FACT SHEET FOR HEALTHCARE PROVIDERS

Emergency Use of the COViage System During the COVID-19 Pandemic

September 24, 2020

Coronavirus Disease 2019 (COVID-19)

This Fact Sheet informs you of the significant known and potential risks and benefits of the emergency use of the *COViage* System (or "COViage") for use by healthcare providers (HCP) in the hospital setting for adult patients (18 years of age or older who are admitted to the hospital) with confirmed COVID-19 (based on 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 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.

During hospitalization, monitoring using electronic medical record (EMR) systems results in the accumulation of a significant amount of individualized patient data. Without predictive analytics, identification of clinically meaningful data can be more easily overlooked. Thus, while decisions can be made based on the patient's current state of health, consideration of data and future potential events may help. The *COViage* System analyzes data obtained from the EMR, including age, gender, and vital signs (heart rate, temperature, diastolic and systolic blood pressure, and respiratory rate) to compute patient status indices to predict a patient's potential for hemodynamic instability or respiratory decompensation for use by HCP. The *COViage* System generates these two patient status indices only once during the patient's hospitalization.

All patients who are monitored with this device during the COVID-19 pandemic will receive the Fact Sheet for Patients: Emergency Use of the COViage System During the COVID-19 Pandemic

What do I need to know about COVID-19 treatment?
Current information on COVID-19 infection, including case definitions and information about clinical signs and symptoms and/or epidemiological criteria, is available on the CDC website listed at the end of this fact sheet.
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What is the *COViage* System?
The *COViage* System is a non-interventional software program that uses vital signs and patient demographic data from EMR systems. It uses models derived from machine learning on patient data from EMRs to calculate the likelihood of the occurrence of certain clinically significant events, specifically, hemodynamic instability or respiratory decompensation. It then notifies HCP of patients who, according to the algorithm, are expected to experience either of these events, which often lead to treatment with vasopressors/inotropes or mechanical ventilation, respectively, at any point during the patient's hospitalization. The *COViage* System consists only of software that integrates with a hospital's existing EMR system and medical devices (i.e., the system is installed on user-provided hardware). HCP notifications from the *COViage* System are displayed on a user interface on the user-provided hardware.

The *COViage* System was validated on a dataset of hospitalized, adult patients diagnosed with COVID-19 and 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 age, gender, temperature, heart rate, respiration rate, systolic blood pressure, and diastolic blood pressure data was 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:

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 they were 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.

The following table outlines the performance of the *COViage* System on the validation dataset.

Metric	**Hemodynamic Instability** Mean (Two-sided 95% CI)	**Respiratory Decompensation** Mean (Two-sided 95% CI)
Sensitivity	0.708, 95% CI: (0.5261, 0.8899)	0.720, 95% CI: (0.5440, 0.8960)
Positive Predictive Value (PPV)	0.205, 95% CI: (0.1181, 0.2919)	0.186, 95% CI: (0.1086, 0.2634)

Personnel operating or maintaining the *COViage* System should read the user manual and be thoroughly familiar with all safety requirements and operating procedures before operating the system.

All personnel using the *COViage* System must also be trained in and be familiar with the interpretation of results of the COViage System.

Due to possible variability in *COViage* System results, system outputs should be viewed as just one clinical data point that should be integrated 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.

What are the known and potential benefits and risks of the COViage System?

The known and potential benefits of the *COViage* System include:

- The *COViage* System provides HCP with an early notification that a patient may be at risk for deterioration. Early prediction of deterioration may:
  - help identify patients who would benefit from increased clinical care;
  - assist with the optimal allocation of limited resources for patient monitoring;
  - help providers make proactive treatment decisions, which may allow for earlier intervention, possibly preventing the need for more invasive therapy; and/or
  - allow the providers more time to prepare for escalating care, if necessary**.**

Known and potential risks of the *COViage* System include:

- Failure of the product to perform as indicated (false positive result or false negative result).

- Overreliance on the COViage results and notification, which may lead to a clinical misdiagnosis, or the failure to respond to the notification, which may lead to withholding the appropriate treatment.

- Delayed or incorrect treatment may occur due to an erroneous product output (false positive result) or failure to provide a notification in the event that a COVID-19 patient is actually at risk for hemodynamic instability or respiratory decompensation (false negative result). Both may result from either a software malfunction or software algorithm error.

Because the *COViage* System does not deliver negative alerts, the risk of missing a patient at risk of hemodynamic instability or respiratory deterioration is low. This risk is further mitigated by limitations for use stated in the Instructions for Use (IFU), which include:

- COViage results should not be used as the sole basis to determine risk of hemodynamic instability or respiratory decompensation in a patient.

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

There is no physical risk to the patient for COViage because it is a non-interventional tool. However, to alleviate the risk of overreliance on the algorithm predictions to predict hemodynamic instability or respiratory decompensation, clinicians will receive training that will indicate that the *COViage* System should not be the sole basis for hemodynamic instability or respiratory decompensation prediction for COVID-19 positive patients.

Overall, it is reasonable to conclude that the known and potential benefits of the *COViage* System outweigh the known and potential risks.

What are the Alternatives to the *COViage* System?
There are several other available solutions for helping hospitals manage their workload and/or providing predictions for patient status, such as products that make use of Early Warning Scores (EWS). While these systems assist in identifying patient deterioration, they do not identify specific predicted future clinical events in the hospital setting, namely hemodynamic instability or respiratory decompensation, as the result of COVID-19 complications. This specific supporting functionality may provide benefit when monitoring large numbers of COVID-19 hospitalized patients.

Limitations of the *COViage* System
The *COViage* System is intended to be used as a 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.

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 performance is dependent on the hospital network. If communication between the hospital and system is not provided, then the system will be unable to provide results for the patients. The user is notified of this situation.

The *COViage* System has been authorized only for the measurement of risk of hemodynamic instability or respiratory decompensation using the COViage algorithm.

The *COViage* System has neither been cleared or approved to provide predictive screening information to assist with the early identification of adult COVID-19 patients who are likely to be diagnosed with hemodynamic instability or respiratory decompensation, which are common complications associated with COVID-19.

What is an Emergency Use Authorization (EUA)?
The United States Food and Drug Administration (FDA) has authorized the emergency use of the *COViage* System for use by HCP in the hospital setting for adult patients with confirmed COVID-19 (based on 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 COVID-19 outbreak. The *COViage* System 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.

The authorized use of the *COViage* System under this EUA has not undergone the same type of review as an FDA-approved or cleared device. FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, available alternatives. In addition, the FDA's determination is based on the totality of scientific evidence available showing that it is reasonable to believe that the *COViage* System may be effective for the authorized emergency use.

The EUA for the *COViage* System is in effect for the duration of the COVID-19 declaration justifying

emergency use of medical devices, unless terminated or revoked (after which the product may no longer be used).

How can I learn more?

CDC websites:
General: https://www.cdc.gov/COVID19
Healthcare Professionals:
https://www.cdc.gov/coronavirus/2019-nCoV/guidance-hcp.html

FDA websites:
General: www.fda.gov/novelcoronavirus
EUAs: https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations

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