cmaj OPEN

Post discharge after surgery Virtual Care with Remote Automated Monitoring technology (PVC-RAM) versus standard care randomized controlled trial

Journal:	*CMAJ Open*
Manuscript ID	CMAJOpen-2020-0176
Manuscript Type:	Protocol
Date Submitted by the Author:	22-Jul-2020

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Keywords:	Cardiovascular medicine, Community medicine, Diagnostics, Health services research, Nursing, Surgery
More Detailed Keywords:	Remote automated monitoring technology, Virtual care, Non-elective surgery, Randomized controlled trial, Standard care, Days alive at home
Abstract:	Background: After non-elective (i.e., semi-urgent, urgent, and emergent) surgeries, patients discharged from hospitals are at risk of re-admissions, emergency department visits, or death. During the Coronavirus Disease 2019 (COVID-19) pandemic, we are undertaking a trial to determine if virtual care with remote automated monitoring (RAM) compared to standard care will increase days alive at home, in adults being discharged after non-elective surgery. Methods: We will randomize 900 adults, being discharged after non-elective surgery, to virtual care with RAM or standard care, at 8 Canadian hospitals. Patients and health-care providers know treatment assignments. Outcome adjudicators are masked to treatment allocations. Patients in the experimental group learn how to use the tablet computer and RAM technology, which measures the following biophysical parameters: blood pressure, heart rate, respiratory rate, oxygen saturation, temperature, and weight. For 30 days, patients take daily biophysical measurements and complete a recovery survey. Patients interact with a virtual nurse daily on days 1-15 and every other day from days 16-30. Nurses escalate care to pre-assigned and available physicians if RAM measurements exceed predetermined thresholds, patients report specific symptoms (e.g., syncope), a medication error is identified, or nurses have concerns they cannot resolve. The primary outcome is days alive at home during the 30 days after randomization. Interpretation: This trial will answer an important question informing how to manage surgical patients after discharge in the setting of the COVID-19 pandemic and offer insights for management of non-elective surgical patients in general. Trial Registration: NCT04344665.

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym- page 1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry- Abstract, page 2
	2b	All items from the World Health Organization Trial Registration Data Set page 2
Protocol version	3	Date and version identifier Not applicable
Funding	4	Sources and types of financial, material, and other support- page 13
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors- page 13
	5b	Name and contact information for the trial sponsor- page 13
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities- page 13
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)- page 11
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention- page 3
	6b	Explanation for choice of comparators- page 3
Objectives	7	Specific objectives or hypotheses- page 7

Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)- page 4

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained- page 4
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) page 4 and Supplemental Documents
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered pages 5 and 6
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) Supplemental Documents
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) page 6
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial pages 5 and 6
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended page 7
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) pages 7 and 8
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations pages 8 and 9
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size page 4

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions pages 4 and 5
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned page 5
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions pages 5
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how page 5
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial not applicable
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol page 8
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols Supplemental Documents
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol page 8
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol pages 9 and 10
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) pages 9 and 10
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) page 9

Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed. Page 10
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial. Page 10
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct. Page 8
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor. Page 8

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval page 11
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) page 11
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) Page 4
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable not applicable
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial. Pages 8 and 11
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site. Page 13
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators page 13
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation. not applicable

Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions page 12
	31b	Authorship eligibility guidelines and any intended use of professional writers page 13
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code pages 13 and 14
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates Supplemental Documents
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable not applicable

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

Post discharge after surgery Virtual Care with Remote Automated Monitoring technology (PVC-RAM) versus standard care randomized controlled trial

PVC-RAM Investigators

Word count: 2428

ABSTRACT

Background: After non-elective (i.e., semi-urgent, urgent, and emergent) surgeries, patients discharged from hospitals are at risk of re-admissions, emergency department visits, or death. During the Coronavirus Disease 2019 (COVID-19) pandemic, we are undertaking a trial to determine if virtual care with remote automated monitoring (RAM) compared to standard care will increase days alive at home, in adults being discharged after non-elective surgery.

Methods: We will randomize 900 adults, being discharged after non-elective surgery, to virtual care with RAM or standard care, at 8 Canadian hospitals. Patients and health-care providers know treatment assignments. Outcome adjudicators are masked to treatment allocations. Patients in the experimental group learn how to use the tablet computer and RAM technology, which measures the following biophysical parameters: blood pressure, heart rate, respiratory rate, oxygen saturation, temperature, and weight. For 30 days, patients take daily biophysical measurements and complete a recovery survey. Patients interact with a virtual nurse daily on days 1-15 and every other day from days 16-30. Nurses escalate care to pre-assigned and available physicians if RAM measurements exceed predetermined thresholds, patients report specific symptoms (e.g., syncope), a medication error is identified, or nurses have concerns they cannot resolve. The primary outcome is days alive at home during the 30 days after randomization.

Interpretation: This trial will answer an important question informing how to manage surgical patients after discharge in the setting of the COVID-19 pandemic and offer insights for management of non-elective surgical patients in general.

Trial Registration: NCT04344665.

INTRODUCTION

At the start of the Coronavirus Disease 2019 (COVID-19) pandemic, many hospitals cancelled elective surgeries for various reasons (e.g., reduce the risk of COVID-19 transmission, facilitate physical distancing, preserve personal protection equipment, and maximize bed availability for patients with COVID-19); however, throughout the pandemic, the need for semi-urgent (e.g., oncology), urgent (e.g., hip fracture), and emergent (e.g., abdominal aortic aneurysm rupture) surgeries remained. Patients discharged after non-elective (i.e., semi-urgent, urgent, or emergent) surgeries are at substantial risk of hospital re-admissions, presentation to emergency departments or urgent-care centres, or death in the 30 days following discharge.[1-3] Many centres are now resuming elective surgeries. To facilitate management of the backlog of individuals waiting for elective surgeries, ensure hospital capacity for patients with COVID-19, and minimize the spread of COVID-19, there is a need to reduce non-elective surgical patients' subsequent use of acute-hospital care.

A strong rationale and encouraging evidence suggests that virtual care with remote automated monitoring (RAM) will increase days alive at home, in adults discharged after surgery.[4] We are undertaking the Post discharge after surgery Virtual Care with Remote Automated Monitoring technology (PVC-RAM) Trial to address the following question: among adults discharged after non-elective surgery, does virtual care with RAM increase days alive at home during the first 30 days after randomization, compared to standard care?

METHODS

Design and setting

The PVC-RAM trial is a multicentre, parallel-group, superiority, randomized controlled trial (RCT) of 900 patients being discharged from the hospital after non-elective surgery. PVC-RAM will determine the effects of virtual care with RAM compared to standard care. Eight, Canadian, academic, tertiary-care hospitals are participating, Table 1.

Trial population

We are including patients who: 1. are ≥40 years of age; 2. have undergone same-day or inpatient non-elective surgery and are being discharged home or are within 24 hours after discharge home, as long as they have not had acute-hospital care since discharge; and 3. provide informed consent to participate. Table 2 reports the exclusion criteria. Patients with COVID-19 are not excluded from the trial.

Patient recruitment

The first patient was randomized on April 23, 2020. Study personnel are using efficient recruitment strategies previously utilized in perioperative trials.[5,6] These include identifying eligible patients through screening of daily surgical lists in the operating room, surgical wards, and intensive care units. Investigators ask clinicians working in anesthesiology, surgery, and medicine to contact the study personnel regarding patients who have undergone non-elective surgery. Research personnel approach eligible patients after surgery to obtain written informed consent, Supplemental Appendix. Study personnel can obtain consent via the telephone, if the patient has already been discharged home and they are within 24 hours of discharge.

Randomization and blinding

Randomization occurs when a patient is deemed eligible and informed consent is obtained. Patients are only randomized after the most responsible physician has decided to discharge the patient home. Although our goal is to randomize patients before hospital discharge, some patients may be discharged before study personnel can randomize the patient.

Research personnel randomize patients via an Interactive Web Randomization System. This 24-hour computerized randomization internet system is maintained at the Population Health Research Institute (PHRI), which is part of Hamilton Health Sciences and McMaster University in Hamilton, Ontario, Canada. The randomization procedure ensures allocation concealment.

The randomization process uses block randomization stratified by centre and type of surgery (i.e., cardiac versus non-cardiac). We use randomly varying block sizes, and study personnel and investigators do not know the block sizes. We randomize patients in a 1:1 fashion to receive virtual care with RAM or standard care. Patients, healthcare providers, and data collectors are aware of patients' treatment assignment. Outcome adjudicators are masked to treatment allocation.

Trial interventions

Patients are randomized to virtual care with RAM for 30 days after randomization or standard care. Research staff teach patients allocated to virtual care with RAM how to use the cellular, modem-enabled, tablet computer and RAM technology from Cloud DX, Figure 1. This RAM technology will measure the following biophysical parameters: blood pressure, heart rate, respiratory rate, oxygen saturation, temperature, and weight. Daily for 30 days, patients take biophysical measurements and complete a recovery survey, and nurses review these results, Supplemental Appendix.

Patients interact daily with a virtual nurse (i.e., a nurse via the tablet computer) on days 1-15 after randomization and every other day from days 16-30. On days without planned virtual visits, nurses organize unscheduled virtual visits if patients' biophysical measurements or recovery survey responses exceed predetermined thresholds or the nurse identifies another reason for concern.

During virtual visits, nurses discuss any patient symptoms, evaluate their wound and obtain a picture, reinforce principles related to recovery after surgery and the need for physical distancing, and undertake medication review and reconciliation on days 1, 8, 15, 22, and 30 after randomization. Virtual nurses escalate care to pre-assigned and available physicians (i.e., perioperative physicians or surgeons) if patients' RAM measurements exceed predetermined thresholds, patients report specific symptoms (e.g., syncope), drug errors are identified, or virtual nurses have concerns about patients' health that they cannot resolve. Physicians will add or modify treatments as indicated and, if required, have patients come to an outpatient facility for evaluation or management. Patients have access to a nurse or physician 24 hours a day, 7 days per week.

In the standard-care group, patients receive post hospital management as per the standard of care at the hospital in which they underwent surgery. No changes to surgeons' standard of care regarding post discharge management occurs for patients randomized to the standard-care group, as a result of the trial.

Trial outcomes

The primary outcome is days alive at home during the first 30 days after randomization. Secondary outcomes during the first 30 days after randomization include: 1. hospital re-

admission; 2. emergency department visit; 3. urgent-care centre visit; 4. acute-hospital care; 5. brief acute-hospital care; 6. all-cause hospital days; 7. COVID-19 infection; 8. medication error detection; 9. medication error correction; 10. delirium; 11. surgeon, family physician, or specialist in-person clinic visit; 12. surgeon, family physician, or specialist virtual clinic visit; 13. sepsis; 14. acute heart failure; and 15. death. An additional secondary outcome is pain, assessed at days 7, 15, and 30 and 6 months after randomization. Tertiary outcomes and outcome definitions are reported in the Supplemental Appendix. We hypothesize that virtual care with RAM will improve the primary, secondary, and tertiary outcomes. We expect to detect more medication errors in the intervention group compared to the control group and would interpret this as an improvement in care.

Follow-up

The day of randomization is day 0 of follow-up and the day after randomization is day 1 of follow-up after randomization, etc. Because patients are followed from the day of randomization (i.e., day 0 of follow-up) until day 30 after randomization, patients have 31 days of follow-up. Study personnel will contact all study patients at 31 days and 6 months after randomization and collect data on the following outcomes: 1. days alive at home; 2. hospital re-admission; 3. emergency department visit; 4. urgent-care centre visit; 5. all-cause hospital days; 6. delirium; 7. sepsis; 8. acute heart failure; 9. death; 10. patient-level cost of recovery; 11. arrhythmia resulting in electrical cardioversion; 12. acute renal failure resulting in dialysis; 13. respiratory failure; 14. infection; 15. surgical site infection; 16. life-threatening, major, or critical-organ bleeding; 17. ileus; 18. myocardial infarction; 19. clinically important atrial fibrillation; 20. symptomatic proximal venous thrombo-embolism; 21. stroke; 22. non-fatal

cardiac arrest; 23. clostridium difficile-associated diarrhea; and 24. indwelling device inappropriately left in patient. Study personnel contact patients in the standard-care group and collect data on the following outcomes: 1. Brief Pain Inventory-Short Form (BPI-SF) on days 7, 15, and 30 and 6 months after randomization; and 2. medication error detection and medication error corrections on day 31 after randomization.

For patients in the virtual care and RAM group, virtual nurses will collect data on the following outcomes: 1. medication error detection; 2. medication error corrections; and 3. the BPI-SF. Through the Institute for Clinical Evaluative Sciences (ICES) and the Canadian Institute of Health Information (CIHI), we will collect data on the following outcomes up to 6 months after randomization: 1. acute-hospital care; 2. COVID-19 infection; 3. re-operation; 4. surgeon, family physician, or specialist clinic visit; and 5. health services utilization-related costs.

Data Management

Study personnel and virtual nurses record data on Case Report Forms (CRFs) and submit the CRFs through a secure computerized database (i.e., iDataFax) via the internet. Patients are identified using a unique numeric code and all patient data are anonymized to ensure confidentiality. Data validity checks are preprogrammed in the database and are monitored by data management assistants from the Project Office through multi-level data validation of CRFs.

Sample size

Table 3 reports the trial power based on a 2-sided α=0.05 and a sample size of 450 patients in each treatment group. We expect patients in the control group to have on average

29.60 days alive at home, of 31 potential days. If on average virtual care with RAM results in 29.81 days alive at home, we will have 89% power. For other possible estimates of days alive at home in the control group (i.e., 29.40, 29.50, 29.60), for absolute increases of 0.21 to 0.30 days alive at home in the intervention group, we have 89%-99% power.

Statistical analyses

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

Main analyses

For the primary analysis, we will use Poisson regression to estimate the 31-day effect of virtual care and RAM technology compared with standard care on the primary outcome of days alive at home, with stratification by centre and type of surgery. For the primary outcome, we will use the Mann-Whitney-Wilcoxon test to establish the p value. We will infer statistical significance if the computed 2-sided p-value is less than α=0.05.

For the binary secondary and tertiary outcomes, we will compare the effect of virtual care and RAM technology using modified Poisson regression,[7] and we will report the corresponding relative risk reductions or increases and 95% CIs. For continuous outcomes, we will evaluate treatment effects using the regression approach to fitting the analysis of co-variance (ANCOVA) models, so we can obtain estimates and their 95% CIs for the independent variables. We will

also conduct economic analyses to assess the cost-impact and cost-effectiveness of virtual care with RAM.

Interim Analyses

Two interim analyses based on the primary outcome will occur when 50% and 75% of the patients have been followed for 30 days after randomization. The Data Monitoring Committee (DMC) will use the modified Haybittle-Peto rule of 4 standard deviations (SDs) ($\alpha = 0.00006$) for the first planned interim analysis and 3.5 SDs ($\alpha = 0.00047$) for the second planned interim analysis. 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 months apart. The α-level for the final analysis will remain at the conventional $\alpha = 0.05$ given the infrequent interim analyses, their extremely low α-levels, and the requirement for confirmation with subsequent analyses.

At any time during the trial, if safety concerns arise the DMC chairperson will assemble a formal meeting of the full committee. The DMC will make their recommendations to the Project Office Operations Committee after considering all available trial data and any external data from relevant studies. If a recommendation for termination is being considered, the DMC will invite the Operations Committee to explore all possibilities before a decision is made. A detailed charter has been developed and governs the activities of the DMC. The DMC members have expertise in clinical trials, perioperative medicine, and biostatistics.

Trial organization

The PHRI is the sponsor and coordinating centre for this trial and is primarily responsible for the organization of the trial, development of the randomization scheme, the study database, data consistency checks, data analysis, and coordination of the study centres. The trial structure includes the following groups: Project Office, Operations Committee, Steering Committee, Site Principal Investigators, Investigators, and Adjudication Committee.

Patient and public involvement

A panel of four patient partners reviewed the daily symptom survey for clarity and perceived ease of use. Given rules on social distancing and limitations to in-person meetings, all feedback was provided via email. We will conduct semi-structured interviews to understand the experience of the PVC-RAM intervention.[8,9] Interview questions will focus on the recovery experience through PVC-RAM, compared to having experienced surgical recovery in the past (patients, family), or compared to caring for surgical patients previously (nurses, physicians). Inductive thematic analysis will be used to code and analyze these data, with NVivo used to facilitate analysis.[10] We plan to interview up to 20 nurses, 20 physicians, and 20 patients/families but will cease once data saturation is reached.[11]

ETHICS AND DISSEMINATION

We require documentation of research ethics committee or institutional review board (REC/IRB) approvals before sites are activated to enroll patients. Investigators are informed of protocol amendments, and REC/IRBs are requested to approve them. Research personnel obtain written informed consent for each patient before randomization. Data are stored on a central encrypted, high-security computer system and kept strictly confidential.

Planned knowledge translation activities are: a) Elsevier will develop an integrated, online, multimedia resource centre as a platform for large scale dissemination of knowledge gleaned from PVC-RAM; this will include multimedia slide and audio programs, patient testimonial interviews, and fact sheets; b) policy brief, supporting evidence-informed transformations at all levels of the health system, which includes a synthesis of research and systematic reviews; c) presentation at national and international conferences; d) peer reviewed journal publications; and e) public relations with national coverage through a high-impact media release of the trial results.

DISCUSSION

Hospitals need to facilitate management of the backlog of patients waiting for elective surgery, ensure hospital capacity for patients with COVID-19, and minimize the spread of COVID-19. Hospitals have a continuing obligation to treat non-COVID-19 patients with semi-urgent, urgent, or emergent conditions. Post discharge after non-elective surgery, these patients are at high risk (i.e., 15-25%) of needing subsequent acute-hospital care and mortality.[1-3] A strong rationale and promising data suggest that virtual care with RAM technology can increase days alive at home, among adults discharged after undergoing non-elective surgery. The PVC-RAM trial will answer an important question that will inform how to manage surgical patients after discharge in the setting of a pandemic and beyond, and offer insights for management of non-elective surgical patients in general.

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protocol. All members of the writing committee contributed to critical revisions of the current manuscript and approved the manuscript for submission.

FUNDING: This trial is supported by the following grants: Roche Innovation Challenge Application Grant; McMaster COVID-19 Research Fund Grant; The Research Institute of St. Joseph's Healthcare Hamilton Grant; COVID-19 Innovation funding grant from the Ottawa Hospital Academic Medical Association (TOHAMO); and Queen's University Department of Anaesthesiology Award and Department of Medicine Research Award to help fund the trial at Kingston Health Sciences. This trial received in-kind support to cover the salaries of the virtual nurses from the Hamilton Health Sciences, Kingston Health Sciences, London Health Sciences, St. Joseph's Healthcare Hamilton, the Ottawa Hospital, and the University of Alberta Hospital. MHM holds the Heart and Stroke Foundation/Michael G. DeGroote Endowed Chair in Cardiovascular Nursing. CO and SOf received internship funding from Mitacs Accelerate to support work on the PVC-RAM Trial. FKB and MM hold McMaster University Department of Medicine Career Research Awards. DC holds a McMaster University Department of Medicine Mid-Career Research Award. PJD holds the McMaster University / Hamilton Health Sciences Chair in Perioperative Care and a Tier 1 Canada Research Chair in Perioperative Medicine.

DISCLAIMER: The members of the writing committee are solely responsible for the trial design, conduct, management, analyses, data interpretation, writing of this paper, and decision to submit this paper for publication.

COMPETING INTERESTS: CloudDX undertook training sessions for virtual nurses and perioperative physicians and surgeons regarding how to use their technology. DC received

consultation fees from Servier, Canada, outside of the current work. EPBC has received grants from Roche and Bayer. PJD has received grants from Philips' Healthcare and Covidien.

Data Sharing Statement: The Population Health Research Institute (PHRI) is the sponsor of this trial. The PHRI believes the dissemination of clinical research results is vital and sharing of data is important. PHRI prioritizes access to data analyses to researchers who have worked on the trial for a significant duration, have played substantial roles, and have participated in raising the funds to conduct the trial. PHRI balances the length of the research study, and the intellectual and financial investments that made it possible with the need to allow wider access to the data collected. Data will be disclosed only upon request and approval of the proposed use of the data by a Review Committee. Data are available to the journal for evaluation of reported analyses. Data requests from other non-PVC-RAM investigators will not be considered until 5 years after the close out of the trial. Regarding the ICES data, while data sharing agreements prohibit ICES from making the data set publicly available, access can be granted to those who meet prespecified criteria for confidential access, available at www.ices.on.ca/DAS.

Dedication: We dedicate this paper to the memory of Dr. Yannick Le Manach, who was a colleague and PVC-RAM investigator. Yannick was a brilliant biostatistician, clinical epidemiologist, and anesthesiologist. Unfortunately, depression cut his life short. His tragic loss highlights the need for more trials to inform how to better prevent and manage depression and suicide.

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Table 1. Canadian hospitals participating in the PVC-RAM trial

Hospital	City, Province
Hamilton Health Sciences, Hamilton General Hospital	Hamilton, Ontario
Hamilton Health Sciences, Juravinski Hospital and Cancer Centre	Hamilton, Ontario
Kingston Health Sciences	Kingston, Ontario
London Health Sciences, Victoria Hospital	London, Ontario
London Health Sciences, University Hospital	London, Ontario
St. Joseph's Healthcare Hamilton	Hamilton, Ontario
The Ottawa Hospital	Ottawa, Ontario
University of Alberta Hospital	Edmonton, Alberta

Table 2. Patients fulfilling any of the following criteria are excluded

underwent same-day surgery and the surgeon or anesthesiologist believe the case reflects a traditional same-day surgery case with a low likelihood of needing acute-hospital care;
went to rehabilitation or convalescent care for more than 7 days after undergoing surgery;
are unable to communicate with research staff, complete study surveys, or undertake an interview using a tablet computer due to a cognitive, language, visual, or hearing impairment; or
reside in an area without cellular network coverage and no home Wi-Fi.

Table 3. Power using 2-sided α=0.05, with 450 subjects per arm

Control group Days alive at home	Virtual Care with RAM Days alive at home	Power
29.40	29.61	89%
29.40	29.69	99%
29.50	29.71	89%
29.50	29.80	99%
29.60	29.81	89%
29.60	29.90	99%

Figure 1. Cloud DX Connected Health kit

SUPPLEMENTARY DOCUMENTS

Supplementary Table of Contents

Supplemental Trial Groups and Investigators

Participating centres and investigators – *Kingston Health Sciences:* Darrin Payne, Rachael DaCunha, Sunil Patel, Michael Yacob, Siddhartha Srivastava, Lisa Nguyen, Curtis Nickel, Tyler Hands, Elorm Vowotor, Emile Peponoulas, Angela Webster, Tammy Doyle; *Hamilton Health Sciences, Hamilton General Hospital*: Kajenny Srivaratharajah, Dave Szalay, Deborah Bedini, Victor Chu, Jason Busse, Sandra Carroll, Jeremy Petch, Duane Bender, Dina Brooks, Krysten Gregus, Patricia Power, Dale Williams; *Hamilton Health Sciences, Juravinski Hospital and Cancer Centre*: Amitabha Chakroborty, Samir Raza, Amna Ahmed, Kelly Lawrence, Derek Hunt, David Cowan, Jehonathan Pinthus, David Wilson, Clare Reade, Leslie Gauthier, Stephen Kelly, Kirsten Krull, Kim Alvarado, Susan Reid, Mohit Bhandari; *University of Alberta Hospital*: Derek Dillane, James Greene, David Bigam, Ryan Snelgrove, Brian Buchanan, Oleksa Rewa, Ronald Brisebois, Nadr Jomha, Bruce Ritchie, Sherry Reid, Adrian Fairey, Greg Hrynchyshyn; *St. Joseph's Healthcare Hamilton*: Bobby Shayegan, Christian Finley, Wendy Lim, Maria Tiboni, David Choi, Anne-Marie MacDonald, Deanna Burnette, Tom Stewart, Melissa Farrell, Carolyn Goss, Faraaz Quiraishi; *The Ottawa Hospital*: Daniel McIsaac, Sarah Tierney, Shawn Hicks, Kathryn Wheeler, Josh Robert, Colleen McFaul, Greg Krolczyk, Purnima Rao, Stephane Moffett, Dan Dubois, Catherine Code, Heather Clark, Melissa Rousseau, Catherine Gray, Dominique Yelle, Youssef Tawil, Babak Rashidi, Weiwei Beckerleg, Shipa Gupta, Sudhir Sundaresan, Suzanne Madore, Andrew Seely, Reece Bearnes, Dean Fergusson, Susan Madden, Jad Abou Khalil, John Sinclair, Moein Momtazi, Rodney Breau, Humberto Vigil, James Chan; *London Health Sciences (University and Victoria Hospitals)*: George Nicolaou, Yamini Subramani, Ashraf Fayad, Amit Garg, Cathy Vandersluis, Glen Kearns, Cheryl Churcher, Carla Cormack, Brenda Maxwell, Johana Halabi, James Calvin, Douglas Naudie, Melfort Boulton, Stephanie Handsor, Heather Whittle, Charlotte Kenning.

Population Health Research Institute Coordinating Centre: Lori Blake, Sanela Dragic-Taylor, Arielle Fernandez, Peggy Gao, Valerie Harvey, Peter Koh, Louise Mastrangelo, John Liu, Yan Yun Liu, Rajibul Mian, Wesley Tong, Jessica Vincent, Heidi Wilton.

Event Adjudication Committee: Flavia K Borges (Chair), Sandra Ofori, Michael Wang, James Khan, Rahima Nenshi, Maura Marcucci.

Data Monitoring Committee: Victor M. Montori (Chair), Finlay McAlister, Kristian Thorlund.

APPENDIX 1. Sample consent form

Informed Consent Form for Participation in a Research Study

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

Study Doctor: Dr. X

Co-Investigator: Dr. Y

Sponsor/Funder(s): Population Health Research Institute (PHRI)

INTRODUCTION

You are being invited to participate in a clinical trial (a type of study that involves research). You are invited to participate in this trial because you are aged 40 or older and have recently had urgent or emergency surgery. This consent form provides you with information to help you make an informed choice. Please read this document carefully and ask any questions you may have. All your questions should be answered to your satisfaction before you decide whether to participate in this research study.

The study staff will tell you about the study timelines for making your decision.

Taking part in this study is voluntary. You have the option to not participate at all or you may choose to leave the study at any time. Whatever you choose, it will not affect the usual medical care that you receive outside the study.

You will not be able to participate if you are unable to communicate with research staff, complete study surveys, or undertake an interview using a tablet computer due to a cognitive, language, visual, or hearing impairment; and/or reside in an area without cellular network coverage.

IS THERE A CONFLICT OF INTEREST?

There are no conflicts of interest to declare related to this study.

WHAT IS THE BACKGROUND INFORMATION FOR THIS STUDY?

Surgery is done to improve survival and quality of life. Unfortunately, complications like pain and infection can be a problem for some people during their recovery after surgery. Your risk of

wound infection, hospital readmission, or need to go to an emergency department or urgent care centre, is greatest in the first 30 days following your surgery. You may not see your surgeon, cardiologist or family doctor for several days or weeks after surgery. For example, it is common to wait up to 4 to 6 weeks to begin cardiac rehabilitation after cardiac surgery. Many complications, such as infection, pain, and medication errors can happen in the first few days following discharge home. If these problems are not dealt with fast enough, people can end up being readmitted to hospital or going to the emergency room. With the current pandemic of COVID-19, there may be COVID-19 positive patients in the hospital and it is important to reduce the risk of COVID-19 transmission to surgery patients if they need treatment or care from a nurse or doctor. We need to evaluate better ways of managing people's care after surgery, which helps prevent problems and helps people recover safely at home, and, at the same time, is sustainable for the healthcare system.

The standard or usual follow up timeline after surgery is a follow up visit or call from your surgeon. Depending on the type of surgery you have had, this follow up could be a telephone call or visit within a few days of your surgery, or up to 8 weeks after your surgery. During the COVID-19 pandemic, these timelines may be even longer.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to evaluate the use of hospital-to-home care tools to monitor recovery safely at home after surgery and to determine if home monitoring can prevent hospital readmission, emergency department or urgent-care centre visits, or other new admissions to healthcare facilities (e.g. rehabilitation centres), by catching and managing health related issues before they become larger problems for you.

WHAT OTHER CHOICES ARE THERE?

You do not have to take part in this study in order to receive treatment or care. Currently, home monitoring is not part of the standard of care after surgery. Your doctor will provide the best care for you.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

It is anticipated that about 900 people will take part in this study, from research sites located in Canada. This study should take less than one year to complete and the results should be known in about one year.

WHAT WILL HAPPEN DURING THIS STUDY?

ASSIGNMENT TO A GROUP

If you decide to participate then you will be "randomized" into one of the groups described below. Randomization means that you are put into a group by chance (like flipping a coin). There is no way to predict which group you will be assigned to. You will have an equal chance of being placed in either group. Neither you, the study staff, nor the study doctors can choose

what group you will be in. After randomization, you will be told which group you are in. The study doctors, study nurses, and research teams will also know which group you are in.

WHAT IS THE STUDY INTERVENTION?

Group 1 (Virtual Care and remote monitoring): Standard care (contact or visit with your surgeon after discharge and within the usual timeframe determined by your surgeon), plus virtual care and remote automated monitoring. If you are randomized to this group you will be monitored at home by study nurses for 30 days after discharge. You will be provided with a hospital to home kit that contains the following technologies: tablet computer (with stand), wrist–based blood pressure cuff (for blood pressure, pulse and breathing rate), finger worn pulse oximeter (for measuring your oxygen levels), thermometer (for temperature) and weigh scale (to monitor your weight). Monitoring will include daily video visits with a nurse for the first 15 days of the program and every other day after this. These video visits will take between 20-30 minutes to start. As you recover and become more comfortable with the technologies, the visits may become shorter.

Prior to discharge, or shortly after discharge (by mail), you will receive the hospital to home kit which will include instructions on how to set up the devices, and the planned 30-day monitoring schedule. You will review the kit and follow up schedule with your virtual care nurse during your first video visit. You will be provided with training on how to use monitoring devices and the tablet application during the first video call. Study nurses will also answer any questions you have.

The measurements collected from the monitoring devices will be uploaded automatically to the companion tablet provided in the monitoring kit. The study nurse will then be able to review these measurements with you during your video visits. The frequency of daily biophysical measurements will be 3 times a day for the first 15 days, and then twice a day from day 16 until 30 days after your start the study. Weight will be measured daily in the morning before breakfast. Vital signs and weight measurement frequency can be adjusted according to your tolerance based on the virtual nurse's judgement or based on directions from the most responsible physician. It is expected that at least one full set of biophysical parameters will be recorded each day of the study. In addition to the vitals collection, each day, for 30 days, you will answer surveys about how you are feeling. Your answers will be uploaded to the study nurse for review and may be discussed with you during the video visit. During the video visit, the study nurse will also ask you questions about your pain level and take a photograph of your wound to look for signs of infection.

After the 30-day monitoring period has ended, you will be contacted by a member of the study team by phone at approximately 31 days and 6 months after hospital discharge and asked a few questions about your overall health, any complications you had during the follow up period, any time spent in a hospital or other health care facility, and medical related expenditures. You will be asked to package up the kit and prepare the kit for return using the prepaid slip and contacting the shipping company to confirm the kit is ready for pick up.

Group 2 (<u>Standard Care</u>): Standard care (contact or visit with your surgeon after discharge and within the usual timeframe determined by your surgeon).

If you are randomized to this group you will receive the usual care provided for your recovery after surgery. You will be contacted by a study team member via telephone on approximately day 7, 15, 30, 31, and 6 months after you have been discharged from the hospital. The phone calls on days 7, 15 and 30 will last approximately 10 minutes. During these calls, you will be asked any pain you may be experiencing and if you have recently been to a hospital or other healthcare facility. During the 31-day call (approximately 31 days after discharge), you will be asked about any medications you are taking, if you have recently been to a hospital or other healthcare facility., any complications that happened during your recovery, pain, health and medical related expenditures. This call will take 20-30 minutes. The last call from the study team at approximately 6 months after your discharge will take 10 minutes. You will be asked about any medications you are taking, pain, and any time spent in a hospital or other healthcare facility since the last telephone call. This final call will take approximately 10 minutes.

WHAT ELSE DO I NEED TO KNOW ABOUT THE STUDY INTERVENTION?

If at any point the study nurse feels your condition has worsened or thinks that you may experience a complication based on your vitals and video interview, the study nurse will have access to a study doctor 24 hours a day/ 7 days a week, to escalate your care. The study doctor will be able to assess you through telephone or video conferencing, and or may make clinical decisions (e.g., add or modify any of your treatments, refer you to other specialists, etc.) as they deem appropriate.
Outside of the regularly scheduled video visits you will also have access to a study nurse, 24 hours a day/ 7 days a week, should you feel that a change in your condition requires urgent contact with a healthcare provider.
The at home monitoring system from CloudDX used in the PVC-RAM study has previously been approved by Health Canada as monitoring systems. The monitoring system is not being tested in this study. We are investigating the clinical workflow and clinical and patient application of these approved devices.

WHAT ARE THE RESPONSIBILITIES OF STUDY PARTICIPANTS?

If you choose to participate in this study, you will be expected to:

- Tell the study doctor about your current medical conditions;
- Tell the study doctor about all prescription and non-prescription medications and supplements, including vitamins and herbals, and check with the study doctor before starting, stopping or changing any of these;
- Tell the study doctor if you are thinking about participating in another research study; and
- Return the monitoring kit and all devices at the end of the follow up period.

HOW LONG WILL PARTICIPANTS BE IN THE STUDY?

The study intervention will last for about 30 days and total follow up is 6 months. The study team will collect information from your hospital chart relevant to your time in hospital for the surgery that made you eligible to participate in this trial. This may include items like your medical history prior to surgery, laboratory assessments performed as part of your routine care, details of your operation, and information on your recovery between surgery and hospital discharge.

No matter which group you are randomized to, and even if you stop the study intervention early, we would like to keep track of your health for up to 6 months after hospital to provide data on health system use and cost after surgery. We also require your permission to collect information on your clinical outcomes (e.g., hospitalizations). This will be done by linking information like your health card number, name, date of birth to health care databases held at the Institute for Clinical Evaluative Sciences (ICES). The ICES databases contain information about physician, hospital, home care services and medications that are paid for by the Ontario government. The linkage of your data with ICES databases will be done in order to evaluate the efficacy of the intervention and assess its long-term outcomes.

CAN PARTICIPANTS CHOOSE TO LEAVE THE STUDY?

You can choose to end your participation in this research (called withdrawal) at any time without having to provide a reason. If you choose to withdraw from the study, you are encouraged to contact the study doctor or study staff and discuss the level of withdrawal. Information that was recorded before you withdrew will be used by the researchers for the purposes of the study, but no information will be collected or sent to the sponsor after you withdraw your permission.

CAN PARTICIPATION IN THIS STUDY END EARLY?

The study doctor may stop your participation in the study early, and without your consent, for reasons such as:

- You are unable to complete all required study procedures;
- The Sponsor decides to stop the study; or
- The Regulatory Authority/ies (for example, Health Canada) or research ethics board withdraw permission for this study to continue

If this happens, it may mean that you would not receive the study intervention for the full period described in this consent form. If you are removed from this study, the study doctor will discuss the reasons with you.

WHAT ARE THE RISKS OR HARMS OF PARTICIPATING IN THIS STUDY?

If you are randomized to the intervention, you will be required to use a wrist-based blood pressure monitor, and a wireless pulse oximeter. These devices may feel uncomfortable at times. You may discuss comfort of these devices with the virtual care nurse during your daily video visits.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

If you are randomized to the Virtual care and remote monitoring arm of the study you may benefit from the increased monitoring. Due to the increased monitoring, you will also have increased contact with study nurses compared to standard care. Study nurses may be able to identify health issues faster than usual. Your participation in this study may add to the medical knowledge about remote monitoring in patients after surgery.

HOW WILL PARTICIPANT INFORMATION BE KEPT CONFIDENTIAL?

If you decide to participate in this study, the study doctors and study staff will only collect the information they need for this study. Records identifying you at this centre will be kept confidential and, to the extent permitted by the applicable laws, will not be disclosed or made publicly available, except as described in this consent document.

Authorized representatives of the following organizations may look at your original (identifiable) medical/clinical study records at the site where these records are held, to check that the information collected for the study is correct and follows proper laws and guidelines.

- Population Health Research Institute, the Sponsor of this study
- The research ethics board who oversees the ethical conduct of this study in Ontario
- This institution and affiliated sites, to oversee the conduct of research at this location

Information that is collected about you for the study (called study data) may also be sent to the organizations listed above. Representatives of Clinical Trials Ontario, a not-for-profit organization, may see study data that is sent to the research ethics board for this study. Your name, address, email, or other information that may directly identify you will not be used. The records received by these organizations may contain your participant code, initials, sex, and date of birth.

The following organizations will also receive study data:

- Institute for evaluative clinical sciences (ICES)
- CloudDX Diagnostics Inc., technology service provider for in home monitoring and video follow up

Studies involving humans sometimes collect information on race and ethnicity as well as other characteristics of individuals because these characteristics may influence how people respond to different interventions. Providing information on your race or ethnic origin is voluntary.

This study requires the transfer of identifiable information to the Institute of Evaluative Clinical Sciences (ICES) for the purposes of longer term (6 month) follow up, health systems costs and health system use analysis.

To do this we would like to gather more information about your medical care from the Institute for Clinical Evaluative Sciences (ICES). ICES is an independent research facility in Toronto, ON that studies the impact of health care and diseases in Ontario. ICES has special status under Ontario privacy law, allowing for the collection and use of patient data, including information about the use of physician services, hospitalizations, and prescriptions for patients residing in this province. In order to have this special status, ICES is required by law to have its policies and procedures, related to the security and privacy protection of data, reviewed and approved by the Information and Privacy Commissioner of Ontario every three years. All data are coded and kept in a secure environment, to maintain individual confidentiality.

Your study data will be entered into a password-protected database and kept in a secure location at the PHRI. This database can only be accessed by authorized members of our research team and will be used to study health outcomes related to surgery and use of health services during your hospitalization and up to 6 months after your participation in the trial began. The risks associated with allowing ICES to use your information are minimal, as the data at ICES are anonymized using unique identifiers and kept in a secure environment, and individuals are never identified.

By providing your consent to participate you are agreeing that the following information will be transferred:

- OHIP number
- Full first name
- Full last name
- Date of birth
- Sex
- Postal code

This information will be securely transferred from Population Health Research Institute (where the research is taking place) by or on behalf of the study investigators to the Institute for Clinical Evaluative Sciences (ICES) so the required linkages can be made to gather the information for the study. The study investigators will be permitted to access de-identified information only for analysis (i.e., any information that can directly identify a person like health card number or name will be removed or replaced with a code that is not known to the study investigators).

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during this study will be used in analyses and will be published/ presented to the scientific community at meetings and in journals. This information may also be used as part of a submission to regulatory authorities around the world to support the approval of the study intervention.

The at-home system is not connected to the hospital. The Connected Health mobile application was designed by Cloud DX. The Cloud DX system will be receiving your personal data entered and it will be stored. Cloud DX will have access to your de-identified data for internal research, development, and regulatory filings. The Cloud DX Connected Health platform is a secure remote patient monitoring solution with all cloud data residing on secure Microsoft Azure servers. The cloud data storage resides entirely in Canada on servers physically located in

Toronto and Quebec (including all backup images), which meet HIPAA compliance for cloud services against ISO 27001 and SOC 2 certifications. During the study, your personal health information will be visible to research team members located across the participating hospital sites, and on restricted access by Cloud DX personnel for technical support. To ensure cybersecurity and patient privacy, the Samsung tablet supports cellular communications through Health Insurance Probability and Accountability Act (HIPAA)-compliant cloud infrastructure. Any data stored in the CloudDX cloud will be de-identified before exporting to our research database.

This study will use the CloudDX pulsewave platform to perform intervention/collect data, which is an externally hosted cloud-based service. A link to their privacy policy is available here (https://www.clouddx.com/#/privacy). Please note that whilst this service has been approved by the Hamilton Integrated Research Ethics Board for collecting data in this study, there is a small risk, as with any platform such as this, of data collected on external servers falling outside the control of the research team. Please talk to the researcher if you have any concerns.

WILL FAMILY DOCTORS/HEALTH CARE PROVIDERS KNOW WHO IS PARTICIPATING IN THIS STUDY?

Your surgeon and your family doctor/health care provider may be informed that you are taking part in a study so that you can be provided with appropriate medical care. If you do not want your family doctor/health care provider to be informed, please discuss this with the study team.

WILL INFORMATION ABOUT THIS STUDY BE AVAILABLE ONLINE?

A description of this clinical trial will be available on *https://clinicaltrials.gov*. This website will not include information that can identify you. You can search this website at any time.

WHAT IS THE COST TO PARTICIPANTS?

The virtual care and remote monitoring technologies will be supplied at no charge while you take part in this study. Participation in this study will not involve any additional costs to you or your private health care insurance.

ARE STUDY PARTICIPANTS PAID TO BE IN THIS STUDY?

You will not be paid for taking part in this study. In the case of research-related side effects or injury, medical care will be provided by the study investigator, to help you recover from the injury or refer you for appropriate treatment. Costs for medical care that you might incur for injuries or illnesses that are not a direct result of research activities will not be covered by the study.

WHAT ARE THE RIGHTS OF PARTICIPANTS IN A RESEARCH STUDY?

You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study.

You have the right to be informed of the results of this study once the entire study is complete. The results of this study will be available on the clinical trial registry (see the "Will information about this study be available online" section for more details).

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form, you do not give up any of your legal rights against the study doctor, sponsor or involved institutions for compensation, nor does this form relieve the study doctor, sponsor or their agents of their legal and professional responsibilities.

You will be given a copy of this signed and dated consent form prior to participating in this study.

WHAT IF RESEARCHERS DISCOVER SOMETHING ABOUT A RESEARCH PARTICIPANT?

During the study, the researchers may learn something about you that they didn't expect. For example, the researchers may find out that you have another medical condition that was not previously diagnosed. If any new clinically important information about your health is obtained as a result of your participation in this study, it may be shared with your family doctor at your discretion. Should a new medical condition be identified that requires treatment, your care will be directed by study doctors. See the "What else do I need to know about the study intervention?" section for more details.

WHOM DO PARTICIPANTS CONTACT FOR QUESTIONS?

If you have questions about taking part in this study, or if you suffer a research-related injury, you can talk to your study doctor, or the doctor who is in charge of the study at this institution. That person is:

Dr. X XXX XXX XXXX ext XXXXX

If you have questions about your rights as a participant or about ethical issues related to this study, you can talk to someone who is not involved in the study at all. That person is:

Name	Telephone
Office of the Chair of the X Integrated Research Ethics Board	XXX-XXX-XXXX ext. XXXXX

SIGNATURES

- All of my questions have been answered,
- I understand the information within this informed consent form,
- I allow access to medical records and related personal health information as explained in this consent form,

- I do not give up any legal rights by signing this consent form,
- I understand that my family doctor/health care provider may be informed of study participation
- I agree to take part in this study.

_____	_____	_____
Signature of Participant	PRINTED NAME	Date/Time
_____	_____	_____
Signature of Person Conducting the Consent Discussion	PRINTED NAME & ROLE	Date/Time

OR

	_____	_____
Verbal Consent obtained	PARTICIPANT'S PRINTED NAME	Date/Time
_____	_____	_____
Signature of Person who obtained verbal consent	PRINTED NAME & ROLE	Date/Time

APPENDIX 2. Biophysical measurements and recovery survey

Based on a schedule developed by a virtual nurse, the tablet prompts patients to measure their biophysical parameters. The frequency of daily biophysical measurements is 3 times a day for the first 15 days, and then twice a day from day 16 until 30 days after randomization. Weight is measured daily in the morning before breakfast. Measurement of biophysical parameters can be adjusted according to a patient's acuity and tolerance, based on the virtual nurse's judgement or directions from a physician. Patients record at least one full set of biophysical parameters each day of the study. The tablet prompts patients daily to complete the recovery survey. The recovery survey consists of questions related to infection, bleeding, pain, dehydration, ileus, and cardiovascular and respiratory complications.

APPENDIX 3. Tertiary outcomes

Tertiary outcomes during the first 30 days after randomization include: 1. health services utilization-related costs; 2. patient-level cost of recovery; 3. re-operation; 4. arrhythmia resulting in electrical cardioversion; 5. acute renal failure resulting in dialysis; 6. respiratory failure; 7. infection; 8. surgical site infection; 9. life-threatening, major, or critical-organ bleeding; 10. ileus; 11. myocardial infarction; 12. clinically important atrial fibrillation; 13. symptomatic proximal venous thrombo-embolism; 14. stroke; 15. non-fatal cardiac arrest; 16. clostridium difficile-associated diarrhea; and 17. indwelling device inappropriately left in a patient. Additional tertiary outcome during the first 6 months after randomization include: 1. the secondary outcomes; and 2. health services utilization-related costs.

APPENDIX 4. Outcome definitions

Outcome	Definition
Days alive at home	Days alive at home are the number of days patients spend at their usual residence – be it a house or apartment, a group home or shelter, a seniors' residence, or a nursing home – or at a community residence of a relative, friend, or acquaintance without, during that day, being admitted to a hospital or visiting an emergency department or urgent-care centre. Thus, patients lose days alive at home if 1. patients go to an emergency department or urgent-care centre; 2. they become inpatients at a hospital or rehabilitation or convalescence-care facility; or 3. they die. More specifically, our approach to calculating days alive at home follows. If a patient visits an emergency department or urgent-care centre anytime between midnight and 23:59 on a given day, they will lose that day as a day alive at home. If a patient visits an emergency department or urgent-care centre anytime between midnight and 23:59 on a given day and they remain in the emergency department or urgent-care centre past midnight into the next day, then they lose 2 day alive at home. If a patient is admitted to the hospital or rehabilitation or convalescence-care facility anytime between midnight and 23:59 on a given day, they will lose that day as a day alive at home. They will continue to lose days alive at home until the day in which they are home and out of an acute-hospital care or a rehabilitation or convalescence-care facility from midnight for an entire day. Patients randomized before hospital discharge do not lose this day alive at home unless after their discharge they die or visit an emergency department or urgent-care centre on the day of their discharge. Patients randomized before hospital discharge will lose this day alive at home if their discharge is ultimately delayed and they do not go home on their day of randomization. Because patients are followed until day 30 after randomization and the day of randomization is day 0, if a patient is discharged home after randomization and remains at home until death on day 2 after randomization (i.e., they survived at home on the day of randomization and day 1 after randomization, but died on the subsequent day) they would be counted as having had 2 day alive at home, and lose 29 of the possible 31 days alive at home.
Hospital re-admission	Patient admission to an acute-care hospital.

Emergency department visit	Patient visit to an emergency department.
Urgent-care centre visit	Patient visit to an urgent-care centre.
Acute-hospital care	Acute-hospital care is a composite outcome of hospital re-admission and emergency department or urgent-care centre visit
Brief acute-hospital care	Acute-hospital care that last <24 hours from the time of arrival to the time of discharge home.
All-cause hospital days	If a patient is admitted to the hospital for any reason anytime between midnight and 23:59 on a given day, this will count as a day in hospital. Study personnel will determine the total number of days in the hospital for any reason. Patients randomized before hospital discharge do not have this day counted as a hospital day unless after their discharge they are re-admitted to the hospital on the day of their discharge. Patients randomized before hospital discharge will have this day counted as a hospital day if their discharge is ultimately delayed and they do not go home on their day of randomization.
COVID-19 infection	For COVID-19 infection, we will accept any laboratory confirmed evidence of COVID-19 infection.
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. We will record all drug errors identified and also report whether they resulted in harm. We will use the following definitions for harm: 1. no harm – error that does not cause any clinically appreciable harm to the patient; 2. minor harm – error that leads to event resulting in minor treatment or extra monitoring to ensure significant harm is avoided (e.g., mild symptoms or minimal loss of function; one day of symptoms; laboratory abnormality not requiring emergency department or urgent-care centre visit); 3. moderate harm – error that leads to event requiring treatment or extra monitoring and causes temporary but not permanent harm (e.g., laboratory abnormality, symptoms, or condition requiring emergency department or urgent-care centre visit); 4. severe harm – error that

	leads to event that requires treatment or extra monitoring and results in significant or permanent harm (e.g., permanent disability or loss of function; near-death event [e.g., anaphylaxis, cardiac arrest]; serious laboratory abnormality, symptom, or condition requiring intervention to sustain life or leading to prolonged hospitalization); and 5. death – error leading to loss of life.
Medication error correction	Any medication error that is corrected.
Delirium	The diagnosis of delirium based on remote assessment (i.e. telephone or videoconference interview) is met when either 1. or 2. is met: 1. Patient able to complete the interview and meeting the delirium criteria as per the Confusion Assessment Method, (i.e., a. acute onset of symptoms OR fluctuating course of symptoms, AND b. inattention AND either c. disorganized thinking or d. altered level of consciousness. 2. Patient unable to complete the interview because too confused. This criterion is applicable when patients are able to complete telephone interviews at baseline, which is consistent with one of our eligibility criteria. In this case, this is significant for an acute decline in their cognitive performance.
Surgeon, family physician, or specialist in-person clinic visit	Patient in-person visit to a surgeon's, family physician's, or specialist's clinic.
Surgeon, family physician, or specialist virtual clinic visit	Patient has a virtual clinical visit with a surgeon, family physician, or specialist.
Sepsis	Our definition of sepsis is based on the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). Sepsis requires a quick Sequential Organ Failure Assessment (qSOFA) Score ≥2 points due to infection. The qSOFA includes the following items and scoring system: 1. altered mental status (1 point); 2. systolic blood pressure ≤100 mm Hg (1 point); and 3. respiratory rate ≥22 breaths per minute (1 point).
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.
Death	The definition of death is all cause mortality.
Pain	Pain intensity and related interference with usual daily activities, will be measured via the Brief Pain Inventory-Short Form (BPI-SF). 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.
Health services utilization-related costs	Data on hospital re-admission, healthcare utilization, and costs of health service utilization will be obtained from the *Institute for Clinical Evaluative Sciences* (ICES) data repository. Administrative databases used to describe the health service utilization include: 1. Registered Persons Database (RPDB) – demographics and vital statistics of all legal residents of Ontario; 2. Discharge Abstract Database – records of inpatient hospitalizations from the Canadian Institute for Health Information (CIHI); 3. Ontario Health Insurance Plan (OHIP) Database – physician billing claims, and the National Ambulatory Care Reporting System – information on emergency department visits from CIHI. In addition, to capture data on times spent on the Cloud DX Connected Health mobile application by health providers (e.g., virtual nurses), costs of health providers' time will be captured in the system reporting. Costs of health providers' time on the Cloud DX Connected Health mobile application will be calculated by multiplying the time with unit costs from standard costing sources in Ontario.
Patient-level cost of recovery	The Ambulatory and Home Care Record (AHCR) will be used to comprehensively measure patient-level costs of illness from a societal perspective. This approach gives equal consideration to health system costs and costs borne by patients and unpaid caregivers (e.g., family members, friends). AHCR items can be categorized as publicly financed (e.g., public sector paid resources) or privately financed care (e.g., all out-of-pocket and third-party

	insurance payments, and time costs incurred by caregiver). Face validity and reliability of the AHCR is well established in multiple groups, including surgical patients.
Re-operation	Re-operation refers to any surgical procedure undertaken for any reason (e.g., wound dehiscence, infection)
Arrhythmia resulting in electrical cardioversion	Any arrhythmia that leads to electrical cardioversion.
Acute renal failure resulting in dialysis	This outcome is defined as acute renal failure that results in dialysis (i.e., use of hemodialysis machine or peritoneal dialysis apparatus) in a patient who was not on chronic dialysis before randomization.
Respiratory failure	Patient intubated or put on bilevel positive airway pressure (BiPAP).
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.
Surgical site infection	Surgical site infection is an infection that occurs within 30 days after surgery and involves the skin, subcutaneous tissue of the incision (superficial incisional), or the deep soft tissue (e.g., fascia, muscle) of the incision (deep incisional).
Life-threatening bleeding	Life-threatening bleeding is bleeding that is fatal, or leads to: significant hypotension that requires inotrope or vasopressor therapy, urgent (within 24 hours) surgery (other than superficial vascular repair), or intracranial hemorrhage.
Major bleeding	Major bleeding is defined as bleeding that is not specified under "life- threatening bleeding" and results in at least one of the following: 1. a postoperative hemoglobin $\leq$ 70 g/L; 2. a transfusion of $\geq$1 unit of red blood cells; or 3. leads to one of the following interventions: embolization, superficial vascular repair, nasal packing.
Critical-organ bleeding	Critical-organ bleeding is bleeding that is intracranial, intraocular, intraspinal, pericardial, retroperitoneal, or intramuscular with compartment syndrome.
Ileus	Ileus is a physician diagnosis of functional obstruction of the gastrointestinal tract in the absence of an alternative diagnosis that

	leads to postoperative decreased bowel activity. The definition requires the following criteria: 1. inability to pass flatus or stool for >24 hours; and 2. persistence of one or more of the following signs and symptoms for >24 hours: abdominal distention; diffuse abdominal pain; or nausea or vomiting.
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 findings consistent with a procedural flow-limiting complication such as coronary dissection, occlusion of a major epicardial artery or graft, side-branch occlusion-thrombus, disruption of collateral flow or distal embolization, 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
Clinically important atrial fibrillation	The definition of clinically important atrial fibrillation requires the documentation of atrial fibrillation or atrial flutter on a 12 lead electrocardiogram, or confirmed atrial fibrillation or atrial flutter

	(e.g., rhythm strip) that results in angina, congestive heart failure, symptomatic hypotension, or requires treatment with a rate controlling drug, antiarrhythmic drug, or electrical cardioversion.
Symptomatic proximal venous thrombo-embolism	Venous thromboembolism that includes symptomatic pulmonary embolism or symptomatic proximal deep vein thrombosis.
Symptomatic pulmonary embolism	The diagnosis of symptomatic pulmonary embolism requires symptoms (e.g., dyspnea, pleuritic chest pain) and any one of the following: 1. A high probability ventilation/perfusion lung scan; 2. An intraluminal filling defect of segmental or larger artery on a helical CT scan; 3. An intraluminal filling defect on pulmonary angiography; or 4. A positive diagnostic test for DVT (e.g., positive compression ultrasound) and one of the following: A. non-diagnostic (i.e., low or intermediate probability) ventilation/perfusion lung scan, or B. non-diagnostic (i.e., subsegmental defects or technically inadequate study) helical CT scan
Symptomatic proximal deep venous thrombosis	The diagnosis of symptomatic proximal deep venous thrombosis (DVT) requires: 1. symptoms or signs that suggest DVT (e.g., leg pain or swelling), 2. thrombosis involving the popliteal vein or more proximal veins for leg DVT OR axillary or more proximal veins for arm DVTs Any of the following defines evidence of vein thrombosis: A. a persistent intraluminal filling defect on contrast venography (including on computed tomography); B. noncompressibility of one or more venous segments on B mode compression ultrasonography; or C. a clearly defined intraluminal filling defect on doppler imaging in a vein that cannot have compressibility assessed (e.g., iliac, inferior vena cava, subclavian).
Stroke	Stroke is defined as either: 1. a new focal neurological deficit thought to be vascular in origin with signs or symptoms lasting ≥24 hours or leading to death; or 2. a new focal neurological deficit thought to be vascular in origin with signs or symptoms lasting <24 hours with positive neuroimaging consistent with a stroke.
Non-fatal cardiac arrest	Non-fatal cardiac arrest is defined as successful resuscitation from either documented or presumed ventricular fibrillation, sustained ventricular tachycardia, asystole, or pulseless electrical activity

	requiring cardiopulmonary resuscitation, pharmacological therapy, or cardiac defibrillation.
Clostridium difficile-associated diarrhea	This outcome requires diarrhea as a symptom with laboratory documentation of Clostridium difficile.
Indwelling device inappropriately left in a patient	An indwelling device (e.g., drain, catheter, pacemaker wire) inappropriately left in patient is defined as an indwelling device inappropriately being left in a bodily organ or passage longer than it was intended.