**Official Title: A Pilot Feasibility Study of an Ambulatory Multi-Vital Signs Monitor in Perioperative Patients**
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**Study Title:**
**A Pilot Feasibility Study of an Ambulatory Multi-Vital Signs Monitor in Perioperative Patients**

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**Sponsor or funding source:** Caretaker Medical, Inc.

## Background, Rationale and Context

Mounting evidence indicates that preoperative vital signs measurements can reflect undesired perioperative events. However, we rarely measure patients' vital signs in a thorough manner. We generally take a single snapshot and use those values for judging physiologic fitness for surgery and anesthesia.

The Third Perioperative Quality Initiative has identified that ambulatory measurement is the optimal method to establish baseline arterial pressure.[i] Another group determined that preoperative heart rate variability assessment is an objective and useful instrument for identifying patients with low autonomic physiological reserves and high risk of poor post-operative course.[ii] Likewise, Reich et al determined that intraoperative tachycardia was associated with adverse outcome in noncardiac surgery.[iii] Foëx et al found that a preoperative fast heart rate was a harbinger of perioperative adverse cardiac events. Among patients in the INPRESS study who were predominantly undergoing abdominal surgery who were at increased postoperative risk, management targeting an individualized systolic blood pressure, compared with standard management, reduced the risk of postoperative organ dysfunction.[iv]
We believe safer care can be achieved by focusing on patients in whom ambulatory vital signs indicate severe pathophysiology.

## Objectives

Using a portable,wireless multi-Vital Sign (VS) monitoring system developed by Caretaker Medical, we have several objectives:

- Primary:
    - Assess the feasibility of placing a Caretaker monitor on subjects scheduled for surgery for an 18-24 hour preoperative ambulatory monitoring session.
    - Assess the feasibility of placing a Caretaker monitor on subjects scheduled for surgery for the perioperative period defined as 18-24 hour intraoperative and postoperative ambulatory monitoring session.
    - Quantitate the data capture rate (estimated at over 99% in the company's prior studies) in this setting and how reliable our monitor return rate is in this setting.
- Secondary:
    - Assess the prevalence of alterations in VS (HR, RR, SaO2, BP, Cardiac Output, Stroke Volume, and HRV preoperatively) in a group of our highest acuity patients (top quartile of risk score) undergoing non-cardiac surgical procedures requiring at least a 2-day admission.
    - Assess any correlation of concerning ambulatory preoperative VS to postoperative VS.
        - We estimate that the percent of time the patient experiences these concerning preoperative VS values will correlate with a higher risk for a similar range of VS postoperatively, as well as undesired outcomes.
            - Undesired outcomes are defined as a) 30-day mortality, b) longer length of stay, c) higher ICU transfer, and 4) RRT calls).

## Methods and Measures

### Design

The Caretaker device is a wrist device that has a version that has already been approved by the FDA for use amongst medical professionals. For the conduct of this protocol we propose to use a newer version of the device called VitalStream, which has been cleared for use by the FDA. The New Caretaker device being used in the study has successfully passed all safety and accuracy tests by an independent lab, which have been submitted to the FDA already (see attached Declaration of Conformity).

We plan to monitor ambulatory preoperative CareTaker VS (HR, RR, SaO2, BP, Cardiac Output, Stroke Volume, and HRV) in random patients who meet our inclusion criteria for 18-24 hours, beginning during their preoperative (Preoperative Assessment Clinic, PAC) visit then overnight after they leave. Postoperatively, we will measure these VS in the same patients for approximately 24 hours postoperatively.

These monitors transmit VS to a data cloud, where we will be able to store and then later analyze the VS data. Clinical data will be collected from our EPIC Information System in order to provide pre- and postoperative information to examine corresponding risk factors and provide demographics.

### Setting

The subjects will be recruited in the PAC, where their monitoring period will start, and will continue at their residence (or wherever they decide to stay that night). They will return the monitor with them into the holding area on the day of their surgical procedure. We will replace their monitor on them in the Post-Anesthesia Care Unit (PACU) where it will remain with the patient for 24 hours +/- 6 hours continuously monitoring.

## Subjects selection criteria

- **Inclusion Criteria**
  - Age>18 years
  - Scheduled for surgery from an outpatient setting and scheduled for a pre-admission PAC appointment
  - Risk stratification placing them in the top 25th percentile using our internally-validated PAC Risk Score.
- **Exclusion Criteria**
  - Surgery on the day of admission (same-day surgery)
  - Any upper extremity surgery
- **Sample Size**
  - Our power analysis indicates that we need a total number of 150 patients to have at least 90% power in detecting a change in VS assuming a mean population VS (HR or BP) change of 12% from Phase 1 to Phase 2. We estimate a standard deviation of 10%, a type I error rate (2-sided) of 5%, and 1% missing follow-up data. We may have to consent up to 200 subjects in order to obtain the 150 evaluable subjects.
  - We estimate this study lasting up to 12months.

## Interventions and Interactions

*The essential features of interventions and interactions used to generate data for the study should be described.*

- Each participant will have the study summary discussed with them, then allowed to read and sign the informed consent after having the chance to interact with the study equipment and ask questions. This will occur in the PAC prior to their preoperative visit.
- Participants who agree with entering the study will then have the CareTaker monitor placed on their left wrist and calibrated prior to them leaving the PAC.
- No surveys or questionnaires will be administered to subjects.
- An information sheet about the Caretaker device along with an emergency contact number will be given to the study subject at the time the device is placed.
- A description of the monitoring device is located in Appendix B.
- Phase I (preoperative phase) Participants will wear the CareTaker monitor for at least 12 hours (up to 24 hours) in their place of residence during the immediate time period after their initial monitor placement.
- The participants will be asked to remove the monitor and ship it back to us using pre-printed packaging or bring it with them on their day of surgery and admission to the hospital, whichever they prefer.
- For Phase II (intraoperative and postoperative phases) of the study, the participants will then have a monitor placed back on them for intraoperative and postoperative monitoring. The monitor will remain on them for up to 24 hours postoperatively, at which time a member of the research staff will remove the monitor.
- Thus, the total length of time participants will undergo active CareTaker monitoring will be 24-48 hours, divided between pre-and intra- and postoperative phases.
- Participants who complete the entire study will be compensated $50 for their time and efforts.

**Table 1. Intervention Events According to Timeline**

| EVENT | PAC VISIT | DAY AFTER PAC VISIT | DAY OF ADMISSION | POSTOPERATIVE DAY 1 |
|---|---|---|---|---|
| Recruitment | **X** | | | |
| Consent | **X** | | | |
| Placement of monitor | **X** | | **X** | |
| Monitor removal | | **X** | | **X** |

**Outcome Measure(s)**

- Primary outcomes:
  - Phase I: Quantitate the data capture rate and how reliable our monitor return rate is in this setting.
  - Phase 2: Quantitate the data capture rate in this setting for the perioperative period.
- Secondary:
  - Assess the prevalence of alterations in VS (HR, RR, SaO2, BP, Cardiac Output, Stroke Volume, and HRV preoperatively) in a group of our highest acuity patients (top quartile of our internal PAC risk score) undergoing non-cardiac surgical procedures requiring at least an overnight admission. See Table 2 for ranges.

**Table 2. Data Sorted into Ranges for each parameter**

| Heart rate (bpm) | Systolic Blood pressure (mmHg) | Diastolic Blood Pressure (mmHg) | RR (bpm) |
|---|---|---|---|
| <50 | <90 | <50 | <8 |
| 51-70 | 91-100 | 51-65 | 9-12 |
| 71-90 | 101-120 | 65-80 | 13-16 |
| 91-100 | 121-140 | 81-90 | 17-20 |
| 101-110 | 141-160 | 91-100 | 21-25 |
| >110 | >160 | >100 | >25 |

- Assess any correlation of range data of ambulatory preoperative VS to postoperative VS.
- Determine if specific VS ranges are associated with undesired outcomes (defined as 1) 30-day mortality, 2) hospital length of stay, c) ICU transfer rate, and 4) Rapid Response Team calls).

**Analytical Plan**

- For the feasibility portion of the study, we will describe descriptive results of subjects' time of use of the monitor, their description of ease of use (difficult or easy), and the quantity of non-artifactual VS data.
- Results will be analyzed initially using descriptive statistics (percent of time VS remained in one of the ranges listed in Table 2) and means/standard error.
- We will compare relative incidence with matched cohort undergoing surgery using univariate analyses (categorical variables: chi-square test, continuous variables: Student's t-test or Mann–Whitney U test). We will use multivariable Cox proportional hazards regression modeling to assess VS risk factors associated with the postoperative undesired outcomes mentioned in outcome measures above.
- Statistical methods data will be expressed as mean ± SD, number (percentage), odds ratio, and 95% CI. All P values will be two-tailed, and a P value less than 0.05 is considered significant.

**Human Subjects Protection**

**Subject Recruitment Methods**

Subjects scheduled for surgery and to have a preoperative visit in our Preoperative Assessment Clinic (PAC) will be identified using their medical information in our EHR (Epic) to see if they fit our study criteria, and interviewed by research staff in the PAC. We ensure equal access to participation among women and minorities because we see both who fit our study criteria adequately on a daily basis. We will protect the privacy of potential subjects during recruitment by not using names or date of birth, and we will assign a unique study identifier to their medical record number.

- We do not plan to use recruitment flyers and advertisements.
- We will use limited PHI to identify subjects via medical records search.
    - We will use only the minimum amount of PHI necessary to review eligibility criteria and method to contact potential subjects. The information we plan to collect for this purpose includes:
        - Medical history
        - Planned surgical procedure

- Age
- PAC appointment time

Confidentiality/privacy will be protected prior to ascertaining desire to participate. Subjects who appear to be eligible for the study on the PAC appointment list will be marked for a conversation with a member of the study staff that will occur during their PAC visit. If they do not wish to participate, any record of their PHI will be immediately erased if electronic or shredded if on pa**Informed Consent**
Signed informed consent will be obtained from each subject by a member of the study staff while the patients are present in the PAC.

**Confidentiality and Privacy**
Confidentiality will be protected by collecting only information needed to assess study outcomes, minimizing to the fullest extent possible the collection of any information that could directly identify subjects, and maintaining all study information in a secure manner. To help ensure subject privacy and confidentiality, only a unique study identifier will appear on the data collection form. Any collected patient identifying information corresponding to the unique study identifier will be maintained on a linkage file, store separately from the data. The linkage file will be kept secure, with access limited to designated study personnel. Following data collection subject identifying information will be destroyed by securely wiping data 3 years after closure of the study, consistent with data validation and study design, producing an anonymous analytical data set. Data access will be limited to study staff. Data and records will be kept locked and secured, with any computer data password protected. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study.

**Data and Safety Monitoring**
Since this is a feasibility study of the Caretaker monitor, we will disable the data screen from displaying vital signs. Stored data will later be analyzed for proximity to standard vital signs measured during the subject's hospital stay. No vital signs from the monitor will be used for actionable interventions.
The principal investigator will be responsible for the overall monitoring of the data and safety of study participants. The principal investigator will be assisted by other members of the study staff.

**Reporting of Unanticipated Problems, Adverse Events or Deviations**
Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB and sponsor.

SUBSTUDY
Since our hypotheses are 1) the percent of time the patient experiences significantly abnormal or concerning preoperative vital signs (VS) values will correlate with a higher risk for a similar range of VS postoperatively, and 2) undesired outcomes such as myocardial infarction or higher 30-day readmission rates, we need to assure that the CareTaker monitors we use have relative accuracy. This will be important to help assure that the CareTaker device measures will be generalizable to the current standards used in clinics.

In order to investigate the accuracy and precision of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and oxygen saturation (SpO2) measurements of the CareTaker monitoring devices we are using, we plan to compare the values obtained by CareTaker devices to standard clinic VS measurements.

In order to accomplish this, we will measure VS using hospital-grade standard monitors at intake into the Preoperative Assessment Clinic. We will then discuss the study with the patient. If the patient accepts entry to the study, we will then place the CareTaker monitor on the patient and record the VS. We will then recheck VS with standard monitors every 20 minutes while the patient is in clinic. Within 60

seconds, each VS measure will be immediately followed by recording the VS from the CareTaker monitor.

**References**


[i] Perioperative Quality Initiative consensus statement on the physiology of arterial blood pressure control in perioperative medicine. Miller, Timothy E., Ackland, Gareth, L.Sanders, Robert, Sessler, Daniel, I.McEvoy, Matthew D. et al. British Journal of Anaesthesia, Volume 122, Issue 5, 542 - 551

[ii] Reimer P, Máca J, Szturz P, Jor O, Kula R, Ševčík P, Burda M, Adamus M. Role of heart-rate variability in preoperative assessment of physiological reserves in patients undergoing major abdominal surgery. *Ther Clin Risk Manag*. 2017;13:1223-1231.

[iii] Reich DL, Bennett-Guerrero E, Bodian CA, Hossain S, Winfree W, Krol M. Intraoperative tachycardia and hypertension are independently associated with adverse outcome in noncardiac surgery of long duration. Anesth Analg. 2002 Aug;95(2):273-7.

[iv] Futier E, Lefrant JY, Guinot PG, Godet T, Lorne E, Cuvillon P, Bertran S, Leone M, Pastene B, Piriou V, Molliex S, Albanese J, Julia JM, Tavernier B, Imhoff E, Bazin JE, Constantin JM, Pereira B, Jaber S; INPRESS Study Group. Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery: A Randomized Clinical Trial. JAMA. 2017 Oct 10;318(14):1346-1357. doi: 10.1001/jama.2017.14172. PMID: 28973220; PMCID: PMC5710560.


**Appendix A.**

1. Copies of questionnaire that will be used
    a. Verbal question: Did you find the wearing of the monitor difficult or easy?
    b. Verbal question: If difficult, what exactly made it difficult?
        i. Free text answer: _____
        _____
    c.

Appendix B.

CareTaker Monitor brochure is a separate attachment (pdf).