CRACoV-HHS: an interdisciplinary project for multi-specialist hospital and non-hospital care for patients with SARS-CoV-2 infection as well hospital staff assessment for infection exposure

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Acknowledgment
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Abstract: The complex course of the COVID-19 and the distant complications of the SARS-CoV-2 infection still remain an unfaded challenge for modern medicine. The care of patients with the symptomatic course of COVID-19 exceeds the competence of a single specialty, often requiring a multispecialist approach. The CRACoV-HHS (CRAcow in CoVid pandemic — Home, Hospital and Staff) project has been developed by a team of scientists and clinicians with the aim of optimizing medical care at hospital and ambulatory settings and treatment of patients with SARS-CoV-2 infection. The CRACoV project integrates 26 basic and clinical research from multiple medical disciplines, involving different populations infected with SARS-CoV-2 virus and exposed to infection.

Between January 2021 and April 2022 we plan to recruit subjects among patients diagnosed and treated in the University Hospital in Cracow, the largest public hospital in Poland, i.e. 1) patients admitted to the hospital due to COVID-19 [main module: 'Hospital']; 2) patients with signs of infection who have been confirmed as having SARS-CoV-2 infection and have been referred to home isolation due to their mild course (module: 'Home isolation'); 3) patients with symptoms of infection and high exposure to SARS-CoV-2 who have a negative RT-PCR test result. In addition, survey in various professional groups of hospital employees, both medical and non-medical, and final-fifth year medical students (module: 'Staff') is planned.

The project carries both scientific and practical dimension and is expected to develop a multidisciplinary model of care of COVID-19 patients as well as recommendations for the management of particular groups of patients including: asymptomatic patient or with mild symptoms of COVID-19; symptomatic patients requiring hospitalization due to more severe clinical course of disease and organ complications; patient requiring surgery; patient with diabetes; patient requiring psychological support; patient with undesirable consequences of pharmacological treatment.

Keywords: SARS-CoV-2 infection, patients with COVID-19, hospital care, non-hospital care, remote care, multi-specialists care, observational study, medical staff.

Introduction

The occurrence of an unusual form of severe pneumonia in December 2019 surprised first the health services of the nearly 9 million-population Wuhan city of China's Hubei province, and shortly thereafter the entire province with a population of 58.4 million. Experience gained in the fight against AIDS and SARS and improvements in PCR techniques made it possible to identify SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) as the cause of COVID-19 disease in just a dozen days — between December 2019 and January 2020. The epidemic quickly reached Europe and Poland, where the first case of COVID-19 was reported on March 4 2020 and the first death from the disease was registered on March 12 2020 [1].

The SARS-CoV-2 infection causes variable, often unpredictable symptoms — from scanty, resembling a typical cold, to severe respiratory distress accompanied by symptoms of the so-called cytokine storm. In the course of the disease, any organ may be affected, which results from the inclusion of the microcirculatory network into the disease process, the total length of which in humans is about 100 thousand km and the cross-sectional area 3500 cm^2 [2].

Fairly early in the SARS-CoV-2 pandemic, it was noted that patients treated in Chinese centers for COVID-19 had complex and variable coagulation abnormalities indicative of a hypercoagulable state. The inflammatory response induced by SARS-CoV-2 causes small vessel inflammation and abnormal activation of the coagulation system, leading to extensive thrombosis. Although the clotting abnormality is initially localized in small vessels, many patients die from thrombotic complications of the vascular bed, mainly due to pulmonary embolism and myocardial infarction [3, 4].

Hospitalized patients with COVID-19 need a multidisciplinary approach due to a plethora of clinical scenarios — from respiratory insufficiency requiring oxygen administration to acute respiratory distress syndrome, multiple organ failure, septic shock and death. Recently published data from our hospital database confirm, that advances age, male sex, diabetes and pre-existing heart failure are the main predictors of unfavorable course of COVID-19 [5].

The positions of international and national scientific societies (e.g. continuously updated recommendations of the National Institute of Health, International Society on Thrombosis and Haemostasis, Anticoagulation Forum, American College of Chest Physicians) or expert boards are helpful. At the end of March 2021, Position Paper No. 3 of the COVID-19 Scientific Forum of the Supreme Medical Council (pol. *Naczelna Izba Lekarska*) on thromboprophylaxis in COVID-19 was published in Poland, and on April 26, the recommendations of the Polish Society of Epidemiologists and Infectious Diseases Physicians (pol. *Polskie Towarzystwo Epidemiologów i Lekarzy Chorób Zakaźnych*) on the management of SARS-CoV-2 infections were updated [6, 7].

On March 11, 2020, the World Health Organization (WHO) announced that we are dealing with a pandemic, an epidemic of global dimensions. This unprecedented situation has raised concerns about the availability of a sufficient number of free beds in wards and intensive care, forcing far-reaching changes in the structure and organization of work of hospitals, including the establishment of new departments and temporary hospitals. The world faced a new challenge — to understand the course of the disease as quickly as possible, to develop treatments and a vaccine, and to develop an optimal model of COVID-19 treatment in various settings — during home isolation, in-hospital stay and post-discharge follow-up as well as medical staff surveillance [8].

Rationale

The **CRACoV-HHS** (**CRA**cow in **CoV**id pandemic — **H**ome, **H**ospital and **S**taff) project involving applied research has been developed by a team of scientists and clinicians from the largest clinical hospital in Poland with the aim of optimizing medical care at each stage of care and treatment of patients with SARS-CoV-2 infec-

tion. It takes into account a multidirectional approach to the patient with SARS-CoV-2 infection and will be implemented at the University Hospital in Cracow, which serves as a hospital for over 3 million people from the Malopolska Region. The project assumes medical care for patients with COVID-19 and monitoring their health status for the duration of the project. Among the modern solutions proposed in the project, it is planned to use ICT tools, implement applications for patients and staff with research and educational potential, which will have an impact on controlling the spread of the SARS-CoV-2 epidemic.

COVID-19 is a complex disease syndrome, and rapid detection of risk factors for early and late complications in the course of the disease may be crucial in clinical practice. Therefore, close monitoring of the patient's vital signs, identification of comorbidities, identification of an appropriate panel of laboratory tests, and careful analysis of imaging studies are necessary to delineate a management algorithm for the care of patients with COVID-19.

The complex course of the disease and the distant complications of infection present a challenge to modern medicine. The care of patients with the symptomatic course of COVID-19 exceeds the competence of a single specialty, therefore diagnosis and treatment of this group of patients require a new, multispecialist model of medical care.

Objective

The CRACoV-HHS project integrates basic and clinical research, conducted in inpatient and out-of-hospital settings, involving different populations infected with SARS-CoV-2 virus and exposed to infection. The primary goal of the project is to better understand the pathomechanisms that influence the course of infection and prognosis, including early and long-term physical and mental health complications of COVID-19.

Among the specific tasks of the project are:
1. developement of new methods to identify the infection — microbiologically and by improving analytical methods for diagnostic imaging;
2. identification of factors that determine the different clinical picture of the SARS-CoV-2 infection;
3. to understand the risk factors of cardiovascular complications, including the risk of venous thromboembolism and respiratory complications;
4. to recognize the risk factors of complications of metabolic and excretory functions;
5. to assess the incidence of early and distant organ and functional complications in patients with a mild, moderate and severe course of infection;
6. evaluation of the immune system response in terms of antibody production and determination of the dynamics of antibody titer changes after COVID-19 infection and/or vaccination;

7. evaluation of the safety of the administered pharmacotherapy, with identification of risk factors for the development of nephro- and hepatotoxicity;
8. development of IT solutions to remotely monitor health status and thereby improve patient safety in home isolation;
9. development of IT solutions to support the development of defense mechanisms in the fight against stress associated with illness;
10. assessment of exposure of medical and non-medical hospital staff to SARS-CoV-2 infection with determination of knowledge of principles of infection prevention and control among staff;
11. assessment of environmental safety — in hospital, operating block settings;
12. creation of databases containing clinical and biochemical data of patients hospitalized at UHK since the beginning of the pandemic.

Study design and settings

Study design

The project, named CRACoV-HHS, is an interdisciplinary effort that brings together 26 research projects from multiple medical disciplines. A simplified scheme of the project is shown in Diagram 1.
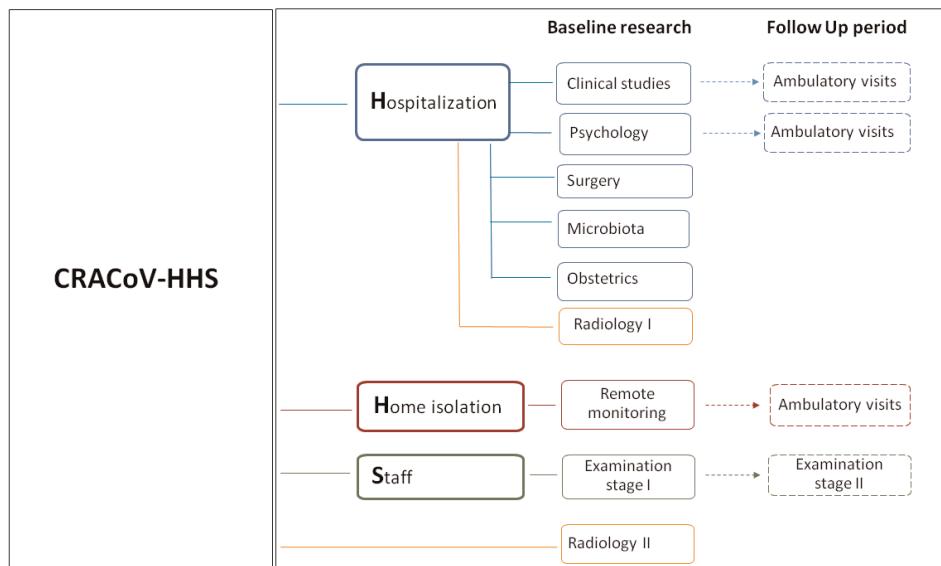
Diagram 1. The CRACoV-HHS project design.

The main module of the project is the "Hospitalization" part with 23 projects in clinical medicine, mental health, diagnostic microbiology and imaging, and environmental assessment in the operating suite. The characteristics of the subprojects, i.e., main objectives, description of the population and planned number of participants, as well as the main outcomes of each project are presented later in this article (Section 2.5).

Additional modules in the CRACoV project are:

a. Home Isolation module — remote monitoring of patients with a confirmed diagnosis of COVID-19, asymptomatic or with mild symptoms, qualified for home treatment;

b. Staff module — examination of medical and non-medical staff of the University Hospital in Cracow;

c. studies in the group of patients with high risk of COVID-19 infection and negative RT-PCR test — the sub-study called 'Radiology II'.

Among the tasks carried out within the framework of the CRACoV main module, there are also projects aimed at performing retrospective analyses of clinical, laboratory and imaging data concerning patients hospitalized due to COVID-19 at the Cracow University Hospital since the beginning of the pandemic, i.e. since March 2020.

Time periods of the study

Primary recruitment period for the main module: January 2021 to June 2021.
Completion of follow-up recruitment for selected sub-studies: April 2022.
Period of follow-up outpatient visits: March 2021 to April 2022.

Study settings

Studies carried out for the CRACoV-HHS project are conducted within the University Hospital in Cracow, which is the largest teaching hospital in southern Poland. It has a database of over 1300 hospital beds, located in 39 departments of conservative and surgical specialties. In the years preceding the pandemic, the annual number of hospitalizations was about 70,000.

As of March 2020, the University Hospital of Cracow has been designated as the single-named hospital, and for a later period of the pandemic, as the coordinating hospital in the region for the care of patients with SARS-CoV-2 infection, both with COVID-19 symptoms and those requiring hospitalization for other reasons (e.g., heart attack, stroke, pregnancy and childbirth, trauma, psychiatric disorders).

Depending on the period of the pandemic, the number of sites dedicated to COVID-19 patients ranged from 200 to 500 hospital beds. The total number of hospitalizations due to COVID-19 between March 2020 and June 2021 was 5,500.

Organizational structure

The study is implemented by approx. 200 members of research teams and expert committees performing scientific and research tasks and approx. 350 employees of the University Hospital (i.e. staff of COVID departments, laboratory and imaging diagnostics staff, CRACoV-HHS outpatient clinic staff) performing medical procedures and tasks defined within the main and supplementary modules.

The organization of the CRACoV-HHS project is summarized in Diagram 2. The members of the different expert teams and representatives of the units involved in the organization and implementation of the study are summarized in Table S1 in the supplementary materials.
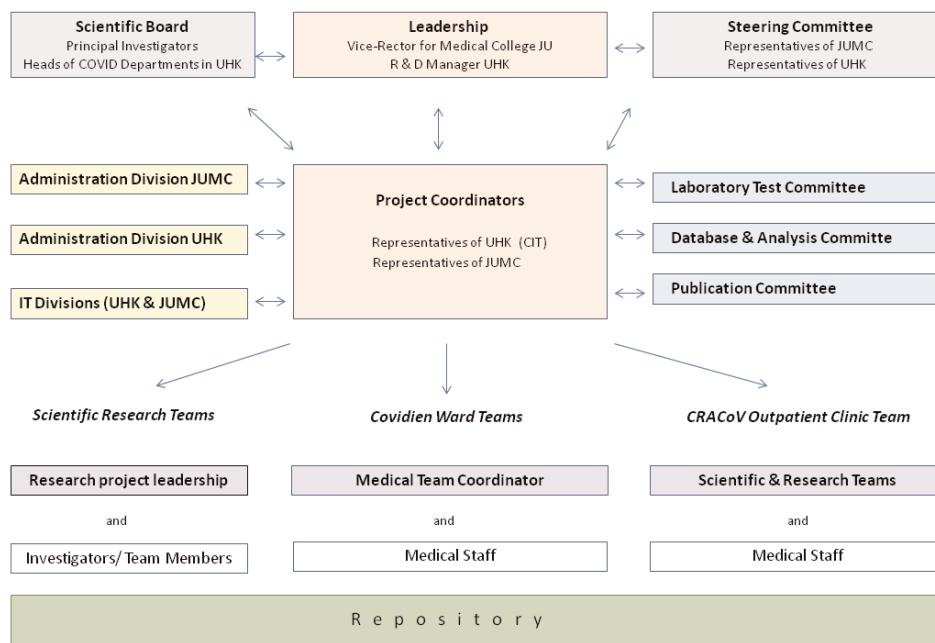
Diagram 2. Organizational structure of the CRACoV-HHS project.

General information about the project

The project was submitted to the competition launched by the National Centre for Research and Development (pol. *NCBiR — Narodowe Centrum Badań i Rozwoju*) for Single Name Hospitals dedicated to COVID-19 as part of the so-called fast track procedure on July 14, 2020 by the Project Leader i.e. University Hospital in Cracow and Jagiellonian University Collegium Medicum as the Consortium Partner.

The project has received funding in the amount of PLN 25 million.

The start date of the project is October 30, 2020.

After obtaining the NCBiR consent in September 2021 to extend the study by 6 months, the completion of the research part is planned for 29th April 2022.

Methods

1. STUDY POPULATIONS

The CRACoV-HHS project includes patients under the medical care of the University Hospital in Cracow, i.e.:

— patients admitted to the hospital due to COVID-19;

— patients with COVID-19 transferred to the University Hospital as a highly specialized unit for treatment of the complications or for highly specialized procedures;

— patients with signs of infection who have been confirmed as having SARS-CoV-2 infection and have been referred to home isolation due to their mild course;

— patients with symptoms of COVID infection and high exposure who have a negative RT-PCR test result.

In addition, the project planned to survey various professional groups of hospital employees, both medical and non-medical, and final-fifth year medical students.

Table 1 summarizes the characteristics of the CRACoV-HHS study populations that constitute the main modules of the project, along with the estimation of the number of participants at the project design stage.

Table 1. Characteristics of studied population in the CRACoV-HHS project.

The CRACoV-HHS modules		Studied population	Estimated no. of participants
Abbreviation	Full name		
H	Hospitalization	Patients with SARS-CoV-2 infection hospitalized in different COVID units in UHK	600
H	Home isolation	Asymptomatic patients or with mild COVID-19 symptoms eligible for home isolation	100
S	Staff	Hospital staff (medical and non-medical staff, students of medical school)	880
—	Radiology II sub-study	Symptomatic patients with high risk COVID-19 infection and negative RT-PCR test	250

Abbreviations: UHK — University Hospital in Cracow, RT-PCR test — reverse-transcription polymerase chain reaction test

1.1. General assumptions regarding sample size

Due to the nature of the project, estimates of the minimum number of patients in the main module 'Hospitalization' (n = 600) are the outcome of:
— assumptions regarding the duration and pace of active recruitment to the main module, to ensure up to 12 months of post-hospital follow-up;
— the presence of additional inclusion criteria for each clinical sub-studies;
— calculation of the population size in the clinical sub-studies;
— estimation of patient loss during post-hospital follow-up (30% to 50%).

The number of patients in the 'Home Isolation' module (n = 100) takes into account the estimated assumptions regarding the minimum recruitment falling in the next stage of project implementation, i.e. after completion of patient recruitment for the main module.

In the module covering hospital staff, the following assumptions were made at the survey planning stage for sample size calculation:
— total sample size i.e. total number of hospital staff: 5000;
— expected prevalence: 0.5; margin of error: 3%; confidence level: 95%.

2. CORE MODULE: HOSPITALIZATION. DESIGN AND METHODS

2.1. Standard of care (SOC)

2.1.1. SOC prior to patient recruitment into the project

On admission, each patient hospitalized for COVID had an initial health assessment including a physical examination, physical examination, measurements of basic vital signs including blood saturation on ambient air and/or oxygen therapy) even before the patient recruitment stage of the study. As part of the standard laboratory diagnosis, a defined panel of laboratory tests included the following blood tests in each patient with SARS-CoV-2 infection on admission: morphology with smear, glucose, glycosylated hemoglobin (HbA1c), urea, creatinine, alanine aminotransferase (ALAT), aspartate aminotransferase (ASPAT), gamma-glutamyl transferase (GGTP), alkaline phosphatase, Na, K, Ca, procalcitonin, C reactive protein (CRP), creatine kinase (CK), d-dimers, lactate, troponin, lactate dehydrogenase (LDH), myoglobin, prothrombin time, ferritin, interleukin-6, N-terminal pro B-type natriuretic peptide (NTproBNP), thyroid-stimulating hormone (TSH), free triiodothyronine (fT3), free tyroxine (fT4), vitamin D, total bilirubin, total protein, albumin, and urinalysis.

Imaging examinations were performed depending on medical indications, according to the standard of care of the University Hospital in Cracow for patients with COVID-19 infection.

2.1.2. SOC after patient recruitment to the project

Of the laboratory determinations routinely performed at the University Hospital, the following time points were defined for subsequent biological material collection for the CRACoV study:

   a. during hospitalization: day 7 and day of hospital discharge (day 14 ± 4 days);
   b. during the outpatient follow-up period: 1, 3, 6 and 12 months after hospitalization.

2.2. Recruitment to the main module and qualification for sub-studies

Recruitment to the various sub-projects was scheduled on the first day of patient admission to the ward. According to the eligibility criteria for the main module, the patient will be included in the study after signing an informed consent to participate in the proposed medical procedures during hospitalization and at the end of hospitalization, accepting further follow-up up to 12 months after hospitalization.

After meeting the main conditions for inclusion in the study, the patient will be evaluated by the recruiting physician for additional eligibility criteria for the clinical sub-studies (cardiology, nephrology, geriatrics, laryngology, etc.). The time points and general scheme of the main module 'Hospitalization' are presented in Diagram 3.
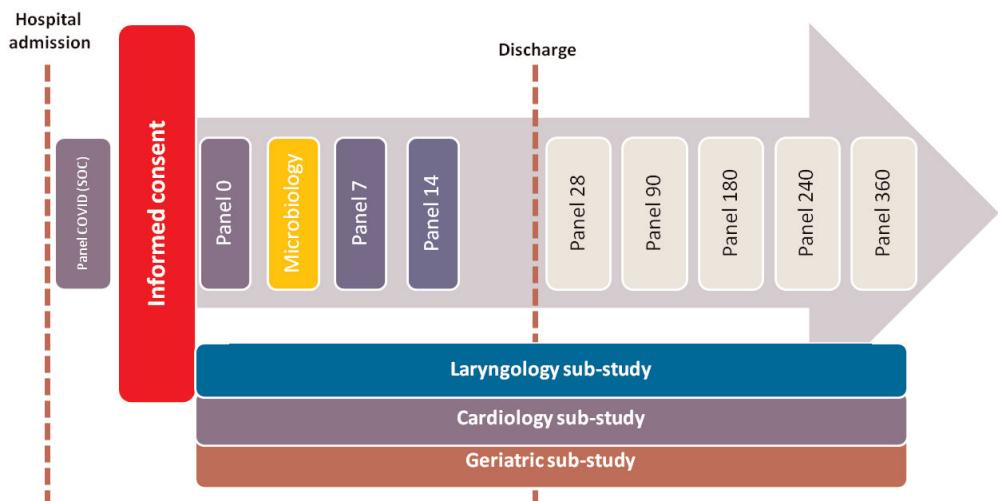
Diagram 3. General scheme of the CRACoV main module: the 'Hospitalization' with time points in the study.

Primary Inclusion / Exclusion criteria
Inclusion criteria
1. informed consent to participate in the study,
2. confirmed COVID-19 infection (positive RT-PCR or antigen test),
3. age ≥18 years of age.

Exclusion criteria
1. inability to give informed consent to participate in the study.

Specific inclusion / exclusion criteria
Inclusion criteria (specific for sub-studies of the Hospitalization Module)
1. age ≥65 years (Geriatric sub-study),
2. age 45–70 (Cardiology I and II, Nephrology sub-study),
3. age 20 and over (Microbiota sub-study),
4. up to 14 days after symptoms of COVID-19 infection (Microbiology sub-study),
5. taste and smell disturbances (Laryngology sub-study),
6. absence of cognitive or psychiatric abnormalities that could significantly affect neurological assessment (Neurology sub-study).

Exclusion criteria (specific to sub-studies of the Hospitalization module)
1. a most recent positive test for SARS-CoV-2 obtained more than 14 days regardless of length and location of hospitalization,
2. confirmation/suspicion of allergic rhinitis,
3. confirmation of chronic sinusitis; condition after sinus surgery,
4. confirmation/suspicion of cancer within the nasal cavity and paranasal sinuses,
5. pregnancy,
6. suspected high-risk VTE (sudden cardiac arrest, hemodynamic instability, shock symptoms),
7. history of interstitial lung disease,
8. hemodynamic instability,
9. chest deformity preventing lung ultrasound examination,
10. severe general condition of the patient and the need for oxygen therapy >5 l/min since the beginning of hospitalization,
11. previous diagnosis of left ventricular systolic dysfunction with EF <40%,
12. previously diagnosed severe valvular heart defect,
13. history of cardiovascular incident of atherosclerotic etiology within 6 months before study entry (stroke, myocardial infarction, coronary or peripheral artery angioplasty, coronary artery bypass grafting),
14. chronic kidney disease with eGFR <30 ml/min/1.73 m^2 on examination at admission,

15. patients with chronic kidney disease (CKD) or suspected CKD with at least one abnormal urinalysis (including proteinuria and/or hematuria within 3 months prior to study inclusion),

16. patients who are on a chronic dialysis therapy program,

17. renal transplant patients,

18. time from intubation and start of mechanical ventilation >24 hours (for ICU patients).

2.3. Medical and scientific research procedures

2.3.1. Common to the main module

a. Collection of clinical information based on a standardized clinical interview questionnaires developed for the study and made available in the hospital informatics system:

   i. *CRF_H_Admission* (Clinical Report Form for assessment at hospital admission) — symptoms of COVID, pre-hospital medical management, presence of chronic conditions and ongoing medications/over-the-counter drugs, severity of COVID course, information on vaccinations, data from physical examination, anthropometric measurements, in case of administered oxygen therapy — information on the method, the flow parameters;

   ii. *CRF_HAE* (Clinical Report Form for Hospital Adverse Events) — reporting of new diagnoses/clinical events/therapeutic procedures/pharmacotherapy during hospitalization, disease progression, transfer to another ward and basic vital parameters.

b. Collection of biological material:

   i. Additional nasopharyngeal and/or oral swab for infections with respiratory viruses (e.g., influenza) or bacteria other than COVID-19;

   ii. Among mechanically ventilated patients microbiological samples will be collected twice — first and seventh day, from each subject materials will be collected from various habitats of the oral cavity: (a) gingival pocket (fluid), (b) dental plaque, (c) swab of the soft palate, buccal and tongue;

   iii. Additional fasting blood samples to secure biological material and perform laboratory assays for:

   - genetic testing for blood hypercoagulability
   - telomere and netosis assessment
   - COVID-19 and RNA
   - level of antibodies against COVID-19 in blood
   - inflammatory biomarkers

- coagulation biomarkers
- biomarkers of vascular endothelial damage
- assessment of the blood-brain barrier
- assessment of angiogenesis and myocardial fibrosis
- profiling of plasma proteins
- assessment of liver and kidney specific plasma miRNA levels and profile (in selected patients only).

iv. Additional urine samples to preserve biological material and search for biomarkers of subacute kidney injury (subAKI).

2.3.2. Additional medical procedures performed in specific patient groups qualified for the research sub-studies

— photographic documentation of oral cavity dentition,
— serial ultrasound examinations of the lungs,
— 2-point compression ultrasound for the diagnosis of deep venous thrombosis of lower extremities,
— quality of life assessment questionnaires,
— geriatric assessment questionnaires and functional tests,
— assessment of strength and muscle mass in geriatric patients,
— immunological consultation,
— psychological and/or psychiatric consultation,
— geriatric consultation,
— laryngological examination evaluating taste and smell disorders and nasal cytology — on selected patients,
— neurological examination to evaluate neurological symptoms and syndromes associated with COVID-19,
— dental examination and assessment of the oral health (BOAS — Beck Oral Assessment Scale) of mechanically ventilated patients.

2.4. Out-of-hospital phase

Post-infection patients will receive medical care at University Hospital until the end of the project duration. The follow-up phase will last up to 12 months from the beginning of hospitalization. According to the study design, the first outpatient visit will take place at the end of the 1st month after hospitalization, the second visit in the 3rd month after hospitalization and subsequent visits at three-month intervals.

Procedures performed during follow-up visits:

1. assessment of basic vital signs;
2. collection of fasting blood and urine to secure biological material for laboratory determinations defined in individual observation periods;

3. medical examination, including standardized interview based on the electronic 'CRF_FU' completed in subsequent months of follow-up of patients after discharge from the hospital (months: 1, 3, 6, 9 and 12);

4. patient self-assessment regarding quality of life and presence of neuropsychological symptoms after COVID-19;

5. functional tests, imaging — according to the schedule of individual sub-studies.

Detailed summary of medical procedures performed within the main module of the CRACoV project in the hospital and post-hospital phase is presented in Table 2.

Table 2. Hospitalization module in the CRACoV project: in-hospital and out-of-hospital phase procedures performed under the various sub-studies.

Procedures	Hospitalization month (day)				Ambulatory visit month (day of FU)				
	0 admission	0 (1)	0 (7)	0 (14)	1 (28)	3 (90)	6 (180)	9 (240)	12 (360)
SOC	X								
Consent to participate in the study and qualification for study panels [a]		X							
A visit to the hospital out-patient clinic					X	X	X	X	X
Physical examination		X	X	X	X	X	X	X	X
Measurement of vital signs		X	X	X	X	X	X	X	X
Microbiological swabs (nasopharynx)		X							
Microbiological oral swab from mechanically ventilated patients	X		X						
Microbiological swabs (oral cavity) in patients recovering from COVID-19				X					
Electrocardiogram		X			X		X		X
Echocardiography		X			(X)	X	X		X
Pulmonary function tests (spirometry and DLCO)						X			X
6-minute walk test						X			X
Lung ultrasound		X	X	X		X			X
Ultrasound of veins of lower limbs with 2-point compression test		X							

Table 2. cont.

Evaluation of taste and smell		X	(X)	(X)	X	X	X		
Nasal cytology		X			X	X	X		
Psychological teleconsultations		X - X							
Blood and urine tests to measure biomarkers of the course of infection COVID-19		X	X		X		X		X
Fasting blood test to measure antibodies to COVID-19				X		X		X	X
Blood test for clotting disorders		X			X				
Blood tests to assess liver function		X	X	X	X	X	X	X	
Blood tests to measure biomarkers of angiogenesis		X	X		X		X		X
Blood tests to measure biomarkers of myocardial fibrosis		X			X		X		X
Blood tests to measure biomarkers of endothelial dysfunction		X			X		X		X
Blood tests for telomere assessment		X							
4Geriatric panel [c]		X		X		X			
Blood test for biomarkers of blood-brain barrier damage		X				X			
Urine tests for measurement of renal biomarkers		X	X		X		X		X
Blood tests to measure renal biomarkers		X	X						
Blood tests for proteomic measurements		X		X			X		
Pharmacotherapy [b]		X [b] —————X			X	X	X		X

Abbreviations:
SOC — blood and urine tests within standard of care procedures in UHK; UHK — University Hospital in Cracow; FU — follow up; DLCO — diffusion lung capacity for carbon monoxide.
Legend:
[a] depending on clinical indications
[b] first sampling on the day of starting pharmacotherapy (dexamethasone, remdesivir, antibiotic or other drug according to current guidelines), every 48 h, last sampling on day 14
[c] only patients ≥65 years of age
(X) — optional procedure

2.5. Characteristics of the research sub-studies carried out within the 'Hospitalization' module

An summary description of the research projects concerning the different groups of patients hospitalized at the University Hospital and the clinical-epidemiological aspects is summarized in Table 3.

The simplified characteristics of the sub-studies presented in this publication include:

— study area (the working name of the sub-study under which it operates);
— main objective of the sub-study;
— description of the population, including specific eligibility criteria for the sub-study;
— the number of patients in the sub-study estimated by the Investigators;
— time points of post-hospital follow-up defined for the sub-study;
— assumed effects of a sub-study implementation.

Details regarding the methodology of the research and analysis conducted will be reported in detail in the sub-study publications.

3. CHARACTERISTICS OF ADDITIONAL MODULES OF THE CRACoV-HHS PROJECT

3.1. Home isolation

Home isolation is an important strategy to manage the SARS-CoV-2 pandemic ("keep COVID-19 out of hospitals"). When qualifying patients for home isolation, it is important to remember that the course of COVID-19 is difficult to predict and even asymptomatic or poorly symptomatic patients may deteriorate suddenly. Therefore, it is essential to supervise patients in home isolation to ensure early and optimal treatment, including referral to hospital, in the event of deterioration.

Objective. The aim of the project is to develop and implement a system for remote monitoring of the health status of a patient with COVID-19, qualified for home treatment, based on an informatics system taking into account the use of a web and mobile application.

Population. Adults with confirmed SARS-CoV-2 infection, qualified for home isolation.

Estimated number of population: approximately 100 individuals.

Description of intervention. Through the developed application, the patient participating in the project will report on a daily basis: a) his health status by answering questions contained in a specially designed questionnaire, b) selected vital parameters

Table 3. Characteristics of the sub-studies carried-out under the CRACoV-HHS project — the Hospitalization module.

No.	Research area (alphabetical order)	Main objective	Population Specific inclusion / exclusion criteria	Estimated no. of subjects	Follow-up (months)	Results / Achievement
1.	Cardiology I (interdisciplinary project)	To establish retrospectively a COVID-19 patient database containing clinical data on patient profile, course of infection and treatment.	COVID-19 patients hospitalized at the University Hospital in Krakow (UHK).	—	*Not applicable*	A large database of patients treated to a defined standard at a single hospital.
2.	Cardiology I	1. To determine whether expanding the diagnostic biochemical panel to include parameters of impaired angiogenesis will more effectively predict the worsening clinical course of COVID-19 depending on the coexistence of hypertension. 2. To define a procedure for monitoring and detecting heart failure based on fibrosis markers, echocardiography, and vascular stiffness assessment in patients after SARS-CoV-2 infection to prevent potential late complications of COVID-19 disease.	Patients hospitalized for COVID-19. No previously diagnosed left ventricular systolic dysfunction, severe valvular heart defect, No history of cardiovascular incident of atherosclerotic etiology within the last 6 months and renal failure (eGFR <30 ml/min/ 1.73 m^2).	200	FU: 1, 3, 6, 12 m	Development of a procedure to predict and detect early cardiac dysfunction after COVID-19.
3.	Cardiology II	To assess to what extent COVID-19 infection impairs vascular endothelial	Patients hospitalized for COVID-19. Inclusion/exclusion criteria	200	FU: 1, 6, 12 m	An attempt to associate the degree of endothelial dysfunction and its changes

No.	Research area (alphabetical order)	Main objective	Population Specific inclusion / exclusion criteria	Estimated no. of subjects	Follow-up (months)	Results / Achievement
		function and whether assessment of markers of endothelial dysfunction may be useful in risk stratification of these patients.	same as in Cardiology I project.			over time with adverse clinical course after COVID-19 infection. An attempt to use assessment of endothelial dysfunction to optimize risk stratification and plan prophylactic management in patients after COVID-19 infection.
4.	Diabetology	Building a database of patients with COVID-19 — with and without coexisting diabetes.	Patients hospitalized at UHK for COVID-19 with and without diabetes. Nationwide data from hospitalizations of patients with diabetes.	5000	*Not applicable*	To develop recommendations for the management of diabetic patients affected by COVID (or another infection similar in nature) and principles for safe glycemic monitoring in patients with different types of diabetes in hospital and out-of-hospital settings.
5.	Immunology	Determination of IgM, IgA and IgG antibody titers in the first year after infection to evaluate changes in antibody titers, persistence of antibody titers after infection and/or vaccination. To evaluate the relationship between antibody titers and	Patients hospitalized for COVID-19. Patients referred to a monitored home isolation project. Medical staff.	500 100 1000	FU: 1, 3, 6, 9, 12 m	To evaluate the humoral response to SARS-CoV-2 infection. To assess the risk and monitor for possible reinfection.

No.	Research area (alphabetical order)	Main objective	Population Specific inclusion / exclusion criteria	Estimated no. of subjects	Follow-up (months)	Results / Achievement
		the clinical course of the infection.				
6.	Geriatrics	To assess the risk and incidence of acute sarcopenia and reserve depletion syndrome (aka weakness syndrome) in association with COVID-19. To determine the trajectory and dynamics of recovery and the incidence of complications in these patients.	Patients hospitalized for COVID-19, age: 65 years and above.	180	Re-evaluation at discharge. FU: 3 m Phone calls: 6 and 12 m	Identification of risk factors for the development of acute sarcopenia in COVID-19 infection in older hospitalized patients. To develop recommendations for the management of the elderly patient with a severe infectious process at risk of developing acute sarcopenia.
7.	Hepatology	To evaluate the association between SARS-CoV-2 infection and serum levels of selected adipokines and hepatokines, taking into account the presence of co-morbidities, particularly metabolic diseases, liver diseases and gastrointestinal symptoms.	Patients hospitalized for COVID-19. No additional inclusison / exclusion criteria.	270	FU: 1 m	To determine the utility of measuring selected adipokines and hepatokines and their prognostic value for assessing disease progression and mortality in COVID-19 patients.
8.	Laryngology	Smell and taste examination in patients with COVID-19 — to determine whether olfactory disturbances in the course of COVID-19 are always accompanied by taste disturbances.	Patients hospitalized for COVID-19. No previously diagnosed allergic rhinitis; chronic sinusitis; sinus surgery; neoplastic disease within the	50	FU: 1, 3, 6 m	To determine the role of olfactory and taste dysfunction in patients with COVID-ID-19 in predicting the severity of infection.

No.	Research area (alphabetical order)	Main objective	Population Specific inclusion / exclusion criteria	Estimated no. of subjects	Follow-up (months)	Results / Achievement
		To attempt to establish the olfactory and taste profile. Determine risk factors for the onset or persistence of olfactory/taste disorders.	nasal cavity and paranasal sinuses.			To perform a qualitative assessment of sensory dysfunction. To develop a management strategy in persistent olfactory/taste dysfunction — attempt to establish a treatment regimen with adjunctive substances/intranasal medications.
9.	Lung ultrasound	To determine the utility of lung ultrasonography, performed according to a standard protocol, in the diagnosis, monitoring, and prognosis of pneumonia in COVID-19 virus infection.	Patients hospitalized for COVID-19. Without previously diagnosed interstitial lung disease, chest deformity preventing lung ultrasonography.	80	FU: 3 and 12 m	To evaluate the diagnostic and prognostic potential of ultrasonography in patients with COVID-19 infection. To include ultrasonography in diagnosis as an alternative to more expensive and time-consuming radiologic procedures with a higher risk of infection transmission.
10.	Microbiology	Development of an assay based on fluorescence in situ hybridization (FISH) to differentiate SARS-CoV-2 virus from influenza viruses. Additionally, to investigate the frequency of viral upper respiratory tract	Patients hospitalized for COVID-19. Time from onset of symptoms — max. 14 days	300	*Not applicable*	Improving the efficiency of diagnosis of SARS-CoV-2 infection and the occurrence of COVID-19. Prediction of the clinical course of infection.

No.	Research area (alphabetical order)	Main objective	Population Specific inclusion / exclusion criteria	Estimated no. of subjects	Follow-up (months)	Results / Achievement
		co-infections in the course of COVID-19 as well as to evaluation of effectiveness of antigen tests in rapid laboratory diagnostics of infections caused by SARS-CoV-2 virus in comparison to qPCR as a gold standard.				
11.	Microbiology Antibiotic consumption	To review the use of antibiotics and other antimicrobial drugs during the pandemic, both in COVID-19 patients and in other patients in the context of suspected or confirmed of different clinical forms of infections, with different etiologies, including bacterial and fungal. Analyze whether and how the use of antibiotics, other antimicrobial drugs, and drugs from other groups used for symptomatic treatment has changed over time, i.e., comparing the period before and during the pandemic, including periods of increased mor-	Patients treated for COVID-19 and other patients of UHK hospitalized during the pandemic.	51 832 patients without COVID-19 symptoms and 5160 patients with confirmed COVID-19	Data from March 2020 to February 2021	Described in detail: — consumption of antibiotics, other antimicrobial drugs, and drugs used for symptomatic treatment COVID-19; — epidemiology and microbiology of co-infections with bacterial and fungal etiology; — patient demographics and characteristics of selected clinical parameters, patients hospitalized during the different stages of pandemic development. The analysis will use stratification of patients into cohorts: COVID-19 (+) vs. COVID-19 (–);

No.	Research area (alphabetical order)	Main objective	Population Specific inclusion / exclusion criteria	Estimated no. of subjects	Follow-up (months)	Results / Achievement
		bidity (first vs. subsequent pandemic waves).				intensive care units vs. other units.
12.	Nephrology	To evaluate the feasibility and utility of early and rapid diagnosis of renal tubular injury using novel markers of renal injury.	Patients hospitalized for COVID-19. Aged 45–70 years, up to 14 days after symptoms of infection. Without previously diagnosed or suspected chronic kidney disease, excluding dialysis and kidney transplantation.	270	FU: 1, 6, 12 m	Assessment of subacute kidney injury using biomarkers of early damage. Create a kidney injury risk calculator for all patients with SARS-CoV-2 infection.
13.	Neurology	Assessment of early and late onset neurological symptoms and syndromes in COVID-19 infection. Neuropsychological evaluation following SARS-CoV-2 infection.	Patients hospitalized for COVID-19, without previously diagnosed cognitive or psychiatric disorders.	500	FU: up-to a year after acute Sars-CoV-2 infection	Epidemiology of the occurrence and severity of neurological signs and symptoms in the course of acute infection and after infection. Occurrence and dynamics of neuropsychological symptoms after COVID-19 infection.
14.	Obstetrics	Evaluation of pre-eclampsia parameters, including sFlt1/PlGF index as its predictor, in women with SARS-CoV-2	Pregnant women hospitalized for COVID-19 or obstetric complications with concomitant SARS-CoV-2 infection.	144	*Not applicable*	This study will contribute to defining the COVID-19 phenotype in pregnancy by understanding aspects of pathophysiology in the

No.	Research area (alphabetical order)	Main objective	Population Specific inclusion / exclusion criteria	Estimated no. of subjects	Follow-up (months)	Results / Achievement
		infection with assessment of severity. To establish a retrospective database to evaluate the general status and obstetric outcomes of women with SARS-CoV-2 infection. To review cases of patients with coagulation disorders and pregnancies complicated by SARS-CoV-2 infection.	,			context of maternal immune response.
15.	Oral Microbiota — ICU	Evaluation of the oral microbiome in mechanically ventilated patients in the course of SARS-CoV-2 infection — analysis of the dynamics of changes taking into account different oral ecological niches and assessment of the influence of oral hygiene on the dynamics and direction of microbiota changes.	Patients with COVID-19 transferred to the ICU, Age: 20–70 years, Mechanically ventilated (time from intubation to initiation of mechanical ventilation <24 hours). Randomization to two oral hygiene methods.	40 2×20	FU: 1, 3, 6 m	Development of principles for effective prevention of oral colonization by undesirable exogenous microorganisms. Develop separate recommendations for the prevention of pneumonia in mechanically ventilated patients with COVID-19.
16.	Oral Microbiota — post COVID-19	Microbiome characteristics of selected oral areas in patients recovering from COVID-19 with prior hospitalization.	The recovered patient, aged 20 years or older, diagnosed with hypertension, hypertension and diabetes mellitus.		*Not applicable*	Evaluation of abnormalities in the composition of the oral microbiota in patients recovered from COVID-19 as a result of oxygen therapy, pharmacotherapy, will

No.	Research area (alphabetical order)	Main objective	Population Specific inclusion / exclusion criteria	Estimated no. of subjects	Follow-up (months)	Results / Achievement
			Study group: hospitalized for COVID-19, examination on the day of discharge. *Control group*: without antibiotic therapy for 6 months.	20–25 20–25		allow to develop of interventions to restore the normal state.
17.	Pharmacotherapy	Identification of predictive factors for the risk of developing drug-induced liver and kidney damage in patients with COVID-19. Monitoring of nephro- and hepatotoxicity by assaying classical biochemical indicators and molecular indicators (assessment of specific miRNA expression in plasma).	Patients hospitalized for COVID-19 undergoing pharmacotherapy who consented to additional blood draws during hospitalization every 48 hours.	50	FU: 1, 3, 6, 12 m	To develop procedures to prevent the occurrence of acute or chronic hepatic and renal failure during pharmacotherapy administered to patients with COVID-19.
18.	Proteomics	Search for protein blood biomarkers to indicate the potential onset or severity of late cardiac complications associated with SARS-CoV-2 infection.	Patients hospitalized for COVID-19. Inclusion / exclusion criteria same as in Cardiology I (project no. 2).	120	FU: 6 m	To determine qualitative differences between patients who developed organ damage and those in whom no such changes were observed. To quantify the relationship between potential protein biomarkers and observed functional and/or morphological changes.

No.	Research area (alphabetical order)	Main objective	Population Specific inclusion / exclusion criteria	Estimated no. of subjects	Follow-up (months)	Results / Achievement
19.	Psychology	Preparation of an application and web platform for the patient's self-activity on strengthening psychological resilience in relation to treatment with COVID-19. Evaluation of a model of psychological assistance in the situation of COVID-19 treatment aimed at strengthening psychological resilience and evaluation of psychological consequences of COVID-19 disease.	Patients hospitalized for COVID-19. *Study group:* consecutively admitted patients who agree to participate in the sub-study and to participate in the E-KOP application, which includes interactive exercises, visualizations, psychoeducation and tests to assess psychological parameters. *Control group:* subjects hospitalized at least 6 months previously, without prior participation in the sub-study.	200 100	FU: 2–8 weeks, 6 m FU: 6 m	Development of an application aimed at strengthening psychological resilience to the stress of illness, which will be available to other patients after the end of the project. To monitor the process of psychological adaptation of patients in the context of reactions to COVID-19 stress (indicators: levels of anxiety, depressiveness, sleep disturbances, later PTSD symptoms) and resources that strengthen psychological resilience. To identify psychological predictors (psychosocial resources and deficits) relevant to adaptation to treatment with COVID-19. To develop a management scheme of psychological and medical psychological support in the study group.

No.	Research area (alphabetical order)	Main objective	Population Specific inclusion / exclusion criteria	Estimated no. of subjects	Follow-up (months)	Results / Achievement
20.	Psychiatry	In some patients, SARS-CoV-2 infection may cause psychiatric and cognitive disturbances. These tend to persist even after the acute infection has resolved. The patient's response to the disease or treatment may also be relevant. The aim of this study is to evaluate the association of psychopathological symptoms and stress caused by the disease and treatment with the presence of impaired intestinal and brain barrier permeability and microbiome composition in patients with SARS-CoV-2 infection.	Patients with confirmed SARS-CoV-2 infection; age less than 70 years; without psychiatric disorders in the pre-infection period.	60	FU: 1, 6 m	Research on the mechanisms that occur in SARS-CoV-2 infection may advance the understanding of the etiological mechanisms that occur in psychiatric disorders.
21.	Pulmonology	1. To evaluate coagulation and fibrinolytic activity in the context of the incidence of venous thromboembolism (VTE) in patients with COVID-19. 2. Assessment of pulmonary impairment in long-term follow-up after COVID-19;	Patients with confirmed infection SARS-CoV-2, with exclusion of pregnant women. Patients without suspected high-risk VTE (sudden cardiac arrest, hemodynamic instability, shock symptoms).	1: 200 2: 100	FU1: 3 m FU2: 3, 12 m	To determine the relationship between the activity of the coagulation and fibrinolysis systems and the incidence of VTE in patients with active screening for proximal deep vein thrombosis of the lower extremities.

No.	Research area (alphabetical order)	Main objective	Population Specific inclusion / exclusion criteria	Estimated no. of subjects	Follow-up (months)	Results / Achievement
		identification of risk factors for pulmonary dysfunction.				To identify predictors of severe disease course and to indicate potential targets for preventive and therapeutic interventions. To determine the extent of respiratory dysfunction in short- and long-term follow-up and to assess potential predictors of persistence of such dysfunction.
22.	Radiology I	To develop and implement a software system using deep machine learning (artificial intelligence) techniques to analyze images of chest CT scans taken in patients hospitalized for COVID-19 infection.	Hospitalized patients with COVID-19 infection confirmed by RT-PCR of a throat/nasopharyngeal swab who had a chest CT scan for inflammatory changes in the lungs/pulmonary embolism.	1000	*Not applicable*	Use of artificial intelligence techniques: 1. for quantitative assessment of the extent and morphology of inflammatory lesions in the lung in the course of COVID-19 infection, including determination of the proportion of "ground glass" zones and consolidation within inflammatory lesions, and 2. for quantitative assessment of the dynamics of inflammatory changes in the course of treatment. To evaluate the correlation of the above results of CT analysis with laboratory findings.

No.	Research area (alphabetical order)	Main objective	Population Specific inclusion / exclusion criteria	Estimated no. of subjects	Follow-up (months)	Results / Achievement
23.	Surgery	1. Assessment of the presence and density of viral particles in the air depending on a distance from the patient infected with SARS-CoV-2 hospitalized in the intensive care department. 2. Detection of possibility of viral particles spreading to the environment during high-risk procedures such as intubation. 3. Measurement of the air contamination with viral particles in the sluice and areas of the hospital building perceived as free from SARS-CoV-2 after standard decontamination procedures. The air samples will be analyzed using molecular diagnostic methods with qualitative and quantitative analysis as well as cultured to assess the infectivity of the virus present in the air.	Collection of air samples from various areas of the the COVID-19 intensive care unit, sluices, lifts and corridors.	*Not applicable*	*Not applicable*	1. Define the risk of SARS-CoV-2 infection in the various areas of the intensive care department dedicated for treatment of COVID-19 infected patients. 2. Refine the safety of standard decontaminating procedures.

(saturation, temperature, pulse,) and c) other alarm symptoms (hemoptysis, chest pain). The information provided by the patient will be monitored regularly by the medical team appointed for this purpose. In addition, when the report data indicate a significant deterioration in the health of the person being treated in home isolation, the application will send the supervising team a notification that the patient needs to be contacted urgently. Monitoring will be conducted for a maximum of 14 days, which may be shortened to 10 days for an asymptomatic patient. If symptoms persist beyond 14 days, the patient will be referred to the Infectious Disease Unit Emergency Department for clinical reassessment of the patient.

Follow-up period. After completion of monitoring in the home isolation setting and termination of SARS-CoV-2 infection, follow-up will be conducted in these individuals to assess late complications of COVID-19. Follow-up visits are scheduled for up to 1 year, at the following times: 28 days after COVID-19 diagnosis, 3, 6, 9, and 12 months.

Expected results. Development and implementation of an IT tool that can be used to remotely monitor the health status of a COVID-19 patient residing at home. The solution will provide a secure form of surveillance of COVID-19 treatment in home isolation, minimizing the risk of a patient with respiratory failure symptoms reporting to the hospital too late, and thus contributing to an improved prognosis. In addition, this arrangement will help to relieve the burden on a hospital care system inefficient during a pandemic.

3.2. Staff

Health care personnel are the most important element in the fight against any outbreak, but unfortunately they are also the most vulnerable to infection. The practice of personal protective equipment, including hand hygiene, is often suboptimal.

Objective. The purpose of the study was to assess hospital staff exposure to SARS-CoV-2 virus and knowledge of infection prevention and control.

Additionally, the project planned to:
a. to assess the actual spread of infection among hospital staff based on serological response;
b. to assess the level of vaccination of medical staff and final year medical students against COVID-19;
c. assessment of the impact of the pandemic on the quality of life of the staff;
d. assessment of psychophysical status, including occupational burnout and chronic fatigue.

Population. Medical and non-medical staff of University Hospital in Cracow. Students of the 5th year of the Faculty of Medicine at Jagiellonian University Medical College.

Estimated number of population. The project was originally planned to involve 880 people. The final number of subjects was: 1412 persons, including 129 medical students of the 5th year of Faculty of Medicine.

Study period. The project has two phases of research planned:

Phase I: January 2021;

Phase II: June 2021.

Expected results. The project will result in a detailed description of:

1. the epidemiology of COVID-19 infections among personnel in the context of prevalence expressed by IgG antibody positivity;

2. the level of immunization of particular groups of personnel with analysis of selected clinical, epidemiological and other parameters.

The results obtained in the questionnaire study will be combined with the results of laboratory tests, which will make it possible to develop a list of risk factors for SARS-CoV-2 infection and to verify the thesis on the occurrence of chronic fatigue syndrome as a complication of COVID-19. The subject of the analysis will be particularly the impact of selected exposure factors, including workplace, occupation, knowledge of the principles of prevention and control of infection, availability and use of personal protective equipment and attitude to vaccination against COVID-19.

3.3. Radiology II

Clinical practice shows that there is a group of patients whose baseline RT-PCR evaluation of nasopharyngeal swabs does not show COVID-19 infection, but these patients present with clinical signs of infection verified by subsequent PCR evaluations as COVID-19.

Objective. The research project plans to develop and launch an informatics system, using deep machine learning techniques (artificial intelligence), for the analysis of chest CT images taken in patients with high risk of COVID-19 infection and negative smear results (RT-PCR).

High-resolution computed tomography (HRCT) is a well-established method for CT examination of the lungs especially for suspected inflammatory lung lesions. The lack of need for intravenous contrast agent during the examination and the relatively low dose of X-rays further reduce the potential negative effects of the CT examination on the patient.

Population. Patients with clinical symptoms suggestive of COVID-19 infection, i.e. at least one of the following: cough, fever (temperature >38°C), dyspnea, loss of sense of smell with sudden onset, loss or disturbance of taste with sudden onset, and no confirmation of COVID-19 infection by RT-PCR of a throat/nasopharyngeal swab performed within seven days prior to study inclusion.

Estimated group size: approximately 250 subjects.

Expected results. Qualitative and quantitative results of analysis of abnormal structures in the lung parenchyma, with differentiation of lesions characteristic of "atypical" and viral inflammations, including COVID-19, from bronchopneumonia.

To assess the presence of a certain pattern of lung tissue involvement characteristic of COVID-19, impossible to assess by humans but available for analysis by machine learning techniques.

Demonstration of atypical inflammatory features may result in a change in management and treatment of the patient as potentially infectious, with the need for further observation and repeat swabs.

Ethical issues

All patients signed an informed consent to participate in the project conducted in accordance with the principles of Good Clinical Practice in Clinical Trials. The study was approved by the Bioethics Committee of the Jagiellonian University in Cracow. Due to the different nature of the population participating in the individual modules of the project and the tasks performed, applications for consent to conduct research were submitted separately for some module of the project. Table 4 summarizes the research approvals received for the CRACoV project modules and specific sub-studies.

Table 4. Summary of Bioethics Committee approvals for the CRACoV-HHS project.

CRACoV-HHS modules	Sub-study	Bioethics Committee Approval (no. and date)
Hospitalization	Clinical sub-studies	No. 1072.6120.333.2020 dated December 7, 2020
	Cardiology I (retrospective database)	No. 1072.6120.279.2020 dated October 28, 2020
	Antibiotic consumption	No. 1072.6120.2.2021 dated January 20, 2021
	Obstetrics	No. 1072.6120.86.2021 dated April 21, 2021
Home isolation	—	No. 1072.6120.334.2020 dated December 7, 2020
Staff	—	No. 1072.6120.353.2020 dated December 16, 2020
	Radiology II	No. 1072.6120.363.2020 dated December 16, 2020

Discussion

The CRACoV-HHS study in its assumptions refers to the development of multidisciplinary care and the development of such recommendations for the management of patients infected with SARS-CoV-2 in different areas of medical care.

The project will result in the development of management guidelines for:

1. with asymptomatic or mild symptoms of COVID patients treated in home isolation;
2. with symptomatic patients — hospitalized without clinical complications;
3. with patients developing more severe clinical course of disease and organ complications;
4. patient requiring surgery;
5. patient with diabetes;
6. patient requiring psychological support;
7. patient with undesirable consequences of pharmacological treatment.

Furthermore, the development of a multidisciplinary model of care was assumed, depending on the clinical course of SARS-CoV-2 infection.

Innovative technology solutions being developed as part of the project include:

a. an informatics system for monitoring the health status of patients remaining in home isolation together with the launch of an application for self-reporting of health status;
b. an application for patient self-management strengthening psychological resistance to stress related to illness and prevention of trauma resulting from isolation;
c. test-method for detection of SARS-CoV-2 infection, differentiation of infection with influenza virus;
d. risk calculators for unfavorable course of COVID-19, including transfer for ICU or death, and organ complications after COVID-19.

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Author contributions and disclosure

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Disclosure

The authors have nothing to declare.

Conflict of interest

None declared.

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Supplementary material

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Iwona Gregorczyk-Maga (PI), Mateusz Fiema, Jolanta Kędzierska, Anna Pałka, Dorota Romaniszyn, Anna Sepioło, Magdalena Skóra, Zuzanna Tokarczyk, Jadwiga Wojkowska-Mach.

Oral Microbiota-post COVID:
Joanna Zarzecka (PI), Monika Brzychczy-Włoch, Barbara Brzychczy, Wojciech Ostrowski, Agnieszka Sroka-Oleksiak, Katarzyna Talaga-Ćwiertnia, Elżbieta Zarzecka-Francica.

Pharmacotherapy:
Jarosław Woroń (PI), Beata Bujak-Giżycka, Klaudia Czepiel, Przemysław Kapusta, Barbara Lorkowska-Zawicka, Justyna Totoń-Żurańska.

Proteomics:

Maciej Suski (PI), Anna Kiepura, Józef Madej, Rafał Olszanecki, Aneta Stachowicz.

Psychiatry:

Maciej Pilecki (PI), Katarzyna Furman, Wirginia Krzyściak, Marta Szwajca, Natalia Śmierciak, Aleksander Turek.

Psychology:

Barbara Bętkowska-Korpała (PI), Kinga Ciesielska, Katarzyna Cyranka, Aleksandra Ćwięk, Katarzyna Dembe, Dominika Dudek, Natalia Kowina, Anna Laskowska-Wronarowicz, Donata Liberacka, Beata Lickiewicz, Stanisław Łukasik, Wojciech Majka, Magdalena Noga, Katarzyna Olszewska-Turek, Ewa Pałczyńska, Anna Pastuszak-Draxler, Adrian Podolski, Krzysztof Pytel, Gabriela Rudnik, Łukasz Rudzki, Dominika Sarna-Palacz, Jakub Sewiło, Małgorzata Skalska, Anna Starowicz-Filip, Alicja Widera, Barbara Zawadzka.

Pulmonology:

Krzysztof Sładek (PI), Natalia Celejewska-Wojcik, Karolina Górka, Iwona Gross-Sondej, Aleksander Kania, Łukasz Kasper, Jacek Krawczyk, Sabina Lichołai, Marcin Mrugacz, Paweł Nastałek, Kamil Polok, Marek Przybyszowski, Tomasz Stachura, Anna Trojan-Królikowska, Krzysztof Wójcik, Bożena Żurowicz.

Radiology:

Robert Chrzan (PI), Monika Bociąga-Jasik, Łukasz Brandt, Amira Bryll, Paulina Karcz, Tadeusz Popiela, Andrzej Urbanik.

Staff:

Jadwiga Wójkowska-Mach (PI), Ilona Barańska, Tomasz Burliga, Estera Jachowicz, Violetta Kijowska, Wojciech Majka, Barbara Maziarz, Dorota Romaniszyn, Anna Różańska, Magdalena Strach, Michał Struś, Wojciech Sydor, Katarzyna Szczerbińska, Barbara Żółtowska.

Surgery:

Michał Pędziwiatr (PI), Jarosław Garlicki, Piotr Major, Andrzej Matyja, Michał Nowakowski, Krzysztof Pyrć, Justyna Rymarowicz, Mateusz Wierdak.

Table S1. Organizational Structure of the CRACoV-HHS Project.

Management		
R & D Manager	Monika Bociąga-Jasik, M.D., Ph.D.	Department of Infectious and Tropical Diseases
Representatives of the Project Leader (UHK)	Krzysztof Mydel, M.D.	Deputy Director of Coordination and Development in UHK
	Joanna Konopka, M.A. (starting December 2021)	
Research consultant (JUMC)	prof. Tomasz Grodzicki, M.D., Ph.D.	Jagiellonian University Vice-Rector for Medical College, Department of Internal Medicine and Gerontology
Coordination Team		
Project Manager (UHK)	Wojciech Sydor, M.D., Ph.D.	Head of the Center for Innovative Therapies, Department of Rheumatology and Immunology
Project Manager (JUMC)	Barbara Wizner, R.N., Ph.D.	Department of Internal Medicine and Gerontology
Coordinators (UHK)	Barbara Żółtowska, M.A.	Center for Innovative Therapies
	Barbara Miśtal, R.N., M.Sc.	Center for Innovative Therapies
	Magdalena Zawadzka, M.D.	Center for Innovative Therapies
Coordinators (JUMC)	Magdalena Łopuszańska-Rusek, D.Eng.	Research Support Department JUMC
	Agnieszka Kwietniewska-Śmietana, M.Sc.Eng.	Research Support Department JUMC (starting 1st February 2021)
	Katarzyna Friedlein-Wójtowicz, M.A.	Research Support Department JUMC (until 28th February 2021)
Steering Committee		
Representatives of the Project Leader (UHK)	Marcin Jędrychowski, M.A.	Director of the University Hospital in Cracow
	Marcin Krzanowski, M.D., Ph.D.	Deputy Medical Director
	prof. Aleksander Garlicki, M.D., Ph.D.	Head of Department of Infectious and Tropical Diseases
	Stefan Bednarz, M.D., Ph.D.	Manager of Primary Health Care Clinic
	Jarosław Surowiec, M.D.	Head of Quality, Hygiene and Infection Control Section
	prof. Tomasz Grodzicki, M.D., Ph.D.	

Group	Name	Affiliation / Role
Consortium Representatives (JUMC)	prof. Marek Sanak, M.D., Ph.D.	Jagiellonian University Vice-Rector for Medical College, Department of Internal Medicine and Gerontology
	prof. Maciej Małecki, M.D., Ph.D.	Vice-Rector's Proxy for Research and International Cooperation at the JUMC, Molecular Biology and Clinical Genetics Unit
		Dean of the Faculty of Medicine, Department of Metabolic Diseases
	prof. Tomasz Gosiewski, M.D., Ph.D.	Division of Molecular Medical Microbiology, Department of Microbiology, Faculty of Medicine, JUMC
Expert Committees		
Databases & Analysis Committee	Agnieszka Olszanecka, M.D., Ph.D. (Chair)	1st Department of Cardiology and Interventional Electrocardiology and Hypertension JUMC
	prof. Jerzy Gąsowski, M.D., Ph.D.	Department of Internal Medicine and Gerontology JUMC
	prof. Tomasz Klupa, M.D., Ph.D.	Department of Metabolic Diseases and Diabetology JUMC
	Magdalena Strach, M.D., Ph.D.	Department of Rheumatology and Immunology JUMC
	Wojciech Sydor, M.D., Ph.D.	Center for Innovative Therapies UHK, Department of Rheumatology and Immunology
	Barbara Wizner, R.N., Ph.D.	Department of Internal Medicine and Gerontology JUMC
Laboratory Tests Committee	prof. Marek Sanak, M.D., Ph.D. (Chair)	Vice-Rector's Proxy for Research and International Cooperation at the JUMC, Division of Molecular Biology and Clinical Genetics, Department of Internal Medicine, JUMC
	Marcin Surmiak, M.Sc, Ph.D.	Division of Molecular Biology and Clinical Genetics, Department of Internal Medicine, JUMC
	Jolanta Kędzierska, D.Biol.	Department of Microbiology UHK
	prof. Beata Kuśnierz-Cabala, M.D., Ph.D.	Department of Diagnostics, Department of Clinical Biochemistry JUMC
	Barbara Maziarz, M.D., Ph.D.	Head of Diagnostic Facility UHK, Department of Clinical Biochemistry JUMC
Publication Committee	prof. Maciej Małecki (Chair)	Dean of the Faculty of Medicine JUMC, Department of Metabolic Diseases and Diabetology JUMC
	prof. Małgorzata Bala, M.D., Ph.D.	Department of Epidemiology and Preventive Medicine JUMC
	prof. Grażyna Bochenek, M.D., Ph.D.	Department of Pulmonology JUMC
	prof. Rafał Olszanecki, M.D., Ph.D.	Chairman of the Disciplinary Council of JUMC, Department of Pharmacology JUMC

prof. Marek Sanak, M.D., Ph.D.	Vice-Rector's Proxy for Research and International Cooperation at the JUMC, Division of Molecular Biology and Clinical Genetics, Department of Internal Medicine, JUMC
Scientific Council	
(Representatives of Investigators, Hospital Emergency Unit Department and Medical Department transformed into COVID-19 departments in the UHK)	
Monika Bociąga-Jasik, M.D., Ph.D.	Department of Infectious and Tropical Diseases
prof. Robert Chrzan, M.D., Ph.D.	Department of Diagnostic Imaging Unit
prof. Barbara Gryglewska, M.D., Ph.D.	Department of Internal Medicine and Geriatrics
prof. Tomasz Gosiewski, M.D., Ph.D.	Division of Molecular Medical Microbiology, Department of Microbiology, Faculty of Medicine, JUMC
prof. Hubert Huras, M.D., Ph.D.	Department of Obstetrics and Perinatology
prof. Katarzyna Krzanowska, M.D., Ph.D.	Department of Nephrology
prof. Andrzej Matyja, M.D., Ph.D.	2nd Department of General Surgery
prof. Michał Pędziwiatr, M.D., Ph.D.	2nd Department of General Surgery
Maciej Pilecki, M.D., Ph.D.	Department of Child and Adolescent Psychiatry
prof. Marek Rajzer, M.D., Ph.D.	1st Department of Cardiology and Interventional Electrocardiology and Hypertension
prof. Krzysztof Sładek, M.D., Ph.D.	Department of Pulmonology
prof. Agnieszka Słowik, M.D., Ph.D.	Department of Neurology
prof. Katarzyna Szczerbińska, M.D., Ph.D.	Department of Sociology of Medicine, Department of Epidemiology and Preventive Medicine, JUMC
prof. Jerzy Tomik, M.D., Ph.D.	Department of Otolaryngology
prof. Jerzy Wordliczek, M.D., Ph.D.	Department of Interdisciplinary Intensive Care
Aleksandra Załustowicz, M.D., Ph.D.	2nd Department of General Surgery

Legend:
JUMC — Jagiellonian University Medical College, UHK — University Hospital in Cracow