User Manual for the Etiometry Platform DAV 5.4 and RAE 10.0

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The Etiometry Platform software is a medical device complying with Regulation (EU) 2017/745 (EU MDR) concerning Medical Devices. Any serious incident that occurs in relation to the Etiometry Platform should be reported to Etiometry (the manufacturer) and to the competent authority of the EU Member State in which the user and/or patient is located.

> **CAUTION**: The sale of this device is restricted by or on the order of a physician.

1. Indications for Use

The Etiometry Platform™ features the Data Aggregation & Visualization module version 5.4 and the Risk Analytics Engine module version 10.0.

The application is intended to record and display multiple physiological parameters of adult, pediatric, and neonatal patients from supported bedside devices. The application is not intended for alarm notification nor to control any of the independent bedside devices to which it is connected. The application is intended to be used by healthcare professionals for the following purposes:

- To remotely consult regarding a patient's status and
- To remotely review other standard or critical near real-time patient data to utilize this information to aid in clinical decisions and deliver patient care in a timely manner.

The Data Aggregation & Visualization module can display numeric physiologic data and waveforms captured by other medical devices:

- Airway flow, volume, and pressure
- Arterial blood pressure (invasive and non-invasive, systolic, diastolic, and mean)
- Bispectral index (BIS, signal quality index, suppression ratio)
- Cardiac Index
- Cardiac output

- Central venous pressure
- Cerebral perfusion pressure
- End-tidal CO2
- Heart rate
- Heart rate variability
- Intracranial pressure
- Left atrium pressure
- Oxygen saturation (intravascular, regional, SpO2)
- Premature ventricular counted beats
- Pulmonary artery pressure (systolic, diastolic, and mean)
- Pulse pressure variation
- Pulse Rate
- Respiratory rate
- Right atrium pressure
- Temperature (rectal, esophageal, tympanic, blood, core, nasopharyngeal, skin)
- Umbilical arterial pressure (systolic, diastolic, and mean)
- Electrocardiogram
- Plethysmograph

The Data Aggregation & Visualization module can display laboratory measurements, including arterial and venous blood gases, complete blood count, and lactic acid. It can display information the Risk Analytics Engine module provides.

The Risk Analytics Engine module calculates four indices: the IDO2 Index™ for inadequate delivery of oxygen, the IVCO2 Index™ for inadequate ventilation of carbon dioxide, the ACD Index™ for acidemia, and the HLA Index™ for hyperlactatemia. Mathematical manipulations of the physiologic data and laboratory measurements derive the indices. The indices present partial quantitative information about the patient's cardiovascular or respiratory condition. No therapy or drugs can be administered based solely on the interpretation statements.

The IDO2 Index is indicated for use by health care professionals with patients under intensive care, not on mechanical circulatory support, weighing 2 kg or more, and 0 to 12 or 18 years of age or older. When the IDO2 Index increases, there is an increasing risk of inadequate oxygen delivery, and attention should be given to the patient.

The IVCO2 Index is indicated for use by health care professionals with invasively ventilated patients not on mechanical circulatory support and 0 to 12 or 18 years of age or older. When the IVCO2 Index increases, there is an increasing risk of inadequate carbon dioxide ventilation, and attention should be given to the patient.

The HLA Index is indicated for use by health care professionals with patients under intensive care, not on mechanical circulatory support, weighing 2 kg or more, and 0 to 12 or 18 years of age or older. When the HLA Index increases, there is an increasing risk of hyperlactatemia, and attention should be given to the patient.

The ACD Index is indicated for use by health care professionals with invasively ventilated patients not on mechanical circulatory support, weighing 2 kg or more, and 0 to 12 or 18 years of age or older. When the ACD Index increases, there is an increasing risk of acidemia, and attention should be given to the patient.

WARNINGS:

- Do not use the application as an active patient monitoring system.
- Do not use the application to replace any part of the hospital's device monitoring.
- Do not rely on the application as the sole source of patient status information.
- Do not use any indices as a substitute for taking blood samples.
- Do not use the IDO2 Index for adult patients on Mechanical Circulatory Support.
- The indices present qualitative and potentially imperfect information about the patient's condition; in certain scenarios, the indices may contradict each other.
- The primary data should be reviewed as part of standard patient evaluations, and no decisions should be solely based on the indices.

2. Overview

The Etiometry Platform is an application developed for clinical use with patients being closely monitored. The aims are of the application to:

1. Capture and store continuous physiologic data streams from monitored patients.
2. Provide meaningful visualization of near real-time data to make informed decisions through data integration, analytics, and calculations.
3. Develop algorithms and models from stored and shared data to reduce practice variability and unnecessary resource utilization.

This user manual describes the User Interface (UI) and the fundamental features of the application. The application's features, layout, and appearance may differ in future releases.

3. Introduction

Figure 1: Etiometry Platform Icon

The web-based application is designed to leverage near real-time patient data by presenting complex information in an elegant display to improve clinical decision-making. The application may be accessed online by clicking on the following icon (icon1, p. 6) on a network computer's desktop or by navigating a web browser to the hospital's installed instance of the Etiometry Platform.

4. User Interface (UI)

The following sections describe the User Interface - what each feature is and how the user can interact with the application. These sections are separated by functionality. A key element or concept will appear bold when initially defined. These key elements and concepts can also be found in the glossary.

4.1. Modes of Operation

The application functions in either **Persistent Display mode** or **Individual User mode**.

- The Persistent Display mode displays data about the patient in a particular bed space. It continues to show information on the patient assigned to the location, even as patients are admitted, transferred, and discharged. Having a dedicated Persistent Display monitor for a bed space saves clinicians the time and effort of logging in and navigating to the patient's data.
- The Individual User mode is for people logging in through a web browser for a defined period. This document will first describe the Individual User mode and then discuss the differences introduced by the Persistent Display mode.

4.2. Login Screen

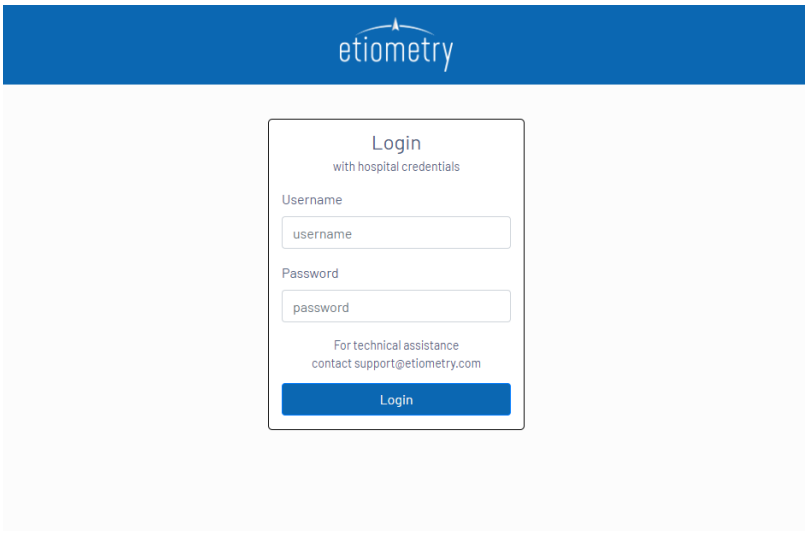

Figure 2: Login Screen

The login screen is the first page accessed when the application initially launches. An error message will be displayed if a login attempt is made with an incorrect username or password.

The application authenticates with a Lightweight Directory Access Protocol (LDAP). Contact your Help Desk if you cannot log in.

4.3. Census Overview

The user will be directed to the **Census Overview screen** after successfully authenticating into the application. This page displays all the current patients for that user's authorized ICUs, along with their bed assignment, name, medical record number (MRN), sex, age, recent activity, i.e., when a patient has entered or left the ICU, and Clinical Pathway activity. The data here originates from information entered into the patient's bedside monitor. If an incorrect name, bed assignment, or MRN is displayed, the user should correct the monitor, and the Census Overview screen will automatically update its content. For example, if the user corrects a patient's medical record number on the monitor, the Census Overview screen will make the corresponding change. Furthermore, if a new patient has just been connected to the monitor, the patient will automatically appear on the census screen. Overall, the Census Overview screen provides a high-level view of all current patients in the ICU.

Patients in the user's authorized units will be shown on the Census Overview screen by default. In the upper right-hand corner of the screen is a Filter drop-down menu, through which users can select a subset of units and beds to view. When set, this preference will carry through to the Patient View dropdown and Surveillance View. This can also be defined in the Surveillance View and carried through to the other two previously mentioned areas. This setting will persist between login sessions. A Clinical Pathway filter can also be defined to help filter patients based on a specific pathway. When applied, this patient list will show any patient that has started, completed or is eligible for the selected pathway. More information on the user preferences can be found below in the Welcome Banner section.

> **Note:** The application also supports an alternative workflow where the hospital provides a data interface from the patient registration system (an Admit, Discharge, Transfer interface, also known as an ADT interface). In this workflow, the interface from the patient monitor contains bed location along with the data values for the patient but no medical record number (MRN) identifying the patient. Instead, the application derives the MRN by matching the bed location sent in the patient monitor interface with the bed location / MRN pairing sent in the ADT interface.

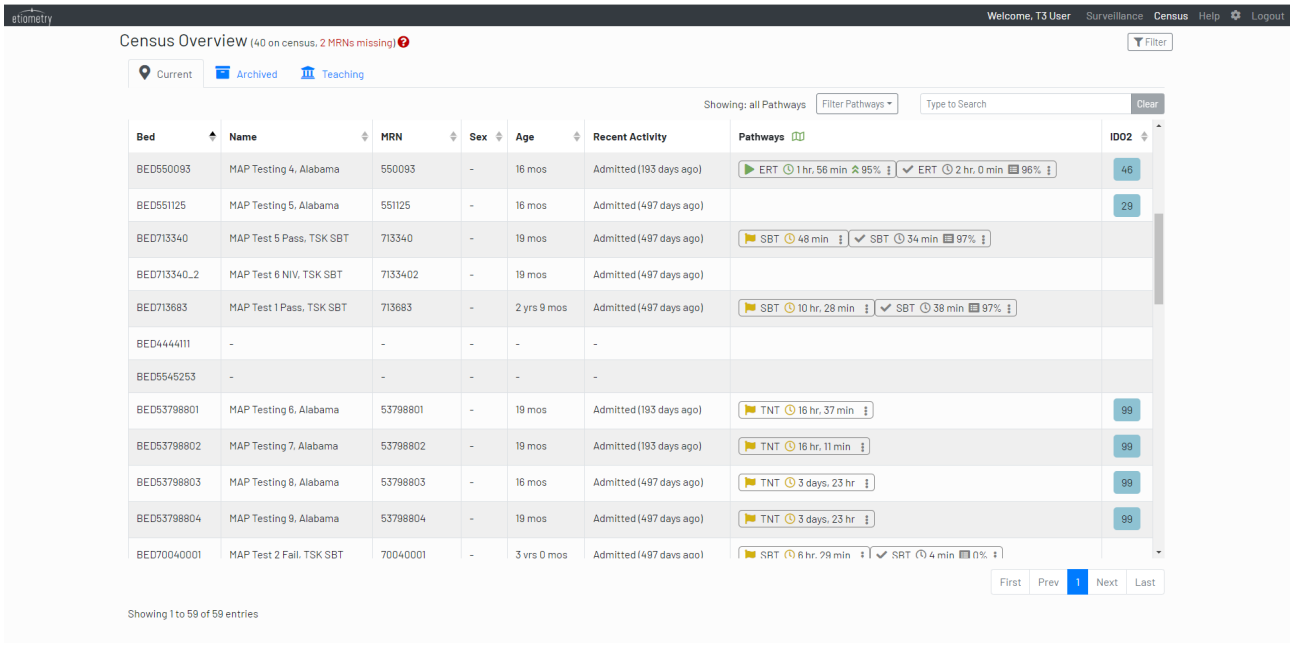

Figure 3: Census View

Census table entries are sorted by bed number by default in the Census View (um_census_view3, p. 9). The user may click on the header of any column (e.g., name or MRN) to sort the entries in ascending or descending order for that column. To navigate to a specific patient for a closer look at physiometric trends, click on that patient's row in the Census Overview.

If a patient's MRN is assigned to a bed, but the application is not receiving data from that bed, its entry will appear grayed out. These rows may still be clicked to access the Patient View.

4.4. Archived Census

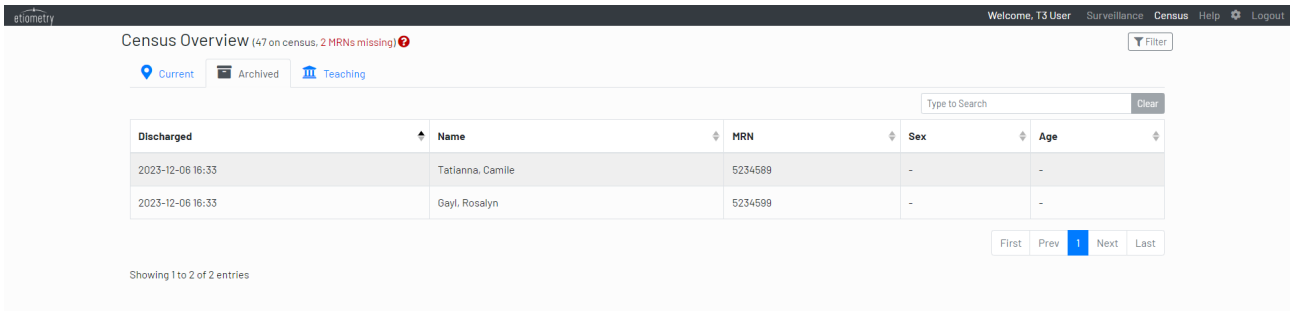

Figure 4: Archived Census

Using the tab atop the Census Overview screen, the user can access the Archived Census (see f_arcCen4,

p. 9). This displays all patients from the application has received data in the past two months. The Archived Census can access patient data for event review and deconstruction.

The Archived Census is sorted by the patient's last observation time by default. The user may click on the header of the other columns to sort the rows by those respective fields. Like the Census Overview screen, click on that patient's row to navigate to a specific patient.

4.5. Welcome Banner

In the Individual User mode, the welcome banner appears at the top of every page in the application. The welcome banner displays the name of the ICU or hospital location the user is logged into, the user's full name (when available; otherwise, the username is displayed), the Census button, the Help button, and the logout button. Clicking on the logout button will end the current user's session, and re-authentication will be necessary to access the application again. Staying idle in the application for fifteen minutes will prompt a warning dialog that alerts the user that they will be automatically logged out in another fifteen minutes with a countdown.

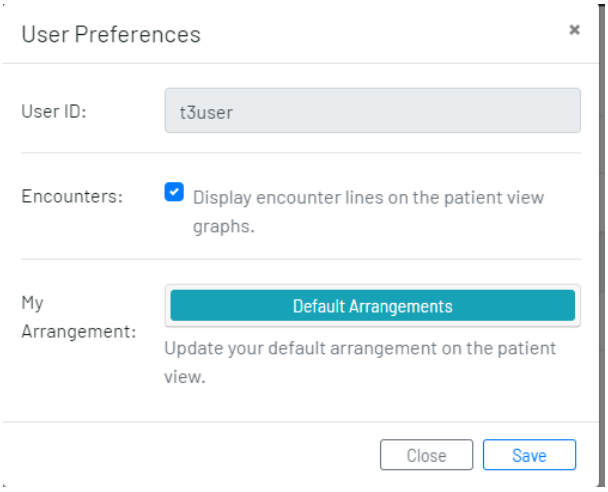

Figure 5: User Preferences

Clicking the gear icon will allow you to access your user preferences, where you can manage your default Patient View arrangement and toggle the Encounter boundaries shown on the graphs (see f_userPer5, p. 10). This menu can revert your default Patient View arrangement to the site default. A default arrangement can be set on any Patient View. More information on Encounters can be found in the *Encounters* section of the user manual.

4.6. Patient View

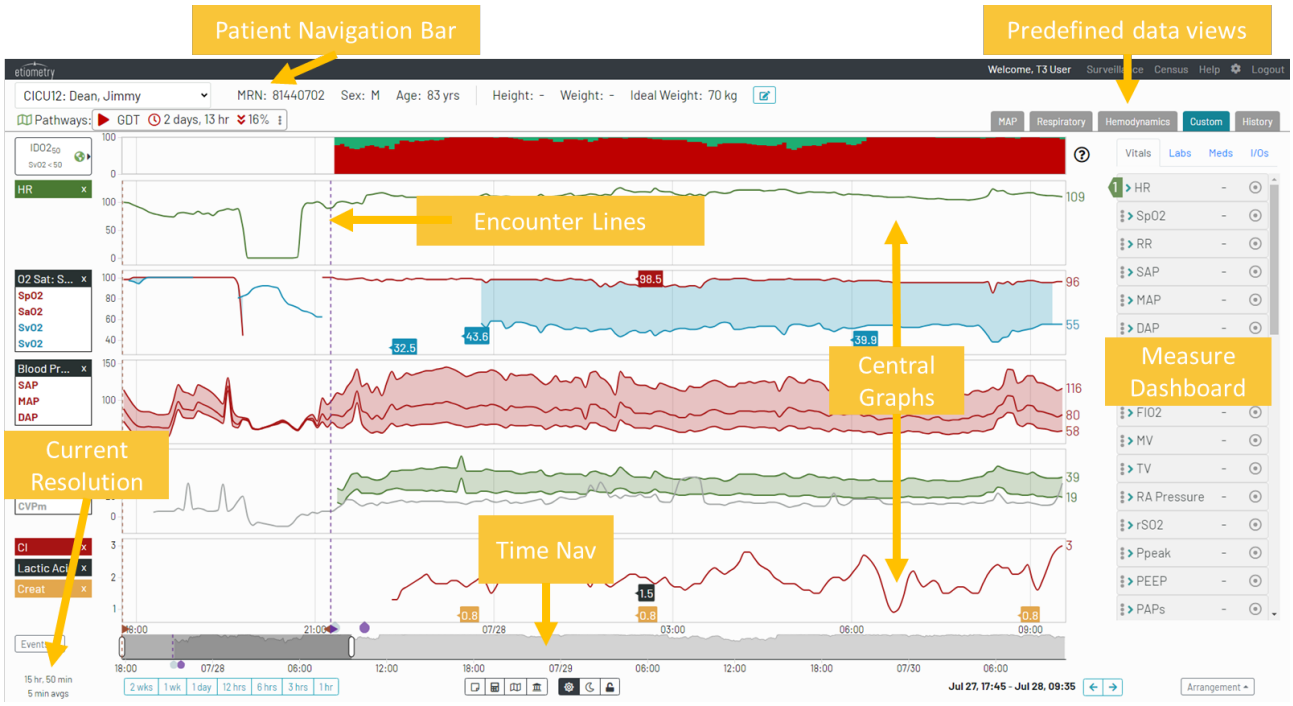

Figure 6: Patient View

When you click on any patient entry, the application displays the Patient View (see f_patientView, p. 11). In this view, the patient's physiometric trends are displayed for the care team's analysis. Features described in the following sections are all accessed through the Patient View and are designed to improve clinical decision-making.

4.7. Patient Navigation Bar

Beneath the welcome banner on the Patient View is the patient navigation bar. It contains a dropdown that shows the name and bed location of the current patient and has a list of all patients in the hospital location. It allows you to navigate to a specific patient easily by clicking on their name or bed location. The patient navigation bar also shows the medical record number (MRN), the patient's sex, age, height, weight, and ideal weight. The default setting will appear blank and allow manual entry of these values. You can determine if this data should be pulled from elsewhere (i.e., monitor, ventilator, etc.) or manually entered by the users. If this data should be pulled in from another source, you must work with the Etiometry support team to set up the configurations. Additionally, the ideal weight will not automatically be calculated but can be if given the desired configuration to be set up.

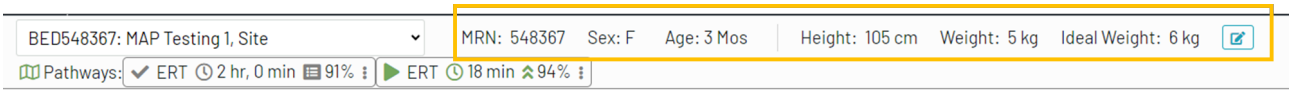

Figure 7: Patient Navigation Bar

A set of tabs for switching among predefined patient data views is on the right side of the navigation bar.

- Respiratory: shows measures and laboratory results related to the body's respiratory system.
- Hemodynamics: shows measures and laboratory results related to the hemodynamic system.
- Custom: shows the patient's measures and laboratory results and lets users create data arrangements.
- History: displays a history of all global actions performed on this patient. See the *Patient History* section of this user manual to learn more.

4.8. Central Graphs Area

The center section of the page is called the Central Graphs Area. This is the main area for patient data investigation and analysis of physiometric trends. There are five graphs in the Central Graphs Area, each capable of simultaneously displaying as many as four individual measures. The user may use the time navigation feature below the graphs to go forward or backward in time and zoom in or out of the data shown in the Central Graphs Area. The Central Graphs Area is very flexible, so the user can drag any measure from graph to graph and overlay them on top of others for visual comparison. If a measure is not displayed in the Central Graphs Area, the user can drag the measure from the Measures Dashboard on the right side of the page to the Central Graphs Area.

Measures may be continuous or intermittent. Intermittent measures such as noninvasive blood pressure (NBP) are shown on the graph as discrete data points, while continuous measures are shown as a line. No measurement data is captured when a patient is disconnected from physiometric devices (for example, while being transferred between bed locations). Later, if they are reconnected to the physiometric devices, the period they were disconnected appears on the graph as a gap. Likewise, during relatively rare periods, while the application is being maintained, patient measure data is not captured, and the period later appears on the graph as a gap.

The application creates **Measure Groups**, collections of measures, and laboratory results that are graphed together as a unit. Additional measures (up to 8 items overall) can be added for any pre-configured groups with four parameters defined. The application can insert shading, vertical lines, and other visual cues to emphasize relationships in the data. Individual parameter target shading does not appear for measures when plotted as part of a measure group.

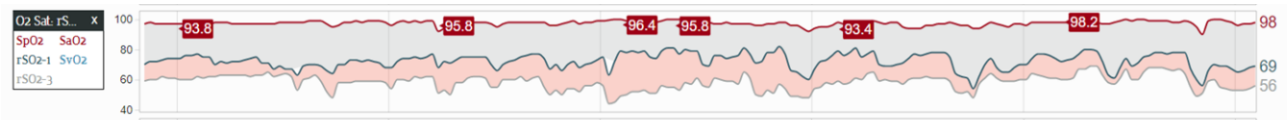

Figure 8: Measure Group

Above the Central Graphs Area, the application may display an aggregate score derived from the patient data. On the Hemodynamic View or the Custom View, this score is the IDO2 Index.

The application may also display dashed lines, which indicate various patient Encounters. More details can be found in the *Encounters* section.

4.9. Advanced indices

As the application continuously collects patient physiologic measures and laboratory test results, the Advanced Indices are computed using Bayes' theorem to interpret the newly acquired data given its previous assessment of the patient's physiologic state. It then uses the interpreted data to update its assessment of the patient's state. The patient's state is represented as a set of patient physiologic variables, each modeled with a probability distribution to account for patient-to-patient variations and measurement uncertainty. Physiologic variables representing the patient's state are also related to one another using established relationships of human physiology. Finally, the physiological variables are related to the physiological measures and laboratory test results collected by the application using models of the measurement collection devices and sensors that account for potential errors in the data. These elements make up the software physiology model. Note that some of the parameters of the physiology model are continuously dependent on the patient's age.

Mixed venous oxygen saturation (SvO2), partial pressure of carbon dioxide (PaCO2), whole blood lactate concentration (LA), and arterial blood pH (pHa) are four of the patient physiologic variables that the algorithm keeps updated, given new data. These four variables are then used to compute four distinct indices in the following way:

- Inadequate delivery of oxygen index (IDO2 Index) by calculating the cumulative probability of the SvO2 probability distribution between 0% and 30%, 0% and 40%, or 0% and 50%, depending on the threshold chosen by the user.
- Inadequate ventilation of carbon dioxide index (IVCO2 Index) by calculating the cumulative probability of the PaCO2 probability distribution above 50 mmHg or 60 mmHg depending on the threshold chosen by the user.
- The Acidemia index (ACD Index) is computed by the probability density estimated of pHa by computing the cumulative probability of pHa being below 7.25.

- The Hyperlactatemia Index (HLA Index) is computed by the probability density estimated of LA by computing the cumulative probability of LA being above 4 mmol/L.

WARNING:

- The IDO2 Index should not be used as a substitute for taking central or mixed venous blood gas samples.
- The IVCO2 Index should not be used as a substitute for taking arterial blood gas samples.
- The ACD Index should not be used as a substitute for taking arterial blood gas samples.
- The HLA Index should not be used as a substitute for taking measurements of the whole blood concentration of lactate.

In certain scenarios, the interrelationships between indices may provide additional information, for example:

- The IDO2 Index and the HLA Index afford comprehensive tracking of adequate oxygen delivery, including the downstream effect of lactate production due to anaerobic metabolism.
- The ACD Index and the IVCO2 Index afford comprehensive tracking of adequate ventilation, including periods when the patient is managed with permissive hypercapnia.

In certain scenarios, discordance may be observed, for example:

- Elevated lactate post-cardiac surgery (**High HLA**) without impaired oxygen delivery (**Low IDO2**)
- Hypercapnia (**High IVCO2**), which is compensated (**Low ACD**)
- Rising lactate detection by a series of lactate measurements (**High HLA**) due to impaired elimination (e.g., liver failure) and normal oxygen delivery (**Low IDO2**)
- Decreasing pH is detected by a series of blood gas measurements (**High ACD**) during normocapnia (**Low IVCO2**) due to metabolic reasons.

As a result of the model-based approach used, the indices exhibit the following properties:

- The indices can continue to be computed based on previously acquired data even when data is missing at particular points in time.
- The algorithm used for the indices computation can incorporate and reconcile multiple measurements of the same physiologic variable (e.g., heart rate can be derived from ECG and the arterial line waveform) because it accounts for the noise and common errors inherent in each possible measurement source.
    - Suppose redundant sources of measurements of the same physiologic variable are available, and one source produces erroneous measurements in general. In that case, the indices will be more accurate than if only the erroneous source were available.
- The algorithm used for the indices computation analyzes the likelihood of particular measurement values given other collected data values and its current patient state assessment. It can reject potential measurement artifacts contradicting the physiology model or the other physiologic measurements.

- If a measurement source produces erroneous measurements, e.g., faulty blood pressure measurements from an arterial line, the algorithm's performance will benefit from the redundant sources and maintain accuracy in most instances.

The model incorporates the following physiological effects:

- Oxygen and Carbon Dioxide gas exchange dynamics circulate in three interconnected compartments: alveolar, arterial, and venous. Ventilation rate, *V*, and cardiac output, *Q*, drive this exchange.
- *V-Q* mismatch using alveolar variables for dead space and pulmonary shunting represents idealized portions of the lung that are ventilated but not perfused and perfused but not ventilated, respectively.
- Mixed venous oxygen saturation depends on oxygen consumption, oxygen delivery (Stroke Volume x Heart Rate x Oxygen Content), and arterial oxygen saturation.
- The model's nominal value of oxygen consumption depends on the current body temperature.
- Heart rate, systemic vascular resistance, and unstressed venous blood volume are affected by autonomic regulation.
- Stroke volume depends on mean arterial pressure, central venous pressure, and ventricular function.
- Pulse pressure depends on stroke volume.
- A dynamic relationship accounts for kidney response to increases in CO2 and decreasing blood pH. The dynamic response model is focused on accounting for HCO3 retention and, as a result, gradual compensation of respiratory failure and respective acidemia.
- A dynamic relationship between computed oxygen delivery and lactic acid production tracks the likelihood of increased whole blood concentration of lactate as a function of changes to the patient's perfusion status.

The model incorporates the following measurement effects:

- Physiologic measurements are modeled as corrupted by the normally distributed noise with a zero mean and a standard deviation specific to the measurement source.
- The model accounts for a potential persistent bias between arterial oxygen saturation derived from arterial blood gas and pulse oximetry.
- The model utilizes regional oxygenation measurements from Near-Infrared Spectroscopy sensors to inform the algorithm's estimate of the patient's current mixed venous oxygen saturation level.
- Error mechanisms in EtCO2 measurements make that measurement source less reliable.

The model utilizes adaptable parameters that adjust to the individual patient to account for the patient-to-patient variability.

The algorithm employed for indices computation classifies venous oxygen saturation measurements as either validated or non-validated and incorporates the measures under different conditions based on that classification. The algorithm will always incorporate validated samples. Non-validated samples will only be incorporated if a central venous, a right atrial, or a pulmonary artery catheter is present when the sample was taken, as determined by pressure measurements from one of these sources. The validation process continually assesses a site's adherence to a protocol of correctly labeling true mixed venous (or central venous) oxygen saturation measurements within their laboratory system.

Note: Inaccurate labeling of venous blood gas samples, e.g., labeling arterial samples as venous samples, will degrade the indices' accuracy and overall performance.

Note: The IVCO2 and ACD indices are only computed if the patient is invasively ventilated at a particular time. The algorithm determines this based on whether or not it has received FiO2, Airway Respiration Rate, and Tidal Volume measurements from the patient in the past 10 minutes.

Note: The application includes an IVCO2 Index indicated for patients with a weight of less than 2kg. However, the IDO2, HLA, and ACD indices are not intended for patients with a weight less than 2 kg, and as such, the IDO2, HLA, and ACD indices are not enabled in neonatal intensive care units. Enabling indices is a configuration completed at the time of installation by Etiometry.

AIM, p. 16 and summarizes the data that can be ingested by the algorithms and the minimum frequency required for the display of each index:

Physiologic variables	Employed measurements	Minimally Required for IDO2 Index (Pediatric)	Minimally Required for IDO2 Index (Adult)	Minimally Required for HLA Index (Pediatric or Adult)	Minimally Required for IVCO2 Index (Pediatric or Adult)	Minimally Required for ACD Index (Pediatric or Adult)
Heart rate	HR (ECG) HR (Pulse)	**Yes, at least every minute**	**Yes, at least every 5 seconds**	**Yes, at least every minute**	**Yes, at least every minute**	**Yes, at least every minute**
Mean blood pressure	(ABPm/ ARTm) Arterial line (NiBPm) Blood pressure cuff	**Yes, at least every 10 minutes**	**Yes, at least every 5 seconds (Invasive Arterial Line Only)**	**Yes, at least every 10 minutes**	No	No

Physiologic variables	Employed measurements	Minimally Required for IDO2 Index (Pediatric)	Minimally Required for IDO2 Index (Adult)	Minimally Required for HLA Index (Pediatric or Adult)	Minimally Required for IVCO2 Index (Pediatric or Adult)	Minimally Required for ACD Index (Pediatric or Adult)
Systolic blood pressure	(ABPs/ ARTs) Arterial line					
	(NiBPs) Blood pressure cuff					
Diastolic blood pressure	(ABPd/ ARTm) Arterial line					
	(NiBPd) Blood pressure cuff					
Filling pressure	RAPm (Right atrium pressure)	No	**Yes, at least every 5 seconds (CVPm Only)**	No	No	No
	CVPm (Central venous pressure)					
Pulmonary Artery Pressure	PAP (Pulmonary Arterial Line)	No	No	No	No	No
SpO2	SpO2	**Yes, at least every 10 minutes**	**Yes, at least every 5 seconds**	**Yes, at least every 10 minutes**	**Yes, at least every 10 minutes**	**Yes, at least every 10 minutes**
	SpO2 (Left)					
	SpO2 (Right)					
	SpO2 (Pre-ductal)					
	SpO2 (Post-ductal)					
Hemoglobin	Laboratory result	No	**Yes, at least every 24 hours**	No	No	No
SvO2	Venous blood gas	No	No	No	No	No

Physiologic variables	Employed measurements	Minimally Required for IDO2 Index (Pediatric)	Minimally Required for IDO2 Index (Adult)	Minimally Required for HLA Index (Pediatric or Adult)	Minimally Required for IVCO2 Index (Pediatric or Adult)	Minimally Required for ACD Index (Pediatric or Adult)
	Pulmonary artery blood gas	No	No	No	No	No
	Continuous from central oximetry catheter	No	No	No	No	No
SaO2	Arterial blood gas	No	No	No	No	No
Temperature	Temp	No	No	No	No	No
	Temp (Skin)					
	Temp (Rectal)					
	Temp (Core)					
	Temp (Oral)					
	Temp (Esophagus)					
	Temp (Blood)					
Respiration rate (Airway)	RR (Airway)	No	No	No	**Yes, at least every minute**	**Yes, at least every minute**
Respiration rate (ECG)	RR (ECG)	No	No	No	No	No
Tidal volume	TV (Expired)	No	No	No	No	No
	TV (Inspired)					
Minute Ventilation	MV (Expired)	No	No	No	**Yes, at least every minute**	**Yes, at least every minute**
	MV (Inspired)					
Fraction of inspired oxygen	FIO2	No	No	No	**Yes, at least every minute**	**Yes, at least every minute**

Physiologic variables	Employed measurements	Minimally Required for IDO2 Index (Pediatric)	Minimally Required for IDO2 Index (Adult)	Minimally Required for HLA Index (Pediatric or Adult)	Minimally Required for IVCO2 Index (Pediatric or Adult)	Minimally Required for ACD Index (Pediatric or Adult)
PaCO2	Arterial blood gas	No	No	No	**Yes, interchangeably with PvCO2, every 12 hours or EtCO2 every minute (or PcapCO2 every 12 hours if the patient is less than 29 days old)**	**Yes, interchangeably with PvCO2, every 12 hours or EtCO2 every minute**
End Tidal CO2	etCO2	No	No	No	**Yes, interchangeably with PvCO2 or PaCO2, every 12 hours (or PcapCO2 every 12 hours if the patient is less than 29 days old)**	**Yes, interchangeably with arterial/ venous pH, every 12 hours**
Arterial pH	Arterial blood gas	No	No	No	No	**Yes, interchangeably with venous pH, every 12 hours**
PvCO2	Venous blood gas	No	No	No	**Yes, interchangeably with PaCO2, every 12 hours or EtCO2 every minute (or PcapCO2 every 12 hours if the patient is less than 29 days old)**	**Yes, interchangeably with PaCO2, every 12 hours or EtCO2 every minute**

Physiologic variables	Employed measurements	Minimally Required for IDO2 Index (Pediatric)	Minimally Required for IDO2 Index (Adult)	Minimally Required for HLA Index (Pediatric or Adult)	Minimally Required for IVCO2 Index (Pediatric or Adult)	Minimally Required for ACD Index (Pediatric or Adult)
Venous pH	Venous blood gas	No	No	No	No	**Yes, interchangeably with arterial pH, every 12 hours**
Whole blood concentration of lactate	Various blood panels	No	No	**Yes, every 24 hours**	No	No
Mean Airway Pressure	Mean Airway Pressure	No	No	No	**Yes, at least every minute**	**Yes, at least every minute**
Regional Oxygenation	NIRS (channel 1)	No	No	No	No	No
	NIRS (channel 2)					
	NIRS (channel 3)					
	NIRS (channel 4)					
Cardiac Index	Continuous cardiac index from pulmonary artery catheter	No	No	No	No	No
	Intermittent cardiac index from pulmonary artery catheter	No	No	No	No	No

Physiologic variables	Employed measurements	Minimally Required for IDO2 Index (Pediatric)	Minimally Required for IDO2 Index (Adult)	Minimally Required for HLA Index (Pediatric or Adult)	Minimally Required for IVCO2 Index (Pediatric or Adult)	Minimally Required for ACD Index (Pediatric or Adult)
PcapCO2	Capillary blood gas	No	No	No	**Yes, interchangably with PaCO2 or PvCO2, every 12 hours or EtCO2 every minute (only if the patient is less than 29 days old)**	No

Table 1: Advanced Indices Measurements

Note: For patients less than 29 days of age, the IVCO2 Index can use capillary PCO2 blood gas measurements in addition to arterial PCO2 or venous PCO2 blood gas measurements to satisfy the required minimum data for computation.

Note: The indices' performance, as assessors of physiologic states implied by their associated biomarkers, improves as more data becomes available (see AIM, p. 16 for all of the data types considered for the indices computation.)

The following sections about each index provide more detailed explanations and performance analysis.

4.9.1. Sensor reading acquisition factors affecting data quality that may impact advanced indices performance

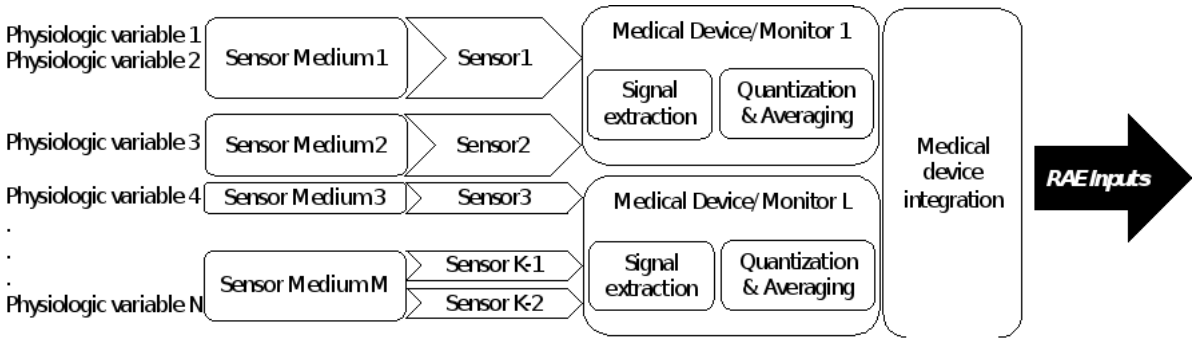

Figure 9: Data Acquisition Environment

RMGFL, p. 22 summarizes the data acquisition pathway that feeds the algorithms that compute the advanced indices. This pathway has several layers, each subject to potential deviations that may affect the indices' performance:

1. In the first layer, the physiologic variables correspond to vital signs, biomarkers, and device support settings captured by the system.
2. Sensors capture physiologic variables through multiple media. One medium and a single sensor operating in it can be used to capture multiple physiologic signs, e.g., using the chest as a medium, ECG leads can capture both heart and respiratory rates. Similarly, multiple media and multiple sensors can be used to capture a single physiologic variable, e.g., a mainstream capnography sensor measures EtCO2 directly in the medium of the endotracheal tube. In contrast, side-stream capnography measures this variable outside of the endotracheal tube.
3. Sensor data is processed by medical devices/monitors through a two-step process: a signal extraction; examples include R-R detection for HR extraction, plethysmography analysis for SpO2 extraction, etc., and signal averaging, which applies a quantization and moving average algorithm to generate a stream of this data with particular resolution and frequency. Some multiple monitors/ devices may be processing data from the patient, e.g., a bedside monitor which can process data such as heart rate, blood pressure (both invasive and non-invasive), pulse-oximetry, etc., a regional oximetry monitor, which can process data from multiple anatomic locations of the body, or a mechanical ventilator, which can provide data on respiratory rate, EtCO2, tidal volume, minute ventilation, etc.
4. The multiple monitoring data sources are then connected to a Medical Device Integrator (MDI), which further conditions the data by downsampling. Up to the output of the MDI, data acquisition and processing rely on commercially available, compatible third-party devices.

To assure appropriate performance, the data acquisition should be configured to achieve the following:

- Minimum frequency of continuous data acquisition of one point every minute
- Minimum specific resolution for each acquired physiologic variable as stated in meas_resolutions, p. 23
- Appropriate tagging of the sampling medium of different blood gases (e.g., appropriate identification of venous versus arterial, central venous vs peripheral venous)

Physiologic variables	Employed measurements	Minimum Required Resolution
Heart rate	HR (ECG)	1 BPM
	HR (Pulse)	
Mean blood pressure	(ABPm/ARTm) Arterial line	1 mmHg
	(NiBPm) Blood pressure cuff	
Systolic blood pressure	(ABPs/ARTs) Arterial line	
	(NiBPs) Blood pressure cuff	
Diastolic blood pressure	(ABPd/ARTm) Arterial line	
	(NiBPd) Blood pressure cuff	
Filling pressure	RAPm (Right atrium pressure)	1 mmHg
	CVPm (Central venous pressure)	
SpO2	SpO2	1 %
	SpO2 (Left)	
	SpO2 (Right)	
	SpO2 (Pre-ductal)	
	SpO2 (Post-ductal)	
Hemoglobin	Laboratory result	0.1 g/DL
SvO2	Venous blood gas	1 %
SaO2	Arterial blood gas	1 %
Temperature	Temp	0.1 degrees C
	Temp (Skin)	
	Temp (Rectal)	
	Temp (Core)	
	Temp (Oral)	
	Temp (Esophagus)	
	Temp (Blood)	
Respiration rate (Airway)	RR (Airway)	1 BPM
Respiration rate (ECG)	RR (ECG)	1 BPM
Minute Ventilation	MV (Expired)	100 mL/min

Physiologic variables	Employed measurements	Minimum Required Resolution
	MV (Inspired)	
Fraction of inspired oxygen	FIO2	1 %
PaCO2	Arterial blood gas	1 mmHg
End Tidal CO2	etCO2	1 mmHg
Arterial pH	Arterial blood gas	0.01
PvCO2	Venous blood gas	1 mmHg
Venous pH	Venous blood gas	0.01
Whole blood concentration of lactate	Various blood panels	0.1 mmol/L
Mean Airway Pressure	Mean Airway Pressure	1 cmH20
Regional Oxygenation	NIRS (channel 1)	1 %
	NIRS (channel 2)	
	NIRS (channel 3)	
	NIRS (channel 4)	
PcapCO2	Capillary blood gas	1 mmHg
Cardiac index	Continuous Cardiac Index	0.1 L/min/m^2
	Aperiodic Cardiac Index	

Table 2: Required Measurement Minimum Resolutions

The advanced indices algorithms have build-in functionality to automatically handle certain deviations in the data acquisition continuum that may affect index performance:

- No index is displayed if data are not acquired within the required minimum frequency
- The algorithm employed for indices computation classifies venous oxygen saturation measurements as either validated or non-validated based on hospital practices of distinguishing between central/ mixed and peripheral venous blood gases. Non-validated samples will only be incorporated if a central venous, a right atrial, or a pulmonary artery catheter is present when the sample was taken, as determined by pressure measurements from one of these sources.

In addition, the indices have been tested against various factors that may not be controllable in the specific operational environment. These factors include the following:

- The indices have been validated to exhibit robust performance against possible deviations of signal extraction technique and against variation in the time-based averaging methodology by artificially adding white noise into the continuously ingested sensor inputs.

- The indices performance has been validated against specific variations in physiologic variables medium acquisition:
  - Variations in the availability of mainstream or sidestream capnography when such sensor data is available
  - Variations in possible anatomic location placement of tissue oximetry when such sensor data is available
- The indices performance has been evaluated when point-of-care (PoC) blood gas diagnostic is used either instead of or as a complete substitute for laboratory testing since PoC may be subject to more frequent mistagging.

The results reported in the performance analysis below include confidence intervals and ranges that are inclusive of the effects on the performance of these factors.

WARNING: To minimize degraded algorithm performance, the data collection system should be configured such that:

- data sources meet the required minimum frequencies (see AIM, p. 16)
- data sources meet the required minimum resolutions (see meas_resolutions, p. 23)

WARNING: Incorrect tagging of the source of blood gases, arterial, peripheral venous, or central venous, may significantly degrade the indices' performance

4.10. IDO2 Index

The Etiometry Platform continuously computes and displays the IDO2 Index, reflecting the likelihood of the patient experiencing inadequate oxygen delivery. Assuring adequate tissue oxygen delivery is the central tenant of critical care (Checchia et al. 2011). Mixed venous oxygen saturation is considered a gold standard in detecting a mismatch between oxygen delivery and demand and, therefore, is an important biomarker for assessing the potential presence of inadequate oxygen delivery (Gutierrez et al. 2012; Martin et al. 2009). The IDO2 index reflects the likelihood of mixed venous oxygen saturation (SvO2) below a particular threshold. For adults, the IDO2 Index is the cumulative probability of the SvO2 probability distribution between 0% and 50%. For neonates, infants, and children, the threshold is either 30%, 40%, or 50% and can be selected by the user based on clinical preference. For neonates, infants, and children, the default threshold for the IDO2 Index is SvO2 below 40% because mixed venous oxygen saturation levels below this have been documented to correspond with inadequate oxygen delivery levels (Walley 2011, Martin et al. 2009; Hoffman et al. 2000, and Hoffman et al. 2005). However, the user may select the other thresholds based on individual provider preferences, clinical judgment, or patient needs. As referenced (Walley 2011), Walley states, "SvO2 less than 50% is low and, depending on tissue oxygen extraction capabilities, could be approaching values associated with [critical oxygen extraction]". Meanwhile, SvO2 less than 30% is specifically associated with the onset of anaerobic metabolism (Martin et al. 2009, Hoffman et al. 2000).

The IDO2 Index varies between 0 and 100 and is displayed on the Patient View screen. When the IDO2 Index increases, there is an increasing risk of inadequate oxygen delivery, and attention should be given to the patient.

The IDO2 Index is computed based on multiple physiologic measures and laboratory test results collected by the Etiometry Platform. The algorithm that computes the IDO2 Index uses a software model of human physiology. The IDO2 Index is solely indicated for post-surgical patients 0 to 12 years of age and weighing 2 kg or more under intensive care and patients 18 years or older under intensive care and not on Mechanical Circulatory Support.

To compute reliable results, the algorithm requires physiologic variables as minimum input requirements (see AIM, p. 16). If data are received with a lower frequency, or if these data types are unavailable, the IDO2 Index is not computed, and the user is informed that no computation is available.

References

1. P. Checchia and P. Laussen, “The cardiac intensive unit perspective on hemodynamic monitoring of oxygen transport balance,” *Pediatr. Crit. Med.*, vol. 12, no. 4, pp. S69–S71, 2011.
2. J. A. Gutierrez and A. A. Theodorou, “Oxygen Delivery and Oxygen Consumption in Pediatric Critical Care,” in *Pediatric Critical Care Study Guide*, Springer, 2012, pp. 19–39.
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4.10.1. The IDO2 User Interface

Figure 10: Patient view enables easy analysis of patient physiometric data.

The IDO2 Index is displayed on the Patient View in a dedicated graph above the Central Graphs Area (see f_patViewIDO2, p. 27). The IDO2 Index cannot be removed from its graph, and the application does not allow other measures to be overlaid on top of it. The Y-Axis for this canvas extends from zero to one hundred, and the IDO2 Index is graphed in red against a green background.

Suppose needed clinical data is missing or the application determines that an Index calculation does not apply to the patient because of their age or other characteristics. In that case, it will not show an Index; the relevant section of the Index graph will be blank. Suppose the Index is not currently being calculated. In that case, the application will display a tooltip that states the Index is not being calculated for this patient either because it doesn't apply to them or because the required data are missing.

Users can select which threshold for the IDO2 Index to display via the threshold selector. The index with the selected threshold will then populate the graph above the Central Graphs Area, and the index will be overlaid in the time navigation below the Central Graphs Area.

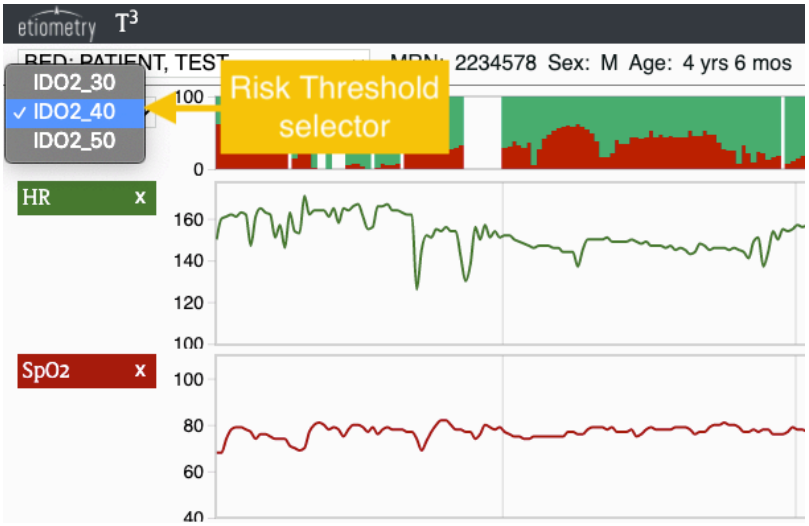

Figure 11: Configurable IDO2 Threshold Selector

This selection will become saved as part of the user's arrangement. Specifically, thresholds for the IDO2 Index and their associated notations are described as follows:

Risk	Threshold	Description
IDO2	IDO2_30	Likelihood that SvO2 < 30%
	IDO2_40 *	**Likelihood that SvO2 < 40% ***
	IDO2_50	Likelihood that SvO2 < 50%
	• Default threshold	

Table 3: Various risk thresholds

Note: The IDO2_30 Index threshold is not available or validated for patients above two years of age.

4.10.2. The IDO2 Index Performance (Neonates, Infants, and Children)

The association of the IDO2 Index with inadequate oxygen delivery was established through a retrospective study of a patient population that included neonates (0-28 days of age), infants (29 days to 2 years of age), and children (2-12 years of age) from multiple institutions and intensive care units. This validation patient population group included 3,017 patients.

The study used periodic measurements of proxies of mixed venous oxygen saturation (SvO2proxy) measurements sampled from various access points, e.g., superior vena cava catheters or right atrium catheters. A total of 19,448 measurements were included in the reported performance assessment.

For each SvO2proxy measurement in the first ten postoperative days, the average IDO2 Index was computed in the 30 minutes immediately before the measurement and used as a predictor score for the different selectable thresholds of the index, i.e., SvO2proxy < 30%, SvO2proxy < 40%, or SvO2proxy < 50%. The resulting Receiver Operating Characteristic (ROC) curve was generated, and the Area Under the Curve (AUC) was computed. The specification for the AUC performance is that the 95% confidence interval must be above 0.7.

4.10.3. Default IDO2 Index configuration (IDO2_40)

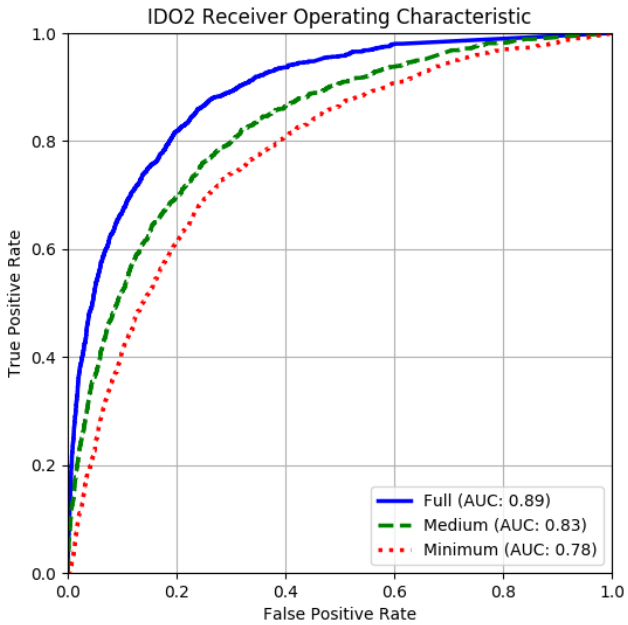

Figure 12: ROC curves for Minimum, Medium and Full Data sets for the IDO2 Index

f_ROC_min_med_full_30, p. 29 shows the receiver operating characteristic with SvO2proxy < 40% by using the IDO2 Index computed by the model-based IDO2 algorithm. There were three datasets examined. In the first dataset, full measurement data composed of all possible measures listed above were used by the algorithm for the IDO2 computation, which included past mixed venous oxygen saturation measurements. A “medium” dataset was curated in the second dataset by removing all SvO2 lab measurements. In the third dataset, the algorithm used only the minimum measurement data for the computation, i.e., heart rate every 60 seconds, SpO2 every 10 minutes, and blood pressure every 10 minutes. Note these datasets are defined in t_ido2_datasets, p. 30. The area under the curve (AUC) for the prediction with the full data set is AUC = 0.89, with a 95% confidence interval of 0.88-0.90. The AUC for using the medium data set is AUC = 0.83, with a

95% confidence interval of 0.81-0.84. The AUC for the minimum data set is AUC = 0.78, with a 95% confidence interval of 0.77- 0.80. This is shown in the figure.

Data set	Downsampling
Full	No downsampling - all data sources are fully available; see AIM, p. 16
Medium	No downsampling - all data sources are fully available, with the removal of all SvO2 lab measurements
Minimum	Reduced data rates for the minimal set (eleven measurements): • The following measures downsampled to 1 data point every 10 minutes - SpO2 and Arterial Blood Pressure • The following measures downsampled to 1 data point every 60 seconds - Heart rate No other measurements above the minimal measurements are processed through the algorithm (i.e., excluding central venous pressure, Hemoglobin, SvO2, and temperature)

Table 4: The data sets employed in the analysis

The significance of different values of the IDO2 Index is illustrated (see f_ab_risk, p. 30), by calculating the risk for SvO2 < 40% in various index bins. The figure shows a consistent increase in the risk in bins with higher values.

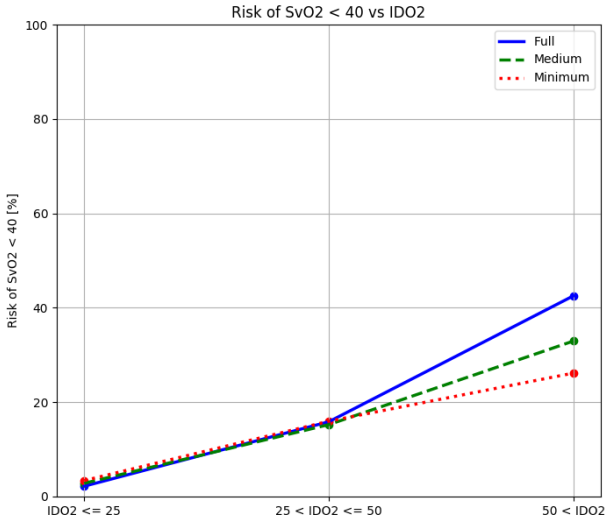

Figure 13: The risk of SvO2 < 40% for different bins of the IDO2 Index

Data Set	IDO2 ≤ 25	p-value	25 < IDO2 ≤ 50	p-value	50 < IDO2
Full	2.16	<0.0001	16.09	<0.0001	42.42
Medium	2.56	<0.0001	12.97	<0.0001	28.34
Minimum	3.28	<0.0001	16.47	<0.0001	26.06

Table 5: Statistics of the increase of risk of SvO2 < 40% between different bins of the IDO2 Index

The risk of SvO2 < 40% for different IDO2 bins is summarized in the table above for all three datasets (see table_of_risks, p. 31). The dataset is shown in the left-hand column, and each bin's risk is under the corresponding bin label. The p-values listed specify whether the increases in risk between two adjacent bins are statistically significant.

4.10.4. Additional IDO2 index thresholds (IDO2_30 and IDO2_50)

IDO2_30IDO2_50AUCsummary, p. 31 includes the AUC performance of the additional thresholds selectable for the index denoted as IDO2_30 for SvO2 < 30% and IDO2_50 for SvO2 < 50%.

Threshold	Data set	AUC	95% Confidence Interval
IDO2_30	Full	0.9077	[0.8883 - 0.925]
	Medium	0.8422	[0.8173 - 0.8675]
	Minimum	0.7957	[0.7664 - 0.8238]
IDO2_50	Full	0.8535	[0.8473 - 0.8601]
	Medium	0.7758	[0.7673 - 0.785]
	Minimum	0.7451	[0.7367 - 0.7552]

Table 6: AUCs for each data set type given with 95% confidence bounds - IDO2_30 and IDO2_50

IDO2_30and50_risk_summary, p. 31 shows how the risk of SvO2 < 30% and SvO2 < 50% change for different ranges of the index thresholds. Note that the p-values demonstrate the risk increase is significant between the different ranges, the only notable exception being the increase of the IDO2 Index between the 25-50 and 50-100 ranges in the minimum data set.

Threshold	Data Set	IDO2 ≤ 25	p-value	25 < IDO2 ≤ 50	p-value	50 < IDO2 ≤ 100
IDO2_30	Full	0.75	<0.0001	12.93	<0.0001	30.64
	Medium	0.92	<0.0001	7.61	<0.0001	15.94

Threshold	Data Set	IDO2 ≤ 25	p-value	25 < IDO2 ≤ 50	p-value	50 < IDO2 ≤ 100
	Minimum	1.29	<0.0001	8.82	=0.5289	11.20
IDO2_50	Full	6.21	<0.0001	23.43	<0.0001	53.55
	Medium	8.16	<0.0001	19.03	<0.0001	43.75
	Minimum	9.28	<0.0001	22.69	<0.0001	42.65

Table 7: AUCs for each data set type given with 95% confidence bounds - IDO2_30 and IDO2_50

4.10.5. The IDO2 Index Performance (Adults)

The association of the IDO2 Index for adults with inadequate oxygen delivery was established through a retrospective study of patients admitted to an adult ICU from a single institution. The performance disclosed in this labeling was evaluated on an independent data set not utilized for any development or calibration of the algorithm consisting of 783 adult patients.

The study used periodic measurements of mixed venous oxygen saturation (SvO2) sampled from pulmonary artery catheters, with 4,667 measurements included in the reported performance assessment.

For each SvO2 measurement, the average IDO2 Index was computed in the 30 minutes immediately before the measurement and used as a predictor score for SvO2 < 50%. The resulting Receiver Operating Characteristic (ROC) curve was generated, and the Area Under the Curve (AUC) was computed.

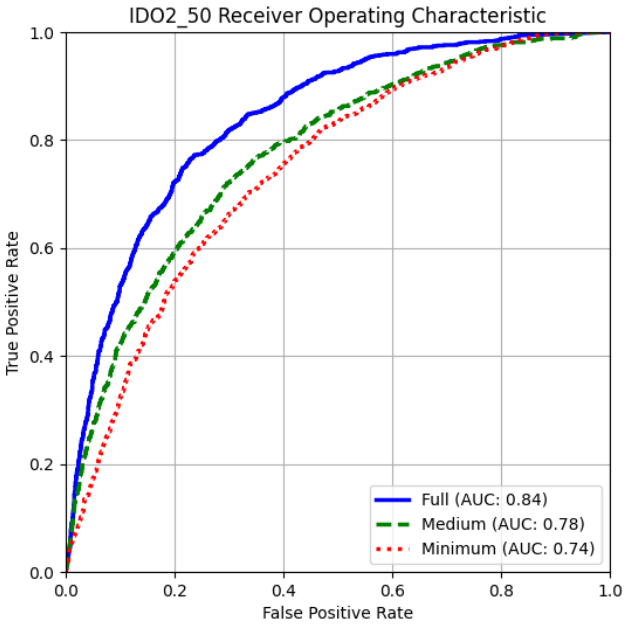

Figure 14: ROC curves for Minimum, Medium and Full Data sets for the IDO2 Index (adults)

D9FX8, p. 33 shows the receiver operating characteristic with SvO2 < 50% by using the IDO2 Index. There were three datasets examined. In the first dataset, full measurement data composed of all possible measures listed above were used by the algorithm for the IDO2 computation, which included, when available, past mixed venous oxygen saturation measurements and continuous venous saturation evaluated through an infrared catheter. In the second dataset, a “medium” dataset was curated by removing all SvO2 measurements, both continuous and labs. In the third dataset, only the minimum measurement data was used by the algorithm for the computation (see AIM, p. 16).

The following table summarizes the results for each group:

Data set	AUC	95% Confidence Interval
Full	0.8375	[0.8238 - 0.8513]
Medium	0.7751	[0.7582 - 0.7898]
Minimum	0.744	[0.7278 - 0.7608]

Table 8: AUC and 95% confidence intervals for each measurement configuration

The significance of different values of the IDO2 Index is illustrated (see YG4O1, p. 34), by calculating the risk for SvO2 < 50% in various index bins. The figure shows a consistent increase in the risk in bins with higher values.

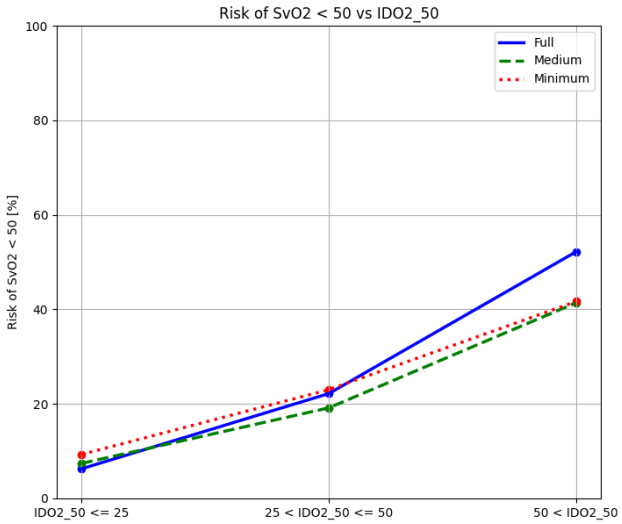

Figure 15: The risk of SvO2 < 50% for different bins of the IDO2 Index (adults)

Data Set	IDO2 ≤ 25	p-value	25 < IDO2 ≤ 50	p-value	50 < IDO2
Full	6.27	<0.0001	22.18	<0.0001	52.18
Medium	7.41	<0.0001	19.16	<0.0001	41.39
Minimum	9.31	<0.0001	23.01	<0.0001	41.66

Table 9: Statistics of the increase of risk of SvO2 < 50% between different bins of the Adult IDO2 Index

The risk of SvO2 < 50% for different Adult IDO2 bins is summarized in the table above for all three datasets (see Z60X1, p. 34). The dataset is shown in the left-hand column, and each bin's risk is under the corresponding bin label. The p-values listed specify whether the increases in risk between two adjacent bins are statistically significant.

4.10.6. The IDO2 Index Limitations

Healthcare professionals should consider the following limitations when employing the IDO2 Index for the evaluation of indicated patients:

- The IDO2 Index cannot be used to diagnose or treat a disease or condition.
- The IDO2 Index is not validated and should not be used for patients on Mechanical Circulatory Support.
- The IDO2 Index is a trend monitor and, as such, has been validated and intended to be interpreted in the context of its entire range, not versus a specific threshold.

- The IDO2 Index accuracy depends on the intensity of patient monitoring. The more measurements collected as inputs, the more accurate the IDO2 Index will be. See the table in the Measurements section for all the data types the algorithm considers.
- The IDO2 Index will not be displayed if the following minimum measurements are not available:
  - Heart rate from ECG or pulse at least once every 60 seconds.
  - SpO2 from pulse oximetry at a minimum of once every 10 minutes.
  - Blood Pressure (mean/diastolic/systolic) at least once every 10 minutes.
- The IDO2 Index has not been validated for patients weighing less than two kilograms.
- When the IDO2 Index is at its minimum value and not trending, there is still a residual risk for inadequate oxygen delivery.
- When the IDO2 Index is at its maximum value and not trending, there is still a residual risk for adequate oxygen delivery.
- The IDO2 Index uses the patient's date of birth to compute the patient's age and continuously updates certain parameters of the physiology model.
- The IDO2 Index requires initialization time to calibrate to a particular patient once data starts streaming. The IDO2 Index will not be displayed during the initial calibration period of five minutes. If the patient's heart rate is subsequently lost for one hour, the algorithm will wait for the minimum measurements to be restored. It will re-enter a calibration period before reporting a new value. If the algorithm re-initializes at any time, it will also re-enter a calibration period. No IDO2 Index will be displayed while the index is calibrating.
- The IDO2_30 is unavailable or validated for patients above two years of age.
- At extreme data sparsities (minimally available data sets), the IDO2_30 may not increase throughout its range.

Note: The scale for the IDO2 Index is the opposite of the saturation scale for oxygen saturation measurements such as those provided by pulse oximetry. When the index increases, there is an increasing risk of inadequate oxygen delivery, and attention should be given to the patient.

4.11. IVCO2 Index

The application continuously computes and displays the IVCO2 Index, which reflects the likelihood that a patient is experiencing inadequate carbon dioxide ventilation, defined as the arterial partial pressure of carbon dioxide (PaCO2) greater than a specific threshold. The threshold is selectable by the user based on clinical judgment. One of these thresholds is a PaCO2 value greater than 50 mmHg, which is an established sign of ventilation failure, i.e., failure of CO2 removal (Sue & Lewis 2008). Another is PaCO2 of 60 mmHg, which can be used for patients whose nominal PaCO2 is above 50 mmHg, such as patients with permissive hypercapnia (Miller & Carlo 2007 and Thome & Carlo 2012).

The IVCO2 Index varies between 0 and 100 and is displayed on the Patient View screen. When the IVCO2 Index increases, there is an increasing risk of inadequate carbon dioxide ventilation, and attention should be given to the patient.

The IVCO2 Index is computed based on multiple physiologic measures and laboratory test results collected by the application. The algorithm that computes the IVCO2 Index uses a software model of human physiology. The IVCO2 Index is solely indicated for use for invasively ventilated patients 0 to 12 years of age or 18 years of age under intensive care and not on Mechanical Circulatory Support.

To compute reliable results, the algorithm requires the following physiologic variables as minimum input requirements: heart rate, pulse oximetry, respiration rate, minute ventilation, a fraction of inspired oxygen, end-tidal carbon dioxide, and mean airway pressure. The heart rate, airway respiration rate, minute ventilation, the fraction of inspired oxygen, end-tidal carbon dioxide, and mean airway pressure must be acquired at least every 60 seconds, while pulse oximetry must be acquired at least every 10 minutes. The end-tidal carbon dioxide can be substituted with an arterial or venous PCO2 measurement (or capillary PCO2 measurement if the patient is less than 29 days old), acquired at least every 12 hours (see AIM, p. 16).

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4.11.1. The IVCO2 Index User Interface

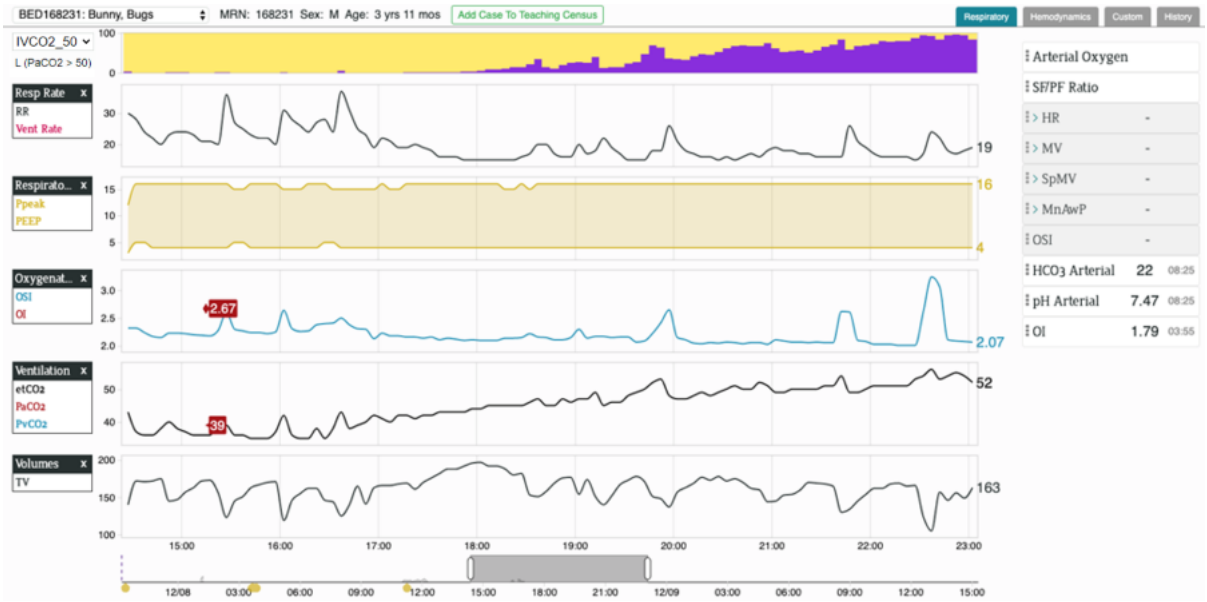

Figure 16: IVCO2 is displayed on the respiratory tab - patient view screen

The IVCO2 Index is displayed on the Patient View screen in a dedicated canvas above the five Central Graphs Area (see user_IVCO2, p. 37). The IVCO2 Index cannot be deleted from its graph canvas, and the application does not allow other measures to be overlaid on top of it. The Y-Axis for this canvas extends from zero to one hundred, and the IVCO2 Index is graphed in purple against a yellow background.

If needed clinical data is missing, or if the application determines that the index calculation does not apply to the patient because of the patient's age or other characteristics, it will not show an index: the relevant section of the IVCO2 Index graph canvas will be blank. Suppose the IVCO2 Index is not currently being calculated. In that case, the application will display an icon beside the canvas with a tooltip that says, "IVCO2 Index is not being calculated for this patient either because it doesn't apply to them or because required data is missing."

Users can select which threshold for the IVCO2 Index to display via the threshold selector. The index with the selected threshold will then populate the graph above the Central Graphs Area, and the index will be overlaid in the time navigation below the Central Graphs Area.

Figure 17: Configurable IVCO2 Threshold Selector

This selection will become saved as part of the user's arrangement. The following table summarizes the available thresholds respected notation for the IVCO2 Index:

Risk	Threshold	Description
IVCO2	IVCO2_50 (default threshold)	Likelihood that PaCO2 > 50 mmHg
	IVCO2_60	Likelihood that PaCO2 > 60 mmHg

Table 10: Various risk thresholds

4.11.2. The IVCO2 Index Performance

The association of the IVCO2 Index with hypercapnia was established through a retrospective study of a pediatric patient population that included neonates (0-28 days of age), infants (29 days to 2 years of age), and children (2-12 years of age), and an adult patient population including patients 18 years and older. Data were gathered from multiple institutions and intensive care units in both patient groups. The pediatric validation patient population group included 2,270 patients, and the adult validation patient population included 862 patients.

The study used periodic measurements of PaCO2 sampled from arterial blood gas. In the pediatric performance assessment, 30,870 measurements were included in the analysis. In the adult performance assessment, 6859 measurements were included in the analysis.

For each PaCO2 measurement in the first ten postoperative days, the average IVCO2 index was computed in the 30 minutes immediately before the measurement and used as a predictor score for PaCO2 > 50 mmHg (or PaCO2 > 60 mmHG for IVCO2_60 mmol). The resulting Receiver Operating Characteristic (ROC) curve was generated, and the Area Under the Curve (AUC) was computed. The specification for the AUC performance is that the 95% confidence interval must be above 0.7

4.11.3. Pediatric IVCO2 Performance

IVCO2_50 (Default IVCO2 Index configuration)

AUCFigure, p. 39 illustrates the ROC curves and respective AUC values for detecting points positive for inadequate ventilation of carbon dioxide (PaCO2 > 50 mmHg) evaluated under the three different datasets.

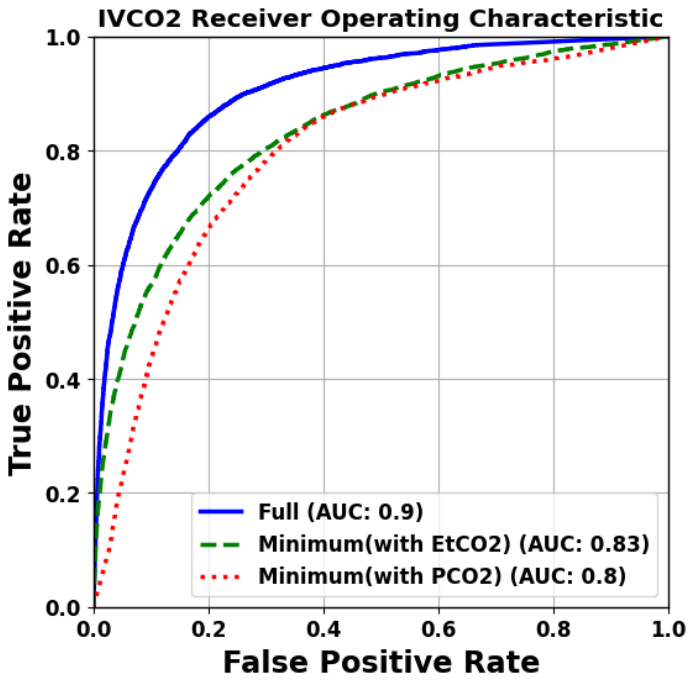

Figure 18: The ROC for detecting points positive for inadequate ventilation of carbon dioxide for full and minimum datasets

In the first dataset, the algorithm used full measurement data composed of all possible measures listed above for the IVCO2 computation. In the second and third datasets, the minimum data was derived by down-sampling the full dataset to include only the minimum data required to compute the IVCO2 Index. The minimum data either included only EtCO2 measurements or PCO2 measurements. This was used to evaluate the robustness of the performance of the IVCO2 Index under limited monitoring levels. Note that these datasets are defined below in t_DataSets, p. 39.

Data set	Downsampling
Full	No downsampling - all data sources are fully available; see AIM, p. 16

Data set	Downsampling
Minimum (with EtCO2)	Reduced data rates for the minimal set: • The following measures downsampled to 1 data point every 10 minutes - SpO2 • The following measures downsampled to 1 data point every 60 seconds - FiO2, Heart rate, Respiratory rate, Tidal Volume, and Mean Airway Pressure • The following measures downsampled to 1 data point every 60 seconds - EtCO2 No other measurements above the minimal set are processed through the algorithm (i.e., central venous pressure, Hemoglobin, SvO2, and temperature)
Minimum (with PCO2)	Reduced data rates for the minimal set: • The following measures downsampled to 1 data point every 10 minutes - SpO2 • The following measures downsampled to 1 data point every 60 seconds - FiO2, Heart rate, Respiratory rate, Tidal Volume, and Mean Airway Pressure • The following measurements were downsampled to one every 12 hours - arterial or venous PCO2 (or, if the patient was less than 29 days old, capillary PCO2) No other measurements above the minimal set are processed through the algorithm (i.e., central venous pressure, Hemoglobin, SvO2, and temperature)

Table 11: The data sets employed in the analysis

These results are also summarized in AUCValidationSummary, p. 40, which includes the error around the means of the reported AUCs.

Data set	AUC	95% Confidence Interval
Minimum (with EtCO2)	0.8248	[0.819 - 0.8305]
Minimum (with PCO2)	0.7852	[0.7777 - 0.7925]
Full	0.8881	[0.8842 - 0.8922]

Table 12: AUCs for each data set type, given with confidence bounds

The risk for PaCO2>50mmHg (the fraction of positive points) in different bins of the index is summarized in ValidationRisk, p. 41, which shows a monotonically increasing risk between bins in all three datasets, as summarized in ValidationRiskSummary, p. 41, is statistically significant.

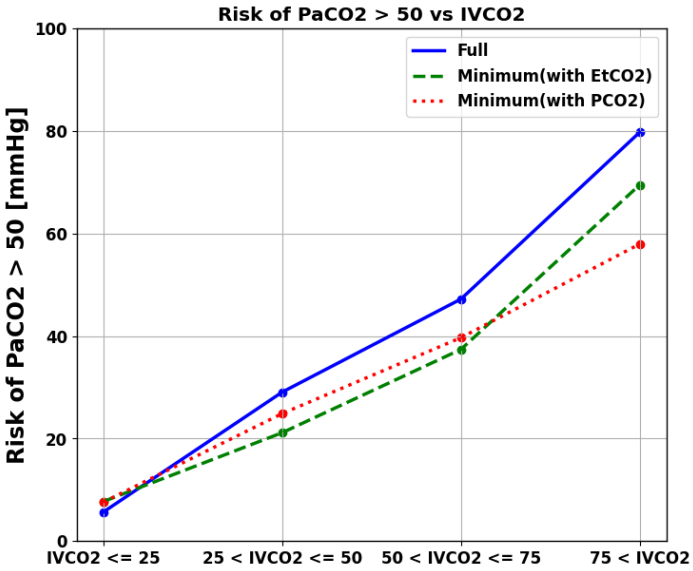

Figure 19: The risk of inadequate ventilation of carbon dioxide for different bins of the IVCO2 index

Data Set	0-25	p	25-50	p	50-75	p	75-100
Minimum (with EtCO2)	10.09	<0.0001	30.02	<0.0001	43.88	<0.0001	70.59
Minimum (with PCO2)	9.95	<0.0001	26.72	<0.0001	40.49	<0.0001	58.47
Full	6.43	<0.0001	29.06	<0.0001	45.67	<0.0001	75.85

Table 13: Statistics of the increase of inadequate ventilation of carbon dioxide risk between different bins of the IVCO2 index

Note that when the IVCO2 Index is below its minimum value, i.e., IVCO2 < 1, or above its maximum value, i.e., IVCO2 > 99, there is still a residual risk for inadequate ventilation of carbon dioxide (i.e., PaCO2 > 50 mmHg), or adequate ventilation of carbon dioxide (i.e., PaCO2 ≤ 50 mmHg) in the latter case. The following approach is used to quantify this limitation:

- The risk for inadequate ventilation of carbon dioxide is evaluated given the IVCO2 Index < 1
- The risk for adequate ventilation of carbon dioxide is evaluated given the IVCO2 Index > 99
- The relative risk between these risks and the total risks (prevalence) in the study population is quantified with its 95% confidence interval

ExtremeRelativeRisks50, p. 42 shows the computed relative risk of PaCO2 > 50 at IVCO2 Index < 1 defined as the minimum relative risk, and PaCO2 ≤ 50 mmHg at IVCO2 Index > 99 defined as the maximum relative risk.

Data Set	Minimum relative risk	95% Confidence Interval	Maximum relative risk	95% Confidence Interval
Minimum (with EtCO2)	0.23	[0.21-0.25]	0.22	[0.20-0.24]
Minimum (with PCO2)	0.31	[0.29-0.34]	0.54	[0.51-0.58]
Full	0.13	[0.11-0.14]	0.19	[0.17-0.21]

Table 14: The minimum relative risk for patients in the validation data set

The following conclusion can be drawn from these results:

- When a patient has both an IVCO2 Index < 1 and a **full** set of observations (see t_DataSets, p. 39), this patient is **8 times** less likely to have inadequate ventilation of carbon dioxide than the patient population (i.e., 1/0.13 = 8, where 0.13 is the minimum relative risk value from the full dataset, ExtremeRelativeRisks50, p. 42).
- When a patient has both an IVCO2 Index > 99 and a **full** set of observations (see t_DataSets, p. 39), this patient is **6 times** less likely to have adequate ventilation of carbon dioxide than the patient population (i.e., 1/0.19 = 6, where 0.17 is the maximum relative risk value from the full data set, ExtremeRelativeRisks50, p. 42).

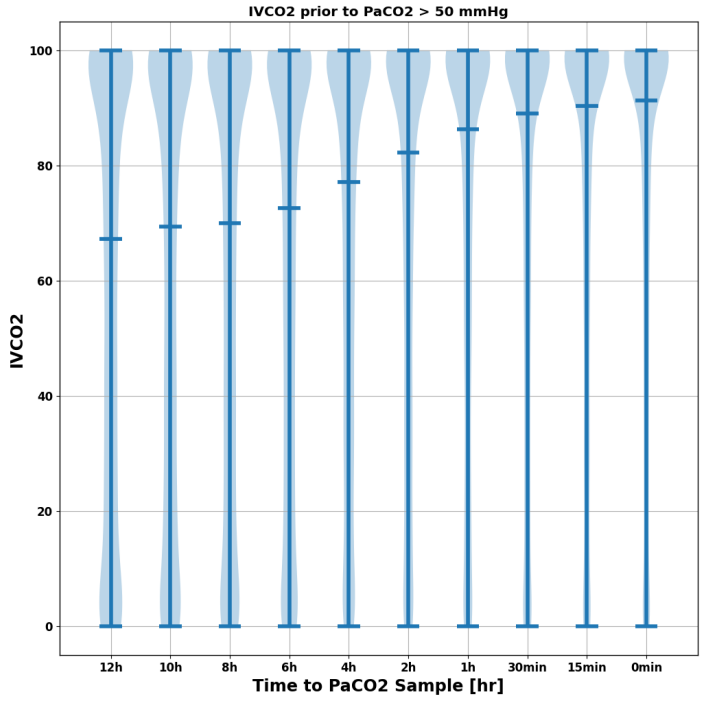

Figure 20: IVCO2 Distribution Prior to PaCO2 > 50 mmHg

The IVCO2 index is intended to be used as a trend monitor. 3U9C3, p. 42 summarizes the trend of the IVCO2 index before an arterial blood gas with PaCO2 > 50 mmHg, which illustrates the following key elements of the index:

- Before a PaCO2 measurement associated with inadequate ventilation of carbon dioxide (PaCO2 > 50 mmHg), from 12 hours to 4 hours, the distribution of IVCO2 values is bi-modal, with the larger portion from 60-100, and the smaller portion from 0 - 20. This illustrates the fact that some patients experience chronic hypercapnia with chronically elevated IVCO2. In contrast, others experience acute periods of hypercapnia and, as a result, have lower IVCO2 values further away from a blood gas sample.
- From 4 hours to the draw time of an ABG with PaCO2 > 50 mmHg, 3U9C3, p. 42 depicts a rise in the median IVCO2 value and a shift of the distribution from bi-modal to uni-modal with the majority of density > 60, indicating that an increasing IVCO2 Index correctly identifies an increasing risk for inadequate ventilation of carbon dioxide.

Additional IVCO2 threshold (IVCO2_60)

AUCValidationSummary_60, p. 43 summarized the AUC values for IVCO2_60 in detecting points positive for inadequate ventilation of carbon dioxide (PaCO2 > 60 mmHg) under the three different datasets.

Data set	AUC	95% Confidence Interval
Minimum (with EtCO2)	0.8665	[0.857 - 0.875]
Minimum (with PCO2)	0.8369	[0.8258 - 0.8489]
Full	0.9114	[0.9042 - 0.9187]

Table 15: AUCs for each data set type, given with confidence bounds

The risk for PaCO2 > 60 mmHg (the fraction of positive points) in different bins of the index is summarized in ValidationRisk_60, p. 43, which shows a monotonically increasing risk between bins in all three datasets.

Data Set	0-25	p	25-50	p	50-75	p	75-100
Minimum (with EtCO2)	2.76	<0.0001	19.19	<0.0001	34.65	<0.0001	59.87
Minimum (with PCO2)	2.34	<0.0001	13.92	=0.0007	27.61	=0.0007	34.58
Full	1.84	<0.0001	22.98	<0.0001	33.96	<0.0001	59.46

Table 16: Statistics of the increase of inadequate ventilation of carbon dioxide risk between different bins of the IVCO2 index

ExtremeRelativeRisks60, p. 44 shows the computed minimum and maximum relative risks for inadequate ventilation of carbon dioxide. Given these performance metrics:

- When a patient has both an IVCO2_60 < 1 and a **full** set of observations (see t_DataSets, p. 39), this patient is **7 times** less likely to have inadequate ventilation of carbon dioxide than the patient

population (i.e., 1/0.14 = 7, where 0.14 is the minimum relative risk value from the full dataset, ExtremeRelativeRisks60, p. 44).

- When a patient has both an IVCO2_60 > 99 and a **full** set of observations (see t_DataSets, p. 39), this patient is **4 times** less likely to have adequate ventilation of carbon dioxide than the patient population (i.e., 1/0.29 = 4, where 0.29 is the maximum relative risk value from the full data set, ExtremeRelativeRisks60, p. 44).

Data Set	Minimum relative risk	95% Confidence Interval	Maximum relative risk	95% Confidence Interval
Minimum (with EtCO2)	0.23	[0.20-0.26]	0.27	[0.22-0.32]
Minimum (with PCO2)	0.23	[0.20-0.27]	0.72	[0.68-0.76]
Full	0.14	[0.12-0.16]	0.29	[0.26-0.33]

Table 17: The minimum relative risk for patients in the validation data set

4.11.4. Adult IVCO2 Performance

IVCO2_50

HE8N5, p. 45 illustrates the ROC curves and respective AUC values for detecting points positive for inadequate ventilation of carbon dioxide (PaCO2 > 50 mmHg) evaluated under two different datasets.

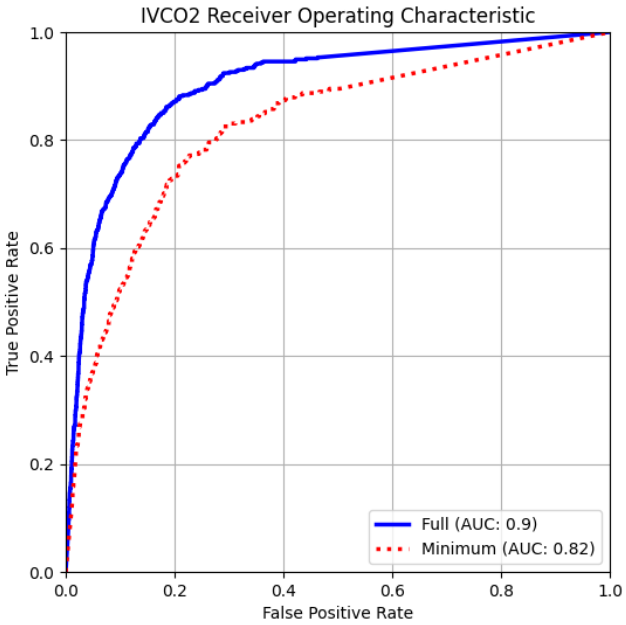

Figure 21: the ROC for detecting points positive for inadequate ventilation of carbon dioxide for all validation patients when run with full and minimum data sets

In the first dataset, the algorithm used full measurement data composed of all possible measures listed above for the IVCO2 computation. Second, the minimum data was derived by down-sampling the full dataset to include only the minimum data required to compute the IVCO2 Index. This was used to evaluate the robustness of the performance of the IVCO2 Index under limited monitoring levels. Note these datasets are defined below in ERG1E, p. 45.

Data set	Downsampling
Full	No downsampling - all data sources are fully available; see AIM, p. 16
Minimum	Reduced data rates for the minimal set: • The following measures downsampled to 1 data point every 10 minutes - SpO2 • The following measures downsampled to 1 data point every 60 seconds - FiO2, Heart rate, Respiratory rate, Tidal Volume, and Mean Airway Pressure • The following measurements were downsampled to one every 12 hours - arterial or venous PCO2 No other measurements above the minimal set are processed through the algorithm (i.e., central venous pressure, Hemoglobin, SvO2, and temperature)

Table 18: The data sets employed in the analysis

These results are also summarized in Z660T, p. 46, which includes the error around the means of the reported AUCs.

Data set	AUC	95% Confidence Interval
Full	0.9009	[0.8867 - 0.9156]
Minimum	0.8226	[0.798 - 0.8453]

Table 19: AUCs for each data set type, given with confidence bounds

The risk for PaCO2>50mmHg (the fraction of positive points) in different bins of the index is summarized in Y72PD, p. 46, which shows a monotonically increasing risk between bins in all three datasets, as summarized in METZX, p. 46, is statistically significant.

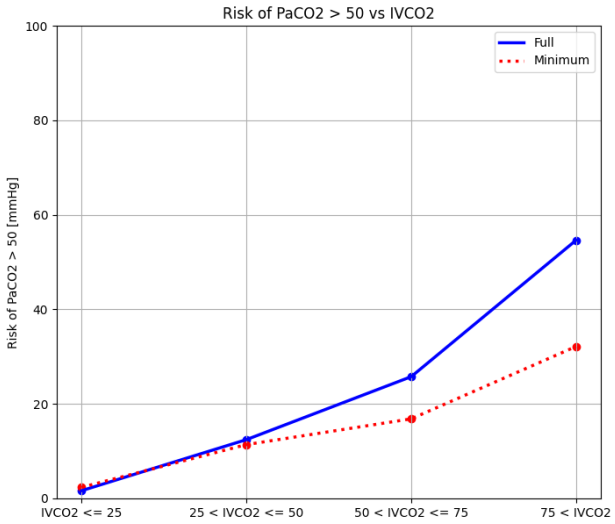

Figure 22: The risk of inadequate ventilation of carbon dioxide for different bins of the IVCO2 index

Data Set	0-25	p	25-50	p	50-75	p	75-100
Minimum	2.36	<0.0001	11.39	=0.0252	16.84	<0.0001	32.15
Full	1.64	<0.0001	12.44	<0.0001	25.76	<0.0001	54.62

Table 20: Statistics of the increase of inadequate ventilation of carbon dioxide risk between different bins of the IVCO2 index

Note that when the IVCO2 Index is below its minimum value, i.e., IVCO2 < 1, or above its maximum value, i.e., IVCO2 > 99, there is still a residual risk for inadequate ventilation of carbon dioxide (i.e., PaCO2 > 50 mmHg), or adequate ventilation of carbon dioxide (i.e., PaCO2 ≤ 50 mmHg) in the latter case. The following approach is used to quantify this limitation:

- The risk for inadequate ventilation of carbon dioxide is evaluated given the IVCO2 Index < 1
- The risk for adequate ventilation of carbon dioxide is evaluated given the IVCO2 Index > 99
- The relative risk between these risks and the total risks (prevalence) in the study population is quantified with its 95% confidence interval

G8TU3, p. 47 shows the computed relative risk of PaCO2 > 50 at IVCO2 Index < 1 defined as the minimum relative risk, and PaCO2 ≤ 50 mmHg at IVCO2 Index > 99 defined as the maximum relative risk.

Data Set	Minimum relative risk	95% Confidence Interval	Maximum relative risk	95% Confidence Interval
Minimum	0.22	[0.16-0.30]	0.57	[0.48-0.67]
Full	0.10	[0.07-0.14]	0.42	[0.32-0.52]

Table 21: The minimum relative risk for patients in the validation data set

The following conclusion can be drawn from these results:

- When a patient has both an IVCO2 Index < 1 and a **full** set of observations (see ERG1E, p. 45), this patient is **10 times** less likely to have inadequate ventilation of carbon dioxide than the patient population (i.e., 1/0.10 = 10, where 0.10 is the minimum relative risk value from the full dataset, G8TU3, p. 47).
- When a patient has both an IVCO2 Index > 99 and a **full** set of observations (see ERG1E, p. 45), this patient is **2 times** less likely to have adequate ventilation of carbon dioxide than the patient population (i.e., 1/0.42= 2, where 0.42 is the maximum relative risk value from the full data set, G8TU3, p. 47).

Additional IVCO2 threshold (IVCO2_60)

AUCValidationSummary_60, p. 43 summarized the AUC values for IVCO2_60 in detecting points positive for inadequate ventilation of carbon dioxide (PaCO2 > 60 mmHg) under the three different datasets.

Data set	AUC	95% Confidence Interval
Minimum	0.862	[0.8197 - 0.9008]
Full	0.9212	[0.8944 - 0.947]

Table 22: AUCs for each data set type, given with confidence bounds

The risk for PaCO2 > 60 mmHg (the fraction of positive points) in different bins of the index is summarized in ValidationRisk_60, p. 43, which shows a monotonically increasing risk between bins in all three datasets.

Data Set	0-25	p	25-50	p	50-75	p	75-100
Minimum	0.56	<0.0001	4.8	=0.1407	8.61	=0.0536	15.38
Full	0.46	<0.0001	6.96	=0.0002	20.59	=0.0602	30.38

Table 23: Statistics of the increase of inadequate ventilation of carbon dioxide risk between different bins of the IVCO2 index

ExtremeRelativeRisks60, p. 44 shows the computed minimum and maximum relative risks for inadequate ventilation of carbon dioxide. Given these performance metrics:

- When a patient has both an IVCO2_60 Index < 1 and a **full** set of observations (see ERG1E, p. 45), this patient is **8 times** less likely to have inadequate ventilation of carbon dioxide than the patient population (i.e., 1/0.12 = 8, where 0.12 is the minimum relative risk value from the full dataset, RR8L7, p. 48).
- When a patient has both an IVCO2_60 Index > 99 and a **full** set of observations (see ERG1E, p. 45), this patient is **1.3 times** less likely to have adequate ventilation of carbon dioxide than the patient population (i.e., 1/0.8= 1.3, where 0.80 is the maximum relative risk value from the full data set, RR8L7, p. 48).

Data Set	Minimum relative risk	95% Confidence Interval	Maximum relative risk	95% Confidence Interval
Minimum	0.22	[0.13-0.39]	0.75	[0.63-0.90]
Full	0.12	[0.06-0.22]	0.80	[0.68-0.95]

Table 24: The minimum relative risk for patients in the validation data set

4.11.5. The IVCO2 Index Limitation

Healthcare professionals should consider the following limitations when employing the IVCO2 Index for the evaluation of indicated patients:

- The IVCO2 Index cannot be used to diagnose or treat a disease or condition.
- The IVCO2 Index is not validated and should not be used for patients on Mechanical Circulatory Support.
- The IVCO2 Index is a trend monitor and, as such, has been validated and intended to be interpreted in the context of its entire range, not versus a specific threshold.
- The precision and accuracy of the IVCO2 Index algorithm improve as more data becomes available. The performance of the IVCO2 Index shows a statistically significant improvement in the presence of arterial blood gases. (See AUCValidationSummary, p. 40.)
- When the IVCO2 Index is at its minimum value and not trending, there is still a residual risk for inadequate ventilation of carbon dioxide.

- When the IVCO2 Index is at its maximum value and not trending, there is still a residual risk for adequate ventilation of carbon dioxide.
- The IVCO2 Index will not be displayed if the following minimum measurements are not available:
  - Heart rate from ECG or pulse, respiration rate, tidal volume, the fraction of inspired oxygen, and mean airway pressure at a minimum of once every 60 seconds
  - SpO2 from pulse oximetry at a minimum of once every 10 minutes
  - Either EtCO2 at a minimum of every 60 seconds OR arterial or venous PCO2 (or capillary PCO2 when the patient is under 29 days of age) at a minimum of once every 12 hours
- The IVCO2 Index requires initialization time to calibrate to a particular patient once data starts streaming. The IVCO2 Index will not be displayed during the initial calibration period of five minutes. If the patient's heart rate is subsequently lost for one hour, the algorithm will wait for the minimum measurements to be restored. It will re-enter a calibration period before reporting a new value. If the algorithm re-initializes at any time, it will also re-enter a calibration period. No IVCO2 Index will be displayed while the index is calibrating.
- The IVCO2 Index uses the patient's date of birth to compute the patient's age and continuously update certain parameters of the physiology model.

4.12. The HLA Index

The application continuously computes and displays the HLA Index, reflecting the likelihood of the patient experiencing hyperlactatemia. Impaired tissue oxygenation leads to anaerobic metabolism manifested by the production of lactic acid and the respective elevation of its conjugated base (lactate) concentration in the blood (Minton and Sidebotham 2017). In this respect, the HLA Index as the means of tracking the likelihood of whole blood concentration of lactate above 4 mmol/L provides a supplemental assessment that an increasing risk for inadequate oxygen delivery (increasing IDO2 Index) has led to an increasing risk for hyperlactatemia. The threshold of 4 mmol/L has been chosen based on the association of this threshold with poor outcomes in different patient populations (Minton and Sidebotham 2017, Casserly et al. 2015, Kogan et al. 2012) and specific feedback from current clinical users.

The HLA Index varies between 0 and 100 and is displayed on the Patient View screen. When the HLA Index™ is increasing, there is an increasing risk of hyperlactatemia, and attention should be brought to the patient.

The HLA Index is computed based on multiple physiologic measures and laboratory test results collected by the application. The algorithm that computes the HLA Index uses a software model of human physiology. The HLA Index is solely indicated for post-surgical patients 0 to 12 years of age and weighing 2 kg or 18 under intensive care and not on Mechanical Circulatory Support.

To compute reliable results, the algorithm requires the following physiologic variables as minimum input requirements: heart rate, blood pressure, pulse oximetry, and whole blood concentration of lactate. The heart rate needs to be acquired at least every 60 seconds, while the blood pressure and pulse oximetry need to be acquired at least every 10 minutes. The lactate measurements need to be acquired with a frequency of at least once every 24 hours. If data is received with lower frequency, or if these data types are unavailable, the HLA Index is not computed, and the user is informed that no computation is available.

References

1. J. Minton and D. A. Sidebotham, “Hyperlactatemia and cardiac surgery,” *J. Extra. Corpor. Technol.*, vol. 49, no. 1, pp. 7–15, 2017
2. B. Casserly *et al.*, “Lactate measurements in sepsis-induced tissue hypoperfusion: Results from the surviving sepsis campaign database,” *Crit. Care Med.*, vol. 43, no. 3, pp. 567–573, 2015.
3. Kogan *et al.*, “The impact of hyperlactatemia on postoperative outcome after adult cardiac surgery,” *J. Anesth.*, vol. 26, no. 2, pp. 174–178, 2012.

4.12.1. HLA Index User Interface

Figure 23: HLA is displayed on the Hemodynamics tab - patient view screen

The HLA Index is available to be displayed on the Patient View in a dedicated graph above the Central Graphs Area (see ZM5D8, p. 50) if requested as a configuration change by a specific hospital or unit. Additionally, it is always available as a plottable measure from the Measure Dashboard.

If configured in the dedicated Risk Analytics graph, the HLA Index cannot be removed from its graph, and the application does not allow other measures to be overlaid. The Y-Axis for this canvas extends from zero to one hundred, and the HLA Index is graphed in red against a green background. Suppose needed clinical data is missing or the application determines that an Index calculation does not apply to the patient because of their age or other characteristics. In that case, it will not show an Index; the relevant section of the Index graph will be blank. Suppose the Index is not currently being calculated. In that case, the application will display a tooltip that states the Index is not being calculated for this patient either because it doesn't apply to them or because the required data are missing.

4.12.2. The HLA Index performance

The association of the HLA Index with hyperlactatemia was established through a retrospective study of a pediatric patient population that included neonates (0-28 days of age), infants (29 days to 2 years of age), and children (2-12 years of age), and an adult patient population including patients 18 years and older. Data was gathered from multiple institutions and intensive care units in both patient groups. The pediatric validation patient population group included 3,491 patients, and the adult validation patient population included 1293 patients.

The study used periodic measurements of whole blood concentration of lactate sampled from various blood panels, e.g., Point-of-Care diagnostics and blood chemistry. In the pediatric performance assessment, 58,181 measurements were included in the analysis. In the adult performance assessment, 15,331 measurements were included in the analysis.

For each lactate measurement in the first 10 postoperative days, the average HLA index was computed in the 30 minutes immediately before the measurement and used as a predictor score for LA > 4 mmol /L. The resulting Receiver Operating Characteristic (ROC) curve was generated, and the Area Under the Curve (AUC) was computed. The specification for the AUC performance is that the 95% confidence interval must be above 0.7

4.12.3. Pediatric HLA Performance

The HLA ROC Performance

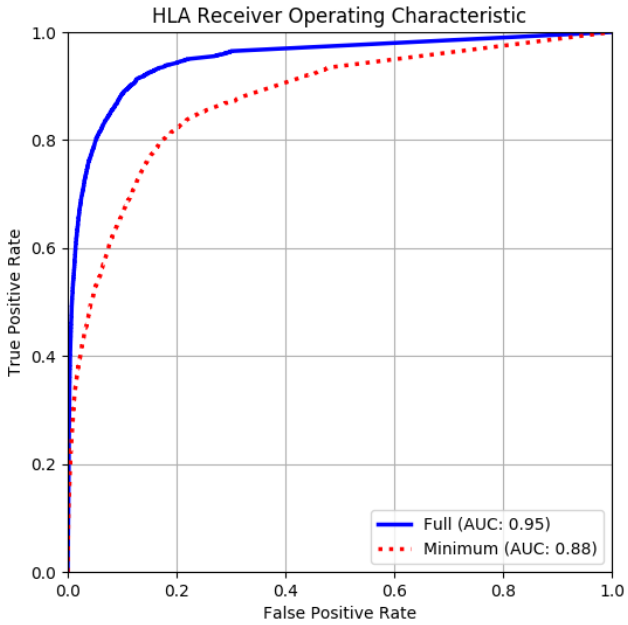

Figure 24: ROC Curves for Full and Minimum Validation sets for the HLA Index

hla_roc_fig, p. 52 shows the receiver operating characteristic with LA > 4 mmol/L using the HLA Index computed by the model-based Risk Analytics algorithm. There were two datasets examined. In the first dataset, the algorithm used full measurement data composed of all possible measures listed above for the HLA computation. In the second dataset, the algorithm used only the minimum measurement data for the computation, i.e., heart rate every 60 seconds, SpO2 every 10 minutes, blood pressure every 10 minutes, and whole blood lactate once every 24 hours. Note these datasets are defined below in hla_data_sets, p. 52.

Data set	Downsampling
Full	No downsampling - all data sources are fully available; see AIM, p. 16
Minimum	Reduced data rates for the minimal set (eleven measurements): • The following measures downsampled to 1 data point every 10 minutes - SpO2 and Arterial Blood Pressure • The following measures downsampled to 1 data point every 60 seconds - Heart rate • The following measures downsampled to 1 data point every 24 hours - Whole blood lactate No other measurements above the minimal measurements are processed through the algorithm

Table 25: The data sets employed in the HLA analysis

hla_auc_table, p. 53 includes the resulting AUCs and 95% confidence intervals.

Data set	AUC	95% Confidence Interval
Full	0.9654	[0.9628 - 0.968]
Minimum	0.9104	[0.9056 - 0.9154]

Table 26: AUCs for each data set type given with 95% confidence bounds for the HLA Index

The HLA Risk Performance

The risk for LA > 4 mmol/L in different bins of the HLA Index is summarized in risk_figure_hla, p. 53. Note the monotonic increase of risk between bins in both data sets, which, as summarized in risk_table_hla, p. 53, is statistically significant.

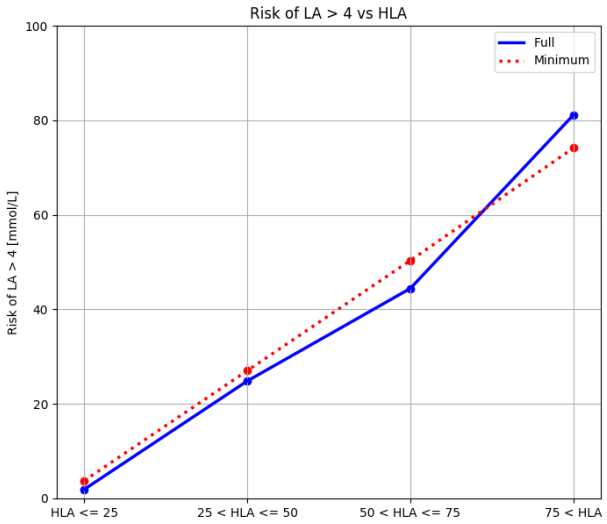

Figure 25: The risk of LA > 4 mmol/L for different bins of the HLA Index

Data Set	HLA ≤ 25	p-value	25 < HLA ≤ 50	p-value	50 < HLA ≤ 75	p-value	75 < HLA
Full	1.19	<0.0001	16.35	<0.0001	36.81	<0.0001	82.58
Minimum	2.88	<0.0001	21.72	<0.0001	34.14	<0.0001	70.58

Table 27: Statistics of the increase of hyperlactatemia risk between different bins of the HLA Index

Note that when the HLA Index is below its minimum value, i.e., HLA < 1, or above its maximum value, i.e., HLA > 99, there is still a residual risk for hyperlactatemia (i.e., LA > 4 mmol / L), or LA ≤ 4 mmol / L in the latter case. The following approach is used to quantify this limitation:

- The risk for hyperlactatemia is evaluated given the HLA Index < 1
- The risk for LA LA ≤ 4 mmol / L is evaluated given the HLA Index > 99
- The relative risk between these risks and the total risks (prevalence) in the study population is quantified with its 95% confidence interval

min_max_rel_risk_table_hla, p. 54 describes the minimum relative risk for hyperlactatemia, which is 0.09 and 0.03 for the minimum and full data sets, respectively. These numbers can be interpreted as a patient with a minimum value of the HLA Index and a full set of observations is **33 times less likely** to have hyperlactatemia than their peers. The table also describes the maximum relative risk for Lactate < 4 mmol/L, which is 0.06 and 0.16 for both the minimum and full data sets. These numbers can be interpreted as a patient with a maximum value of the HLA Index and a full set of observations is **17 times less likely** to have Lactate ≤ 4 mmol/L than their peers.

Data Set	Minimum relative risk	95% Confidence Interval	Maximum relative risk	95% Confidence Interval
Minimum	0.09	[0.07-0.11]	0.16	[0.15-0.18]
Full	0.03	[0.02-0.04]	0.06	[0.05-0.07]

Table 28: The minimum and maximum relative risk for patients in the validation data set for the HLA Index

4.12.4. Adult HLA Performance

The HLA ROC Performance

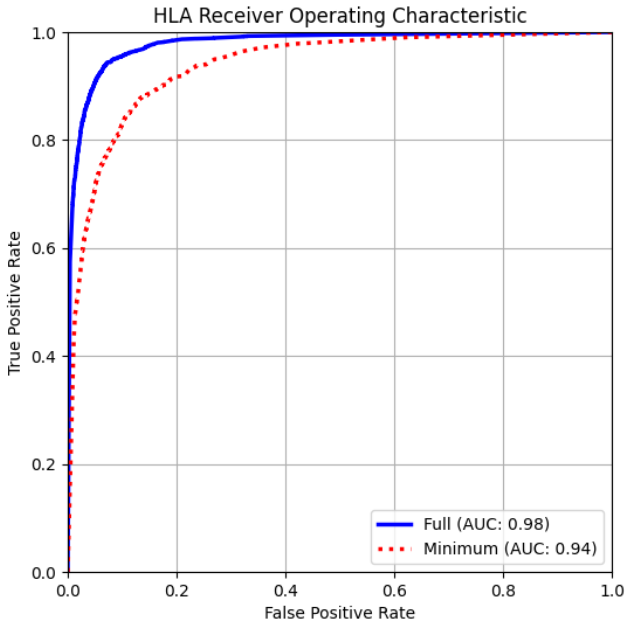

Figure 26: ROC Curves for Full and Minimum Validation sets for the HLA Index

L7MV9, p. 55 shows the receiver operating characteristic with LA > 4 mmol/L using the HLA Index computed by the model-based Risk Analytics algorithm. There were two datasets examined. In the first dataset, the algorithm used full measurement data composed of all possible measures listed above for the HLA computation. In the second dataset, the algorithm used only the minimum measurement data for the computation, i.e., heart rate every 60 seconds, SpO2 every 10 minutes, blood pressure every 10 minutes, and whole blood lactate once every 24 hours. Note these datasets are defined below in NNPSL, p. 55.

Data set	Downsampling
Full	No downsampling - all data sources are fully available; see AIM, p. 16
Minimum	Reduced data rates for the minimal set (eleven measurements): • The following measures downsampled to 1 data point every 10 minutes - SpO2 and Arterial Blood Pressure • The following measures downsampled to 1 data point every 60 seconds - Heart rate • The following measures downsampled to 1 data point every 24 hours - Whole blood lactate No other measurements above the minimal measurements are processed through the algorithm

Table 29: The data sets employed in the HLA analysis

FI5TS, p. 56 includes the resulting AUCs and 95% confidence intervals.

Data set	AUC	95% Confidence Interval
Full	0.9789	[0.9759 - 0.9818]
Minimum	0.9383	[0.9322 - 0.9439]

Table 30: AUCs for each data set type given with 95% confidence bounds for the HLA Index

The HLA Risk Performance

The risk for LA > 4 mmol/L in different bins of the HLA Index is summarized in E3LLP, p. 56. Note the monotonic increase of risk between bins in both data sets, which, as summarized in T2VY0, p. 56, is statistically significant.

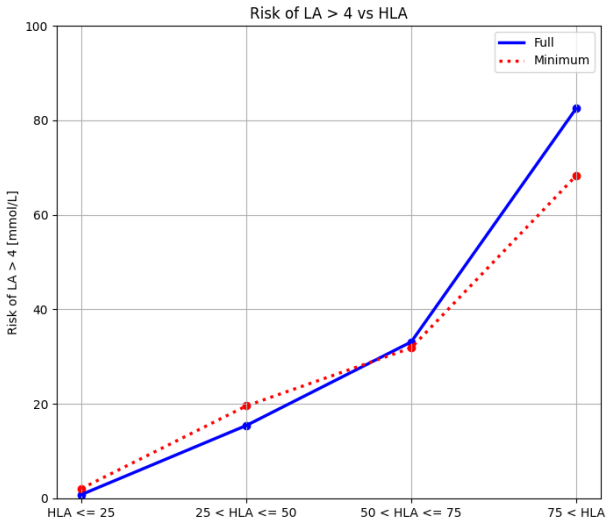

Figure 27: The risk of LA > 4 mmol/L for different bins of the HLA Index

Data Set	HLA ≤ 25	p-value	25 < HLA ≤ 50	p-value	50 < HLA ≤ 75	p-value	75 < HLA
Minimum	2.1	<0.0001	19.58	<0.0001	31.85	<0.0001	68.26
Full	0.83	<0.0001	15.44	<0.0001	33.11	<0.0001	82.47

Table 31: Statistics of the increase of hyperlactatemia risk between different bins of the HLA Index

Note that when the HLA Index is below its minimum value, i.e., HLA < 1, or above its maximum value, i.e., HLA > 99, there is still a residual risk for hyperlactatemia (i.e., LA > 4 mmol / L), or LA ≤ 4 mmol / L in the latter case. The following approach is used to quantify this limitation:

- The risk for hyperlactatemia is evaluated given the HLA Index < 1
- The risk for LA LA ≤ 4 mmol / L is evaluated given the HLA Index > 99
- The relative risk between these risks and the total risks (prevalence) in the study population is quantified with its 95% confidence interval

1Y304, p. 57 describes the minimum relative risk for hyperlactatemia, which is 0.01 and 0.03 for the minimum and full data sets, respectively. These numbers can be interpreted as a patient with a minimum value of the HLA Index and a full set of observations is **100 times less likely** to have hyperlactatemia than their peers. The table also describes the maximum relative risk for Lactate < 4 mmol/L, which is 0.05 and 0.18 for both the minimum and full data sets. These numbers can be interpreted as a patient with a maximum value of the HLA Index and a full set of observations is 50 **times less likely** to have Lactate ≤ 4 mmol/L than their peers.

Data Set	Minimum relative risk	95% Confidence Interval	Maximum relative risk	95% Confidence Interval
Minimum	0.03	[0.02-0.05]	0.18	[0.15-0.21]
Full	0.01	[0.01-0.02]	0.05	[0.04-0.07]

Table 32: The minimum and maximum relative risk for patients in the validation data set for the HLA Index

4.12.5. The HLA Index Limitations

Healthcare professionals should consider the following limitations when employing the HLA Index for the evaluation of indicated patients:

- The HLA Index cannot be used to diagnose or treat a disease or condition.
- The HLA Index is not validated and should not be used for patients on Mechanical Circulatory Support.
- The HLA Index is a trend monitor and, as such, has been validated and intended to be interpreted in the context of its entire range, not versus a specific threshold.
- The HLA Index accuracy depends on the intensity of patient monitoring. The more measurements collected as inputs to the application, the more accurate the HLA Index will be. See the table in the Measurements section for all the data types the algorithm considers.
- The HLA Index will not be displayed if the following minimum measurements are not available:
  - Heart rate from ECG or pulse at least once every 60 seconds.
  - SpO2 from pulse oximetry at a minimum of once every 10 minutes.
  - Blood Pressure (mean/diastolic/systolic) at least once every 10 minutes.
  - Whole blood concentration of lactate acquired at a minimum of every 24 hours
- The HLA Index has not been validated for patients weighing less than two kilograms.

- When the HLA Index is at its minimum value and not trending, there is still a residual risk for hyperlactemia.
- When the HLA Index is at its maximum value and not trending, there is still a residual risk for LA ≤ 4 mmol / L.
- The HLA Index uses the patient's date of birth to compute the patient's age and continuously update certain parameters of the physiology model.
- Once data starts streaming, the HLA Index requires initialization time to calibrate to a particular patient. The HLA Index will not be displayed during the initial calibration period of five minutes. If the patient's heart rate is subsequently lost for one hour, the algorithm will wait for the minimum measurements to be restored. It will re-enter a calibration period before reporting a new value. If the algorithm re-initializes at any time, it will also re-enter a calibration period. No HLA Index will be displayed while the index is calibrating.

4.13. The ACD Index

The application continuously computes and displays the ACD Index, reflecting the likelihood of a patient experiencing acidemia, defined as arterial pH below 7.25. In some circumstances, the risk of inadequate ventilation of carbon dioxide, as trended by the IVCO2 index, is acceptable (see permissive hypercapnia by Miller & Carlo 2007 and by Thome & Carlo 2012). Interpreting ventilation failures in the context of arterial pH provides supplemental information, bringing attention to a patient who may need further clinical evaluation. The ACD Index explicitly achieves this objective by tracking the likelihood of arterial pH less than 7.25. The specific threshold of 7.25 has been chosen because arterial pH less than this value has been clinically recognized as a sign of severe respiratory acidosis (Crummy et al. 2007). It provides a meaningful threshold for an attention trigger in managing a pediatric patient with permissive hypercapnia (Jouvet et al. 2015)

The ACD Index varies between 0 and 100 and is displayed on the Patient View screen. When the ACD Index increases, there is an increasing risk of acidemia, and attention should be given to the patient.

The ACD Index is computed based on multiple physiologic measures and laboratory test results collected by the application. The algorithm that computes the ACD Index uses a software model of human physiology. The ACD Index is solely indicated for use for invasively ventilated patients 0 to 12 years of age and weighing 2 kg or 18 years of age under intensive care and not on Mechanical Circulatory Support.

To compute reliable results, the algorithm requires the following physiologic variables as minimum input requirements: heart rate, blood pressure, pulse oximetry, respiration rate, tidal volume, a fraction of inspired oxygen, end-tidal carbon dioxide, mean airway pressure, and interchangeable arterial or venous blood gases. The heart rate, airway respiration rate, tidal volume, the fraction of inspired oxygen, end-tidal carbon dioxide, and mean airway pressure need to be acquired at least every 60 seconds, while pulse oximetry needs to be acquired at least every 10 minutes, the blood pressure needs to be acquired at least every 60 minutes, and the arterial or venous blood gasses need to be acquired every 24 hours (see AIM, p. 16).

Note: The presence of respiratory acidosis predominantly drives the ACD index, but it may indicate metabolic acidosis or both respiratory and metabolic acidosis.

References

1. Miller, J. D., & Carlo, W. A. (2007) Safety and effectiveness of permissive hypercapnia in the preterm infant Current Opinion in Pediatrics. 19(2):142–144, APR 2007
2. Thome, U. H., & Carlo, W. A. (2002). Permissive hypercapnia. *Seminars in Neonatology*, *7*(5), 409–419. https://doi.org/10.1053/siny.2002.0135
3. F. Crummy, C. Buchan, B. Miller, J. Toghill, and M. T. Naughton, “The use of noninvasive mechanical ventilation in COPD with severe hypercapnic acidosis,” *Respir. Med.*, vol. 101, no. 1, pp. 53–61, 2007.
4. P. Jouvet *et al.*, “Pediatric Acute Respiratory Distress Syndrome: Consensus Recommendations from the Pediatric Acute Lung Injury Consensus Conference,” in *Pediatric Critical Care Medicine*, 2015, vol. 16, no. 5, pp. 428–439.

4.13.1. The ACD Index User Interface

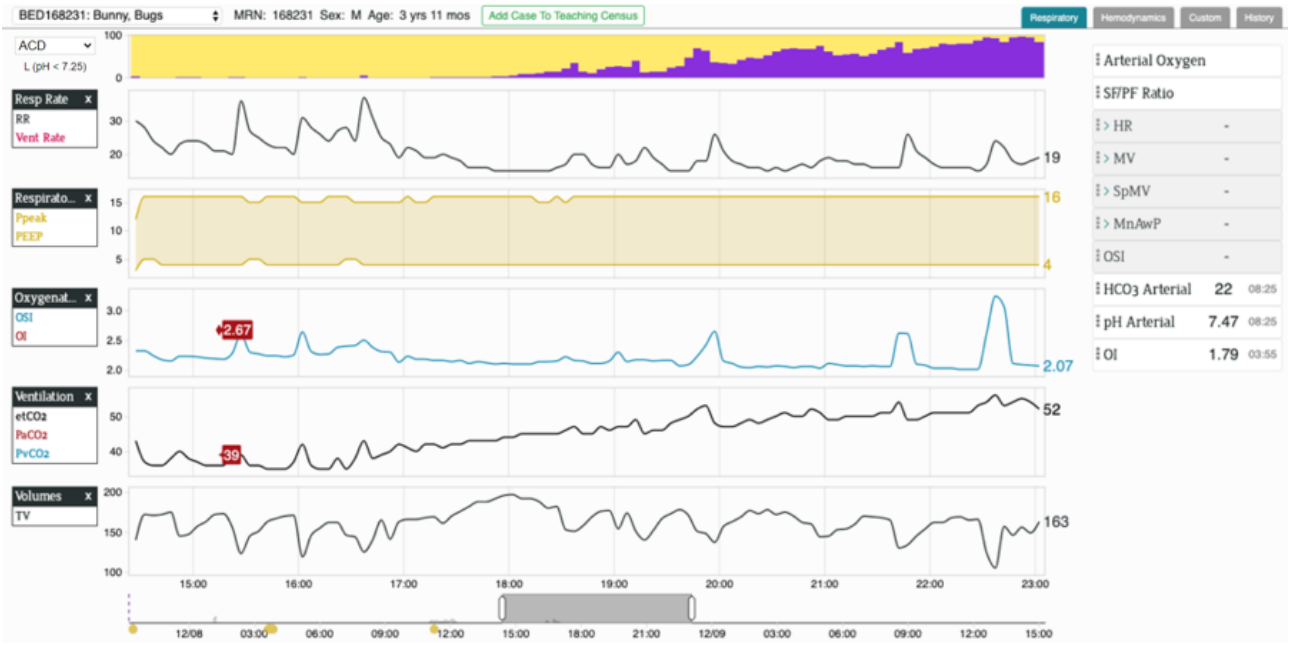

Figure 28: ACD is displayed on the Respiratory tab - patient view screen - in T3

The ACD Index is available to be displayed on the Patient View in a dedicated graph above the Central Graphs Area (see E5GDV, p. 60) if requested as a configuration change by a specific hospital or unit. Additionally, it is always available as a plottable measure from the Measure Dashboard.

If configured in the dedicated Risk Analytics graph, the ACD Index cannot be removed from its graph, and the application does not allow other measures to be overlaid. The Y-Axis for this canvas extends from zero to one hundred, and the ACD Index is graphed in purple against a yellow background. Suppose needed clinical data is missing or the application determines that an Index calculation does not apply to the patient because of their age or other characteristics. In that case, it will not show an Index; the relevant section of the Index graph will be blank. Suppose the Index is not currently being calculated. In that case, the application will display a tooltip that states the Index is not being calculated for this patient either because it doesn't apply to them or because the required data are missing.

4.13.2. The ACD Index Performance

The association of the ACD Index with acidemia was established through a retrospective study of a pediatric patient population that included neonates (0-28 days of age), infants (29 days to 2 years of age), and children (2-12 years of age), and an adult patient population including patients 18 years and older. Data was gathered from multiple institutions and intensive care units in both patient groups. The pediatric validation patient population group included 1863 patients, and the adult validation patient population included 793 patients.

The study used periodic measurements of pH sampled from arterial blood gas. In the pediatric performance assessment, 24,879 measurements were included in the analysis. In the adult performance assessment, 6414 measurements were included in the analysis.

For each arterial pH measurement (pHa), the average ACD index was computed in the 30 minutes immediately before the measurement and used as a predictor score for pHa < 7.25. The resulting Receiver Operating Characteristic (ROC) curve was generated, and the Area Under the Curve (AUC) was computed. The specification for the AUC performance is that the 95% confidence interval must be above 0.7.

4.13.3. Pediatric ACD Performance

The ACD ROC Performance

The figure below (see roc_fig_acd, p. 61) shows the receiver operating characteristic of predicting pHa < 7.25 using the average ACD Index averaged 30 minutes before an arterial blood gas sample.

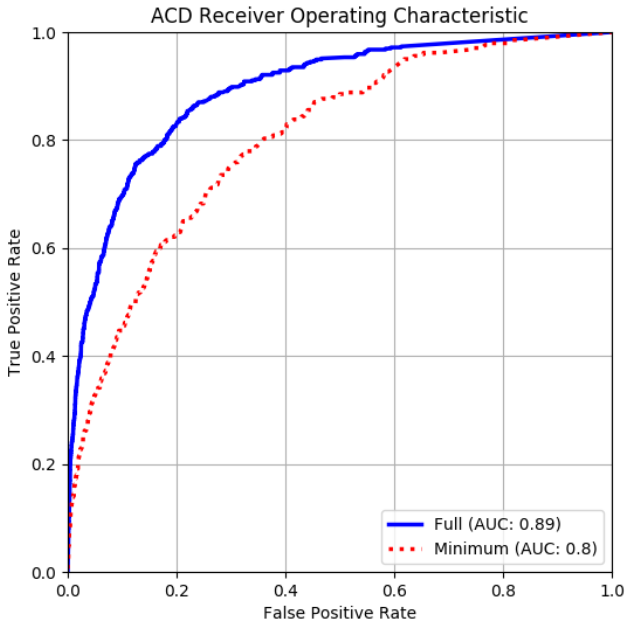

Figure 29: ROC Curves for Full and Minimum Validation sets of the ACD Index

Three different sets (see acd_data_sets, p. 62) were derived from the original data: 1) a full data set, which included the unaltered original data for the available patients, and 2) two minimum data sets, which were derived by down-sampling the original dataset to include only the minimum data required for the computation of the ACD Index. These minimum sets were used to evaluate the robustness of the performance of the ACD Index under limited monitoring levels.

Data set	Downsampling
Full	No downsampling - all data sources are fully available; see AIM, p. 16
Minimum (with EtCO2)	Reduced data rates for the minimal set: • The following measures downsampled to 1 data point every 60 minutes - Arterial Blood Pressure • The following measures downsampled to 1 data point every 10 minutes - SpO2 • The following measures downsampled to 1 data point every 60 seconds - FiO2, Heart rate, Respiratory rate, Tidal Volume, and Mean Airway Pressure • The following measurements were downsampled to one every 12 hours - arterial or venous pH • The following measures downsampled to 1 data point every 60 seconds - EtCO2 No other measurements above the minimal set are processed through the algorithm (i.e., central venous pressure, Hemoglobin, SvO2, and temperature)
Minimum (with PCO2)	Reduced data rates for the minimal set: • The following measures downsampled to 1 data point every 60 minutes - Arterial Blood Pressure • The following measures downsampled to 1 data point every 10 minutes - SpO2 • The following measures downsampled to 1 data point every 60 seconds - FiO2, Heart rate, Respiratory rate, Tidal Volume, and Mean Airway Pressure • The following measurements were downsampled to one every 12 hours - arterial or venous pH • The following measurements were downsampled to one every 12 hours - arterial or venous PCO2 No other measurements above the minimal set are processed through the algorithm (i.e., central venous pressure, Hemoglobin, SvO2, and temperature)

Table 33: The data sets employed in the analysis

auc_table_acd, p. 62 includes the resulting AUCs and 95% confidence intervals. Note that all intervals are above the 0.7 AUC acceptance criterion.

Data set	AUC	95% Confidence Interval
Full	0.9154	[0.9047 - 0.926]
Minimum (with EtCO2)	0.8988	[0.8865 - 0.9125]
Minimum (with PCO2)	0.8514	[0.8348 - 0.8666]

Table 34: AUCs for each data set type given with 95% confidence bounds for the ACD Index

ACD Risk Performance

The risk for pHa < 7.25 in different bins of the ACD Index is summarized in risk_fig_acd, p. 63. Note the monotonic increase of risk between bins in both data sets, which, as summarized in risk_table_acd, p. 63, is statistically significant.

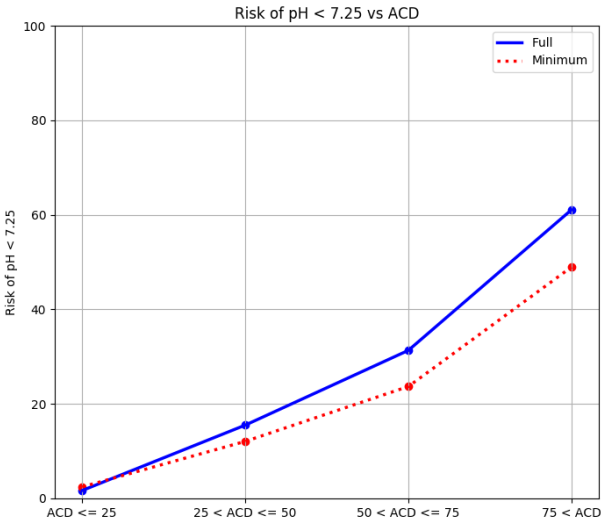

Figure 30: The risk of pH < 7.25 for different bins of the ACD Index

Data Set	ACD ≤ 25	p-value	25 < ACD ≤ 50	p-value	50 < ACD ≤ 75	p-value	75 < ACD
Full	0.74	<0.0001	5.21	<0.0001	18.70	<0.0001	42.76
Minimum (with EtCO2)	0.79	<0.0001	5.13	<0.0001	15.37	<0.0001	45.19
Minimum (with PCO2)	1.02	<0.0001	4.89	<0.0001	12.60	<0.0001	23.62

Table 35: Statistics of the increase of acidemia risk between different bins of the ACD Index

Note that when the ACD Index is below its minimum value, i.e., ACD < 1, or above its maximum value, i.e., ACD > 99, there is still a residual risk for acidemia (i.e., pHa < 7.25), or pHa ≥ 7.25 in the latter case. The following approach is used to quantify this limitation

- The risk for acidemia is evaluated given ACD Index < 1
- The risk for pHa ≥ 7.25 is evaluated given the ACD Index > 99
- The relative risk between these risks and the total risks (prevalence) in the study population is quantified with its 95% confidence interval

min_max_rel_risk_table_acd, p. 64 describes the minimum relative risk for acidemia, which is 0.07, 0.15, and 0.11 for the minimum and full data sets, respectively. Note that these numbers can be interpreted as a patient with a minimum value of the ACD Index and a full set of observations is 9 **times less likely** to have acidemia than their peers. The table also describes the maximum relative risk for pHa ≥ 7.25, which is 0.31, 0.71, and 0.49 for both the minimum and full data sets. Note that these numbers can be interpreted as a

patient with a maximum value of the ACD Index and a full set of observations is 2 **times less likely** to have pHa ≥ 7.25 mmol/L than their peers.

Data Set	Minimum relative risk	95% Confidence Interval	Maximum relative risk	95% Confidence Interval
Minimum (with EtCO2)	0.07	[0.04-0.12]	0.31	[0.23-0.43]
Minimum (with PCO2)	0.15	[0.11-0.21]	0.71	[0.67-0.76]
Full	0.11	[0.08-0.14]	0.49	[0.45-0.54]

Table 36: The minimum and naximum relative risk for patients in the validation data set for the ACD Index

4.13.4. Adult ACD Performance

The ACD ROC Performance

The figure below (see OCXAE, p. 65) shows the receiver operating characteristic of predicting pHa < 7.25 using the average ACD Index averaged 30 minutes before an arterial blood gas sample.

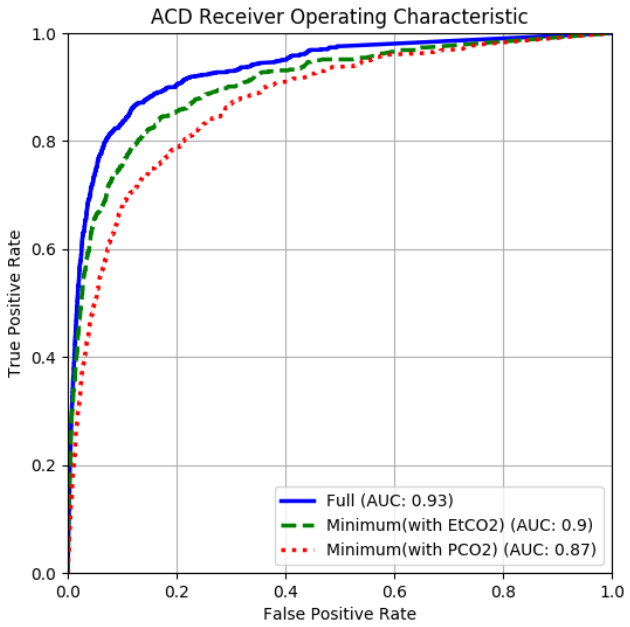

Figure 31: ROC Curves for Full and Minimum Validation sets of the ACD Index

Two different sets (see OCXAE, p. 65) were derived from the original data: 1) a *full data set*, which included the unaltered original data for the available patients, and 2) a *minimum data set*, which was derived by down-sampling the original dataset to include only the minimum data required for the computation of the ACD Index, which was used to evaluate the robustness of the performance of the ACD Index under limited monitoring levels.

Data set	Downsampling
Full	No downsampling - all data sources are fully available; see AIM, p. 16
Minimum	Reduced data rates for the minimal set: • The following measures downsampled to 1 data point every 60 minutes - Arterial Blood Pressure • The following measures downsampled to 1 data point every 10 minutes - SpO2 • The following measures downsampled to 1 data point every 60 seconds - FiO2, Heart rate, Respiratory rate, Tidal Volume, and Mean Airway Pressure • The following measurements were downsampled to one every 12 hours - arterial or venous pH • The following measurements were downsampled to one every 12 hours - arterial or venous PCO2 No other measurements above the minimal set are processed through the algorithm (i.e., central venous pressure, Hemoglobin, SvO2, and temperature)

Table 37: The data sets employed in the analysis

NVBC4, p. 65 includes the resulting AUCs and 95% confidence intervals. Note that all intervals are above the 0.7 AUC acceptance criterion.

Data set	AUC	95% Confidence Interval
Full	0.9207	[0.9019 - 0.9379]
Minimum	0.8201	[0.7864 - 0.8512]

Table 38: AUCs for each data set type given with 95% confidence bounds for the ACD Index

4.13.5. ACD Risk Performance

The risk for pHa < 7.25 in different bins of the ACD Index is summarized in Y6KIW, p. 66. Note the monotonic increase of risk between bins in both data sets, which, as summarized in 9DE0A, p. 66, is statistically significant.

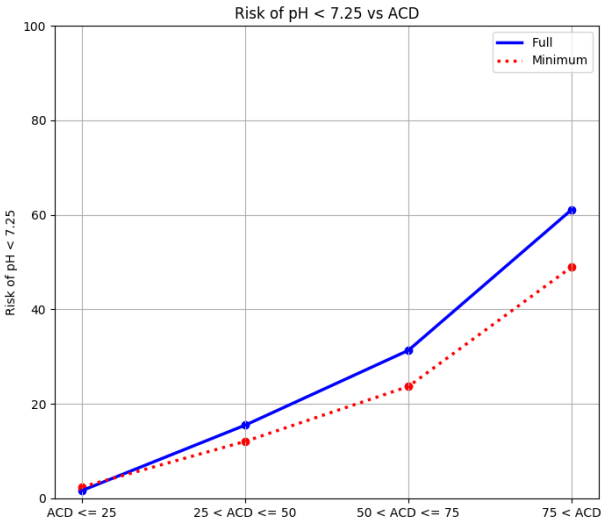

Figure 32: The risk of pH < 7.25 for different bins of the ACD Index

Data Set	ACD ≤ 25	p-value	25 < ACD ≤ 50	p-value	50 < ACD ≤ 75	p-value	75 < ACD
Minimum	1.23	=0.0004	3.4	=0.0007	9.59	=0.0008	18.64
Full	0.59	<0.0001	7.06	<0.0001	9.39	<0.0001	35.61

Table 39: Statistics of the increase of acidemia risk between different bins of the ACD Index

Note that when the ACD Index is below its minimum value, i.e., ACD < 1, or above its maximum value, i.e., ACD > 99, there is still a residual risk for acidemia (i.e., pHa < 7.25), or pHa ≥ 7.25 in the latter case. The following approach is used to quantify this limitation

- The risk for acidemia is evaluated given ACD Index < 1
- The risk for pHa ≥ 7.25 is evaluated given the ACD Index > 99
- The relative risk between these risks and the total risks (prevalence) in the study population is quantified with its 95% confidence interval

IFFWP, p. 67 describes the minimum relative risk for acidemia, 0.2 and 0.07 for the minimum and full data sets, respectively. Note that these numbers can be interpreted as a patient with a minimum value of the ACD Index and a full set of observations is 14 **times less likely** to have acidemia than their peers. The table also describes the maximum relative risk for pHa ≥ 7.25, 0.75, and 0.59 for the minimum and full data sets. Note that these numbers can be interpreted as a patient with a maximum value of the ACD Index and a full set of observations is 2 **times less likely** to have pHa ≥ 7.25 mmol/L than their peers.

Data Set	Minimum relative risk	95% Confidence Interval	Maximum relative risk	95% Confidence Interval
Minimum	0.20	[0.11-0.36]	0.75	[0.69-0.81]
Full	0.07	[0.04-0.13]	0.59	[0.52-0.66]

Table 40: The minimum and naximum relative risk for patients in the validation data set for the ACD Index

4.13.6. ACD Index Limitations

Healthcare professionals should consider the following limitations when employing the ACD Index for the evaluation of indicated patients:

- The ACD Index cannot be used to diagnose or treat a disease or condition.
- The ACD Index is not validated and should not be used for patients on Mechanical Circulatory Support.
- The ACD Index is a trend monitor and, as such, has been validated and intended to be interpreted in the context of its entire range, not versus a specific threshold.
- The ACD Index accuracy depends on the intensity of patient monitoring. The more measurements collected as inputs to the application, the more accurate the ACD Index will be. See the table in the Measurements section for all the data types the algorithm considers.
- The ACD Index will not be displayed if the following minimum measurements are not available:
  - Heart rate from ECG or pulse, respiration rate, tidal volume, end-tidal-CO2, the fraction of inspired oxygen, and mean airway pressure at a minimum of once every 60 seconds
  - SpO2 from pulse oximetry at a minimum of once every 10 minutes
  - Blood Pressure (mean/diastolic/systolic) at a minimum of once every 60 minutes
  - Venous or arterial pH acquired every 12 hours
  - Either EtCO2 at a minimum of every 60 seconds OR arterial or venous PCO2 at a minimum of once every 12 hours
- The ACD Index has not been validated for patients weighing less than two kilograms.
- When the ACD Index is at its minimum value and not trending, there is still a residual risk for acidemia.
- When the ACD Index is at its maximum value and not trending, there is still a residual risk for pHa ≥ 7.25
- The ACD Index uses the patient's date of birth to compute the patient's age and continuously update certain parameters of the physiology model.
- The ACD Index requires initialization time to calibrate to a particular patient once data starts streaming. The ACD Index will not be displayed during the initial calibration period of five minutes. If the patient's heart rate is subsequently lost for one hour, the algorithm will wait for the minimum measurements to be restored. It will re-enter a calibration period before reporting a new value. If the algorithm re-initializes at any time, it will also re-enter a calibration period. No ACD Index will be displayed while the index is calibrating.

4.14. Index Measure Contributions

As the Etiometry Platform continuously processes patient measurements to compute a particular index, the Measure Contribution calculation assesses how much each measurement contributes to the elevation of that index. Each index represents the estimated likelihood that a particular physiological variable is within a given range, e.g., SvO2 < 40% for IDO2_40 and PaCO2 > 50 mmHg for IVCO2_50, estimated through applying Bayes' Theorem. In this Bayesian framework, each measurement and its history can be viewed as independent evidence contributing to the probability reflected by the particular index. The Measure Contribution calculation aims to evaluate the importance of this evidence in assessing the elevated likelihood performed by the algorithm. This is accomplished by reversing the Bayesian update process by which evidence is incorporated into the likelihood estimate, and the change in likelihood is assessed after the removal of the measurement and its history. When an index is above 25%, hovering over the central graph lists the top 3 measures that significantly contribute to the index elevation (see DRHT7, p. 68).

> **Note:**
> The Measure Contributions feature is not validated or meant to facilitate patient diagnosis. It is solely intended to provide an interpretation of the computational relationship between a particular index and the raw measures that inform it.

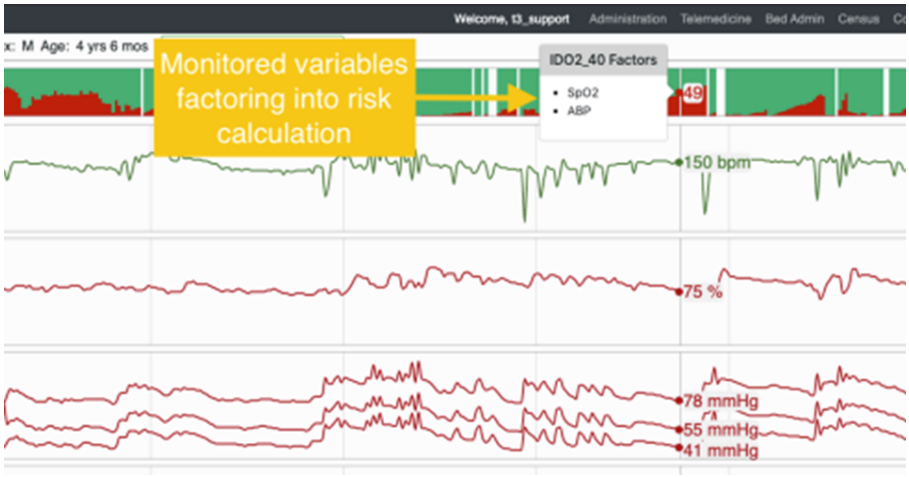

Figure 33: Risk Measure Contributions

4.15. Grayed-Out Period and Warnings Prompt

The Etiometry Platform is not indicated for active patient monitoring. When in Persistent Display mode, the User Interface includes the following to safeguard against the misuse of active patient monitoring:

1. The Index is grayed out for five minutes (see ABSoftwareDesignRiskMitigationUM, p. 69)
2. A warning label is displayed warning against active patient monitoring (see ABSoftwareDesignRiskMitigationUM, p. 69)
3. A user is prompted to acknowledge the warnings when selecting an Index to be graphed in the Central Graphs Area (see CSoftwareDesignRiskMitigationUM, p. 69)

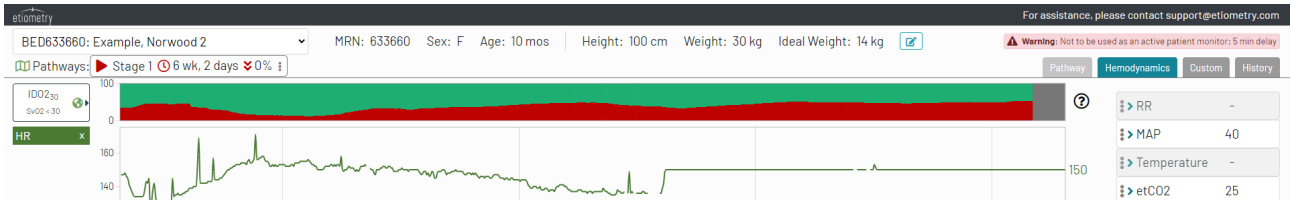

Figure 34: (1) Grayed-out Index, see upper graph and (2) warning label, see upper right

Figure 35: (3) Warnings prompt

4.16. Measure Synonyms

While not identical, certain measures are nevertheless closely related and can be considered "synonyms" for each other. For example, "Temp" (Generic Temperature), "Tairwy" (Airway Temperature), "Tesoph" (Esophageal Temperature), and "Ttymp" (Tympanic Temperature) are all measures of the patient's temperature. In this example, the measure synonym feature would allow the application to continuously report a value for "Temperature" based on whatever values were received for Temp, Tairwy, Tesoph, and Ttymp.

Measure synonyms are based on a three-level hierarchy for a small set of important measures. The top-level (1) Physiologic variables are measurements of patient status or a condition like heart rate, respiratory rate, systolic blood pressure, temperature, etc. Each physiologic variable is calculated from one or more related

(2) channel variables. A channel refers to how a measure is captured via a specific device or lab at a bodily site. A single physiologic variable is sometimes measured through multiple channels simultaneously. For example, systolic blood pressure may be captured from an arterial catheter simultaneously as measured with a noninvasive blood pressure cuff. When this occurs, the application computes the measure synonym based on a preference order defined for related channels. A physiologic variable is calculated for each point in time by evaluating its related channel variables and choosing the data value from the highest priority channel. Finally, channel variables are obtained from mutually exclusive (3) vendor sources. A vendor source is a particular vendor's implementation of the channel device. This is the lowest level of the hierarchy.

As raw data flows into the application from vendor sources, the application calculates the value of the corresponding channel and physiologic variables. These variables, as well as the raw vendor sources, can all be graphed in the application. The physiologic and channel variable names constitute a vendor-neutral lexicon useful in hospitals with multiple vendors. In addition, you can graph physiologic variables over a trended period. This saves clinicians the time and effort of locating the raw measurements and then evaluating them individually to decide the preferred value at each point. Since different clinicians might come to different conclusions depending on what they were seeing or might miss a raw reading, other benefits of measure synonyms include simplification, standardization, and error reduction.

Physiologic Variable	Pref. Order	Channel Variables
Diastolic Blood Pressure (DAP)	1	ABPd
	2	ARTd
	3	UAPd
	4	NBPd
Heart Rate	1	HR (EKG)
	2	HR from ABP
	3	HR from CVP
	4	HR from LAP
	5	HR from UAP
	6	HR from FEM
	7	HR from SpO2
	8	HR from Pulse
	9	HR from an external device
	10	HR from NBP
Mean Blood Pressure (MAP)	1	ABPm
	2	ARTm
	3	UAPm
	4	NBPm

Physiologic Variable	Pref. Order	Channel Variables
rSO2 (from NIRS)	1	StO2
	2	StO2_l
	3	StO2_r
	4	rSO2-1
	5	rSO2-2
	6	rSO2-3
	7	rSO2-4
RFP (Right Filling Pressure)	1	RAPm
	2	CVPm
Respiratory Rate	1	Airway RR
	2	Resp
SpO2	1	SpO2
	2	SpO2_l
	3	SpO2_r
	4	SpO2-pr
	5	SpO2-po
Systolic Blood Pressure (SAP)	1	ABPs
	2	ARTs
	3	UAPs
	4	NBPs
Temperature	1	Temp (core)
	2	Temp (rectal)
	3	Temp (esophageal)
	4	Temp (nasopharyngeal)
	5	Temperature
	6	Temp (skin)
	7	Temp (oral)
	8	Temp (brain)

Physiologic Variable	Pref. Order	Channel Variables
	9	Temp (blood)
	10	Temp (myocardial)
	11	Temp (airway)
	12	Temp (urometer)
	13	Temp (tympanic)
	14	Temp (axillary)

Table 41: Measure Synonyms

The measure synonyms table (see t_MeasureSynonyms, p. 70) shows the configuration of the physiologic variables and channels for the application.

4.17. Display of Laboratory Results

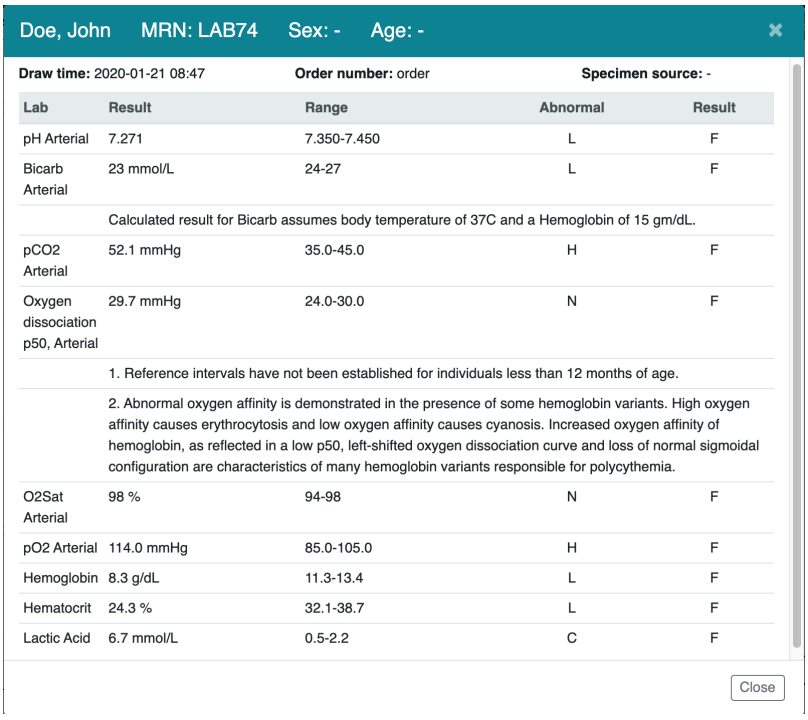

Figure 36: Additional information about a lab result

Lab results can be graphed by dragging the lab label from the Lab panel of the Measures Dashboard and dropping it onto the Central Graphs Area. Results are shown as discrete data points. If you click a lab on a

graph, information about all the labs in the panel associated with the plotted lab will be displayed. The information shown includes the lab names, the time taken, reference ranges of expected results, the actual results, and any applicable abnormal status flags (see f_lab_result, p. 72). The lab names displayed will be specific to the hospital's naming conventions, not the standardized labels.

4.18. Fluid Balance - Ins and Outs

Etiometry displays fluid intakes and outputs with other contextual physiologic data on the Patient View.

An additional tab is presented on the measure dashboard label I/Os, which displays net fluid balance over the timeframe displayed on the Patient View.

Figure 37: fluid_balance_dashboard

In addition to the total fluid balance, all the contributing inputs and outputs are displayed and available to be trended on the Central graphs.

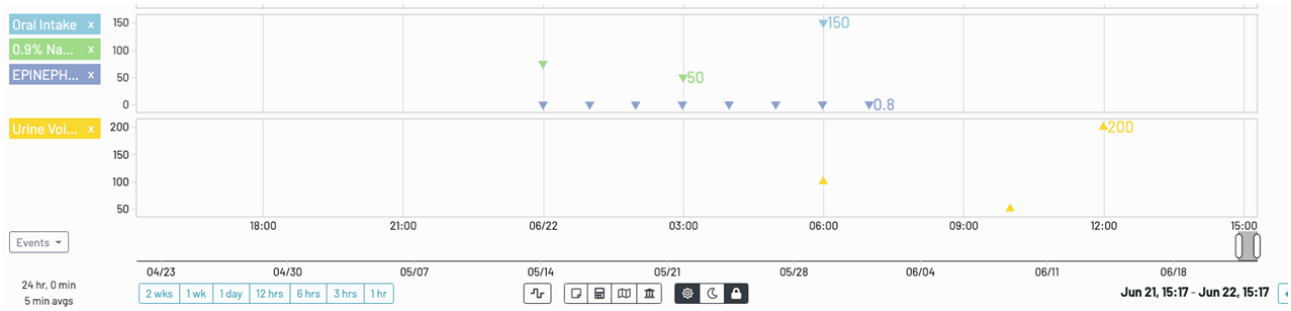

Figure 38: inputs_outputs_plots

4.19. Medications

Etiometry displays medication infusion rates with other contextual physiologic data in the Patient View. Medication infusions are shown as weight-normalized doses, which can be trended with other parameters.

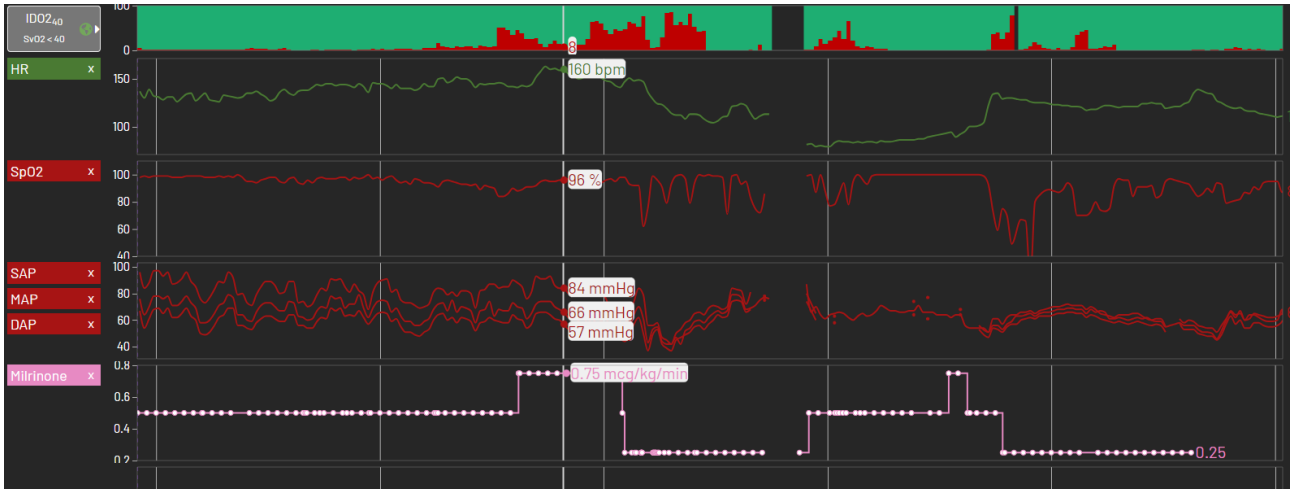

Figure 39: medication_plot

Certain subsets of medications can also be grouped. For example, Etiometry has a default measure group that shows a stacked graph representation of a patient's vasoactive medication support.

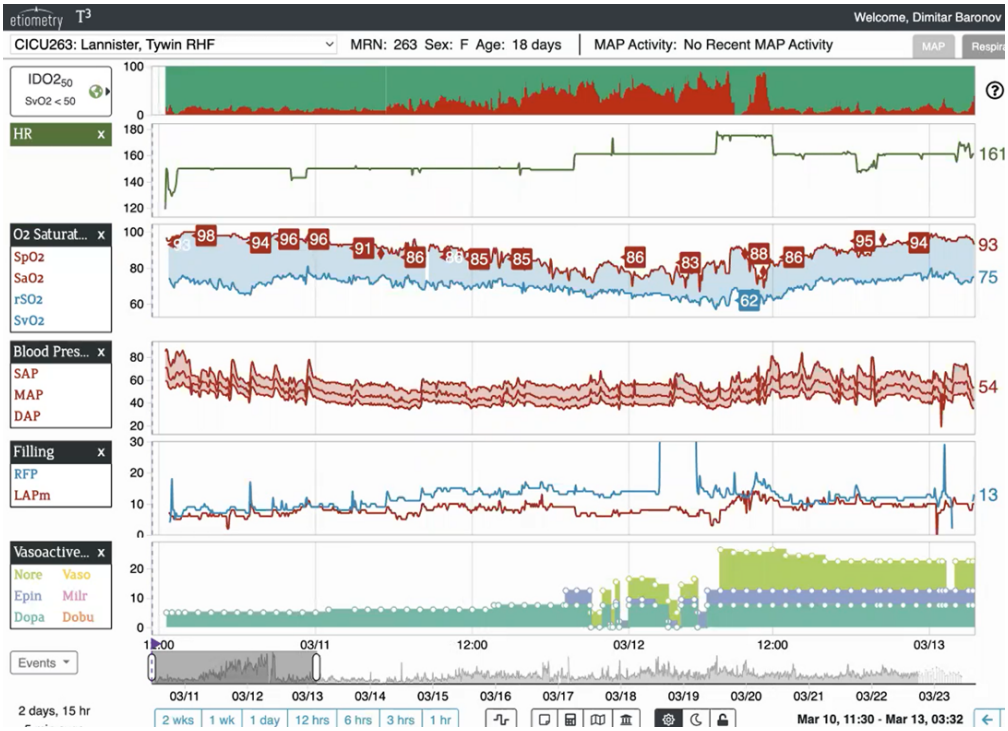

Figure 40: vasoactive_group

4.20. Contextual Waveform Visualization

Waveform signals can be viewed in Etiometry from the Patient View. Select the wave icon from the toolbar and click on a period of interest on the Central Graphs. This will raise a modal view that shows all available waveform data for that patient surrounding the selected time.

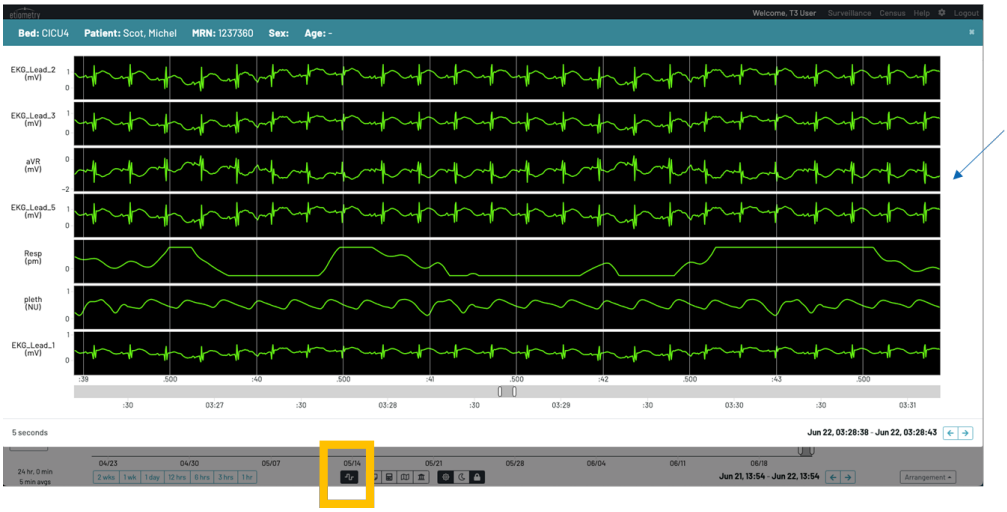

Figure 41: waveform_modal

4.21. Navigation

Figure 42: Time Navigation Bar

The Time Navigation Bar is located below the Central Graphs Area and allows the user to zoom in and out of the data (see f_timeNavigationSlider, p. 76). The data displayed on the Central Graphs Area can span as little as one minute and as long as two weeks. By dragging either end of the **Time Navigation Slider**, the user can extend or condense the time range of data displayed. The user can change the amount of time being graphed using the various zoom levels (e.g., 2 weeks, 1 day, 6 hours, etc.). The user can drag the slider horizontally to pan across a consistent time range. The user can pan across the Central Graphs Area to move the graphs forward or backward in time. Another way to pan through time is by clicking the forward and back arrows to jump forward or backward by the amount of time currently displayed.

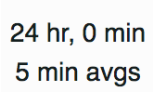

Figure 43: Data resolutions

Normally, four different data resolutions are available to be displayed: 5 seconds, 1 minute, 5 minutes, and 30 minutes. The application receives data points at 5-second intervals. Hence, the 5-second resolution is the raw data the application receives from the bedside monitor. If, for instance, a one-minute resolution is displayed, the average of 12 raw data points forms one data point. The application automatically selects the best resolution to display based on the selected timeframe by the user. The shorter the timeframe, the higher the resolution of the data displayed. The current resolution is displayed at the lower-left corner of the Time Navigation Bar (see f_dataResolutions, p. 77).

> **Note:** Not all physiometric sources can send data at 5-second intervals, and the application will then use the highest frequency available from the physiometric source.

4.22. Dashboard

For a complete list of measures displayed in the application, refer to the *List of Common Measures,* Common Laboratory Results, and *Clinical Calculations* in the Appendix. The software is an expandable platform and will allow more variables to be displayed as this data becomes available.

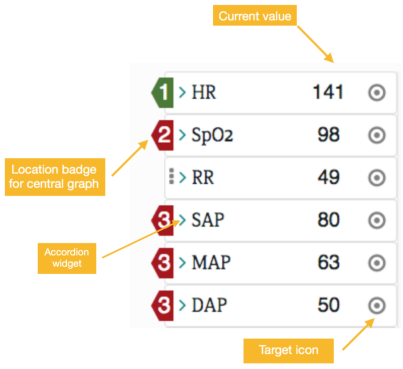

Figure 44: Measures Dashboard

The area on the right-hand side of the Patient View holds physiology measures for the current patient collected by the bedside monitor (e.g., heart rate, respiratory rate, and oxygen saturation; see f_measuresDashboard, p. 77). The data will automatically be captured, stored, and displayed in the application if a new lead is attached to a patient. A measure's current value is shown next to its abbreviation.

Some measures, such as pulse width, are derived from other measures, called clinical calculations, and appear exactly like ordinary measures. If a measure is not displayed on any central graphs, the user can drag the measure from the Measures Dashboard to the Central Graphs Area. If a measure is already graphed, a badge appears on the left side of the measure in the Measures Dashboard, indicating the placement and color of the measure on the Central Graphs Area. Subsequent sections of this user manual explain each element of a measure shown in the figure above.

When data is received from one or more vendor source variables, their corresponding channel and physiologic variables are also shown on the Measures Dashboard. The measure synonyms are grouped on the Measures Dashboard. You can click on the measure synonym to expand the hierarchy and then drag any related variables (physiological variable, channel variable, or vendor sources) to the Central Graphs Area to display them.

4.23. Encounters

Figure 45: Encounter arrow badges

Patient location history during their stay in the ICU is tracked through Encounters (see f_encounterArrowBadges, p. 78). An Encounter is a block of time determined by the entry and exit of the patient in a specific bed. Encounter start and end times will be denoted on the Patient View with dashed lines on the Central Graphs Area and Time Navigation Bar. In addition, the Encounter lines on the Central Graphs Area will be labeled with a triangle, pointing to the right, indicating entry into the unit, and left, indicating an exit. The triangle icon can be clicked to view more specific information on the Encounter. A chronological list of Encounters can be found in the patient's History tab.

4.24. Targets

The application allows users to manage and track patient physiometric data trends against customized target ranges or standard range sets.

> **WARNING:** The application does not replace the bedside monitor auditory alerts, alarms, or warnings. While the application displays Targets set by the clinicians, clinicians must use primary monitors appropriate for those indications, which appropriately alert, alarm, and warn.

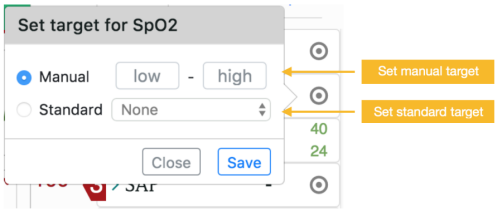

Figure 46: Set targets

You set a target range for a measure by clicking its bulls-eye icon in the Measures Dashboard. This brings up the "Set target" dialog (see f_setTargets, p. 79). In the dialog, you can:

1. Enter the low and high Targets and save them by clicking the Set Target button. Creating Targets with this method is called setting manual Targets or
2. Select a Target range from a set of common predefined Targets. Click on the "standards" drop-down to select an appropriate Target range for this patient.

Once targets are set, the application will monitor this measure against the target range and display indicators when the physiological variable drifts outside the desired range (see section *Out of Range Measure)*. Targets for a patient are global and immediately displayed for all other users viewing that patient. This feature is known as a **Global Feature**.

To remove Targets, click on the Target values, select "Remove Target," and click the "Save" button. To assist the care team in communication, the dialog shows the last user to change this measure's Target. The Patient History tab records the time, date, and name of the clinician making changes to the Targets.

Targets cannot be set on laboratory values and will not show on parameters when displayed as part of a measure group.

4.25. Out-of-Range Measures

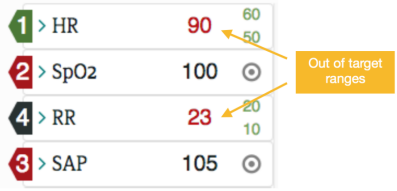

Figure 47: Out of range

After the user sets Targets on a measure via the manual or standard method, the application tracks how the patient fares against the Targets (see f_outRrange, p. 80). For instance, when the current value of heart rate drifts outside of the desired range, the current value in the Measures Dashboard becomes red and italicized to emphasize that it has fallen outside of the Target range. Furthermore, if the measure is on a central graph, the application applies colored shading between its value and the Target range to show how far it has drifted. The shading on the central graphs appears only when a measure drifts out of its desired range.

4.26. Measure Statistics

Figure 48: Statistics button

Basic statistics about the measures currently on the graphs can be calculated over a specific range. When clicking on the Statistics button on the toolbar, the tool will calculate statistics for all measures on the Central Graphs Area for the current period (see f_statisticsButton, p. 80). Selecting the Statistics button option will open the baseline dialog.

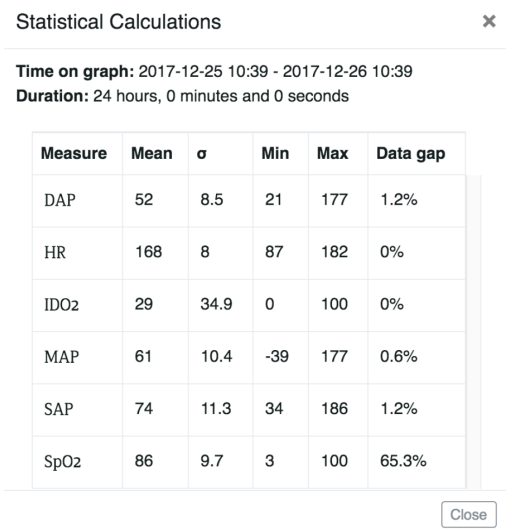

Figure 49: Calculating statistics

The application can use the selected period to calculate key statistics for all measures that are graphed (see f_calculatingStatistics, p. 81). The application generates statistics for all graphed measures containing averages, standard deviations, minimums, maximums, and data gap percentages. A data gap percentage is the time in the selected range where data were not collected for the patient. For example, if a patient's heart rate lead was disconnected for one hour in four hours, the data gap percentage is 25%.

4.27. Events

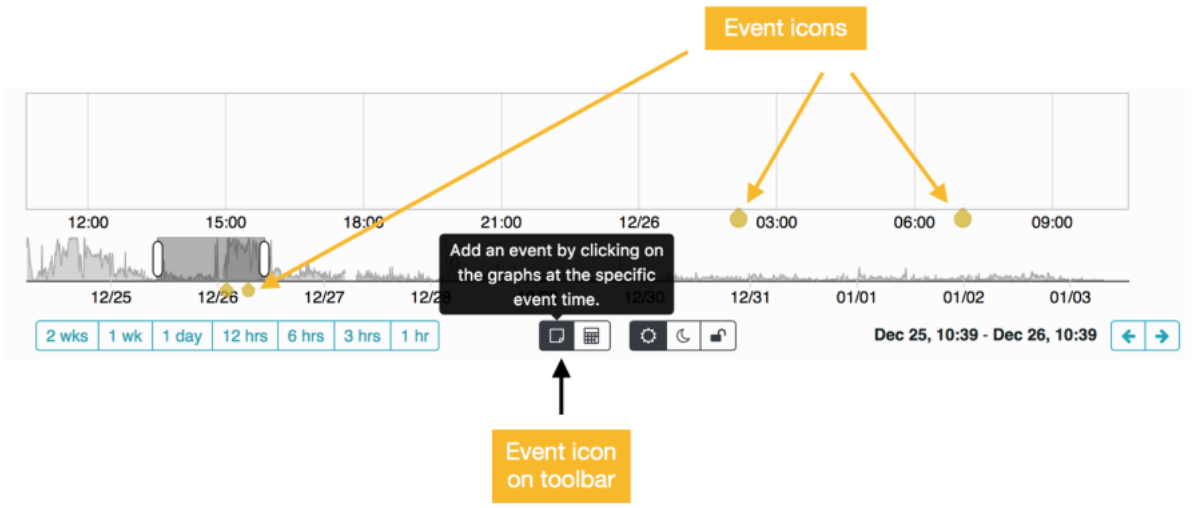

Figure 50: Annotate an event

The application lets the user create customized annotations for the patient to record events and decisions. The user clicks the Event button on the toolbar and then clicks on the Central Graphs Area on the Patient View, bringing up the "Event" dialog (see f_annoEvent, p. 81).

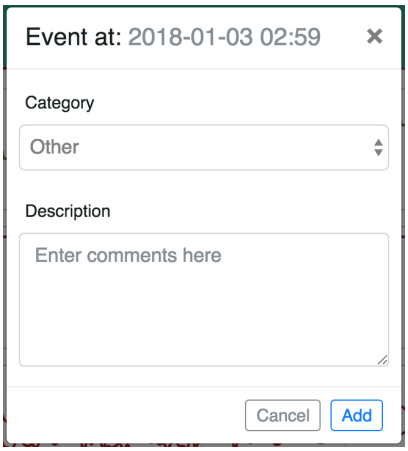

Figure 51: Add an event

In the dialog, the user selects a category from a list of common categories and can enter a description of the event (see f_addEvent, p. 82). After the user saves the Event, it will be added to the point where the user prompted the add event dialog. Events are displayed as icons below the Time Navigation Bar. The user can click on an existing Event icon to view or append it. As with setting targets, creating Events is a Global Feature; all users can see all Events for a patient.

4.28. Y-Axis Control

When you graph a measure or laboratory result in the application, each point on the graph represents a value at a moment. The item's value is represented on the Y-axis, and a point in time is represented on the X-axis. By default, the application selects "auto-select" as the range for the Y-axis. Auto-select means that the application will calculate a Y-axis range so that the minimum and maximum data values for the specified period will be shown on the graph.

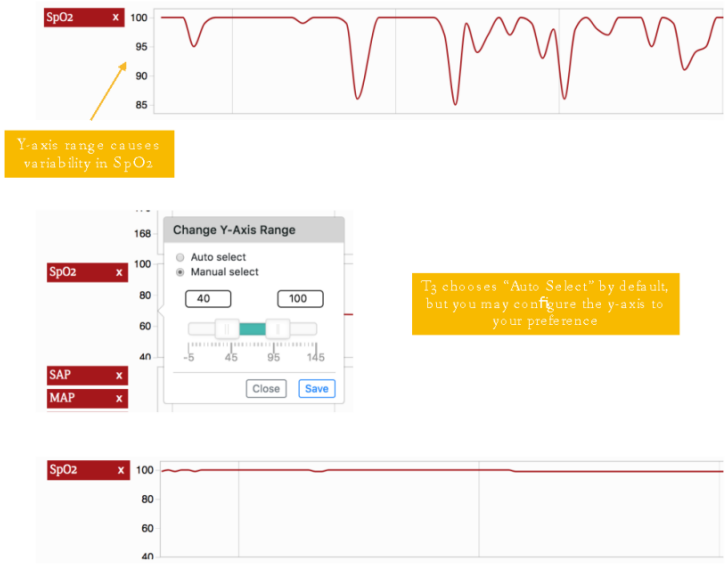

Figure 52: Custom Y-axis ranges

The application enables users to select **custom Y-axis ranges** by hovering and clicking on the Y-axis range of a graph and using the sliders to select a new range (see f_customYAxisRanges, p. 83). Y-Axis ranges can be configured to automatically adjust the scale based on patient age for any of the "Group" measures (discussed in section 4.8) found on the Custom screen. These are not delivered with any configurations and must be reviewed to be implemented. Unlike targets and Events, the user's choice of Y-axis range is not a Global Feature and only affects the user's view of the patient.

> **Note:** Auto-select works well for most measures, but for a select few, like oxygen saturation and SpO_2, clinicians may want to view the data using a different Y-axis. Because variations in oxygen saturation are usually very small, the auto-select range results in a Y-axis range where a small change in SpO_2's value may be depicted on the central graph with a significant dip or spike. This may be alarming if the user doesn't notice the range on the Y-axis. When SpO2 is graphed in a central graph by itself, the application will choose a Y-axis range of 40 to 110. In all other situations, the application will choose auto-select by default.

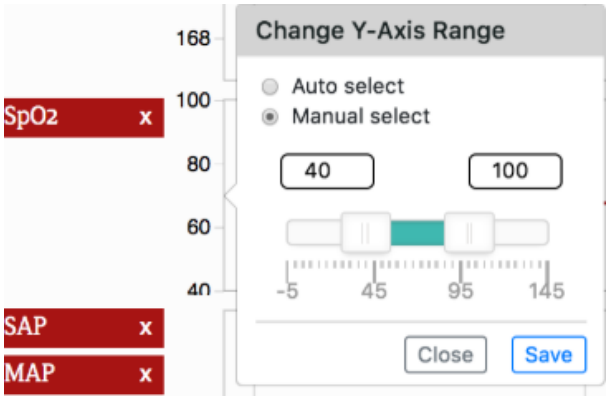

Figure 53: Change Y-Axis Range

To change the Y-axis range (see f_YAxisRange, p. 84), click on the Y-axis values on the left-hand side of the graph. Select "Manual select" and drag the sliders, or manually enter values to set a new minimum and maximum. Click "Save" to save your choice. Select "Auto select" to return to an automatically determined range.

4.29. User Arrangement

The user's choice of Y-axis control setting is saved as a **User Arrangement**, which the application defines on a per-user and per-patient basis. It is important to know the distinction between User Arrangements and Global Features. User Arrangement changes are only displayed for the user and no one else, whereas Global Features are shown for all users. Furthermore, no matter which computer the user logs into the application on, their unique personal arrangements are saved for each specific patient where arrangements are set. In addition to Y-axis control, User Arrangements also save the measures on the Central Graphs Area.

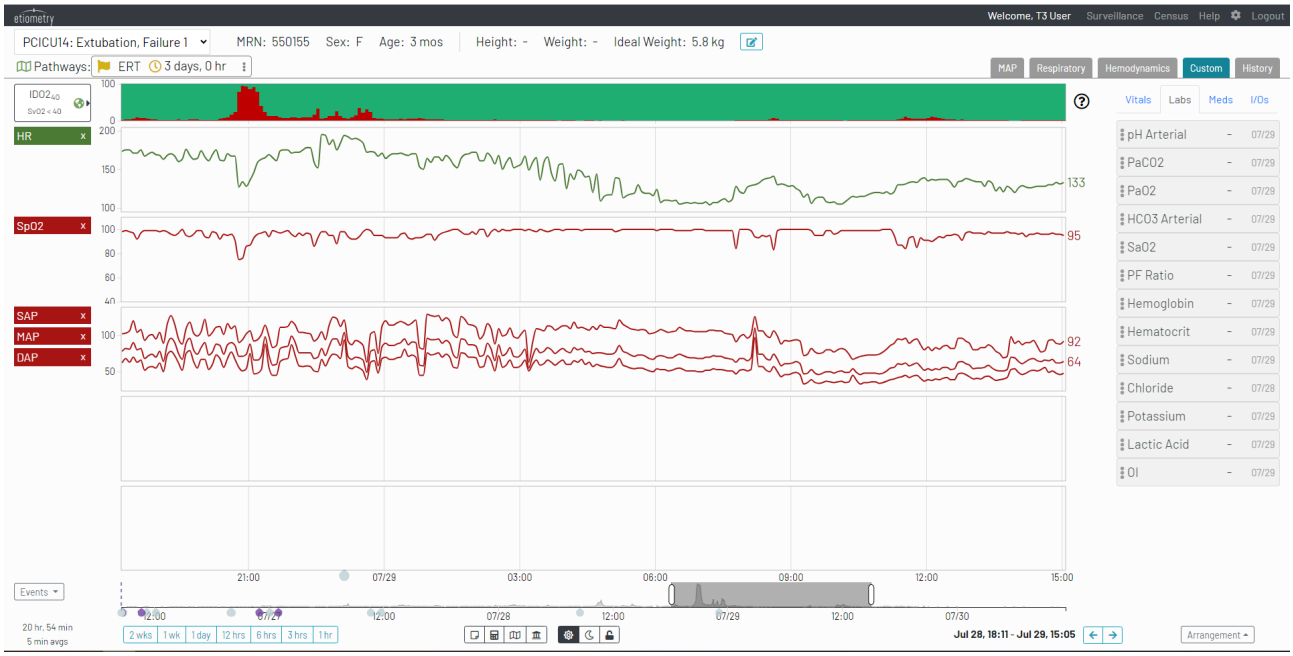

Figure 54: Default arrangement of Custom View

The default User Arrangement is loaded the very first time the user navigates to a Patient View (see f_defaultArrangementCustom, p. 85). For example, the default arrangement might place heart rate on the first central graph, oxygen saturation on the second, and the three pressures, systolic, mean, and diastolic, if available, on the third central graph. The Y-axis control for all graphs might be set to auto-selected. A message appears on the application's bottom right corner when the default arrangement is shown. When the user adds or removes a measure on the Central Graphs Area, rearranges the Central Graphs Area ordering, or changes the Y-axis control, the user's arrangement is saved. The user's preferences form their User Arrangement for the current patient only. The default User Arrangement will be loaded if the user navigates to a different patient not previously viewed. However, if the user returns to the previous patient, their User Arrangement will be loaded for this patient. Each Y-axis in the Central Graphs Area is individually configurable, whereas the top graph of the algorithm is not configurable and is fixed from zero to one hundred.

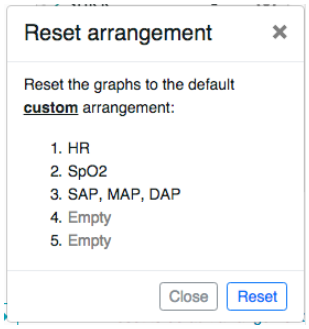

Figure 55: Default arrangements

On the bottom right corner of the application, the application displays a label that restores the Patient View to the default arrangements (see f_defaultArrangements, p. 85). Clicking this label displays a confirmation dialog to verify that default User Arrangements should be restored.

Each unit has a globally set default arrangement, but users can update this configuration to set a personal default arrangement. This personal default arrangement behaves the same way as the global default - if the user sets a patient-specific arrangement, that will be maintained whenever that patient is viewed.

To set a personal default arrangement, (1) select a patient from the Census view to (2) display their Custom View. (3) Drag and drop parameters into the appropriate visualization field, (4) select the "Arrangement" icon in the lower right, and select the "Update" option. This will save the current arrangement as the user's new default.

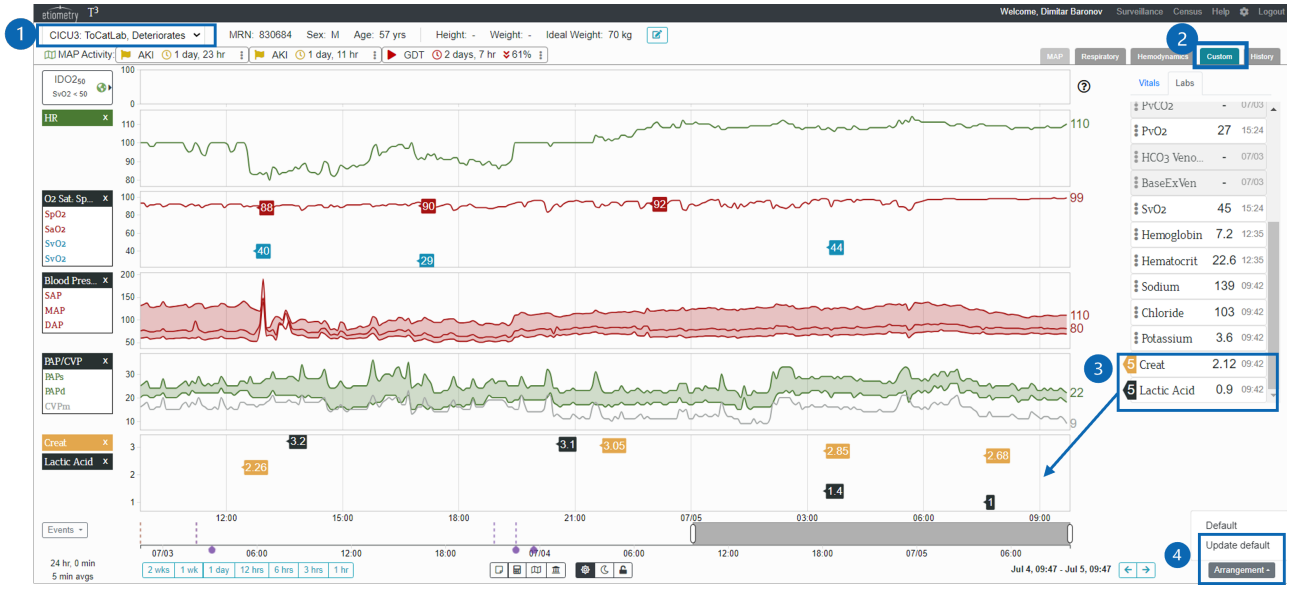

Figure 56: custom_default

The default arrangements are unit-specific. So, if the user can access multiple units, they can set different defaults depending on the unit. If the user wishes to review their default views or revert to the site's global default, they can do so from the User Preferences dialogue.

4.30. Patient History

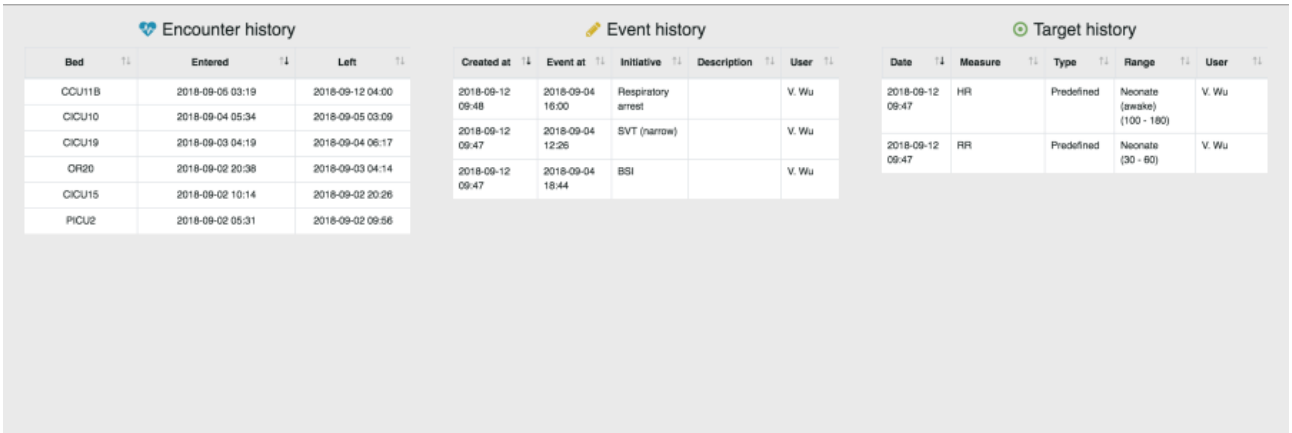

Figure 57: Patient history

The application keeps a history of all global actions performed on a patient (see f_patientHistory, p. 87). All Targets and Events are recorded within the **patient history**. Clicking on the "History" tab will open the patient's history, consisting of Encounters, Events, and Targets recorded for that patient. The Events history list contains the time an event was added or modified, the initiative, and the user who created the event. The Target history list contains standard, manual, or removed targets. The History tab will also contain a chronological list of the patient's Encounter history, detailing when they entered and exited their previous units.

4.31. Archive View

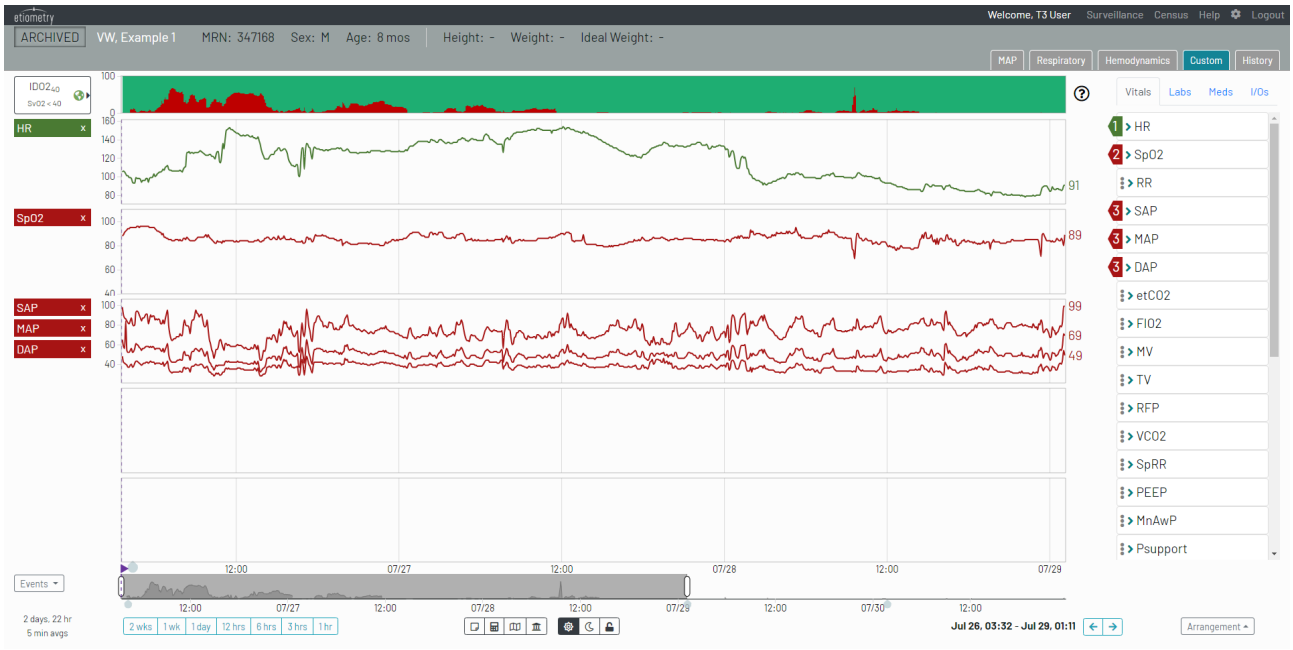

Figure 58: Archive view

The Archive View presents patient data for retrospective analysis like those for active patients. All functionality available for an active patient is available in the Archive View (see f_archiveView, p. 88). Zooming and statistic calculation functionality are enabled.

4.32. Nighttime Display

Figure 59: Dark background at night

The application has application-wide configuration settings that specify when "nighttime" starts and ends (see f_darkNight, p. 89). For example, nighttime can be defined as starting at 7 PM and ending at 7 AM - or whatever times are desired. When the application runs "at night," it recognizes that it is night based on the system clock and automatically uses a dark background when showing the Patient View. This reduces the ambient light the application monitor emits, promoting a restful environment for the patient if the application is displayed in their room. When it runs during the day, the application similarly recognizes that it is day and automatically uses a light background. Depending on site-wide preference, night-time display either is limited to the Persistent Display mode or applies to both Persistent Display and individual user modes.

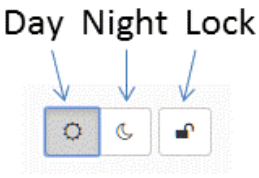

Figure 60: Nighttime Display Buttons

It is also possible for individual users to manually override the **Nighttime display** function (see f_nighttimeDisplayButt, p. 89). At the bottom of the Patient View screen, the application has three buttons that let the user manually control night mode. A sunshine button makes the background light, and a moon button makes the background dark. A lock button toggles between locked and unlocked.

When locked, the setting of the sun or moon takes precedence. These buttons let the user run a light background at night or a dark background during the day - whatever the user selects. When unlocked, the time of day takes precedence. For example, if a Persistent Display monitor runs unlocked, it will switch backgrounds without the user having to do anything. However, if they desire, a clinician can switch to light or dark modes using the sun or moon buttons and lock their choice in. The application will continue with the background of choice until the button is unlocked, the user changes patients, or logs off.

4.33. Teaching Census

While real-time observation of patients can create good learning opportunities, more complex patients require deeper introspection to understand etiologies and treatment strategies better. The Teaching Census allows clinicians to create case reviews (“Teaching Census Cases”) from patients monitored using the application. Teaching Census cases are stored, de-identified, and then presented in a format conducive to case presentation and training. The Teaching Census allows clinical leaders to identify opportunities to use targeted training for continuous improvement. Click on “Add Case to Teaching Census” to start the case review creation workflow.

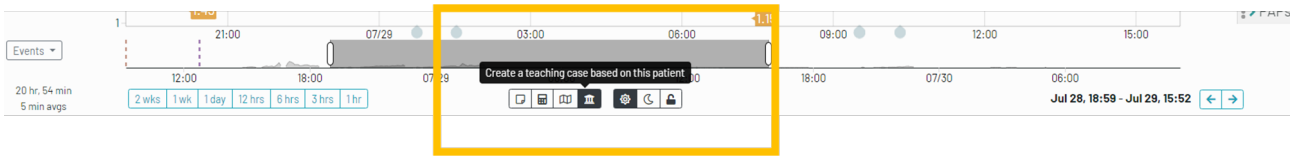

Figure 61: Adding To Teaching Census

Teaching Census will then walk through the necessary steps to create a Teaching Census case:

Create the Teaching Census Case Profile. Fill out the following information to describe the case

- Case Title: The title for the Teaching Census case
- Diagnosis: Patient diagnosis (diagnosis as it relates to the case). If the diagnosis does not appear in the list, you can add a diagnosis
- Key findings: Important notes related to the case (e.g., What was learned? What could be improved?)

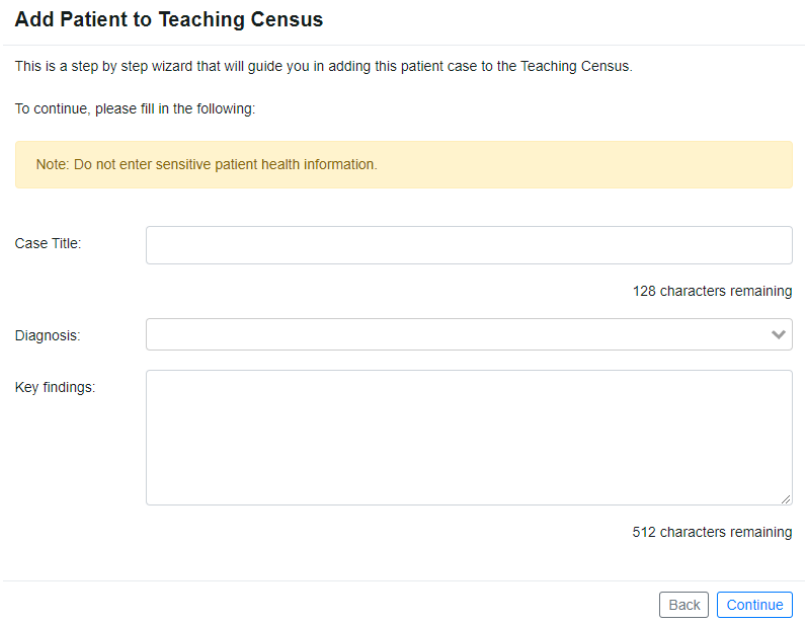

Figure 62: Create the Teaching Census Case

Set Desired Time Range. Frame the start and end times of the case. Please note that the maximum timeframe for Teaching Census cases is two weeks. Update the graphs to select the desired time range and click “Next” when you are finished to confirm your selection. The time range shown on the graphs will then be used.

Set Measure Arrangement. Select the desired view in the upper-right-hand corner of the Patient Dashboard and set the graphs with any measures, labs, or groups. This will then be the default arrangement seen for the Teaching Census case. Click “Next” when you are finished to confirm your selection.

Create Event Sequence. Create a chronological sequence of events for the Teaching Census case. Use the Event tool in the bottom center of the page to annotate events. Existing Events can be added to the Event Sequence by selecting the desired event and “Add to Event Sequence.”

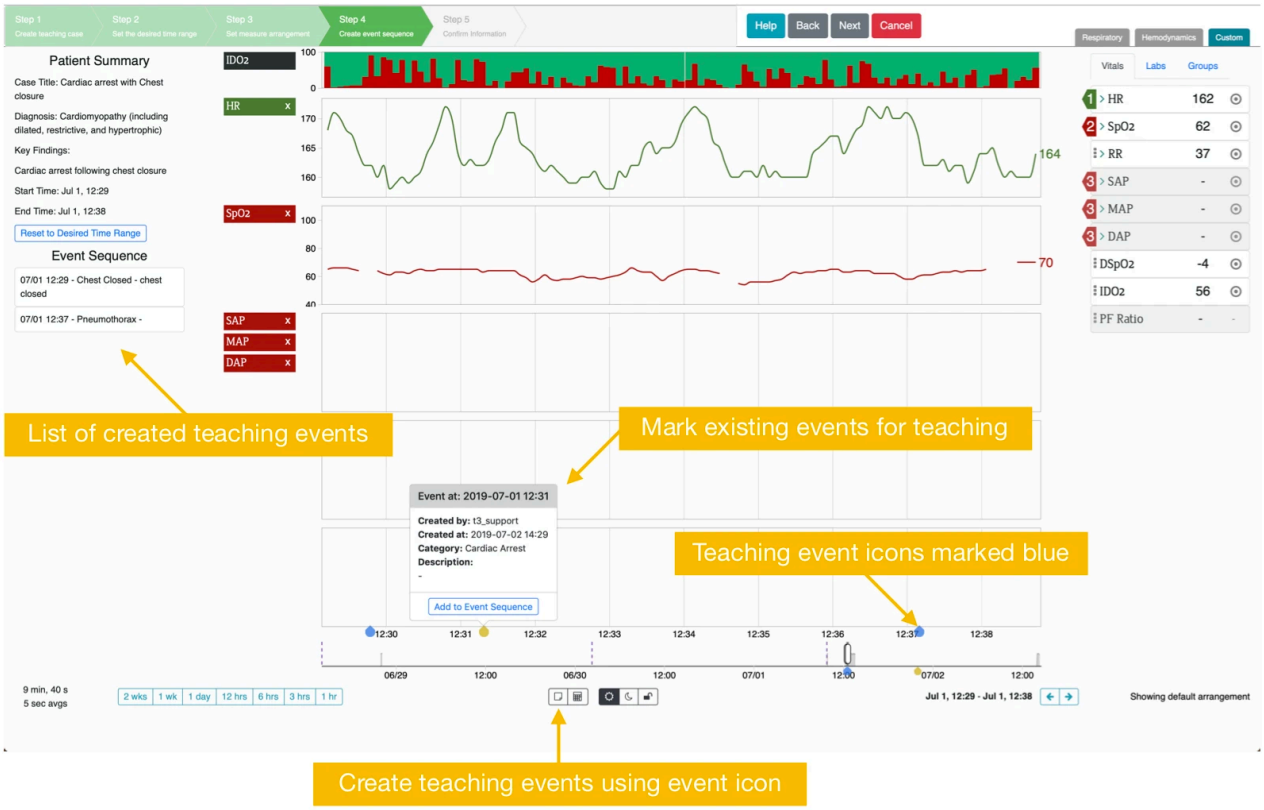

Figure 63: Event Sequence

The event timeline will be listed under “Event Sequence.” Events can be updated and deleted from the event timeline by selecting them here.

Verify Information. Confirm all information and click “Submit”.

Teaching Census cases can be accessed via the Census Overview page. Select the “Teaching” tab to view all existing Teaching Census cases. To select a specific Teaching Census case, click the Case Title.

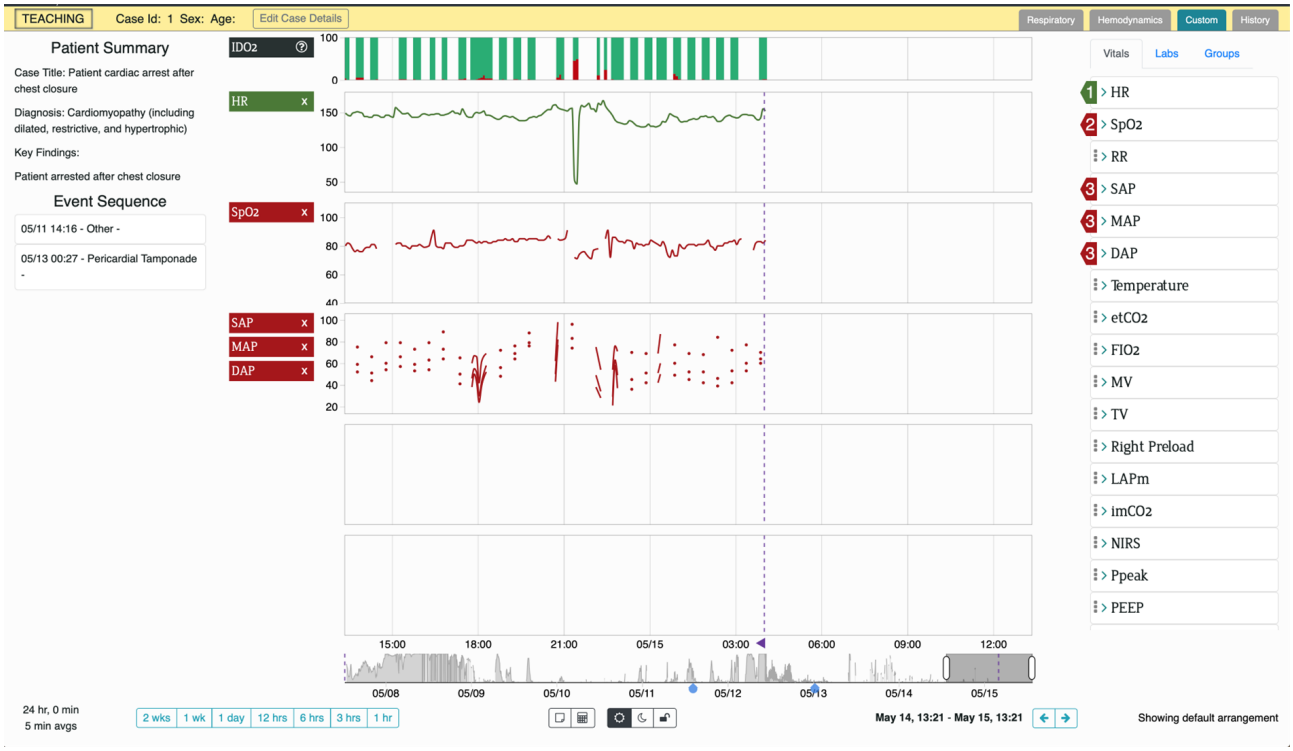

Figure 64: Viewing a Teaching Case

Any graph arrangements, not the default graphs, will not be saved upon leaving the current Teaching Census case.

To protect patient information, the Teaching Census case will not display the original patient's demographic information, except for the patient's age. The patient's data will also be day-shifted for a random number of days.

Users must have the Etiometry Platform Clinical Educator access level to create and edit Teaching Census cases. The Teaching Census case summary and patient timeline events can be modified after case creation. If you believe you should have this level of access, please get in touch with your administrator.

4.34. Surveillance View

The Surveillance View is a tool to view the ICU patients' status on one central display. The tool supports interpreting trends for selected variables, understanding the trajectory of patients, and supporting bedside clinicians in their decision-making.

4.34.1. Default View

For each bed in the ICU, the bed number is displayed along with the last name and age of the patient in that bed. This tool differs from the Census Overview by displaying the most recent vital signs and algorithm values for each patient in tiles containing graphs instead of a table of rows. The Surveillance View can be filtered by unit, similar to the Census Overview, by clicking the unit dropdown in the top right corner. Beds

may also be filtered by searching by unit, bed number, MRN, or first and last name. Clicking on a Surveillance tile will navigate the user to Patient View for that particular patient.

White tiles with patient demographic information and graphs indicate a bed with a patient currently receiving data. These boxes can be clicked to navigate to the Patient View for that particular patient. The pathway summaries presented in each tile can be interacted with similarly from the Census view (see Clinical Pathways below). Grey tiles with patient demographic information indicate beds where patients are not receiving data. These may also be clicked to navigate to the Patient View. Blank grey tiles indicate beds with no current patient. There is no interaction with these blank grey tiles.

Figure 65: Surveillance View display

Each Surveillance tile will show the previous 12 hours of data by default at a time resolution of 5-minute averages. This information can be seen at the top of the page beside the search bar. This can be configured to your desired time window and resolution by contacting Etiometry Support. The timeframe can be altered to 24, 12, 6, 3, or 1-hour increments within the Time Window filter. Default measures for the tiles will display the IDO2 algorithm, Heart Rate, SpO2, and MAP. The measure arrangements can be set on a per-unit basis and can be configured by contacting Etiometry Support.

Each graph will display that particular measure's most recent current value in the 'Last' column. Each graph will also show the low and high values of the y-axis to provide more context for the displayed graph. These values will update accordingly when new averaged values are drawn onto the graph.

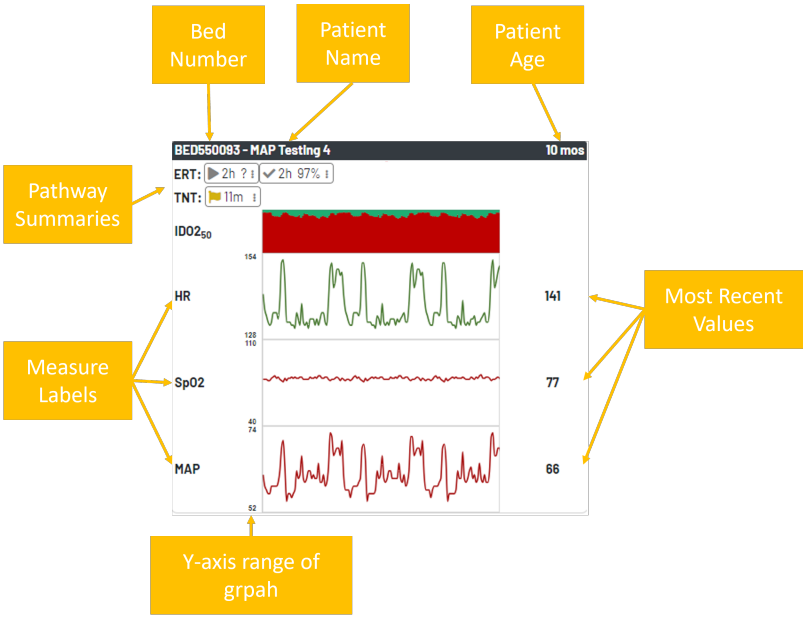

Figure 66: Surveillance View Patient Tile

The tiles will dynamically resize based on the number of tiles shown on the screen, and if an entire row of beds is empty, that row will collapse to show the header rather than populate the row with empty tiles.

4.34.2. Waveforms View

The Surveillance View has a Waveform View, which presents streaming waveforms for the beds being monitored on the view. The tiles present two streaming signals and four numeric values that update as they are streamed from the monitoring system. The default is to show an ECG trace, the Pleth wave, and HR, BP, SpO2, and RR.

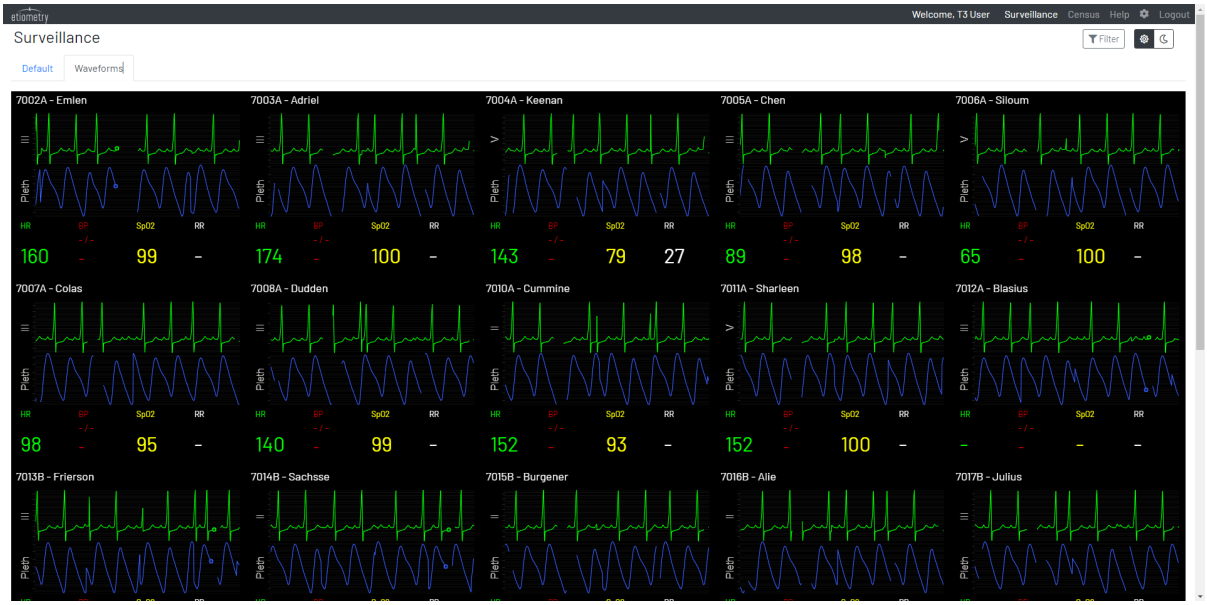

Figure 67: Surveillance View Waveforms display

The tiles display a fixed time window, and the displayed beds can be controlled through the Filter dialog. The presented measures are configurable on a site-wide basis. This view is only enabled if the site has waveform connectivity configured for Etiometry.

> **Note:** Streaming depends on the available resources of the end-user device. Limited resources can result in degraded visualization. To alleviate visualization issues, ensure the device meets the minimum client specification in the Technical Manual, minimize the number of other applications running on the system, and reduce the number of beds using the Filter dialog.

4.35. Clinical Pathways

Clinical Pathways assist clinicians in following and applying their protocols for patient care. Pathways allow the application to host protocols defined and implemented by institutions and ICUs, which leverage the application's existing functionality of Targets and User-defined arrangements. Pathways support protocols that consist of data-driven eligibility and compliance criteria.

Pathways will only be active at sites with defined protocols; no default definitions are available. For a full summary of the available configuration options, see the Technical Manual associated with this release.

Pathways continuously and automatically screen all patients and identify those who have met protocol eligibility criteria defined by the specific protocol on both the Census View and the Patient View. Flagged patients display a timer on the Census View of how long criteria have been met. If a patient complies, the Pathway measures will appear green (see legend). If the patient is out of compliance, Pathway measures will

appear red. Multiple Pathways can be embedded simultaneously. Clicking on the ellipsis will allow the user to choose between several actions.

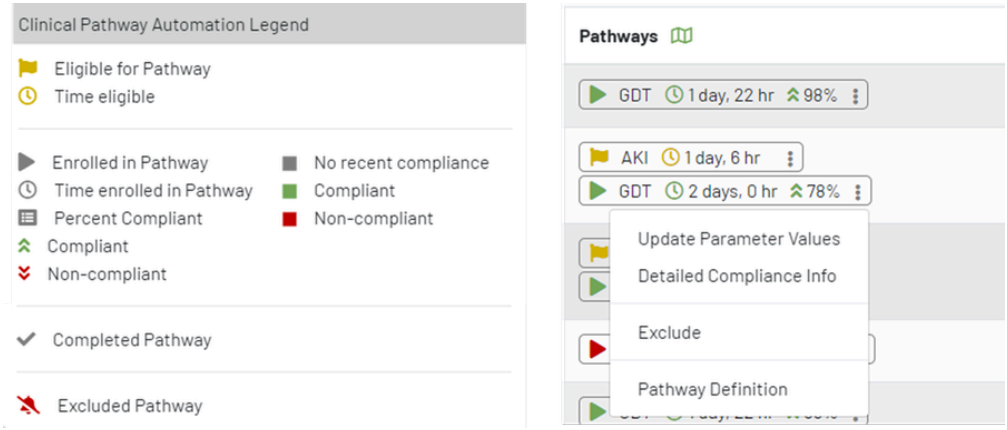

Figure 68: Clinical Pathway Activity

Update Parameter Values: When applicable, this will allow clinicians to update compliance parameters manually.

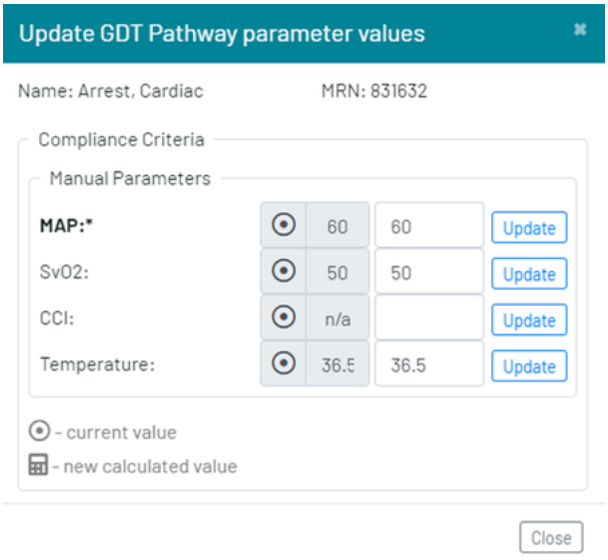

Figure 69: Update Parameters View

Detailed Compliance Info: This shows a quick summary of the period (per compliance criteria) when a patient was in or out of compliance.

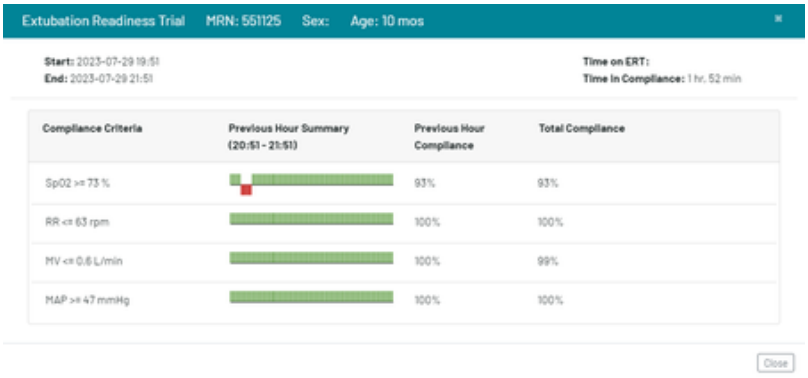

Figure 70: Detailed Compliance Screen

Exclusions: This allows the clinician to exclude the patient from protocol. The patient will not be tracked for eligibility or completion.

Definition: This brings the user to a specialized view that displays the parameters relevant to eligibility criteria for the protocol. The specific eligibility criteria, including default values, can be viewed by clicking the Pathway name on the census.

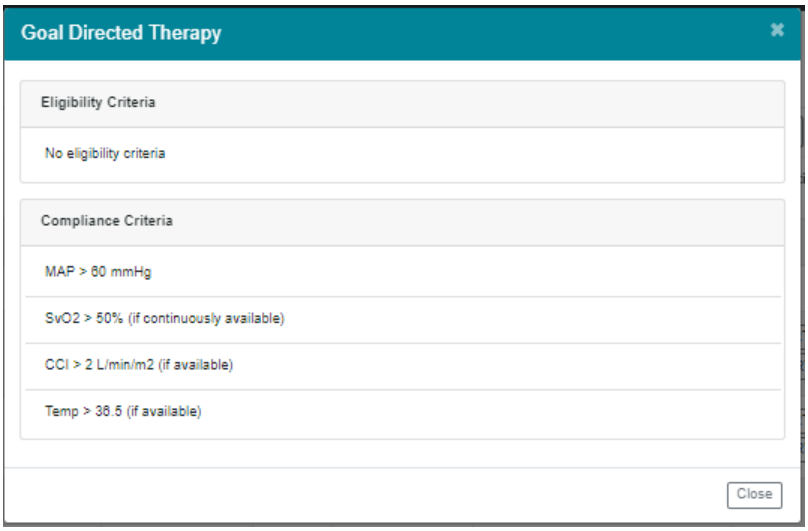

Figure 71: Definition View

There are two mechanisms for enrolling a patient in a Clinical Pathway: manual enrollment, where the user can click a start button in the UI or a triggered enrollment that uses a predefined set of activation criteria to enroll a patient. The Start button will bring up a dialog that prompts the user for any additional necessary information and allows for the adjustment of certain criteria. If the Pathway is started based on a set of predefined activation criteria, the Start dialog will still be available and allow for the adjustments of predefined criteria. Still, it will include a description of the activation criteria rather than presenting a clickable Start button.

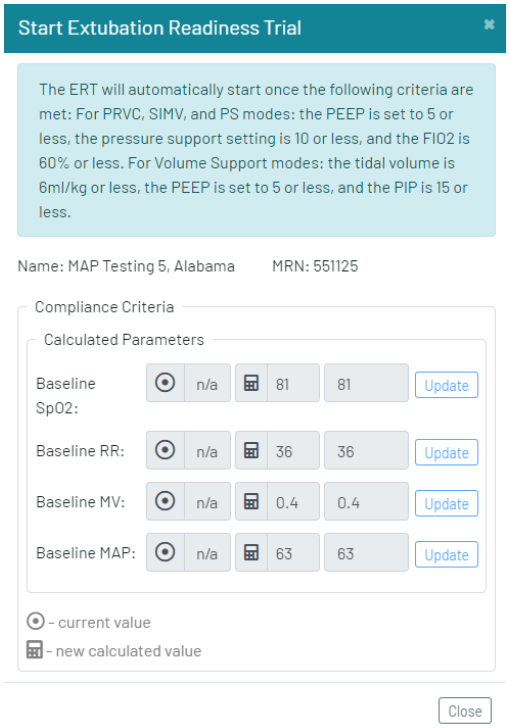

Figure 72: Example Start Dialog

Once a patient is enrolled in or has completed a Clinical Pathway, a summary of the enrollment period is presented on the Census View. An additional patient-specific Pathway View is available. This summary includes the duration for which the patient has been enrolled or was enrolled for a completed Pathway and their compliance as measured by adherence to all applicable compliance rules. The compliance criteria are available by clicking on the Pathway name. A user can click the summary values of an active or completed Pathway. They will be brought to the Pathway view, which will snap to the relevant period and visually show compliance using Targets.

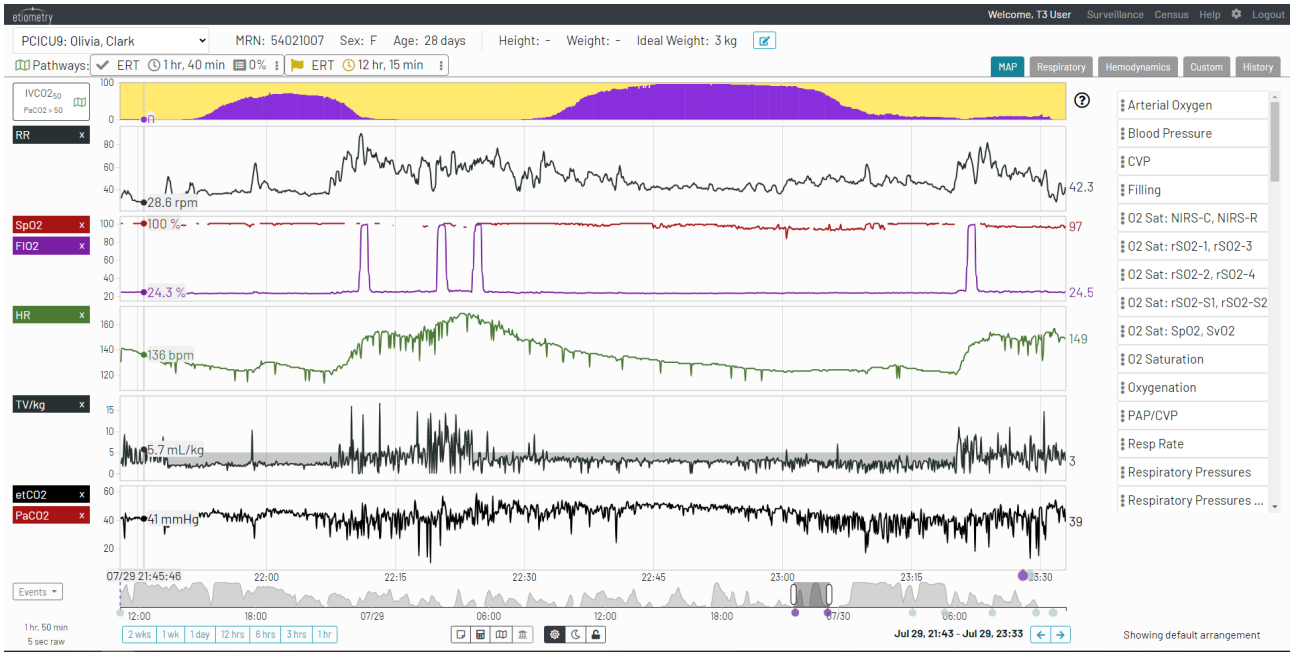

Figure 73: Patient Pathway View

Past Pathways can be reviewed by selecting the checkbox icon in the bottom center of the page. This dialog can also force enrollment in a protocol even if a patient is not currently flagged as eligible.

Figure 74: Pathway History

4.36. Persistent Display Mode

As noted in the "Modes of Operation" Section above, one of the ways the application can be viewed is on a dedicated monitor that shows data for a single location. The default operating mode of the Persistent Display is that any adjustments made to the arrangement on the default view are reverted after a configurable idle period. The view will revert to the default after the same configurable idle period.

Optionally, there is a mechanism to lock the Persistent Display to a custom arrangement on the Custom View. The action can be toggled on or off in the lower right-hand side of the screen. This allows users to set any desired default screens (including Pathway Views). An active Pathway can be a default (more meant for long-term Pathway). However, if the Pathway has been completed on the patient, the default screen will return to the global view screen defined during the implementation.

To set this, select the lock icon on the desired screen on which you would like to log back into the system. This will be the new default screen. If you want to change your default, go to the new desired default screen and select the lock icon again.

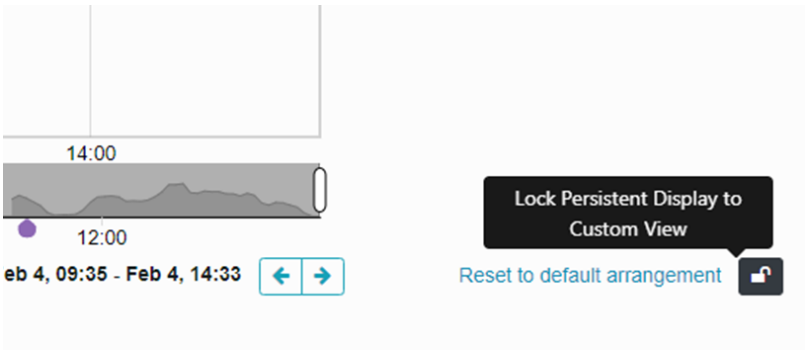

Figure 75: Persistent Display Lock

The User will be asked to authenticate this change because the Persistent Display View represents a shared configuration.

5. Support and Maintenance

If you cannot run the application or encounter a problem, please report it to your hospital Help Desk. They will ask you to describe the sequence of steps leading up to the issue so they can attempt to reproduce it.

If you are accessing your hospital network over a wireless connection, verify that you can access other websites. If you cannot, the problem may be caused by your network connection rather than the application.

Occasionally, you may notice differences in the application's functionality. The application is being enhanced, and new software releases are periodically installed on your hospital servers to correct problems or improve functionality.

6. Appendix

6.1. List of Graphical Icons in the User Interface

Description	Icon
Location Badge (appears on Measures Dashboard)	
Target icon (no targets)	
Target icon (with targets)	
Add Event (appears on the toolbar)	
Encounter – entry into the unit (appears on Time Navigation)	
Encounter – exit out of the unit (appears on Time Navigation)	
Event (appears on Time Navigation)	
Calculate Statistics (appears on the toolbar)	
Day Mode (appears on the toolbar)	
Night Mode (appears on the toolbar)	
Lock (appears on the toolbar)	
Clinical Pathways (appears on the toolbar)	
Create a Teaching Case (appears on the toolbar)	

Description	Icon
Waveforms (appear in the toolbar)	
Time Navigation Increment (appears next to display dates)	
Edit demographics (appears in the patient nav bar)	

Table 42: Application icons and graphics

t_appIconsGraphics, p. 102 displays icons and graphics for the application's features.

6.2. List of Common Measures

Abbreviation	Name	Units
ABPd	Arterial blood pressure (diastolic)	mmHg
ABPm	Arterial blood pressure (mean)	mmHg
ABPs	Arterial blood pressure (systolic)	mmHg
ARTd	Arterial blood pressure (diastolic)	mmHg
AR	Arterial blood pressure (mean)	mmHg
ARTs	Arterial blood pressure (systolic)	mmHg
CPP	Cerebral perfusion pressure	mmHg
CVPd	Central venous pressure (diastolic)	mmHg
CVPm	Central venous pressure (mean)	mmHg
CVPs	Central venous pressure (systolic)	mmHg
dSpO2	Difference between two SpO2 values (like Left-Right)	%
etCO2	End-tidal carbon dioxide concentration	mmHg
FiO2	Fraction of inspired oxygen	%
HR	Heart rate	bpm
ICPm	Intracranial pressure (mean)	mmHg

Abbreviation	Name	Units
LAPd	Left atrial pressure (diastolic)	mmHg
LAPm	Left atrial pressure (mean)	mmHg
LAPs	Left atrial pressure (systolic)	mmHg
MV	Minute volume	L/min
PAPd	Pulmonary arterial pressure (diastolic)	mmHg
PAPm	Pulmonary arterial pressure (mean)	mmHg
PAPs	Pulmonary arterial pressure (systolic)	mmHg
PB	Barometric pressure	mmHg
Peep	Positive-end expiratory pressure	cmH2O
Ppeak	Peak airway pressure	cmH2O
Pulse	Pulse	bpm
RAPd	Right atrial pressure (diastolic)	mmHg
RAPm	Right atrial pressure (mean)	mmHg
RAPs	Right atrial pressure (systolic)	mmHg
RR	Impedance respiratory rate	rpm
SpMV	Spontaneous minute volume	L/min
SpO2	Peripheral oxygen saturation	%
SpO2 l	Arterial oxygen saturation (left)	%
SpO2 r	Arterial oxygen saturation (right)	%
SpRR	Spontaneous respiration rate	rpm
Tcore	Core (body) temperature	°C
Temp	Temperature	°C
Tesoph	Tesoph esophageal temperature	°C
Trect	Rectal temperature	°C
TV	Tidal volume	mL
UAPd	Umbilical arterial pressure (diastolic)	mmHg

Abbreviation	Name	Units
UAPm	Umbilical arterial pressure (mean)	mmHg
UAPs	Umbilical arterial pressure (systolic)	mmHg
UVPd	Umbilical venous pressure (diastolic)	mmHg
UVPm	Umbilical venous pressure (mean)	mmHg
UVPs	Umbilical venous pressure (systolic)	mmHg

Table 43: Common measures

t_CommonMeasures, p. 103 lists common measures displayed in the application.

6.3. List of Common Laboratory Results

Name
Arterial blood gases
Venous blood gases
Hemoglobin
Hematocrit
Lactic acid

Table 44: Common laboratory results

t_CommonLab, p. 105 lists common laboratory results displayed in the application.

6.4. List of Clinical Calculations

Abbreviation	Name	Units	Formula (60-second averages used when data are not aligned)
PW	Pulse width	mmHg	ABPs – ABPd
CPP_LAP	Cerebral perfusion pressure	mmHg	ABPm – LAPm
CPP_RAP	Cerebral perfusion pressure	mmHg	ABPm – RAPm

Abbreviation	Name	Units	Formula (60-second averages used when data are not aligned)
CPP_CVP	Cerebral perfusion pressure	mmHg	ABPm – CVPm
CorPP_r	Coronary perfusion pressure	mmHg	ABPd – RAPm
CorPP_l	Coronary perfusion pressure	mmHg	ABPd – LAPm
CorPP_c	Coronary perfusion pressure	mmHg	ABPd – CVPm
RPP	Rate pressure product (myocardial oxygen demand indicator)	1000 mmHg*bpm	ABPs * HR / 1000
P/F	P/F Ratio	n/a	PaO2 / FiO2
S/F	S/F Ratio	n/a	SpO2 / FiO2
OI	Oxygenation Index	n/a	(FiO2 * Mean Airway Pressure * 100) / PaO2
OSI	Oxygen Saturation Index	n/a	(Mean Airway Pressure * FiO2 * 100) / SpO2
PRx	Pressure Reactivity Index	n/a	Pearson Correlation between ICP and MAP
PCI	ICP-PCO2 Compliance Index	n/a	Pearson Correlation between ICP and EtCO2

Table 45: Clinical calculations and their formulas

t_calForm, p. 105 contains clinical calculations and their formulas included in the application.

7. Glossary

Term	Description
Central Graphs Area	The configurable plotting area in the center of the patient view.
Census Overview screen	Upon logging into the application, the initial page displays all current patients in the unit. The Current Census tab shows patients occupying a bed space, while the Archived Census tab shows patients who have been in the ICU in the past two months.
Clinical calculation	A measure derived by computation from one or more other measures. See *List of Clinical Calculations* for more information.
Data resolutions	Four different data resolutions are available: 5 seconds, 1 minute, 5 minutes, and 30 minutes. The application selects the most appropriate resolution based on how far the user zooms in or out.

Term	Description
Global Features	Actions performed on the Patient View screen that display to all other patient users, e.g., Targets and Events.
Central graphs	Five central graphs are available for users to analyze physiometric trends. Each graph can hold up to four measures.
Individual User mode	The mode of the application for situations where a user logs in and uses the application for a defined period.
Legend Label	The label of the currently plotted measure on a graph is located to the left of the graph in the Central Graphs Area.
Measures Dashboard	The list of all available measures is presented on the right-hand side of the Central Graphs Area.
Measure group	A collection of measures and laboratory results is graphed together as a unit. Because the constituent labs and measures are predefined, The application can add visual elements such as shading to emphasize data relationships.
Measure Statistics	A table displaying the average, standard deviation, maximum, minimum, and data gap percentage calculated for measures displayed in the Central Graphs Area for the selected time range.
Measure Synonyms	The logic recognizes parameters that measure the same physiologic condition and determines which one of several synonymous measures has the highest priority at each point in time.
Nighttime display	A configurable feature where the Patient View is displayed with a dark background at night and a light background during the day.
Patient History	A table that displays details (time, user, action) for all global actions done on the patient.
Persistent Display	The mode of the application for situations where the application is meant to display data for a specific bed space constantly.
Time Navigation Bar	A navigation tool that allows users to condense or extend the amount of data displayed in the Central Graphs Area.
User Arrangement	Actions performed on the Patient View that are saved only for the current user for the current patient (e.g., Central Graphs Area arrangement and placement and y-axis control).
Y-axis control	Users can change the Y-axis for each graph by clicking on the Y-axis range of a graph and selecting the Y-axis range.

8. Help Link

The Help features training materials. Users may access site-specific training materials through the Help link to receive training updates. Educators may support their users with access to the training materials on devices they use regularly. The educators may know which training materials users have accessed to determine when their users have trained.

FAQ on Views

How can I look at a different unit in Census Overview?

In the upper right-hand corner is a “Filter” dropdown to filter patients by unit and bed. The default option is to view all patients. You can adjust the Filter settings, which will persist throughout the different views and between different login sessions.

Can I look at old data for a patient who has been re-admitted?

Yes, a patient's data is accessible from the past two months. Use the time navigation to browse back to view historical data.

Can I look at patients no longer in the ICU?

Yes, patients in the unit within the last two months can be viewed. Click on the "Archive" tab to see all the patients in the unit for the last two months.

Why does the MRN field say 'MRN Required'?

If 'MRN Required' is shown, the MRN has not been entered into the bedside monitor, and thus, the patient cannot be displayed in the application.

What is 'Recent Activity'?

Recent Activity indicates when this particular patient entered the unit or, if applicable, the unit they were in before transferring to the current unit.

Why is this patient grayed out on the Census Overview screen?

If a patient's MRN is assigned to a bed, but the application is not receiving data from that bed, its entry will appear grayed out. These rows may still be clicked to access the Patient View.

How is the Persistent Display mode used in clinical workflows?

Persistent Display mode displays high-resolution trended device and lab data for the patient. It can be used in several clinical workflows, such as during an escalation procedure or resuscitation, rounds, nursing hand-offs, and post-event quality reviews. It is also a good source of information for the bedside nurse or other clinicians evaluating and making clinical decisions about the patient.

FAQ on Measurements

How often does a measurement update?

The frequency of updates depends on the device capturing the measurements. For example, Philips monitors deliver measurements to the application every five seconds.

Why is there no value shown for a measure?

No value will be shown if it has been more than 5 minutes since the application received a new measurement.

Why is the measure grayed out?

A grayed-out measure signifies a measure that, at one point during the patient’s stay, was accumulating data but later stopped. A measure turns gray after 5 minutes if there is no new measurement.

What does the colored number on the left of some of the measures mean?

The colored arrow with the number on the left side of a measure indicates which graph the measure is currently graphed on and under what color it is displayed on the graph. The numbers range from 1-5, where 1 is the top graph, and 5 is the bottom.

What are the tabs above the measures?

The measures are grouped by category. Vitals are measurements coming from devices attached to the patient. Labs are values coming from laboratory results. Groups are collections of measures and laboratory results graphed together as a unit. The application can insert shading, vertical lines, and other visual cues to emphasize relationships in the data.

How do I learn more about a measure synonym's value?

The application continues to make the channel variables available for display. You can graph them by going to the Measures Dashboard, expanding the accordion widget for the physiological variable, and graphing each channel separately.

FAQ on Central Graphs Area

How do I graph a particular measure?

A measure can be graphed by clicking and dragging the associated measure strip to the desired graph and releasing the mouse button. The measure will be graphed in the time range designated by the time navigation utility.

Why can I not drag a measure to the graphs?

This can be for two different reasons. Measures cannot be dragged to a new graph if the measure is already associated with another graph. Click and drag the legend label to re-arrange the measure. Graphs cannot have more than four associated measures. Remove an existing measure before attempting to add a new one. Remove an existing measure by clicking the 'X' on the right side of the legend label before attempting to add a new one.

How do I reset the arrangement back to the default one?

All the measures dragged to the Central Graphs Area by a single user are remembered for that user and patient. If you want to return to displaying the default measures on the graph with the default Y-axis ranges, you can press "Reset to default arrangement" to clear your arrangement. This is an irreversible action, so make sure you want to clear your arrangement before taking action.

FAQ on Time Navigation

What are the Quick Select Buttons (1 day, 12 hrs, etc) and arrows of the Time Navigation?

Clicking a "Zoom level" will modify the time viewed based on the zoom level selected, allowing you to change the time range of the graphs quickly. Clicking the left or right arrows will jump the time viewed backward or forward, respectively.

I can only drag the slider to the left edge; how do I see data from a longer time than that?

The Time Navigation Bar's left edge represents the patient's oldest viewable time. Since no data is available before this time, you cannot move the time window.

What is the data shown on the Time Navigation Bar?

The IDO2 Index is overlayed on the Time Navigation bar to see how the patient has progressed. If the IDO2 Index hasn't been calculated for the patient, the Time Navigation bar won't show any data overlaid.

FAQ on Targets

Why is there shading on some of the center graphs?

The shading on the center graphs represents periods where the measure's value was outside the range specified by its Targets. The shading on the center graphs always goes from where you would like to be, so shading below the graphed measure indicates a value above its Target while shading above the line indicates that the value was below the Target.

FAQ on Events

How do I change an Event?

To change an Event, click on the Event icon in the Time Navigation Bar for the Event you wish to change.

Can I remove an event?

Events cannot be removed from the application.

FAQ on IDO2 Index

Why is the IDO2 Index not showing up?

IDO2 values will appear for patients between birth and 12 years of age and above the age of 18 years. If a patient transitions past 12 years but is not yet 18, IDO2 will no longer be calculated, but the historically computed IDO2 values will be available in the application.

FAQ on IVCO2 Index

Why is the IVCO2 Index not showing up?

IVCO2 values will appear for patients between birth and 12 years and above the age of 18 years. If a patient transitions past 12 years but is not yet 18, IVCO2 will no longer be calculated, but the historically computed IVCO2 values will be available in the application.

FAQ on User Preferences

What is the "Encounters" option?

You may deselect this preference to hide Encounter lines and labels on the Patient View if you prefer only measures and labs on your Central Graphs Area and Time Navigation Bar.

Contact Us

How can I contact Etiometry?

Etiometry's support staff is always ready to help with any questions.

Want to Talk?

You can reach us by phone at (US) +1 857-366-9333.

Want to send us an email?

Contact us through email at support@etiometry.com

Want to learn more about Etiometry, Inc?

For more general information, check out our website, www.etiometry.com.

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