient for use by the staff (at the entrance to the ward, at the bedside of the patient, etc.).

Taking into account epidemiological risks and if possible, it is recommended to organize a dormitory for personnel working in a medical organization (structural subdivision) providing care to patients with COVID-19 in inpatient settings.

Reception of patients should be organized in reception and examination boxes or separate rooms with independent waiting areas should be allocated for the reception of patients with a confirmed diagnosis, with suspected disease. Sanitary treatment of incoming patients is carried out in the sanitary passageway of the reception department or in the wards. The patient's outer clothing, if there is consent, is treated in the disinfection chamber, stored in the storeroom in individual bags. In the emergency room, current disinfection (after admission of each patient) and final disinfection (at the end of the working shift) are carried out.

In the absence of mechanical ventilation systems in the medical organization, equipped in accordance with the requirements for the organization of air exchange in infectious diseases hospitals, supply ventilation systems that use recirculated air shall be turned off. At the same time, exhaust ventilation in the sanitary rooms of wards must be in working condition. It is allowed to use supply systems that provide the necessary air exchange rate and supply of clean outdoor air with increasing the degree of filtration to the maximum possible values, eliminating defects in the seals of filter housings and filter holders. The use of split-systems, vacuum dust removal systems, pneumatic mail is not allowed in the rooms of the «red» zone. In wards and rooms with a permanent stay of staff install air disinfection devices approved for use in the presence of people, and ensure their operation in a continuous mode (ultraviolet bactericidal irradiators of closed type (recirculators), installations based on various types of electrostatic precipitators, permanent magnetic fields, etc.). The required number of air disinfection devices is calculated in accordance with the instructions for their use, taking into account the volume of the room in which they will be installed.

Monochromatic ultraviolet bactericidal irradiators of open type, pulsed xenon bactericidal irradiators of continuous spectrum, aerosol disinfection units can be used for final disinfection in wards, as well as for disinfection of indoor air in the absence of people.

In a general hospital, the admission of patients with infectious manifestations should be organized separately from somatic patients. Admission of patients with signs of respiratory diseases is carried out in a specially allocated box.

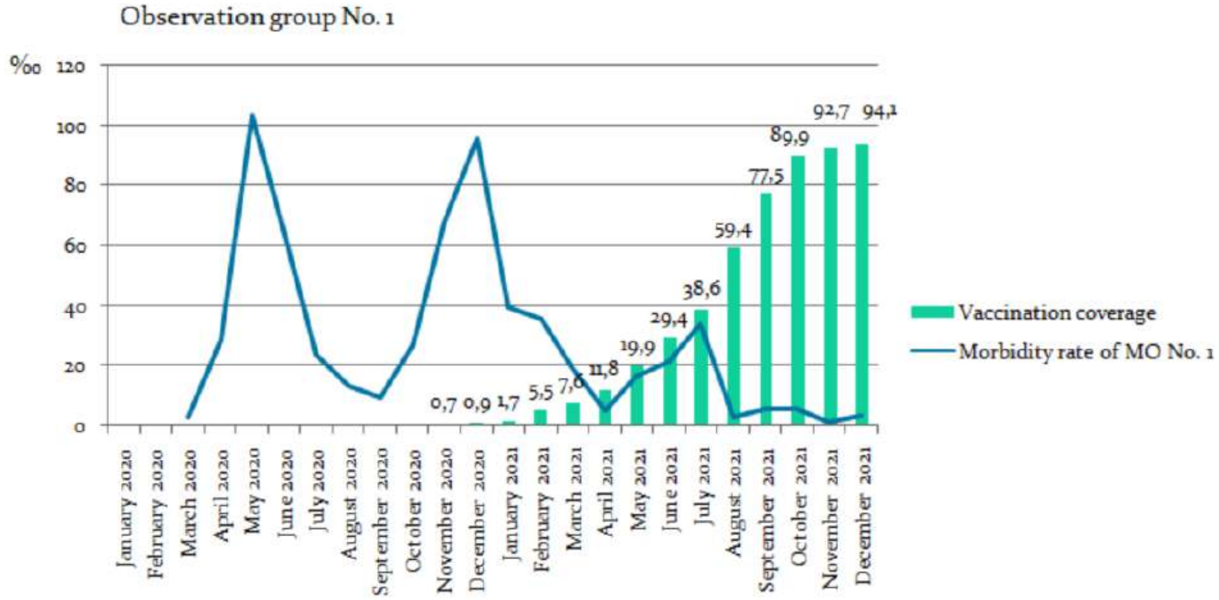
Medical care should be organized with the performance of as many procedures as possible and the use of portable equipment (ultrasound, X-ray, ECG, etc.) in the wards. Pulse oximeters, phonendoscopes, thermometers, portable glucometers, blood pressure monitors, oxygenators, ultrasound machines, ECG and other equipment should be treated with disinfectants after each patient (it is recommended to use disinfectants that do not require prolonged exposure, for example, alcohol-containing disinfectants). Diagnostic rooms with large-size equipment (CT, etc.) are used according to the schedule with separation of the flow of patients with confirmed diagnosis and suspected COVID-19 and with current disinfection. In case of emergency investigations of patients with COVID-19 (suspected) outside the schedule in the room is carried out current disinfection. After completion of admission of patients with COVID-19 (suspected) in the office (department) is carried out final disinfection. The personnel of diagnostic units involved in the provision of medical care to patients with COVID-19 (suspected) should use protective clothing and personal protective equipment that ensures biosafety. Our proposed measures have been implemented in practice:

1. Organization of work of radiology diagnostic departments and algorithms of examination during the spread of acute respiratory viral infections, influenza and new coronavirus infection (COVID-19). Methodical recommendations / O. V. Mironenko, T. N. Trofimova, O. V. Lukina, P. V. Gavrilova, V. A. Ratnikov, A. K. Ratnikova, V. A. Kashchenko, E. A. Fedorova, A. A. Tovanova, D. A. Obukhov, M. G. Stupin - St. Petersburg: publishing house Federal State Budgetary Educational Institution of Higher Education of I.I. Mechnikov NWSMU, 2022. - 60 pages.

2. Individual protection means in professional activity of medical workers of stomatological profile: educational and methodical manual / O. V. Mironenko, A. S. Nekhoroshev, O. I. Kopytenkova, S. N. Noskov, Kh. K. Magomedov, A. A. Tovanova, E. A. Fedorova, A. A. Kulieva. - SPb.: Federal State Budgetary Educational Institution of Higher Education VO NWGMU named after I.I. Mechnikova, 2024. - 79 pages.

Specific activities. Medical personnel who provide medical care and care for COVID-19 patients, except for those who have IgG - antibodies to RBD fragment of S-protein S-protein of SARS-CoV-2 virus as a result of immunization or transferred disease, shall be under medical surveillance for the entire period of work and until the expiry of 14 days from the last contact with the diseased. Laboratory examination of personnel in order to detect SARS-CoV-2 virus shall be carried out in the presence of medical indications in accordance with the established procedure, as well as in a planned order upon entering the workplace, further - once every seven days, except for persons who have IgG-antibodies to RBD fragment of S-protein S-protein of SARS-CoV-2 virus as a result of immunization or transferred disease (within six months from the date of detection of such antibodies). It is recommended to restrict admission to the red zone to personnel who do not have IgG-antibodies to the RBD fragment of the S-protein S-protein of SARS-CoV-2 virus.

Personnel of medical organizations are subject to prophylactic immunization against COVID-19 in accordance with the calendar of prophylactic vaccinations for epidemic indications. Providing vaccination coverage of more than 77.50% ±0.05 (in a «covid» hospital) and 67.60% ±0.05 (in a general hospital), there is a significant decrease in the incidence rate among health care workers by 8 and 3 times, respectively (p-value < 0) (Figure 31).



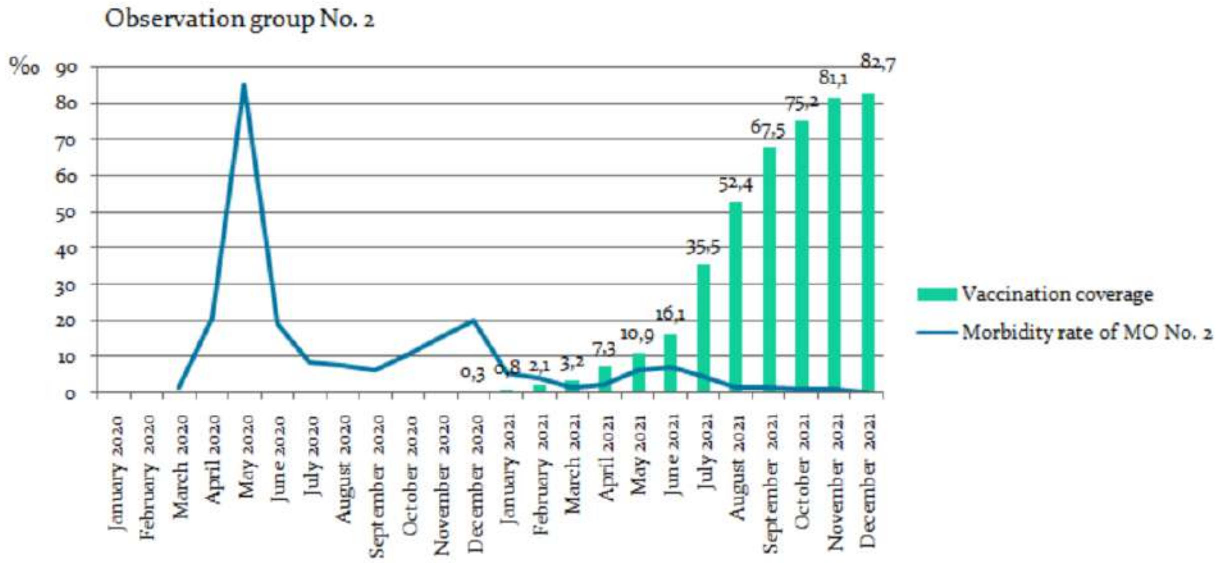


Figure 31 - Morbidity of health workers and vaccination coverage in the post-vaccination period

Thus, in compliance with a set of anti-epidemic measures, the leading of which are immunization and monitoring the structure of collective immunity, there is a significant significant reduction in the incidence of staff morbidity, as well as the spread of COVID-19 in hospitals, regardless of their profile.

CONCLUSION

At the time of the beginning of material collection in 2020, there were no scientifically substantiated data on effective preventive measures against COVID-19, aimed at preventing the spread of this infection among professional groups of medical workers and ensuring the efficiency of inpatient health care systems both in the Russian Federation and abroad.

In order to evaluate organizational measures and mechanisms of collective immunity formation as a result of analysis of databases created by us, statistical hypotheses were selectively put forward, which were subjected to testing by means of mathematical tests.

It was found that depending on the period of observation and the development of the epidemiological process, the structure of collective immunity, preventive and organizational measures have differences. Thus, if during the period of the beginning of the spread of COVID-19, there were two groups of hospital staff (those who had contracted the disease and those who had not), then during the late postvaccinal period, there were four groups:

1.Vaccinated.

2.Over-vaccinated (not more than six months ago), unvaccinated.

3. Those who haven't been sick, unvaccinated.

4.Those who haven't been sick, unvaccinated, with medical contraindications.

These factors influenced the choice of statistical methods for testing mathematical hypotheses.

The mathematical assessment of morbidity levels revealed that the median values of morbidity of medical workers in a general hospital are lower than the morbidity of workers in a «covid» hospital. At the same time, there are no gender differences when studying morbidity rates.

This fact is related to the fact that medical workers of the «covid» hospital primarily provided care to patients with a confirmed diagnosis of COVID-19 and were exposed to a high viral load.

When compared with the city-wide morbidity rate in the pre-vaccination period, the median value of morbidity of medical workers in hospitals is significantly higher than the similar value of the city-wide indicator (Figure 32). At the same time, the dynamics of morbidity has similar trends: peaks of morbidity are observed in May 2020, December 2020 and June-July 2021.

One of the first contingents of mass vaccination were medical workers - in the studied hospitals, workers started to be vaccinated from November 2020.

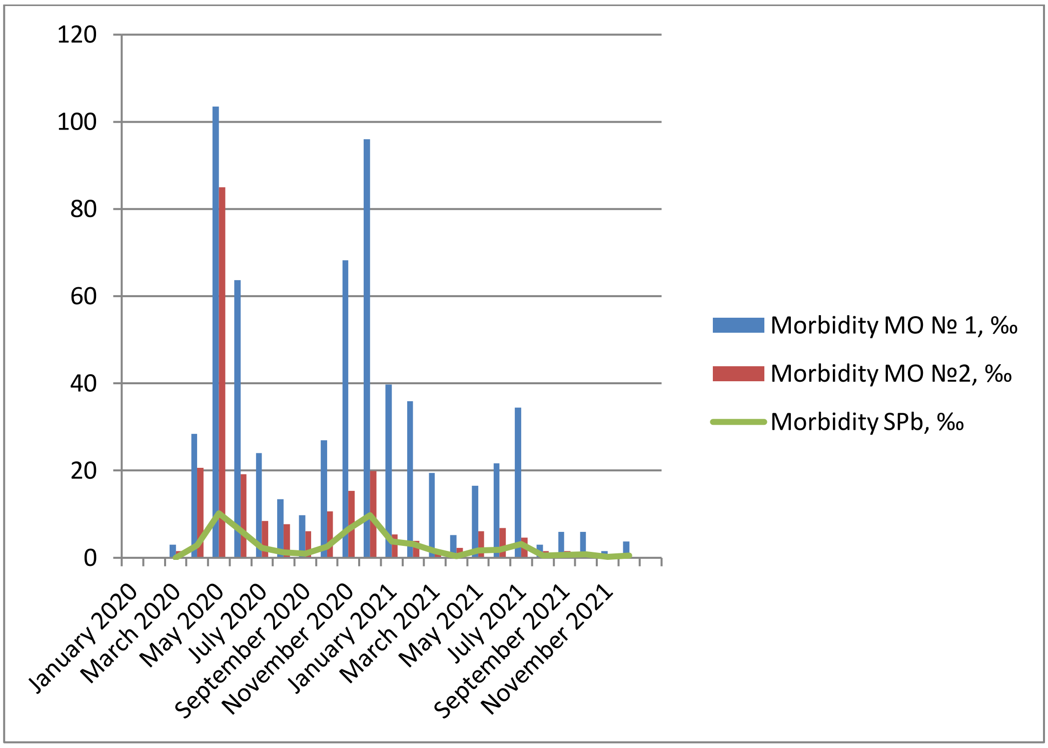


Figure 32 - Dynamics of morbidity among medical workers in hospitals and residents of St. Petersburg

Since November 2020, medical workers in the «covid» inpatient unit have been vaccinated more intensively, and the range of vaccines used is diverse, in contrast to the general inpatient unit, where employees were vaccinated only with «Sputnik V» and «Sputnik Lite». The majority of medical workers in both hospitals were vaccinated with "Sputnik V" (double vaccination).

The structure of collective immunity in both hospitals had similar trends when formed at different stages of the epidemic process. During the period of active spread of COVID-19 and the beginning of vaccination in both hospitals, the groups of those who were already sick prevailed. In the postvaccination period, the proportion of those vaccinated in observation group no. 1 (94.20%) was statistically significantly higher than the proportion of those vaccinated in observation group no. 2 (82.70%), which explains the differences in the structure of collective immunity in these institutions (Table 16).

Table 16 - Structure of collective immunity of medical workers at different stages of the COVID-19 epidemic process

Observation period	A set of preventive and organizational measures	The structure of collective immunity
Commencement of COVID-19 dissemination (March-November 2020)	Architectural and planning Disinfection Isolation Application of personal protective equipment Modern methods of laboratory diagnostics (PCR)	1. Those who were sick 2. Uninfected
Vaccination start period (December 2020 - August 2021)	Architectural and planning Disinfection Isolation Vaccination (double vaccination) Application of personal protective equipment Modern laboratory diagnostic methods (PCR, ELISA)	1. Those who have already been sick 2. Vaccinated and those who have already been sick 3. Vaccinated and those who haven't gotten sick. 4. Those who have never been sick and unvaccinated
Late post-vaccination period (September-December 2021)	Architectural and planning Disinfection Isolation Vaccination (double vaccination, single vaccination) Application of personal protective equipment	1.Vaccinated 2.Those who have been sick (not more than six months ago), unvaccinated. 3. those who have not been sick, unvaccinated. 4.Those who have not been sick, unvaccinated, with medical contraindications.

The effectiveness of vaccination as a preventive measure can be assessed by the number of illnesses in the late vaccination period. The number of repeated illnesses after vaccination in vaccinated persons in percentage terms is significantly lower than in unvaccinated persons in both hospitals.

At the same time, the number of repeated illnesses after vaccination in the «covid» hospital is significantly lower in percentage than in the similar group of the general hospital. This fact may be associated with the application and tighter control of other organizational measures: these are architectural and planning decisions (creation of a "red" zone), the use of personal protective equipment, disinfection measures, and the attitude to each patient as a "dangerous" patient.

The researchers argue that, because of the significant mortality from COVID-19, the acquisition of immunity solely through natural infection is not effective enough, and alternative strategies, including mass immunization, are needed. Therefore, an important step in the study was to assess the relationship between morbidity and vaccination.

In the post-vaccine period, cases of COVID-19 have been reported in both pre-vaccinated and subsequently vaccinated individuals and in vaccinated individuals who have not previously had the disease.

The incidence of disease among those who were not sick before vaccination and vaccinated employees of the «covid» hospital (15.40%), which is more than the same indicator for those who were sick and vaccinated (7.42%). Thus, the fact of having had a disease and vaccination really statistically significantly reduces the probability of recurrent disease. In our opinion, this fact is associated with the presence of cellular immunity in COVID-19 survivors, which provides more pronounced protection.

Preserving the duration of humoral immunity and determining the time during which disease will not develop after vaccination are relevant for evaluating vaccine prophylaxis as one of the main organizational measures in the hospital during the period of active spread of COVID-19. To evaluate this hypothesis, we determined the period between the first vaccination and the incidence of disease after vaccination. During mathematical processing of the databases statistically significant differences were established for the indicator "period of COVID-19 disease onset" after vaccination with "Sputnik V", which ranges from 6.9 to 8 months in the «covid» hospital (maximum 7.5 months) and from 5.46 to 6.34 months in the general hospital (maximum 5.9 months).

In employees of the study groups vaccinated with "Sputnik V", the median value of IgG titers reaches the maximum value in the period from 60 to 90 days after the first dose of the vaccine and amounts to 1144.30 BAU/ml.

When assessing the dynamics in the period from 0 to 90 days, an increase in IgG titers was noted, peaking between 60 and 90 days. In the period from 90 to 180 days the level decreases, and after 180 days reaches the minimum level.

In the late vaccination period, it was recognized that re-vaccination of medical personnel was necessary to maintain the level of collective immunity. Based on calculations of the period of recurrent disease and recommendations of the Russian Ministry of Health, the probability of disease five and six months after vaccination was calculated.

In order to substantiate the necessity of revaccination, the indicator "probability of morbidity of employees of the studied groups after vaccination" was assessed in five months from the date of the first dose, which amounted to 3.53% - with a median IgG value of 330.80 BAU/ml, and in 6 months - 5.41% with a median IgG value of 274.05 BAU/ml, which can be a reference point of indications for revaccination.

In assessing the recurrent morbidity, we have previously statistically proved the fact that the recurrent morbidity in those who have been re-infected and vaccinated is significantly lower than in those who have only been vaccinated. This conclusion is associated with the presence of cellular immunity and its active function in protecting the organism from recurrent disease.

To assess the significance of cellular immunity, we analyzed the data of patients who underwent tests for the state of humoral and cellular immunity, who were over-vaccinated and then vaccinated with Sputnik V six months after vaccination.

The median level of T-cell response to NMO protein peptides (Me = 26.50): N, M, ORF3a, ORF7a (cellular response as a result of disease) was significantly higher than the median level of cellular response to S-protein peptides (Me = 51.00) (cellular response to vaccination).

The recurrent morbidity in the group of employees of the studied hospitals "re-infected and vaccinated" is reliably lower than in those only vaccinated, which is confirmed by the data on the level of cellular immunity six months after vaccination - in the group "re-infected and vaccinated" the value of the median level of cellular immunity NMO is reliably higher than the median level of cellular immunity S than in the group «vaccinated», and this result has no gender differences.

Thus, the complex of preventive measures in hospitals includes five main groups of measures:

1. Architectural and planning, which include:

- Room layout.
- Organization and maintenance of ventilation systems.
- At a «covid» inpatient facility, compliance during reassignment:
  - al location of «red» zones;
  - a system of sanitary gates and airlocks;
  - use of portable equipment;
  - obtaining a laboratory license with COVID-19.

2. Disinfection and sterilization measures

- Hand hygiene.
- Peculiarities of application of personal protective equipment in hospitals of different profiles - higher degree of protection in a «covid» hospital (e.g. for a «covid» hospital - a suit corresponding to type I of the anti-plague suit, respirator or filtering half-mask of protection class FFP3, extended medical gloves, and for a general hospital - a medical gown (disposable or reusable) with a cap, supplemented with a medical mask and goggles (shield), gloves, shoe covers (or replacement shoes with closed toe, made of materials that allow daily disinfection) [49]. Our proposed options are included in the methodological recommendations for physicians of radiology departments and dental physicians.
- Compliance with the procedure of medical waste management.

- Prevention of infections associated with the provision of medical care, microbiological monitoring.

- Rational selection of antibacterial therapy and disinfectants.

3. Administrative:

- Staff training.

- Compliance monitoring.

- Development of up-to-date algorithms, instructions, schemes for personnel.

- Monitoring of personnel health status (thermometry, PCR diagnostics).

4. Insulation:

- Separation of patient flows.

- In «covid» hospitals:

- Prohibition of admission of visitors, unassigned staff;

- isolation of patients with a confirmed diagnosis.

At the same time, PCR examination before hospitalization is obligatory for general hospitalization.

- Temporary isolation and transfer of patients to a «covid» hospital for patients with a confirmed diagnosis.

5. Vaccination.

The whole complex of preventive measures, where vaccination takes the leading place, led to a statistically significant reduction in the incidence of disease among the staff, and it was found that in the «covid» hospital, when the vaccination coverage of the staff is more than 77.5%, there is a reliable decrease in the incidence rate by 8 times, and in the general hospital - when the vaccination coverage is more than 67.7%, the incidence rate decreases by 3 times (Figure 33).

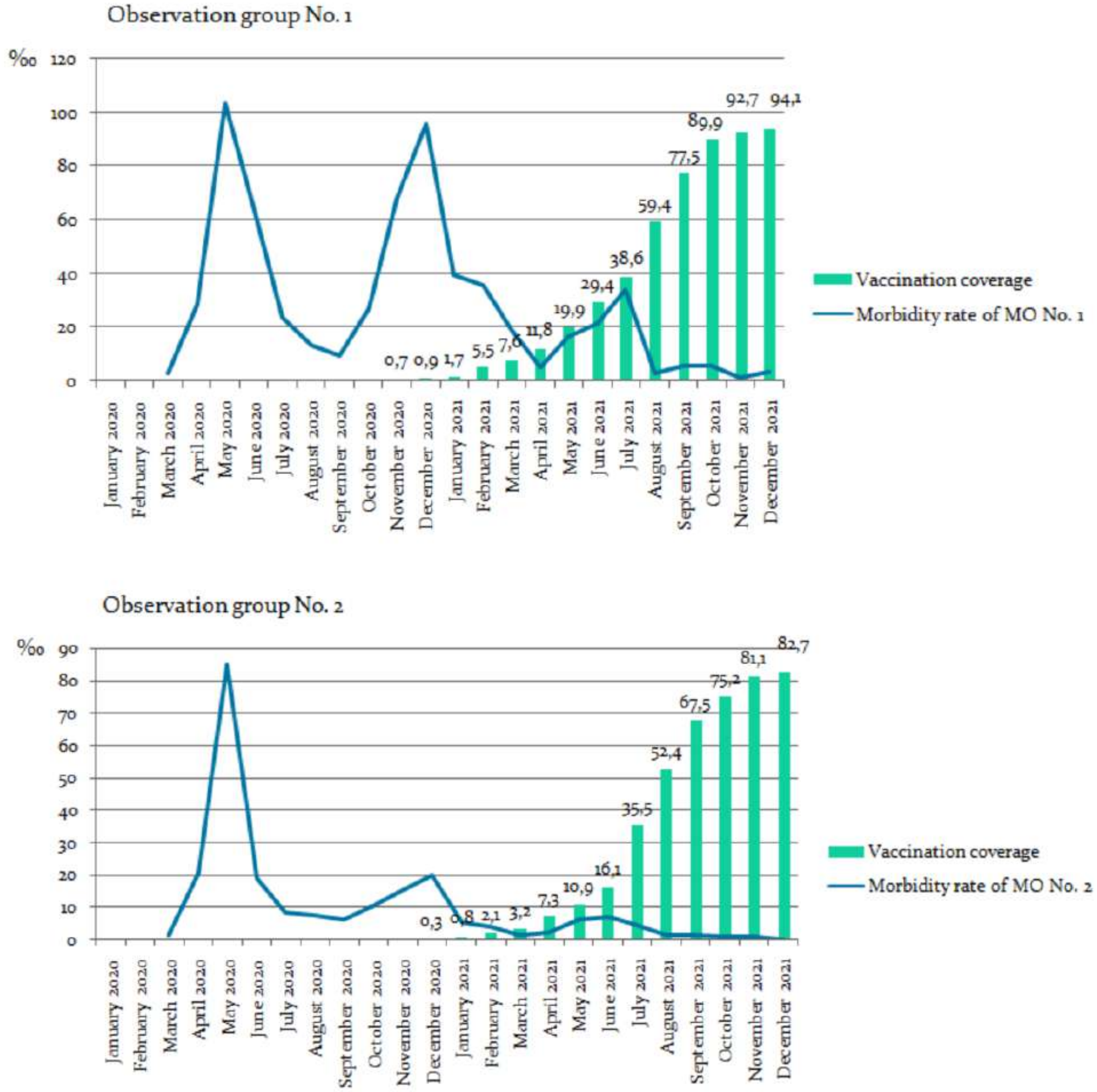


Figure 33 - Morbidity of health care workers (per 1000 people) and vaccination coverage during the post-vaccination period

RESULTS

On the basis of the conducted work and fulfillment of the set tasks we have formulated results:

1. The incidence of staff morbidity in the studied hospitals in the pre-vaccine period has no gender differences and is significantly higher than the city-wide population level, but the incidence of staff morbidity is higher in the «covid» hospital than in the general hospital (Me = 20.6; Me = 5.75) and is respectively 62.2% (men), 61.4% (women) - x-square = 0.56, p > 0.05; and 24.8% (men) - 22.2% (women) – x-square = 0.776, p > 0.05).

2. The number of vaccinated employees in the «covid» hospital is statistically significantly higher than in the general hospital and is 94.2% vs. 82.7% (X-squared = 82.433, p-value < 2.2e-16) respectively, which determines the profile of collective immunity of the studied groups.

3. Statistically significant differences were found for the COVID-19 disease onset period after Sputnik V vaccination, ranging from 6.9 to 8 months (maximum after 7.5 months, p-value = 0.9242) in the «covid» hospital, and from 5.46 to 6.34 months (maximum 5.9 months, p-value = 0.6612 in the general hospital).

4. In employees of the study groups vaccinated with Sputnik V, the median value of antibody titers (IgG) reaches its maximum value between 60 and 90 days after the first dose of vaccine and is 1144.30 BAU/ml (with 95% confidence interval [498.25; 1886.00]); in the period from 0 to 60 days after vaccination - 892.70 BAU/ml (with 95% confidence interval [428.90; 1359.90]), and in the period from 90 to 180 days decreases to 268.53 BAU/ml (with 95% confidence interval [171.30; 455.60]), after 180 days reaches the minimum level - 164.35 BAU/ml (with 95% confidence interval [208.50; 761.05]);

5. In order to justify the necessity of revaccination after six months, the indicator «probability of incidence of the study group employees after vaccination» was assessed five months after the date of the first dose, which amounted to 3.53% (in the range from 2.29% to 4.79%) with a median IgG value of 330.80 BAU/ml, and after six months - 5.41% (in the range from 3.89% to 6.92%), with a median IgG value of 274.05 BAU/ml, which can be a reference point of indications for revaccination.

6. Repeated morbidity in the group of employees of the studied hospitals "over-infected and vaccinated" is reliably lower than in the vaccinated group only

(z = -4.40, p = 1.07e-05), which is confirmed by the data on the level of cellular immunity six months after vaccination - in the group "over-vaccinated and vaccinated" the value of the median level of cellular immunity NMO is significantly higher than the median level of cellular immunity S (W = 2063.00, p-value = 3.979e-09) than in the "vaccinated" group, and this result has no gender differences (W = 610.50, p-value = 4.804e-05).

7. Application of a complex of measures, including architectural and planning solutions, isolation measures, disinfection and sterilization, use of PPE, as well as vaccination of the employees of the «covid» hospital and general hospital, respectively, more than 77.50% and 67.60% cause a significant reduction in the incidence of disease among health workers in 8 (observation group №1) and 3 times (observation group №2).

PRACTICAL RECOMMENDATIONS

In order to promptly carry out anti-epidemic measures and prevent the spread of COVID-19 in hospitals, regardless of the profile, it is necessary to develop an operational plan of action when identifying a patient suspected of this disease. All personnel should be familiarized and clearly follow the instructions, algorithms, standard operating procedures for therapeutic and diagnostic manipulations, hand hygiene, disinfection and sterilization measures and handling of medical waste. Control of personnel actions for compliance with the requirements may be carried out using checklists (e.g. checklist of readiness of the Radiation Diagnostics Department (computed tomography) to work in the conditions of pandemic COVID-19 is presented in Annex No. 3).

When a patient is admitted to a **general hospital**, PCR-diagnostics is mandatory, with subsequent transfer of the patient to a «covid» hospital if the diagnosis of COVID-19 is established.

Medical and service personnel should be equipped with working clothes and use personal protective equipment when providing medical care. For "covid" hospital: protective overalls or plague coat, high waterproof shoe covers; to protect the respiratory and visual organs use an anti-aerosol respirator (filtering half-mask) protection class FFP3 or insulating half-mask with anti-aerosol or combined filter protection class P3, sealed goggles; disposable medical gloves with extended cuffs. For general hospital: medical gown with cap, medical mask and goggles, gloves, closed-toe shoes made of materials that allow daily disinfection [49, 52, 105].

In the «covid» hospital it is necessary to provide redesign with the allocation of «dirty» and clean zones, airlocks for changing staff. For general hospital - separation of patient flows on admission with the allocation of patients with signs of infectious diseases to separate wards. During the period of active spread, ensure that visits by relatives and other persons who are not employees of the medical facility are prohibited. Movement of patients within the hospital is also restricted, and medical care with the use of portable/portable equipment is favored.

Special attention is paid to the operation and maintenance of ventilation systems, with regular cleaning, disinfection and efficiency checks of ventilation systems.

In order to protect staff, daily thermometry at the entrance to the institution and at the end of the working day, interviewing of staff before starting work are organized. Personnel with symptoms of acute respiratory infections (fever, cough, runny nose) are not allowed to work, it is recommended to ensure self-isolation [105].

Staff of health care organizations should be vaccinated against COVID-19 (two times vaccination) followed by revaccination after six months. In the absence of vaccination, weekly testing of staff to determine IgG levels is required. Individuals with titers less than 274.05 BAU/ml are suspended from work until vaccination. Reduction in the incidence of the disease is ensured when vaccination coverage exceeds 77.50% of employees in the general hospital and 67.60% in the «covid» hospital, provided that the entire set of measures is observed.

TOPIC DEVELOPMENT PROSPECTS

Due to the importance of the biological factor at the present stage of society development, with the emergence of new topical infectious agents in the population, it is necessary to continue research in the following directions: to assess the consequences of the new coronavirus infection on the human body, the so-called «postcovirus syndrome», in which the state of the immune system and susceptibility to viral infections are of particular importance, as well as to continue research on the state of humoral and cellular immunity in various categories of the immune system.

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LIST OF ABBREVIATIONS

HIV - human immunodeficiency virus

AVL - artificial ventilation of the lungs

HCAI - health care-associated infections

ELISA - enzyme-linked immunosorbent assay

CT - computer tomography

MRSA - Methicillin-resistant Staphylococcus aureus (MRSA).

ARI - acute respiratory infection

PCR - polymerase chain reaction

PPE - personal protective equipment

UV - ultraviolet

COVID-19 - Corona Virus Disease 2019,- infection caused by the new coronavirus SARS-CoV-2.

IgG - class G immunoglobulins.

SARS-CoV-2 is the new coronavirus that caused the COVID-19 pandemic.

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APPENDICES

Appendix 1

Etiology and pathogenesis COVID-19

COVID-19 is an acute viral disease with predominantly upper respiratory tract involvement. The causative agent is a single-stranded RNA-containing virus of the genus Betacoronavirus of the family Coronaviridae, line Beta-CoV B.

The Coronaviridae family includes more than 40 species of RNA-containing viruses that have a supercapsid. They are capable of infecting both animals (their natural hosts) and humans. Virions range in size from 80 to 220 nm. The nucleocapsid is a flexible helix consisting of genomic plus-strand RNA and a large number of nucleoprotein N molecules. Coronaviruses have the largest genome among RNA-genomic viruses. Its structure includes a supercapsid, which contains glycoprotein trimeric spikes (peplomers), membrane glycoprotein, small envelope glycoprotein, and hemagglutinin esterase. The presence of peplomers, which define the name of this family, is associated with a specific mechanism of penetration through the cell membrane by mimicking molecules to which transmembrane cell receptors respond.

The main target cells for coronaviruses are cells of the alveolar epithelium, in the cytoplasm of which the virus replicates. After virions are assembled, they are transferred into cytoplasmic vacuoles that migrate to the cell membrane and exit into the extracellular space by exocytosis. Expression of virus antigens on the cell surface before virions exit the cell does not occur, so antibody formation and interferon synthesis are stimulated relatively late. The formation of syncytium under the influence of the virus determines the ability of the latter to spread rapidly into tissues. The action of the virus causes an increase in the permeability of cell membranes and increased transport of albumin-rich fluid into the interstitial tissue of the lung and the lumen of the alveoli. This destroys surfactant, which leads to collapse of the alveoli, as a result of a sharp violation of gas exchange develops acute respiratory distress syndrome (ARDS). Immunosuppressive state of the patient contributes to the development of opportunistic bacterial and mycotic infections of the respiratory tract.

Pathogenesis

The entry gate of the pathogen is the epithelium of the human upper respiratory tract and epitheliocytes of the stomach and intestine [138, 174].

Infection of alveolocytes, cardiomyocytes, and endothelium of the vascular system by the virus leads to inflammatory changes including edema, degeneration, and necrotic changes. These changes are mainly associated with proinflammatory cytokines including interleukin IL-6, IL-10 and tumor necrosis factor α. This factor stimulates the growth of granulocyte colonies, increased programmed expression of macrophages inflammatory protein 1α, monocyte chemotaxis protein 1, and pathogenetic ability to develop viral pneumonia, cardiomyocyte damage, microcirculatory disorders, and small fiber neuropathy.

The respiratory system is the main system affected by SARS-CoV-2 virus. There are microscopic bilateral diffuse diffuse alveolar lesions, cellular fibromyxoid infiltrates, and interstitial mononuclear inflammatory infiltrates with a predominance of lymphocytes. The pathologoanatomical feature of alveolar lung lesions is dyschrony and prolongation with an infrequent combination of its two phases - exudative and proliferative. In this case, there is an increase in lung both in volume and mass, the organ itself is dark red (cherry) in color, very dense in consistency, there is a concept of airlessness and/or small airiness of the lung. When pressing from the surfaces of the incisions, dark-red fluid flows down, with difficulty squeezed out of the tissue.

Cardiovascular disorders in COVID-19 are described as diffuse microangiopathic thrombi, cardiomyocyte inflammation, cardiac arrhythmias, heart failure, and evolving acute coronary syndrome.

ACE2 is expressed in epithelial cells of the gastrointestinal tract, suggesting that the virus enters through ACE2 receptors and replicates, causing inflammatory changes in the GI tract (diarrhea, nausea, vomiting, and abdominal pain). SARS-CoV-2 also causes liver damage, which is manifested by elevated serum alanine aminotransferase and aspartate aminotransferase levels, and serum bilirubin and γ-glutamyltransferase levels may be elevated.

The lymphocytopenia seen during infection is due to CD4+ and some CD8+ T cells, and causes delayed virus elimination, which promotes hyperstimulation of macrophages and neutrophils in cells.

SARS-CoV-2 has potential neuropathologic properties. In the brain, ACE2 expression has been established in endotheliocytes, astrocytes, oligodendrocytes, microgliocytes, and neurons, i.e., in virtually all cells that support the vital activity and functional activity of the brain, as well as visceral regulation of organs and tissues. The pathogenic factors of COVID-19 should include, in addition to the direct action of the virus on cells, hypoxia with the development of acidosis, impaired microcirculation due to immune damage with the development of coagulation disorders, manifested by thrombosis and hemorrhage, the launch of autoimmune processes. Myelitis and neuropathies due to the development of Guillain-Barré syndrome are not uncommon. Psychiatric consequences of SARS-COV-2 are associated with prolonged depression (reported in 60% of survivors) and suicidal ideation (20%). Studies show an increased incidence of post-traumatic stress disorder, panic attacks, obsessive-compulsive disorders on the background of COVID-19 compared to the pre-infection period. The degree and duration of psychiatric and neurologic disorders and syndromes are highly variable during and after coronavirus infection.

Among the first COVID-19 symptoms reported are increased body temperature (90%), cough - dry or with little sputum (80%), dyspnea (55%), myalgias and fatigue (44%), feeling of tightness in the chest (20%), and headaches (8%), hemoptysis (5%), diarrhea and nausea (3%). These symptoms may also be present at the onset of infection in the absence of fever [150].

Clinical variants and manifestations of COVID-19:

1) acute respiratory viral infection of mild course;

2) pneumonia without respiratory failure;

3) pneumonia with acute respiratory failure (ARF);

4) acute respiratory distress syndrome;

5) sepsis;

6) septic (infectious-toxic) shock;

7) hypoxemia (decrease in SpO2 less than 88%) develops in more than 30% of patients.

Epidemiology

The natural reservoir of SARS-CoV-2 virus is bats. An additional reservoir may be mammals that eat them, with further spread to humans. Phylogenetic studies of isolated strains have shown that the genomic sequences of viruses found in bats are 99% identical to those isolated from COVID-19 patients.

The source of infection is an infected person at all stages of the disease, including the greatest risk for spread is a patient in the incubation period and an asymptomatic carrier of SARS-CoV-2 at the end of the incubation, prodromal period (the beginning of virus release from target cells) and during clinical manifestations.

The mechanism of transmission is aspiration. The leading route of transmission is airborne (virus release by coughing, sneezing, talking) through close contact (Table 1). The contact route of transmission is realized during handshakes and other types of direct contact with an infected person, as well as through surfaces and objects contaminated with the virus [99].The household contact route is realized through transmission factors: water, food and objects (door handles, smartphone screens) contaminated with the pathogen. The fecal-oral mechanism is possible (the pathogen was detected in fecal samples from patients infected with SARS-CoV-2). The fact of realization of the artificial mechanism of SARS-CoV-2 transmission has been established.

The role of SARS-CoV as a healthcare-associated infection (nosocomial [124, 138, 174]), has been established according to the following scenario: patient's admission to a COVID-19 hospital, neglect of epidemiologic data (contact, arrival from an endemic area), false-negative results of virus tests, stay in a general ward, and even admission to the intensive care unit on a ventilator with virus dissemination in the hospital. It has been shown that the seasonal increase of ozone in the surface atmosphere, occurring during spring and summer, can increase the severity of COVID-19 disease course and lead to additional deaths [31].

The incubation period for COVID-19 ranges from 2 to 14 days, more commonly 5 to 8 days (for comparison, the incubation period for seasonal influenza is about 2 days) [99]. For some strains (e.g., Omicron strain), it can be shortened to 2 to 3 days.

Table 1- Mechanisms and pathways of transmission of COVID-19

№п/п	Mechanism of transmission	Transmission path	Factors
1.	Airborne	air-drop Airborne	Droplet particles of respiratory secretion Dust particles Air
2.	Contact	Householdcontact	Hands Household items Medical instruments and materials
3.	Fecal-oral	Householdcontact	Hands Householditems

Based on data on epidemiology and transmission routes, susceptibility to the pathogen is high in all population groups. Risk groups for severe course of the disease and risk of lethal outcome include people over 60 years of age, patients with chronic diseases (respiratory diseases, cardiovascular diseases, diabetes mellitus, oncologic diseases). Lethality varies from 2 to 4%.

Appendix 2

Data bases

Covid inpatient staff database

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V
1	n/n	Gender	AGE	Date of birth	Medical department	Position	Medical staff	sickB1	sickB2	sickB3	AT 1	тиrp	sput1	sput2	lite	vaccine	sickA1	Anti-body after vaccination	titer			
2	1	F		29.09.1976	Therapy	Procedural nurse	nursing staff	May 2021			June 2021	319,3			Апрель 2021	Sputnik Light						
3	2	F		02.09.1999	Gastroenterology	nurse	nursing staff						May 2021	June 2021		Gam-Covid-Vac	January 2022	July 2021	330,8			
4	3	F		08.10.1973	Neurology №1	Trainee doctor	senior medical staff	December 2020	February 2021				May 2021	May .2021		Gam-Covid-Vac						
5	4	F		16.08.1986	Reception department	Medical registrar	junior medical staff						August 2021	August 2021		Gam-Covid-Vac	February 2022	November 2021	267,1			
6	5	F		03.02.1961	Medical Rehabilitation Department	Senior nurse	nursing staff	April 2020							August 2021	Fizer						
7	6	M		15.11.1986	FD room	Head of the office - FD doctor	senior medical staff								July 2021	Sputnik Light						
8	7	F		21.01.1967	Gynecology	Ward nurse (post nurse)	nursing staff	February 2021	July 2021				June 2021	June 2021		Covivac						
9	8	F		13.11.1966	MXO-4	Sanitation worker	junior medical staff	May 2020							October 2021	Sputnik Light						
10	9	F		30.11.1994	Neurology №3	Neurologist	senior medical staff						March 2021	April 2021		Gam-Covid-Vac						
11	10	F		18.07.1977	Department of X-ray EM of DaT	Operating room nurse	junior medical staff						March 2021	April 2021		Gam-Covid-Vac	March 2022	July 2021	79,34			
12	11	F		10.04.1954	btd	Nurse hostess	nursing staff						April 2021	May 2021		Gam-Covid-Vac						
13	12	M		08.10.1973	craniofacial surgery	Maxillofacial Surgeon	senior medical staff						March 2021	April 2021		Gam-Covid-Vac						

Database of general hospital staff

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S
1	п/п	Gender	AGE	Date of birth	Medical department	Position	Medical staff	sickB1	sickB2	sickB3	Antibody 1 (before vaccination)	titer	sput1	sput2	lite	vaccine	sickA1	Antibody 1 (after vaccination)	titer
2	1	f		02.06.1999	1 Anesthesiology-	Anesthesia nurse	nursing staff						November 2021	December 2021		Sputnik	February 2022		
3	2	f		28.02.1972	2 Pulmonology department	Ward nurse	nursing staff						September 2021	October2021		Sputnik	February 2022		
4	3	M		05.07.1987	Cardiosurgery department	Doctor-cardiovascular surgeon	senior medical staff						September 2021	October 2021		Sputnik			
5	4	M		06.11.1987	Cardiosurgery Department	Physician-cardiovascular surgeon	senior medical staff								September 2021	Light			
6	5	f		02.09.1975	Radiodiagnostic	X-ray laboratory	junior medical	Март 2020					September 2021	October 2021		Sputnik			
7	6	f		09.03.1990	1 therapeutic	General practitioner	senior medical	Март 2020			March 2021	156,4			September 2021	Light			
8	7	M		17.08.1983	2 Neurosurgery Department	Neurosurgeon Doctor (for emergency care)	senior medical staff						May 2021	Май 2021		Sputnik			
9	8	M		15.3.1991	Computer	Radiologist	senior medical								October 2021	Light			
10	9	f		04.08.1958	LFC	Physical therapy instructor	senior medical staff						December 2021	December2021		Sputnik		Feb.2022	67,6
11	10	f		13.12.1968	1 Pulmonology department	Procedure room nurse	nursing staff						September 2021	October 2021		Sputnik			
12	11	f		21.04.1980	1 therapeutic department	Head of department-physician-physician-therapist	senior medical staff	Апрель 2020			February 2021	15,6	July 2021	August 2021		Sputnik	November 2021		
13	12	M		06.10.1964	Traumatology department	Traumatologist-orthopedist doctor	senior medical staff	Апрель 2020					August 2021	September 2021		Sputnik			
14	13	f		10.02.1959	1 Pulmonology department	Ward nurse	nursing staff								July 2021	Light	January 2022		
15	14	f		22.07.1957	1 Pulmonology Department	Senior nurse	nursing staff						August 2021	September 2021		Sputnik	February 2022		

Patient database of a commercial medical center

1	2	3	4	5	6	7	8	9	10	11
п/п	Пол	ВОЗРАСТ	Дата рождения	Пациент, ЭМК	Заболевание 1	Вакцинация	Дата сдали (белок S)	Панель АГ к пептидам белка S	Дата сдачи (белок NMO)	Панель АГ к пептидам белка NMO
1	ж	43	27.11.1978	5638	да	29.07.2021	17.06.2021	27	17.06.2021	30
2	м	63	12.08.1959	8681	да	15.11.2021	22.07.2021	31	22.07.2021	42
3	м	59	01.03.1946	4008	да	03.11.2020	01.05.2021	80	01.05.2021	83
4	ж	55	02.02.1967	197943	да	27.01.2021	29.07.2021	12	29.07.2021	55
5	ж	76	01.03.1946	44173	да	22.06.2021	26.08.2021	93	26.08.2021	108
6	м	62	20.08.1960	136803	да	03.12.2021	05.04.2021	22	05.04.2021	78
7	м	67	14.08.1955	54021	да	11.12.2020	09.06.2021	28	09.06.2021	39
8	м	67	24.12.1954	41762	да	13.01.2021	12.07.2021	34	12.07.2021	18
9	ж	69	28.07.1953	42588	да	14.10.2020	12.04.2021	74	12.04.2021	76
10	м	48	26.04.1974	15409	да	15.12.2020	14.06.2021	57	14.06.2021	222
11	ж	67	16.03.1955	20016	да	21.10.2021	19.04.2021	24	19.04.2021	36
12	ж	66	23.03.1956	2918	да	21.11.2020	22.05.2021	26	22.05.2021	101
13	ж	23	04.02.1999	677443	да	25.02.2021	28.08.2021	35	28.08.2021	126
14	ж	64	11.08.1958	677434	да	29.01.2021	28.07.2021	24	28.07.2021	161
15	ж	44	08.02.1978	677438	да	29.01.2021	28.07.2021	69	28.07.2021	225
16	м	65	17.09.1957	677435	да	29.11.2020	28.05.2021	53	28.05.2021	45
17	м	38	14.12.1983	677433	да	01.02.2021	28.08.2021	13	28.08.2021	16
18	м	23	11.07.1999	677440	да	20.12.2020	28.06.2021	22	28.06.2021	120
19	ж	68	12.08.1954	693779	да	27.10.2020	04.05.2021	23	04.05.2021	32
20	м	58	16.06.1964	694339	да	29.10.2020	06.05.2021	31	06.05.2021	13
21	м	55	20.10.1967	510664	да	16.11.2020	24.05.2021	12	24.05.2021	16
22	м	55	20.10.1967	510665	да	17.12.2020	25.06.2021	17	25.06.2021	22
23	м	55	20.10.1967	510666	да	02.03.2021	29.08.2021	24	29.08.2021	8
24	м	42	01.10.1980	709225	да	28.11.2020	06.06.2021	309	06.06.2021	740
25	м	41	12.05.1981	9225	да	30.04.2021	05.11.2022	96	05.11.2022	245

Appendix 3

Readiness checklist for the Radiologic Diagnostic Department (CT) to work under COVID-19 pandemic conditions

1. Key activities to prepare radiology departments to work with patients with suspected and confirmed COVID-19

1	Separation of patient flows: different appointment times, different rooms for patients with suspected COVID-19 and patients with other pathologies	yes	no
2	Application of CT-surveys as a screening method for asymptomatic patients during hospitalization in order to prevent the introduction of infection into the medical organization.	yes	no
3	Training and briefing of medical personnel on prevention and prophylaxis of COVID-19 spread, including the use of PPE.	yes	no

2. Maintaining stable operation of the computer tomography room

1	The medical staff of the Department of Radiation Diagnostics is aimed at strengthening the work of CT rooms. Training of nursing staff to work on CT equipment was carried out	yes	no
2	Additional medical personnel were allocated to assist in the work of CT rooms	yes	no

3. Compliance with the requirements of sanitary and epidemiological regime

1	Patients with signs of acute respiratory infections and/or suspected pneumonia are examined in a designated CT room or at a designated time	yes	no
2	Control over the use of PPE (masks, shoe covers) by patients in the Department of Radiologic Diagnostics.	yes	no
3	Medical personnel in direct contact with patients are provided with PPE (masks, shoe covers, respirators, face shields, disposable gowns, caps).	yes	no
4	A monthly stock of PPE for medical personnel has been calculated and created	yes	no
5	Visual instructions on the rules of hand washing and treatment are placed in specially equipped places	yes	no

Continuation of Table 3

6	Visual instructions on removing/ putting on PPE have been placed in the places designated for removing/ putting on PPE	yes	no
7	Disinfection means - elbow or non-contact dispensers (sanitizers) with skin antiseptics are available at the entrance, in all rooms and resident rooms of the Department of Radiologic Diagnostics.	yes	no
8	Social distance of 1.5-2 meters in the waiting area of patients is ensured.	yes	no
9	Air disinfection devices are used: closed-type air recirculators - continuously during the working shift, in the presence of patients; open-type irradiators - according to the quartz schedule.	yes	no
10	Disinfection measures: current cleaning is carried out at least twice a day, general cleaning - once a week with fixation in the general cleaning log.	yes	no
11	Treatment of high-contact surfaces every two hours with disinfectants according to the antiviral regime: switches, door handles, etc.	yes	no
12	Disinfection of equipment parts touched by the patient after each appointment (treatment of the room with disinfectants (alcohol-based, ChAS) approved by the equipment manufacturer with a short exposure time)	yes	no

4. Maintenance requirements for the equipment of the radiology department

1	CT calibration is performed according to the manufacturer's documentation (periodicity for a particular device according to the manufacturer's recommendations)	yes	no
2	Evaluation of technical parameters of the scanning protocol (optimization of the study protocol to obtain the necessary diagnostic information with minimal radiation dose and increase the equipment resource).	yes	no

5. Documents on organization and control of sanitary and epidemic regime

1	Availability of orders on appointment of persons responsible for organization and implementation of anti-epidemic measures (availability of orders to be brought to the attention of employees)	yes	no
2	Availability of an industrial control program and protocols of tests/measurements approved by the head of the organization	yes	no
3	Presence of standard operating procedures and instructions on hand treatment, cleaning, diagnostic tests execution	yes	no
4	Availability of briefing of employees on organization of work in COVID-19 conditions.	yes	no
5	Daily thermometry of employees with recording of data in the journal	yes	no
6	Weekly PCR-examination of the staff of the radiation diagnostics department	yes	no
7	Vaccine prophylaxis of employees against COVID-19 once every 6 months or more often according to the results of antibody tests.	yes	no
