Beyond wellness monitoring: Continuous multiparameter remote automated monitoring of patients

Michael H. McGillion, RN, PhD, Katherine Allan, MASc, PhD, Sara Ross-Howe, BASc, MASc, PhD(c), Wenjun Jiang, Michelle Graham, MD, Maura Marcucci, MSc, Ana Johnson, PhD, Ted Scott, MAppSc, PhD, Carley Ouellette, RN, BScN, Dejan Kocetkov, Jennifer Lounsbury, RN(EC) MN, Marissa Bird, BSN, RN, Prathiba Harsha, MBBS, CCRA, Karla Sanchez, BSc, Valerie Harvey, BSc, Jessica Vincent, MSc, Flavia K. Borges, MD, PhD, Sandra L. Carroll, RN, PhD, Elizabeth Peter, RN, PhD, Ameen Patel, MD, Sverre Bergh, PhD, P.J. Devereaux, MD, PhD, FRCPC

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Michael H. McGillion, RN, PhD, Katherine Allan, MASC, PhD, Sara Ross-Howe, BASc, MASC, PhD(c), Wenjun Jiang, Michelle Graham MD, Maura Marcucci, MSc, Ana Johnson, PhD, Ted Scott, MApSc, PhD, Carley Ouellette, RN, BScN, Dejan Kocetkov, Jennifer Lounsberry, RN(EC) MN, Marissa Bird, BSN, RN, Prathiba Harsha, MBBS, CCRA, Karla Sanchez, BSc, Valerie Harvey, BSc, Jessica Vincent, MSc, Flavia K Borges, MD, PhD, Sandra L Carroll, RN, PhD, Elizabeth Peter, RN, PhD, Ameen Patel, MD, Sverre Bergh, PhD, P.J. Devereaux, MD, PhD, FRCPC, McMaster University, Faculty of Health Sciences, Hamilton, Ontario, Canada; Population Health Research Institute, Hamilton, Ontario, Canada; Unity Health Toronto, Division of Cardiology, Toronto, Ontario, Canada; University of Waterloo, Waterloo, Ontario, Canada; Cloud DX, Kitchener, Waterloo, Ontario, Canada; Hamilton Health Sciences, Hamilton, Ontario, Canada; University of Alberta, Edmonton, AB, Canada; Queen’s University, Kingston, Ontario, Canada; University of Toronto Faculty of Nursing, Toronto, Ontario, Canada; Research Centre for Age-related Functional Decline and Diseases, Innlandet Hospital Trust, Ottestad, Norway.

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Corresponding Author:
Michael McGillion, RN PhD
School of Nursing, Faculty of Health Sciences
McMaster University
1280 Main Street West
HSC 2140E
Hamilton, ON
L8S 4K1
Phone: 905 525 9140 ext. 20275
Email: mmcgill@mcmaster.ca
Abstract

The pursuit of more efficient patient-friendly health systems and reductions in tertiary health services use has seen enormous growth in the application and study of remote patient monitoring systems for cardiovascular patient care. While there are many consumer-grade products available to monitor patient wellness, the regulation of these technologies varies considerably, with most products having little to no evaluation data. As the science and practice of virtual care continues to evolve, clinicians and researchers can benefit from an understanding of more comprehensive solutions, capable of monitoring three or more biophysical parameters (e.g., oxygen saturation, heart rate) continuously and simultaneously. These devices, herein referred to as continuous multiparameter remote automated monitoring (CM-RAM) devices, have the potential to revolutionize virtual patient care. Through seamless integration of multiple biophysical signals, CM-RAM technologies can allow for the acquisition of high-volume big data for the development of algorithms to facilitate early detection of negative changes in patient health status and timely clinician response. In this article, we review key principles, architecture, and components of CM-RAM technologies. Work to date in this field and related implications are also presented, including strategic priorities for advancing the science and practice of CM-RAM.

Brief Summary

Recent years have seen enormous growth in the application and study of remote patient monitoring systems for cardiovascular patient care. Continuous multiparameter remote automated monitoring (CM-RAM) devices, have the potential to revolutionize virtual patient care. In this article, we review key principles, architecture, and components of CM-RAM technologies. Work to date in this field is also presented, including strategic priorities for advancing the science and practice of CM-RAM.
The pursuit of more efficient patient-friendly health systems and reductions in need for tertiary health services use has seen enormous growth in the application and study of remote patient monitoring systems in cardiovascular patient care over the last two decades.\textsuperscript{1-3} More recently, the coronavirus 2019 (COVID-19) pandemic has catapulted this area of clinical practice and research to new heights—health system innovators have worked feverishly to deploy non-invasive systems that facilitate remote patient surveillance and monitoring, as well as the physical and social distancing of patients and families to prevent viral spread.\textsuperscript{4} During the COVID-19 crisis, allowances made by regulatory agencies such as the United States Food and Drug Administration (FDA) have permitted health systems to leverage legally marketed patient monitoring solutions, with modifications beyond their original indications for clinical use.\textsuperscript{5} The expansion of the capabilities, reach, and availability of these technologies has resulted in an unprecedented number of patient biophysical parameters being monitored remotely. The widespread proliferation of consumer-grade wearable remote patient monitoring devices for wellness monitoring has also changed the face of home-based surveillance of patients’ cardiovascular parameters, beyond the use of the original Holter electrocardiogram.\textsuperscript{1-3,6}

While there are many available consumer products to measure patient biophysical parameters, few have stood out in terms of moving these devices forward for clinical-grade application. Wellness devices are limited in the claims they can make regarding the diagnosis, prevention, or treatment of a disease or condition.\textsuperscript{7} Manufacturers can suggest they may help to reduce the risk for chronic disease or conditions such as high blood pressure (BP) or type 2 diabetes, where a healthy lifestyle has been generally well accepted to have demonstrated risk reduction or help with living well.\textsuperscript{7} The Apple Watch is an example of a product that has impressively featured a number of measurable biophysical parameters over the course of product releases, including heart rate (since Series 1), on-demand lead-1 ECG tracing (Series 4), and blood oxygen saturation (Series 6).\textsuperscript{8-10} While Apple Watch on demand-ECG tracings are approved by the FDA for arrhythmia detection, the blood oxygen saturation sensor is
for wellness monitoring only; it employs reflectance pulse oximetry—a technique that can be vulnerable to artifact from patient motion.\textsuperscript{11}

Furthermore, the regulation of consumer-grade wearable patient monitoring products varies considerably, with most available products having little to no published evaluation data.\textsuperscript{12} The majority of wellness monitoring devices are capable of measuring a maximum of 1 to 2 episodic (e.g., on-demand ECG) or continuous (e.g., temperature) biophysical parameters simultaneously, thereby limiting clinical utility for patient surveillance, diagnoses, and timely management of changes in health status. While single parameter monitoring (e.g., heart rate) has important application in certain situations (e.g., atrial fibrillation monitoring), many patients require continuous measurement of a diversity of biophysical parameters, similar to what happens among inpatients in hospital. Innovators working with market-ready solutions are also often faced with the inherent complexities of intermingling proprietary systems,\textsuperscript{13} each with operational independence that features unique biophysical parameters and data communication channels, as well as data storage and health system integration requirements.

As the science and practice of virtual care and remote patient monitoring evolves, clinicians and researchers can benefit from an understanding of more comprehensive solutions, capable of monitoring three or more biophysical parameters continuously and simultaneously. These systems target optimal efficiency by maximizing the metrics collected and by streamlining processes through the application of a single integrated solution. More advanced systems are also capable of collecting raw biometric waveforms, such as photoplethysmography and ECG, that can be used to derive non-invasive estimates of more complex biophysical parameters that would normally be measured continuously through invasive means (e.g., continuous BP via invasive arterial catheter). These devices, hereafter referred to as continuous multiparameter remote automated monitoring (CM-RAM) devices, have the potential to revolutionize patient monitoring through seamless integration of
multiple, time-synchronized biophysical parameter signals. These technologies can also yield high 
frequency/high volume big data for the development of algorithms to facilitate early detection of 
negative changes in patient health status and timely clinician response. Figure 1 illustrates the purpose 
of CM-RAM devices, versus wellness monitoring and other medical grade devices.

[Insert Figure 1 here].

**CM-RAM Architecture: Principles and components**

*Body Sensor Network*

CM-RAM systems include sensors that can be either attached directly to the body or integrated 
into different materials for indirect body sensing. The interconnection of these sensors forms a ‘Body 
Sensor Network’ (BSN) (see Figure 2). BSNs consist of three layers, with each layer communicating 
either wirelessly or through hardwired channels.14 First is the body sensor layer, that includes wearable 
sensor ‘nodes’, each capable of measuring, sampling (i.e., digitizing) and processing multiple 
biophysical signals.14 BSNs can be sub-categorized into sensors affixed to the patient versus the main 
processing unit where signals are digitized, filtered, and processed. The second layer is the personal 
area network layer, containing the coordinating device that runs the end user applications. These are 
typically hand-held devices (e.g., smartphone) or tablet-based computer devices (e.g., tablet) that can 
perform either limited or more advanced forms of local data processing to display the metrics being 
collected or integrate and analyze them to assist in clinical decision making. Signal transmission from 
the body sensor layer to the personal area network layer is typically through a wireless communication 
protocol, configured for short-range, low power radio frequency communication (e.g., Bluetooth, 
Zigbee). The third layer is the global network layer, a back-end cloud infrastructure to support data 
storage, analytics, and interfacing with dashboards via web portals.

[Insert Figure 2 here]

**Body Sensing Layer**
CM-RAM devices utilize fundamental principles of biomedical engineering to measure and derive clinically relevant biophysical parameters. Sensors convert physical measurements into electrical output that can be quantified and analyzed utilizing digital signal processing. These signals can either be measured in an analog format as continuous measurements, or in a digital format with samples taken at a defined sampling frequencies (e.g., ECG signal sampled at 500 Hz [times per second]). Sensors are classified based on the mode of transduction, including mechanical, electrical, optical, and chemical modalities. See Supplementary Table S1 for details on sensor categories by transduction method.

**Common Biometric Sensors, continuous biophysical parameters, and sensor placement**

Figure 3 presents common forms of biometric sensors and related positioning for optimal signal quality. *Electrocardiography* draws upon the principles of biopotentials measured through wet or dry electrodes. Wet electrodes consist of a solid conductive pad that interface with the skin via an electrolyte containing hydrogel that minimizes the electrical impedance of skin. Dry electrodes do not contain any electrolyte materials and instead rely on direct skin contact. Disposable wet electrodes typically use silver-silver chloride (Ag-AgCl) contacts with electrolyte gel for conduction and dry electrodes use metal plating. Specialized electrodes have been developed to support short- or long-term monitoring and different activities (e.g., resting versus stress testing).

Within CM-RAM devices, electrodes are paired to measure the voltage potential difference between two points. Common examples of this include the electrocardiogram (ECG), electroencephalogram, and Electromyography. Minimum three-lead (Leads I – III) ECG electrode positioning is desired for CM-RAM devices (Figure 3). Most commercial grade products featuring ECG patches are limited to a single lead configuration due to limitations with local data storage (within the device), power, and the need for wearability. More complex systems, such as Visi Mobile (Sotera Visi Mobile, San Diego, California) (see Work to date) offer multiple lead configurations.
Photoplethysmography (PPG) captures volumetric changes in blood flow measured through optical sensors, which consist of light-emitting diodes (LEDs) at defined wavelengths and photo diodes for measuring transmitted light. CM-RAM devices can measure PPG at varying wavelengths, including 660 nanometres (nm) (visible red light); 940 nm (infrared light) to capture SP02;\textsuperscript{10} and 525 nm (visible green light) for pulse detection. These sensors can be arranged in a ‘transmittance’ orientation, where the LEDs and photo diodes are positioned on opposite surfaces of the peripheral site under measurement. Alternatively, the optical sensors can be positioned in a ‘reflectance’ orientation where the LEDs and photo diodes are positioned on the same tissue surface. Oxygen saturation is measured by determining the ratio of absorption between red and IR channels. Green PPG is a movement-resilient signal, frequently used for pulse rate detection in ambulatory devices. Reflective PPG sensors are commonly placed on the forehead and wrist locations, and transmittance-based orientations are facilitated on the fingers, toes, ear lobes, and nasal cavity (Figure 3).\textsuperscript{19} These optical sensors are vulnerable to artifact from patient motion, as well as intrusion by ambient (environmental) light.\textsuperscript{19} Moreover, accuracy testing in patients with a range of skin pigmentation has been limited.

Body temperature is measured with thermo resistors via conduction through a metal contact point with the skin or thermopiles as IR sensors that measure thermal levels.\textsuperscript{20} Core body temperature is a more challenging metric to capture than skin temperature, with tympanic, forehead, and under arm sensor sites demonstrating the greatest promise for accuracy.\textsuperscript{21} Many CM-RAM devices to date capture surface skin temperature and ongoing research is focused on the development of advanced algorithms to map these metrics to a core body temperature for clinical-grade application.\textsuperscript{21} For clinical decision making, core temperature is the preferred measurement as skin temperature can be impacted by a number of environmental factors, such as ambient room temperature or climate.\textsuperscript{21}

Continuous respiration rate is among the most infrequently measured vital signs, yet the importance of this metric has become paramount during the COVID-19 pandemic. The gold standard
for capturing continuous respiration rate includes the use of capnography and nasal cannula. Wearable CM-RAM devices commonly measure respiration rate with elastomeric plethysmography through belts placed snugly around the chest that utilize piezoelectric (i.e., electrical detection of mechanical stress) sensors to register expansion and contraction, or through impedance plethysmography where bioimpedance (i.e., estimation of body composition) is measured between chest-mounted ECG electrodes. Discrete respiration measurements can also be derived from ECG or PPG signals by identifying the amplitude and frequency deviations caused by respiration. Both these modalities pose challenges to patient comfort; the respiration belt can be uncomfortable for female or obese patients, and wet electrodes can cause skin irritation with extended wear. Further confounding can occur by artifact related to patient vocalizations and coughing. A challenging area is the use of these sensors in patients with underlying chronic respiratory conditions that feature irregular breathing patterns, such as COPD and asthma. Advances are being made in contactless sensing systems, which show promise for accurate respiratory rate and heart rate measurement at a distance, while overcoming these types of movement and artifact-related challenges.

[Insert Figure 3 here]

**Movement and Position**

Some CM-RAM devices also track patient position and movement through inertial measurement units, which include accelerometer, gyroscope and magnetometer sensors placed on the limbs or torso. Accelerometers and gyroscopes utilize either piezoresistive or piezoelectric sensors to measure the acceleration of an object (or rate of change of velocity) and angular velocity, respectively. A magnetometer measures the strength and direction of magnetic fields to establish patient position. These signals have been utilized for human activity recognition (HAR), activity indexes, step counting, energy output, sleep quality and fall risk assessment and detection. Ballistocardiography (BCG) utilizes specially located (typically on the chest) inertial measurement units to measure small
movements caused by the mechanical output of the heart and is often used to derive a heart rate. Although some CM-RAM devices, such as VitalPatch (VitalConnect, California, San Jose, CA), feature inertial measurement units to capture motion and position metrics, these outputs are not subject to regulatory standards or widely adopted in clinical settings at this time. Often, these signal inputs are included in CM-RAM systems to support advanced digital signal processing (DSP) of incoming vital signs data, such as identification and mitigation of the confounding effects of patient motion artifact.

**Personal Area Network Layer**

Signals generated in the BNS sensor layer are typically wirelessly transmitted to a base station (i.e., tablet or smartphone) within the personal area network layer through wireless body area networks (WBAN). Almost universally, CM-RAM systems use Bluetooth Low Energy (BLE) transmission due to low power requirements, high speed data transmission rates of up to 1 megabit per second (Mbps), and an operating range of up to 100 metres from device to base station. More advanced systems have sufficient on-board data storage to allow for delayed signal transmission if the base station is out of range. Once transmitted, the raw signals are digitized and pre-processed to remove noise artifacts and biophysical parameters metrics are derived.

**Global Network Layer**

Originating from the patient at home (Body Sensing Layer), pre-processed vital signs data within CM-RAM devices can be transmitted from the base station (Personal Area Network Layer) to a cloud infrastructure in the Global Area Network Layer from the base station and relayed to clinical support teams. These communications can be bi-directional (Figure 2) and are achieved through cellular 3G, 4G, 5G or Wi-Fi networks. More sophisticated CM-RAM systems feature cloud infrastructures that support long-term storage of biophysiological signals, as well as web-based clinician portals or dashboards for remote monitoring of patient status. With some systems, early
warning scores are applied to collected biophysical data within the central infrastructure of hospital information systems to identify patients at risk for clinical deterioration and facilitate early intervention.

**CM-RAM: Work to date**

The science of CM-RAM implementation and evaluation is developing rapidly. A literature search on studies employing CM-RAM technologies yielded 38 studies of various technologies published between 2012 and 2021 (see the Supplemental Methods for details). Table 1 provides a summary of devices and their features and Supplementary Table S2 is a summary of all studies. While preliminary effectiveness data are accruing, most studies focus on clinical validation, feasibility of implementation, and patient wearability and acceptability.

Three of the most well-studied CM-RAM technologies to date are the VitalPatch, the SensiumVitals System (Sensium Healthcare Ltd, Oxford, UK), and Visi Mobile. The VitalPatch and SensiumVitals systems consist of a disposable, adhesive wireless ECG patch sensor with 3-axis accelerometer (VitalPatch only) and thermoresistor affixed to the patient’s chest that captures multiple biophysical parameters, including heart rate, respiratory rate (i.e, impedance pneumography) and skin temperature. Visi Mobile also includes a wrist-worn device that captures SpO₂, BP and features a touch screen vital signs display. These systems transmit vital signs in real time to patients and clinicians. Data are transmitted to cloud platforms for storage and further analysis.

All three devices have undergone clinical validation testing comparing their metrics against manual vital signs measurements taken by nurses. In a feasibility study (n= 20), patients admitted to internal medicine and surgical wards were monitored with the VitalPatch and Visi Mobile devices for 2 to 3 days. Vital signs collected by both devices and nurses were used to calculate and compare Modified Early Warning Scores for clinical deterioration. The clinical measurements and both device measurements were in agreement within accepted limits, although wide limits of
agreement were found. In 15% and 25% of the Visi Mobile and VitalPatch cases, respectively, clinically relevant differences in Modified Early Warning Scores comparisons were found based on inconsistent respiratory rate measurements; both devices overestimated respiratory rate in comparison to nurses. Technical issues also differed by device; over 50% of VitalPatch artifacts and data losses had no discernable cause while the rest were due to loss of skin contact, transmission problems or the patient leaving the ward without their mobile device. For Visi Mobile, almost 70% of all reported artifacts were caused by a connection failure between the mobile device and chest patch sensor. During the study, one patient monitored with Visi Mobile had clinical deterioration detected 3 days postoperatively after elective colorectal surgery. The device alerted the patient’s nurse that he developed both tachycardia and tachypnea; this adverse event detection occurred between two scheduled nurse vital signs measurements and could have otherwise been missed.

Verrilo et al. evaluated the feasibility of the Visi Mobile device for improving patient outcomes by comparing the prevalence and incidence rates of postoperative complications, rapid response team, intensive care unit (ICU) transfers, and death rates after admission in 422 postoperative patients (general care, orthopedics, trauma) with continuous vital signs monitoring versus standard of care; nurse satisfaction with the device was also examined. Patients were asked to wear the device for at least the first 48 hours of unit admission. The incident rate of complications declined significantly in the Visi Mobile group compared to the control group, i.e., 9.6 versus 34.3 per 1000 patient days (p<0.05). Clinically significant decreases in transfers to ICU and failure-to-rescue events in the Visi Mobile group were also observed. By incorporating Visi Mobile data into their patient assessments, nurses reported they were able to prioritize patient care with greater accuracy, identify signs of clinical deterioration, and facilitate early intervention.

The accuracy and feasibility of the SensiumVital System was assessed in a series of RCTs in patients undergoing major elective general surgery. The reference standard was nurse-recorded
vital signs, factored into the National Early Warning Score for adverse event prediction. Participants were individually randomized 1:1 to receive either CM-RAM with Sensium plus National Early Warning Score monitoring or monitoring by National Early Warning Score, alone. In a small pilot RCT (n=51), comparison showed reasonable correlation between nurse and Sensium-recorded heart rate ($R^2=0.67$, $p<0.001$), but poor correlation between these approaches for measurement of respiratory rate ($R^2=0.01$, $p<0.001$) and temperature ($R^2=0.13$, $p<0.001$). Ambient room temperature was thought to be a confounding factor for the Sensium device, given that skin temperature measured by thermoresistor sensors can be affected by environmental factors. Data completeness for continuous vital signs recorded varied (respiratory rate, 31%, skin temperature, 72.8%) and data losses were attributed to artifact from patient ambulation. In a follow-up larger feasibility RCT (n=136), preliminary clinical outcomes explored included time to antibiotics for sepsis cases, length of hospital stay, number of critical care admissions and rate of hospital readmission within 30 days of discharge. Time to antibiotics was similar in both arms; participants monitored with Sensium had a shorter average length of stay, i.e., 11.6 days (95% Confidence Interval [CI], 9.5-13.7 days) vs 16.2 days (95% CI, 11.3-21.2 days).

The VitalPatch, SensiumVitals and Visi Mobile systems have also undergone wearability and usability assessments. A pilot RCT of 90 post-surgical patients randomized to CM-RAM using Visi Mobile or VitalPatch for 2-3 days found that patients and nurses had overall positive feelings about both devices—earlier identification of clinical deterioration, shorter hospital stay and increased feelings of safety were frequently mentioned as positive benefits. A feasibility and acceptability study (30 patients, 23 nurses) of SensiumVitals compared to VitalPatch and Visi Mobile in abdominal surgery patients found the majority of patients rated the Sensium sensor patch as comfortable, felt safer, and would choose to wear it again when next in hospital. Results for wearability across devices have been mixed and speak to the need for CM-RAM technologies to be lightweight, unobtrusive, and
low-maintenance. The VitalPatch was rated as positive due to its small size and “invisibility” under patient clothing, whereas the Visi Mobile device was felt by some patients to be ‘big’ or ‘heavy’ with many cables and a short battery life.  

Large scale prospective observational studies of other hospital-based CM-RAM systems have also shown positive results. In a before (n=2139) and after (n=2263) study of patients admitted to two general medicine wards in the United Kingdom, Subbe et al.\textsuperscript{37} examined the effect of automated continual vital signs monitoring, with relay of abnormal vital signs to rapid response teams. The Philips Guardian solution (Royal Philips, Amsterdam, Netherlands)—featuring cableless transmittance-based finger SpO\textsubscript{2} sensor, oscillometric BP cuff, and respiratory rate derived from accelerometer and gyroscope sensors applied to the patient, paired with a bedside spot-check vital signs monitor—was used to remotely monitor respiratory rate, heart rate, BP, and SpO\textsubscript{2}; temperature was acquired intermittently. During the intervention period on each ward notifications to rapid response teams increased significantly (from 405 to 524, p=0.001), resulting in interventions for intravenous fluid therapy, antibiotics and bronchodilators.\textsuperscript{37} Reduction in mortality was also observed from pre (n= 173) to post (n= 147) intervention (p=0.042).\textsuperscript{37} Bellomo et al.\textsuperscript{38} found similar results in a before and after study conducted on a cohort of 18,305 patients across 12 general wards (10 hospitals) in Australia, the US, and Europe. The use of the Guardian system led to an increased proportion of response team calls related to detection of abnormal respirations (from 21% to 31%; difference 9.9% [95% CI: 0.1-18.5]); and improvements in survival following treatment to 90 days or discharge (from 86% to 92%; difference 6.3 [95% CI: 0.0-12.6]).\textsuperscript{38} Guardian was also associated with significantly decreased nurse time required to record vital signs (from 4.1 ± 1.3 minutes [min] to 2.5 ± 0.5 min; difference 1.6 min [95% CI: 1.4 to 1.8]).\textsuperscript{38}

Some studies have focused on pilot testing these systems in the home setting, sometimes in combination with environmental ambient sensors. Saner et al.\textsuperscript{39} tested a multimodal sensor system in a
cohort of 24 community dwelling seniors over a period of 1-2 years. Vital signs and contextual data were collected using integrated sensors including a passive infrared motion sensing system (Domosafety, S.A., Switzerland) to detect physical activity, toileting, refrigerator use and door openings; as well as an upper armband sensor (Everion, Biovotion AG, Zurich Switzerland) to collect heart rate, heart rate variability, respiratory rate and skin temperature. An accelerometer (Axivity Ltd, Newcastle, UK) evaluated patient motion. A bed sensor beneath the mattress also collected heart rate, respiratory rate and sleep quality. Data were transmitted automatically each night via cellular network to a secured cloud platform for hosting and analyses. A total of 92,592 person hours were recorded by the Everion® device over the course of the study. Several episodes of health deterioration, including worsening heart failure and heart rhythm disturbances, were captured by sensor signals from different sources, supporting the idea that multiple sensor streams holds promise for detecting patient deterioration and diagnosing health problems at home. Participant feedback supported the use of contactless ambient sensors in the home, where possible, to reduce feelings of intrusion that can be associated with wearable devices.

More recently, Keogh et al. investigated the usability of 7 wearable continuous remote patient monitoring devices, including the CM-RAM Everion solution®, by asking 8 older adults to wear them in their home environment for a minimum of one week. Participants believed that light weight wrist-worn sensors were the most versatile and easy to use, and therefore more suitable for longer term use. Most also agreed that long battery life was essential; a minimum of one week was considered ideal. The need to charge systems daily was deemed unacceptable and was considered a barrier for extended use of the Everion® device. Participants expressed willingness to accept some device-related discomfort, inconvenience, and intrusion at home for systems perceived as useful through the provision of real-time feedback on their health status. Systems designed to only inform remote observers were perceived as less tolerable.
Some advances are also being made in the use of CM-RAM systems for acuity prediction in trauma and emergency patients. Meizoso et al.\textsuperscript{41} used the MiniMedic wireless vital signs monitor (MiniMedic, Athena GTX, Des Moines, Iowa) to remotely monitor 59 trauma ICU patients to predict shock index, i.e., \( \frac{\text{heart rate}}{\text{systolic BP}} \). Developed by the US Military, MiniMedic acquires vital signs from small surface sensors placed on up to 5 patients simultaneously before wirelessly transmitting these data to monitors carried by any first responder within a 100-metre range.\textsuperscript{41} The system incorporates an injury acuity algorithm, the Murphy Factor, which summarizes overall patient status, accounting for changes in vital signs every 30 seconds. Pulse wave transit time (PWTT) is used in place of systolic blood pressure.\textsuperscript{41} MiniMedic sensors were applied to the forehead and finger of each patient to measure PWTT, temperature, heart rate and \( \text{SpO}_2 \), which were recorded and displayed on a standard bedside monitor for 60 minutes. Shock index was calculated using bedside measured vital signs and compared to the Murphy Factor. The shock index categorized patients equally as “routine,” “priority,” and “critical,” whereas the Murphy Factor over-riaged to “routine” and under-riaged to “critical”\textsuperscript{41}. The discrepancies were attributed to erroneous PWTT estimations of BP. Refinement of the algorithm thus requires improved accuracy of PWTT measurement or replacement of this metric with continuous non-invasive BP estimation.\textsuperscript{41}

Liu et al.\textsuperscript{42} pilot tested the Athena Wireless Vital Signs Monitor (WVSM) (Athena GTX, Inc., Des Moines, Iowa) to predict the need for lifesaving interventions in the emergency department (ED) using data collected from 305 consecutive trauma patients during transport via helicopter to a Level I trauma center. WVSM records continuous 3-lead (Lead II) ECG, intermittent non-invasive BP and \( \text{SpO}_2 \); data are transmitted wirelessly to a mobile device or desktop computer. Participants were randomized to either routine vital signs monitoring with a standard bedside monitor or the WVSM.\textsuperscript{42} The WVSM system demonstrated better prediction for life-saving interventions (e.g., thoracotomy, cricothyrotomy, pericardiocentesis) performed in the ED compared to standard monitoring (Area
Under the Curve [AUC], 0.86 vs. 0.81, respectively). A challenge identified was increased clinician workload due to lack of integration of the WVSM with the hospital EMR resulting in the need for duplicate documentation. Personnel also recorded the timing of life-saving interventions manually, which could hinder precision of future algorithm development given the potential for human error and time discrepancies.42

In the hospital setting, feasibility, pilot and observational studies reflect continued growth in field of CM-RAM, with more sophisticated systems capable of real-time, simultaneous integration of multiple vital signs, prediction of patient future status, and informing clinical decision making. Adequately powered randomized controlled trials with representative patient samples are needed to make more definitive conclusions about clinical benefits. The acquisition of accurate vital signs data is technically challenging in real-world environments, particularly when measuring continuous respiratory rate. Availability of continuous non-invasive BP is also a gap as most technologies are incapable of capturing this metric. The study of CM-RAM technologies in the home setting is less mature, but the available data corroborate what has been observed in hospital-based studies (i.e., to be acceptable and wearable, devices should be unobtrusive, lightweight, and of perceived clear benefit to patients). Deployment and utility of CM-RAM systems can be hindered by lack of attention to these human factors, as well as interfacing with surrounding information systems that can result in increased clinician workload.

Future Directions

Economic evaluation

Few studies have evaluated the effect of CM-RAM technologies on resource utilization (hospitalizations, length of stay, emergency department visits) and costs.43,44 There are important considerations for future economic evaluations of CM-RAM. Analyses may be conducted from the healthcare system perspective (i.e., resource utilization components and costs from the healthcare
system) and/or from the societal perspective (i.e., all costs and benefits are included regardless of who incurs costs or benefits, e.g., savings in patient related travel). Different economic evaluation designs and several analytic approaches can be adopted. It is important to consider time frame/horizon, patient populations being targeted, and the number of vital signs parameters monitored. In future evaluations, implementation costs should be subdivided into individual categories (e.g., capital costs, software licenses, maintenance, and upgrades) to measure the efficiency of CM-RAM programs. Additional cost considerations may also be warranted, depending on system configuration and workflows. For example, whether clinical staff would act on system notifications generated through pre-existing health system infrastructure (e.g., workstations, tablets) or on extrinsic mobile devices will have implications for any potential cost savings.

**Big data and advanced prediction modeling**

Early Warning Scores (EWSs) are clinical prediction models that use measured vital signs to predict likelihood of clinical deterioration, using pre-established likelihood thresholds to trigger a warning so that care can be escalated. While EWSs are now ubiquitous and drive several CM-RAM systems, they can have significant limitations. In a systematic review describing external validation of EWSs for adult inpatients, Gerry et al. found that all 95 studies appraised were at high risk of bias. In addition to poor reporting, they identified several methodological weaknesses, including limited sample sizes and event rates, inadequate handling of missing data and regression models, and focus on discrimination (i.e., ability of the model to stratify patients according to higher or lower risks of events) rather than on calibration (i.e., correspondence between observed and predicted absolute event rates). Moreover, EWSs are static systems, based on the same predictors and cut-offs across populations, which may be neither accurate nor efficient.

CM-RAM devices offer a way forward. These systems can generate Gigabytes of biophysical and raw physiological data on patients over a 24-hour period, allowing for the application of machine
learning (ML) models, which are increasingly being leveraged to harness the potential of patient-centric big data to develop more complex predictive models.48,49

Our group is soon commencing the international Vascular events In noncardiac Surgery patients cOhort evaluatioN study-2 (VISION-2) study, where we will apply the Vitaliti™ Continuous Vital Signs Monitor (CVSM)49 by Cloud DX to 20,000 patients undergoing noncardiac surgery for the first 30 postoperative days. Vitaliti™ continuously measures 5-lead ECG, heart rate and heart rate variability, respiratory rate, core temperature (infrared sensor applied to the ear), SpO2, continuous non-invasive BP and pulse wave velocity. In addition, the device records multiple continuous, high-fidelity biometric raw waveforms underpinning these metrics (e.g., photoplethysmography for core temperature and BP) that can be inputted directly into deep learning predictive algorithms. These signals are collected non-invasively at high sampling frequencies (i.e., ECG at 1kHz or 1000 cycles per second).49

VISION-2 will result in a comprehensive data set suitable for deep predictive modelling research that overcomes challenges (e.g., missing data, representation biases) experienced by retrospective machine learning studies that rely on electronic health record data to train models.50 Moreover, wide-spread deployment of 5G broadband cellular networks51 are in progress across most continents. 5G promises increased bandwidths and low latency (i.e., minimal lag time) communications to many under-serviced areas,51 which will help support data collection in VISION-2 across participating collection sites. Our aim is to build classification models for the prediction of postoperative serious adverse events associated with mortality including myocardial injury, major bleeding, sepsis, and infection.52

Conclusion

Technologies that offer continuous multiparameter vital signs monitoring hold great promise for comprehensive clinical-grade remote care of patients, beyond what wellness monitoring can
provide. Successful deployment and evaluation of these systems requires an understanding of the architecture of body sensor networks and related technical and operational challenges of their use in clinical and home environments. Scale and spread of these technologies will require attention to comprehensive economic evaluation. Harnessing the power of machine learning will advance the science and practice of CM-RAM for the prediction of critical adverse events, and provision of timely interventions.

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n/a

**Disclosures**

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**References**

5. United States Food and Drug Administration. Enforcement Policy for Non-Invasive Remote Monitoring Devices Used to Support Patient Monitoring During the Coronavirus Disease 2019


Figure 1. Purpose of CM-RAM devices versus wellness monitoring and other medical grade devices.

Health and Wellness Devices
- Used to encourage healthy lifestyles.
- Most capable of measuring a maximum of 1 to 2 episodic (e.g., on-demand ECG) or continuous (e.g., temperature) biophysical parameters simultaneously.
- Limited in the claims they can make regarding the diagnosis, prevention, or treatment of a disease or condition.
- Manufacturers can suggest they may help to reduce the risk for chronic disease or conditions, where a healthy lifestyle has been generally well accepted to have demonstrated risk reduction or help with living well.

Regulated Medical Devices
- Intended for the diagnosis, prevention, or treatment of a disease or condition.
- Have regulatory clearance and evidence that they are safe and effective.

Continuous Multiparameter Remote Automated Monitoring (CM-RAM) Devices
- Comprehensive regulated medical devices, capable of monitoring three or more biophysical parameters (e.g., oxygen saturation, heart rate) continuously and simultaneously.
- Target optimal efficiency by maximizing the metrics collected and streamlining RAM processes through the application of a single integrated solution.
Figure 2. Body Sensor Network
Figure 3. Biometric Sensor Placement on the Body

- **Respiration Rate:** Respiration belt or impedance-based measurement through electrodes.

- **Position and Movement:** Inertial Measurement Unit utilizing accelerometers, gyroscopes, and sometimes magnetometers. Ballistocardiography (BCG) to detect small movements caused by the mechanical output of the heart.

- **Electrocardiography:** ECG for up to 12-lead configurations.

- **Core Body Temperature:** Forehead or tympanic measurement.

- **Photoplethysmography:** PPG measured with LEDs (Red, IR, and sometimes Green) and photo diode for pulse rate measurements and SpO2 derivations. Transmittance or reflectance orientation.
<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>Vital Signs Measured</th>
<th>Other Parameters Measured</th>
<th>Location</th>
<th>Battery Life</th>
<th>Connection Type</th>
<th>Connection Range (meters)</th>
<th>EMR</th>
<th>SOA</th>
<th>D</th>
<th>W</th>
<th>Setting</th>
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<tr>
<td>VitalPatch® (Previous version was HealthPatch MD, which is no longer available)</td>
<td>VitalConnect</td>
<td>ECG, HR, RR, ST</td>
<td>HRV, steps, body posture, fall detection, activity</td>
<td>Chest</td>
<td>5 days</td>
<td>Bluetooth</td>
<td>Max 10</td>
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<td>Sensium Healthcare</td>
<td>HR, RR, ST</td>
<td>None</td>
<td>Chest, armpit</td>
<td>5 days</td>
<td>Wi-Fi 802.11 b/g</td>
<td>180</td>
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<td>Clinic</td>
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<td>Visi Mobile®</td>
<td>Sotera Wireless</td>
<td>HR, BP, RR, SpO2, ST, ECG</td>
<td>Body posture, fall detection</td>
<td>Chest, wrist and thumb</td>
<td>14-16 h</td>
<td>Wi-Fi 802.11 radio</td>
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<td>Body Guardian®</td>
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<td>None</td>
<td>Chest</td>
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<td>HR, HRV, RR, SpO2, ST, Blood Pulse Wave, Energy Expenditure</td>
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<td>Upper arm</td>
<td>5-46 h</td>
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<td>Activity, body posture</td>
<td>Chest</td>
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<td>Zephyr ECHO gateway, Bluetooth 2.1+, 3G</td>
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<td>Water Resistant</td>
<td>System of Alerts</td>
<td>Disposal</td>
<td>Available Locations</td>
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<td>Forehead, Fingertip</td>
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</table>

EMR Electronic Medical Record; SOA – System of Alerts; D – Disposable; W – Waterproof; HR = Heart Rate; RR = respiration rate, ST = skin temperature, CT - Core Temperature; CDMA: code-division multiple access, CT: core temperature, PWTT: pulse wave transit time; - = could not locate information