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(54) **METHODS AND APPARATUS FOR
DETECTING HEART FAILURE EVENT
USING PATIENT CHRONIC CONDITIONS**

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(71) Applicant: **Cardiac Pacemakers, Inc.**, St. Paul,
MN (US)

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(72) Inventors: **Robert J. Sweeney**, Woodbury, MN
(US); **Yi Zhang**, Plymouth, MN (US);
Qi An, Blaine, MN (US); **Pramodsingh
Hirasingh Thakur**, Woodbury, MN
(US)

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(73) Assignee: **Cardiac Pacemakers, Inc.**, St. Paul,
MN (US)

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Primary Examiner — Eric J Messersmith

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(74) *Attorney, Agent, or Firm* — Schwegman Lundberg &
Woessner, P.A.

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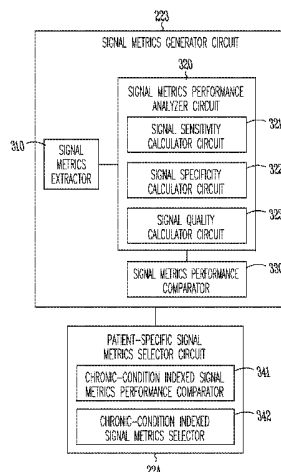
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(57) **ABSTRACT**

Devices and methods for detecting physiological target event such as events indicative of HF decompensation status are described. A medical device is configured to receive at least a first and a second chronic condition indicators of a patient, receive one or more physiologic signals from the patient, and generate a plurality of signal metrics when the first and the second chronic condition indicators meet their respective criterion. The medical device can detect the target event or condition using one or more patient-specific signal metrics selected from a group including both the first and the second set of the signal metrics. The medical device and the methods can be configured to detect an event indicative of HF decompensation.

18 Claims, 6 Drawing Sheets



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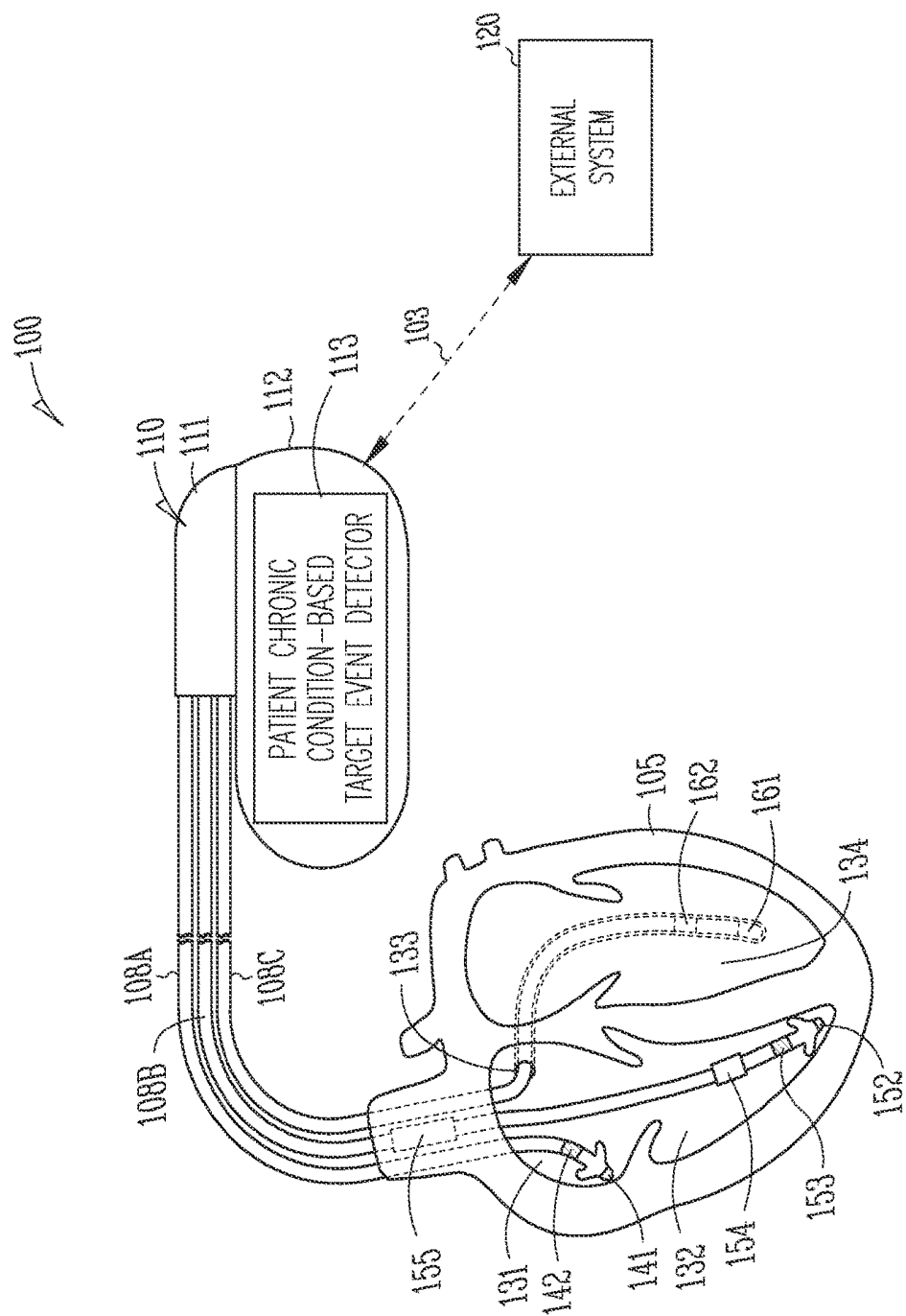
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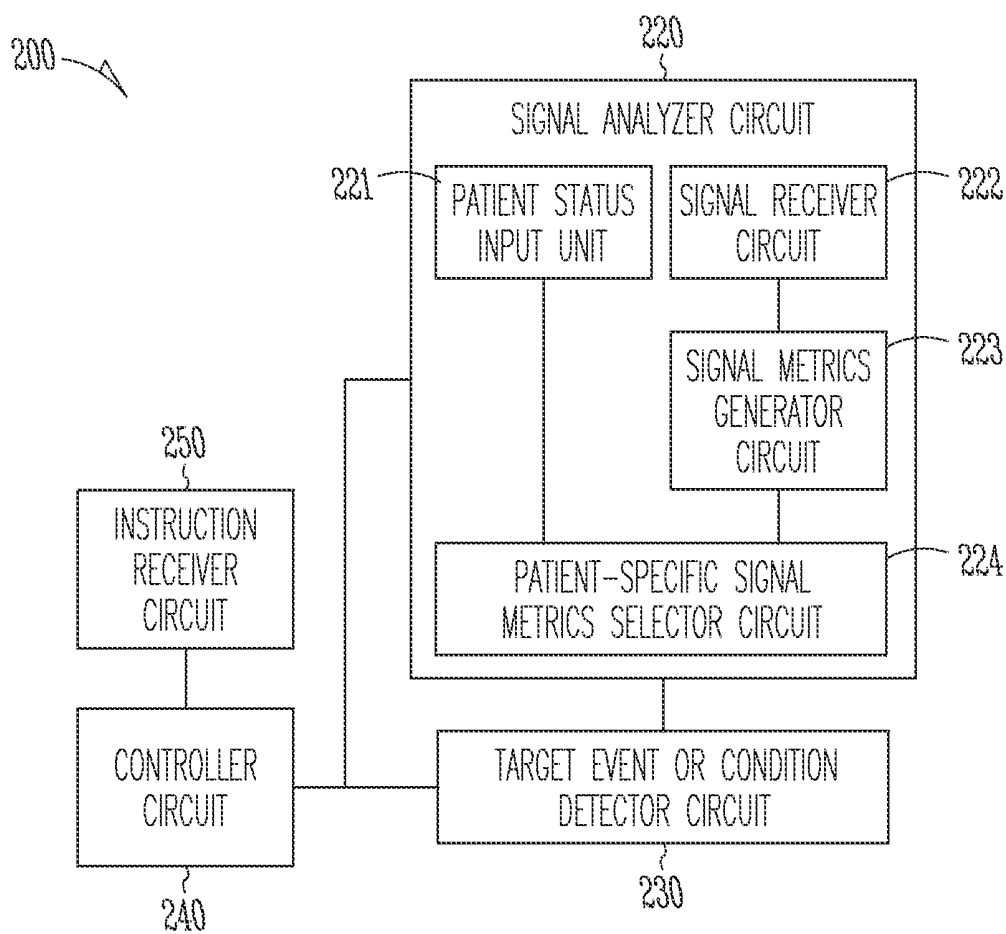
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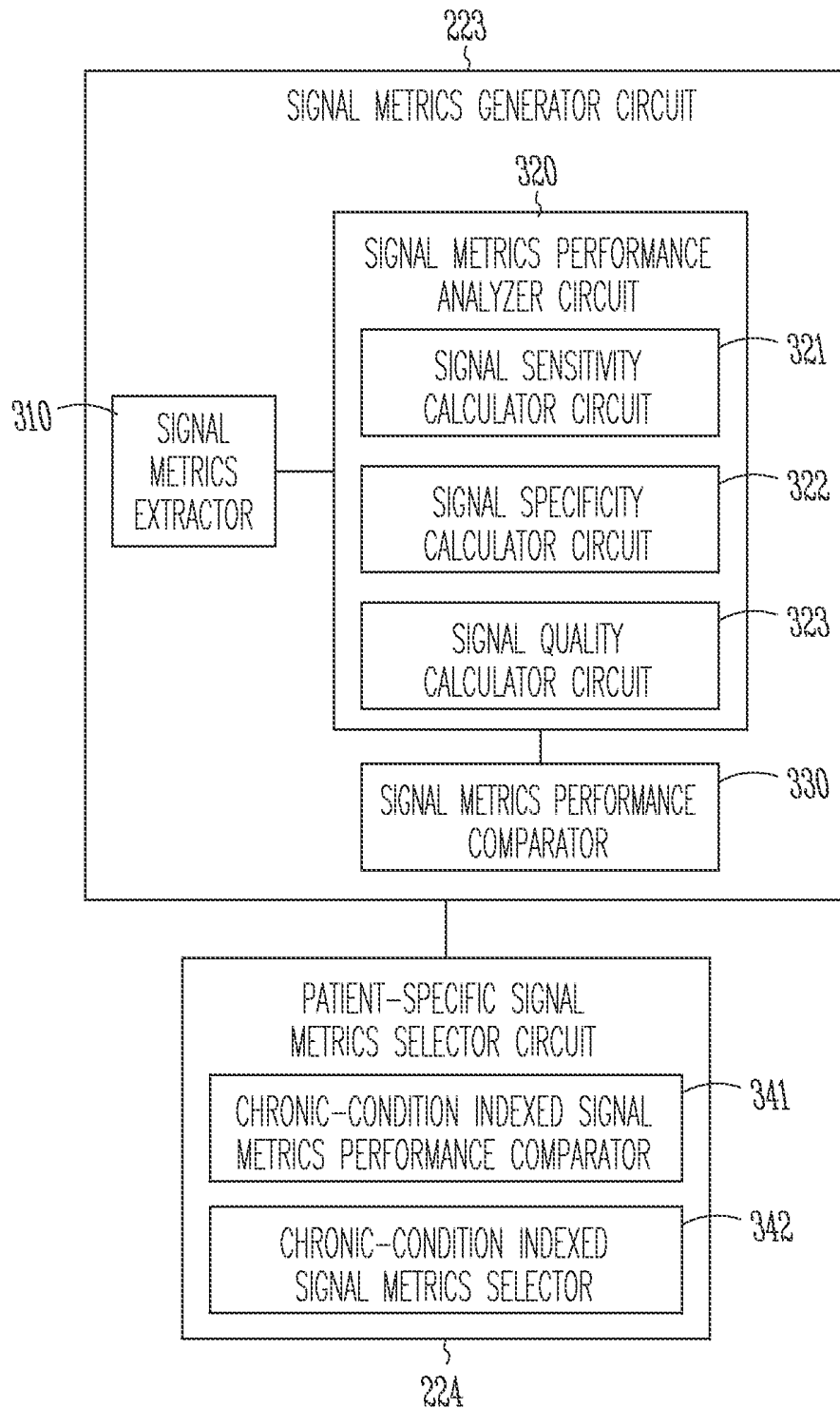
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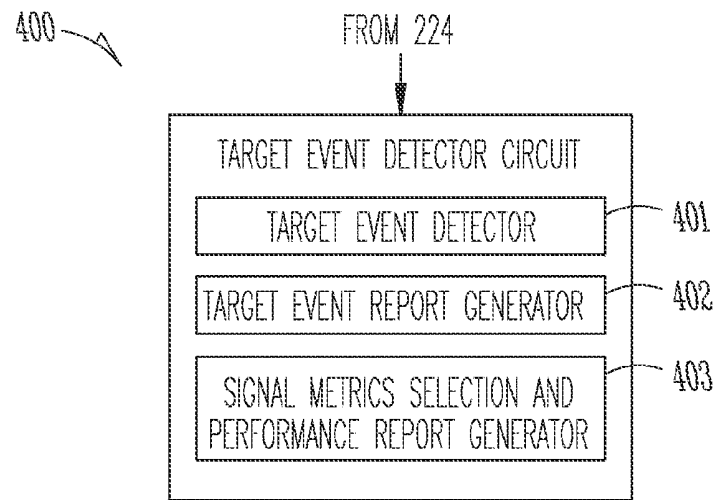
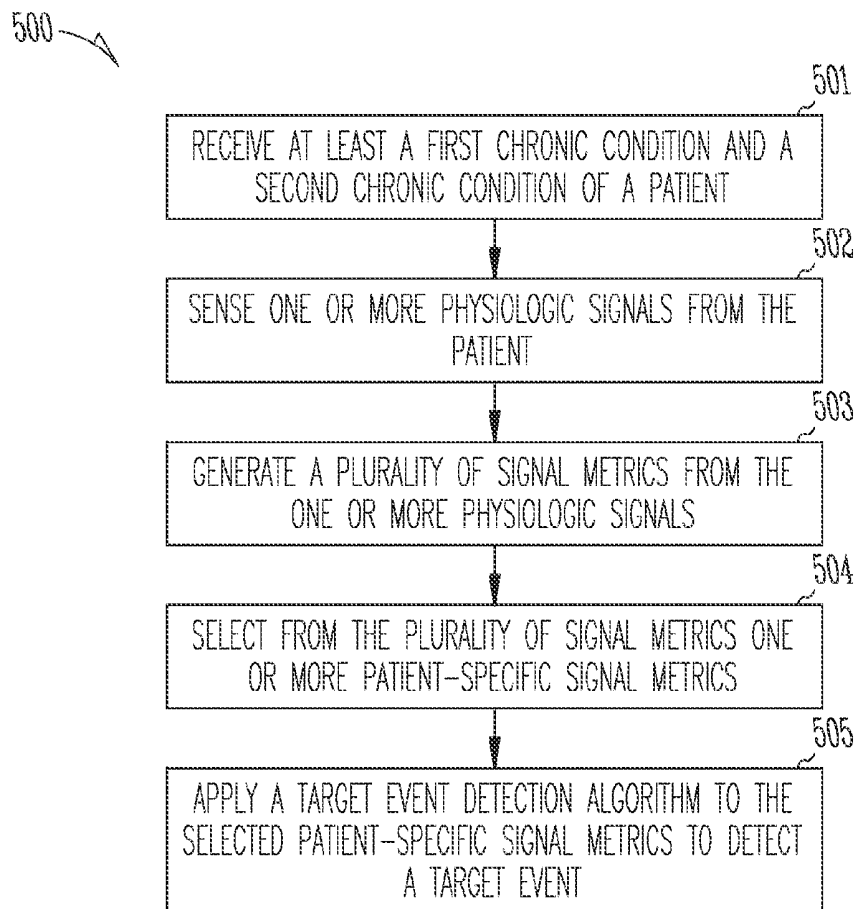
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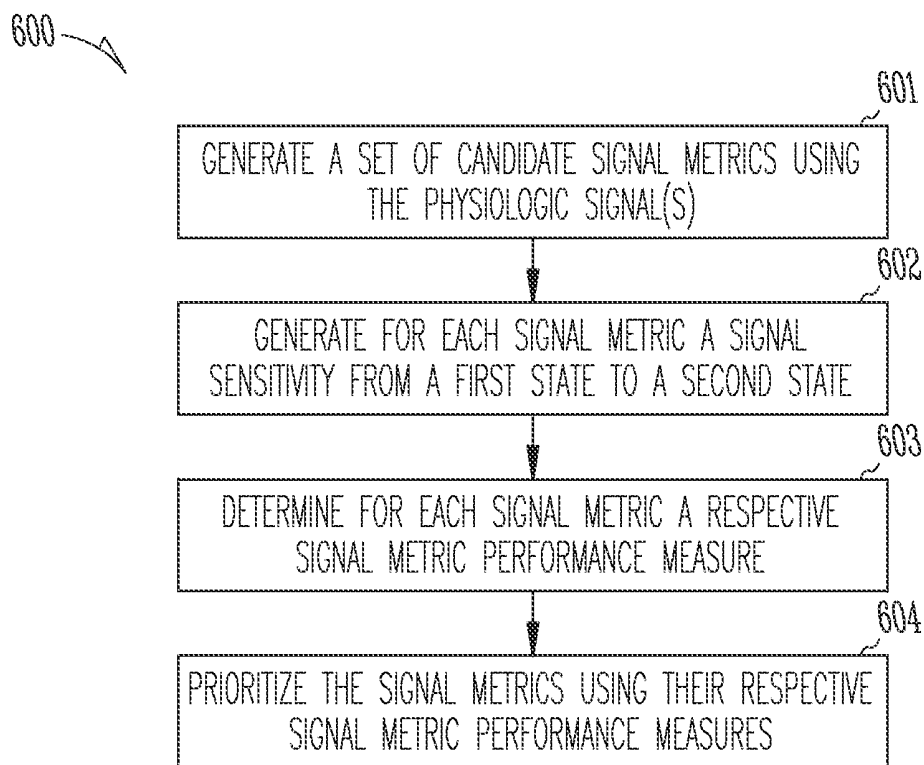


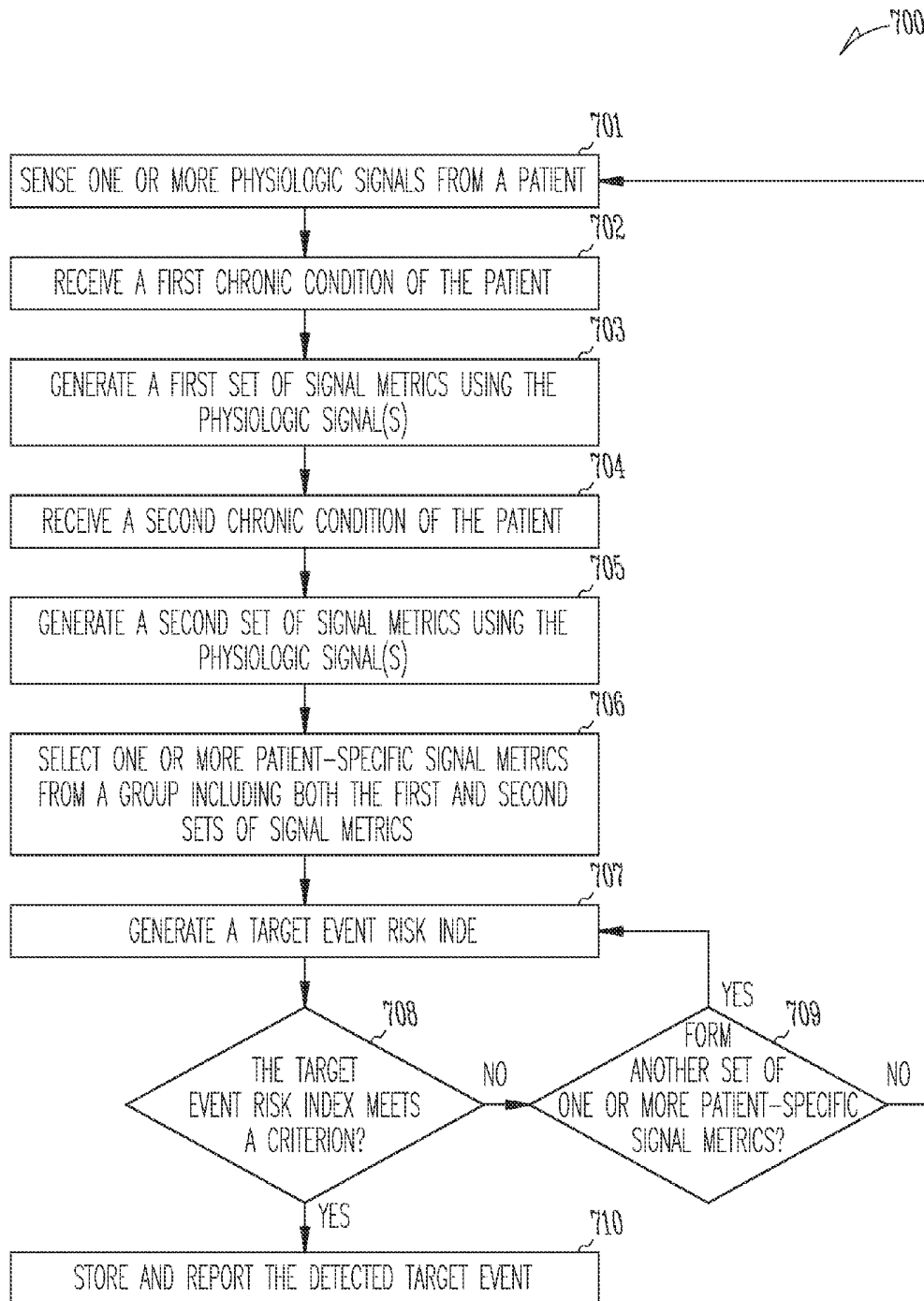
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*Fig. 2*

*Fig. 3*

*Fig. 4**Fig. 5*

*Fig. 6*

*Fig. 7*

METHODS AND APPARATUS FOR DETECTING HEART FAILURE EVENT USING PATIENT CHRONIC CONDITIONS

CLAIM OF PRIORITY

This application claims the benefit of priority under 35 U.S.C. § 119(e) of U.S. Provisional Patent Application Ser. No. 61/825,172, filed on May 20, 2013, which is herein incorporated by reference in its entirety.

TECHNICAL FIELD

This document relates generally to medical devices, and more particularly, to systems, devices and methods for detecting and monitoring heart failure decompensation.

BACKGROUND

Congestive heart failure (CHF) is a major health problem and affects over five million people in the United States alone. CHF patients typically have enlarged heart with weakened cardiac muscles, resulting in poor cardiac output of blood. Elevated pulmonary vascular pressures can cause fluid accumulation in the lungs over time. In many CHF patients, fluid accumulation precedes episodes of heart failure (HF) decompensation. The HF decompensation can be characterized by pulmonary or peripheral edema, reduced cardiac output, and symptoms such as fatigue, shortness of breath and the like.

Overview

Frequent monitoring of CHF patients and timely detection of intrathoracic fluid accumulation or other events indicative of HF decompensation status can help prevent worsening of HF in CHF patients, hence reducing cost associated with HE hospitalization.

Ambulatory medical devices can be used for monitoring HE patient and detecting HF decompensation events. Examples of such ambulatory medical devices can include implantable medical devices (IMD), subcutaneous medical devices, wearable medical devices or other external medical devices. The ambulatory or implantable medical devices can include physiologic sensors which can be configured to sense electrical activity and mechanical function of the heart, and the medical device can optionally deliver therapy such as electrical stimulation pulses to a target area, such as to restore or improve the cardiac function. Some of these devices can provide diagnostic features, such as using transthoracic impedance or other sensor signals. For example, fluid accumulation in the lungs can decrease the transthoracic impedance due to the lower resistivity of the fluid than air in the lungs. The fluid accumulation can also elevate ventricular filling pressure, resulting in a louder S3 heart sound. Additionally, fluid accumulation in the lungs can irritate the pulmonary system and leads to decrease in tidal volume and increase in respiratory rate.

Desirable performance of a method or a device for detecting HF decompensation can include one or more of a high sensitivity, a high specificity, a high positive predictive value (PPV), or a higher negative predictive value (NPV). The sensitivity can represent a percentage of actual HF decompensation episodes that are correctly recognized by a detection method. The specificity can represent a percentage of actual non-HF decompensation episodes that are correctly

tion method. The PPV can represent a percentage of the detected HF decompensation episodes, as declared by the detection method, which are actual HF decompensation events. The NPV can represent a percentage of the detected non-HF decompensation episodes, as declared by the detection method, which are actual non-HF decompensation events. A high sensitivity or a higher PPV can help ensure timely intervention to a patient with an impending HF decompensation episode, whereas a high specificity or a high NPV can help avoid unnecessary intervention and added healthcare cost due to false alarms. HF decompensation detection may be affected by a number of factors including the choice of physiologic sensors or physiologic signals. For example, a detector using a particular sensor signal may provide desirable accuracy in HF decompensation event detection in one patient but less sensitive or less specific in another patient. Additionally, the performance of a detector using one type of sensor signal may change over time due to patient's disease progression or development of a new medical condition. Therefore, the present inventors have recognized that there remains a considerable need for improving HF decompensation events detection in CHF patients.

Various embodiments described herein can help improve the detection of target physiologic events such as events indicative of HF decompensation status. For example, a medical device (such as an implantable medical device or a wearable medical device) can detect an HF decompensation event, such as using sensor signals or signal metrics selected in accordance with patient chronic condition indicators. A signal analyzer circuit can receive a patient status input which can include at least first chronic condition indicator and a second chronic condition indicator non-identical to the first chronic condition indicator. The signal analyzer can sense one or more physiologic signals from the patient, and generate a plurality of signal metrics from the physiologic signals. The signal metrics including a first set of one or more signal metrics when the first chronic condition indicator meets at least one first specified criterion, and a second set of signal metrics when the second chronic condition indicator meets at least one second specified criterion. The signal analyzer circuit can select one or more patient-specific signal metrics from a group including both the first and the second set of one or more signal metrics. The medical device can include an HF decompensation event detector circuit configured to detect a target event or condition of the patient using the selected one or more patient-specific signal metrics.

A method can include detecting a target physiologic event or condition such as an event indicative of HF decompensation status. The method can include receiving at least a first chronic condition indicator of the patient and a second chronic condition indicator non-identical to the first chronic condition indicator, sensing one or more physiologic signals of the patient, and generating a plurality of signal metrics from the one or more physiologic signals. The signal metrics can include a first set of one or more signal metrics when the first chronic condition indicator meets at least one first specified criterion, and a second set of signal metrics when the second chronic condition indicator meets at least one second specified criterion. The method can include selecting one or more patient-specific signal metrics from a group including both the first and the second set of one or more signal metrics, and applying a target event detection algorithm to the selected one or more patient-specific signal metrics to detect a target event or condition of the patient.

This Overview is an overview of some of the teachings of the present application and not intended to be an exclusive or exhaustive treatment of the present subject matter. Further details about the present subject matter are found in the detailed description and appended claims. Other aspects of the invention will be apparent to persons skilled in the art upon reading and understanding the following detailed description and viewing the drawings that form a part thereof, each of which are not to be taken in a limiting sense. The scope of the present invention is defined by the appended claims and their legal equivalents.

BRIEF DESCRIPTION OF THE DRAWINGS

Various embodiments are illustrated by way of example in the figures of the accompanying drawings. Such embodiments are demonstrative and not intended to be exhaustive or exclusive embodiments of the present subject matter.

FIG. 1 illustrates an example of a cardiac rhythm management (CRM) system and portions of the environment in which the CRM system operates.

FIG. 2 illustrates an example of a patient chronic condition-based target event detector.

FIG. 3 illustrates an example of a signal metrics generator circuit and the patient-specific signal metrics selector circuit.

FIG. 4 illustrates an example of a target event or condition detector circuit.

FIG. 5 illustrates an example of a method for detecting a target event from one or more physiological signals.

FIG. 6 illustrates an example of a method for generating one or more signal metrics from a physiologic signal.

FIG. 7 illustrates an example of method for detecting a target event from one or more physiological signals.

DETAILED DESCRIPTION

Disclosed herein are systems, devices, and methods for detecting one or more physiologic target events or conditions. The events can include early precursors of an HF decompensation episode. That is, these events can occur well before the systematic manifestation of worsening of HF. Therefore, by detecting the precursor events, the present document can provide a method and device to detecting an impending HF decompensation episode. In particular, the methods and devices described herein can be applicable to detecting events that can forecast an impending HF decompensation episode. Such events can include accumulation of intrathoracic fluid, changes in heart sounds, changes in breathing patterns, changes in physiologic response to activity, or changes in posture. More generally, the systems, devices, and methods described herein may be used to determine HF status and/or track HF progression such as worsening and recovery from an event.

FIG. 1 illustrates an example of a Cardiac Rhythm Management (CRM) system 100 and portions of an environment in which the CRM system 100 can operate. The CRM system 100 can include an ambulatory medical device, such as an implantable medical device (IMD) 110 that can be electrically coupled to a heart 105 such as through one or more leads 108A-C, and an external system 120 that can communicate with the IMD 110 such as via a communication link 103. The IMD 110 may include an implantable cardiac device such as a pacemaker, an implantable cardioverter-defibrillator (ICD), or a cardiac resynchronization therapy defibrillator (CRT-D). The IMD 110 can include one or more monitoring or therapeutic devices such as a subcutaneously implanted device, a wearable external device, a

neural stimulator, a drug delivery device, a biological therapy device, or one or more other ambulatory medical devices. The IMD 110 may be coupled to, or may be substituted by a monitoring medical device such as a bedside or other external monitor.

As illustrated in FIG. 1, the MD 110 can include a hermetically sealed can 112 that can house an electronic circuit that can sense a physiological signal in the heart 105 and can deliver one or more therapeutic electrical pulses to a target region, such as in the heart, such as through one or more leads 108A-C. The CRM system 100 can include only one lead such as 108B, or can include two leads such as 108A and 108B.

The lead 108A can include a proximal end that can be configured to be connected to IMD 110 and a distal end that can be configured to be placed at a target location such as in the right atrium (RA) 131 of the heart 105. The lead 108A can have a first pacing-sensing electrode 141 that can be located at or near its distal end, and a second pacing-sensing electrode 142 that can be located at or near the electrode 141. The electrodes 141 and 142 can be electrically connected to the IMD 110 such as via separate conductors in the lead 108A, such as to allow for sensing of the right atrial activity and optional delivery of atrial pacing pulses. The lead 108B can be a defibrillation lead that can include a proximal end that can be connected to IMD 110 and a distal end that can be placed at a target location such as in the right ventricle (RV) 132 of heart 105. The lead 108B can have a first pacing-sensing electrode 152 that can be located at distal end, a second pacing-sensing electrode 153 that can be located near the electrode 152, a first defibrillation coil electrode 154 that can be located near the electrode 153, and a second defibrillation coil electrode 155 that can be located at a distance from the distal end such as for superior vena cava (SVC) placement. The electrodes 152 through 155 can be electrically connected to the IMD 110 such as via separate conductors in the lead 108B. The electrodes 152 and 153 can allow for sensing of a ventricular electrogram and can optionally allow delivery of one or more ventricular pacing pulses, and electrodes 154 and 155 can allow for delivery of one or more ventricular cardioversion/defibrillation pulses. In an example, the lead 108B can include only three electrodes 152, 154 and 155. The electrodes 152 and 154 can be used for sensing or delivery of one or more ventricular pacing pulses, and the electrodes 154 and 155 can be used for delivery of one or more ventricular cardioversion or defibrillation pulses. The lead 108C can include a proximal end that can be connected to the MID 110 and a distal end that can be configured to be placed at a target location such as in a left ventricle (LV) 134 of the heart 105. The lead 108C may be implanted through the coronary sinus 133 and may be placed in a coronary vein over the LV such as to allow for delivery of one or more pacing pulses to the LV. The lead 108C can include an electrode 161 that can be located at a distal end of the lead 108C and another electrode 162 that can be located near the electrode 161. The electrodes 161 and 162 can be electrically connected to the IMD 110 such as via separate conductors in the lead 108C such as to allow for sensing of the LV electrogram and optionally allow delivery of one or more resynchronization pacing pulses from the LV.

The IMD 110 can include an electronic circuit that can sense a physiological signal. The physiological signal can include an electrogram or a signal representing mechanical function of the heart 105. The hermetically sealed can 112 may function as an electrode such as for sensing or pulse delivery. For example, an electrode from one or more of the

leads **108A-C** may be used together with the can **112** such as for unipolar sensing of an electrogram or for delivering one or more pacing pulses. A defibrillation electrode from the lead **108B** may be used together with the can **112** such as for delivering one or more cardioversion/defibrillation pulses. In an example, the IMD **110** can sense impedance such as between electrodes located on one or more of the leads **108A-C** or the can **112**. The IMD **110** can be configured to inject current between a pair of electrodes, sense the resultant voltage between the same or different pair of electrodes, and determine impedance using Ohm's Law. The impedance can be sensed in a bipolar configuration in which the same pair of electrodes can be used for injecting current and sensing voltage, a tripolar configuration in which the pair of electrodes for current injection and the pair of electrodes for voltage sensing can share a common electrode, or tetrapolar configuration in which the electrodes used for current injection can be distinct from the electrodes used for voltage sensing. In an example, the IMD **110** can be configured to inject current between an electrode on the RV lead **108B** and the can housing **112**, and to sense the resultant voltage between the same electrodes or between a different electrode on the RV lead **108B** and the can housing **112**. A physiologic signal can be sensed from one or more physiological sensors that can be integrated within the IMD **110**. The IMD **110** can also be configured to sense a physiological signal from one or more external physiologic sensors or one or more external electrodes that can be coupled to the IMD **110**. Examples of the physiological signal can include one or more of heart rate, heart rate variability, intrathoracic impedance, arterial pressure, pulmonary artery pressure, RV pressure, LV coronary pressure, coronary blood temperature, blood oxygen saturation, one or more heart sounds, physical activity or exertion level, physiologic response to activity, posture, respiration, body weight, or body temperature.

The arrangement and functions of these leads and electrodes are described above by way of example and not by way of limitation. Depending on the need of the patient and the capability of the implantable device, other arrangements and uses of these leads and electrodes are.

As illustrated, the CRM system **100** can include a patient chronic condition-based target event detector **113**. The patient chronic condition-based target event detector **113** can be configured to receive patient chronic condition indicators and one or more physiologic signals from the patient, and select one or more patient-specific signal metrics from the physiologic signals using the information of the patient chronic condition indicators. The physiologic signals from the patient can be sensed using the electrodes on one or more of the leads **108A-C**, or physiologic sensors deployed on or within the patient and communicated with the IMD **110**. The patient chronic condition-based target event detector **113** can detect a target event or condition of the patient such as an HF decompensation event using the selected patient-specific signal metrics. The HF decompensation event can include one or more early precursors of an HF decompensation episode, or an event indicative of HF progression such as recovery or worsening of HF status. Examples of the patient chronic condition-based target event detection are described below, such as with reference to FIGS. 2-3.

The external system **120** can allow for programming of the MD **110** and can receives information about one or more signals acquired by IMD **110**, such as can be received via a communication link **103**. The external system **120** can include a local external IMD programmer. The external system **120** can include a remote patient management sys-

tem that can monitor patient status or adjust one or more therapies such as from a remote location.

The communication link **103** can include one or more of an inductive telemetry link, a radio-frequency telemetry link, or a telecommunication link, such as an internet connection. The communication link **103** can provide for data transmission between the IMD **110** and the external system **120**. The transmitted data can include, for example, real-time physiological data acquired by the IMD **110**, physiological data acquired by and stored in the IMD **110**, therapy history data or data indicating IMD operational status stored in the IMD **110**, one or more programming instructions to the IMD **110** such as to configure the IMD **110** to perform one or more actions that can include physiological data acquisition such as using programmably specifiable sensing electrodes and configuration, device self-diagnostic test, or delivery of one or more therapies.

The patient chronic condition-based target event detector **113** may be implemented in the external system **120**. The external system **120** can be configured to perform HF decompensation event detection such as using data extracted from the **110** or data stored in a memory within the external system **120**. Portions of the patient chronic condition-based target event detector **113** may be distributed between the IMD **110** and the external system **120**.

Portions of the IMD **110** or the external system **120** can be implemented using hardware, software, or any combination of hardware and software. Portions of the MD **110** or the external system **120** may be implemented using an application-specific circuit that can be constructed or configured to perform one or more particular functions, or can be implemented using a general-purpose circuit that can be programmed or otherwise configured to perform one or more particular functions. Such a general-purpose circuit can include a microprocessor or a portion thereof, a microcontroller or a portion thereof, or a programmable logic circuit, or a portion thereof. For example, a "comparator" can include, among other things, an electronic circuit comparator that can be constructed to perform the specific function of a comparison between two signals or the comparator can be implemented as a portion of a general-purpose circuit that can be driven by a code instructing a portion of the general-purpose circuit to perform a comparison between the two signals. While described with reference to the IMD **110**, the CRM system **100** could include subcutaneous medical device (e.g., subcutaneous ICD, subcutaneous diagnostic device), wearable medical devices (e.g., patch based sensing device), or other external medical devices.

FIG. 2 illustrates an example of a patient chronic condition-based target event detector **200**, which can be an embodiment of the patient chronic condition-based target event detector **113**. The patient chronic condition-based target event detector **200** can include one or more of a signal analyzer circuit **220**, a target event detector circuit **230**, a controller **240**, and an instruction receiver **250**.

The signal analyzer circuit **220** can include a patient status input unit **221**, a signal receiver circuit **222**, a signal metrics generator circuit **223**, and a patient-specific signal metrics selector circuit **224**. The patient status input unit **221** can be configured to receive at least a first chronic condition indicator and a second chronic condition indicator of a patient. The second chronic condition indicator can be non-identical to the first chronic condition indicator. The patient chronic condition indicators can be descriptive of the patient characteristics or sustained medical status that do not change or slowly change over a certain specified time, such as approximately at least six months. The first and the

second chronic condition indicators of the patient can respectively include at least one of a chronic disease indicator of the patient, a prior medical procedure indicator of the patient, or a demographic characteristic indicator of the patient. Example of the chronic disease indicator of the patient can include a patient's prior myocardial infarction (MI), ischemic or dilated cardiomyopathy, valvular disease, renal disease, chronic obstructive pulmonary disease (COPD), peripheral vascular disease, cerebrovascular disease, hypertension, hepatic disease, diabetes, asthma, anemia, depression, pulmonary hypertension, sleep disordered breathing, hyperlipidemia, among others. Examples of the prior medical procedure can include prior coronary artery bypass graft (CABG) surgery, thoracic surgery, valvular surgery, or other surgical interventions. Example of demographic characteristic indicator can include a patient's age, sex, race, height, ethnicity, blood type, past or current smoker, New York heart association (NYHA) functional class, among others.

The patient status input unit **221** can be configured to receive at least the first and the second chronic condition indicators from a system user (e.g., a physician) such as via the instruction receiver **250**. In an example, the patient status input unit **221** can be configured to be coupled to a storage device, including an electronic medical record (EMR) system that can store at least the first and the second chronic condition indicators of the patient. When receiving a command from a system user such as via instruction receiver **250**, the patient status input unit **221** can retrieve from the storage device such as the EMR system at least the first chronic condition indicator and the second patient chronic condition indicator non-identical to the first chronic condition indicator. For example, the first chronic condition indicator includes an indicator of the patient's prior thoracic surgery, and the second chronic condition indicator includes an indicator of patient's having a renal disease.

The chronic condition indicators received by the patient status input unit **221** can include binary values indicating the presence or absence of a specified condition. Additionally or alternatively, the chronic condition indicators can include categorical classification or progressive stage information of a demographic characteristic indicator or a chronic disease indicator. For example, the chronic condition indicators can include symptomatic or functional classification of heart failure (e.g., NYHA classes I, II, III, and IV), diabetes mellitus type 1 and type 2, chronic kidney disease (MD) of stage 1 through stage 5, among others. The chronic condition indicator can also include a plurality of value ranges of a physiologic parameter that indicate functional assessment of the patient's chronic condition. For example, the chronic conditions can include a plurality of value ranges of glomerular filtration rate (GFR) indicating the progression of CKD, a plurality of value ranges of ejection fraction (EF) indicating the progression of heart failure, a plurality of value ranges of blood glucose indicating the progression of diabetes, a plurality of value ranges of apnea hypopnea index (AHI) indicating the progression of sleep disordered breathing, a plurality of value ranges of forced expiratory volume in one second (FEV1) indicating the progression of chronic obstructive pulmonary diseases (COPD). The first and the second chronic condition indicators can respectively include non-identical categorical classes from the same or different chronic condition indicators of the patient.

The signal receiver circuit **222** can be configured to receive one or more physiologic signals from the patient, such as for detecting a target event or condition. The signal receiver circuit **222** can be coupled to one or more of:

or more electrodes such as electrodes on one or more of the leads **108A-C** or the can **112**; one or more physiologic sensors; or one or more patient monitors. The physiological signals can be indicative of the target event or condition such as HF decompensation status, including one or more electrograms such as sensed from electrodes on one or more of the leads **108A-C** or the can **112**, heart rate, heart rate variability, intrathoracic impedance, intracardiac impedance, arterial pressure, pulmonary artery pressure, RV pressure, LV coronary pressure, coronary blood temperature, blood oxygen saturation, one or more heart sounds, physiologic response to activity, apnea hypopnea index, one or more respiration signals such as a respiration rate signal or a tidal volume signal. The signal receiver circuit **222** can include one or more modules to perform signal conditioning (e.g., signal amplification, digitization, or filtering) or parameter extraction from the sensed physiological signal. Examples of extracted signal parameters can include: signal mean, median, or other central tendency measures; a histogram of the signal intensity; one or more signal trends over time; one or more signal morphological descriptors; or signal power spectral density at a specified frequency range. In an example, the signal sensing circuit can sense two or more physiological signals and can generate a composite signal parameter set such as using the two or more physiological signals.

The signal metrics generator circuit **223** can be configured to generate a plurality of signal metrics from the one or more physiologic signals. A signal metric can include a sensor signal acquired by a physiologic sensor or from one or more electrodes on one or more of the leads **108A-C** or the can **112**. A signal metric can also include a signal feature extracted from the sensor signal such as a statistical measure (e.g., mean, median, standard deviation, variance, correlation, covariance, or other statistical value over a specified time segment), a morphological measure (e.g., peak, trough, slope, area under the curve), or a feature indicative of a physiologic activity (e.g., P wave and QRS complexes in an electrogram signal, or S1, S2, S3 or S4 components of a heart sound signal, an inspiration phase and expiration phase of a respiration signal). The signal metrics generated by the signal metrics generator circuit **223** can include at least a first set of one or more signal metrics and a second set of signal metrics. The first set of signal metrics can be generated in response to the first chronic condition indicator meeting a first specified criterion, and the second set of signal metrics can be generated in response to the second chronic condition indicator meeting a second specified criterion. For example, the first set of signal metrics can include a five-day average of intracardiac impedance signal and a daily maximum respiration rate (MRR) signal when the patient has a chronic condition of renal disease, and the second set of signal metrics can include a standard deviation of R-R interval signal (such as calculated from an electrogram or an intracardiac electrogram signal) and a five-day average of transthoracic impedance signal when the patient has a chronic condition of diabetes. The signal metrics with respect to the chronic condition indicator can be selected using the population-based information. Examples of the signal metrics generator circuit **223** are described below, such as with reference to FIG. 3.

The patient-specific signal metric selector circuit **224** can be configured to select one or more patient-specific signal metrics from the plurality of signal metrics generated by the signal metrics generator circuit **223**. The patient-specific signal metrics can be used to detect the target event or condition such as an HF decompensation event. The patient-

specific signal metrics can include one or more signal metrics selected from a group including both the first set of one or more signal metrics and the second set of one or more signal metrics. In an example, if there is at least one signal metric shared by the first and the second set of the signal metrics (i.e., the intersection of the first and the second sets of the signal metrics are not empty), the patient-specific signal metrics can include at least one signal metric from an intersection of the first set and the second set of signal metrics. In another example, the patient-specific signal metrics selector circuit can include at least one signal metric from the first set of signal metrics and at least one signal metric from the second set of signal metrics.

The target event or condition detector circuit **230** can receive input from the patient-specific signal metrics selector circuit **224** and be configured to detect a target event or condition using the selected one or more patient-specific signal metrics. A target event or condition can include a physiologic event indicative of an onset of a disease, worsening of a disease state, recovery of a disease state, a response to an intervention, or a change of a disease state. In an example, the target event or condition detector circuit **230** can detect the presence of an event indicative of HF decompensation status. Examples of target event can also include a worsening HP, pulmonary edema, pulmonary condition exacerbation such as COPD, asthma and pneumonia, or myocardial infarction, among others.

The controller circuit **240** can control the operations of the signal analyzer circuit **220** and the subcomponent circuits **221** through **224**, the target event or condition detector circuit **230**, and the data and instruction flow between these components. The controller circuit **240** can receive external programming input from the instruction receiver circuit **250** to control one or more of the receiving patient status, signal sensing, signal metrics generation, patient-specific signal metrics selection, or the target event detection. Examples of the instructions received by the instruction receiver **250** may include: selection of electrodes or sensors used for sensing physiologic signals, selection of chronic conditions of the patient, or configuration of the target event and condition detector **230**. The instruction receiver circuit **250** can include a user interface configured to present programming options to the user and receive user's programming input. The instruction receiver circuit **250** can be coupled to the patient status input unit **221** to receive the patient chronic condition indicators such as via the user interface. In an example, at least a portion of the instruction receiver circuit **250**, such as the user interface, can be implemented in the external system **120**.

FIG. 3 illustrates an example of the signal metrics generator circuit **223** and the patient-specific signal metrics selector circuit **224**, as part of the patient chronic condition-based target event detector **200**. The signal metrics generator circuit **223** can include one or more of a signal metrics extractor **310**, a signal metrics performance analyzer circuit **320**, and a signal metrics performance comparator **330**. The patient-specific signal metrics selector circuit **224** can include a chronic-condition indexed signal metrics performance comparator **341** and a chronic-condition indexed signal metrics selector **342**.

The signal metrics extractor **310** can receive one or more processed physiologic signals sensed from the patient and extract signal features from the physiologic signals. The extracted signal metrics can include a statistical signal feature, a morphological signal feature, or a signal feature indicative of a physiologic activity. Examples of the extracted signal features can include mean, median, standard

deviation, variance, correlation, covariance, or other statistical value over a specified time segment; peak, trough, slope, area under the curve of a sensor signal, P wave and QRS complexes in an electrogram signal, or S1, S2, S3 or S4 components of a heart sound signal, inspiration and expiration phase of a respiration signal, among others.

The signal metrics extractor **310** can extract signal features when a patient chronic condition indicator such as that received by the patient status input unit **221** meets a specified condition. For example, when a patient chronic condition of having a chronic kidney disease is received by the patient status input unit **221**, the signal metrics extractor **310** can extract signal features including daily maximum respiration rate (MRR), transthoracic impedance, and daily S3 heart sound amplitude. When two or more patient chronic condition indicators are received, the signal metrics extractor **310** can extract signal features with respect to each of the patient chronic condition indicator. The association between a chronic condition indicator and the respective signal metrics can be stored in a machine-readable medium such as a memory device, association can be created in a form of searchable data structure such as a lookup table or association map to facilitate automatic selection of signal metrics for any given chronic condition indicator. The data structure can contain a plurality of chronic condition indicators or categorical classifications of a chronic condition indicator, each of which can be associated to the respective one or more signal metrics.

The signal metrics performance analyzer circuit **320** can be configured to generate, for one or more of the signal metrics from the signal metrics extractor **310**, respective performance measures indicative of reliability or accuracy of detecting a target event or condition. As illustrated in FIG. 3, the signal metrics performance analyzer circuit **320** can include at least one of a signal sensitivity calculator circuit **321**, a signal specificity calculator circuit **322**, or a signal quality calculator circuit **323**. Each of the calculator circuits **321** through **323** alone or in any combination can be used to evaluate the performance of the one or more signal metrics provided by the signal metrics extractor **310**.

The sensitivity calculator circuit **321** can be configured to determine the sensitivity of a signal metric in response to a physiologic change associated with the target event or condition, such as using comparison of measurements of the signal metric at two non-identical states. The first and the second states can include non-identical temporal information. In an example, the sensitivity calculator circuit **321** can calculate for a signal metric (X) a relative change (such as a difference ΔX) between the signal metric at a first state (X_{S1}) and the signal metric at the second state (X_{S2}), that is, $\Delta X = X_{S1} - X_{S2}$. The relative change can include a rate of change ($\Delta X / \Delta t$) of the signal metric over the duration between the first and the second state, that is, $\Delta X / \Delta t = (X_{S1} - X_{S2}) / (T_{S1} - T_{S2})$, where T_{S1} and T_{S2} respectively represents occurrence time of the first and the second states. In an example, T_{S1} can be approximately 14-28 days prior to patient's developing a target event such as an decompensation event, and T_{S2} can be a time preceding T_{S1} by specified time duration of approximately 1-6 months or approximately 1-3 months. The second state can be a baseline state representing the historical trend of the signal metric when the patient does not develop the target event. The signal metric at the baseline state can be computed using a linear or nonlinear combination of a plurality of historical measurements of the signal metric. The relative change in the signal metric from the first state (such as the state prior to an BF decompensation event) to the second state (such as a state

preceding the first state or a baseline state) thus can indicate predictive content in the signal metric in response to the progression of a target event. A signal metric with high sensitivity preserves high predictive content in detecting a target event such as an HF decompensation event. In an example, the sensitivity calculator circuit **321** can calculate a statistical significance of relative change ΔX or $\Delta X/X_{S2}$. The significance can be computed as a p-value obtained by fitting relative change data from a group of patients to a statistical model. The sensitivity of a signal metric can be computed using both the p-value as discussed above and the relative change ΔX or $\Delta X/X_{S2}$. A signal metric having a large and significant change, such as large ΔX or $\Delta X/X_{S2}$ and small p value, is more desirable for detecting a target event such as a HF decompensation event. In an example, a sensitivity score can be computed as a product of a relative change $\Delta X/X_{S2}$ and a negative logarithm of the p-value, i.e., $-\log(\text{p-value}) * \Delta X/X_{S2}$. A higher sensitivity score preserves high predictive content in detecting the target event.

The specificity calculator circuit **322** can be configured to determine the specificity of a signal metric in response to a physiologic or non-physiologic change not associated with the target event or condition. For example, in detecting the target event of HF decompensation event, confounding events such as noise, inference, patient activity, lead fracture, lead revision, change of pacing configuration, or a replacement of the device are not physiologic changes associated with an impending HF decompensation event. The specificity can characterize the accuracy of the signal metric in recognizing the confounding events as non-target event. The specificity calculator circuit **322** can determine the specificity using comparison of measurements of the signal metric at two non-identical states. The first and the second states can include non-identical temporal information. The specificity calculator circuit **322** can calculate a relative change in a signal metric (X) from a first state to a second state. The first state can occur at a time such as approximately 14-28 days prior to patient's developing a target event such as an HP decompensation event. The second state can occur at a time preceding the first state by at least specified time duration, such as approximately 1-6 months or approximately 1-3 months. The second state can be a baseline state representing the historical trend of the signal metric. The relative change in the signal metric from the first state (such as the state prior to an IV decompensation event) to the second state (such as a state preceding the first state or a baseline state) thus can indicate response of the signal metric in the absence of the target event. A signal metric with high specificity therefore reduces the rate of false detection of non-target event as a target event.

The signal quality calculator circuit **323** can be configured to determine the signal quality of the signal metric. Signal quality can include signal strength, signal variability, or signal-to-noise ratio, among others. Examples of the signal variability can include range, inter-quartile range, standard deviation, variance, sample variance, or other first-order, second-order, or higher-order statistics representing the degree of variation. For example, in determining the quality of a signal metric of S1 heart sound intensity, the signal quality calculator circuit **323** can perform a plurality of measurements of the S1 heart sound intensity such as from a plurality of cardiac cycles during a specified period of time. The signal quality calculator circuit **323** can determine the variability of the S1 intensity by computing a variance of the plurality of measurements of the S1 intensity. A high signal quality, such as indicated by one or more of a high

signal-to-noise ratio, a high signal strength, or a low signal variability, is desirable for detecting the target event.

The signal sensitivity calculator circuit **321**, the signal specificity calculator circuit **322**, or the signal quality calculator circuit **323** can determine respective signal performance measures (e.g., signal sensitivity, specificity, or quality) using population-based statistics. For example, the signal metric of daily maximum respiration rate (MRR) can be measured in a cohort of patients with the chronic condition (such as renal disease) identical or similar to the present patient. Statistics such as the signal sensitivity, signal specificity, or signal quality with regard to the population-based daily MRR can be determined from the population-based data. These statistical data can be retrieved from a database or otherwise provided to the signal metrics performance analyzer circuit **320** and used by one or more of the signal sensitivity calculator circuit **321**, the signal specificity calculator circuit **322**, or the signal quality calculator circuit **323**. In an example, the signal metrics performance analyzer circuit **320** can determine respective signal performance measures using both the population-based statistics (e.g., population-based sensitivity of daily MRR) and the performance measure of the patient (e.g., sensitivity of daily MRR).

The signal metrics performance comparator **330** can be coupled to the signal metrics performance analyzer circuit **320**, and configured to select one or more signal metrics from a plurality of signal metrics based at least in part on a comparison of the performance measures including the signal sensitivity, the signal specificity, or the signal quality, or any combination thereof. In an example, the signal metrics performance comparator **330** can compute a composite performance score for a signal metric using a linear combination or nonlinear combination of one or more of performance measures. The composite performance score can then be compared to a specified threshold to determine whether the signal metric can be selected. For example, a composite performance score (F_{MRR}) for the signal metric of daily maximum respiration rate (NCR) can be computed as $F_{MRR} = a * Ss + b * Sp + c * Q$, where a, b, c are scalar weights to respective performance measures sensitivity (Ss), specificity (Sp), and quality (Q). The signal metrics performance comparator **330** can select daily MRR for detecting the target event of HF decompensation event if F_{MRR} exceeds a specified threshold, e.g., $F_{MRR} > F_{MRR-TH}$. In another example, the signal metrics performance comparator **330** can select the signal metric when one or more performance measures meet specified criteria. For example, the signal metrics performance comparator **330** can select daily MRR for detecting HF decompensation event if sensitivity, specificity, or quality each exceeds respective threshold, e.g., $Ss > Ss_{TH}$, $Sp > Sp_{TH}$, or $Q > Q_{TH}$.

When the signal metrics extractor **310** generates and provides more than one signal metric to the performance analyzer circuit **320**, the signal metrics performance comparator **330** can organize the signal metrics such as prioritizing the signal metrics. The signal metrics performance comparator **330** can prioritize the signal metrics based at least in part on their respective performance measures. For example, corresponding to a chronic condition indicator of patient having diabetes, the signal metrics extractor **310** can generate a set of signal metrics including standard deviation of average normal RR interval (SDANN), 24-hour max intracardiac impedance (Zmax), daily maximum of respiration rate (MRR), and daily maximum of tidal volume (TV). The signal metrics performance analyzer circuit **320** can compute composite performance score (F) for each of the

signal metrics. If the comparison of the performance measures at the signal metrics performance comparator **330** indicates that $F_{MRR} \geq F_{TV} \geq F_{Zmax} \leq F_{SDANN}$, then the prioritized signal metrics can be in the order of (MRR, TV, Zmax, SDANN).

The patient-specific signal metrics selector circuit **224** can be coupled to the signal metrics generator circuit **223** and receive therein at least a first set of one or more signal metrics corresponding to the first chronic condition indicator and a second set of signal metrics corresponding to the second chronic condition indicator. The chronic-condition indexed signal metrics performance comparator **341** can compare the signal metrics in the first set to the signal metrics in the second set, such as to identify one or more common signal metrics shared by the first and the second sets of the signal metrics. The chronic-condition indexed signal metrics performance comparator **341** can also compare the performance measures such as the signal sensitivity, signal specificity, or signal quality of the signal metrics in the first and the second sets.

The chronic-condition indexed signal metrics selector **342** can be configured to select from the plurality of signal metrics one or more patient-specific signal metrics selected from a group including both the first set of one or more signal metrics and the second set of one or more signal metrics. In an example, the chronic-condition indexed signal metrics selector **342** can select at least one signal metric from an intersection of the first set and the second set of signal metrics, where the intersection includes at least one common signal metric shared by both the first and the second set of signal metrics. The chronic-condition indexed signal metrics selector **342** can select at least one signal metric from the first set of signal metrics and at least one signal metric from the second set of signal metrics. For example, the chronic-condition indexed signal metrics selector **342** can use the prioritized signal metrics such as provided by the signal metrics performance comparator **330**, and select a signal metric with the highest composite performance from the first set, and a signal metric with the highest composite performance score from the second set. Other approaches of selecting patients-specific signal metrics from the first and the second sets based at least in part on the performance measures have also been contemplated.

FIG. 4 illustrates an example of target event or condition detector circuit **400**, which can be an embodiment of the target event or condition detector circuit **230**. The target event or condition detector circuit **400** can receive the chronic-condition indexed signal metrics from the patient-specific signal metrics selector circuit **224**, and detects the target event from the received signal metrics. The target event or condition detector circuit **400** can include a target event detector **401**, a target event report generator **402**, and a signal metrics selection and performance report generator **403**.

The target event detector **401** can detect the target event from the chronic-condition indexed signal metrics. In an example, the target event can be an event indicative of HF decompensation status, and the target event detector **401** can be configured to compute an HF decompensation index such as using the chronic-condition indexed signal metrics, and determine whether the HF decompensation index meets a specified criterion such as by comparing the HF decompensation index to a threshold value. Examples of target HF decompensation event detection using the chronic-condition indexed signal metrics are discussed below, such as with reference to FIGS. 5-7.

The target event report generator **402** can generate a report to inform, warn, or alert the user the detected target event. The report can include recommendations such as confirmative testing, diagnosis, or treatment options. The report can include one or more formats of media including, for example, a textual or graphical message, a sound, an image, or a combination thereof. In an example, the target event report generator **402** can be coupled to the instruction receiver circuit **250** and the report can be presented to the user via an interactive user interface on the instruction receiver circuit **250**. The target event report generator **402** can be coupled to the external device **120**, and be configured to present to the user the detected target event via the external device **120**.

The signal metrics selection and performance report generator **403** can generate, and present to the system user, one or more of a report including the chronic condition indicators such as received from the patient status input unit **221**, signal metrics and the respective performance measures such as generated by the signal metrics generator circuit **223**, or the chronic-condition indexed signal metrics such as generated by the patient-specific signal metrics selector circuit **224**. The signal metrics selection and performance report generator **403** can be coupled to the external device **120** or the instruction receiver circuit **250**, and be configured to present the signal metrics information to the user therein. The user input can include confirmation, storage, or other programming instructions to operate on the patient-specific signal metrics or patient chronic condition indicators.

FIG. 5 illustrates an example of a method **500** for detecting a target event from one or more physiological signals. The method **500** can be implemented and operate in an ambulatory medical device or in a remote patient management system. In an example, the method **500** can be performed by the patient chronic condition-based target event detector circuit **113** implemented in IMD **110**, or the external device **120** which can be in communication with the IMD **110**.

At **501**, at least two chronic condition indicators of a patient can be received. The patient chronic condition indicators can be descriptive of the patient characteristics or sustained medical status that do not change or slowly change over a certain specified time, such as approximately at least six months. The at least two chronic condition indicators, including a first and a second chronic condition indicator of the patient, can be non-identical. For example, the first and the second chronic condition indicators can respectively include at least one of a chronic disease indicator of the patient e.g., prior MI, ischemic or dilated cardiomyopathy, valvular disease, renal disease, COPD), a prior medical procedure indicator of the patient (e.g., CABG, thoracic surgery), or a demographic characteristic indicator of the patient (e.g., age, sex, race, height, NYHA classifications). The chronic condition indicators can include binary values indicating the presence or absence of a specified condition, a plurality of categorical classifications or progressive stages of a particular chronic condition, or a plurality of value ranges of a physiologic parameter.

At **502**, one or more physiological signals can be sensed from the patient. The physiological signal may represent electrical or mechanical activities in the body. Examples of the physiological signal include: heart rate, heart rate variation, conduction times, arrhythmias, intrathoracic impedance, intracardiac impedance, arterial pressure, pulmonary artery pressure, RV pressure, LV coronary pressure, heart sounds, respiration signals including respiration rate or tidal volume, posture, activity, physiologic response to activity;

coronary blood temperature, blood oxygen saturation, electrolyte concentrations, or other measures descriptive of the patient's physiology. The physiological signal can be received from a signal sensing circuit coupled to the electrodes on one or more of the leads such as 108A-C, or implanted or external physiologic sensors associated with an ambulatory medical device. The physiologic signal can also be received from a signal memory where the physiological data are stored.

At 503, a plurality of signal metrics can be generated from the one or more physiologic signals. A signal metric can include signal feature extracted from the one or more physiologic signals, such as a statistical measure, a morphologic measure, or a portion of the physiologic signal indicative of a physiologic activity. Examples of the signal metrics can include: mean, median, or other central tendency of a portion of a physiologic signal; variance, standard deviation, or other second-order or higher-order statistical measure of a portion of a physiologic signal; peak, trough, slope or other morphological features of a portion of a physiologic signal; P wave and QRS complexes in an electrogram signal; S1, S2, S3 or S4 components of a heart sound signal; inspiration phase and expiration phase of a respiration signal.

The generated signal metrics can include a first set of one or more signal metrics when the first chronic condition indicator meets a first specified criterion, and a second set of one or more signal metrics when the second chronic condition indicator meets a second specified criterion. Since the first and the second chronic condition indicators can be non-identical to each other, the first set of the signal metrics may not be identical to the second set of signal metrics. In an example, the first chronic condition indicator is CKD and the second chronic condition indicator is diabetes. When the first chronic condition indicator meets the criterion of "CKD of stage 3 or above", the first set of signal metrics (M_{CKD}) can include: $M_{CKD} = \{\text{daily maximum respiration rate signal (MRR), average of intracardiac impedance signal (AvgZ1), 53 heart sound amplitude (S3Amp)}\}$. When the second chronic condition indicator meets the criterion of "patient having diabetes within the past 5 years", the second set of signal metrics ($M_{Diabetes}$) can include: $M_{Diabetes} = \{\text{standard deviation of average R-R intervals (SDANN), average of intracardiac impedance signal (AvgZ1)}\}$. Examples of the selection of signal metrics in accordance with the patient chronic condition indicator is discussed below, such as with reference to FIG. 6.

At 504, one or more patient-specific signal metrics can be selected from the plurality of signal metrics such as generated at 503. The patient-specific signal metrics can include at least one signal metric from an intersection of the first set of signal metrics corresponding to the first chronic condition indicator and the second set of signal metrics corresponding to the second chronic condition indicator. In an example where the first set of signal metrics corresponding to CKD includes $M_{CKD} = \{\text{MRR, AvgZ1, S3 Amp}\}$ and the second set of signal metrics includes $M_{Diabetes} = \{\text{SDANN, AvgZ1}\}$, the intersection of the two sets M_{CKD} and $M_{Diabetes}$, namely AvgZ1, can be selected as the patient-specific signal metrics, that is, $M_P = \{\text{AvgZ1}\}$. In another example, the patient-specific signal metrics can include at least one signal metric from the first set of signal metrics and at least one signal metric from the second set of signal metrics. Using the example of M_{CKD} and $M_{Diabetes}$ as discussed above, the patient-specific signal metrics can be selected as $M_P = \{\text{MRR, SDANN}\}$. The selection of the signal metric from each set to be a patient-specific signal metrics can be performed using performance measure of respective signal

metrics in each set. Examples of the performance measure of the signal metrics is discussed below, such as with reference to FIG. 6.

At 505, a target event or condition detection algorithm can be applied to the selected patient-specific signal metrics, such as that determined at 504, to detect a target event. The method of target event detection can be performed by the target event detector circuit 400.

The target event detection algorithm can include an algorithm for detecting an event indicative of HF decompensation status of the patient. The HF decompensation event detection algorithm includes computing a decompensation index such as using the patient-specific signal metrics. The decompensation index can be a quantitative parameter indicating the presence or severity of a physiologic condition precipitating an HF decompensation episode, such as excessive intrathoracic fluid accumulation, increased heart sounds, increased heart rate, increased respiratory rate, decreased tidal volume, or reduction in activity. In an example, an HF decompensation event is detected if the decompensation index is greater than a threshold. Examples of the target event detection algorithm is discussed below, such as with reference to FIG. 7.

FIG. 6 illustrates an example of a method 600 for generating a plurality of signal metrics from the one or more physiologic signals. The method 600 can be an example of 503. The method can take the input of a plurality of chronic condition indicators including at least a first and a second chronic condition indicators from a patient and one or more physiologic signals sensed from the patient such as using one or more physiologic sensors, and generate a set of signal metrics corresponding to each respective chronic condition indicator. The method 600 can also generate performance measure of each signal metric, which can be used to select one or more patient-specific signal metrics such as at 504. In an example, the method 600 can be performed by the signal metrics generator circuit 223 as illustrated in FIG. 2.

At 601, for each received chronic condition indicator, a respective set of candidate signal metrics can be generated when the chronic condition indicator meets a specified criterion, such as being categorized as a specified class of status, stage of disease, or a value range of a physiologic parameter. The candidate signal metrics associated with each chronic condition indicator, including the number, type, or methods of generating the candidate signal metrics, can be pre-determined such as using the population-based data. For example, for patient with CKD of stages 3 or above, various signal metrics can be evaluated in a cohort of patients with the similar chronic condition (e.g., CKD of stage 3 or above) and another cohort of patients absent of similar chronic condition. If a signal metric (e.g. daily maximum respiration rate, or MRR) shows a desirable level of difference between the two cohorts of patients, then the signal metric can be determined as a candidate signal metric associated with the chronic condition of CKD.

At 602, a signal sensitivity measure can be generated for each candidate signal metric. A sensitivity measure can be indicative of the ability of a signal metric in predicting a progression of a target event or condition. The sensitivity measure can be computed as a relative change of the respective signal metric from a first state to a second state. In an example, the second state includes temporal information non-identical to that of the first state. For example, in detecting an IV decompensation event, the first state can occur at a time prior to patient's developing a target event such as an HF decompensation event, and the second state can occur at a time preceding the first state by at least

specified time duration, such as approximately 1-6 months or approximately 1-3 months. In another example, the second state can be a baseline state computed using a plurality of historical measurements of the signal metric. The sensitivity measure can include a false negative rate of detecting a target event or condition. A low false negative rate can correspond to a high sensitivity measure. The sensitivity measure can also include a positive predictive value (PPV) which represents likelihood of correctly recognizing a target event or condition. A signal metric with high sensitivity preserves predictive content in detecting a target event such as an HF decompensation event.

The computed signal sensitivity measure can be used to determine a performance measure for the respective signal metric at **603**. The performance measure can indicate how well the signal metric can predict the progression or detect the occurrence of a target event or condition. In an example, the performance measure can include the sensitivity measure of the signal metric and the population-based statistics of the signal metrics. While the sensitivity measure can include “intra-patient” relative change of the signal metrics between two states with non-identical temporal information, the population-based statistics can include “inter-patient” consistency of the signal metric in preserving the predictive content in detecting a target event. For example, population-based statistics, such as average, variance, or statistical distribution of the sensitivity measure of daily MRR across a cohort of patients with similar type of chronic condition e.g., CKD of stage 3 and above), can be retrieved from the patient database, and further be used in determining the performance measure.

The performance measure for the respective signal metric can be determined using other parameters either in conjunction with or as an alternative to the sensitivity measure of the respective signal metric. In one example, the performance measure can include a specificity measure of a signal metric in response to a physiologic or non-physiologic change not associated with the target event or condition. The specificity measure can be calculated as a relative change in a signal metric from a first state such as the state prior to an HF decompensation event) to the second state (such as a state preceding the first state or a baseline state) in the absence of the target event. The specificity measure can include a false positive rate of detecting a target event or condition. A low false positive rate can correspond to a high specificity measure. The specificity measure can also include a negative predictive value (NPV) which represents likelihood of correctly recognizing a non-target event or condition. In another example, the performance measure can include a signal quality measure such as signal strength, signal variability, or signal-to-noise ratio. In various examples, population-based statistics of the specificity measure or of the signal quality measure, such as central tendency or statistical distribution computed using data of a cohort of patient with similar type of chronic condition, can be retrieved from a database and used in determining the performance measure.

At **604**, candidate signal metrics with respect to each chronic condition indicator input can be compared and prioritized using at least their respective performance measures. In an example, for each candidate signal metric, a composite performance score can be computed such as a linear combination or nonlinear combination of one or more of the sensitivity measure, the specificity measure, or the signal quality measure. The candidate signal metrics with respect to each chronic condition indicator can be prioritized such as being organized in a descending order at least based on the their respective composite performance scores. The

prioritized candidate signal metrics and the respective composite performance scores can be to select one or more patient-specific signal metrics such as at **504**.

FIG. 7 illustrates an example of a method **700** for detecting a target event from one or more physiological signals such as using information of the patient chronic condition indicators. The method **700** can be an embodiment of the method **500**. In an example, the method **700** can be performed by the target event detector **200**.

At **701**, one or more physiologic signals of a patient can be received. The physiologic signals may be received from a signal sensing circuit coupled to electrodes or external or implanted physiologic sensors associated with an ambulatory medical device or a physiological monitor, or from a signal memory.

At **702**, a first chronic condition indicator of the patient can be received such as from a system user (e.g., a physician) via a user interface on a transceiver in communication with the ambulatory medical device. The chronic condition indicator can include a chronic disease indicator of the patient, a prior medical procedure indicator of the patient, a demographic characteristic indicator of the patient, or any other condition descriptive of the patient characteristics or sustained medical status that do not change or slowly change over a certain specified time, such as approximately at least six months. The first chronic condition indicator can be compared to a specified criterion at **703**, such as determining if the first chronic condition indicator falls under a categorical class or a progressive stage of a chronic disease. When the first chronic condition indicator meets the specified criterion, a first set of signal metrics can be generated using the one or more physiologic signals at **703**. The signal metrics can be generated according to specified instructions and methods stored in the ambulatory medical device. For each signal metric a respective performance measure can be computed, which includes a sensitivity, a specificity, or a signal quality measure such as the signal-to-noise ration of the signal metric.

At **704**, a second chronic condition indicator of the patient can be received. The second chronic condition indicator can be non-identical to the first chronic condition indicator. A second set of signal metrics can be generated at **705** using a similar approach of signal metrics generation for the first chronic condition indicator at **703**. Because the second chronic condition indicator is not identical to the first chronic condition indicator, the second set of signal metrics can be non-identical to the first set of signal metrics.

At **706**, one or more patient-specific signal metrics can be selected from a group including both the first and second sets of signal metrics. In an example, if there is at least one signal metric shared by the first and the second set of the signal metrics, the patient-specific signal metrics can include at least one signal metric from an intersection of the first set and the second set of signal metrics. Alternatively or additionally, the patient-specific signal metrics can include at least one signal metric from the first set of signal metrics and at least one signal metric from the second set of signal metrics. For example, the signal metrics with respect to each chronic condition indicator can be organized according to their respective performance measure such as the sensitivity to the progression of target event. The patient-specific signal metrics can include the signal metric with the highest performance score from the first set and the signal metric with the highest performance score from the second set.

At **707**, a target event risk index can be generated using the one or more patient-specific signal metrics. The target event risk index can be a quantity indicating the presence or

severity of a physiologic condition precipitating the target event, such as excessive intrathoracic fluid accumulation in a target event indicative of HF decompensation status.

For each patient-specific signal metric selected at 706, a corresponding risk index can be computed such as an accumulated deviation of the signal metric intensity from a reference value over time. The intensity of the signal metric can include a central tendency measure (e.g. a mean or a median) of the signal metric over a specified time such as 3-10 days. The reference value can be a moving average of the signal metric, a low-pass or band-pass filtered signal metric with pre-determined filter coefficients, or other measures representing the trend of the intensity of the signal metric. In some examples, the deviation of the signal metric intensity from a reference value can be accumulated only if a certain criterion is met, such as the difference between the intensity of the signal metric and the decompensation index being greater than a specified threshold. Other examples of decompensation index can include the cumulative sum in detecting persistent shifts in the trended signal found in Brockway et al., U.S. Pat. No. 7,761,158, entitled "Detection of Heart Failure Decompensation Based on Cumulative Changes in Sensor Signals," filed Dec. 20, 2005, which is incorporated herein by reference in its entirety.

The target event risk index at 707 can be a linear or nonlinear combination of the individual risk index associated with each patient-specific signal metric. In an example, the target event risk index can be computed as a sum of individual risk index each scaled by a weight factor. The weight factor can be proportional to the performance measure of the respective signal metric. For example, if at 706 two patient-specific signal metrics, namely daily MRR and SDANN, are selected with respective performance measure F_{MRR} and F_{SDANN} , and the respective individual risk index is R_{MRR} and R_{SDANN} , then the target event risk at 707 can be determined as $R = R_{MRR} * F_{MRR} / (F_{MRR} + F_{SDANN}) + R_{SDANN} * F_{SDANN} / (F_{MRR} + F_{SDANN})$. The target event risk index can also be determined as a parametric or non-parametric model using the individual risk index, such as decision trees, neural network, Bayesian network, among other machine learning methods. In an example, the target event risk index can be computed using a probability model $p(D) = 1 / (1 + \exp(x))$, where $p(D)$ represents a probability of the target event such as a HF decompensation (D) event, and x represents a linear or nonlinear combination of individual risk indices, or a linear or nonlinear combination of measurements of the selected patient-specific signal metrics.

At 708, the target event risk index is checked against a specified criterion, such as compared to a specified threshold value, to determine if a target event is detected. A target event is deemed detected if the target risk index meets the specified criterion, and at 710 a report is generated to inform the user the detected target event. The report can include a textual or graphical message, a sound, an image, or any combination thereof.

If the target event risk index does not meet the specified criterion, then at 709 a decision is made as to whether a new set of patient-specific signal metrics is to be used for computing a target event risk index. The new set of the patient-specific signal metrics can be different than the patient-specific signal metrics used at 706. For example, if at 706 the patient-specific signal metrics include only the intersection between the first set of signal metrics such as generated at 703 and the second set of signal metrics such as generated at 705, then at 709 the patient-specific signal metrics can include the signal metric with the highest performance score from the first set and the signal metric

with the highest performance score from the second set. In another example, if at 706 the patient-specific signal metrics include the signals metrics with the highest performance score from the first and the second sets, then at 709, the patient-specific signal metrics can include the signals metrics with the second highest performance score from the first and the second sets. The decision at 709 can be received from a system user, or automatically executed in response to the target event risk index as determined at 708 fails to meet the criterion (e.g., falling below the detection threshold) by a narrow margin. If a different set of patient-specific signal metrics is decided to be used, then a new target event risk index can be generated at 707; otherwise, no target event is deemed detected, and the detection can continue with receiving the physiological signals at 701.

The above detailed description includes references to the accompanying drawings, which form a part of the detailed description. The drawings show, by way of illustration, specific embodiments in which the invention can be practiced. These embodiments are also referred to herein as "examples." Such examples can include elements in addition to those shown or described. However, the present inventors also contemplate examples in which only those elements shown or described are provided. Moreover, the present inventors also contemplate examples using any combination or permutation of those elements shown or described (or one or more aspects thereof), either with respect to a particular example (or one or more aspects thereof) or with respect to other examples (or one or more aspects thereof) shown or described herein.

In the event of inconsistent usages between this document and any documents so incorporated by reference, the usage in this document controls.

In this document, the terms "a" or "an" are used, as is common in patent documents, to include one or more than one, independent of any other instances or usages of "at least one" or "one or more." In this document, the term "or" is used to refer to a nonexclusive or, such that "A or B" includes "A but not B," "B but not A," and "A and B," unless otherwise indicated. In this document, the terms "including" and "in which" are used as the plain-English equivalents of the respective terms "comprising" and "wherein." Also, in the following claims, the terms "including" and "comprising" are open-ended, that is, a system, device, article, composition, formulation, or process that includes elements in addition to those listed after such a term in a claim are still deemed to fall within the scope of that claim. Moreover, in the following claims, the terms "first," "second," and "third," etc. are used merely as labels, and are not intended to impose numerical requirements on their objects.

Method examples described herein can be machine or computer-implemented at least in part. Some examples can include a computer-readable medium or machine-readable medium encoded with instructions operable to configure an electronic device to perform methods as described in the above examples. An implementation of such methods can include code, such as microcode, assembly language code, a higher-level language code, or the like. Such code can include computer readable instructions for performing various methods. The code may form portions of computer program products. Further, in an example, the code can be tangibly stored on one or more volatile, non-transitory, or non-volatile tangible computer-readable media, such as during execution or at other times. Examples of these tangible computer-readable media can include, but are not limited to, hard disks, removable magnetic disks, removable optical disks (e.g., compact disks and digital video disks), magnetic

cassettes, memory cards or sticks, random access memories (RAMs), read only memories (ROMs), and the like.

The above description is intended to be illustrative, and not restrictive. For example, the above-described examples (or one or more aspects thereof) may be used in combination with each other. Other embodiments can be used, such as by one of ordinary skill in the art upon reviewing the above description. The Abstract is provided to comply with 37 C.F.R. § 1.72(b), to allow the reader to quickly ascertain the nature of the technical disclosure. It is submitted with the understanding that it will not be used to interpret or limit the scope or meaning of the claims. Also, in the above Detailed Description, various features may be grouped together to streamline the disclosure. This should not be interpreted as intending that an unclaimed disclosed feature is essential to any claim. Rather, inventive subject matter may lie in less than all features of a particular disclosed embodiment. Thus, the following claims are hereby incorporated into the Detailed Description as examples or embodiments, with each claim standing on its own as a separate embodiment, and it is contemplated that such embodiments can be combined with each other in various combinations or permutations. The scope of the invention should be determined with reference to the appended claims, along with the full scope of equivalents to which such claims are entitled.

What is claimed is:

1. A medical device, comprising:

a patient status input unit configured to receive at least a first demographic characteristic indicator and a second demographic characteristic indicator of a patient, the second demographic characteristic indicator non-identical to the first demographic characteristic indicator;

a signal receiver circuit configured to receive one or more physiologic signals of the patient;

a signal metrics generator circuit, coupled to the signal receiver circuit, configured to generate a plurality of signal metrics from the received one or more physiologic signals, including to generate a first set of one or more signal metrics from the received one or more physiologic signals according to a first association with the first demographic characteristic indicator and in response to the first demographic characteristic indicator meeting at least one first specified criterion, and to generate a second set of signal metrics from the received one or more physiologic signals according to a second association with the second demographic characteristic indicator and in response to the second demographic characteristic indicator meeting at least one second specified criterion;

a patient-specific signal metric selector circuit configured to select a subset of patient-specific signal metrics from the first and second sets of signal metrics using signal metric performance measures of at least one metric from the first and second sets of signal metrics; and

a target event or condition detector circuit configured to detect a target heart failure event or condition of the patient when the selected subset of patient-specific signal metrics satisfies a detection threshold criterion, wherein the target event or condition detector circuit is further configured to generate an alert of the detected target heart failure event.

2. The device of claim 1, wherein the target heart failure event or condition includes either an event indicative of heart failure decompensation status of the patient, or an event of worsening heart failure.

3. The device of claim 1, wherein the patient status input unit is configured to receive a first chronic disease indicator

and a second chronic disease indicator of the patient, wherein the signal metrics generator circuit is configured to generate the first set of signal metrics further based on the first chronic disease indicator, and to generate the second set of signal metrics further based on the second chronic disease indicator.

4. The device of claim 3, wherein the first chronic disease indicator includes a renal disease indicator, and the second chronic disease indicator includes a prior thoracic surgery indicator.

5. The device of claim 1, wherein:

the signal receiver circuit is configured to be coupled to at least one physiologic sensor configured to sense the one or more physiologic signals from the patient;

the signal metrics generator circuit comprises a signal metrics performance analyzer circuit configured to generate, for the plurality of signal metrics, respective signal metrics performance measures including at least one of a signal quality measure, a signal sensitivity measure, or a signal specificity measure; and

the patient-specific signal metrics selector circuit is configured to select the subset of patient-specific signal metrics using the respective signal metric performance measures.

6. The device of claim 5, wherein the signal metrics performance analyzer circuit is configured to generate the signal sensitivity measure including a relative change of the respective signal metric from a first state to a second state, the second state including temporal information non-identical to that of the first state.

7. The device of claim 6, wherein the signal metrics performance analyzer circuit is configured to generate a sensitivity of a daily maximum respiration rate (MRR) indicative of a relative change from a baseline daily MRR, and wherein the signal metrics generator circuit is configured to generate a set of signal metrics including the daily MRR when the patient has no prior renal disease.

8. The device of claim 1, wherein the patient-specific signal metrics selector circuit is configured to select, for the subset of patient-specific signal metrics, at least one signal metric from an intersection of the first set and the second set of signal metrics.

9. The device of claim 1, wherein the patient-specific signal metrics selector circuit is configured to select, for the subset of patient-specific signal metrics, at least one signal metric from the first set of signal metrics and at least one signal metric from the second set of signal metrics.

10. A method, comprising:

receiving at least a first demographic characteristic indicator and a second demographic characteristic indicator of a patient, the second demographic characteristic indicator non-identical to the first demographic characteristic indicator;

sensing one or more physiologic signals of the patient;

generating a plurality of signal metrics from the sensed one or more physiologic signals, including generating a first set of one or more signal metrics according to a first association with the first demographic characteristic indicator and in response to the first demographic characteristic indicator meeting at least one first specified criterion, and generating a second set of signal metrics according to a second association with the second demographic characteristic indicator and in response to the second demographic characteristic indicator meeting at least one second specified criterion;

selecting from the first and second sets of signal metrics a subset of patient-specific signal metrics using signal

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metric performance measures of at least one metric from the first and second sets of signal metrics; applying a target event detection algorithm to the selected patient-specific signal metric subset to detect a target heart failure event or condition of the patient; and generating an alert of the detected target heart failure event.

11. The method of claim 10, wherein applying a target event detection algorithm to detect a target heart failure event or condition includes detecting either an event indicative of heart failure decompensation status of the patient, or an event of worsening heart failure.

12. The method of claim 10, further comprising receiving a first chronic disease indicator and a second chronic disease indicator of the patient, generating the first set of signal metrics further based on the first chronic disease indicator, and generating the second set of signal metrics further based on the second chronic disease indicator.

13. The method of claim 10, wherein:
generating the plurality of signal metrics includes generating, for the plurality of signal metrics, respective signal metrics performance measures including at least one of a signal quality measure, a signal sensitivity measure, or a signal specificity measure; and selecting the subset of patient-specific signal metrics includes using the respective signal metric performance measures.

14. The method of claim 13, wherein generating the signal sensitivity measure includes calculating a relative change of

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the respective signal metric from a first state to a second state, the second state including temporal information non-identical to that of the first state.

15. The method of claim 10, wherein selecting the subset of patient-specific signal metrics includes selecting at least one signal metric from an intersection of the first set and the second set of signal metrics.

16. The method of claim 10, wherein selecting the subset of patient-specific signal metrics includes selecting at least one signal metric from the first set of signal metrics and at least one signal metric from the second set of signal metrics.

17. The method of claim 10, wherein applying the target event detection algorithm includes:

generating a target event risk index using the selected subset of patient-specific signal metrics;

determining a detection criterion associated with the target heart failure event or condition using the at least one first or second demographic characteristic indicator; and

detecting the target heart failure event or condition when the target event risk index meets the detection criterion.

18. The method of claim 17, wherein generating the target event risk index includes generating, for each signal metric of the selected subset of patient-specific signal metrics, a respective weight factor, and calculating the target event risk index using a combination of the subset of patient-specific signal metrics each being weighted by the respective weight factor.

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IPC分类号	A61B5/08 A61B5/0205 A61B5/145 A61B5/00 A61B5/1455 A61B5/11 A61B5/024 A61B5/0245		
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摘要(译)

描述了用于检测生理目标事件的装置和方法，例如指示HF代偿失调状态的事件。医疗设备被配置为接收患者的至少第一和第二慢性病症指示物，从患者接收一个或多个生理信号，并且当第一和第二慢性病症指示符满足它们各自的时候产生多个信号指标标准。医疗设备可以使用从包括第一和第二组信号度量的组中选择一个或多个患者特定信号度量来检测目标事件或状况。医疗设备和方法可以被配置为检测指示HF代偿失调的事件。

