**Cardiac complicAtions in Patients with SARS Corona vIrus 2 regisTrY (CAPACITY)**

**Version 2.0 May 2020**



**PROTOCOL TITLE: Cardiac complicAtions in Patients with SARS Corona vIrus 2 regisTrY (CAPACITY)**

|  |  |
| --- | --- |
| **Short title** | **CAPACITY** |
| **Version** | **2.0** |
| **Date** | **08-05-2020** |
| **Principal Investigator** | **Prof. Dr. F.W. Asselbergs** |
| **Local coordinating investigator:**  ***Multicenter research: per site*** | ***<please include name and contact data>***  ***<please include name of hospital of local coordinating investigator>*** |
|  |  |
| **Other investigator(s)** | ***<please include name and contact data>*** |
| **Sponsor** | **UMC Utrecht, Utrecht, the Netherlands** |
|  |  |
| **Subsidising party** | **Not applicable.** |
|  |  |
| **Laboratory sites** | **Not applicable.** |
|  |  |

**PROTOCOL SIGNATURE SHEET**

|  |  |  |
| --- | --- | --- |
| **Name** | **Signature** | **Date** |
| **Head of Department:**  **Prof. dr. P. van der Harst, cardiologist** |  |  |
| **Principal Investigator:**  **Prof. dr. F.W. Asselbergs, cardiologist** |  |  |
| **Local Coordinating Investigator:**  ***<please include name>*** |  |  |

**TABLE OF CONTENTS**

1. INTRODUCTION AND RATIONALE 6

2. OBJECTIVES 6

3. STUDY DESIGN 6

4. STUDY POPULATION 6

4.1 Population (base) 6

4.2 Inclusion criteria 6

4.3 Exclusion criteria 7

4.4 Sample size calculation 7

5. INVESTIGATIONAL PRODUCT 7

5.1 Name and description of investigational product(s) 7

5.2 Summary of findings from non-clinical studies 7

5.3 Summary of findings from clinical studies 7

5.4 Summary of known and potential risks and benefits 7

5.5 Description and justification of route of administration and dosage 7

5.6 Dosages, dosage modifications and method of administration 7

5.7 Preparation and labelling of Investigational Medicinal Product 7

5.8 Drug accountability 7

6. METHODS 7

6.1 Study parameters/endpoints 7

6.1.1 Main study parameter/endpoint 7

6.1.2 Secondary study parameters/endpoints (if applicable) 7

6.1.3 Other study parameters (if applicable) 8

6.2 Study procedures 8

6.3 Withdrawal of individual subjects 8

6.3.1 Specific criteria for withdrawal (if applicable) 9

6.4 Replacement of individual subjects after withdrawal 9

6.5 Follow-up of subjects withdrawn from treatment 9

7. STATISTICAL ANALYSIS 9

7.1 Primary study parameter(s) 9

7.2 Secondary study parameter(s) 9

7.3 Other study parameters 9

8. ETHICAL CONSIDERATIONS 9

8.1 Regulation statement 9

8.2 Recruitment and consent 9

9. ADMINISTRATIVE ASPECTS AND PUBLICATION 10

9.1 Handling and storage of data and documents 10

9.2 Amendments 10

10. REFERENCES 10

**SUMMARY**

**Rationale:** Coronavirus disease (COVID-19) is a rapidly emerging pandemic in which cardiovascular complications are increasingly described. Furthermore, underlying cardiovascular disease seems to be of prognostic importance in patients with COVID-19. In prior pandemics, data collection was not performed in a standardized manner. Data collection during the COVID-19 pandemic should therefore be standardized, to improve data quality and allow high-quality research with data collected across multiple centres. Cardiac complicAtions in Patients with SARS Corona vIrus 2 regisTrY (CAPACITY) is an extension of the ISARIC-WHO case report form (CRF)(<https://isaric.tghn.org/covid-19-clinical-research-resources/> ). CRF extensions have been developed to capture information on cardiac history, use of cardiac medications and the occurrence of cardiac complications. CAPACITY offers a comprehensive data collection tool that facilitates uniform data collection of patients with COVID-19.

**Objective**: To participate in the WHO-recommended standardized data collection of patients infected with SARS-CoV-2 and gain additional insight into the role of cardiovascular disease in this pandemic.

**Study design:** Patient registry (observational in nature). Data can be collected in a prospective manner during hospital admission or retrospectively after discharge.

**Study population:** Patients that have been or are currently admitted the hospital with (highly suspected) COVID-19.

**Main study parameters/endpoints:** NA

**Nature and extent of the burden associated with participation, benefit and group relatedness:** Patients will not undergo any additional investigations. Only data that has been generated during routine clinical care will be collected within CAPACITY.

# INTRODUCTION AND RATIONALE

# Coronavirus disease (COVID-19) is a rapidly emerging pandemic caused by an infection with SARS-CoV-2. Most patients require admission to the hospital due to the development of pneumonia, which may necessitate mechanical ventilator support. Besides the respiratory symptoms, some patients develop severe cardiac damage (1, 2). In addition, underlying cardiovascular disease may worsen the prognosis of these patients (2). There are concerns that the use of angiotensin-converting enzyme (ACE) inhibitors, angiotensin II type-I receptor blockers (ARBs), ibuprofen and thiazolidinedione’s can worsen the course of COVID-19. These concerns are based on the fact that SARS-CoV-2 bind to their target cells through the ACE2 receptor. The expression of the ACE2 receptor can be substantially increased with the use of these drugs (3). To gain insight into the rate of cardiac complications and the course of COVID-19 in patients with underlying cardiac disease, high-quality data collection is needed. In prior pandemics data collection was not done in a standardized manner. It is of pivotal importance that the data collection during the COVID-19 pandemic is standardized. Cardiac complicAtions in Patients with SARS Corona vIrus 2 regisTrY (CAPACITY) offers a WHO-recommended comprehensive data collection tool that facilitates uniform data collection on patients infected with SARS-CoV-2 with cardiovascular disease.

# OBJECTIVES

Standardised data collection of patients infected with SARS-CoV-2 which should eventually be helpful in answering questions on the role of cardiovascular disease in this pandemic.

# STUDY DESIGN

This is an international multicenter registry that will collect data from multiple centers.

# STUDY POPULATION

## Population (base)

## All patients (that have been) admitted at one of the participating centres with a highly suspected/confirmed infection with SARS-CoV-2.

## Inclusion criteria

In order to be eligible to participate in this study, a subject must meet the following criteria:

1. Highly suspected/confirmed infection with SARS-CoV-2
2. Age ≥18 years

## Exclusion criteria

1. Age <18 years

## Sample size calculation

NA

# INVESTIGATIONAL PRODUCT

## Name and description of investigational product(s)

NA

## Summary of findings from non-clinical studies

NA

## Summary of findings from clinical studies

NA

## Summary of known and potential risks and benefits

NA

## Description and justification of route of administration and dosage

NA

## Dosages, dosage modifications and method of administration

NA

## Preparation and labelling of Investigational Medicinal Product

NA

## Drug accountability

NA

# METHODS

## Study parameters/endpoints

### Main study parameter/endpoint

NA

### Secondary study parameters/endpoints (if applicable)

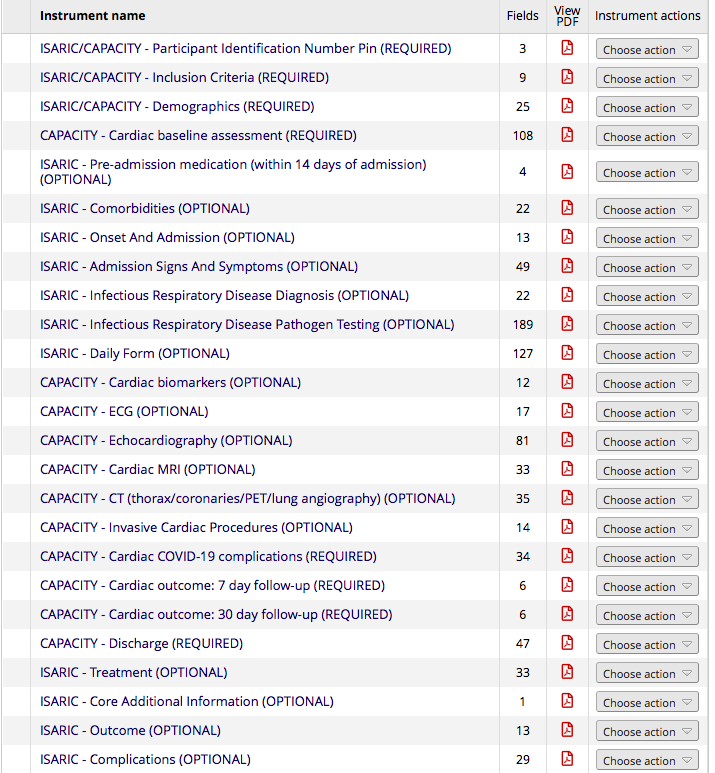
NA

### Other study parameters (if applicable)

NA

## Study procedures

For every participating centre, new eligible cases will be reported to one responsible coordinating researcher. The research team will subsequently collect the following data from electronic health records and enter these data in an pseudonimised electronic case report form (eCRF). Data can be collected during admission or retrospectively after discharge. All data collection instruments in REDCap are visualized below. Patients are not subjected to any additional procedures besides standard clinical care. The data collection instruments will only be filled with data that is generated during routine care.



## Withdrawal of individual subjects

Individual subjects / participants can leave the study at any time for any reason if they wish to do so without any consequences when they express they do not want their data to be used in the context of this study.

### Specific criteria for withdrawal (if applicable)

## Replacement of individual subjects after withdrawal

NA

## Follow-up of subjects withdrawn from treatment

NA

# STATISTICAL ANALYSIS

NA

## Primary study parameter(s)

NA

## Secondary study parameter(s)

NA

## Other study parameters

NA

# ETHICAL CONSIDERATIONS

## Regulation statement

The study will be conducted according to ‘Gedragscode Gezondheidsonderzoek’ and in accordance with the EU GDPR (General Data Protection Regulation) and the Declaration of Helsinki.

## Recruitment and consent

For every participating centre, new eligible cases will be reported to one responsible coordinating researcher. The research team will collect relevant data from electronic health records, and enter these data in an pseudonymized electronic case report form (eCRF). All eligible patients will be informed of the study during admission to the hospital through written information. In this document, patients are informed about the possibility to refuse the use of their data (i.e. opt-out-procedure). Obtaining informed consent is not feasible during this pandemic, considering the acute setting (i.e. emergency department/intensive care) in which a large number of COVID-19 patients are currently being admitted. Besides, obtaining informed consent during this pandemic will induce selection bias, since only mildly symptomatic patients can be included through a classic informed consent procedure. Lastly, informed consent requires extra contact with the patients, which is absolutely undesirable as per judgement of the National Institute for Public Health and the Environment (RIVM)(4). A detailed rationale for this opt-out strategy is addressed in the GDPR-Justification document of this study. The Privacy Officer of the UMC Utrecht, the Dutch Health and Youth Care Inspectorate and the Board of Directors of the UMC Utrecht have been informed about this opt-out procedure. In the case that a patient refuses the use of his/her data after it was collected, collected data will be destroyed.

# ADMINISTRATIVE ASPECTS AND PUBLICATION

## Handling and storage of data and documents

For every participating centre, one coordinating researcher will be responsible for giving patients a pseudo-ID. Only this coordinating researcher will be able to create a new patient ID in REDCap to prevent that the same patient being entered multiple times under different pseudo-IDs. Every participating centre will have an identification list which will be encrypted and stored in a protected folder according to a SOP. All data that is entered in the eCRFs is non-retraceable (no address, date of birth, etc.). Researchers with access to the Research Electronic Data capture (REDcap) platform will only see non-retraceable, pseudonimised data.

## Amendments

Amendments are changes made to the research after an ethical committee gave an advice non-WMO. Any change that may cause the investigation to fall within the scope of the WMO is submitted to the ethical committee that gave the non-WMO advice.

# REFERENCES

(1) Zheng Y. et al. COVID-19 and the cardiovascular system. Nat Rev Cardiol 2020 [Online ahead of print]

(2) Huang, C. et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395, 497–506.

# 3) Fang, L. et al. Are Patients With Hypertension and Diabetes Mellitus at Increased Risk for

# COVID-19 Infection?

(4) https://www.rijksoverheid.nl/onderwerpen/coronavirus-covid-19 Accessed on 19th of March 2020.

**Revisions:**

|  |  |  |
| --- | --- | --- |
| 24-03-2020 | Version 1.0 | First version |
| 08-05-2020 | Version 2.0 | Page 5 and 8: Clarification that data collection can take place prospectively during admission or retrospectively after discharge.  Page 6-7: Age <18 added as exclusion criteria.  Page 8: New figure with overview of data collection instruments due to additions with the release of new ISARIC CRF (version 24APR20)  Page 9: Changed the manner of withdrawal of individual subjects from “handing in an opt-out form” to “when they express they do not want their data to be used in the context of this study”. |