Review

Postoperative Remote Automated Monitoring: Need for and State of the Science

Michael H. McGillion, RN, PhD,[a,b] Emmanuelle Duceppe, MD, FRCPC, PhD(c),[a,c]

Katherine Allan, MASc, PhD,[a] Maura Marcucci, MSc,[a] Stephen Yang, MDCM, FRCPC,[a,b]

Ana P. Johnson, PhD,[d] Sara Ross-Howe, BASc, MASc, PhD(c),[e] Elizabeth Peter, RN, PhD,[f]

Ted Scott, MAppSc, PhD,[b] Carley Ouellette, RN, BScN,[a,b]

Shaunattonie Henry, RN, MN, MAEd, PhD(c),[a,b] Yannick Le Manach, MD, PhD,[a]

Guillaume Paré, MD, MSc, FRCPC,[a] Bernice Downey, RN, PhD,[a] Sandra L. Carroll, RN, PhD,[a,b]

Joseph Mills, BChir, MD, MA, MB, FRCP,[g] Andrew Turner, PhD, HCPC, RHP, MBPsS,[h]

Wendy Clyne, PhD,[i] Nazari Dvirnik, BHSc, MD, MS,[a,b] Sandra Mierdel, MA, BScPT,[j]

Laurie Poole, BScN, MHSA,[j] Matthew Nelson, MBA, MSc, PhD(c),[j] Valerie Harvey, BSc,[b]

Amber Good, MSc, CCRP,[b] Shirley Pettit, RN,[b] Karla Sanchez, BSc,[b]

Prathiba Harsha, MBBS, CCRA,[a,b] David Mohajer, BComm,[k]

Sem Ponnambalam, BA(Hons), MA,[k] Sanjeev Bhavnani, MD,[l]

Andre Lamy, MD, MHSc, FRCSC,[b] Richard Whitlock, MD, PhD, FRCSC,[b] and

P.J. Devereaux, MD, PhD, FRCPC;[a,b] on behalf of the PROTECT Network Investigators

[a] McMaster University, Faculty of Health Sciences, Hamilton, Ontario, Canada; [b] Population Health Research Institute, McMaster University and Hamilton Health Sciences, Hamilton, Ontario, Canada; [c] Centre Hospitalier de l'Université de Montréal, Montreal, Quebec, Canada; [d] Queen's University, Kingston, Ontario, Canada; [e] Univerity of Waterloo, Waterloo, Ontario, Canada; [f] University of Toronto, Toronto, Ontario, Canada; [g] Liverpool Heart and Chest Hospital, Liverpool, United Kingdom; [h] Coventry University, Coventry, United Kingdom; [i] Hope for the Community, Community Interest Company, Coventry, United Kingdom; [j] Ontario Telemedicine Network, Toronto, Ontario, Canada; [k] XAHIVE, Toronto, Ontario, Canada; [l] Scripps Clinic and Research Institute, La Jolla, California, USA

ABSTRACT

Worldwide, more than 230 million adults have major noncardiac surgery each year. Although surgery can improve quality and duration of life, it can also precipitate major complications. Moreover, a substantial proportion of deaths occur after discharge. Current systems for monitoring patients postoperatively, on surgical wards and after transition to home, are inadequate. On the surgical ward, vital signs evaluation usually occurs only every 4-8 hours. Reduced in-hospital ward monitoring, followed by no vital signs monitoring at home,

RÉSUMÉ

Chaque année, plus de 230 millions d'adultes à travers le monde subissent une chirurgie non cardiaque majeure. Si les interventions chirurgicales peuvent améliorer la qualité et prolonger la durée de la vie, elles peuvent aussi précipiter l'apparition de complications majeures. De plus, une proportion appréciable des décès se produit après la sortie de l'hôpital. Les systèmes actuels de surveillance des patients après l'opération, dans les services de chirurgie et après leur retour à la maison sont insuffisants. Lorsque le patient est hospitalisé

Worldwide, more than 230 million adults (>500,000 Canadians) have major noncardiac surgery annually. Among those having surgery, average age and comorbidities are rising.[1] Although surgery can improve patient outcomes, it can also precipitate major complications.[1] More than 10% of surgical patients, age 45 and older, will suffer a major postoperative

leads to thousands of cases of undetected/delayed detection of hemodynamic compromise. In this article we review work to date on postoperative remote automated monitoring on surgical wards and strategy for advancing this field. Key considerations for overcoming current barriers to implementing remote automated monitoring in Canada are also presented.

dans le service de chirurgie, l'évaluation de ses signes vitaux n'est en général effectuée que toutes les 4 à 8 heures. Une surveillance réduite pendant l'hospitalisation, suivie de l'absence de surveillance des signes vitaux à la maison conduit à la non-détection ou à la détection tardive de milliers de cas de troubles hémodynamiques. Dans le présent article, nous passons en revue les travaux effectués à ce jour sur la surveillance postopératoire automatisée à distance dans les services de chirurgie et les stratégies envisageables pour favoriser le progrès dans ce domaine. Nous présentons également les éléments clés à considérer pour surmonter les obstacles actuels à la mise en œuvre de la surveillance automatisée à distance au Canada.

complication.[1] Worldwide, >1.5% of adults die within 30 days of noncardiac surgery.[2] Few of those patients die in the operating room, the period when patients should be most vulnerable.[3] Moreover, a substantial proportion of postoperative deaths occur after discharge.[2]

Medical complications are the main cause of mortality in surgical patients.[4-7] In the **P**eri**o**perative **Is**chemic **E**valuation (POISE) trial 8351 noncardiac surgery patients (191 centres, 23 countries) were randomized to extended-release metoprolol (mean age 68.9 years) or placebo (mean age 69.1 years).[4] The primary outcome, a composite of cardiovascular death, nonfatal myocardial infarction (MI), and nonfatal cardiac arrest, was observed in 6.4% of participants at 30 days. Seventy-seven percent of surgical patients died in-hospital, whereas 23.0% of patients died postdischarge. Of those who died postdischarge, 64% of deaths were from preventable vascular causes, the most common being MI, arrhythmia, stroke, and hemorrhage. The most common nonvascular cause of preventable death was infection/sepsis.[4]

The **V**ascular Events **i**n Noncardiac **S**urgery Pat**i**ents C**o**hort Evaluati**o**n (VISION) study—a prospective study of 21,842 noncardiac surgery patients (23 centres, 3 countries)—examined risk factors independently associated with postoperative mortality. Myocardial injury after noncardiac surgery (MINS; ie, myocardial injury caused by ischemia within 30 days postoperatively [hazard ratio (HR), 3.69; 95% confidence interval (CI), 2.80-4.85]), bleeding (HR, 2.77; 95% CI, 2.11-3.62), and sepsis (HR, 4.96; 95% CI, 3.54-6.96) were the 3 strongest independent predictors of 30-day mortality.[1]

Data from large randomized controlled trials (RCTs) suggest that blood pressure (BP) is also associated with postoperative vascular complications and death. In POISE, although a reduction in MI was found in the metoprolol group, there was a significant increase in death (HR, 1.33; 95% CI, 1.03-1.74) and postoperative stroke (HR, 2.17; 95% CI, 1.23-3.74).[4] These postoperative complications were partly mediated by clinically important hypotension, and metoprolol increased the risk (HR, 1.55; 95% CI, 1.38-1.74). Clinically important hypotension, defined as systolic BP < 90 mm Hg that required a medical intervention, had the largest population-attributable risk for postoperative death (37.3%) and stroke (14.7%).[4]

There is also a strong association between the duration of clinically important hypotension and incidence of vascular complications. In a substudy cohort of VISION (n = 14,687), increased duration of intraoperative hypotension led to increased composite risk of 30-day mortality, MINS, and stroke.[6] For instance, when the duration of intraoperative hypotension was more than 30 minutes, the adjusted relative risk of the composite outcome was 1.19 (95% CI, 0.95-1.15). As the duration of hypotension increased to > 120 minutes, the adjusted relative risk became statistically significant at 1.66 (95% CI, 1.03-2.69).[6] Clinically important hypotension also remains a concern beyond the intraoperative period. In the same cohort, those who were hypotensive postoperatively (postoperative days 0-3) were at significant increased risk for death (adjusted odds ratio, 2.64; 95% CI, 2.16-3.22).[6]

In POISE-2, a blinded factorial RCT of 10,010 patients (135 centres, 23 countries) allocated to aspirin or clonidine vs placebo (primary outcome: composite of death, nonfatal MI at 30 days), the median duration of clinically important hypotension in the operating room was 15 minutes (95% CI, 5-30 minutes).[7] However, on postoperative day 1, the median duration was 150 minutes (95% CI, 60-374 minutes).[7] Multivariable analyses showed that clinically important hypotension was an independent predictor of subsequent risk of perioperative MI (adjusted HR, 1.37; 95% CI, 1.16-1.62).[7]

Patients die after surgery because of cardiovascular and infectious complications, often preceded by potentially detectable, early signs of hemodynamic compromise.[8] Anaesthetic-related mortality has decreased 100-fold over the past 100 years.[9] An important part of this progress relates to intraoperative monitoring to facilitate early detection of hemodynamic compromise, intervention, and prevention of complications. After transfer to the surgical ward, however, vital signs are evaluated just every 4-8 hours.[10] Such reduced monitoring, followed by no monitoring at home, leads to undetected/delayed detection of hemodynamic compromise, associated with morbidity and mortality.[11]

In a study from the Cleveland Clinic,[11] nurses blinded to continuous pulse oximetry (SpO_2) assessed patients (n = 564) postoperatively according to normal practice and detected a 5% incidence of hypoxemia (SpO_2 < 90%). Among the 95% of patients in whom hypoxemia went undetected by nurses, blindly captured SpO_2 detected that 38% had at least 1 continuous episode of hypoxemia, lasting at least 1 hour. Of these, 10% had at least 1 continuous episode of hypoxemia, lasting $\geq$ 1 hour with an SpO_2 of < 85%.[11] Because hypoxemia for > 5 minutes is associated with increased risk of myocardial ischemia, suboptimal monitoring presents risk to patients.[11]

New models of postoperative remote automated monitoring (RAM) are needed on surgical floors and at home if

postoperative care is to achieve improvements similar to those achieved intraoperatively. Our group formed a multidisciplinary consortium of experts, the Reducing Global Perioperative Risk and ImprOving Global Health outcomes Through Innovation, Excellence, and appliCation of Digital Health Technologies (PROTECT) Network. The aim is to reduce perioperative mortality, complications, and hospital readmissions by 50% within the next decade. In this article we review preliminary work on postoperative RAM on surgical wards and at home. Strategic priority research areas for advancing this field are presented, as well as considerations for overcoming current barriers to implementing RAM.

RAM: Key Components

RAM is a subcomponent of telemedicine encompassing a range of audio-, digital-, and video-based telecommunications infrastructures that facilitate clinical health care at a distance. RAM refers to systems that include wearable sensors that transmit vital signs data from patients to clinicians.[12] Nangalia et al.[13] identified key components of RAM, including data acquisition from sensors, transmission and integration of these data to describe patient status, synthesis of appropriate action of the front-line nurse, and escalation of care in the context of real-time decision support. Over the past decade, a variety of physiologic parameters have been captured using wearable sensor technology.[14] Wearable sensor models have evolved rapidly, for which sensor measurements might be continuous, intermittent, or both.[14] Automation level also varies from fully automatic to semiautomatic (ie, requires clinician or patient prompt to initiate vital signs measurement).

Vital signs transmission modalities have evolved from wired connections to wireless deployments and are becoming more common, particularly in research.[15] Current wireless transmission protocols enable biometric sensors to be small and portable and to support long-term data-gathering. These wireless networks, collectively referred to as the "Internet of Things" (IoT), include WiFi, ZigBee, Bluetooth low-energy, and cellular networks, each with expanding global coverage. Challenges with the IoT include limited power consumption and range, cybersecurity, and constrained data rates. To support the complete data life cycle, wireless biometrics gathered in-hospital must be transferred and integrated to electronic health records (EHRs) and support real-time notifications to clinical care teams. Initiatives such as the Health Level Seven International (HL7) consortium[16] are facilitating standardization of this process through international standards for data exchange and messaging.

Models for data integration, synthesis of appropriate clinician action, and related decision support vary depending on patient acuity and context. More sophisticated systems now go beyond "pushing" data to clinicians to support data interpretation and clinical decision-making. For example, Philips' Guardian Solution (GS) (Philips Canada, Markham, ON) is programmable according to hospital early warning score (EWS) parameters.[17,18] The GS features cableless sensors and a bedside MP5 spot-check monitor, which transmits and displays respiratory rate (RR), BP, heart rate, SpO$_2$, and temperature on the bedside MP5 spot-check monitor, and a central monitoring station (Fig. 1). The GS integrates these vital signs data and automatically calculates patients'

EWSs.[17,18] Notifications are sent to front-line nursing staff, calling for early attention to care should patients' EWS risk level be elevated to the next actionable band. The system monitor also prompts the clinician according to EWS-prespecified interventions.[17,18] The system features built-in reassurance measurements to prevent notification fatigue.

RAM in Surgical Populations: Work to Date

RAM on surgical wards and in the home remains a burgeoning field. We performed a literature search following the criteria for RAM according to Nangalia et al.[13] (see the Supplemental Methods for details). Early in-hospital automated monitoring studies (Table 1) suggested benefit from automated monitoring for patients age 19-100 years. In an RCT, Watkinson et al.[20] compared mandated multichannel physiologic monitoring (electrocardiogram [ECG], heart rate, RR, BP, SpO$_2$, and temperature) vs standard care in 402 patients. Although > 50% of major events were reported, no difference was observed in the number of alarms between the 2 study arms. This precluded any observed difference in clinical outcomes; the primary composite end point (ie, one or more major adverse events, urgent staff calls, changes to higher care levels, and cardiac arrests or death) was not significantly different between groups at 4 days.[20] Only 16% of the patients in the mandatory monitoring arm were monitored for the full 72 hours specified, and some patients in the control arm received multiparameter monitoring, leading to concern regarding protocol nonadherence and contamination biases. Many of the continual physiologic data and related alarms were also likely unnoticed by busy nursing staff because no automated risk score calculation or protocolized response was in place.[20] The study results emphasized the importance of addressing protocol adherence, coordinated alarm parameters, and meaningful (actionable) notifications to front-line nurses.

In a larger RCT (n = 1219), Ochroch et al.[19] assessed the effect of continuous SpO$_2$ (CPOX) monitoring on the rate of intensive care unit (ICU) transfer and ICU and overall hospital length of stay. A CPOX monitor was installed on a postcardiothoracic surgery care unit; patients were enrolled over a 26-month period and randomly allocated to CPOX or standard monitoring. Although CPOX influenced reasons for ICU transfer, the overall rate of transfers between groups remained similar.[19] Unfortunately, the rate of alarms and the group imbalance by virtue of the randomization method limited interpretation of this study. A key issue for both early trials[19,20] was the absence of data integration and synthesis, along with absence of support for interpretation of monitor data and related escalation of care—likely a limitation of the technology at the time.

RAM is improving with recent technological advances that enable data integration and synthesis, as well as directed front-line nurse response. In the prospective before (n = 2139) and after (n = 2263) study of Subbe et al.,[17] patients admitted to 1 of 2 general medicine wards in a United Kingdom hospital were connected to the Philips GS remote, automated advisory vital signs, and notification system, configured to relay abnormal vital signs to a rapid response team. During the intervention period (14 months), the number of rapid response team notifications increased from 405 to 524 (P = 0.001; 1.43 notifications per patient that led to a change
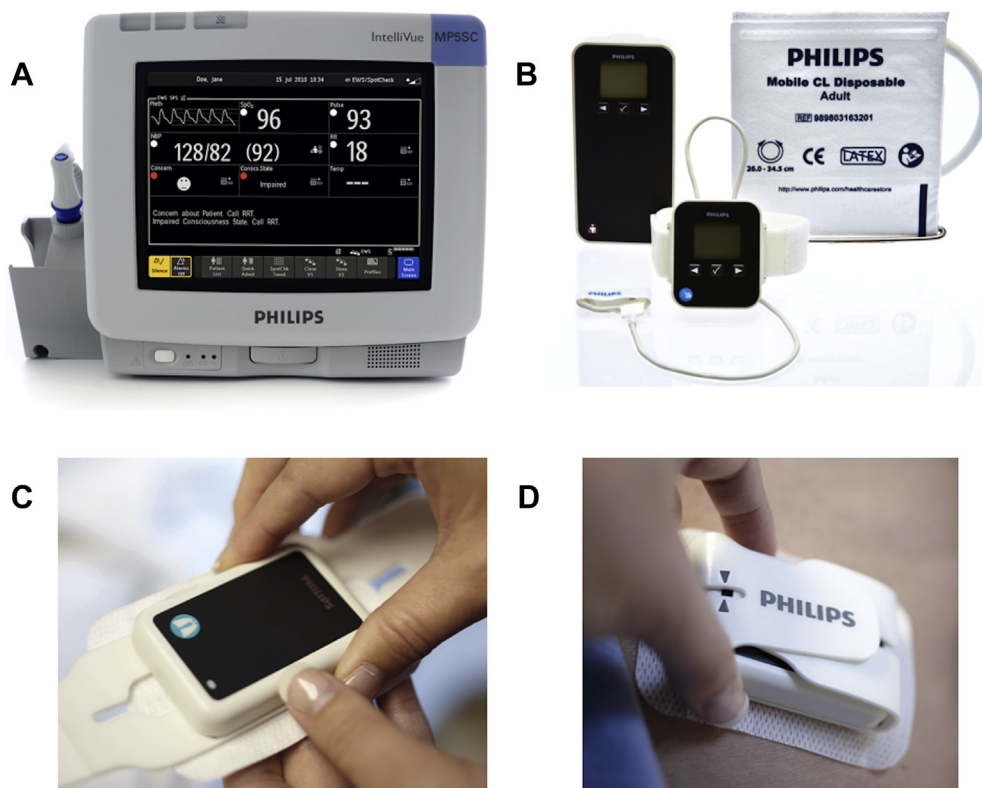
Figure 1. The Philips Guardian Solution. (**A**) MP5 spot-check monitor, (**B**) wireless blood pressure monitor, (**C**) wireless continuous pulse oximetry monitor, and (**D**) wireless respiratory sensor. Reproduced with permission from Philips Canada, (Markham, ON).

in care), triggering fluid therapy, bronchodilators, and antibiotics. Mortality and nonfatal cardiac arrests decreased from 173 to 147 ($P = 0.042$) and from 14 to 2 events ($P = 0.002$), respectively.[17] A key driver of notifications in this study population was abnormal RR.

Subbe et al.[17] were the first to document detailed investigation of the effect of RAM—with cableless sensors generating real-time, actionable notifications—on nurses' responses and related clinical outcomes. The results are encouraging, and robust clinical trials are needed to reach definitive conclusions about effectiveness. It is reasonable to expect that similar effects can be realized in surgical populations. A large part of physiologic derangement after surgery, however, is likely due to clinically important hypotension.[6,7] A challenge to RAM to date is reliance on intermittent, pneumatic BP cuffs. Their use in the context of RAM might lead to suboptimal clinician notification and response times in cases in which BP is the predominant driver of patient deterioration.

The latest technologies show high potential for addressing the gap in continuous noninvasive BP (NIBP) measurement. Advanced NIBP technologies leverage fundamental principles of biomechanics as modelled through Moens—Korteweg equations, which map pulse wave velocity to characteristics of the neighbouring arterial wall. With an initial BP calibration step, these equations can then be manipulated to derive systolic and diastolic BP estimates from pulse transit time, measured between ECG and photoplethysmography peak-to-peak calculations.[23]

Weenk at al.[12] recently piloted (n = 20) remote automated continuous in-hospital monitoring with the Sotera Wireless ViSi Mobile (VM; San Diego, CA) device. This device features continuous, cableless ECG, heart rate, RR, skin temperature, SpO$_2$, and NIBP measurement. Bland—Altman analyses revealed that mean differences in vital signs and EWSs measured by nurses and the VM were within the range of predefined accepted discrepancies. An ongoing study is under way[12] to address further validation work, clinical work flows, and VM connectivity challenges. In similar work, our group is currently engaged in clinical pilot studies evaluating the Cloud DX Vitaliti solution (Cloud DX, Kitchener, ON) (Fig. 2), a multibiometric-channel lightweight monitor that captures continuous NIBP, ECG, heart rate, and heart rate variability, RR, core temperature, SpO$_2$, and pulse wave velocity.

Recent feasibility studies[21,22] have examined the application of RAM systems in combination with hospital-to-home virtual patient engagement interfaces. Such combined systems typically include a Bluetooth-enabled vital signs monitor, a patient/family tablet interface featuring interactive symptom surveys, and a secure video connection to facilitate clinician assessment and follow-up.[18,21,22]

Connectivity and Alarm Fatigue

Connectivity issues remain a challenge, particularly in remote areas that lack cellular communications infrastructure and densely populated areas, where Bluetooth low-energy and cellular networks might be subject to overcrowding.[13] WiFi networks are common installations in home health care environments but require significant power draw from wearable devices than Bluetooth low-energy alternatives and can be

Table 1. Available postoperative remote automated monitoring studies

	Study	Design	Population	Intervention	Comparator	Follow-up	Outcome	Conclusion
In-hospital monitoring								
Effectiveness and feasibility	Ochroch et al.[19]	Single-centre RCT	N = 1219 Age: monitored = 61.8 ± 13.3; unmonitored = 59.9 ± 15.3 years Men: monitored = 59.9%; unmonitored = 64.4%	Continuous	Standard	LOS	(1) Monitored patients transferred to ICU 1 day earlier (2) Mean estimated costs lower in monitored patients ($15,481 vs $18,713 USD) and ICU stay $23,262 USD less	Benefit for high-risk population
Effectiveness	Watkinson et al.[20]	Single-centre RCT	N = 402 Age: monitored = 72 (19-92) unmonitored = 73 (23-100) years Men: monitored = 60%; unmonitored = 62%	Continuous	Standard	Discharge and 30 days	(1) Major events similar (56% monitored; 58% unmonitored) (2) Acute treatment changes similar (53% monitored; 50% unmonitored) (3) 30-day mortality similar (34 monitored; 35 unmonitored)	No effect on adverse events or mortality
Feasibility	Weenk et al.[12]	Single-centre pilot RCT	N = 20 Age: 49.9 ± 13.4 years Men = 65%	Continuous and simultaneous using 2 devices	Manual	3 days	(1) VS measurements consistent (2) Relevant early warning scores on the basis of respiration	Monitoring technologies promising
In-home monitoring								
Effectiveness and feasibility	Ertel et al.[21]	Single-centre, nonrandomized pilot	N = 20 Age: 56 ± 7 years Men = 80%	Tablet-based home monitoring	Booklet and class	90 days	(1) 30-day readmission 20%; median LOS 5.5 days (usual 7 days) (2) 90-day readmission 30% (3) No patient with completed daily assessments readmitted within 30 days	Feasible and enhances monitoring
Effectiveness and feasibility	McElroy et al.[22]	Single-centre, pilot trial	N = 443 Age: monitored = 62.9 ± 9.8; unmonitored = 65.9 ± 14.1 years Men: monitored = 85.2%; unmonitored = 65.9%	Tablet-based home monitoring	Booklet and class	30 days	(1) Readmission similar (7.4% monitored; 9.9% unmonitored) (2) Correlation between abnormal biometric and intervention ($r = 0.62$; $P = 0.001$) (3) Mean satisfaction score: patient 4.9 ± 0.5; clinician 4.9 ± 0.2	Portal for telemonitoring

ICU, intensive care unit; LOS, length of stay; RCT, randomized controlled trial; VS, vital sign.

Figure 2. The Cloud DX Vitaliti multibiometric channel vital signs monitor. Reproduced with permission from Cloud DX (Kitchener, ON).

insecure if not properly configured and maintained. Bluetooth is an efficient, low-power wireless communication alternative, but the theoretical transfer range of 100 m is often degraded because of physical barriers in hospitals and residential settings. Cellular capabilities allow built-in wireless transfer capabilities but could be expensive if a wearable device transfers significant amounts of raw sensor data.[24]

Striking a balance between alarm fatigue and missed events is also an important consideration. A systematic review of 62 articles did not seem to reach consensus on the correct balance because suggested alarm rates range from 0.03 to 4 alerts per patient.[25] Alarm fatigue—associated with delayed/no response to alarms—results from desensitization due to increased exposure to alarms, especially to nonactionable or false alarms.[26] Combined measures of customizing alarm parameters and displays, introducing notification systems with better algorithms, changing batteries, electrodes, and sensors regularly, and careful attention to practice change have all been documented as key strategies for reducing the number of alarms from 18.5% to 89.0%.[25,26] Winters et al. argue that decreasing the number, duration, and noise level of alarms is a top priority for RAM implementation to improve satisfaction among front-line nurses.[26]

Moving Forward: Strategic Priority Research Areas

To move RAM forward, the PROTECT network identified strategic priority research areas through discussions with leading industry partners, health policy experts, health system executives, and government officials. Discussions were focused on the inter-related "clusters" of concentrated scientific effort required to accelerate RAM in Canada and overcome barriers to implementation and scale-up. On the basis of this process, the following strategic priority research areas were identified.

Effectiveness evaluation

As previously discussed, adequately powered RCTs are needed to make substantive conclusions about the effect of RAM after surgery. Moreover, studies to date have focused on either in-hospital[12,19,20] or at-home[21,22] monitoring; no studies have examined models in which RAM spans the surgical ward stay and post-discharge transition to home. Multiple prospective studies from our group confirm that patients are vulnerable in the first 30 days after surgery.[1,4,6,7,11]

The PROTECT network is working to address the hospital-to-home monitoring gap with the current **T**echnology **E**nabled Remote Automated Monitoring and **S**elf-**Man**agement: **Vi**sion for Patient Empowerment Following **C**ardiac and **V**ascular Surgery (THE SMArTVIEW, CoVeRed) trial.[18] Patients undergoing cardiac and major vascular surgery at participating sites in Canada and the United Kingdom are eligible. The SMArTVIEW intervention includes RAM in hospital with the Philips GS system. Postdischarge, patients are followed by daily hospital-to-home monitoring for 30 days with the Philips electronic Transition to Ambulatory Care Program (Fig. 3), a tablet-based solution that combines clinical software for care management with Bluetooth-enabled monitoring devices measuring SpO$_2$, heart rate, BP, temperature, and weight.[18] Specially trained hospital-to-home nurses review patients' vital signs daily and conduct secure video visits to assess for patient concerns and early signs of postoperative complications that require medical intervention. Patient symptom surveys are factored into an embedded triage score to flag recovery issues and prioritize nursing assessment.[18]

Eight hundred patients will be randomized to the SMArTVIEW intervention or standard postoperative care; the trial will examine various feasibility and clinical outcomes, including 45-day hospital readmission and emergency department visits, total system notifications generated, and the proportion of system notifications that lead to actionable changes in care in hospital as well as at home (eg, treatment for hypotension, infection). Our phase 1 usability study[27] indicated high user acceptance ratings for the remote monitoring protocol and devices from patients (mean score 9.4 of 10 [10 indicating complete acceptance]) and nurses (mean acceptance score 8.9 of 10); all patients were 65 years of age or older. Feedback from these end users was used to optimize intervention training and clinical work flows at study sites.[27] Trial recruitment is now under way.

Deterioration: Toward more nuanced appreciation of "signal"

Key to the optimal design of future RAM trials is the acquisition of big data through large-scale, prospective, observational studies. In the upcoming VISION-2 study, our network will use the Cloud DX Vitaliti solution to collect prospective, continuous biometric data on 10,000 patients

Figure 3. The Philips electronic Transition to Ambulatory Care system, featuring tablet interface and Bluetooth-enabled vital signs monitors. Reproduced with permission from Philips.

undergoing noncardiac surgery. This study will be a critical step in obtaining sufficient big data to determine "signal" (ie, prognostically important physiologic precursors of postoperative hemodynamic compromise and adverse events) from "noise" (ie, benign physiologic abnormalities that do not affect prognosis). VISION-2 will allow us to potentially move beyond RAM systems driven by static hospital EWSs.

Hospital EWSs are expected to modify patient outcomes through the identification of patients with initial clinical deterioration in whom an early intervention can prevent a major event. Thus, evaluating the predictive ability of EWSs, in real-life settings, is challenging because the outcomes targeted in prediction models can—and ideally should—be prevented by timely interventions that EWSs have triggered. To minimize bias, observational studies have focused on the ability of EWSs to predict short-term death and/or cardiac arrest (ie, within 48 hours).[28] A systematic review reported that among observational studies in urban hospitals (in developed countries), EWSs have high discriminative ability for death (area under the receiver operating characteristic curve, 0.88-0.93) and cardiac arrest (area under the receiver operating characteristic curve, 0.74-0.86) within 48 hours.[28] In terms of effect on processes, EWSs have been shown to increase the number of calls to rapid response teams (RRTs) and ICU outreach teams, as well as "code blue" calls for patients with pulse and RR abnormalities, suggesting that EWSs trigger interventions earlier.

Although EWSs have been shown to have high predictive value for death and cardiac arrest, they are not patient-specific.[28] Rather, they are on the basis of standardized parameters derived from thresholds for adverse outcomes across multiple clinical settings and conditions.[22] A limitation of this model is that EWSs represent a "one size fits all" approach, which might lack sensitivity to detect more subtle signs of early deterioration in individual patients. For example, some EWSs used in cardiac and other surgical populations specify upper systolic BP thresholds between 170 and 200 mm Hg.[21,23] However, among patients who are recovering from aortic surgery, the upper limit should be lower (140-150 mm Hg) to decrease the risk of internal bleeding.[21,22]

Accrual of big data in VISION-2 and related large-scale prospective cohort studies will facilitate more nuanced understanding of subtle signs of early deterioration and future design of configurable RAM models, not driven by static parameters.

Efficiency of deployment

Appropriate selection of patients at risk for home events remains unknown. Preoperative risk stratification presents an opportunity to identify those at sufficient risk to warrant RAM interventions. The ability to be selective will be an important consideration in terms of the feasibility and sustainability of RAM—in hospital as well as at home. Cardiac risk assessment before noncardiac surgery, in patients who are 45 years of age or older or who have significant cardiovascular disease, is now considered best practice.[29] Although validated clinical risk indices, such as the **R**evised **C**ardiac **R**isk **I**ndex (RCRI),[30] are available for preoperative cardiac risk assessment, prospective observational studies[31,32] show high predictive and reclassification ability of the brain natriuretic peptides (BNPs) and N-terminal fragment of proBNP (NT-proBNP) for cardiovascular complications after noncardiac surgery. On the basis of the available evidence,[31,32] the Canadian Cardiovascular Society guidelines on perioperative cardiac risk assessment and management for patients who undergo noncardiac surgery strongly recommend[29] the use of preoperative NT-proBNP/BNP for those undergoing

noncardiac surgery to enhance cardiac risk estimation. Risk assessment on the basis of clinical indices and biomarkers is evolving and shows promise in terms of directing selective deployment of RAM.

Application of machine learning

Classical biostatistical analyses, on the basis of distribution assumptions, will be of limited utility in the context of continuous multibiometric big data with—likely—multiple nonlinear interactions between variables. With deep learning,[33] a form of artificial intelligence, we will use representation learning to organize and automatically extract progressive layers of features directly from raw data. Machine learning presents an opportunity for new forms of analyses. On the basis of inter-related clusters of physiologic data, our goal is to predict, rather than detect, physiologic derangements after surgery to facilitate timely (pre)intervention. Machine learning architectures, such as generative adversarial networks and convolution networks, have been shown to surpass previous methods in machine vision, speech recognition, and natural language processing.[33] We will use such machine and deep learning methods to develop classification models for identification of physiologic "sentinels" of patient deterioration.[33]

Health research has more slowly adopted machine learning algorithms than other fields, likely because of a lack of precedent for approval by the Food and Drug Administration, Health Canada, and the European Commission. Recent developments are promising, however, including Food and Drug Administration approval of the first deep learning algorithm for analyses of cardiac magnetic resonance imaging data[34] and Cardiogram's recent development of a sensitive (98.04%) and specific (90.02%) deep neural network for detecting atrial fibrillation via Apple Watch (Cadiogram, Inc, San Francisco, CA).[35]

Prevalent strategies for training machine learning models include supervised, unsupervised, and reinforcement techniques.[33] Supervised learning is associated with regression (continuous values or ordinal values) and classification problems (categorical or unordered), where labels exist to define desired network input-output mappings. Unsupervised techniques are used for data sets without associated labels and include clustering and generative modelling approaches.[33] Reinforcement learning defines a reward mechanism for networks to measure performance against and faults that bear on performance. An iconic demonstration of this method was staged by the Google DeepMind team with an artificial intelligence system that outperformed all previous methods of playing Atari video games.[36] Supervised learning is preferred for developing predictive models because it leverages gold standard case labels. Capture of continuous biometric data on 10,000 patients undergoing noncardiac surgery in VISION-2 will allow for design of adverse event labels in support of supervised machine learning activities.

Incorporation of biomarkers

Blood biomarkers are routinely used for preoperative risk stratification (eg, NT-proBNP/BNP)[31,32,37] and postoperative diagnosis of adverse coronary events (eg, high-sensitivity cardiac troponin T).[38] Research has been conducted on a small number of biomarkers that, although useful, do not reflect the spectrum of biologic disease pathways seen in the perioperative context. Complementary to the collection of continuous prospective biometric data, the advent of highly multiplex biomarker measurements provides a unique opportunity for postoperative risk stratification on the basis of identification of novel biomarkers. Refinements in point-of-care testing, foregoing the need for phlebotomy, further introduce possibilities for incorporating biomarkers into future RAM schemas.

The PROTECT network will use biobanks, created from our large international perioperative studies,[1,5,39] to undertake case-control studies using platforms such as SOMAmer or OLink. These studies will allow for identification of risk stratification biomarkers, diagnostic panels, and testing of new hypotheses related to the etiology and pathophysiology of perioperative complications. Incorporating these new biomarkers into risk scores could enhance precision of discrimination of at-risk patients[4] and timely initiation of preemptive therapy to prevent progression of postoperative complications and death.

Economic evaluation and payment models

If the Centers for Disease Control and Prevention classified perioperative death as its own category, it would be the third leading cause of death in the United States.[40] Major cardiovascular events are important on their own because they account for a third of postoperative deaths after noncardiac surgery, resulting in substantially increased medical costs.[5,41] In a study of high-risk gastrointestinal surgeries (n = 935) from Maryland, perioperative MI was among postsurgical complications that resulted in the greatest increase in resource use ($9,573 USD, 95% CI, $4,512-14,633).[42] A large retrospective cohort study of all hospital discharges between 2003 and 2010 from the California State Inpatient Database also showed the incremental cost associated with perioperative MI.[43] The median total hospital costs per patient, with and without perioperative MI, were $154,180 USD (interquartile range, $85,910-$280,110) and $52,040 USD (interquartile range, $29,500-$91,100), respectively.[43] Similar cost increases were shown in a vascular surgery study in the United States (n = 236), in which the total cost of index hospital stay per patient without postoperative MINS was $13,660 USD, compared with $23,640 USD in patients who sustained postoperative MINS.[44] Patients who suffered postoperative MINS were more likely to visit the emergency room postdischarge (23.8% vs 20.3%; P < 0.02) and require ICU stay during rehospitalization (7.1% vs 1.6%; P < 0.04).[44]

As evidence accrues and models for deployment of RAM evolve, economic evaluations will need to consider clinician roles, rates of adoption and diffusion, budget impact analyses, and development of alternative payment and reimbursement mechanisms to facilitate scale-up. The optimal clinical model for deploying RAM and the related costs are not yet known. Hence, comprehensive approaches to economic analyses are necessary. In the SMArTVIEW trial,[18] ward nurses are using the Philips GS to support RAM on surgical wards, and a trained subteam of nurses is responsible for hospital-to-home monitoring via the electronic Transition to Ambulatory Care system.

Our network will address economic evaluation of this model by adopting a payer's (Ministry of Health and

Long-Term Care) as well as a societal (all intervention costs and consequences, regardless of who pays or benefits) perspective. There will be multiple outcomes for the analytic techniques used,[45-47] including cost-effectiveness analysis (CEA; eg, cost per life-year saved, cost per pain-free days), cost-utility analysis (CUA; cost per quality-adjusted life-year saved), and cost analysis (cost of implementation of the SMArTVIEW intervention compared with costs averted [postoperative complications]). Incremental costs and effects of the SMArTVIEW intervention, compared with usual care, will also be calculated. Incremental cost analyses will indicate what the cost savings will be for implementation of the intervention, taking postoperative complications into consideration. Incremental CEA will denote additional costs to save an additional life or result in complication-free recovery. Finally, incremental CUAs will calculate additional costs to save an additional quality-adjusted life-year when comparing SMArTVIEW with standard care. Probabilistic sensitivity analyses will be conducted to assess how sensitive trial results are to changes in values of key parameters (eg, uptake of SMArTVIEW). Finally, an acceptability curve (95% CIs) will be used to characterize the uncertainty in the findings with respect to a range of maximum monetary values that a decision-maker would be willing to pay given a certain change in outcome.[47]

The time horizon chosen for this approach is 45 days and 6 months for the cost analyses and 6 months for CEA and CUA. Supplemental Tables S1 and S2 illustrate cost definitions and the steps required for these planned analyses, which might inform approaches to economic evaluation in future RAM trials.

The ability of postoperative RAM to transgress hospital-to-home boundaries will also challenge the scientific community to generate an evidence base for the implementation of new care-related billing systems for virtual care that fulfil ethical and economic requisites.[48] Because of the rapid pace of technological development, payment models must also follow an iterative process that allows for adjustment and incorporation of continual new data. The adaptation of the current billing system to accommodate telemedicine health care services and premiums in Ontario, undertaken by the Ontario Ministry of Health and Long-Term Care,[49] provides key examples of issues that will likely need to be tackled, including updates to billing software, classification of specific services under new care models for billing, site approvals, certifications for the provision of RAM services, and accounting for technical difficulties.

Incentives are needed to stimulate clinician involvement and incorporation of time spent on documentation requirements related to virtual patient-clinician interactions and follow-up.[50] Switching from fee-for-service reimbursements to value-based payment approaches might address these principles. For example, in early 2017, the US Centers for Medicare and Medicaid Services implemented a merit-based incentive payment system for ambulatory care services.[51] The model was predicated on a composite performance score, which incorporates subscores for quality measures and advancing care information through information technologies.[51]

When optimal implementation and cost evaluation models are realized, the potential cost savings for RAM are considerable. The 3 highest-volume surgeries performed in Canada from 2015 to 2016 (excluding caesarean section delivery) were for knee and hip replacement and fractures. Across Canada, 171,308 in-patient orthopaedic surgeries were performed, representing 11.6% of all annual in-hospital surgeries.[52] The median length of acute hospital stay was 6.8 days and average hospitalization cost was $9106 CAD. This cost equates to >1.5 billion dollars annually in hospital-related expenses.[52] RAM strategies targeted at reducing perioperative events related to hemodynamic compromise could lead to significant reductions in surgery-related economic burden.

Ethical implications: Access and effect on home life

RAM technologies will also have implications from a social justice and equity perspective in terms of access to services, effect on home life, patient autonomy, and interpersonal relationships. Recent reviews exploring the social and ethical dimensions of various digital health technologies in the home[53,54] highlight the importance of examining these factors. Balance needs to be struck with respect to privacy and patient need to conform to the requirements of using these technologies vs their potential to reduce the need for appointments or hospitalization.[55-57] Additional considerations include ease of patient/family use, effect on activities of daily life, and perceived stigma of wearing monitoring devices.[53,54]

Consideration should be paid to equity through identification of the "social locations" of patients, referring to factors such as social class, gender, and race.[54] Because Canadians live in geographically diverse places, attention to how RAM technologies affect access to health care services, across locations, will also be needed. A recent review of communications infrastructure showed that differences in quality of data infrastructure between urban and rural areas is growing despite rural communities being most in need of connectivity.[55]

Lack of Internet and cellular access is particularly evident in rural and remote Indigenous communities, where resources to support connectivity are largely unavailable.[55] Affordability is also a concern.[56] Despite these barriers, a 2017 critical review[55] showed that adaptation of assistive technologies, for health purposes, by Indigenous peoples is growing. Indigenous community engagement and feasibility studies—inclusive of diverse Indigenous group end-user needs and connectivity capabilities—are needed to inform the development of culturally safe models for adoption of RAM strategies.

Implementation of RAM in Canada: Overcoming Barriers

Importance of interoperability and cybersecurity

A recent health policy review by the Personal Connected Health Alliance identified the promotion of interoperability standards as crucial to the success of scaling remote patient monitoring programs.[57-59] Presently, the PROTECT network engages in proprietary, custom installations of monitoring solutions to conduct research—a commonplace scenario in Canada. Such custom deployments reflect ongoing, pragmatic efforts to manage technical complexity, maintain vendor confidentiality, and ensure regulatory compliance.[58]

More open and interoperable solutions will be needed to facilitate efficiency of clinical trials. Common interfaces that
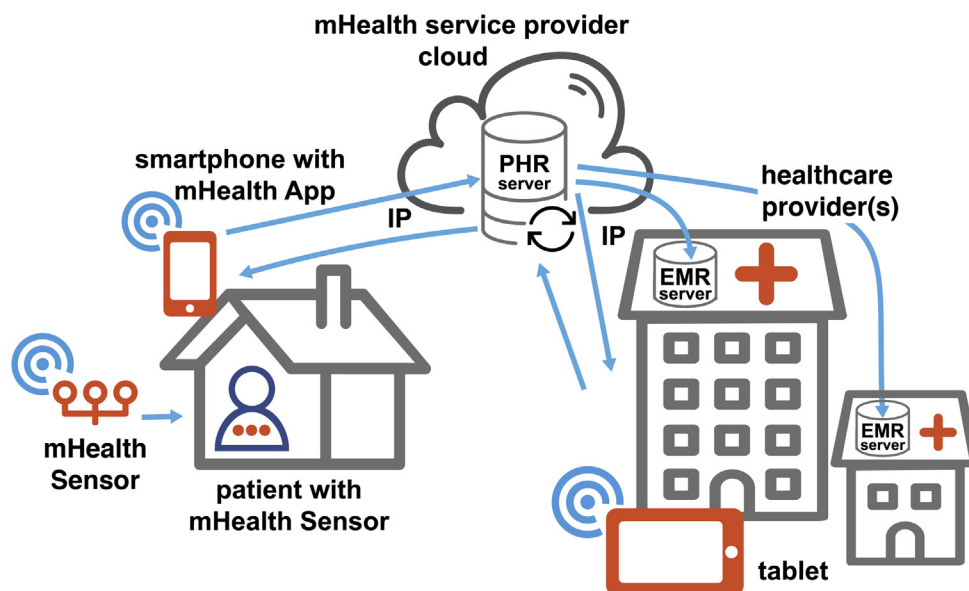
Figure 4. Conceptual schema of a remote monitoring device integration model using mobile services. Typically, the medical device or sensor will transmit vital signs and related patient information via Bluetooth low-energy or ZigBee protocols to a mobile device and application (app). From the mobile device, data can be shared with personal health records and stored in hospital information systems, community clinical data repositories (for access by primary/community care providers), or primary care electronic medical records through Web-enabled transactions. EMR, electronic medical record; IP, Internet provider; PHR, personal health record.

support "plug-and-play" device-level exchange[59] through to back-end hospital EHR systems will need to be leveraged. The conceptual system diagram presented in Figure 4 depicts this principle for end-to-end (hospital-to-home) integration of a patient RAM device, connected to an IoT network, through ZigBee low-power radio or Bluetooth low-energy protocols.[57]

Leading not-for-profit organizations such as Continua Health Alliance and Integrating the Healthcare Enterprise have established product certification programs that leverage personal health data, integration, and interoperability standards for wireless data transmission set by the International Standards Organization, the Institute of Electrical and Electronics Engineers, and HL7.[16] They are also working on guidelines for systems interoperability by grouping standards into profiles against which monitoring solutions can be certified. However, there is still some way to go before the health sector has a fully interoperable set of standards that can be universally adopted and can support RAM.

The PROTECT network hopes to overcome barriers promulgated by low adoption rates of RAM pilots and insufficient volumes of patients to justify investment in standardized integration protocols that connect mobile health networks to hospital-based EHRs.

Another important consideration is cybersecurity. Implementation of RAM requires interfacing with legacy hospital information systems. Installations can therefore feature architecture constituted by decentralized and heterogeneous subsystems, each with operational and managerial independence. These conditions can confer security risk, even under conditions in which solutions meet HL7 standards[16] for seamless connection and bidirectional data exchange. Cybersecurity experts have predicted that between 2015 and 2019, data breaches will cost hospitals $305 billion (USD).[60] The average cost of a health care breach is estimated at more than

$2.2 million (USD), with the average stolen record costing $355 (USD).[61] As the RAM field grows, attention to cybersecurity issues will be a key factor in the development and governance of research infrastructure and databases with extensible architecture (to accommodate big biometric data), supplier networks, and portal access points that meet regulatory compliance requirements.[61]

Importance of stakeholder engagement in system design and implementation

Evidence supports the importance of sustained stakeholder engagement for the viability of RAM. Since 2007, for example, the Ontario Telemedicine Network Telehomecare program has enrolled > 14,600 patients (living with congestive heart failure and/or chronic obstructive pulmonary disease) in a 6-month program to increase self-management skills via RAM and health coaching. A study of stakeholder facilitators and barriers to program implementation and adoption identified the importance of user-friendly technology to facilitate equitable access, motivational skills of the clinical team to keep people engaged, and manageable patient—clinician ratios.[62]

In the perioperative setting, suboptimal processes of care can be co-responsible for adverse events.[63] If RAM is to be expected to reduce preventable adverse events related to the lack of detection of early signs of clinical deterioration, it will be crucial to engage stakeholders in system design[18] to address user acceptance and training, prevention of notification fatigue, and effective communication around implementation.[8,27] Evidence supports the positive effect of engaging stakeholders early, with respect to training in particular, because RAM models should target postsurgical wards, where clinicians are unaccustomed to responding to continuous

monitoring data in real time. In the study by Subbe et al.,[17] nursing staff underwent systems training ahead of time. A dedicated on-site trainer further supported model implementation until 80% of ward staff were trained in clinical work flows.

At an organizational level, the Ontario Telemedicine Network reported[62] that structured, consistent, and ongoing engagement with primary care providers to increase awareness and facilitate referrals, partnering with hospitals to improve care transitions into the community, and sustained change management practices have been central to the sustainability of the telehomecare program.

Drawing from these lessons, consideration of barriers and facilitators to RAM, across network studies, will include a structured, tiered scaling and uptake model with clearly defined users, programs, organizations, and regions of focus. Practice-level adoption will address the needs of nurses, physicians, allied health support staff, patients, and family members in terms of technology user-friendliness, acceptance, and ease of work flows. At the organizational level, perioperative pathways and programs will need to be analyzed to identify opportunities for early stakeholder adoption, motivation, and change leading to organizational-level application. At the regional level, collaborative efforts will be made to connect hospital and regional health executives to network leaders, with a focus on enabling the adoption, scale, and spread of network monitoring solutions.

Advancing RAM: The PROTECT Network

Advancing the field of RAM requires innovation and strategy to overcome implementation barriers. PROTECT moves beyond traditional discipline-specific approaches, comprising an international, multidisciplinary group of researchers, administrators, and leaders in health policy. Progress will require the ability to capitalize on preexisting databases and infrastructure to address issues such as preoperative risk prediction and intelligent deployment of RAM models. Strategies will be drawn from multiple international perioperative studies[1,4,7,64-66] completed by network members (see Supplemental Table S3).

Conclusion

Perioperative complications are a major neglected public health issue with substantial economic implications. The PROTECT network anticipates showing that RAM of continuous physiologic parameters, along with biomarker measurements, has the potential to reduce major perioperative complications and hospital readmissions by up to 50%. As a field, RAM remains in the early stages. Strategic priorities for research in this arena represent key areas of inter-related focus that can fulfil the enormous potential of postoperative RAM to address an important void in Canadian and global research and health care.

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Disclosures

See the *Disclosures* section of the Supplementary Material.

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Supplementary Material

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