RED CORAL Study Documents

Note: The PETAL CIRB reviewed the RED CORAL protocol and assessed that it meets 45 CFR 46.104 (d) category (4)iii for Exempt Review and Secondary research for which consent is not required.

RED CORAL

PETAL Retrospective Electronic Data COVID-19 Observational Study

Enrollment Goals

- Retrospective registry of 1500 patients
- Each clinical center (CC) will contribute ~125 patients, most of whom will have "focused" data collected
    - Up to 25 ICU patients at each CC will have more thorough "detailed" data collected

Inclusion Criteria

- Adults hospitalized with positive test for COVID-19 within 14 days of admission
- Evidence of acute COVID-19 with fever or respiratory manifestations, as characterized by signs and symptoms such as fever, cough, dyspnea, tachypnea, hypoxemia, and infiltrates on chest imaging.
    - Note: this includes patients who were admitted for reasons unrelated to COVID-19, but are displaying sign/symptoms of COVID-19

Exclusion Criteria

- Inability to access medical records
- Known prisoner at time of data collection

Patients cared for in the ICU with COVID-19 *contributing* to their need for hospital admission may be eligible for "detailed" data collection. For example, a COVID positive patient admitted to the hospital/ICU with a head injury and a cough would be eligible for RED CORAL but would not be eligible as an ICU patient with "detailed" data collection because COVID did not contribute to their reason for hospitalization.

Clinical Center Enrollment Strategy

Starting with patients admitted March 1st, consecutive COVID patients at all participating sites should be enrolled in chronological order. They will all contribute to a center's 125 total. Eligible patients cared for on the acute care ward will undergo "focused" data collection. Eligible patients cared for in the ICU at any point of their hospital stay will be eligible for "detailed" data collection. After the first 25 ICU patients across a center's sites have been identified for detailed data collected, all following patients can be assigned to either detailed or focused data collection, but payment will be at the "focused" level. Centers are free to determine how many patients each site will contribute.

- Example: Center has two sites
    - Site #1 has 62 patients, but only can contribute 20 patients due to workforce. Of these, 6 are eligible ICU patients for whom the site plans to do detailed data collection.
    - Site #2 has 135 patients. This site plans to collect data on their first 105 eligible patients. They will perform detailed data collection on the first 19 ICU patients. They will collect focused data for any additional ICU patients after these.

Focused Collection

- Floor patients, and ICU patients after the first 25 who are eligible for detailed data.
- Data collection consists of:
    - Baseline data (day of presentation)
    - Daily assessments on Days 1, 4, 8, 15, 21, 28, In addition, daily data form is collected on ICU day 1, if patient received care in the ICU during hospitalization and ICU day 1 does not overlap with other listed days.*
    - Discharge data (up to study day 60)

Detailed Collection

- At least 25 patients per CC who received ICU care, chronologically (at each site within the CC). Centers can elect to do detailed collection for more/all patients if desired but will be paid at the higher "detailed collection" level for a maximum of 25 patients.
- Data collection consists of:
    - Baseline data (day of presentation)
    - Daily assessments on hospital days 1-15, day 21 & 28. In addition, ICU days 1-15 if they do not overlap with other listed days.*
    - Discharge data (up to study day 60)

*Redcap will automatically generate correct data forms based on user selection of detailed vs focused collection

Study: PETAL Repository of Electronic Data COVID-19 Observational Study

Acronym: RED CORAL

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ABBREVIATIONS

ABG = Arterial blood gas
ARDS = Acute Respiratory Distress Syndrome
CORAL= COVID-19 Observational Study
COVID-19 = Coronavirus disease due to SARS-CoV2
ED = Emergency Department
FiO_2 = Fraction of Inspired Oxygen
ICU = Intensive Care Unit
IMV = Invasive Mechanical Ventilation
ISARIC= International Severe Acute Respiratory Illness Consortium
MV= Mechanical Ventilation
NHLBI = National Heart Lung and Blood Institute
PETAL = Prevention and Early Treatment of Acute Lung Injury
P/F = PaO2/FiO2 ratio
$PaCO_2$ = Partial pressure of arterial carbon dioxide
PACU = Post anesthesia care unit
PaO_2 = Partial pressure of arterial oxygen
PBW = Predicted Body Weight
PEEP = Positive End-Expiratory Pressure
POCUS = Point of care ultrasound
Ppl = Plateau pressure
PS = Pressure Support Ventilation
PUI= Person under investigation (Test pending for COVID-19)
RED CORAL= Repository of electronic data for COVID-19
S/F = SpO2/FiO2 ratio
SARS-CoV2= Severe acute respiratory syndrome coronavirus 2
SOFA = Sequential Organ Failure Assessment
SBP = Systolic Blood Pressure
SpO_2 = Oxygen Saturation via pulse oximetry
WHO = World Health Organization

DEFINITIONS

CORAL: PETAL Network's observation research program studying severe COVID-19. RED CORAL is a component of CORAL.

Confirmed COVID-19: Defined as a person with a laboratory confirmed SARS-CoV2 infection

Extubation: Removal of an orotracheal tube, nasotracheal tube, or unassisted breathing with a tracheostomy

Home: Level of residence or health care facility where the patient was residing prior to hospital admission

Invasive Mechanical Ventilation (IMV): Assisted positive pressure ventilation delivered by a nasotracheal, orotracheal, or tracheostomy tube

Mortality at hospital discharge: This includes deaths from all causes at the time of discharge from the hospital

Funder: National Institutes of Health and the National Heart Lung and Blood Institute

Study Day: The day of presentation to hospital associated with COVID-19 admission is study day 1. The day of ICU admission is ICU day 1.

Study hospital: Defined as the hospital where the patient was enrolled in study procedures.

1. PROTOCOL SUMMARY

Title	PETAL COVID-19 Observational Study
Short Title	CORAL
Clinical Phase	Observational Study
Number of Sites	Participating PETAL hospitals
IND Sponsor/Number	Not Applicable
Study Objectives	**Primary Aim** • Provide data for investigation of demographics, clinical characteristics, risk factors, care practices, outcomes and resource utilization of patients with severe acute COVID-19 **Secondary Aims** • Characterize the severity and course of acute clinical manifestations of COVID-19 • Identify risk factors and create prediction models for COVID-19 outcomes, including acute respiratory failure, prolonged mechanical ventilation, cardiomyopathy, and death • Describe care processes for hospitalized patients with COVID-19, including resource allocation, utilization of palliative care services, and causes of death • Assess the state of emergency activation and capacity strain in the health systems providing care to hospitalized patients with COVID-19, in order to describe practice, and to inform interpretation of clinical care provision and outcomes.
Study Design	Retrospective observational study of hospitalized patients with COVID-19
Accrual Objective	1500 patients
Study Duration	12 months
Treatment Description	Not Applicable
Inclusion Criteria	1. Adult patient with confirmed COVID-19 within 14 days of hospital admission 2. Evidence of acute COVID-19, with fever or respiratory manifestations, as characterized by signs and symptoms

	such as fever, cough, dyspnea, tachypnea, hypoxemia, and infiltrates on chest imaging.
Exclusion Criteria	1. Prisoners
Study Stopping Rules	There are no safety-related stopping rules

2. TRIAL DESCRIPTION

2.1 Background

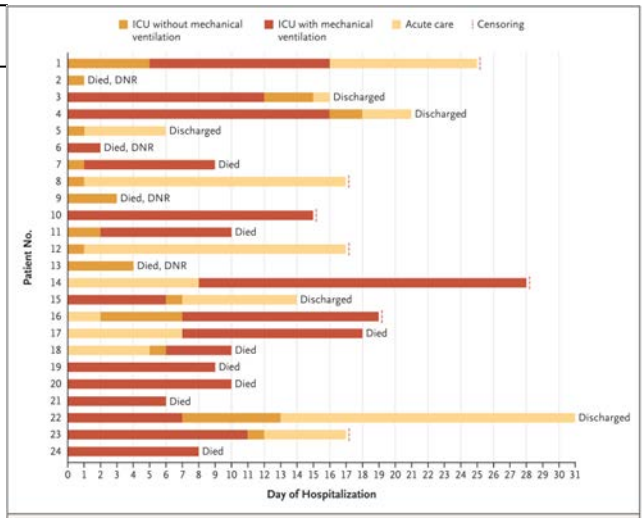
Not even three months have passed since the initial report of a cluster of 27 cases of pneumonia of unknown etiology in Wuhan, China on December 31st, 2019. One week later, the pathogen was identified as a novel coronavirus, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV2). By the end of January, there were nearly 8000 cases of coronavirus disease 2019 (COVID-19) in China and 80 travel-related cases confirmed outside China, leading to declaration of "a public health emergency of international concern" by the World Health Organization. In just three weeks more, there were over 70,000 cases and 200 deaths in China and 1000 cases around the world.[1] Since that time, COVID-19 has raged across the earth like wildfire. On March 28th, 2020, there were over 650,000 cases around the world, with over 115,000 in the US, and a global death toll of over 30,000; one week later, these numbers had doubled (over 1.2 million cases worldwide, over 63,000 deaths, and over 300,000 cases in the United States). By early May 2020, there have been over 4.5 million cases and over 300,000 deaths worldwide. The United States has been hard hit, with over 1.4 million cases and over 86,000 deaths on May 14, 2020.

The scientific literature regarding COVID-19 is, unsurprisingly, still in its infancy. The first large population-level report came from China late February, describing 44,415 patients with confirmed COVID-19. Most patients were between 30-79 years old, with only 3% of cases in people $\geq$ 80 years. Mild disease was common (81%), although it is not clear if care was received in a hospital setting. Hospitalized patients had signs of lower respiratory infection with cough, shortness of breath, and abnormal chest radiographs. Nearly 20% of patients were critically ill with hypoxemic respiratory failure. Overall case fatality rates was 2.3%, with the oldest and most severely ill at higher risk of death.[1]

Single center reports from China describe high rates of critical illness syndromes among hospitalized patients, with acute respiratory distress syndrome (ARDS) in 22-42%, arrhythmias in 16%, and shock in 11%. [2,3]Early reports describe prolonged respiratory failure and hospitalization, with extended periods of mechanical ventilation. Reports from 1-2 centers in China present clinical risk factors for ARDS and death, describing advancing age, co-morbid hypertension and diabetes, and fever. Patients with poor outcomes were more likely to have abnormal laboratory findings, including neutrophilia, evidence of organ dysfunction (thrombocytopenia and elevated liver enzymes, creatinine, and troponin) and markers of inflammation and dysregulated coagulation (including

interleukin-6, ferritin, d-dimer, prothrombin time).[2,4] Case fatality among the severely ill in these Chinese reports is very high, ranging from 49-95%.

Figure 1[5]



The first case series of critically ill patients in the United States is from King County, Washington, where 21 patients with COVID-19 due to community spread were hospitalized at a single hospital between February 20th and March 5th, 2020. All but one developed ARDS, 67% developed shock, and 33% had evidence of cardiomyopathy. As of March 17th, 14 had died, 5 remained critically ill, and just 2 had left the ICU alive.[5] The second case series, also from Seattle, described 24 critically ill patients, 18 of whom received mechanical ventilation (MV).[6] Median duration of MV was 10 days (interquartile range 7-12), but only four patients had successfully liberated from MV at the time of the report, while three remained ventilator dependent and 8 had died. Although informed by a small number of patients, this report demonstrates major challenges in the care and investigation of severely ill COVID-19 patients; duration of MV and hospitalization is often long, and critical illness may develop later than a week into hospitalization, as shown in **Figure 1.**

Currently, little is known about the epidemiology of COVID-19 in the United States. Best estimates as of mid-March suggested that 20-30% of confirmed COVID-19 cases required hospitalization, and that 5-12% of the overall population with confirmed COVID-19 required intensive care.[7] It is difficult to generalize these findings, given rapid changes in COVID-19 testing and profound evolution of the population at risk from day to day. There are key knowledge gaps regarding clinical characteristics, biology, risk factors, outcomes, and resource utilization for acutely ill COVID-19 patients, especially in the United States. There are no proven treatments, despite high health care utilization and high case fatality, particularly among the elderly and the critically ill. It is unclear how generalizable current knowledge of ARDS biology and treatment may be in COVID-19, since most biomarker profiling and approaches informing prognostication and treatment of ARDS have considered underlying bacterial infections, rather than viral infections.

Thus, there exists little understanding of biologic pathways that might be optimal for targeting therapeutics in this deadly syndrome, nor for understanding which patients are at highest risk for ARDS development or prolonged critical illness. Rapid expansion of cases across this country and others necessitates urgent study of severe acute COVID-19 in order to care for patients, inform and develop treatments, target therapeutics, prognosticate, and understand health system impacts.

2.2 Study Objectives

The epidemiology of patients hospitalized with severe COVID-19 has not been well defined, especially in the American context. There are significant knowledge gaps regarding demographics, clinical characteristics, trajectory of disease, timing of recovery, predictors of organ failure and death, resource utilization, and post-hospital outcomes. Furthermore, there exists limited understanding of biologic pathways activated by this viral syndrome and which patients are at risk for progression to more severe illness. There are reports of unusual features of COVID-19 critical illness, such as high prevalence of cardiomyopathy as well as catastrophic arrhythmias during recovery, which need further study. In response, the purpose of the RED CORAL study is to inform epidemiology and resource utilization through data collection and creation of a data repository.

2.2.1 Specific Aims

We will identify acute and critically ill patients with COVID-19 and collect detailed data from their hospital stay. We will contribute data to the WHO/ ISARIC COVID registry and to the scientific community in order to advance United States participation in studies of global epidemiology. We will use the data to increase understanding of the clinical course of COVID-19.

Our specific aims are to:

a. Provide data for investigation of demographics, clinical characteristics, risk factors, care practices, outcomes and resource utilization of patients with severe acute COVID-19
b. Characterize the severity and course of acute clinical manifestations of COVID-19
c. Identify risk factors and create prediction models for COVID-19 outcomes, including acute respiratory failure, prolonged mechanical ventilation, cardiomyopathy, and death
d. Describe care processes for hospitalized patients with COVID-19, including resource allocation, utilization of palliative care services, and causes of death
e. assess the state of emergency activation and capacity strain in the health systems providing care to hospitalized patients with COVID-19, in order to describe practice, and to inform interpretation of clinical care provision and outcomes

The Prevention and Early Treatment of Acute Lung Injury (PETAL) Network is a consortium of academic and affiliated hospitals across the United States, funded by the NHLBI to conduct clinical trials in patients with or at risk for critical illness, including ARDS. Our Network's goal is to improve outcomes of patients with acute and critical illness through research. We have deep expertise in severe acute respiratory infections and critical illness, and the existing infrastructure to rapidly investigate acute and critical illness caused by SARS CoV-2. We are integrated with complimentary efforts in children (PALISI), outpatients (CDC), and the global community (SCCM, WHO/ISARIC). We are perfectly positioned to investigate the burden of disease, severity of illness, clinical course, and impact on the health system of severe COVID-19.

3. RESEARCH APPROACH

3.1 Previous Work

There have been no similar studies of epidemiology of hospitalized patients with COVID-19 in the United States at this time, and only limited reports worldwide. There are growing efforts to create registries of patients with COVID-19 in the United States and around the world, including work by the WHO (ISARIC registry), the Centers for Disease Control (CDC-IVY), the Society for Critical Care Medicine (SCCM-VIRUS), and the pediatric community (PALISI). There are also proposals for bio-specimen collection, including the newly funded COVID Immunophenotyping study by NIAID, IMPACC. This PETAL proposal (CORAL) is deliberately designed to harmonize and synergize with these existing and proposed efforts.

At the same time, CORAL is unique, leveraging the expertise of PETAL in order to conduct detailed phenotyping of the clinical course, and outcomes of acutely and critically ill patients with COVID-19, and use this information to understand and improve clinical care, with a particular focus on critical illness. PETAL has successfully completed a large scale observational study of ventilator practices across Network hospitals, [8] and many of the PETAL hospitals, investigators, and staff contributed to a successful observational registry of pandemic H1N1 in 2009-2010 as part of the NHLBI ARDS Network and in conjunction with PALISI.[9] The proposed studies are feasible in our hands.

3.2 Overall Approach

RED CORAL is a multicenter, observational medical record review study of 1500patients with COVID-19 admitted to PETAL Network hospitals. Data Collection may occur remotely in order to accommodate stay-at-home orders and other social distancing procedures.

3.3 Study Population

RED CORAL will include adult patients with confirmed COVID-19 hospitalized at participating sites who have available clinical data. The study period will include patients who present for admission to study hospitals between March 1st and April 1st, 2020.

Inclusion criteria:

1. Adult patient with confirmed COVID-19 within 14 days of hospital admission
2. Evidence of acute COVID-19, with fever or respiratory manifestations, as characterized by signs and symptoms such as fever, cough, dyspnea, tachypnea, hypoxemia, and infiltrates on chest imaging.

Exclusion criteria:

1. Prisoners

3.4 Selection of Clinical Sites

RED CORAL will recruit at all volunteering PETAL Network hospitals. The only requirements are capacity to identify hospitalized patients with COVID-19 and resources to complete the case report forms with high fidelity. In addition, resources and procedures will be developed to facilitate the participation of hospitals outside of the PETAL Network as well.

4. STUDY PROCEDURES

4.1 Screening

Research staff sites will identify potentially eligible COVID+ patients hospitalized during the study period using medical records and lists maintained for clinical operations. A log of hospitalized COVID+ patients during the study period will be compiled by participating sites. This log will include simple information: patient name, medical record number, age, sex at birth, date of admission, admission location (ward or ICU), race and ethnicity. This log will be used to select patients and to describe the relationship between selected patients and the larger population. Patient names and medical record numbers from this log will only be used at the local sites and not transmitted to the Clinical Coordinating Center (CCC). Research staff will use the medical records for patients on the log to determine study eligibility. Patient names and medical record numbers will be removed from screening logs, which will then be uploaded by each site into REDCap. This information will be used to describe basic characteristics of the entire population of patients with COVID-19 hospitalized at PETAL hospitals between March 1st and April 1st, 2020.

4.2 Enrollment

Patients admitted for hospitalization with test-confirmed COVID-19 may be eligible for inclusion in CORAL. The study period will be March 1st through April 1st, 2020. Individual patients will only be eligible for inclusion once; if readmitted during the study period, the first hospitalization to a study hospital will be selected.

Each clinical center will be paid for entry of 125 patients. Patients should be selected beginning with the earliest cases, ideally at institutions within each center that can complete data entry most quickly. Patients should be selected chronologically at each site. If a clinical center cannot complete data entry rapidly or does not have 125 patients to contribute, the quota may be shared by other clinical centers. This will sum to 1500 patients across PETAL Sites. Beyond this quota, clinical centers may contribute additional patients, but will not be guaranteed compensation.

From this group of 125 patients, clinical centers will chronologically identify 25 patients who received care in the ICU for detailed data collection. Centers will receive additional compensation for this detailed data collection. Centers may choose to perform detailed data collection on all patients (floor, and ICU patients after the first 25) but will not receive extra compensation for doing so. All patients will be included via waiver of informed consent.

4.3 Data Collection

RED CORAL elements include all data needed for participation in the ISARIC/WHO registry, in addition to selected variables important for understanding COVID-19 in the context of acute and critical illness in the United States. Data will be collected in three modules: admission, daily and discharge or study termination. Timing and included data elements are presented in the table.

CORAL Data Collection Timing & Description		
Module	Timing	Data Elements
Admission	Calendar day of presentation to study hospital (Day 1) and 24-hour period	COVID testing, symptoms, demographics, exposures, comorbidities, home medications, vital signs, labs, supportive care & treatments, research trial enrollment, medications, ventilator settings
Daily Data	Focused: Days 1,4,8,15,21,28, & ICU Day 1 Detailed: Days 1-15, 21,28, & ICU days 1-15	Vital signs, labs, supportive care & treatments, research trial enrollment, medications, ventilator settings
Discharge or study termination	Hospital discharge or study day 60	Disposition, cause of death, care limitations, functional status, infections, organ support at discharge, summative treatments, summative complications, summative diagnostics

The detailed mainly differs from the focused data collection in terms of daily data. For the study period, ICU patients with COVID-19 contributing to their need for hospital admission may be eligible for detailed data collection, which will include ICU days 1-15.

The case report form (CRF) is built in RED Cap which can be imported as a local instance or centrally through the PETAL CCC. Manual data entry of all elements into REDCap may not be required depending on the site's ability to extract data from the EMR. It is important for data collection to begin promptly so that these studies can rapidly inform care of the thousands of COVID-19 patients in hospitals.

4.4 Images for Repository

Data collection include abstracting presence of infiltrates as noted on radiologists' reports from chest radiographs and computed tomography (CT) scans. RED CORAL also will collect all clinical radiographs and CT scans available from the course of illness as well as clinically performed cardiac evaluations. All image types will be uploaded by study staff into the imaging coordinating center at the American College of Radiology's Center for Research and Innovation. We will use the TRIAD image collection system which removes all identifiers and codes images with study labels in DICOM format. The CORAL

Figure 3.
Chest CT of COVID-19 ARDS (ref. 5)

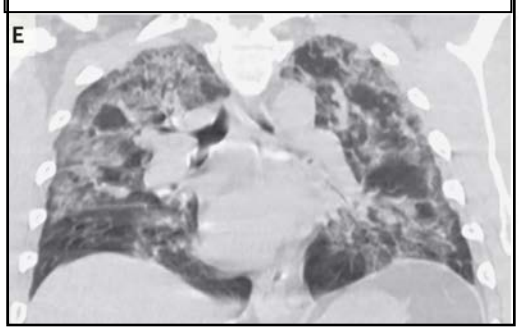


Image Repository will be maintained on ACR CRI servers through the course of the study. ACR CRI will collect all diagnostic images, create a link between the images and clinical data collected by PETAL, and archive images throughout study duration and after study close to make accessible to researchers.

4.5 Human Subjects Considerations

COVID-19 is a global pandemic. Obtaining information about patients with COVID-19 is an important response to a public health emergency. Given that this is a data repository of data and images that are available in the medical record and already being collected as part of routine care, the only risk of the research is loss of confidentiality. Patients hospitalized with COVID-19 at participating hospitals are eligible for enrollment regardless of age, gender, ethnicity, race, sexuality, or religion. Previous reports suggest that males may have higher rates of infection than females meaning that males might be slightly over presented – however, distribution of different demographics will be similar to the demographics of admitted patients. Children aged less than 18 years old appear to have milder disease when infected with SARS-CoV2 and in general, are not routinely hospitalized. As such, enrollment will be restricted to adults. However, data will be harmonized with aligned research efforts of pediatric patients.

4.6 Risks and Benefits of Participation

The only risk is potential invasion of privacy and stress. Data will be secured and password protected. RED CORAL is an observational study; there are no clinical benefits to participation. However, many patients report benefits of altruism through study participation. This study has the potential to help future patients with COVID-19 and those stricken in future pandemics.

4.7 Study Withdrawal or Discontinuation

Study withdrawal or discontinuation is not relevant to RED CORAL.

4.8 Statistical Considerations

It is anticipated that there will be thousands of patients eligible at PETAL hospital for entry into the registry and cohort. This proposal is to begin by collecting data on 1500 patients. It is difficult to predict what proportion of included patients will be acutely ill, critically ill, receiving mechanical ventilation, developing ARDS, receiving prolonged mechanical ventilation, and dying during initial hospitalization—early reports have been small and incomplete. Describing these aspects of the clinical epidemiology, with special attention to ARDS and cardiac complications, and course of acute severe COVID-19 is an important early contribution from this work.

RED CORAL proposes to focus early efforts on describing the clinical characteristics of COVID-19. Similarly, early efforts will focus on identifying risk factors and developing prediction models for key outcomes (including respiratory failure, shock, cardiac complications, prolonged mechanical ventilation, and death). These analyses need to be completed and published expeditiously in order to make an impact on clinical care and

research in the early days of the COVID-19 pandemic. There will also be plans for data cleaning, model validation, analysis, and publication of findings from the final study population. There are many important research questions that these data will be able to address. Statistical analysis plans will be developed and approved before any analyses begin.

We have identified key research questions and will refine more as additional information accumulates. We will estimate the proportion of patients with ICU admission, respiratory failure, prolonged mechanical ventilation (more than 7 days of mechanical ventilation), and death We will estimate the duration of mechanical ventilation, ICU stay, and hospital stay. Using both floor and ICU patients, we will estimate what proportion are in each state of the COVID Outcome Scale on days 8, 15, 21 and 28. Increasing the size of the sample will increase the precision around these estimates. We will then use the number of patients in each outcome group to design adequately powered multivariate models.

We anticipate sufficient power to evaluate at least 20 variables for association with these outcomes of respiratory failure, prolonged mechanical ventilation, and death. We will focus on key demographic factors, such as age, sex at birth, comorbidity, race/ethnicity, and pre-morbid functional status. We will develop multivariable models to evaluate the association of additional laboratory and physiologic variables with these outcomes and compare with existing risk prediction models.

The sample size for the overall cohort was determined to allow early hypothesis testing on at least 300 patients with respiratory failure and 200 patients who die from COVID-19. This number of patients with expected outcomes are required to create appropriately adjusted multivariable models to predict outcomes, and to look for associations between treatments and outcomes

4.9 Data management, data sharing, quality assurance and security of data

Data collected by study staff will contain identifiers at local sites. For transmission of data to the PETAL CCC, a unique study identifier will be assigned to each subject. All RED CORAL data will be shared in order to facilitate rapid knowledge generation and dissemination. this study was specifically designed to allow data sharing with the ISARIC registry. RED CORAL data and images may be shared with other projects, both at the site and network level, provided that human subjects' protections are followed. CORAL's case report forms, data dictionaries, and REDCap builds will be available on the public-facing PETAL website. The CORAL committee will work with the PETAL CCC and Steering Committee to create a solid approach to early data sharing that accelerates knowledge while minimizing potential threats of invasion of privacy. Sharing of data will be reviewed by the PETAL Network Natural History Committee, according to current PETAL network policies.

ISARIC data elements from all completed cases will be shared with ISARIC's Oxford Data Coordinating center. The PETAL Network will receive reports from ISARIC describing numbers and features of the cases contributed. In addition, these data will be easily shared with other efforts to understand COVID-19 and will be expeditiously made publicly available.

Data quality and consistency of approach to data collection is very important. We will follow the previously successful approach to multi-faceted quality assurance which includes: (1) use of Manuals of Operation for training and reference, (2) regular meetings between local Investigators and study coordinators to answer questions and ensure consistency in evaluations across study sites, (3) regular conferences between all Investigators for the same purposes, (4) ongoing quality assurance review and training updates, (5) data entry into a database with extensive automated checks of data validity, and (6) ongoing review of descriptive statistics by Investigators with detailed review of selected data. We will use best practice physical and electronic security and back-up procedures as well.

4.10 Privacy and Confidentiality

Data will be collected into the HIPAA compliant REDCap database. Only study personnel will have access to the REDCap database. The CCC will download data from the database with limited identifiers (limited to dates and zip codes). Identifiers will only be shared in accordance with all relevant human subjects' protections.

4.11 Record Retention

One year after the primary manuscript is published or after data collection ends, whichever is last, any identifiable data in the database will be deleted and the data will be transferred to an NIH controlled, de-identified database.

5. REFERENCES

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RED CORAL REDCap Data Entry: Process Document

CREATING A COPY OF RED CORAL REDCap in your local REDCap System:

These files are for sites which intend to create a copy of the PETAL RED CORAL REDCap system locally. Steps to extract data from your EMR system and import it into CORAL REDCap: 1) ***create*** a local REDCap instance, 2) ***import*** the data there and add any manually extracted data, and 3) ***export*** the data from the local instance and import into the CCC's instance (titled Partners REDCap).

There are three files in each .zip file:

1. CORAL codebook PDF, which shows the data elements
2. CORAL XML upload, which is for creating the project the first time
3. CORAL CSV upload, which is for updating an existing CORAL project with any changes

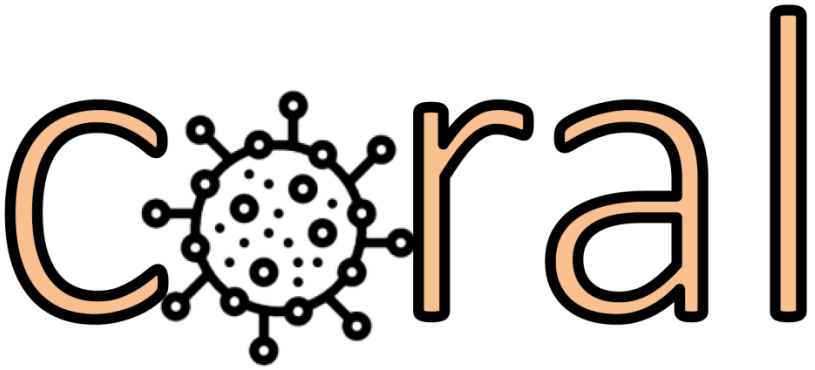
Always **download and use the most recent version of the .zip files**. Older versions are kept posted for tracking purposes.

CREATING the RED CORAL project in your local REDCap system for the first time:

1. Download the most recent .zip file and extract it
2. Log in to your local REDCap
3. From the main page, click on the "New Project" button at the top of the page
4. Fill out the submission form and enter the name of the project (listed as "PETAL CORAL Registry" in CCC REDCap).
5. Provide any locally required information
6. Chose "Upload a REDCap project XML file" from the list of options (which start with "start project from scratch")
7. Upload the XML upload file ("CORAL XML upload vX.YY.xml")
8. Click "create project"

UPDATING an existing PETAL RED CORAL project on your local REDCap system:

1. Use the CSV data dictionary file
2. Go to the "PETAL CORAL Registry" project>>"Project Setup" page>>"Data Dictionary"
3. Check project status: If the project is already in production change it to "draft" mode
4. Set the date format for uploads to be "DD/MM/YYYY"
5. Upload the CSV upload file ("CORAL CSV upload vX.YY.csv")
6. Confirm the upload; **Note:** If you had to enter "draft" mode, you will need to "submit changes for review"



NIH/NHLBI PETAL Network

COVID-19 Observational Study

Data abstraction manual

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CORAL section leads: Ithan Peltan, MD, MSc
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PETAL COVID-19 Observational Study

The epidemiology of patients hospitalized with severe COVID-19 has not been well defined, especially in the U.S. context. There are significant knowledge gaps regarding demographics, clinical characteristics, trajectory of disease, timing of recovery, predictors of organ failure and death, resource utilization, and post-hospital outcomes. Furthermore, there exists limited understanding of biologic pathways activated by this viral syndrome and which patients are at risk for progression to more severe illness. There are reports of unusual features of COVID-19 critical illness, such as high prevalence of cardiomyopathy as well as catastrophic arrhythmias during recovery, which need further study. In response, the purpose of the CORAL study is to inform epidemiology and resource utilization through three interrelated approaches: a registry, a detailed prospective cohort including bio-specimen collection that is correlated with clinical phenotyping and outcomes, and a health system assessment.

The dataset will comprise a rich body of data on adult patients hospitalized with COVID-19. Major data domains for inclusion in the final dataset:

1. Demographic characteristics, including baseline and long-term functional status measures
2. Patient comorbidities
3. Patient clinical parameters, including, vital signs, and lab results
4. Patient management, including pharmacologic and organ support therapies
5. Long-term mortality and functional outcomes
6. Biospecimens repository
7. Clinical radiology and EKG repository

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COHORT DESCRIPTION

This study will enroll 3000 adult patients admitted to a PETAL study hospital with COVID-19 disease to both a retrospective registry and to a prospective cohort of patients. Core data collection (termed the RED CORAL dataset) will occur for all patients. Additional data (CORAL REEF) will be collected for prospective patients and a subset of retrospective registry patients whose cause of admission was caused in whole or in part by COVID-19 or an attributable complication.

Figure 1. PETAL Network Clinical Centers. Each clinical center includes 3-7 study hospitals.

Master inclusion criteria (apply to ALL subjects)

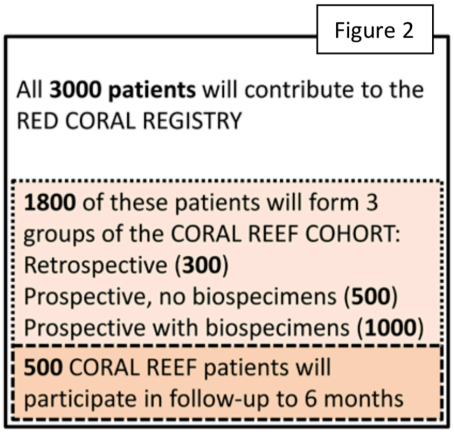
- Age ≥18 years
- Positive PCR test for SARS-CoV-2
- Admitted to a study hospital within 14 days of positive SARS-CoV-2
- One or more of the below signs or symptoms of acute COVID-19 disease:
    a. History of self-reported feverishness or measured fever of ≥38˚C (≥100.4˚F)
    b. Cough
    c. Dyspnea (shortness of breath) OR tachypnea
    d. Clinical suspicion of acute respiratory infection (ARI) despite not meeting criteria above (e.g. hypoxemia, diagnosis of pneumonia)

Master exclusion criteria (apply to ALL subjects)

- Patient known to be a prisoner or in legal custody at the time of hospital admission

Additional inclusion/exclusion criteria applicable to specific arms of the CORAL REEF study.

- *Prospective & retrospective CORAL REEF cohort:* COVID-19 contributed to need for hospital admission
- *Retrospective CORAL REEF:* admit or transfer to ICU during hospitalization
- *Prospective CORAL REEF:*
    - Able to enroll within 48 hours of admission or positive COVID test (whichever is later)
    - Active comfort care orders within 48 hours of admission or at the time of eligibility
- *Prospective CORAL REEF biospecimens:* Inability of hospital site or staff to complete study procedures according to schedule at the time of patient eligibility.
- *Prospective CORAL REEF long-term follow up cohort:* Survival to hospital discharge with ability to participate in telephone follow-up by either patient or caregiver.



Note that <u>all</u> RED CORAL patients can contribute full CORAL REEF data, but the higher level of CORAL REEF payment will only be provided in retrospective cohort for up to 25 ICU patients per Clinical Center.

SCREENING

Study personnel will screen medical records at their institutions in order to identify hospitalized patients with COVID-19 meeting study criteria. Approach to screening is expected to vary by hospital.

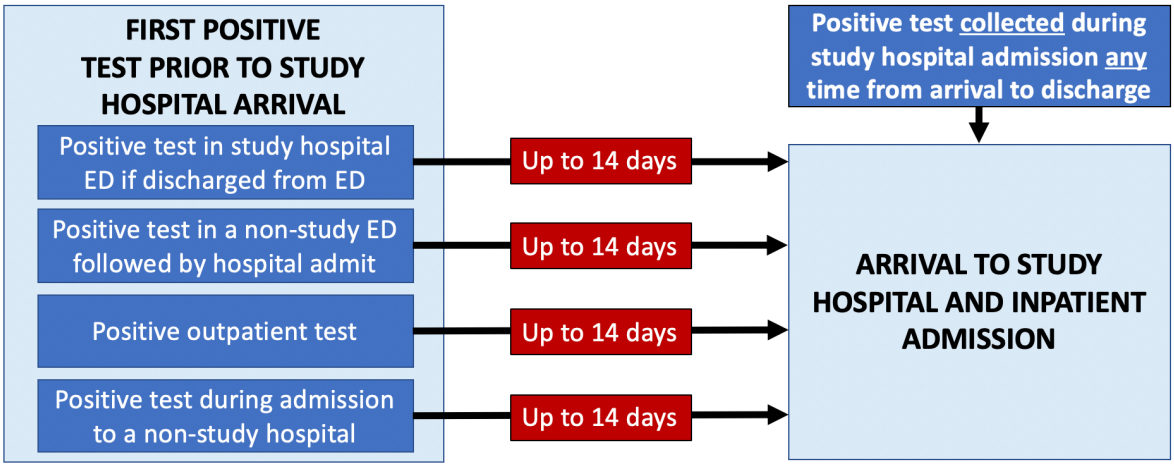
In order to understand how patients enrolled in CORAL and interventional studies reflect the larger population of COVID-19 patients at participating hospitals, all sites will be asked to compile a complete log of all hospitalized COVID+ patients during study periods. This log will include simple information: patient identifier, age, sex at birth, date of admission, and admission location (ward or ICU). This log will be used to select patients and to describe the relationship between selected patients and the larger population.

CORAL Screening Log - All Hospitalized COVID-19 Postive Patients								
ID Number	MRN	Admit Date	Age at Admit	Sex at Birth	ICU Admission (y/n)	Floor/Ward Admission (y/n)	Race	Ethnicity

IDENTIFYING ELIGIBLE INDEX HOSPITALIZATION

The hospitalization of interest is the first hospitalization for the patient where either:

1) The first hospital admission occurring up to 14 days after a positive SARS-CoV-2 test that occurred at an urgent care, clinic, drive-through testing center, outpatient laboratory, or ED visit from which the patient was discharged. The SARS-CoV-2 test does not need to have resulted either before index hospital admission or even before index hospital discharge.
2) A positive SARS-CoV-2 test was obtained within the first 14 days of the admission encounter (including while in the ED). Important note: The SARS-CoV-2 test does not need to have resulted prior to hospital discharge.



SUMMARY OF DATA ELEMENTS

For subjects enrolled in both the retrospective and prospective cohorts, we will collect data for three types of time points. Note that these data can be collected at any time — data do not need to be collected in real time.

1. Baseline assessment
2. Daily assessment: serial daily assessment (frequency dependent on study arm) up to hospital discharge or day 28, whichever comes first
3. Discharge from the study hospital

Additionally, a subset of prospectively enrolled CORAL REEF who survive to hospital discharge patients will be contacted by telephone at 1, 3 and 6 months after hospital discharge. Patients and family members will provide consent for continued involvement at the time of the first call.

Table 3: Data		Admit	Daily	Discharge
	RED CORAL	X	Hospital day 1, 4, 8, 14, 21, 28 ICU Day 1	X
CORAL REEF	**Retrospective**	X	Hospital days 1-14, 21, 28 ICU days 1-15	X
	Prospective	X	Hospital days 1-14, 21, 28 ICU days 1-15	X

Table 7: LTO	Hospital	1 month	3 months	6 months
Detailed contact info	x	x	x	x
EQ5D-5L	x	x	x	x
Activities of daily living (ADL)	x	x	x	x
Instrumental ADLs	x	x	x	x
Financial toxicity		x	x	x
Cardiopulmonary symptoms		x	x	x
Depression (PHQ-9)		x	x	x
Anxiety (GAD-7)		x	x	x
Cognitive function (MOCA /AD8, Hayling)	x	x	x	x
Rehospitalization		x	x	x

DATA ABSTRACTION PROCESS & METHODS

- **Option #1:** Pure manual abstraction into CCC REDCap

- **Option #2:** Pure manual abstraction into local REDCap instance

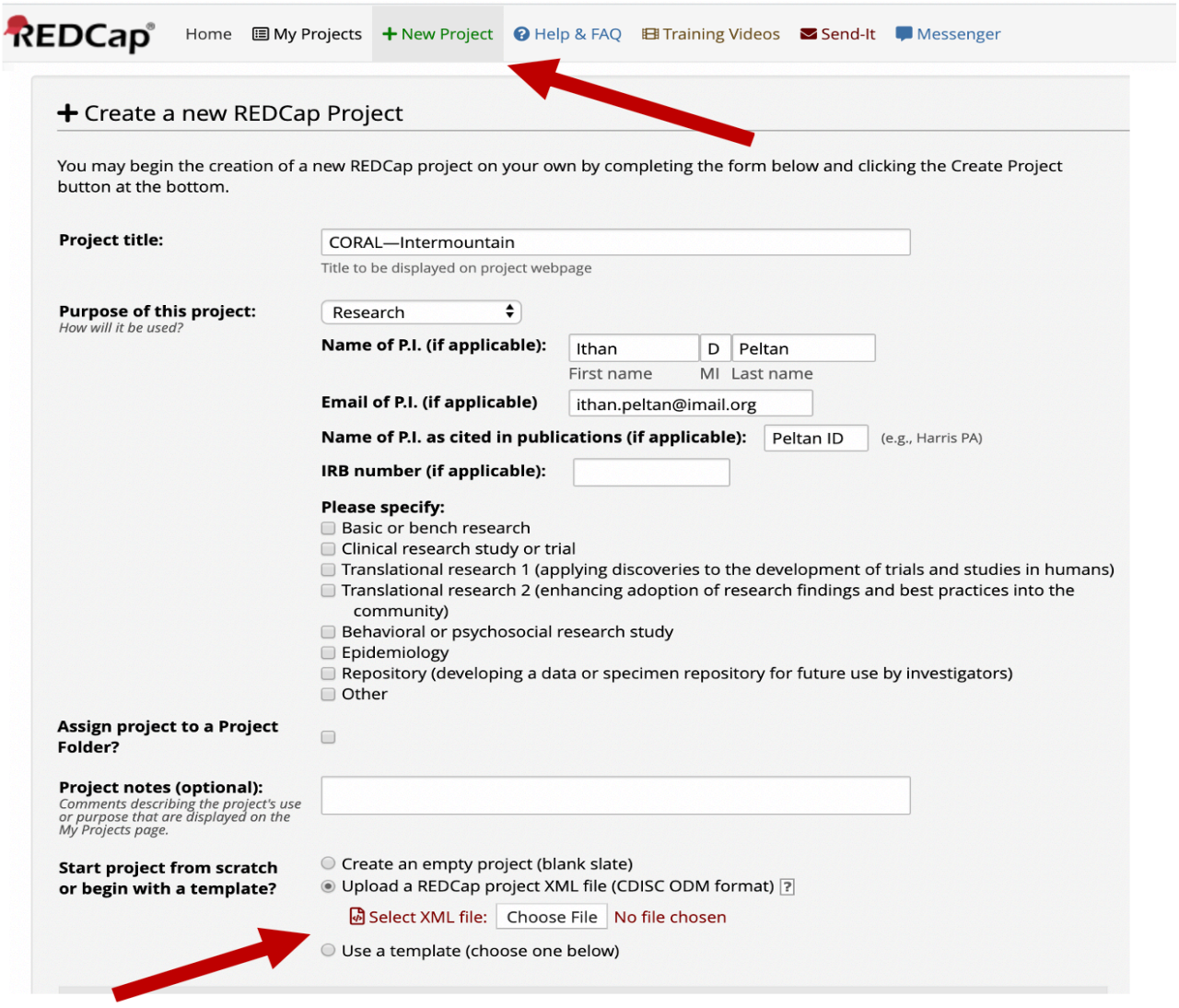
- **Option #3:** Electronic abstraction + manual completion/cleaning which requires
  1. Construction of an electronic query for available data elements (will vary by site)
  2. Convert results of electronic query to match CORAL REDCap data structure
  3. Import/upload file containing electronic query into local REDCap instance
  4. Manual abstraction/cleaning locally

→ Use of a local REDCap will require promptly updating their local REDCap instance (see below) when updates to the data dictionary are issues by the CCC.

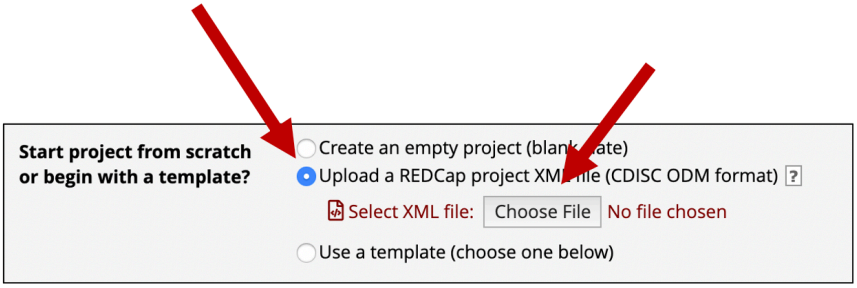
→ For sites entering data to their a local REDCap, final/clean data will be transferred from the local REDCap to the CCC REDCap by exporting a file and then importing that file directly into CCC REDCap.

SET UP LOCAL INSTANCE OF CORAL REDCAP INSTRUMENT

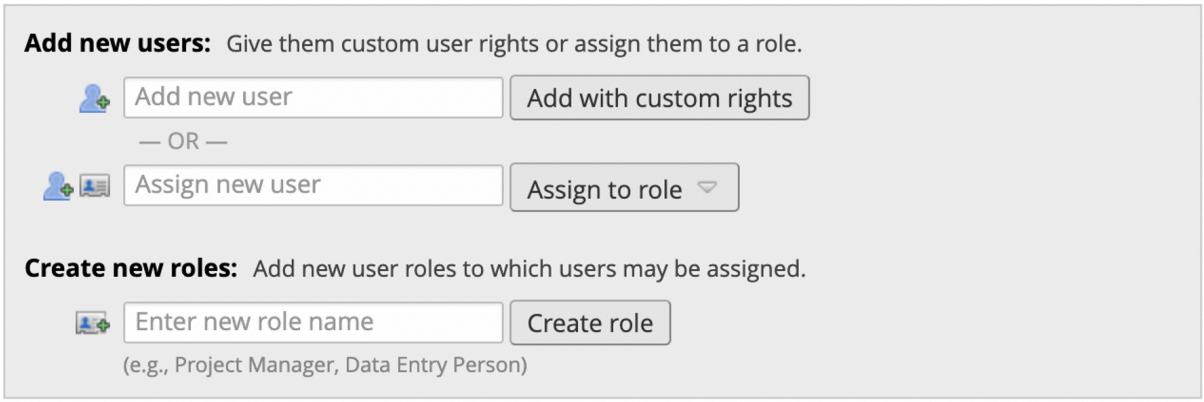
(1) XML file issued to sites by CCC
(2) On REDCap main page, click New Project button (top of page)
(3) Enter study name/purpose/IRB



(4) Choose "Upload a REDCap project XML file" from the list of options with "Start project from scratch
(5) Upload XML file
(6) Click "Create project"



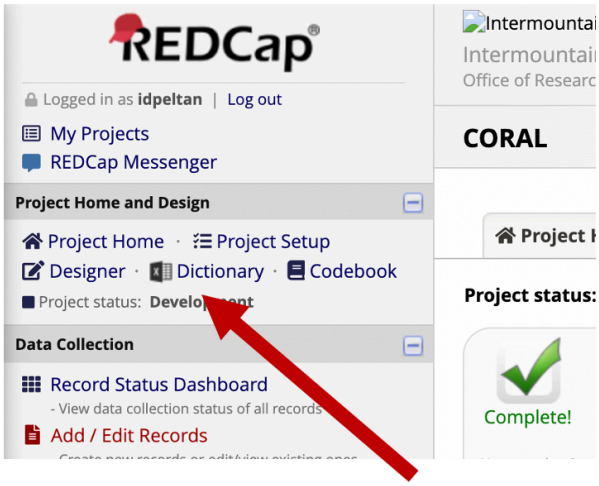
(7) Assign user rights
(8) Move project to production status when CCC says to do so



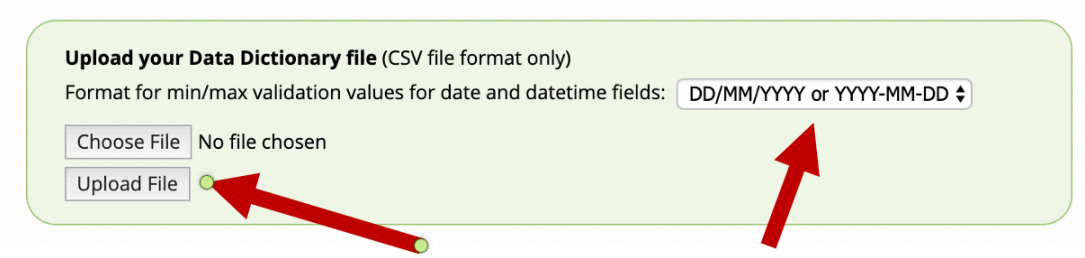
Role name (click role name to edit role)	Username or users assigned to a role (click username to edit or assign to role)	Expiration (click expiration to edit)	Project Design and Setup	User Rights	Data Access Groups
—	idpeltan (Ithan Peltan)	never	✓	✓	✓
Data abstractor	[No users assigned]		✗	✗	✗
Data manager	[No users assigned]		✓	✓	✗

UPDATING LOCAL INSTANCE OF CORAL REDCAP INSTRUMENT

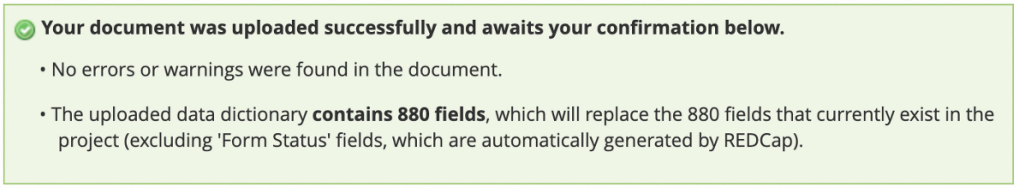
(1) Data dictionary CSV file issued to sites by CCC
(2) Person with "data manager" role or the original project owner must complete upload
(3) Go to "Project Setup" page → "Data dictionary"

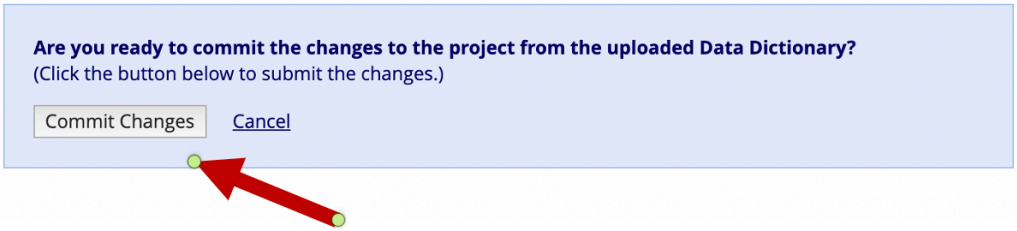


(3) Set date format to "DD/MM/YYYY" format (if necessary)
(4) Upload "CORAL upload" CSV file



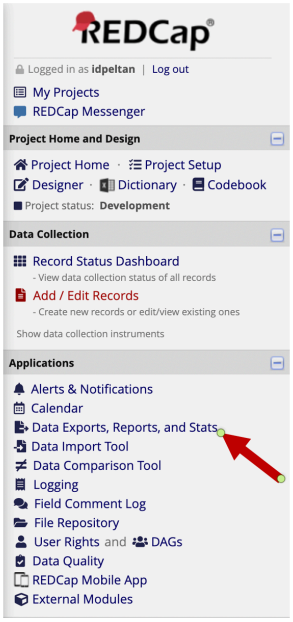
(5) Click "Commit Changes"



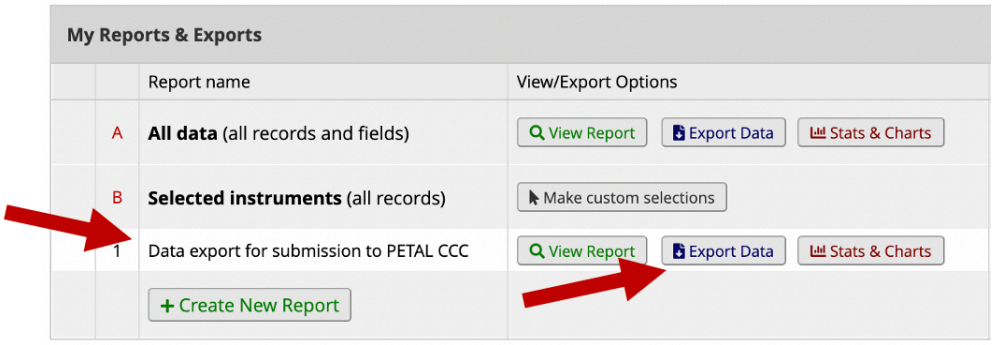


EXPORT LOCAL DATA FOR UPLOADING DATA TO CCC

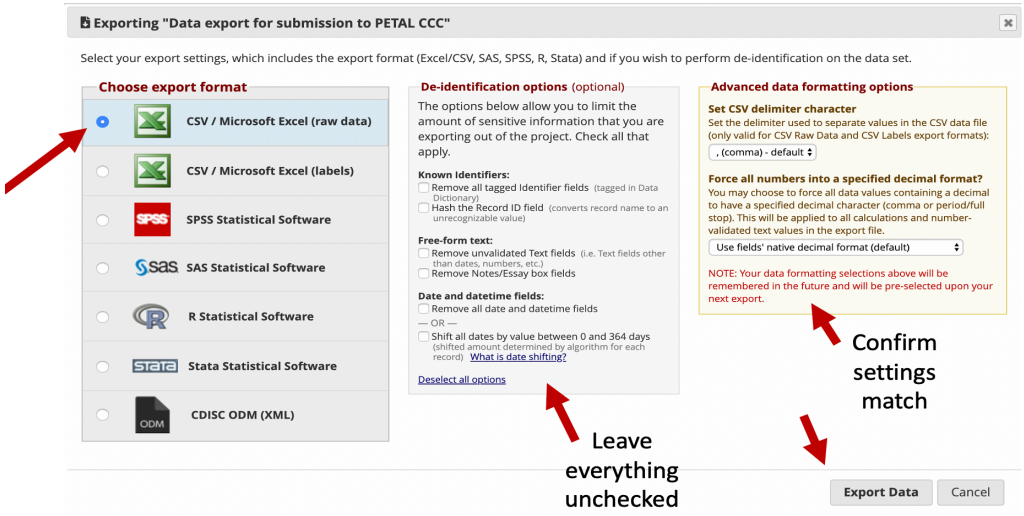
(1) Person with "data manager" role or the original project owner must complete data export
(2) Go to "Data exports" page



(3) IF NEEDED: Follow instructions on next page to update the report titled "Data export for submission to CCC" to align with most recent report data elements released by the CCC
(4) Click "Export data" for the report titled "Data export for submission to CCC"

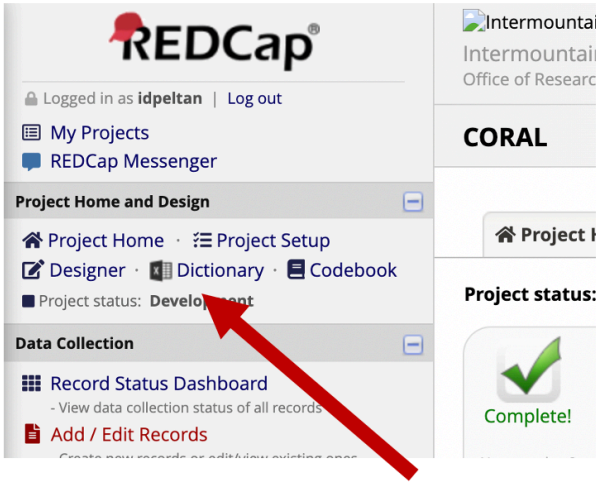


(5) Choose export format "CSV / Microsoft Excel (raw data)"
(6) Ensure deidentification options box hhas nothing checked
(7) Ensure "Advanced data formatting options" match default settings below
(8) Click "Export data" button

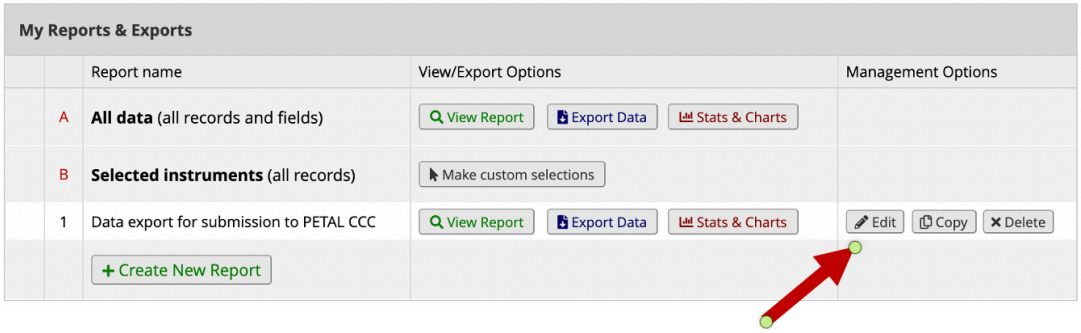


UPDATE UPLOADABLE REPORT PRIOR TO EXPORTING DATA

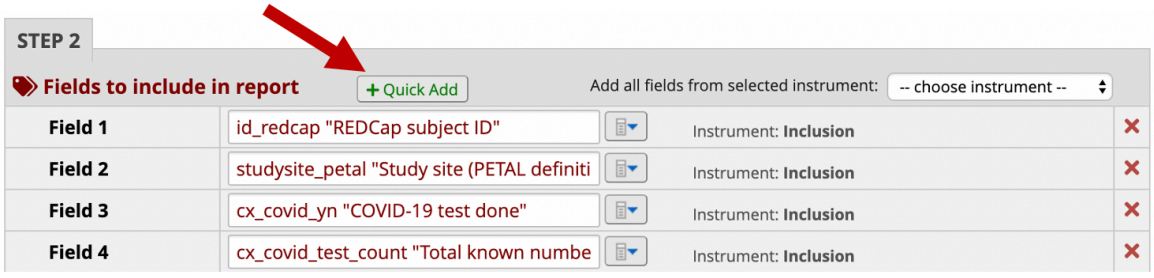
(1) Person with "data manager" role or the original project owner must complete upload
(2) Go to "Project Setup" page → "Data dictionary"



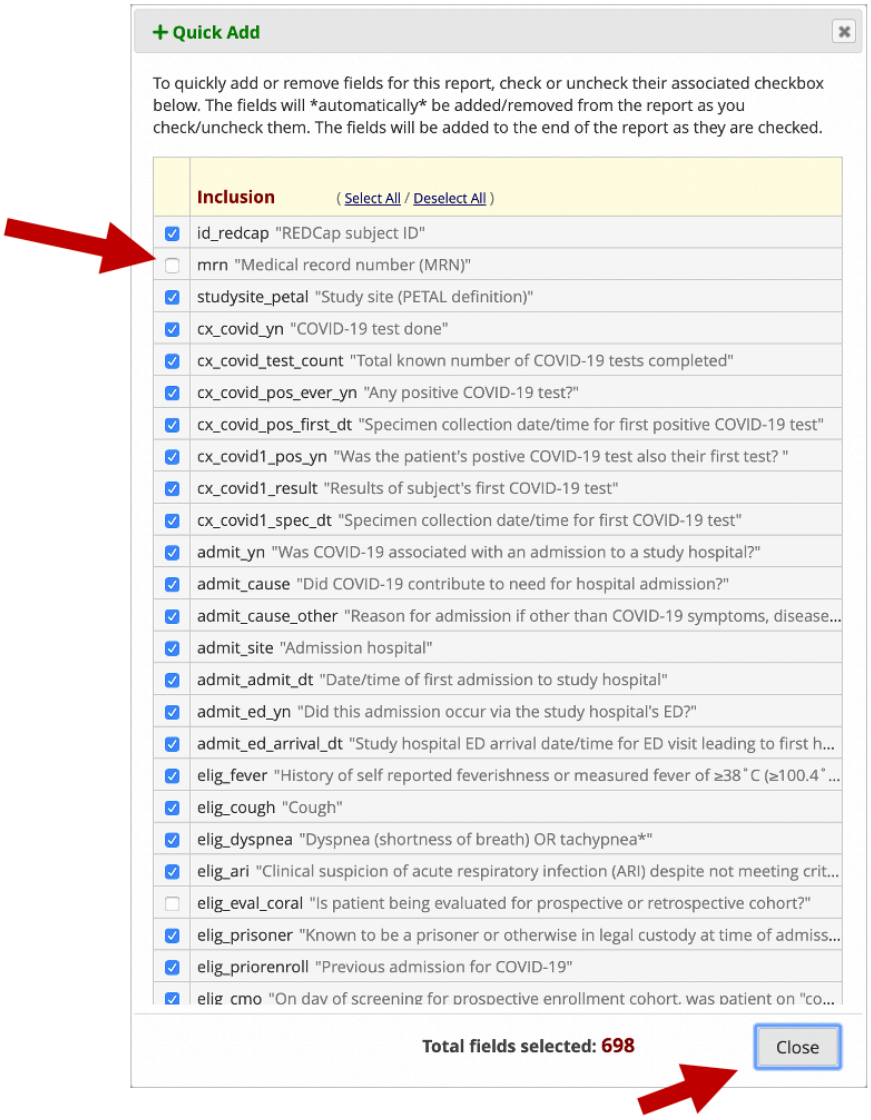
(3) Click the "edit" button for the report titled "Data export for submission to CCC"



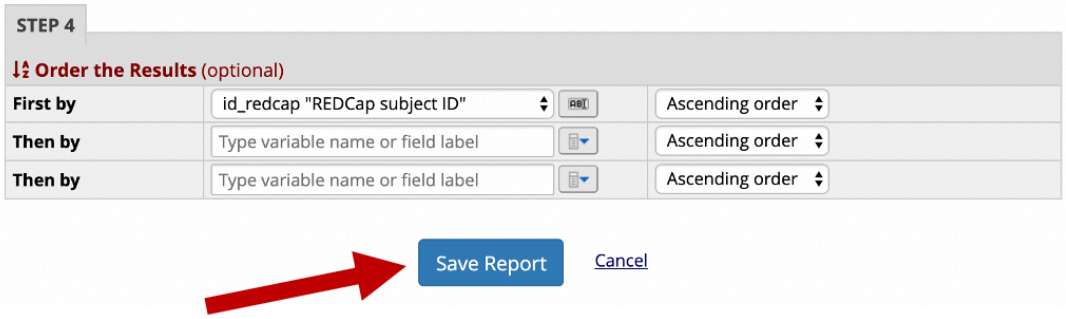
(4) Scroll down to the "Step 2" tab labeled "Fields to Include in Report"
(5) Click "Quick Add"



(4) Add or remove data elements based on instructions from the CCC by activating or inactivating the check box in front of them
(5) Click close when done



(6) Scroll to bottom of page
(7) Click "Save report



DATA ABSTRACTION INSTRUCTIONS

Detailed approaches to abstraction of individual data elements will depend on the electronic medical record and other clinical data systems available to each site as well as the amount of data (if any) that is able to be abstracted electronically. The REDCap instrument itself will help you keep your data aligned with requirements, but ultimately the responsibility is with sites to enter clean data.

A few general principles:

- Do not begin manual abstraction for other instruments until the "Inclusion" instrument is complete.
- Additional instructions are embedded in the REDCap
- Study days use calendar days. Study day #1 is the day of arrival to the study hospital.
- The REDCap instrument built for this project makes extensive use of branching logic to hide unnecessary fields as well as field validation.
  - If a data field is not shown, you do not need to complete it.
  - During manual abstraction, with very few exceptions, almost all fields that appear are mandatory.
  - For sites entering data electronically:
    - Uploaded data will need to match the field validation rules for a given field (e.g. temperature must be uploaded as "37.0" rather than "37")
    - Be aware that it is generally OK to enter more time points of data than necessary. For example, labs can be entered every day for a RED CORAL patient. This should not interfere with REDCap branching logic.
    - Ensure that indicator "-99" rather than empty field is included for missing data in required fields (except for exceptions such as MRN, ZIP code).
- Missing data
  - For numeric data elements, with a few exceptions (including MRN and ZIP code), enter "-99" (without quotation marks) for missing data.
  - For fields that force data entry with a specific number of decimal places (e.g. temperature, pH), missing data indicator must also follow the same pattern (e.g. "-99.00" for missing pH)
  - For missing/unknown date/time data elements, enter "01/01/1900 00:00". If known date but unknown time, enter time as "00:00".

Specific issues arising repeatedly

- *Documentation of oxygen support (FiO2):*
  - Report value as fraction (range 0.21-1.00).
  - Enter "0.21" if breathing room air.
  - If oxygen reported in L/min, calculate FiO2 as 0.21+0.03 x (O2 flow in liters/min). Example: 3L NC oxygen = 0.21+3x(0.03)= 0.21+0.09 = 0.30 If unknown, enter "-99"
- *Documentation of medications given as part of a trial:* In general document medication as usual if the patient was in an "open label" or single arm trial and is therefore known for certain to have received a medication. If the trial was blinded, it is unknown which medication patient received or if they received placebo, so do not document this medication. See "Baseline-Initial Drug Tx" for more information.

The goal is to efficiently obtain accurate data with the bare minimum of missingness. In some cases, this will require "reading between the lines" of physician and nursing notes or other elements of the medical record.

INCLUSION

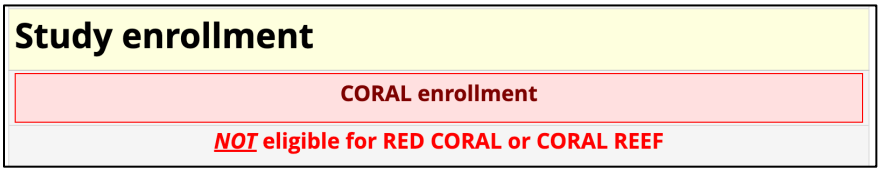
This form MUST be completed before moving on to other forms.

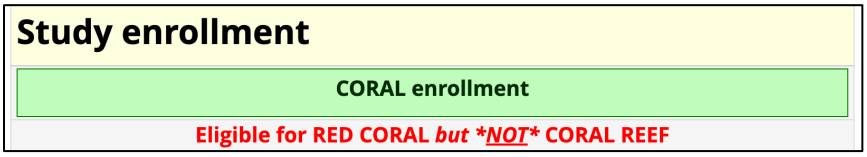
This form acts as an inclusion/exclusion screening tool. For some questions that go to the basic eligibility criteria for all CORAL patients (e.g. "Ever COVID positive?"), all subjects entered into the database will have a "Yes" answer. This is intentional. Other questions will evaluate eligibility for CORAL REEF.

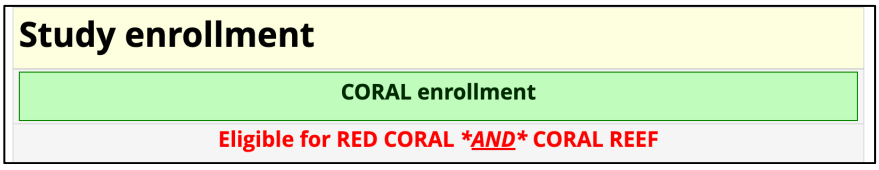
Note: You cannot enroll patient in CORAL until all necessary inclusion/exclusion questions are completed.

Once all necessary questions are answered, the REDCap will provide instructions that either:

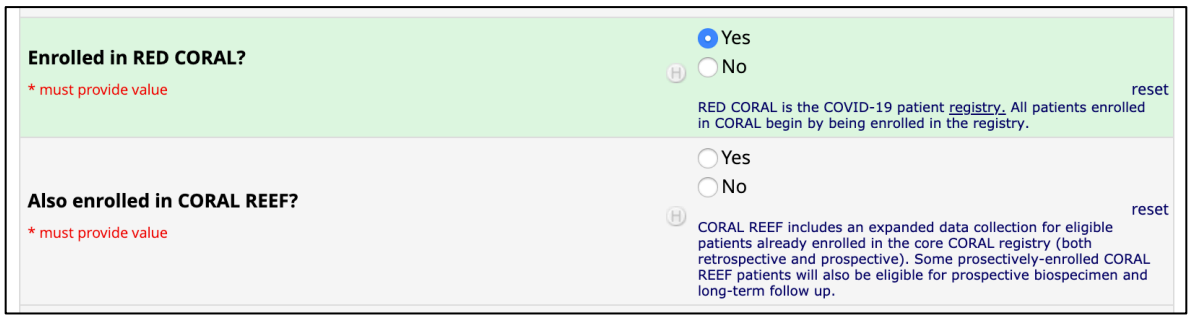
(1) Indicate that patient is not eligible for CORAL
(2) Confirm patient is eligible for RED CORAL but not CORAL REEF
(3) Confirm patient is eligible for both RED CORAL and CORAL REEF.







You will then complete fields to enroll patient in RED CORAL, either include or exclude patient from CORAL REEF, and enter study enrollment date and study ID codes.



SELECT VARIABLES/FIELDS	COMMENT/INSTRUCTION
REDCap subject ID	For most sites, this will be the PETAL subject ID. If electing to use a different number, this should be a code combining PETAL site ID with a UNIQUE number >/= 6 alpha-numeric digits. (Example: 'A03-00001' or 'U01-28453970').
Medical record number (MRN)	Enter "0" if site is not submitting MRN
Total known number of COVID-19 tests completed	Number of times patient was known to have been tested for COVID-19 at study hospital
Any positive COVID-19 test?	This will be YES for all CORAL subjects.
Was positive COVID-19 test the first test?	Answer based on their first test at study hospital
Was COVID-19 associated with an admission to a study hospital?	This will be YES for all CORAL subjects.
Did COVID-19 contribute to need for hospital admission?	Answer "Yes" if COVID-19 symptoms (e.g. fever, shortness of breath), disease (e.g. pneumonia), or complications at least in part attributed to COVID-19 (e.g. hypoxemia, ARDS, encephalitis, renal failure) contributed to need for admission to hospital as documented by treating clinicians.
Date/time of admission to study hospital	Use admit time associated with this acute illness
Eligibility symptoms	When evaluating symptom/history based elements: • If history able to be obtained and symptom noted, choose "Yes" • If history was able to be obtained and symptom is either denied or was not specifically noted, choose "No" • If clinicians unable to obtain any history, choose "unknown"
Clinical suspicion of acute respiratory infection	Answer "YES" if documented diagnosis of respiratory infection OR treatment specifically for a pneumonia OR new hypoxemia OR bilateral opacities on chest imaging. (**AT LEAST ONE SYMPTOM OR "ACUTE RESPIRATORY INFECTION" SHOULD BE "YES" FOR ALL CORAL SUBJECTS)**
ICU admit during hospitalization	Answer "No" if highest level of care was "intermediate care" or "step down" unit.
Comfort care	Comfort care includes patients who are on hospice, "comfort-focused care," "comfort measures, or have "comfort measures only" code status. Review admission and hospital progress note for days #1-2.
PETAL subject ID	Code combining site ID code with a sequential patient ID for all subjects site has enrolled in all PETAL studies (e.g. "A03-00232"). Obtain from PETAL website.
CORAL subject ID	Will only be used for prospective CORAL patients

BASELINE DATA COLLECTION

Includes instruments that collect data about patient's preadmission course and data related to the first 24 hours after hospital arrival. In general, this data can be abstracted any time beginning 24 hours after subject's arrival to the PETAL study hospital. (Note: Hospital arrival refers to the first time patient arrived to the study hospital, whether via the ED or admission to the inpatient floor if they were a "direct admit" or transferred from another hospital.)

CONTACT

This instrument collects patient's home ZIP code and may collect additional patient identifiers for prospective CORAL REEF patients enrolled in long-term follow up arm.

DEMOGRAPHICS

This instrument collects core demographic and baseline functional status on patient. Unless otherwise noted, obtain from ED/admission notes.

SELECT VARIABLES	COMMENT/INSTRUCTION
Sex	Enter sex at birth
Patient location/living situation prior to onset of current illness episode	Obtain data from brief review of ED note and admission note. If no suggestion of living in facility and no suggestion of baseline functional limitation, default to "home independently." If has limitation & lives at home, but no evidence of professional home services, default to "Home with help (unskilled...)"
Other situation	Do not specify incarceration/legal custody in this free text field.
Healthcare worker	Choose "Yes" if patient works in any capacity in a healthcare situation.
Smoking/vaping status	Former smoker/vaper defined as having quit ≥4 weeks prior to presentation. Only answer “unknown” if patient’s history is completely unknown. Otherwise, If not specifically mentioned, assume “No.”
Transferred from another facility	Include only acute care settings (ED, acute care hospital). Does not include nursing homes or long-term acute care hospitals (LTACHs).
External triage limitations on access to intensive care?	Examples include lack of ventilator availability and hospital policies limiting therapies available to that patient (e.g. intubation, ICU admission) based on age, comorbidities, or other factors. This does not include limitations based on patient’s expressed goals of care.
Goals of care include limitations	This is independent of whether an advanced directive or POLST was in place before hospital admission. Applicable data includes decisions made by the patient/LAR up through the time of admission.
Independent for ADLs	ADLs include bathing, dressing, transferring, using the toilet, and eating. Obtain from review of ED, H&P, physical therapy notes, initial rehab admission note (if available after discharge).
Frailty scale	Obtain from review of ED, H&P, physical therapy notes, initial rehab admission note (if available after discharge). For baseline healthy patients without detailed data, assume patient is “well.” • Very fit: Robust, active, energetic, motivated; exercises regularly; they are the fittest for their age • Well: No active disease symptoms; active or exercises occasionally • Managing well: Medical problems are well controlled; not active beyond routine walking • Vulnerable: Slowed down; not dependent on others; symptoms limit activities • Mildly frail: Evident slowing, higher order IADL dependency, impaired shopping or walking outside and housework\ • Moderately frail: Needs help with all outside activities, has trouble with stairs, may need help with bathing and dressing • Severely frail: Completely dependent for personal care, not at high risk of dying within 6 months • Very severely frail: Completely dependent, approaching end of life, typically would not recover from minor illness • Terminally ill: Approaching end of life

SYMPTOMS

This instrument collects signs and symptoms present on hospital arrival/admission that are new or changed from baseline during this episode of illness. Obtain from ED note and admission H&P

Importantly, the absence of symptoms/signs that were not present may not be explicitly documented. When evaluating symptom/history based elements:

- Choose "Yes" if history was able to be obtained and symptom/sign noted.
- Choose "No" if history was able to be obtained and symptom/sign is either denied OR was not specifically noted.
- Choose "unknown" only if clinicians were unable to obtain any meaningful history about patient.

COMORBIDITIES

This instrument collects data on preexisting conditions. Additional summative comorbidity flags are created automatically from this and other data and will be available in the final dataset. Obtain data from ED/admission note. Note that comorbidities (marked with an asterisk) are based on the Charlson Comorbidity Index definitions. Electronic abstraction using validated methods based on ICD-9/10 diagnosis codes is encouraged.

SELECT VARIABLES/FIELDS	COMMENT/INSTRUCTION
Myocardial infarction*	History of diagnosed or symptomatic MI, not ECG changes only
Congestive heart failure*	History of symptomatic heart failure
Atrial arrhythmia	Atrial fibrillation, atrial flutter, sick sinus syndrome
Other (non-atrial) arrhythmia	Ventricular tachycardia, ventricular fibrillation, long QT syndrome, supraventricular tachycardia (SVT)
Peripheral vascular disease*	Claudication, arterial insufficiency, revascularization, AAA ≥6 cm
Cerebrovascular disease (with mild or no residual or TIA)*	Transient ischemic attack (TIA) or CVA/stroke with mild or no residual symptoms
Hemiplegia*	Paraplegia or hemiplegia
Dementia*	Chronic cognitive deficit
Chronic pulmonary disease*	Dyspnea at rest or with mild exertion, chronic O2 use, chronic hypercapnia
Interstitial lung disease	Interstitial lung disease, pulmonary fibrosis, interstitial pneumonitis, cryptogenic or other non-infectious organizing pneumonia, asbestosis, pulmonary sarcoidosis
Asthma	Previously diagnosed by a physician
Home respiratory support	If patient uses >1 type, select the highest intensity item.
Peptic ulcer disease*	History of treatment for ulcer disease
Mild liver disease*	Without portal hypertension, includes chronic hepatitis
Moderate or severe liver disease*	Cirrhosis with portal hypertension
Diabetes without end-organ damage*	Excludes diet-controlled diabetes
Diabetes with end-organ damage	Complicated by retinopathy, neuropathy, nephropathy
Connective tissue disease*	Lupus, polymyositis, MCTD, PMR, mod/severe RA, or other significant autoimmune disease
Moderate or severe renal disease*	Baseline Cr >3, dialysis, or kidney transplant
Tumor without metastases*	Answer "No" if >5 years since diagnosis
Leukemia*	AML, ALL, CLL, CML, and polycythemia vera
HIV	Answer "Yes" if HIV or AIDS
Tuberculosis	Active pulmonary or extra-pulmonary TB. Answer "No" if latent TB only.
Alcohol abuse	Documentation of alcohol use disorder, withdrawal, or abuse
Drug abuse	Use of ilicit drugs (do not include marijuana), or prescription medications (e.g. opiates) without prescription
Psychosis	Includes schizophrenia or other psychosis
Depression	Diagnosis of depression or on current use of an antidepressant including: • SSRI: citalopram (Celexa), escitalopram (Lexapro), fluoxetine (Prozac), fluvoxamine (Luvox), paroxetine (Paxil), sertraline (Zoloft) • SNRI: desvenlafaxine (Pristiq), duloxetine (Cymbalta), venlafaxine (Effexor) • Tricyclic antidepressant: amitriptyline (Elavil], desipramine (Norpramin), doxepine (Sinequan), Imipramine (Tofranil), nortriptyline (Pamelor)
Anxiety	Diagnosis of anxiety disorder or chronically prescribed benzodiazepine (lorazepam [Ativan], clonazepam [Xanax], diazepam [Valium]

HOME MEDICATIONS

This instrument collects data on patients medications at home, as well as their participation in any research study prior to study hospital arrival.

SELECT VARIABLES/FIELDS	COMMENT/INSTRUCTION
Participation in research study involving therapeutic drug.	Includes trial participation as outpatient or at another hospital prior to transfer to study hospital. Answer "No" if patient received only "usual care" as part of the trial (no study drug) or never received any study medication.
Was patient's treatment assignment blinded?	A trial (may or may not be randomized) in which patient and their medical team knew which drug the patient received. Examples include trials that: • Give all patients a single active drug. • Compare active drug to "usual care." • Study arms use same active drug but compare durations or doses. • Compare ≥2 different active drugs with known assignment. Blinded trial: A trial in which patient and their medical team did not know which drug the patient received or if they received an active study drug at all. Examples include trials that: • Compare one or more drugs to a placebo (e.g. ORCHID) • Compare ≥2 different active drugs with unknown assignment.
Medication class members	Specific drugs within larger drug classes are provided within the REDCap instruments and in Appendix 1.
Immunosuppressive medication	Includes chemotherapy, immunosuppression for auto-immune disease, and immunosuppression after bone marrow or solid organ transplant.
Aspirin	Daily use only

INITIAL VITAL SIGNS & LABS

These instruments collect the first and, for select parameters, the highest and/or lowest values during the first 24 hours following hospital arrival.

SELECT VARIABLES/FIELDS	COMMENT/INSTRUCTION
All labs & vital signs	Values do not need to be obtained from the same time. Enter "-99" for missing values (some fields may force 1-2 zeroes after a decimal place).
Was patient's treatment assignment blinded?	If GCS is not explicitly recorded in structured documentation or as part of physical exam documented by physician, use description from HPI and physical exam in ED note or admission H&P to assign values. • GCS 15 = Normal mental status, A&O x3 • GCS 14 = Confused, altered mental status • GCS 13 = Somnolent, opens eyes to voice • GCS 10 = Obtunded, grimaces to pain • GCS 3 = Unresponsive, comatose • If still unable to determine, enter "-99"
Troponin I	Only enter values for troponin I. If only available value is troponin T (normal or high-sensitivity), enter value as missing.

INITIAL SUPPORTIVE TREATMENTS

This instrument collects respiratory and other organ support therapies administered during the first 24 hours following hospital arrival.

SELECT VARIABLES/FIELDS	COMMENT/INSTRUCTION
ICU or ICU step-down/intermediate care unit admission	If admitted to both IMCU and ICU (e.g. transferred from IMCU to ICU within 24 hours), select ICU. "ICU" can include surge, ad hoc, and temporary ICUs.
Non-invasive ventilation (NIPPV, BiPAP, CPAP)	Answer "No" if on home settings, at night only or if used only for sleep apnea.
Inotropes/vasopressors	Includes norepinephrine (Levophed), epinephrine, vasopressin, phenylephrine (Neosynephrine), angiotensin-II (Giapreza), dopamine, dobutamine, milrinone
Therapeutic neuromuscular blockade / therapeutic paralysis	Do not include paralytic given for intubation

INITIAL DRUG TREATMENTS

This instruments collects structured data on drug and related treatments administered during the first 24 hours following hospital arrival.

SELECT VARIABLES/FIELDS	COMMENT/INSTRUCTION
Selection and specification of "other" targeted treatment for COVID-19	Do not include medications for chronic illnesses, complications of acute illness (e.g. amiodarone for arrhythmia, heparin for cardiac ischemia or DVT), and hospital supportive care (e.g. nebulizers, sedatives, DVT prophylaxis).
Sedatives used for patient while on ventilator	Do not include medications given only for initial intubation. Eligible benzodiazepine medications: midazolam (Versed), lorazepam (Ativan), diazepam (Valium)

DAILY ASSESSMENT

Daily assessments will be conducted for patients in both RED CORAL and CORAL REEF, but at different intervals. **Assessments are performed up until hospital day 28 or hospital discharge, whichever occurs first.**

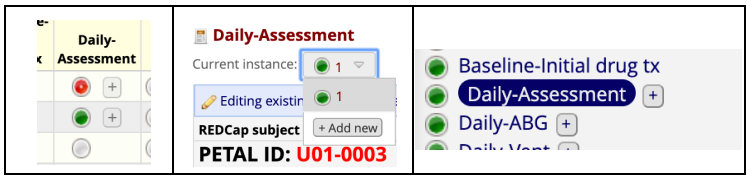
	Hospital day									ICU days*	
	1†	2-3	4	5-7	8	9-14	15	21	28	1	2-14
RED CORAL	X		X		X		X	X	X	X	
CORAL REEF	X	X	X	X	X	X	X	X	X	X	X

† Day 1 is the admission calendar day, not the 1st 24 hrs after hospital arrival.
* If specified ICU days do not overlap with days already being collected

Daily assessments occur by calendar day (i.e. midnight to 11:59 pm). **Calendar day #1 begins with hospital arrival and ends at 11:59 pm on that calendar day.** Note therefore that calendar day #1 only has partial overlap with the first 24 hours from hospital arrival.

Most data elements parallel those already described for the baseline assessments. After documenting the subject's first daily assessment, you will "reuse" this repeating form.

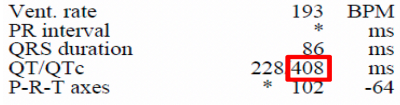
1) Click the plus symbol next to the instrument icon in Record Dashboard or on the subject's instrument menu.
2) Click the dropdown menu at the top left of the instrument and choose "Add New"



Record dashboard | Menu at top of form | Left menu bar

Data entry time points

- *Vital signs:* value closest to 8 am. If no value on study day, enter -99.
- *Labs:* value closest to 8 am. If no value on calendar day, review days between current and prior assessment day and select closest value. Enter "-99" if not done since prior assessment day.
- *ICU care:* Received at any time during calendar day
- *Treatments:* Received at any time during calendar day
- *Medications:* Received at any time during calendar day. If not given on study day, review each calendar days between current and preceding assessment day. Answer "Yes" if medication received since previous assessment day. If not given since previous assessment day, answer "No."

SELECT VARIABLES/FIELDS	COMMENT/INSTRUCTION
Urine output, daily net intake/output	Can use either calendar (as for all other daily data elements) or a can use a 24-hour period based on hospital's standard documentation/flowsheet (e.g. 6am on calendar day to 6 am on the next calendar day) to make abstraction easier. Choice should be applied consistently for each hospital.
WHO ordinal outcome scale	Will auto-populate after all necessary treatments have been documented.
Daily EKG & QTc	If patient had an EKG performed, enter the "QTc" value recorded on the EKG form by the computer. 
Other fields	See instructions provided for baseline data elements.

SERIAL ABGs & VENTILATOR CHECKS

Plan for prospective CORAL REEF is to enter all ABGs and all ventilator checks obtained while the patient is in the ICU. For patients in retrospective cohorts, these forms will not be used.

SUMMATIVE/DISCHARGE DATA

Includes instruments that collect data about patient's overall hospital course. **This data should be finalized on hospital discharge.** If patient is transferred between hospitals within your hospital system, review data from all available hospitalizations to answer summative questions.

OUTCOMES

Instrument collects data on hospital outcome, infections, and discharge status.

SELECT VARIABLES/FIELDS	COMMENT/INSTRUCTION
Date of last update	Enter date that data is being abstracted. *This field should be updated each time the summative/discharge data is updated.*
Hospital disposition at discharge	Aside from death, palliative discharge trumps other disposition statuses. For instance, a patient discharged on home hospice should be recorded as "palliative discharge" rather than "discharge home with services.
Care limitations	Obtain data from review of discharge, interim, and transfer summaries.
Pulmonary infection	Obtain info from discharge, interim, and transfer summaries as well as results of molecular testing for pulmonary pathogens and sputum and other respiratory cultures.
Non-pulmonary infection	Obtain information from discharge, interim, and transfer summaries. Do not include initially suspected infections that are ultimately disproven (may be explicitly documented or may be indicated by decision to stop antibiotics before completing a full course (e.g. after just 1-2 days).
Discharged on new or increased non-invasive positive pressure ventilation (NIPPV/BiPAP/CPAP)	Answer "No" if NIPPV or CPAP only used to treat sleep apnea and not ongoing respiratory failure.
New mechanical ventilation	Answer "No" If a patient is (1) chronically vent-dependent and is discharged on their home support or (2) has a trach on around-the-clock trach collar

TREATMENTS

Instrument collects summative data on supportive treatments provided during the hospitalization.

SELECT VARIABLES/FIELDS	COMMENT/INSTRUCTION
Days of therapies	Count calendar days where patient got any oxygen.
ICU admit/discharge dates	Record admission/discharge date for up to 4 ICU admission episodes. If ≥4 ICU admissions, enter the date of the FINAL ICU for the "ICU discharge FINAL" field or, if in the ICU at discharge, the date of hospital discharge.
Intubation/extubation dates	Record intubation and extubation date for up to 4 intubation episodes. If ≥4 intubations, enter the date of the FINAL extubation for the "extubation #4" field or, if intubated at discharge, the date of hospital discharge.
Other fields	See instructions provided for baseline data elements.

DIAGNOSTICS

Instrument collects data on imaging and microbiologic testing.

SELECT VARIABLES/FIELDS	COMMENT/INSTRUCTION	
Molecular testing	Molecular tests of interest include: • Influenza • Non-COVID coronaviruses • Strep urine antigen • Legionella urine antigen • RSV	• Metapneumovirus • Parainfluenza • Adenovirus • Rhinovirus • Mycoplasma • Chlamydia pneumoniae
"True positive" cultures	"True positive" pulmonary, blood, urine, or other culture per clinical documentation in discharge summary, transfer notes, and/or interim summaries. True positive cultures will usually be matched by an appropriate course of antibiotic treatment. Culture results that are <u>usually</u> false positives include: • Respiratory samples that read “oropharyngeal flora” can be ignored • Samples that grew multiple bacterial types or “multiple colony types” or “mixed flora” can be ignored if antibiotic sensitivities not done • Candida (a fungus/yeast) from urine or sputum (but <u>not</u> from other sources) is assumed to be a contaminant • Coagulase negative staph” is usually, but *not always,* a contaminant. If only one bottle or one set of blood cultures is positive for this, can ignore <u>if</u> clinical notes indicate the team felt this was a contaminant.	

COMPLICATIONS

Instrument collects data on complications observed at any time during hospitalization. Obtain data from review of discharge summary, transfer note, and interim summary as well as ICU admission notes that occur late in hospitalization. Importantly, the <u>absence</u> of a complication will not be explicitly documented. Simply answer "No" if that complication is not documented.

MEDICATIONS

Instrument collects data on treatment with key medications over the entire course of the hospitalization. Obtain data from review of discharge summary, transfer note, and interim summary and the medication administration record. For additional information, see instructions provided for baseline inpatient medications.

CONTACT INFORMATION

To facilitate long-term follow up, instrument collects preferred language and detailed contact information for both subject and up to two backup contacts. **For patients in retrospective cohorts, this form will not be used.**

PLACEHOLDER INSTRUMENTS

These forms are primarily for use by CCC or as optional storage. Abstractors should not need to interact with these forms.

CALCULATION PENDING

This form contains fields for use by CCC to generate values calculated from data entered elsewhere in REDCap. You will never need to enter data for this form.

OPTIONAL

For sites collecting data electronically, this form contains fields to store additional comorbidity data (Elixhauser), ICD-10 discharge diagnosis codes, and a small amount of additional data on COVID-19 testing. All of this data is entirely optional for all sites. **Do NOT enter data manually unless explicitly instructed to do so by your site's investigator.**

APPENDIX 1 — Drug classes and example drugs

DRUG CLASS	COMMON DRUGS IN THIS CLASS	
ACE inhibitors	Benazapril (Lotensin) Captopril (Captoten) Enalopril (Vasotec) Fosinopril (Monopril) Lisinopril (Prinivil, Zestril)	Moexipril (Univasc) Perindopril (Aceon) Quinapril (Accupril) Ramipril (Altace) Trandolapril (Mavik)
Angiotensin receptor blockers (ARBs)	Azilsartan (Edarbi) Candesartan (Atacand) Eprosartan (Teveten) Irbesartan (Avapro)	Telmisartan (Micardis) Valsartan (Diovan) Losartan (Cozaar) Olmesartan (Benicar)
Other anti-hypertensive	Metoprolol (Lopressor/Toprol) Carvedilol (Coreg) Labetalol Atenolol Propranolol Clonidine Hydrochlorothiazide	Amlodipine (Norvasc) Nicardipine Diltiazem Verapamil Hydralazine Isosorbide
NSAIDs (non-steroidal anti-inflammatory drugs)	Ibuprofen (Advil, Motrin) Naproxen (Aleve, Naprosyn) Diclofenac (Voltaren) Indomethacin (Indocin)	Ketorolac (Toradol) Piroxican (Feldene) Celecoxib (Celebrex)
Diuretics	Furosemide (Lasix) Torsemide (Demadex) Metolazone	Chlorothiazide (Diuril) Bumetanide (Bumex) Ethacrynic acid
Statin	Atorvastatin (Lipitor) Fluvastatin (Lescol) Lovastatin (Mevacor, Altoprev) Pravastatin (Pravachol)	Rosuvastatin (Crestor) Simvastatin (Zocor) Pitavastatin (Livalo)
Inhaled steroids	Includes only steroids inhaled into lungs, not nasal steroids inhalers/sprays	Fluticasone (Flovent, Arnuity) Budesonide (Pulmincort) Mometasone (Asmanex) Beclomethasone (QVAR) Flunisolide (QVAR) Ciclesonide (Aerobid) Triamcinolone (Azmacort)
Systemic/oral steroids	Requires oral, IV or IM administration	Prednisone Dexamethasone (Decadron) Methylprednisone (Solumedrol, Medrol) Prednisolone Hydrocortisone
Inotropes/vasopressors	Norepinephrine (Levophed) Epinephrine Vasopressin	Phenylephrine (Neosynephrine) Angiotensin-II (Giapreza), Dopamine Dobutamine Milrinone
Sedatives for intubated patients	Propofol Dexmedetomidine (Precedex) Ketamine	Benzodiazepines: -Midazolam (Versed) -Lorazepam (Ativan)

DRUG CLASS	COMMON DRUGS IN THIS CLASS
	-Diazepam (Valium)
Prophylactic anticoagulation	Subcutaneous heparin Enoxaparin (Lovenox) ≤40 mg daily or ≤30 mg twice daily Dalteparin (Fragmin) ≤5000 units daily Fondaparinux (Arixtra) ≤2.5 mg daily
Therapeutic anticoagulation	IV heparin (continuous infusion) Enoxaparin (Lovenox) ≥40 mg twice daily Dalteparin (Fragmin) >5000 units total per day Fondaparinux (Arixtra) ≥5 mg/day Warfarin (Coumadin) R ivaroxaban (Xarelto) Dabigatran (Pradaxa) Apixaban (Eliquis) Exodaban (Savaysa) Bivalruidin Argatroban
Fibrinolytic ("lytic") therapy	Exclude if used just to manage of clotted catheters (e.g. ≤8 mg of tPA) Alteplase ("tPA" or "tissue plasminogen activator") Streptokinase Urokinase
Antiretroviral therapy (ART/HAART) for HIV/AIDS	See NIH list of FDA-approved ART medications.

APPENDIX 2 — Categories/examples of non-pulmonary infection

Main infection category	Specific diagnosis examples (not necessarily comprehensive)	Abbreviation(s)
Urinary tract	Urinary tract infection Catheter-associated UTI Cystitis Pyelonephritis Prostatitis Infected nephrolithiasis	UTI CAUTI
Intraabdominal	Peritonitis Spontaneous bacterial peritonitis Mesenteric ischemia Perforated bowel, intestine, colon etc Diverticulitis Appendicitis Gastritis Enteritis Infecious diarrhea Salmonella Shigella Intraabdominal abscess Cholecystitis Cholangitis Ascending cholangitis Pancreatitis (<u>only</u> if ED attending believes necrotic/infected or treats empirically as infected due to illness severity) Heptatits Gastroenteritis Colitis Clostridium difficile colitis Toxic megacolon Retroperitoneal abscess Psoas abscess Abdominal mesh infection Enterocutaneous fistula Infection involving chronic biliary or abdominal drain (<u>unless</u> infection is restricted to the skin)	 SBP “Perf” CCY C diff, CDI
CNS/meningitis	Meningitis Encephalitis Epidural abscess West Nile Virus Ventriculitis VP shunt infection	

Main infection category	Specific diagnosis examples (not necessarily comprehensive)	Abbreviation(s)
Skin and soft tissue	Cellulitis Soft tissue infection Necrotizing soft tissue infection Necrotizing fasciitis Abscess (in skin or muscle) Folliculitis Erysipelas Myositis Lymphadenitis Myonecrosis Diabetic foot infection Infected wound Post-operative infection (if of skin) Infected decubitus or pressure ulcers Orbital cellulitis Otitis externa Mastitis Perirectal abscess	
Primary bloodstream/endocarditis	Bacteremia (but **only** if does not have another source of infection) Catheter-associated bloodstream infection Endocarditis Line infection Pacemaker infection PICC infection Port-a-cath infection Candidemia	BSI CLABSI SBE
Osteoarticular (bones & joints)	Osteomyelitis Discitis Septic arthritis Infected ortho hardware (ex. artificial knee) Mastoiditis	

Other specific source	Use if source identified but does not fit into a category above. Two major groups are oropharyngeal disease and infections of the male and female reproductive tracts
	• Neutropenic fever
	• Dental & oropharyngeal infections:
	  ○ Sinusitis
	  ○ Retropharyngeal abscess
	  ○ Pharyngitis
	  ○ Dental infection
	  ○ Dental abscess
	  ○ Tonsilitis
	  ○ Epiglotitis
	• Otitis media (middle ear infection)
	• Reproductive tract infections
	  ○ Endometritis
	  ○ Orchitis
	  ○ Epididymitis
	  ○ Gonorrhea
	  ○ Syphilis
	  ○ Chlamydia
	  ○ Septic abortion	

Main infection category	Specific diagnosis examples (not necessarily comprehensive)	Abbreviation(s)
	○ Cervicitis ○ Pelvic inflammatory disease • Other ○ EBV/mononucleosis (systemic) ○ Babesia ○ Lyme disease ○ Malaria ○ Rocky Mountain Spotted Fever ○ Ehrlichiosis ○ Anaplasmosis ○ Tularemia ○ Many others, if in doubt, ask	
Multiple sources	Use this if physician has identified several sites where they believe they are actually infected (as opposed to simply listing several possibiltiies and they're not sure which). Example: "Patient has evidence of both pneumonia and UTI"	
Infected, source unclear	Sepsis of unclear source. Examples: "Fever of unknown origin," "Unclear source of sepsis, possibilities include …"	
Not infected	Some patients receive antibiotics for reasons other than having an active infection, but rather to reduce the risk of getting one due to another problem • Open fracture • Prophylaxis after other trauma/injury • Cirrhosis/liver failure with GI bleeding • After sexual assault • Prophylaxis prior to surgery • Prophylaxis prior to other invasive procedure (e.g. cardiac cath)	

APPENDIX 3 — INFECTION SOURCE FAQs

- Pyelonephritis is a urinary infection, not abdominal

- Intraabdominal infections with the "-itis" suffix
    - Appendicitis, cholangitis, peritonitis, cholecystitis, gastroenteritis are types of abdominal infections
    - Colitis is either an infection or when it's not caused by infection, is often treated as if it were an infection even when it's due to a non-infectious cause including inadequate blood flow (ischemic colitis) or autoimmune disease (inflammatory bowel disease). Unless MD clearly doesn't believe colitis is an infection, this counts as an abdominal infection if antibiotics are given.
    - Pancreatitis is the most complex intraabdominal "-itis" for our purposes. In contrast to appendicitis, colitis, cholangitis, pyelenonephritis etc etc, pancreatitis MAY be a source of infection, but <u>USUALLY is not</u>. Three situations apply:
        - Pancreatitis is source of infection (look for terms "infected pancreatits" or "necrotizing pancreatitis" or pancreatic abscess")
        - Pancreatitis is present, & MD treats empirically for infection bcause patient is severely ill
        - Pancreatitis is present, but is not belived to be infected, and MD treats patient for a different infection
            - For situations #1 and #2, pancreatitis counts as an intrabdominal infection source
            - For situation #3, do NOT count pancreatitis as an intraabdominal infection source
- "Septic pulmonary emboli" implies that infection observed in the lung originated elsewhere and travelled ("embolized") to the lung. If no other primary source is identified, label these as "primary bloodstream."

- In the case of am endocarditis involving the right heart, where infection spreads to the lung from the infected heart valve or pacer wires (and especially if the bug is Staph aureus) often will be endocarditis as the primary source rather than pneumonia. If in doubt, ask me or flag.

- Prostate infections are classified as urinary tract infections

- Other specific source: ***pharyngitis*** (includes "strep pharyngitis," has been misclassified several times), epiglottitis, tonsillar abscess, retropharyngeal abscess

- Skin infections and osteomyelitis can occur together when a penetrating skin infection extends to the bone. This is particularly common in patients with chronic wound or diabetic foot infections. So there are four situations that may occur for recording ED and final source of infection. Please particularly note situation #3, which has been a source of confusion.
    - Skin infection alone/cellulitis --> skin and soft tissue
    - Diabetic foot infection or other infected chronic wound but NO mention of coexisting bone infection → <u>skin and soft tissue infection</u>
    - Diabetic foot infection or ulcer WITH mention that MD strongly suspect or believes patient has both an active wound infection osteomyelitis → <u>multiple sources</u>
    - Bone infection below chronic wound with no suspicion that the soft tissues are actively infected → <u>Osteoarticular</u>

APPENDIX 4 — LIST OF ANTIBIOTICS

Antibiotic	Bramd names	Routes
Amikacin	Amikin	IV
Amoxicillin	Amoxicillin	PO
Amoxicillin/clavulanate	Augmentin	PO
Amphotericin	Amphotec, Ambisome	IV
Ampicillin	Principen	IV/PO
Ampicillin/sulbactam	Unasyn	IV
Anidulafungin	Eraxis	IV
Azithromycin	Zithromax, Zmax, Sumamed	IV/PO
Aztreonam	Azactam	IV
Caspofungin	Cancidas	IV
Cefaclor	Ceclor	PO
Cefadroxil	Duricef, Ultracef	PO
Cefazolin	Ancef	IV
Cefdinir	Omnicef	PO
Cefditoren	Spectracef, Meiact	PO
Cefepime	Maxipime	IV
Cefixime	Suprax	PO
Cefoperazone	Cefobid	IV
Cefotaxime	Claforan	IV
Cefotetan	Cefotan	IV
Cefoxitin	Mefoxin	IV
Cefpodoxime	Vantin	PO
Cefprozil	Cefzil	PO
Ceftaroline	Teflaro	IV
Ceftazidime	Fortaz	IV
Ceftazidime/avibactam	Avycaz	IV
Ceftibuten	Cedax	PO
Ceftizoxime	Cefizox	IV
Ceftolozane/tazobactam	Zerbaxa, Ceftolozane	IV
Ceftriaxone	Rocephin	IV
Cefuroxime	Ceftin, Zinacef	IV/PO
Cephalexin	Keflex	PO
Chloramphenicol	Chloromycetin	IV
Ciprofloxacin	Cipro, Ciprobay, Ciproxin	IV/PO
Clarithromycin	Biaxin	PO
Clindamycin	Cleocin	IV/PO
Colistin	Colymycin	IV
Dalbavancin	Dalvance	IV
Daptomycin	Cubicin	IV
Delafloxacin	Baxdela	IV/PO
Dicloxacillin		PO
Doripenem	Doribax	IV
Doxycycline	Doxychel, Vibramycin	IV/PO
Eravacycline	Xerava	IV
Ertapenem	Invanz	IV
Erythromycin	Erythocin, Erythroped	IV/PO

Antibiotic	Bramd names	Routes
Fidaxomycin	Dificid	PO
Fluconazole	Diflucan	IV/PO
Flucytosine	Ancobon	PO
Ganciclovir	Cytovene	IV
Gentamicin	Garamycin	IV
Imipenem/cilastin	Primaxin	IV
Isavuconazole	Cresemba, Isavuconazonium	IV/PO
Itraconazole	Sporanox, Onmel	PO
Levofloxacin	Levaquin	IV/PO
Linezolid	Zyvox	IV/PO
Meropenem	Merrem	IV
Meropenem/vaborbactam	Vabomere	IV
Metronidazole	Flagyl	IV/PO
Micafungin	Mycamine	IV
Minocycline	Minocin	IV/PO
Moxifloxacin	Avelox	IV/PO
Nafcillin	Unipen, Nallpen	IV
Nitrofurantoin	Macrobid, Macrodantin	PO
Ofloxacin	Floxin	PO/IV
Omadadcycline	Nuzyra, Paratek	PO/IV
Oritavancin	Orbactiv	IV
Oxacillin	Bastocillin	IV
Penicillin	Penicillin V, Pencillin G, Pen VK, Bicillin, Veetids, Pentids, Permapen, Pfizerpen	IV/PO
Peramavir	Rapivab	IV
Plazomicin	Zemdri	IV
Piperacillin/tazobactam	Zosyn	IV
Posaconazole	Noxafil	IV/PO
Quinuopristin/dalfopristin	Synercid	IV
Rifampin	Rifadin	IV/PO
Telavancin	Vibativ	IV
Tetracycline	Achromycin, Tetracyn, Sumycin, Tetrachel	IV/PO
Ticarcillin/clavulanate	Timentin	IV
Tidezolid	Sivextro	IV/PO
Tigecycline	Tygacil	IV
Tobramycin		IV
Trimethoprim/ sulfamethoxazole	Bactrim, Septra, Sulfatrim, TMP/SMX	IV/PO
Valacyclovir	Valtrex	PO
Valganciclovir	Valcyte	PO
Vancomycin	Vancocin	IV
Vancomycin	Vancocin	PO
Voriconazole	Vfend	IV/PO