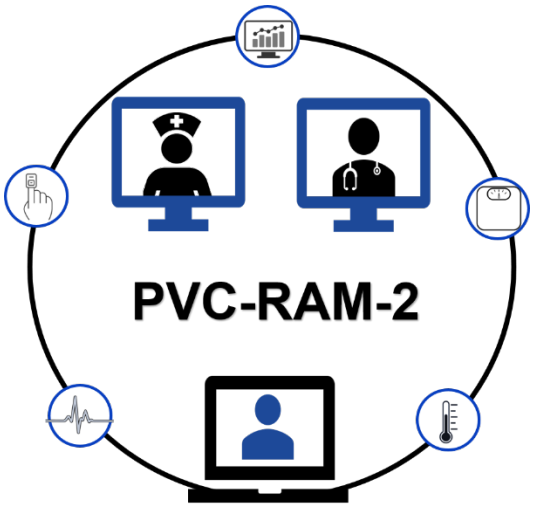

Post discharge after surgery Virtual Care with Remote Automated Monitoring technology-2 (PVC-RAM-2) Trial

Final Protocol v2.0
Dated June 9, 2025

Sponsor and Study Coordinating Group:
PVC-RAM-2 Project Office
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CLINICAL TRIAL SUMMARY

Title	**P**ost discharge after surgery **V**irtual **C**are with **R**emote **A**utomated **M**onitoring technology-2 (PVC-RAM-2) Trial
Project Office	PVC-RAM-2 Project Office, Population Health Research Institute Hamilton General Hospital Campus, DBCVSRI 237 Barton Street East, Hamilton, Ontario, Canada L8L 2X2
Study Size	2000 patients
Study Design	Multicentre, parallel group, superiority, randomized controlled trial.
Primary Objectives	To determine the effect of virtual care with remote automated monitoring (RAM) technology, compared to standard care, on acute-hospital care post-discharge following the index surgery, during the first 45 days after randomization, in adults who have undergone semi-urgent (e.g., oncology), urgent (e.g., hip fracture), or emergency (e.g., ruptured abdominal aortic aneurysm) surgery.
Secondary Objectives	To determine, during the first 45 days after randomization the effect of virtual care with RAM technology on the following secondary outcomes: 1) days in hospital; 2) index length of hospital stay; 3) hospital re-admission; 4) emergency department visit; 5) medication error detection; 6) medication error correction; and 7) surgical site infection. Additional secondary outcomes are pain of any severity, and moderate-to-severe pain assessed at 15 and 45 days post randomization. We will also assess optimal management of long-term health by evaluating among self-reported current smokers and those with atherosclerotic disease, whether patients are taking classes of efficacious medications at 45 days post randomization.
Tertiary Objectives	To determine, during the first 45 days after randomization, the effect of virtual care with RAM technology on the following tertiary outcomes: 1) infection; 2) re-operation; 3) myocardial infarction; 4) acute heart failure;5) arrhythmia that results in patient presenting to an emergency department or being admitted to hospital; 6) death; 7) health-related quality of life (HRQL); and 8) health services utilization-related costs.
Eligibility Criteria	Patients are eligible to participate if they fulfill all the following criteria: 1) are ≥40 years of age; 2) will undergo or have undergone semi-urgent, urgent, or emergency surgery requiring expected hospital stay of ≥2 days; and 3) provide informed consent to participate. Patients fulfilling any of the following criteria will be ineligible to participate: 1) planned transfer to a rehabilitation or convalescent facility, or repatriation from trial hospital site to local community hospital following surgery; 2) are unable to communicate with research staff, complete study surveys, or undertake an interview using a tablet computer due to a language barrier or a cognitive, visual, or hearing impairment; or 3) reside in an area without cellular network coverage.
Treatment Regimen	Patients randomized to the PVC-RAM-2 intervention will be taught how to use the cellular modem-enabled tablet computer and RAM technology, from Cloud DX. The RAM technology will measure the following biophysical parameters: 1. blood pressure, 2. heart rate, , 3. oxygen saturation, 4. temperature, and 5. weight. Patients will start using this technology after they are discharged from the hospital post-surgery. The day

	after the index hospital discharge will be day one of the intervention. Nurses and study personnel will establish contact and system set up with the patient as soon as possible after surgery. Nurses will ensure patients know how to connect to them if they need help or are experiencing any symptoms. Patients will take biophysical measurements with the RAM technology and complete a daily recovery survey for 14 days, and nurses will review these results daily. Through scheduled video visits, patients will interact with a nurse, virtually, on days 1, 3, 7 and 14 after the index hospital discharge. Using the Cloud DX tablet, patients will take a photograph of their wound daily for the first 7 days after the index hospital discharge, and nurses will review these pictures. If the patient's RAM measurements exceed predetermined thresholds, the patient reports specific symptoms (e.g., shortness of breath), a drug error is identified, or the nurse has concerns about the patient's health that require a physician's attention, the nurse will escalate care to a pre-assigned and available perioperative physician. Physicians will add or modify treatments as needed, and if required, they will have the patient come to an outpatient facility for evaluation or management. Via secure video, patients will also have virtual access to a nurse or physician 24 hours a day, 7 days a week. On days 1 and 14 after the index hospital discharge, the perioperative physician will also have a scheduled video visit with the patient to assess the patient, address any immediate medical needs, optimize their treatments including medications, and ensure they are adhering to directions for all prescription medications. A video visit with the physician will occur on day 7 to ensure optimization of medical therapy if the patient has atherosclerotic disease or is an active smoker. A maximum of two 7-day extensions to the virtual care with RAM intervention will be possible, depending on the patient's need for continued virtual nursing and medical support. The decision to extend will be based on standardized criteria. Patients randomized to standard care will receive post discharge care as per the standard of care at the hospital where they undergo surgery.
Follow-up	Outcome ascertainment will occur through direct patient follow-up. Study personnel will contact and assess all patients for the 15 and 45-day outcomes.

PVC-RAM-2 Protocol v1.0 Approval:

By signing the below, I designate my approval of the above-named version of the PVC-RAM-2 protocol.

Dr. Michael McGillion Principal Investigator Population Health Research Institute	_____ Signature	_____ Date
Dr. PJ Devereaux Principal Investigator Population Health Research Institute	_____ Signature	_____ Date
Dr. Sandra Ofori Principal Investigator Population Health Research Institute	_____ Signature	_____ Date

Contents

1 INTRODUCTION AND RATIONALE

Globally over 100 million adults (>500,000 Canadians) ≥45 years of age have major surgery annually; of these, 29% will suffer a prognostically important complication, >1.5% will die, and 7% will be re-admitted to hospital within 30 days of surgery.[1] In Ontario alone, surgical volumes have increased over 400% in the last decade.[2] This growth in surgery, without a corresponding growth in hospital beds, has resulted in a widespread push to prevent hospital readmission after discharge and identify ways to shorten length of hospital stay after surgery.

This major health system challenge has been exacerbated recently by the Coronavirus Disease 2019 (COVID-19) pandemic.[3] At the start of the pandemic, many hospitals canceled elective surgeries; however, the need for semi-urgent (i.e., oncological surgery that is not emergency surgery), urgent (e.g., hip fracture), and emergent (e.g., abdominal aortic aneurysm rupture) surgeries remained. Patients discharged after these non-elective surgeries frequently utilize acute-hospital care (i.e., hospital re-admission and emergency department visit) in the first 30 days following discharge.[4,5] As hospitals continue to struggle with increased patient volume due to backlogs from COVID-19, and have resumed elective surgeries, there continues to be the pressing need to reduce surgical patients' post-discharge use of acute-hospital care to ensure hospital capacity and facilitate management of the backlog of individuals waiting for elective surgeries.[3]

Postoperative virtual delivery of care and remote automated monitoring (RAM) of patients, from hospital-to-home, has garnered significant attention from healthcare providers, provincial ministries of health, and funders throughout COVID-19 as a solution to help address current pressures.[6] Virtual care encompasses all the ways that healthcare providers remotely interact (e.g., telephone, computer) with their patients.[7] RAM refers to the use of technology to remotely obtain data regarding patients' biophysical parameters (e.g., blood pressure).[7] While historically there has been substantial investment in remote patient management; there has been a lack of robust data to support the effectiveness of virtual care with RAM following surgery.[7]

We undertook the Post discharge after surgery Virtual Care with Remote Automated Monitoring technology-1 (PVC-RAM-1) Trial in 2020.[8,9] This randomized controlled trial (RCT) included 905 patients (from 8 centres in Ontario and Alberta), aged ≥40 years who had undergone non-elective surgeries (i.e., semi-urgent cancer surgery, urgent, or emergent surgery) and examined the effect of virtual care with RAM, compared to standard postoperative care.[8,9]

Patients in the experimental group received a cellular modem-enabled tablet computer and RAM technology provided by Cloud DX, which measured blood pressure, heart rate, respiratory rate, oxygen saturation, temperature, and weight (see Figure 1). For 30 days, patients took daily biophysical measurements and wound photographs and interacted virtually with specially trained nurses. These scheduled video visits occurred daily on days 1-15 and every other day from days 16-30.[8,9] On days without planned virtual visits, nurses could perform unscheduled virtual visits if they detected patients' biophysical measurements or recovery survey responses that exceeded predetermined thresholds. During all virtual visits, nurses discussed patients' symptoms, evaluated wounds and obtained pictures, reinforced principles of recovery after surgery and the need for physical distancing due to the COVID pandemic, and undertook medication review and reconciliation.[8,9] Nurses escalated care to pre-assigned and available perioperative physicians if patients' RAM measurements exceeded predetermined thresholds, patients reported specific concerning symptoms (e.g., dizziness), they identified drug errors, or they had concerns about patients' health that required a physician's attention. Physicians could interact with patients virtually via the tablet, and they added or modified treatments as appropriate. In the virtual care group, patients had access to a nurse or physician 24 hours a day, 7 days per week.[8,9]

Early on, the primary outcome of PVC-RAM-1 was changed to days alive at home because of a patient case that identified the potential for death to be a competing outcomes problem with our original primary outcome, acute-hospital care.[8,9] However, with only 3 deaths in each treatment group, the competing outcomes issue proved inconsequential. We found that virtual care and RAM did not significantly affect days alive at home, but raised the possibility of a reduction in acute-hospital care (22.0% in the virtual- care group versus 27.3% in the standard-care group; relative risk, 0.80; 95% CI, 0.64-1.01), brief acute- hospital care (13.7% versus 18.1%, relative risk, 0.75; 95% CI, 0.56-1.02), hospital re-admission (9.5% versus 12.8%; relative risk, 0.77; 95% CI, 0.53-1.11), and emergency department visits (19.7% versus 24.4%; relative risk, 0.81; 95% CI, 0.64-1.04).[9]

We also found that drug errors after hospital discharge post-surgery were common (i.e., 29.7% of virtual-care patients, with a mean of 2.1 drug errors per patient), and that virtual care with RAM demonstrated large absolute benefits in detecting (24.2%; 95% confidence interval [CI], 19.5-28.9) and correcting medication errors (24.4%; 95% CI, 19.9-28.9), compared to standard care.[9] Virtual care also demonstrated substantial absolute reductions in acute postoperative pain at 7 days (13.9% [95% CI, 7.4-20.4]), 15 days (11.9%, [95% CI, 5.1-18.7]) and 30 days (9.6% [95% CI, 2.9-16.3]) post randomization, respectively.[9] We also found improvement in moderate to severe postoperative pain scores (with patients at rest or upon movement), as well as in moderate to severe pain-related interference with recovery, compared to standard care at 15 and 30 days after randomization.

It is only credible to expect virtual care with RAM to impact outcomes if these interventions identify problems and lead to changes in management. In PVC-RAM-1, while we established predetermined thresholds for biophysical measurement in which nurses were to escalate care to a physician, nurses or physicians were at liberty to adjust the frequency of biophysical measurements and parameters for alerts. Across centres in the virtual care with RAM group in PVC-RAM-1, we found there were marked variations in the following: the proportions of patients for whom nurses escalated care to a physician, the number of escalations, the frequency in which biophysical parameters and onset or change in signs or symptoms triggered escalation of care, and the result of the escalation of care (e.g., change in medications).

In post hoc analyses, the patients from centres with the highest escalations of care in response to RAM had a lower risk of acute-hospital care (relative risk, 0.56; 95% CI, 0.38-0.82), brief acute-hospital care (relative risk, 0.47; 95% CI, 0.27-0.80), and emergency department visits (relative risk, 0.54; 95% CI, 0.37-0.81), compared to standard care. In terms of absolute benefit, substantial reductions in these outcomes were realized, as follows: acute-hospital care 14.1% (95% CI: 5.2-23.0); brief acute-hospital care 11.0% (95% CI: 3.6-18.4); and emergency department visits 14.2% (90% CI: 5.4-23.0). PVC-RAM-1 established a viable, adaptable, and scalable model for virtual care with RAM and led to important lessons learned about optimizing intervention effectiveness and efficiency. Our results suggest that virtual care with RAM may substantially affect lowering the risk of acute-hospital care, brief acute-hospital care, and emergency department visits if centres adhere to predetermined biophysical thresholds, escalate care as prespecified, and physicians and nurses then appropriately modify care. Moreover, we have learned that the timing of nursing follow-up and surgical wound photography can be streamlined to correspond to when complications occur and improve the efficiency of the intervention. Building on PVC RAM-1, we will undertake the Post discharge after surgery Virtual Care with Remote Automated Monitoring technology-2 (PVC-RAM-2) Trial to inform this issue.

1.1 Primary Research Question

Among patients who have undergone non-elective surgery, what is the effect of virtual care with RAM on acute-hospital care, post-discharge following the index surgery, during the first 45 days after randomization?

1.2 Need for the PVC-RAM-2 Trial

1.2.1 Patients being discharged from hospital after inpatient non-elective surgery are at substantial risk of subsequent acute hospital care

Our VISION Study, a prospective cohort study of a representative sample of 40,004 adults ≥45 years of age who underwent inpatient non-cardiac surgery at 28 centres across 14 countries,[1] demonstrated a 7% incidence of patient re-admission to hospital within 30 days of surgery. A large administrative database study (n=143,232) from the United States also demonstrated an overall 30-day incidence of unplanned hospital re-admissions after non-cardiac surgery of 7%.[5]

A Canadian Institute of Health Information study evaluated 2.1 million acute hospitalizations in Canada from April 2010 to April 2011.[4] Patients undergoing inpatient and same-day surgery accounted for 31% of participants. Surgical patients had a 7% unplanned 30-day re-admission rate, and the average cost associated with the re-admission was $9,700. Moreover, 19% of the surgical patients presented to an emergency department within 30 days of discharge after their index surgery.[4] Based on these data, it is estimated that 20-25% of adults being discharged after undergoing non-elective surgery will receive acute-hospital care within a 30-day follow-up period.

In a prospective cohort study of 5,158 consecutive patients who underwent cardiac surgery at 10 centres in Canada and the United States, 13% of patients were re-admitted to the hospital within 30 days of discharge.[10] A study of 324,070 Medicare patients in the United States who underwent coronary artery bypass grafting (CABG) surgery had a 22% incidence of emergency department visits within 30 days of discharge after their index hospitalization.[11] Based on these data, it is estimated that at least 25% of cardiac surgery patients will receive acute-hospital care within 30 days after discharge.

The PVC-RAM-1 trial,[8,9] inclusive of noncardiac and cardiac (emergent, urgent, and semi-urgent) surgeries found that the need for acute hospital care following discharge was common— 27% of individuals in the standard care group required acute hospital care following discharge from their index hospitalization, as compared to 22% in the virtual care with RAM group (RR: 0.8, 0.64 to 1.01; absolute difference 5.3%, − 0.3% to 10.9%).[8,9]

1.2.2 PVC-RAM-1 provides a viable virtual care with RAM model for adaptation

The science of virtual care with RAM remains a burgeoning field of study.[7] While there has been substantial investment and great promise of healthcare transformation, research in this area has historically been dominated by low-impact, small pilot studies. Research teams have not been able to predict and meet operational, logistical, technical, and coordination-related challenges. Our recent RAM state of the science review [7] found implementation failure at many levels, including: a) end-user non-adherence to protocols; b) unclear role expectations; c) lack of centralized oversight and coordination; d) underdeveloped intervention workflows; e) logistical problems with shipping monitoring equipment to and from patients' homes; f) failure to respond to patient deterioration in a timely manner; and g) failure to quickly solve technical problems.[7] Predicated on detailed user performance and acceptance testing,[12] as well as proof-of-concept work,[13] PVC-RAM-1[8,9] represented the culmination of our team's work over the last 5 years to overcome these implementation challenges, and offers insights into how best to move forward. As discussed, in PVC-RAM-1[9] in centres with the highest escalation of care, patients in the virtual care with RAM group had a lower risk of acute-hospital care, brief acute-hospital care, and emergency department visits, compared to standard care. In the virtual care with RAM group, there was considerable variation in the frequency with which nurses escalated care to a physician. Post hoc, we evaluated results across centres that had the highest (89.3% of patients had escalation of care), intermediate (54.5%), and lowest escalations of care (34.1%).[9] In the virtual care group, the total number of escalations and the mean escalations per patient, respectively, was 758 and 4.3 in the highest

escalation centres, 227 and 1.2 in the intermediate escalation centres, and 56 and 0.7 in the lowest escalation centres.[9] The total number and the mean escalations per patient varied in the virtual care with RAM group for various triggers across centres. For example, the mean escalations per patient for a biophysical parameter trigger was 1.6, 0.4, and 0.1 in the highest, intermediate, and lowest escalation of care centres, respectively.[9]

Escalations of care to a perioperative physician occurred in the highest escalation centres 747 times, in the intermediate escalation centres 200 times, and in the lowest escalation centres 43 times.[9] In terms of impact on patient management, the results of escalation of care varied across centres. For example, the mean change in medication per patient in the virtual care with RAM group was 1.3 in the highest, 0.7 in the intermediate, and 0.3 in the lowest escalation of care centres.[9]

Our experience in PVC-RAM-1[9] suggests that for optimal intervention effects, centres must adhere to our rigorous, predetermined RAM biophysical thresholds and clinical pathways, and escalate care to assigned perioperative physicians, who then need to actively engage with patients and optimize care as appropriate. In addition, we have gained insights into how to modify the virtual care with RAM intervention for greater efficiency and higher-volume patient throughput. The revised intervention is outlined in section 2.9. Finally, the PVC-RAM-1 data demonstrated that virtual care with RAM also has the potential to impact long-term outcomes through optimization of medical management. For example, in PVC-RAM-1 the use of nicotine replacement or non-nicotine smoking cessation drugs were increased more than 2- fold at 30-days in the virtual-care group (p=0.029). There remains, however, substantial improvements that can occur in optimizing pharmacological therapy to improve long-term health, which we will further develop and evaluate in PVC-RAM-2.

Since the time of PVC-RAM-1, we have been engaged in the PVC-RAM-3 trial, focused on elective surgery patients, with a primary outcome of reduced index hospital length of stay. The intervention in PVC-RAM-3 is a 14-day protocol, as opposed to the 30-day protocol we used in PVC-RAM-1. While focused on elective surgery patients, the Hamilton Health Sciences surgical transition program executed the 14-day PVC-RAM-3 intervention, on an operational level, on both elective and non-elective surgery patients while following them prospectively (i.e., not controlled clinical trial data) from April 2022 to February 2023. During this prospective observation period, 6% of patients enrolled in the 14-day virtual care program (n= 711) were readmitted to hospital within 30 days of index hospital discharge, as compared to 10% of surgical patients who received standard care (n= 3,219), without virtual care support. Moreover, the average length of index hospital stay for those enrolled in the 14-day virtual care program was 5 days, as compared to 7 days for those who received standard surgical care. These data suggest that non-elective surgery patients can be successfully discharged from their index hospitalization early with 14-days of virtual care support in place. While not controlled trial data, these observational data (see Appendix 4) also suggest that not all non-elective surgery patients require 30 days of virtual care support to recover successfully.

Data from PVC-RAM-1 support this argument. In PVC-RAM-1, we found that in the virtual care with RAM intervention group, the majority (i.e., 73%) of post discharge acute hospital care events occurred between days 0 to 15 of patients' recovery period at home, suggesting that a shorter duration of the virtual care intervention, like the PVC-RAM-3 model, may be adequate for the majority of non-elective surgery patients.

Based on our cumulative experience and the data we have accrued to date, we have modified the intervention for PVC-RAM-2 to enhance efficiency. We also included reduction of length of index hospital stay as a secondary outcome. The intervention is now 14 days in length, with the possibility of up to 2 seven-day extensions, as needed (see 2.9.1, Adapted Intervention).

2 PLAN OF INVESTIGATION

2.1 Trial Objectives

2.1.1 Primary objective

To determine the effect of virtual care with remote automated monitoring (RAM) technology, compared to standard care, on acute-hospital care post-discharge following the index surgery, during the first 45 days after randomization, in adults who have undergone nonelective surgery, including semi-urgent (e.g., oncologic surgeries which are not emergency surgeries), urgent (e.g., hip fracture), or emergency (e.g., ruptured abdominal aortic aneurysm) surgery.

2.1.2 Secondary objectives

To determine, during the first 45 days after randomization the effect of virtual care with RAM technology on the following secondary outcomes: 1) days in hospital; 2) index length of hospital stay 3) hospital re-admission; 4) emergency department visit; 5) medication error detection; 6) medication error correction; and 7) surgical site infection. Additional secondary outcomes are pain of any severity, and moderate-to-severe pain assessed at 15 and 45 days post randomization. We will also assess optimal management of long-term health by evaluating among self-reported current smokers and those with atherosclerotic disease, whether patients are taking classes of efficacious medications at 45 days post randomization.

2.1.3 Tertiary objectives

To determine, during the first 45 days after randomization, the effect of virtual care with RAM technology on the following tertiary outcomes: 1) infection; 2) re-operation; 3) myocardial infarction;4) acute heart failure; 5) arrhythmia that results in patient presenting to an emergency department or being admitted to hospital; 6) death; 7) health-related quality of life (HRQL); and 8) health services utilization-related costs.

2.1.4 Machine Learning Algorithm Development & Evaluation

We will use data collected during the trial to develop and evaluate machine learning algorithms for the early detection of clinical deterioration, surgical wound infection, and medication issues. A separate protocol and analysis plan for machine learning development & evaluation will be developed.

2.2 Trial Design

The PVC-RAM-2 trial is a multicentre RCT of 2,000 patients undergoing nonelective surgery and will determine the effects of virtual care with RAM versus standard care. Patients, healthcare providers, and data collectors will be aware of patients' treatment assignment. Outcome adjudicators will be masked to treatment allocation.

2.3 Centres

Numerous sites will participate in PVC-RAM-2.

2.4 Sample Size

Table 1 presents the trial power based on a 2-sided α=0.05, control group event rates of 23%, 24%, 25% and hazard ratios of 0.75 (provided by Power Analysis and Sample Size Software-13, method-Log Rank test accounting for competing risk). For the primary outcome of time to first acute hospital care, we expect to observe a 24% event rate in the Standard Care arm (based on the PVC-RAM-1overall

event rate). Considering a 2% competing risk of death, with a total sample size of N=2000, and 1:1 randomization to study arms, we can achieve more than 90% power to detect a clinically meaningful HR = 0.75 (25% hazard reduction by intervention). Reductions of this magnitude would be meaningful to healthcare decision makers who are calling for innovations in virtual care with RAM, to help alleviate current system pressures.[6]

2.5 Eligibility Criteria

2.5.1 Inclusion Criteria

Patients are eligible if they:

1. are ≥40 years of age;
2. will undergo or have undergone semi-urgent, urgent, or emergency surgery requiring expected hospital stay of ≥2 days; and
3. provide informed consent to participate.

2.5.2 Exclusion Criteria

Patients are ineligible if they:

1. have planned transfer to a rehabilitation or convalescent facility, or repatriation from trial hospital site to local community hospital following surgery;
2. are unable to communicate with research staff, complete study surveys, or undertake an interview using a tablet computer due to a language barrier or a cognitive, visual, or hearing impairment; or
3. reside in an area without cellular network coverage.

2.6 Patient Recruitment and Informed Consent

Participating surgeons will be contacted prior to recruitment start and asked to confirm participation of themselves and potentially eligible patients in the trial. Surgeons will be provided with information on the protocol and objectives of the current trial, the intervention model, and results of the PVC-RAM-1 trial through attendance at rounds, in-service education, and through discussion with other surgeons and trial researchers.

Study personnel will utilize efficient recruitment strategies that we developed in prior perioperative trials.[8,914,15] These include approaches to identify eligible patients through daily screening of surgical lists in the operating room, surgical wards, and intensive care units. Centres will also ask clinicians working in anesthesiology, surgery, and medicine to page the study personnel regarding all patients who will undergo or have undergone non-elective surgery and are admitted through the emergency room or are an inpatient. Research personnel will approach all eligible patients during the perioperative period to obtain informed consent.

2.7 Randomization

Randomization will occur prior to or as soon as possible after surgery when a patient is deemed eligible and informed consent is obtained.

Research personnel will randomize eligible patients via a 24-hour internet-based randomization system maintained by the coordinating centre at the Population Health Research Institute (PHRI), which is part of Hamilton Health Sciences and McMaster University in Hamilton, Ontario, Canada. The randomization process will use block randomization, stratified by centre and type of surgery (i.e., cardiac versus non-cardiac). We will use randomly varying block sizes, and study personnel and investigators will not know the block sizes. We will randomize patients in a 1:1 fashion to receive virtual care with

RAM versus standard care. After participant randomization, research personnel will notify the patient's surgeon of the treatment allocation.

2.8 Minimizing Bias

Our centralized, internet-based randomization procedure ensures concealment of randomization. Outcome ascertainment will occur through direct patient follow-up.

Outcome adjudicators (expert physicians) will be blind to treatment allocation, and all statistical analyses will use adjudicated decisions. We will undertake analyses according to the intention-to-treat principle. We will utilize the same mechanisms for ensuring >99% patient follow-up in PVC RAM-1 and our other large international perioperative trials.[8,9,16,17]

2.9 Trial Intervention

Patients will be randomized to virtual care with RAM technology or standard care. In the standard-care group, patients will receive their post hospital discharge management as per the standard of care at the hospital where they underwent surgery. No changes to surgeons' standard of care regarding post discharge management will occur for patients randomized to the standard-care group, as a result of the trial. For intervention patients, surgeons will receive training as described in section 2.6 and will understand that the decision about whether a patient randomized to the intervention may be discharged home early to virtual care with RAM lies with them, and their decision is based on their clinical judgement on what is best for the patient and understanding of the intervention care model.

2.9.1 Adapted Virtual care and RAM intervention

Patients randomized to the PVC-RAM-2 intervention (see Appendix 3) will be taught how to use the cellular modem-enabled tablet computer and RAM technology from Cloud DX. The RAM technology will measure the following biophysical parameters: 1. blood pressure, 2. heart rate, 3. oxygen saturation, 4. temperature, and 5. weight. The day after the index hospital discharge will be day one of the intervention. Study personnel will establish contact and system set up with the patient as soon as possible after discharge. Nurses will ensure patients know how to connect to them if they need help or are experiencing any symptoms. Patients will take biophysical measurements with the RAM technology and complete a daily recovery survey for 14 days, and nurses will review these results daily. Through scheduled video visits, patients will interact with a nurse, virtually, on intervention days 1, 3, 7 and 14 after the index hospital discharge. On days without planned virtual visits, nurses will organize unscheduled virtual visits if they detect patients' biophysical measurements or recovery survey responses exceed predetermined thresholds or the nurse identifies another reason for concern. During virtual visits, the nurse will discuss any symptoms the patient is experiencing, follow up with the patient on their evaluation of the wound photograph, reinforce principles related to recovery after surgery, assess pain, and undertake medication review and reconciliation on days 1, 3, 7, and 14 after the index hospital discharge. Using the Cloud DX tablet, patients will take a photograph of their wound daily for the first 7 days after the index hospital discharge, and nurses will review and evaluate these images. Patient wound photography and nursing picture review will occur until day 7, unless there is a wound issue that requires specific ongoing surveillance and documentation, such as surgical wound infection or dehiscence.

Nurses will intervene within the nursing scope of practice as needed and document their observations and interventions. If the patient's RAM measurements exceed predetermined thresholds, the patient reports specific symptoms (e.g., shortness of breath), a drug error is identified, or the nurse has concerns about the patient's health that require a physician's attention, the nurse will escalate care to a pre-assigned and available perioperative physician. Physicians will add or modify treatments as needed, and if required, they will have the patient come to an outpatient facility for evaluation or management. Via secure video, patients will also have virtual access to a nurse or physician 24 hours a day, 7 days a

week. On days 1 and 14 after the index hospital discharge, the perioperative physician will also have a scheduled video visit with the patient to assess the patient, address any immediate medical needs, optimize their treatments including medications, and ensure they are adhering to directions for all prescription medications. Should the patient be a confirmed smoker, or have a confirmed history of atherosclerotic disease, the physician will also have a video call with the patient on day 7, to optimize medical therapy to address these issues. By day 14 the physician and nurse will also confer with each other and the patient to determine whether the patient is ready for discharge from the intervention or whether an extension is required.

A maximum of two 7-day extensions to the virtual care with RAM intervention will be possible, depending on the patient's need for continued virtual nursing and medical support. The decision to discharge the patient or continue with extension A (i.e., days 15 to 21) will be made by day 14 of the intervention, and the decision to discharge the patient or continue with extension B (i.e., days 22 to 28) will be made by day 21. Extension to the intervention will be granted if patients meet any of the following requirements, subjecting them to suspected higher risk of post discharge hospital readmission or acute hospital care:

i) recent change in medication within the last 72 hours that requires further follow up for effectiveness evaluation (e.g., increased anti-hypertensives, adjustment of insulin dose, extension opioid use due to unrelieved moderate to severe pain, initiation of smoking cessation therapy, recent hold of pre-operative medications for chronic conditions which require re-initiation, with or without adjustment);

ii) nurse escalation of care to physician for a serious problem within the last 72 hours requiring follow up (e.g., congestive heart failure decompensation, uncontrolled a fib, surgical site infection, uncontrolled severe pain);

iii) recent ER visit, re-hospitalization or clinic visit within the last 72 hours requiring follow up (e.g., new blood work requested and pending, hospital discharge in the last 48-72 hours requiring virtual care team follow up);

iv) Follow up is pending for outstanding tests ordered during hospitalization or during the present intervention period. The results of these tests are anticipated in the next 7 days and it is anticipated that the results may result in a substantive change in care.

v) patient is living in a remote area with limited access to urgent healthcare resources and does not have the possibility of a family doctor/surgeon assessment available in the next 2 weeks should a complication occur.

vi) at request of surgeon, perioperative physician, or member of care team, for any patient not meeting above criteria but for which the care team believes an extension is necessary, e.g. patient has no family physician, support at home and has a history of regular ED visits

Each 7-day extension to the intervention will have a standardized scheduled video visit format and medication reconciliation format, similar to days 1 to 7 of the intervention, as follows:

Extension A): scheduled nurse video visits on days 17 and 21; scheduled physician visits on day 21; medication reconciliation day 21. In cases where a participant was re-admitted to hospital and is resuming

the intervention mid-extension A (e.g. resuming on Day 15) then the nurse will complete an off-schedule visit including medication reconciliation and escalate care to the physician as required.

Extension B): scheduled nurse video visits on days 24 and 28; scheduled physician visits on day 28; medication reconciliation day 28. In cases where a participant was re-admitted to hospital and is resuming the intervention mid-extension B (e.g. resuming on Day 22) then the nurse will complete an off-schedule visit including medication reconciliation and escalate care to the physician as required.

Within extension A and B, patients will routinely record their vital signs twice daily and wound photography may be continued as required. Nurses will continue to perform unscheduled virtual visits with the patients and escalate care to the perioperative physician as required.

Patients randomized to standard care will receive post discharge care as per the standard of care at the hospital where they underwent surgery. All patients will be contacted on day 45 post randomization to assess pain and pain related interference with recovery and to complete final medication audit.

2.9.2 Cloud DX's technology

The primary interface for the virtual care intervention is the Cloud DX Connected Health mobile application, which is embedded in a Samsung Android tablet computer equipped with a camera to facilitate patient and healthcare provider video-based communication. To ensure cybersecurity and patient privacy, the Samsung tablet supports cellular and Wi-Fi communications through Personal Information Protection and Electronic Documents Act (PIPEDA) and Personal Health Information Protection Act (PHIPA)-compliant cloud infrastructure. Bell will provide the cellular data plans. The Connected Health mobile application was designed by Cloud DX for use by patients of varying ages, including seniors. The application features simple menus for scheduling tasks (e.g., video visits with a nurse), measuring biophysical parameters, completing the recovery survey, and educational material.

The Cloud DX RAM technology consists of a group of easy-to-use, Bluetooth-enabled, Health Canada-licensed, biophysical parameters monitoring devices, which will be paired with the pre-programmed Samsung tablet computer. This RAM technology contains the Cloud DX Pulsewave PAD-1A wrist-based or brachial cuff blood pressure monitor, which derives measurements for blood pressure, pulse rate, and respiration rate. Patients will also receive a Cloud DX wireless pulse oximeter and wireless weight scale for measuring blood oxygen saturation and body weight respectively. A wireless digital thermometer will also capture core body temperature. These biophysical parameters will upload automatically to the Samsung tablet, except for temperature, which must be entered manually, depending on the model version of thermometer used. These Cloud DX monitors are certified according to International Standards Organization (ISO) Quality Management Standards and have achieved high patient usability and recommendation scores.

2.9.3 Patients obtaining Cloud DX technology and training

Following randomization, patients will receive the Samsung tablet computer and the RAM technology, instructions on how to use these devices, and their intervention monitoring schedule. This schedule outlines the frequency and timing of daily monitoring of biophysical parameters, recovery survey, and virtual nurse video visits. The Connected Health mobile application will be prepopulated with this program and will guide patients through the daily requirements with interactive prompts.

When on-boarded to the PVC-RAM-2 intervention, patients will be called via telephone and instructed on how to turn the tablet on and navigate to the option of engaging in a video conference call. On the first conference call, research personnel will demonstrate how to complete a full set of vital signs using the Bluetooth-enabled RAM technology. A step-by-step instructional manual, with pictures of each

step, will be used as a visual aid throughout the process; this manual will be provided to each patient/family for future reference at home, at any time. Approximately 30 minutes will be allocated for this initial set-up call with study participants. Based on PVC-RAM-1,[8,9] this allotted time is sufficient to allow for equipment setup, training, and any troubleshooting, if needed. Nurses will welcome family/caregiver involvement in these onboarding and training sessions. As backup, study nurses will also provide a dial-in telephone number to patients and caregivers at home to facilitate immediate connection with the virtual nursing team if technical concerns arise (e.g., patient cannot log on to a scheduled video call with the nurse).

2.9.4 Obtaining measurements of patients' biophysical parameters and recovery survey

Based on the protocol schedule, the tablet will prompt patients to measure their biophysical parameters. The frequency of daily biophysical measurements will be 3 times a day for the first 7 days, and then twice a day from day 8 until day 14 of the intervention. Weight will be measured daily in the morning before breakfast. The tablet will prompt patients daily to complete the recovery survey. The recovery survey consists of questions related to infection, bleeding, pain, dehydration, and cardiovascular and respiratory complications. Should extensions of the intervention be applied, patients' vital signs measurements will be twice daily, as previously described.

2.9.5 Intervention compliance monitoring

Patient compliance with vital sign measurements and completion of daily symptom survey, will be supported through pre-programming of the Cloud DX platform for each patient. Patients will receive prompts when it is time to take their vital signs and to complete the survey. Compliance with these expectations will be tracked within the Cloud DX platform and notifications of non-compliance will be visible to study nurses within the clinician dashboard. These compliance tracking settings will be configured for each site, allowing for centralized monitoring by the coordinating centre. Custom reports will be generated on compliance for individual patients (anonymized), grouped by study site. Over and above patients' routine, scheduled video visits with nurses and perioperative physicians we will also track the following clinician compliance indicators, daily: 1) unscheduled (i.e., extra) nurse-patient interactions (video visit or phone call for patient reassessment) arising from a biophysical parameter or survey result that is of concern; 2) nurse escalations to a perioperative physician; 3) escalation related physician interactions (video visit or phone call) with patient.

2.10 Risk to the Safety of Participants

Patients randomized to virtual care with RAM will be at very low risk of serious harm related to this intervention. No studies of such interventions have reported a serious adverse event related to this intervention, and there was no such occurrence in PVC-RAM-1.[8,9] We are using Health Canada approved RAM technology provided by Cloud DX.

2.11 Trial Outcomes

2.11.1 Primary Outcome

The primary outcome is acute-hospital care post discharge following the index surgery (i.e., a composite of hospital re-admission, emergency department visits and urgent care centre visits) within the 45 days of follow up after randomization.

2.11.2 Secondary Outcomes

Secondary outcomes during the first 45 days after randomization include: 1) days in hospital; 2) index length of hospital stay 3) hospital re-admission; 4) emergency department visit; 5) medication error

detection; 6) medication error correction; and 7) surgical site infection. Additional secondary outcomes are pain of any severity, and moderate-to-severe pain assessed at 15- and 45-days post randomization. Among patients with atherosclerotic disease, we will also assess optimal pharmacological management based upon whether patients are taking classes of efficacious medications at 45 days (i.e., an antiplatelet or anticoagulant drug; an angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker; and a statin). Among patients who report being current smokers at baseline we will assess if patients are receiving pharmacological smoking cessation interventions at 45 days after randomization. Outcome definitions are defined in Appendix 2.

2.11.3 Tertiary Outcomes

Tertiary outcomes during the first 45 days after randomization include: 1) infection; 2) re-operation; 3) myocardial infarction; 4) acute heart failure; 5) arrhythmia that results in patient presenting to an emergency department or being admitted to hospital; 6) death; 7) health-related quality of life (HRQL); and 8) health services utilization-related costs.

2.12 Follow-up

Study personnel will contact all participants 45 days after randomization and collect data on the study outcomes. Study personnel will also administer the EQ-5D-5L (https://euroqol.org/eq-5d-instruments/sample-demo)[16] at baseline and 45 days after randomization for all study patients. Study personnel will contact all patients and collect data on the following outcomes: 1) Brief Pain Inventory-Short Form (BPI-SF)[17] on days 15 and 45 after randomization; and 2) medication error detection and medication error corrections on day 15 and 45 after randomization. For patients in the virtual care with RAM group, the virtual nurse will collect data on the following outcomes while the patient is receiving the intervention: 1) medication error detection; and 2) medication error corrections.

If a patient reports an event, we will collect source documentation through hospital records or family physician reports. If study personnel are unsuccessful in contacting patients, they will contact the patient's primary care physician or a close relative or friend not residing with the patient, whose contact information the patient will provide at the time of enrolment. If patients (or next of kin) indicate that the patient has experienced an outcome, study personnel will contact their physician(s) to obtain documentation. Research personnel will record all trial data on case report forms (CRFs) with information entered directly into an electronic data capture program.

2.13 Statistical Analyses

Following the intention-to-treat principle, we will analyze patients in the treatment groups to which they were randomized. The Project Office Operations Committee will create a separate statistical analysis plan that the statistical analyses will follow. The statistical analysis plan will be developed and finalized before any investigator is unblinded.

2.13.1 Main analyses

We will compare patients allocated to the PVC-RAM-2 intervention to those allocated to standard postoperative care. We will present the survival probability (free from acute hospital care) using the Kaplan-Meier estimator. We will use log-rank tests to compare the survival probability of the primary outcome between the PVC-RAM-2 intervention group versus the standard care group. We will use Cox proportional hazards models, accounting for the competing risk of death using the methods defined by Fine and Gray,[18] to estimate the effect of the PVC-RAM-2 intervention on the primary and secondary outcomes. We will present the hazard ratios and their associated 95% confidence intervals. We will use the relative risk and 95% confidence interval for the binary outcomes. We will infer

statistical significance if the computed 2-sided p-value is <0.05. For continuous outcomes, we will evaluate treatment effects using appropriate statistical techniques, e.g., analysis of co-variance (ANCOVA).

2.13.2 Interim Analyses

Two interim efficacy analyses based on the primary outcome will occur when 50% and 75% of the patients have been followed for 45 days. The Data Monitoring Committee (DMC) will employ the modified Haybittle-Peto rule of 4 standard deviations (SDs) ($\alpha = 0.000067$) for analyses in the first half of the trial (including the first planned interim analysis) and 3.5 SDs ($\alpha = 0.00047$) for all analyses in the second half. For a finding of the treatment to be considered significant, these predefined boundaries will have to be exceeded in at least 2 consecutive analyses, 2 or more weeks apart. The α-level for the final analysis will remain the conventional $\alpha = 0.05$ given the infrequent interim analyses, their extremely low α-levels, and the requirement for confirmation with subsequent analyses.

If at any time during the trial, safety concerns arise, the DMC Chair will assemble a formal meeting of the full committee. The DMC will make their recommendations to the Project Office Operations Committee after considering all the available data and any external data from relevant studies. If a recommendation for termination is under consideration, before a decision is made, the Project Office Operations Committee will explore all possibilities. A detailed charter will be developed and govern the activities of the DMC.

2.13.3 Sub studies and secondary analyses

Separate protocols or statistical analyses plans will be written for all sub studies and secondary analyses.

3 TRIAL MANAGEMENT

3.1 Arrangements for the Day-to-Day Management of the Trial

Figure 2 illustrates the organizational structure of the PVC-RAM-2 Trial. The PHRI Project Office is the coordinating centre for this trial and is responsible for the development of the randomization scheme, trial database, data consistency checks, data analyses, coordination of the trial centres, and conducting the trial. The Co-Principal Investigators, Project Officers, Program Manager, and Research Coordinator are responsible for the activities of the Project Office. No statistician with knowledge of the randomization code will participate in the management or coordination of the PVC-RAM-2.

3.2 Site Principal Investigators

All participating centres will have a site Principal Investigator (PI), and this individual is responsible for ensuring compliance with respect to the intervention, visit schedule, and procedures required by the protocol. The site PI will ensure the provision of all information requested in the trial database in an accurate and timely manner according to instructions provided. The site PI will maintain patient confidentiality with respect of all information accumulated in the course of the trial, other than that information to be disclosed by law.

4 ENSURING DATA QUALITY

The Data Management Plan will outline the procedures to ensure data quality and will include the following: 1) all research personnel will undergo a training session before trial commencement to ensure consistency in trial procedures including data collection and reporting; 2) all centres will have a detailed

trial Manual of Operations that will outline each step of the protocol; 3) the Project Office personnel will review detailed monthly reports on screening, enrollment, patient follow-up, data transmission, thoroughness, and completeness of data collection, and event rates, and they will rapidly address any identified issues; 4) the Project Office, along with programmers, will create internal validity and range checks in TrialMaster that will identify any errors or omissions and notify the sender and Project Office of any such issues; 5) the Project Office will undertake data validation of the trial data forms; and 6) the Project Office will send investigators regular quality control reports.

5 ETHICAL CONSIDERATIONS

This trial will be conducted in compliance with the protocol, principles laid down in the Declaration of Helsinki, Good Clinical Practice (GCP), and all applicable laws and regulations of Canada. Before study initiation, the site PI must have written and dated approval/favourable opinion from the Research Ethics Board (REB) for the protocol and consent form. Amendments to the protocol will require REB approval.

All patient information will be stored in a high security computer system and kept strictly confidential. Subject confidentiality will be further ensured by utilizing subjects' identification code numbers to correspond to treatment data in the computerized files. Patients' medical information obtained as a result of this trial is considered confidential and disclosure to third parties is prohibited. Medical information may be given to patients' personal physicians or to other appropriate medical personnel responsible for the patients' welfare. Data generated as a result of the trial are to be available for inspection on request by the participating physicians, REB, study monitors, and competent authorities.

6 IMPORTANCE OF TRIAL

Patients being discharged from the hospital after inpatient non-elective surgery are at substantial risk of subsequent acute-hospital care. Moreover, eliminating surgical backlogs of the current magnitude we face is unprecedented and innovations in care are needed to manage the crisis. Virtual care with RAM holds promise to reduce acute hospital care among adults discharged following non-elective surgery. Building upon lessons learned in PVC-RAM-1,[8,9] PVC-RAM-2 may have a crucial role to play in relieving current health system pressures.

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8 APPENDIX 1: Tables and Figures

Table 1: Power Calculation for control event rates of 23%, 24% and 25%; hazard ratio of 0.75 and relative risk reduction of 22% and accounting for a 2% competing risk of death.

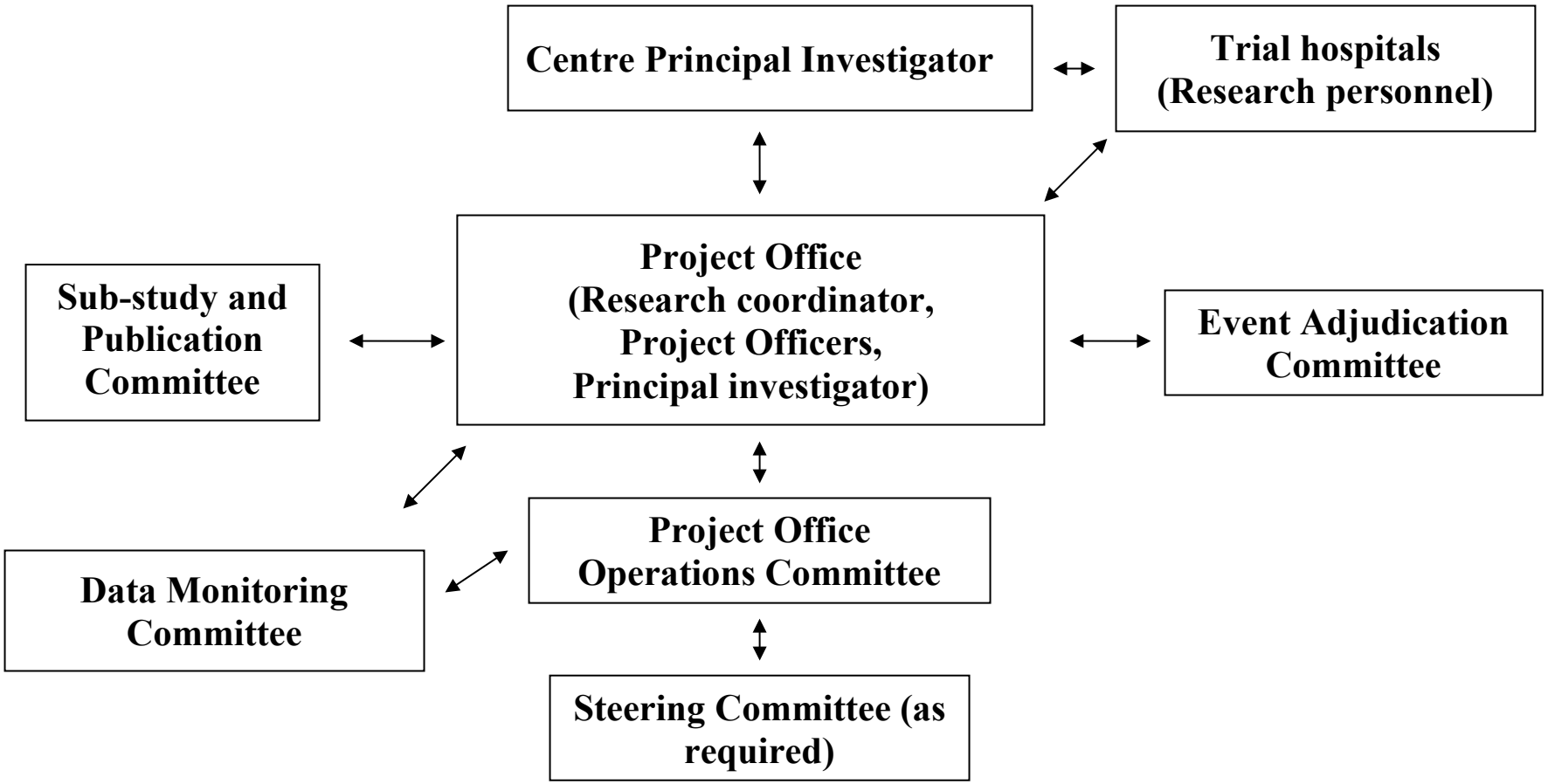
Intervention (22% RRR)	**19.5%**	**18.72%**	**17.94%**
Control	25%	24%	23%
Hazard Ratio	0.75	0.75	0.75
Sample Size	2000	2000	2000
Power	98%	97%	96%

Table 2. Example of vital sign thresholds and recommend nurse and physician actions

SBP measurement	Flag to nurse on CloudDX Connected Health Dashboard	Nurse recommended action	Physician recommended action
100-109 mm Hg	Mild	Nurse to contact and assess patient during scheduled video call. Advise patient to re-check measurement. Nurse to update perioperative care physician, at daily rounds.	Rule out precipitating factors (e.g. sepsis, volume depletion, bleeding, heart failure). Review medication and fluid intake. Decrease blood pressure medication dosage accordingly. Order back to nurse and coordinate follow up with nurse. Reassess in 24 hours.
86-99 mm Hg	Medium	Nurse to contact and assess patient within 30 minutes. Advise patient to re-check measurement. If unresolved, nurse will inform perioperative care physician within 1 hour.	All of the above and the following. Withhold anti-hypertensives until SBP >100 mmHg if patient with no HFrEF. Assess volume status. Order back to nurse and coordinate follow up. Reassess in 4-6 hours
≤85 mm Hg	High	Contact and assist patient immediately. Advise patient to re-check measurement. If unresolved, nurse will inform perioperative care physician within 15 minutes.	Assess patient for symptoms. If patient is asymptomatic then all of the above and the following. Withhold anti-hypertensives. Consider video call with patient. Consider clinic assessment. Order back to nurse and coordinate follow up If patient is symptomatic then all of the above and consider emergency room assessment.

Figure 1. Cloud DX Connected Health kit

Figure 2. PVC-RAM-2 organizational structure



9 APPENDIX 2: Outcome Definitions

Outcome	Definition
Acute-hospital care	Acute-hospital care is a composite outcome of hospital re-admission and emergency department visit, which includes urgent-care centre visit.
Hospital re-admission	Patient re-admission to hospital.
Emergency department visit	Patient visit to an emergency department, which includes urgent-care centre visit.
Days in Hospital	Total number of days in hospital from randomization to 45 days post-randomization, including index hospital stay and any hospital readmission (s). A day in hospital is counted if a participant spends 1 minute of any day admitted to hospital.
Medication error detection	Medication errors include mistakes in medication prescribing, transcribing, dispensing, administering, or monitoring due to preventable events or actions taken by a patient, caregiver, or healthcare worker. Medication errors include: drug omission (i.e., patient did not take a drug they were supposed to take), drug commission (i.e., patient taking a drug they were not supposed to take), duration error, dosing error, frequency error, route error, and timing error.
Medication error correction	Any medication error that is corrected.
Surgical site infection	Surgical site infection is an infection that involves the skin, subcutaneous tissue of the incision (superficial incisional), or the deep soft tissue (e.g., fascia, muscle) of the incision (deep incisional).
Pain	Pain intensity and related interference with usual daily activities, will be measured via the Brief Pain Inventory-Short Form (BPI-SF).[1] The BPI-SF includes four 11-point numeric rating scales (NRS) of pain intensity, which measure “average”, “least”, and “worst” pain intensity in the past 24 hours (hrs.), respectively, as well as pain intensity “now” (0= no pain, 10= pain as bad as you can imagine). The BPI-SF interference subscale will also be used, which measures the degree to which pain interferes with general activity, mood, walking, work, relations with others, sleep, and enjoyment of life (NRS for each item; 0=does not interfere, 10=completely interferes). A total interference score is determined by calculating the sum of these 7 items. The BPI-SF has strong psychometric properties with well-established reliability and validity across divergent surgical groups. Moderate to severe pain is defined by a score of ≥4/10 on a standard numeric rating scale (NRS) for pain.

Index Length of Hospital Stay	Length of hospital stay calculated from time of surgery completion (i.e., time of surgical wound closure) until discharge from the index hospitalization (measured in days and hours).
Optimal pharmacological management among patients with atherosclerotic disease	Among patients with atherosclerotic disease, we will also assess optimal pharmacological management based upon whether patients are taking 0, 1, 2, or 3 of the following classes of efficacious medications at 45 days (i.e., an antiplatelet or anticoagulant drug; an angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker; and a statin).
Optimal pharmacological management self-reported current smokers	Among patient who self-report to be current smokers at baseline, we will assess if patients are receiving pharmacological smoking cessation interventions at 45 days after randomization.
Health services utilization-related costs	Costs associated with hospital re-admission, length of stay, and healthcare utilization will be obtained from administrative datasets.
Health-related quality of life (HRQL)	HRQL will be measured with the EQ-5D-5L instrument (https://euroqol.org/eq-5d-instruments/sample-demo) due to its increased sensitivity and validation in several countries including Canada. [2] The EQ-5D-5L is also recommended in Canada[3] to calculate the Quality Adjusted Life Years (QALYs) when conducting cost-effectiveness analyses.
Infection	Infection is defined as a pathologic process caused by the invasion of normally sterile tissue, fluid, or body cavity by pathogenic or potentially pathogenic organisms.
Re-operation	Re-operation refers to any surgical procedure undertaken for any reason (e.g., wound dehiscence, infection).
Myocardial infarction	The diagnosis of myocardial infarction requires one of the following criteria: 1. Detection of a rise or fall of a cardiac biomarker (preferably troponin) with at least one value above the 99th percentile of the upper reference limit (URL) together with evidence of myocardial ischemia with at least one of the following: A. ischemic signs or symptoms (i.e., chest, arm, neck, or jaw discomfort; shortness of breath, pulmonary edema); B. development of pathologic Q waves present in any two contiguous leads that are ≥ 30 milliseconds; C. new or presumed ECG changes indicative of ischemia (i.e., ST segment elevation [≥ 2 mm in leads V_1, V_2, or V_3 OR ≥ 1 mm in the other leads], ST segment depression [≥ 1 mm], or symmetric inversion of T waves ≥ 1 mm) in at least two contiguous leads; D. new LBBB; or

	E. new cardiac wall motion abnormality on echocardiography or new fixed defect on radionuclide imaging F. identification of intracoronary thrombus on angiography or autopsy 2. Cardiac death, with symptoms suggestive of myocardial ischemia and presumed new ischemic ECG changes or new LBBB, but death occurred before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased. 3. Percutaneous coronary intervention (PCI) related myocardial infarction is defined by elevation of a troponin value (>5 x 99th percentile URL) in patients with a normal baseline troponin value (≤99th percentile URL) or a rise of a troponin measurement >20% if the baseline values are elevated and are stable or falling. In addition, either (i) symptoms suggestive of myocardial ischemia or (ii) new ischemic ECG changes or (iii) angiographic findings consistent with a procedural complication or (iv) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality are required. 4. Stent thrombosis associated with myocardial infarction when detected by coronary angiography or autopsy in the setting of myocardial ischemia and with a rise and/or fall of cardiac biomarker values with at least one of value above the 99th percentile URL. 5. Coronary artery bypass grafting (CABG) related myocardial infarction is defined by elevation of cardiac biomarker values (>10 x 99th percentile URL) in patients with a normal baseline troponin value (≤99th percentile URL). In addition, either (i) new pathological Q waves or new LBBB, or (ii) angiographic documented new graft or new native coronary artery occlusion, or (iii) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. 6. For patients who are believed to have suffered a myocardial infarction within 28 days of a MINS event or within 28 days of a prior myocardial infarction, the following criterion for myocardial infarction is required: Detection of a rise or fall of a cardiac biomarker (preferably troponin) with at least one value above the 99th percentile of the upper reference limit (URL) and 20% higher than the last troponin measurement related to the preceding event together with evidence of myocardial ischemia with at least one of the following: A. ischemic signs or symptoms (i.e., chest, arm, neck, or jaw discomfort; shortness of breath, pulmonary edema); B. development of pathologic Q waves present in any two contiguous leads that are ≥ 30 milliseconds; C. new or presumed new ECG changes indicative of ischemia (i.e., ST segment elevation [≥ 2 mm in leads V_1, V_2, or V_3 OR ≥ 1 mm

	in the other leads], ST segment depression [≥ 1 mm], or symmetric inversion of T waves ≥ 1 mm) in at least two contiguous leads; D. new LBBB; or E. new cardiac wall motion abnormality on echocardiography or new fixed defect on radionuclide imaging F. identification of intracoronary thrombus on angiography or autopsy
Acute heart failure	The definition of acute heart failure requires at least one of the following clinical signs (i.e., elevated jugular venous pressure, respiratory rales or crackles, crepitations, or presence of S3) with at least one of the following: 1. radiographic findings of vascular redistribution, interstitial pulmonary edema, or frank alveolar pulmonary edema, OR 2. heart failure treatment with a diuretic and documented clinical improvement.
Arrhythmia that results in patient presenting to an emergency department or being admitted to hospital	Any arrhythmia that results in patient presenting to an emergency department, which includes an urgent care centre, or being admitted to hospital.
Death	The definition of death is all cause mortality.

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10 APPENDIX 3: Schedule of Assessments

Assessments	Baseline	Day 1	Day 3	Day 7	Day 14	Day 15	Day 17	Day 21	Day 24	Day 28	Day 45
Inclusion/ Exclusion Criteria	X										
Informed Consent	X										
Randomization	X										
Demographics	X										
Vitals/ Labs	X										
Participant Characteristics	X										
Medical History	X										
Substance Use	X										
Con-Meds	X										
Operative Assessment Details	X										
Index Hospitalization Details	X										
VIRTUAL CARE COHORT											
Assessments	**Baseline**	**Day 1**	**Day 3**	**Day 7**	**Day 14**	**Day 15**	**Day 17**	**Day 21**	**Day 24**	**Day 28**	**Day 45**
Virtual Nurse Visit		X	X	X	X ***DTE***		X+	X+ ***DTE***	X++	X++	
Perioperative Physician Visit		X		X*	X ***DTE***			X+ ***DTE***		X++	
Pain Score		X	X	X	X		X	X	X	X	
Medication Reconciliation		X	X	X	X		X	X+	X	X++	
Vitals[a]		X[a]	X[a]	X[a]	X[a]	X+[a]	X+[a]	X+[a]	X++[a]	X++[a]	
Wound Photo[b]		X[b]	X[b]	X[b]							
Medication Audit						X					X
EQ5D5L	X										X

Brief Pain Inventory (BPI)						**X**					**X**
Clinical Events											**X**
Substance Use											**X**
STANDARD OF CARE COHORT											
Assessments	**Baseline**	**Day 1**	**Day 3**	**Day 7**	**Day 14**	**Day 15**	**Day 17**	**Day 21**	**Day 24**	**Day 28**	**Day 45**
Medication Audit						**X**					**X**
EQ5D5L	**X**										**X**
Brief Pain Inventory (BPI)						**X**					**X**
Clinical Events											**X**
Substance Use											**X**

DTE: Decision to Extend virtual care for an additional 7 days

***** Optional physician visit for those with atherosclerotic disease, or current smoker

+ Optional first extension for patients identified by MD and Nurse as requiring additional monitoring per protocol defined criteria

++ Optional second extension for patients identified by MD and Nurse as requiring additional monitoring per protocol defined criteria

a Patients will take biophysical measurements with the RAM technology and complete a recovery survey, daily for 14 days, and nurses will review these results daily. Biophysical parameters include the following: *blood pressure, heart rate, oxygen saturation, temperature, and weight.*

b Using the Cloud DX tablet, patients will also take a photograph of their wound daily for the first 7 days, unless otherwise directed or unable to complete

11 APPENDIX 4: Patients with virtual care vs. control surgical population (non-trial patients April 2022-February 2023)

Virtual Nursing Station Population						
Service	**# Virtual Nursing pts with inpatient surgery**	**Average LOS**	**Unplanned readmits within 30 days of discharge**	**% readmits**	**ED Visits within 30 days of discharge**	**% ED visits**
Cardiac Surgery	259	6.7*	19	7%*	50	19%*
ENT	1	1.0	-	-	-	-
General Surgery	93	6.7*	6	6%*	18	19%
Gynecology	49	3.6*	6	12%	10	20%
Neurosurgery	29	4.2*	-	-	1	3%*
Orthopedic Surgery	203	2.6*	7	3%*	32	16%
Plastic Surgery	3	3.3*	-	-	-	-
Spinal Surgery	22	5.3*	-	-	-	-
Urology	20	5.7*	3	15%	3	15%*
Vascular Surgery	32	4.3*	1	3%*	5	16%*
Grand Total	**711**	**5.0***	**42**	**6%**	**119**	**17%**
Control Surgical Population						
Service	**# Pts with inpatient surgery**	**Average LOS**	**Unplanned readmits within 30 days of discharge**	**% readmits**	**ED Visits within 30 days of discharge**	**% ED visits**
Cardiac Surgery	814	9.7	114	14%	168	21%
ENT	5	1.0	-	-	-	-
General Surgery	582	7.0	51	9%	91	16%
Gynecology	195	4.3	16	8%	31	16%
Neurosurgery	35	7.4	3	9%	4	11%
Orthopedic Surgery	811	4.5	30	4%	114	14%
Plastic Surgery	56	6.8	3	5%	12	21%
Spinal Surgery	304	10.1	49	16%	37	12%
Urology	119	6.6	9	8%	24	20%
Vascular Surgery	299	5.4	39	13%	57	19%
Grand Total	**3219**	**7.0**	**314**	**10%**	**538**	**17%**

*Indicates a lower value (LOS, unplanned readmissions, ED visits) in the virtual nursing station population compared to the control population. The control surgical population might not be an exact match to the VNS population.