



Indications for Use

- The U.S. Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of the COViage Hemodynamic Instability and Respiratory Decompensation Prediction System (*COViage*) to be used by healthcare providers (HCP) in the hospital setting for adult patients (i.e., patients that are 18 years or older who are admitted to the hospital) with confirmed COVID-19 (i.e., a positive PCR test result) for the computation of proprietary patient status indices referred to as Respiratory Decompensation Status and Hemodynamic Instability Status as an adjunct to patient monitoring during the Coronavirus Disease 2019 (COVID-19) outbreak. The COViage indices provide HCP with predictive screening information as a diagnostic aid to assist with the early identification of COVID-19 patients who are likely to be diagnosed with hemodynamic instability or respiratory decompensation, which are common complications associated with COVID-19.
- *COViage* is a cloud-based software tool intended as an aid in identifying adult patients at risk of hemodynamic instability or of respiratory decompensation during their hospitalization. *COViage* is intended for use only in COVID-19 positive patients. Clinicians are instructed to use outputs from the *COViage* algorithm to inform treatment decisions only after a patient has a COVID-19 positive PCR test result during the hospital encounter.
- *COViage* is composed of two algorithms, one that identifies patients at risk of hemodynamic instability during their hospitalization, and another one that identifies patients at risk of respiratory decompensation during their hospitalization. Each algorithm performs a one-time analysis of the following patient health information data fields from electronic medical records (EMRs): age, gender, temperature, heart rate, respiration rate, systolic blood pressure, and diastolic blood pressure.
- *COViage* applies each machine learning algorithm the first time a patient chart in the electronic medical record contains age, gender, and at least one entry of each of the five aforementioned vital signs. Each machine learning algorithm uses the most recently available measurement for each of the vital signs at the time of risk level determination.

Limitations for Use

- *COViage* is intended for use only with COVID-19 positive adult patients aged 18 and over who are admitted to the hospital.
- *COViage* is intended to be used as a clinical decision support tool and is to be used together with the patient's monitoring data, diagnostic test results, best clinical judgment, other clinical observations, patient history, and epidemiological information.

Appendix A: COViage Instructions for Use

- The *COViage* system does not provide a solution for acute situations (such as pulmonary embolism) as the tool analyzes limited data and may not be able to identify suddenly occurring events.
- The *COViage* system has been authorized only for the measurement of risk of hemodynamic instability or respiratory decompensation.
- *COViage* has neither been cleared or approved to provide predictive screening information to assist with the early identification of patients who are likely to be diagnosed with respiratory decompensation or hemodynamic instability, which are common complications associated with COVID-19.

Contraindications

- There are no known contraindications for use of the *COViage* system.

Device Description

The *COViage Hemodynamic Instability and Respiratory Decompensation Prediction System* (“*COViage*” or “*COViage System*”) is cloud-based software that uses a set of two algorithms, one to calculate the risk level determination for hemodynamic instability and the other to calculate the risk level determination for respiratory decompensation, that together:

- Receive patient data from the hospital’s electronic medical record (EMR) system,
- Analyze each patient’s data using each algorithm to compute the patient’s risk level as a one-time assessment, and
- Provide a real-time updated report of risk status for all hospitalized patients aged 18 or over that are diagnosed with COVID-19.

COViage software will run automatically only after all required measurements (described in “Description of algorithm inputs”) are entered into the EMR. At the time that patient age, gender, and all five required vital signs are available in the EMR, the data are inputted by *COViage* autonomously into the algorithm without intervention from the healthcare provider.

- For each vital sign, the most recent measurement of each vital sign is used.
- The data are analyzed and risk level is generated based on individual patient data.
- If the risk level exceeds a predefined threshold, the patient is reported as high risk.
- The risk level determination calculated applies to the duration of the patient’s hospital stay. In other words, *COViage* assesses risk for the patient at any point in their hospital stay after the software receives the minimum required data inputs (described in “Description of algorithm inputs”). There is one risk level determination per visit, and it is made automatically upon the system’s collection of the minimum required data inputs from the EMR. The determination is not recalculated at the provider’s request.

Appendix A: COViage Instructions for Use

COViage has no physical device component. It is cloud-based software. There will be no physical device installation process.

Description of algorithm inputs

Each machine learning algorithm uses the following inputs that together constitute the minimum required data elements. “Minimum” is defined to mean at least one value for each of the data elements listed. There are no additional data elements accepted as inputs to the algorithms. There may, however, be more than one value available per data element, which occurs when a patient has multiple sets of vitals recorded in the EMR at the time the data are made available to COViage.

- Age
- Gender
- Heart Rate (HR)
- Diastolic Blood Pressure (DiasBP)
- Systolic Blood Pressure (SysBP)
- Temperature
- Respiratory Rate

Description of notification configuration

COViage will provide a real-time report in the following form for all hospitalized patients with an age of 18 or older who have been determined to be COVID-19 positive according to a positive PCR test result that is recorded in the EMR during the current hospital stay. “Real-time” is defined to mean that the report is updated virtually instantaneously as a patient’s status changes. COViage generates this risk level determination report only once during the patient hospitalization. The risk level determination report calculated applies to the duration of the patient’s hospital stay. In other words, COViage assesses risk for the patient at any point in their hospital stay after the software receives the minimum required data inputs. There is one risk level determination per visit, and it is made automatically upon the system’s collection of the minimum required data inputs from the EMR. The determination is not recalculated at the provider’s request.

Table 1: Example Report Format (not from actual data)

Patient Last Name	Patient First Name	Medical Record Number	Hemodynamic Instability Status (timestamp)	Respiratory Decompensation Status (timestamp)
Smith	John	1210001	High Risk (June 01, 2020; 16:20)	Not High Risk (June 01, 2020; 16:20)

Appendix A: COViage Instructions for Use

Each Status field will have three possible results¹:

- i) *Insufficient Data*: Patient does not yet have at least one entry for each of the following inputs: age, gender, temperature, heart rate, respiration rate, systolic blood pressure, and diastolic blood pressure. At the first timepoint that all required inputs include an entry, the most recent entries for all inputs (some of which may have been collected earlier) will be used for the algorithm calculations. There will NOT be a prediction from the algorithm displayed if the patient has insufficient data.
- ii) *Not High Risk*: Risk level generated by the respective machine learning algorithm is below the pre-set threshold. This means that the patient is predicted to NOT be at high risk for hemodynamic instability or for respiratory decompensation, as applicable.
- iii) *High Risk*: Risk level generated by the respective machine learning algorithm is above the pre-set threshold. This means that the patient is predicted to be at high risk for hemodynamic instability or for respiratory decompensation, as applicable.

Status fields may be updated from “Insufficient Data” (when the minimum required data inputs are not yet received by COViage) to either “Not High Risk” or “High Risk,” but do not toggle between “Not High Risk” to “High Risk.” There is one analysis made per visit, and no analyses are made when there are not sufficient data collected.

This report is included on a web interface as the sole user interface for COViage. No external software devices are used for the user interface.

Training will be provided by Dascena to users of the COViage System regarding interpretation of the report, including description of the single time point during the hospital stay when each algorithm is applied, descriptions of criteria for “Respiratory Decompensation” and “Hemodynamic Instability” and descriptions of “High Risk,” “Insufficient Data,” and “Not High Risk” status indicators. **The intended user of COViage is a clinician or other authorized user within the hospital who has undergone training by Dascena in the use of the system.**

COViage is not intended to be used on a standalone basis for clinical decision-making.

Summary of Clinical Performance

COViage was validated on a dataset of COVID-19 hospitalized patients admitted between March 1, 2020, and June 3, 2020, from three hospitals. The algorithm was applied to each patient in the validation set at the first time all of age, gender, temperature, heart rate, respiration rate, systolic blood pressure, and diastolic blood pressure were available. There was no overlap among the hospitals used for the training dataset and the validation dataset.

Gold Standard for Hemodynamic Instability: Patients were considered positive for hemodynamic instability if they were given an inotrope or vasopressor at any point during their hospital stay. The following specific medications were included in the characterization:

¹ Note: The thresholds for the risk level status fields have been set by the manufacturer and were derived from prior algorithm development testing. The clinician cannot change the thresholds for the risk levels.

Appendix A: COViage Instructions for Use

- Inotropes: milrinone, digoxin, dobutamine, dopamine, inamrinone
- Vasopressors: isoproterenol, phenylephrine, epinephrine, norepinephrine, dobutamine, ephedrine, angiotensin, droxidopa, vasopressin, dopamine

All patients that did not meet this criterion were considered negative.

Gold Standard for Respiratory Decompensation: Patients were considered to be positive for respiratory decompensation if that the patient was mechanically ventilated (defined as invasive ventilation requiring endotracheal tube or mechanical ventilation not including BIPAP or CPAP) at any point during their hospital stay.

All patients that did not meet this criterion were considered negative.

For prediction of hemodynamic instability at any point during a patients' hospital stay on the validation test set, *COViage* obtained sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 0.708 (95% CI 0.5261, 0.8899), 0.532 (95% CI 0.4496, 0.6144), 0.205 (95% CI 0.1181, 0.2919), and 0.915 (95% CI 0.8546, 0.9754), respectively.

For prediction of respiratory decompensation at any point during a patients' hospital stay on the validation test set, *COViage* obtained sensitivity, specificity, PPV, and NPV of 0.720 (95% CI 0.5440, 0.8960), 0.509 (95% CI 0.4318, 0.5862), 0.186, (95% CI 0.1086, 0.2634), and 0.921 (95% CI 0.8650, 0.9770), respectively.

Warnings, Cautions and Precautions

Warnings

- Do not use before reading instructions for use.
- Use of controls or adjustments, or performance of procedures other than those described herein, may be hazardous. Personnel operating or maintaining the system should read these instructions for use and be thoroughly familiar with all safety requirements and operating procedures before operating the system.
- Only Dascena authorized personnel are allowed to service the system.

Cautions

- Due to possible variability in *COViage* results, algorithm output should be interpreted by an appropriately trained clinician with the patient's monitoring data, diagnostic test results, best clinical judgment, other clinical observations, patient history, and epidemiological information.

Precautions

- Use the system in a hospital environment only.
- The safety and effectiveness of *COViage* has not been established in pediatric patients.

READ BEFORE USING THE SYSTEM

- *COViage* has neither been cleared or approved for the authorized indications for use;
- *COViage* has been authorized for emergency use by FDA under an EUA; and,
- *COViage* has been authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of medical devices under section 564(b)(1) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

Prescription Use Statement

Rx Only: Federal (U.S.) law restricts this device to sale by or on the order of a licensed physician.

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