Statistical Analysis Plan

for
Clinical Investigation Plan
Study Title

A Prospective Evaluation of Surveillance Monitoring as an Alternative to Telemetry in Patients Scheduled for Telemetry without AHA Indication

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Clinical Investigation Plan Title	A Prospective Evaluation of Surveillance Monitoring as an Alternative to Telemetry in Patients Scheduled for Telemetry without AHA Indication
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1. Version History

Version	Summary of Changes	Author(s)/Title
1.0	• New Document	[redacted]
2.0	• Remove the CIP version reference in title page	[redacted]

2. List of Abbreviations and Definitions of Terms

Term	Abbreviation	Definition
Adverse Event	AE	Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the medical device. NOTE 1: This definition includes events related to the medical device or the comparator. NOTE 2: This definition includes events related to the procedures involved. NOTE 3: For users or other persons, this definition is restricted to events related to the medical devices.
American Heart Association	AHA	A non-profit organization in the United States that fosters appropriate cardiac care in an effort to reduce disability and deaths caused by cardiovascular disease and stroke. The AHA published guidelines in 2003 for telemetry monitoring that are still applicable and being used currently.
Adverse Device Effect	ADE	Adverse event related to the use of a medical device.
Clinical Investigation Plan	CIP	The present document describing the study protocol.
CIP Deviation	CIP Deviation	An event when the investigator or site personnel did not conduct the study according to the CIP or the clinical trial agreement. Medtronic's term for protocol deviation.

Term	Abbreviation	Definition
Case Report Forms / Electronic CRF	CRF/eCRF	Forms where the clinical data are collected. eCRF is the electronic version of the CRF.
Device Deficiency	DD	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. NOTE 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the medical device. NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the medical device
Electrocardiogram	ECG	A clinical technique measuring transthoracic electrical activity of the heart over time.
Electronic Data Capture	EDC	Electronic system where the data are collected through the eCRF (Oracle Clinical). May also be referred to as RDC (Remote Data Capture).
Emergency Department	ED	Medical treatment facility specializing in emergency medicine, the acute care of patients who present without prior appointment; either by their own means or by that of an ambulance.
Electronic Medical Record	eMR	Digital version of a patient's medical record within a single facility.
Food and Drug Administration	FDA	Federal agency of the United States Department of Health and Human Services; regulates medical devices.
Heart Rate	HR	A unit of measure that indicates speed of heartbeat in beats per minute.
Intensive Care Unit	ICU	A hospital unit with concentrated special equipment and specially trained personnel for the care of seriously ill patients requiring immediate and continuous attention.

Term	Abbreviation	Definition
Informatics Manager	IM	A type of software that is intended to route and store medical device data and device diagnostic information from supported devices to the VPMP, 3rd Party Annunciation Systems, Electronic Medical Record (eMR) and Clinical Information System (CIS).
Institutional Review Board	IRB	An independent body in US, consisting of healthcare professionals and non-medical members, whose responsibility is to protect rights, safety and well-being of human subjects involved in a clinical trial and to provide public assurance of that protection, by, among other things, expressing an opinion on the clinical trial protocol, the suitability of the investigators involved in the trial and the adequacy of facilities, and on the methods and documents to be used to inform trial subjects and obtain their informed consent.
Investigator Site File	ISF	Regulatory binder supplied by the sponsor.
Length of stay	LOS	The overall hospital length of stay, time of admission to discharge.
Post-anesthesia care unit	PACU	Hospital units typically attached to an operating suite that provide care to patients recovering from anesthesia
Product Accountability Log	PAL	A log maintained by investigative site personnel to document that the study product(s) have been used according to the protocol, and to document the final accounting of study product(s) received at the site, dispensed to subjects, returned by the subjects, and returned to the sponsor.
Patient-controlled analgesia	PCA	A drug-delivery system that dispenses a preset intravascular dose of a narcotic analgesic when the patient pushes a switch on an electric cord.
Rapid Response Team	RRT	A team of health care providers that responds to hospitalized patients with early signs of clinical deterioration on non-intensive care units to prevent respiratory or cardiac arrest.

Term	Abbreviation	Definition
Respiration Rate	RR	A unit of measure that indicates rate of breathing in breaths per minute.
Serious Adverse Event	SAE	Adverse event that 1. led to death, 2. led to serious deterioration in the health of the subject, that either resulted in a. a life-threatening illness or injury, or b. a permanent impairment of a body structure or a body function, or c. in-patient or prolonged hospitalization, or d. medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, 3. led to fetal distress, fetal death or a congenital abnormality or birth defect Note: Planned hospitalization for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered a serious adverse event.
Serious Adverse Device Effect	SADE	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Surveillance Monitoring	SM	The SM group will serve as the group who will be monitored by the study device for the duration of study enrollment on a medical-surgical unit(s).
Standard Operating Procedures	SOP	Medtronic Quality Standard Operating Procedures
Telemetry Monitoring	TM	The TM group will serve as the control group in this study and will be monitored via the site's standard of care telemetry practice/protocol.
Vital Sync™ Informatics Manager & Virtual Patient	Vital Sync™ IM & VPMP	A software only device that provides mobile and centralized remote monitoring.

Term	Abbreviation	Definition
Monitoring Platform		
Virtual Patient Monitoring Platform	VPMP	A display system that provides visual and audible renderings of physiologic data, waveforms, alarms and alerts routed through the Vital Sync™ IM from supported devices. The Vital Sync™ VPMP displays information received from the IM on any web-enabled device.

3. Introduction

This is a single-center, prospective, pilot, pre/post implementation study to collect post-market data on hospitalized subjects monitored via telemetry monitoring and surveillance monitoring.

The purpose of the study is to evaluate the impact of surveillance monitoring versus telemetry monitoring on clinical, healthcare economics, resource utilization, and qualitative outcomes.

4. Study Objectives

4.1. Objectives

4.1.1. Primary Objective

The primary objective of this study is to compare hospital length of stay (LOS) between the surveillance monitoring and telemetry monitoring period on patients without AHA telemetry indication.

4.1.2. Secondary Healthcare Economic and Resource Utilization Objectives

1. Compare telemetry bed, emergency department (ED) bed, and intensive care unit (ICU) bed availability between monitoring periods
2. Compare associated health care costs between monitoring periods
3. Compare the number of ICU, ED, PACU, and telemetry delays in transfer between monitoring periods
4. Compare the number of hospital unit transfers between monitoring groups
5. Compare the number of unplanned ICU transfers between monitoring groups
6. Compare ICU LOS for subjects having unplanned transfers to the ICU between monitoring groups
7. Compare the number of unnecessary diagnostic tests and therapeutic procedures generated by artifacts and/or misdiagnosis between monitoring groups

4.1.3. Secondary Clinical and Qualitative Objectives

1. Compare the number of Rapid Response Team (RRT) interventions between monitoring groups
2. Compare survival rates post RRT interventions between monitoring groups
3. Compare code blue rates between monitoring groups

4. Compare unplanned intubations between monitoring groups
5. Compare time of RRT activation to time of threshold notifications from SM system following clinical deterioration events
6. Assess clinical team satisfaction with surveillance monitoring and study product
7. Assess patient satisfaction with surveillance monitoring and study product
8. Assess perceptions of clinicians who prescribe telemetry to patients without AHA indication
9. Assess clinicians' perceptions on telemetry utilization and impact on hospital resource utilization and patient flow

4.2. Endpoints

4.2.1. Definition of Primary Endpoint

1. Length of stay

   Definition: The overall hospital LOS; time (in minutes) of admission to discharge during indexed hospitalization.

4.2.2. Definition of Secondary Healthcare Economic and Resource Utilization Endpoints

1. Telemetry bed, ED, and ICU bed availability

   Definition: Daily available number of beds available in both telemetry ED, and the ICU measured daily in hours from 12:00 AM to 11:59 PM.

2. Associated health care costs

   Definition: Costs attributable to the primary and secondary clinical and resource utilization endpoints.

3. ICU, ED, PACU, and telemetry delays in transfer

   Definition: Number of patients delayed admission to the ICU, ED, PACU, and to a telemetry bed.

4. Hospital unit transfers

   Definition: Number of inpatient transfers from one unit to another unit during course of hospital stay.

5. Unplanned ICU transfers

   Definition: Direct transfers from either study monitoring group to the ICU where the transfer was not planned during the hospital stay. For example, a transfer may be planned in advance of certain procedures for high risk patient as a preventative measure. The study team will determine if transfer were considered planned versus unplanned by review of the medical record.

6. LOS for ICU transfers

   Definition: The LOS (time in minutes) in the ICU for subjects who have an unplanned transfer to the ICU.

7. Diagnostic tests and therapeutic procedures generated by artifacts and/or misdiagnosis

Definition: Any diagnostic test or therapeutic procedure that was performed because of an ECG artifact or misdiagnosis made by clinician using monitoring technology

4.2.3. Definition of Clinical and Qualitative Endpoints

1. RRT interventions

   Definition: RRT's that are activated due to clinical deterioration as reported by the hospital or subject's medical record.

2. Survival rates post RRT interventions

   Definition: Survival at discharge or study completion following RRT activation.

3. Code blue rates

   Definition: Code blue teams that are initiated due to cardiopulmonary arrest as reported by the hospital or subject's medical record.

4. Unplanned intubations

   Definition: An intubation and mechanical ventilation that was not planned during the course of the hospital stay.

5. Time of RRT activation to time of a threshold notification(s) from the SM system following clinical deterioration events

   Definition: Time of RRT activation is the time that a clinician called or initiated the RRT team. Time of a threshold notification(s) is the time when the SM system alerts or alarms when a hospital protocol-defined threshold is exceeded.

6. Clinical team satisfaction with surveillance monitoring and study product

   Definition: Clinical team (nurse or physician) who treated at least one study subject will be asked to take a qualitative survey on satisfaction and confidence.

7. Patient satisfaction with surveillance monitoring and study product

   Definition: Each subject will be asked to take a qualitative survey on satisfaction and comfort at the end of enrollment.

8. Perceptions of clinicians who prescribe telemetry to patients without AHA indication

   Definition: Each eligible clinician will be asked to take a qualitative survey focused on the AHA guidelines and the monitoring modalities of the study.

9. Clinicians' perceptions on telemetry utilization and impact on hospital resource utilization and patient flow

   Definition: Each eligible clinician will be asked to take a qualitative survey focused on telemetry utilization and the monitoring modalities of the study.

5. Investigation Plan

This will be single-center, prospective, pilot, pre/post implementation study to collect post-market data on hospitalized subjects monitored via telemetry and surveillance monitoring.

Subjects who meet all of the inclusion criteria and none of the exclusion criteria will be assigned to either one of the monitoring groups and then followed for the duration of their hospital stay.

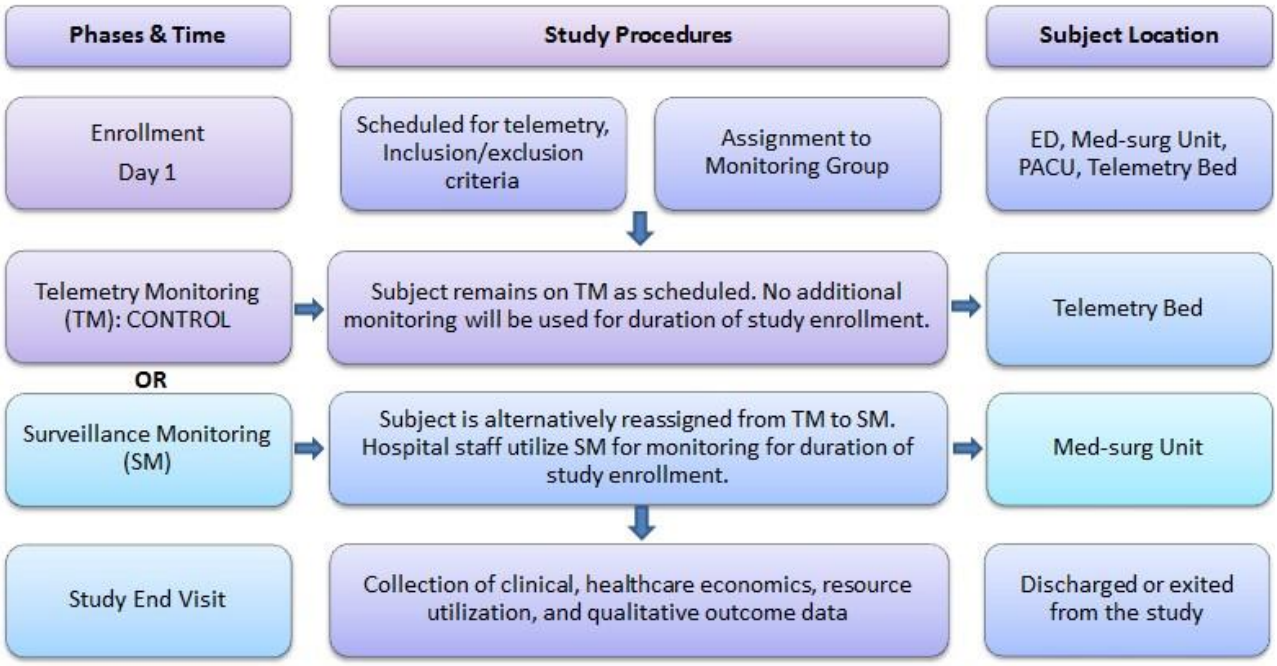
The subject population will include up to a total of 280 subjects with up to 140 subjects in each monitoring group.

Each enrolled subject will be assigned to one of two types of monitoring arms: telemetry monitoring (TM) OR surveillance monitoring (SM) and then followed for the duration of their hospital stay up to 30 days (± 2 days). The monitoring groups described in Section 10.1 of CIP will be enrolled in two prospective phases. The enrollment phase of the TM group will occur first. After TM subjects have completed study participation, the SM phase will initiate. Study flowchart is reported in Figure 1.

No randomization will be used during the course of the study. Assignment to a monitoring arm will be determined by the phase status of the study. During the TM phase, all subjects will be assigned to the TM group. During the SM phase, all subjects will be assigned to the SM group.

No blinding and interim analysis will occur during the course of the study.

Figure 1. Study Flowchart.



6. Determination of Sample Size

The study sample size is based on the primary non-inferiority objective of comparing hospital length of stay (LOS) between the surveillance monitoring (SM) and telemetry monitoring (TM) period on subjects without AHA telemetry indication. From similar study data published in the literature, we assume a similar LOS distribution for both monitoring groups with common coefficients of variation of 0.65. With a pre-specified non-inferiority margin of 0.2 for the mean ratio, a sample size of 132 in each group will provide more than 80% power to assess the objective at the significance level of 0.05. By taking into account potential attrition, a total of 140 subjects in each monitoring group will be used for this study.

7. Statistical Methods

7.1. Study Subjects

7.1.1. Disposition of Subjects

Subject disposition (e.g., number completing the study, number lost-to-follow-up) will be summarized with frequency tables.

7.1.2. Clinical Investigation Plan (CIP) Deviations

The investigator is required to conduct this study in accordance with the CIP, IRB requirements and applicable regulations.

A CIP deviation is defined as an event when the investigator or site personnel did not conduct the study according to the CIP or the clinical trial agreement. Thorough documentation of all deviations in source documents and transcription to eCRF is required, along with notification to your sponsor contact. Additionally, the site must complete the Deviation Log found in the ISF.

Major deviations are associated with subject safety or data integrity. They are defined as deviations with respect to:

- Patient informed consent procedure
- Patient eligibility criteria
- Study data collection and reporting

All deviations and reasons to deviate from the study protocol must be reported prior to deviation when planned or promptly after occurrence when unplanned to the sponsor regardless of whether medically justifiable, pre-approved by the sponsor, or taken to protect the subject in an emergency.

7.1.3. Analysis Sets

The primary effectiveness analysis will be based on all evaluable data from this study. A per protocol analysis will be performed based on all subjects who are compliant with the study protocol, i.e. who provide valid informed consents and do not experience any major protocol deviations.

The safety analysis will be based on all patients participated in the study.

7.2. General Methodology

In general, descriptive statistics will be used to summarize baseline and study outcomes. For continuous variables, number of available observations, mean, standard deviation, median, minimum and maximum values will be provided. For categorical variables, frequency and percentage will be used. Unless otherwise specified, statistical assessments will be based on 2-sided tests at an alpha level of 0.05, which include Student-t or Wilcoxon rank-sum or ANOVA test for continuous variables, and Chi-square or Fisher's exact test for categorical variables. Multivariate regression models will be used to assess impacts of potential confounding variable. Statistical analysis will be performed using [redacted] (SAS Institute Inc., Cary, NC) or other valid statistical software.

The primary effectiveness analysis will be based on all evaluable data from this study. A per protocol analysis will be performed based on all subjects who are compliant with the study protocol, i.e. who provide valid informed consents and do not experience any major protocol deviations.

For safety assessments, adverse events (AEs) will be summarized using frequency counts and percentages. Descriptive statistics will be provided by monitoring group and by severity and relationship. Additionally, differences between the two monitoring groups will be summarized along with 95% confidence intervals. Individual listings of adverse events, including event type, start date, duration, severity, and device-relatedness will be provided as appropriate. The safety analysis will be based on all patients participated in the study.

Further, a health economic analysis will be performed based on healthcare economic and resource utilization data collected in this study. Monitoring effectiveness, QoL in the form of Quality-Adjusted Life-Years (QALYs), life-years gained and other data collected in this study may be used as inputs to the model.

7.3. Center Pooling

N/A – This is a single-center study.

7.4. Handling of Missing Data and Dropouts

Sponsor study personnel will review collected data and create data queries for missing data that impacts data analysis. Subjects may withdraw from the study at any time and for any reason. If a subject officially withdraws from the study, the investigator will document the reason and collect final outcomes data from the subject's medical record. No additional follow-up will occur for withdrawn subjects..

7.5. Adjustments for Multiple Comparisons

N/A

7.6. Demographic and Other Baseline Characteristics

Demographics, medical history, hospital admission data and other baseline charactersitics data listed in section 10.2.1 of CIP will be summarized by descriptive statistics.

7.7. Inpatient Data Characteristics

In general, descriptive statistics will be used to summarize the inpatient data characterstics listed in the Table 1 of CIP. For continuous variables, number of available observations, mean, standard deviation, median, minimum and maximum values will be provided. For categorical variables, frequency and percentage will be used. Unless otherwise specified, statistical assessments will be based on 2-sided tests at an alpha level of 0.05, which include Student-t or Wilcoxon rank-sum or ANOVA test for continuous variables, and Chi-square or Fisher's exact test for categorical variables.

7.8. Interim Analyses

N/A - this study does not have a pre-specified interim analysis.

7.9. Evaluation of Objectives

The primary study endpoint is hospital of length of study (LOS), which is calculated from date of admission and discharge. The primary objective is to demonstrate that LOS of the SM group is similar (non-inferior) to the TM group.

[redacted]

Additionally, if the non-inferiority objective is met, superiority will also be assessed (without statistical penalty) to further understand the effectiveness of SM versus TM. The corresponding superiority hypothesis becomes: [redacted] (i.e., SM has shorter LOS duration than TM).

Secondary clinical and qualitative endpoints include:

- number of RRT interventions between monitoring groups
- survival rates post RRT interventions between monitoring groups
- Time of RRT activation to time of threshold notifications from SM system following clinical deterioration events
- code blue rates between monitoring groups
- unplanned intubations between monitoring groups
- clinical team satisfaction with surveillance monitoring and study product
- patient satisfaction with surveillance monitoring and study product
- perceptions of clinicians who prescribe telemetry to patients without AHA indication
- Clinicians' perceptions on telemetry utilization and impact on hospital resource utilization and patient flow

Additionally, healthcare economic and resource utilization data will be collected to evaluate:

- telemetry bed, ED, and ICU bed availability between monitoring periods
- associated health care costs between monitoring periods

- the number of ICU, ED, PACU, and telemetry delays in transfer between monitoring periods
- the number of hospital unit transfers between monitoring groups
- the number of unplanned ICU transfers between monitoring groups
- ICU LOS for subjects who have an unplanned transfer to the ICU between monitoring groups
- the number of unnecessary diagnostic tests and therapeutic procedures generated by artifacts and/or misdiagnosis between monitoring groups

7.10. Safety Evaluation

Only the following adverse events will be collected for this study:

- Any adverse events noting mild or moderate physiological deterioration
- Any adverse event whose relationship to the study device is: possible, probable, definite, or unknown/ impossible to determine, regardless of what the event may be.
- All SAEs, of any relationship, meeting definition in section 12.2 of the CIP must be reported.

The recording of adverse events for all enrolled subjects begin after the study devices are attached and ends with the subject's completes study enrollment. Completion is defined by when a subject is discharged from the hospital, completes 30 day (± 2 days) enrollment period, or if the subject is withdrawn from the study for any reason.

7.11. Health Outcomes Analyses

N/A

7.12. Changes to Planned Analysis

Any deviations from the original statistical plan will be justified and documented appropriately.

8. Validation Requirements

[redacted]

9. References

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