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Review

Beyond Wellness Monitoring: Continuous Multiparameter Remote Automated Monitoring of Patients

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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

RÉSUMÉ

L'objectif de rendre le système de santé plus efficace tout en étant proche des patients et de réduire le recours aux services de santé tertiaires a entraîné une croissance phénoménale de l'application et de l'étude des systèmes de télésurveillance des patients dans le

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 past 2 decades.[1-3] More recently, the response to coronavirus-2019 (COVID-19) has catapulted this area of clinical practice and research to new heights. Health system innovators have worked feverishly to deploy noninvasive systems that facilitate remote patient surveillance and monitoring, as well as the physical distancing of patients and families, to prevent viral spread.[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.[5] The expansion of the capabilities, reach, and availability of these technologies has resulted in an unprecedented number of patient biophysical parameters

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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 multiple biophysical parameters (eg, 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 revolutionise 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.

domaine des soins cardiovasculaires. Bien qu'il existe de nombreux produits de surveillance grand public axés sur le bien-être des patients, la réglementation de ces technologies varie considérablement, la plupart des produits ne disposant que de peu de données d'évaluation, voire aucune. À mesure que la science et la pratique des soins virtuels évoluent, les cliniciens et les chercheurs peuvent tirer profit de la compréhension de solutions plus complètes permettant de surveiller plusieurs paramètres biophysiques (par exemple, la saturation en oxygène, la fréquence cardiaque) en continu et simultanément. Ces solutions font appel à des dispositifs automatisés de télésurveillance continue multiparamétrique (DATCM), qui pourraient bien révolutionner la prise en charge virtuelle des patients. Grâce à l'intégration transparente de plusieurs signaux biophysiques, les technologies sur lesquelles reposent les DATCM permettent de recueillir de grands volumes de mégadonnées en vue du développement d'algorithmes destinés à faciliter la détection précoce des variations négatives de l'état de santé des patients et l'intervention rapide des cliniciens. Dans cet article, nous examinons les fondements, l'architecture et les composants des technologies propres aux DATCM. Nous présentons aussi les travaux réalisés jusqu'à présent en la matière ainsi que leurs implications, dont les priorités stratégiques axées sur l'évolution des aspects scientifiques et pratiques des DATCM.

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 Holter electrocardiography (ECG).[1-3,6]

Although 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.[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.[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).[8-10] Although 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 artefacts from patient motion.[11]

Furthermore, the regulation of consumer-grade wearable patient monitoring products varies considerably, with most available products having little to no published evaluation data.[12] The majority of wellness monitoring devices are capable of measuring a maximum of 1 to 2 episodic (eg, on-demand ECG) or continuous (eg, temperature) biophysical parameters simultaneously, thereby limiting clinical utility for patient surveillance, diagnosis, and timely management of changes in health status. While single parameter monitoring (eg, heart rate) has important application in certain situations (eg, atrial fibrillation monitoring), many patients require continuous measurement of a diversity of biophysical parameters, similarly to inpatients in the hospital. Innovators working with market-ready solutions are also often faced with the inherent complexities of intermingling proprietary systems,[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 3 or more biophysical parameters continuously and simultaneously. These systems target optimal efficiency by maximising 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 noninvasive estimates of more complex biophysical parameters that would normally be measured continuously through invasive means (eg, continuous BP via invasive arterial catheter). These devices, hereafter referred to as continuous multiparameter remote automated monitoring (CM-RAM) devices, have the potential to revolutionise patient monitoring through seamless integration of multiple time-synchronised 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, vs wellness monitoring and other medical-grade devices.

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

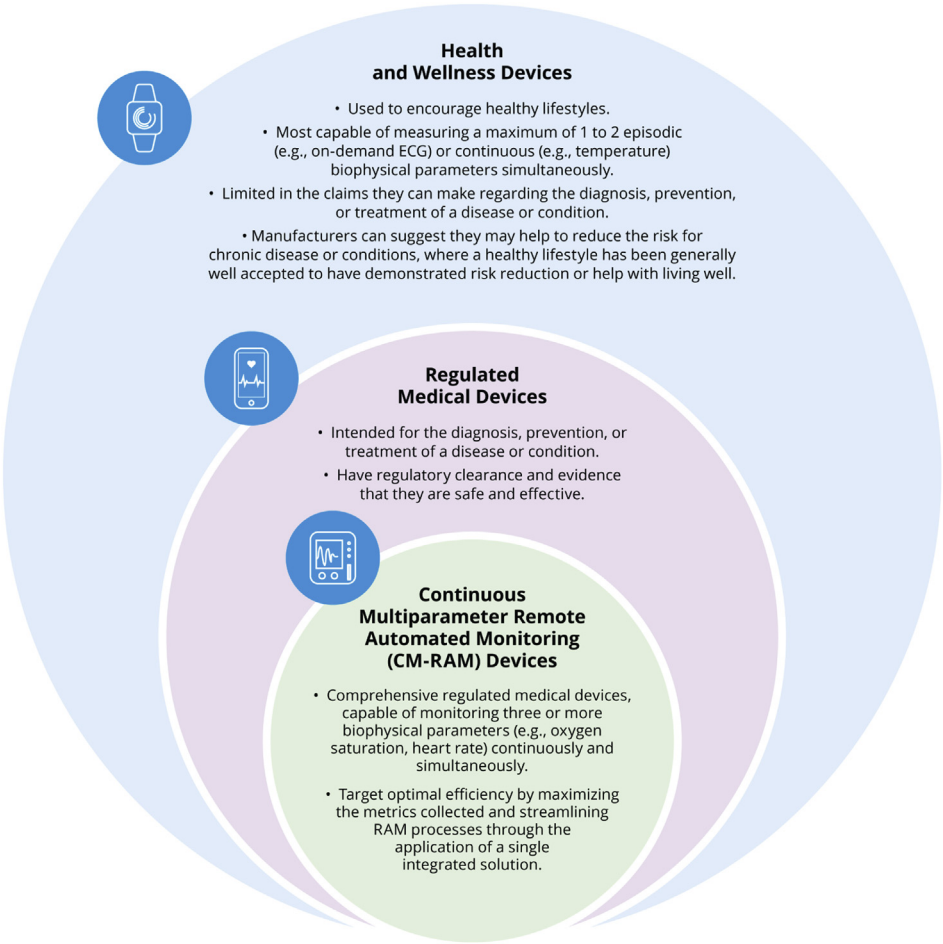

Figure 1. Purpose of continuous multiparameter remote automated monitoring devices vs wellness monitoring and other medical-grade devices. ECG, electrocardiography.

materials for indirect body sensing. The interconnection of these sensors forms a "body sensor network" (BSN) (Fig. 2). BSNs consist of 3 layers, with each layer communicating either wirelessly or through hardwired channels.[14] First is the body sensing layer, that includes wearable sensor nodes, each capable of measuring, sampling (ie, digitising) and processing multiple biophysical signals.[14] BSNs can be subcategorised into sensors affixed to the patient and the main processing unit where signals are digitised, 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 handheld devices (eg, smartphones) or tablet-based computer devices that can perform either limited or more advanced forms of local data processing to display the metrics being collected or integrate and analyse them to assist in clinical decision making. Signal transmission from the body sensing layer to the personal area network layer is typically through a wireless communication protocol, configured for short-range low-power radiofrequency communication, eg, Bluetooth or 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.

Body sensing layer

CM-RAM devices use 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 analysed by means of digital signal processing.[15] These signals can be measured either in an analog format as continuous measurements, or in a digital format with samples taken at defined sampling frequencies (eg, 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.[16] Supplemental Table S1 presents details on sensor categories according to 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. ECG draws on 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 minimises the electrical impedance of skin.[16] Dry electrodes do not contain any electrolyte materials and instead rely on direct skin

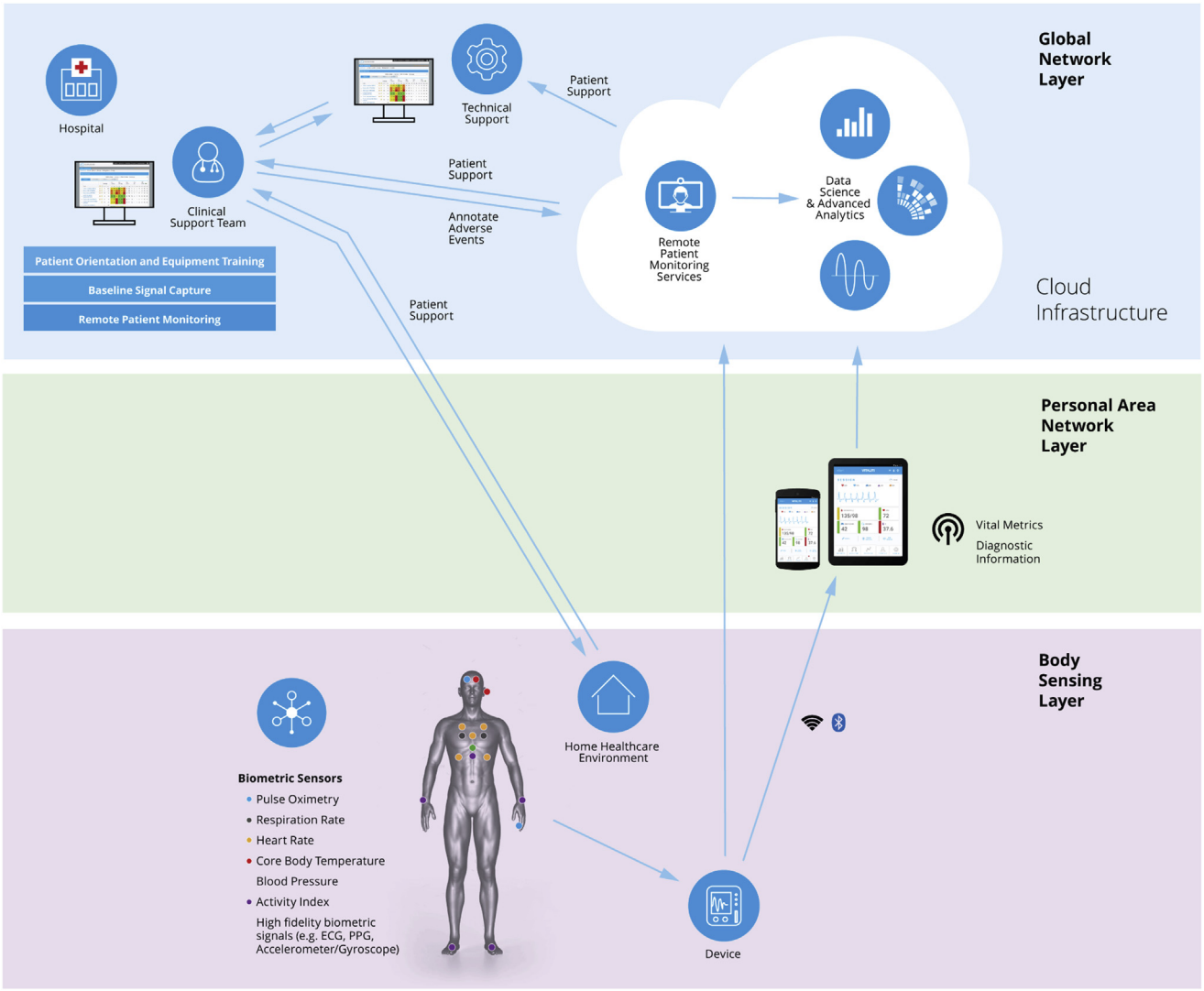

Figure 2. Body sensor network. ECG, electrocardiography; PPG, photoplethysmography.

contact. Disposable wet electrodes typically use silver—silver chloride contacts with electrolyte gel for conduction[17] and dry electrodes use metal plating. Specialised electrodes have been developed to support short- or long-term monitoring and different activities (eg, resting vs stress testing).

Within CM-RAM devices, electrodes are paired to measure the voltage potential difference between 2 points. Common examples of this include ECG, electroencephalography, and electromyography. Minimum 3-lead (leads I-III) ECG electrode positioning is desired for CM-RAM devices (Fig. 3). Most commercial-grade products featuring ECG patches are limited to a single lead configuration owing to limitations with local data storage (within the device), power, and the need for wearability. More complex systems, such as Visi Mobile (Sotera Wireless Inc, San Diego, CA)[18] (see subsequent section, *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 nm (visible red light) and 940 nm (infrared IR] light) to capture oxyhemoglobin saturation (SpO_2),[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 (Fig. 3).[19] These optical sensors are vulnerable to artefacts from patient motion, as well

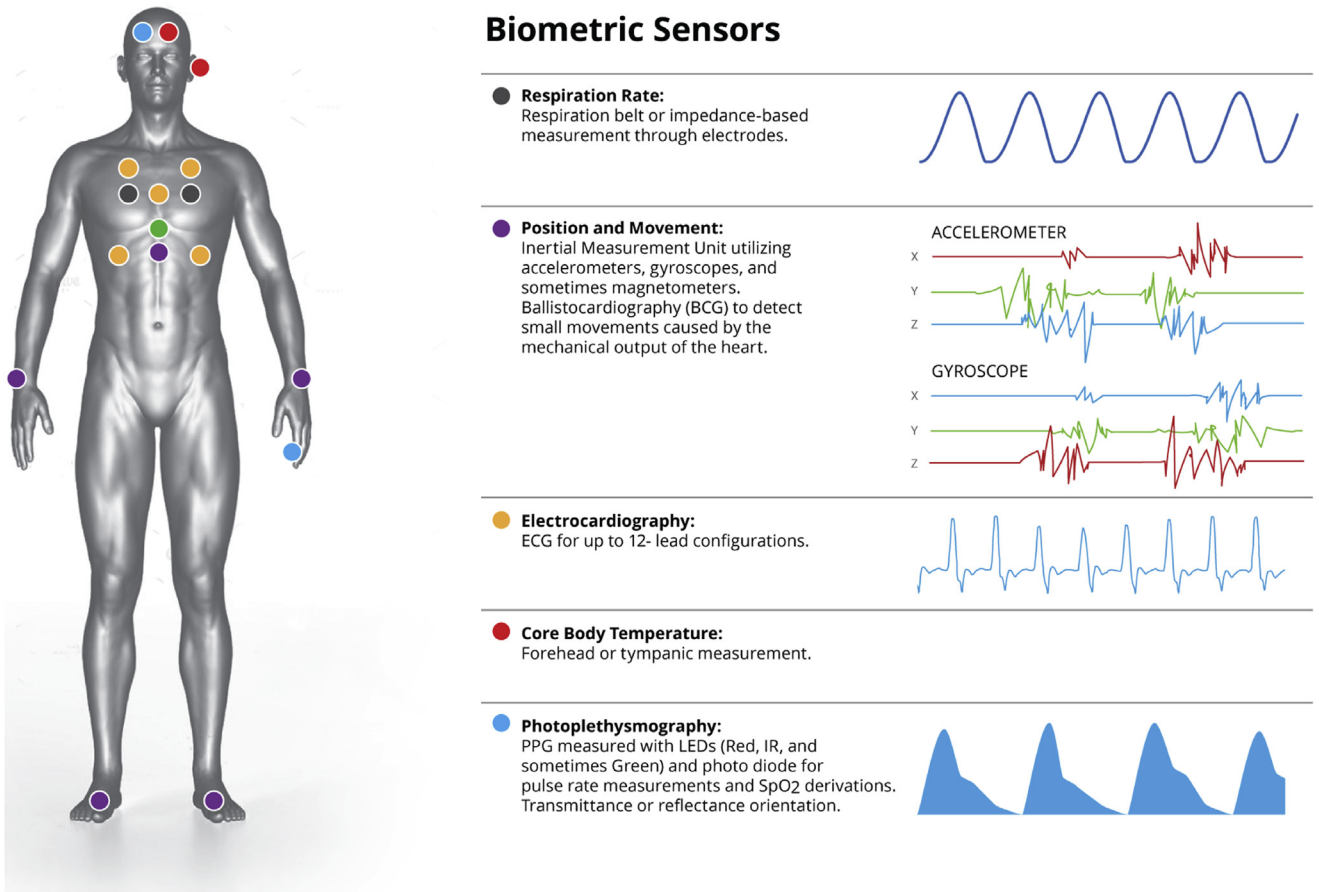

Figure 3. Biometric sensor placement on the body. ECG, electrocardiography, LED, light-emitting diode; PPG, photoplethysmography; SPO_2, oxyhemoglobin saturation.

as intrusion by ambient (environmental) light.[19] Moreover, accuracy testing in patients with a range of skin pigmentation has been limited.

Body temperature is measured with thermoresistors via conduction through a metal contact point with the skin or thermopiles as IR sensors that measure thermal levels.[20] Core body temperature is a more challenging metric to capture than skin temperature, with tympanic, forehead, and underarm sensor sites demonstrating the greatest promise for accuracy.[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.[21] For clinical decision making, core temperature is the preferred measurement because skin temperature can be affected by a number of environmental factors, such as ambient room temperature and climate.[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 criterion 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 use piezoelectric (ie, electrical detection of mechanical stress) sensors to register expansion and contraction, or through impedance plethysmography where bioimpedance (ie, estimation of body composition) is measured between chest-mounted ECG electrodes.[17] Discrete respiration measurements can also be derived from ECG or PPG signals by identifying the amplitude and frequency deviations caused by respiration.[17] Both of 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 artefacts related to patient vocalisations and coughing.[17] A challenging area is the use of these sensors in patients with underlying chronic respiratory conditions that feature irregular breathing patterns, such as chronic obstructive pulmonary disease 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 artefact-related challenges.[22]

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 utilise either piezoresistive or piezoelectric sensors to measure the acceleration of an object (or rate of change of velocity) and angular velocity, respectively. A

Table 1. CM-RAM device characteristics

Device	Manufacturer	Vital signs measured	Other parameters measured	Location	Battery life	Connection type	Connection range (m)	EMR	SOA	D	W	Setting
VitalPatch (previous version was HealthPatch MD, which is no longer available)	VitalConnect (San Jose, CA)	ECG, HR, RR, ST	HRV, steps, body posture, fall detection, activity	Chest	5 days	Bluetooth	Max 10	✓	✓	✓	✓	Clinic, home
SensiumVitals System	Sensium Healthcare (Oxford, UK)	HR, RR, ST	None	Chest, armpit	5 days	Wi-Fi 802.11 b/g	180	✓	✓	✓	✓	Clinic
Visi Mobile	Sotera Wireless, Inc (San Diego, CA)	HR, BP, RR, SpO_2, ST, ECG	Body posture, fall detection	Chest, wrist, thumb	14-16 h	Wi-Fi 802.11 radio	180	✓	✓			Clinic
Body Guardian	Preventice Solutions (Minneapolis, MN)	ECG, HR, RR	None	Chest	12 h	Bluetooth	~ 3		✓			Home
Everion	Biovotion (Zurich, Switzerland)	HR, HRV, RR, SpO_2, ST, blood pulse-wave, energy expenditure	Activity, barometric pressure, sleep, relax indicator, galvanic skin response	Upper arm	5-46 h	Bluetooth	−		✓		✓	Clinic, home
Zephyr System (BioPatch and Harness)	Medtronic Inc (Annapolis, MD)	HR, RR, estimated CT	Activity, body posture	Chest	12-28 h	Zephyr ECHO gateway, Bluetooth 2.1+, 3G	−		✓			Clinic
Mini Medic	Athena GTX (Des Moines, IA)	HR, SpO_2, ST	PR, PWTT, Murphy Factor	Forehead, fingertip	12 h	Zigbee 802.15.4	100		✓		✓	Clinic, home
WVSM	Athena GTX (Des Moines, IA)	HR, BP, RR, SpO_2	None	Chest, upper arm, fingertip	7 h	Athena Device Management Suite	< 183		✓		✓	Clinic, home
Hexoskin	Carré Technologies (Montréal, QC)	HR, ECG, SpO_2, RR, ST	Activity and sleep data	Upper body	12-30+ h	Bluetooth	−	✓	✓		✓	Home
Philips IntelliVue Guardian Solution (IGS)	Philips (Amsterdam, The Netherlands)	HR, RR, SpO_2, BP	None	Upper arm, wrist, belly	12-24 h	Short-range radio to IntelliVue Guardian Software	< 100	✓	✓			Clinic

CDMA, code-division multiple access; CT, core temperature; ECG, electrocardiography; D, disposable; EMR, electronic medical record; HR, heart rate; HRV, heart rate variability; PR, pulse rate; PWTT, pulse-wave transit time; RR, respiration rate; SOA, system of alerts; SpO_2, oxyhemoglobin saturation; ST, skin temperature; W, waterproof; WVSM, Wireless Vital Signs Monitor; −, could not locate information.

magnetometer measures the strength and direction of magnetic fields to establish patient position. These signals have been utilised for human activity recognition (HAR),[23] activity indexes, step counting, energy output, sleep quality and fall risk assessment and detection.[24]Ballistocardiography (BCG) utilises 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.[23] Although some CM-RAM devices, such as VitalPatch (VitalConnect, San Jose, CA),[25] feature inertial measurement units s 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 artefact.

Personal area network layer

Signals generated in the BSN sensing layer are typically wirelessly transmitted to a base station (eg, tablet or smartphone) within the personal area network layer through a wireless body area network (WBAN).[26] Almost universally, CM-RAM systems use Bluetooth low-energytransmission[27] because of low power requirements, high-speed data transmission rates of up to 1 megabit per second, and an operating range of up to 100 metres from device to base station.[28] 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 digitised and preprocessed to remove noise artefacts and biophysical parameters metrics are derived.

Global network layer

Originating from the patient at home (body sensing layer), preprocessed 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 network layer from the base station and relayed to clinical support teams. These communications can be bidirectional (Fig. 2) and are achieved through cellular 3G, 4G, 5G, or Wi-Fi networks.[29] 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[30] 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 using CM-RAM technologies yielded 38 studies of various technologies published from 2012 to 2021 (see Supplemental Appendix S1 for details). Table 1 provides a summary of devices and their features and Supplemental Table S2 summarises all of the 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, Oxford, UK), and Visi Mobile.[18,31,32] 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 (ie, impedance pneumography), and skin temperature. Visi Mobile also includes a wrist-worn device that captures SpO_2 and 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.[18,31,32]

All 3 devices have undergone clinical validation testing comparing their metrics against manual vital signs measurements taken by nurses.[18,31-34] In a feasibility study ($n = 20$),[18] patients admitted to internal medicine and surgical wards were monitored with the VitalPatch and Visi Mobile devices for 2 to 3 days.[18] 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.[18] In 15% of the Visi Mobile and 25% of the VitalPatch cases, clinically relevant differences in modified early warning score comparisons were found based on inconsistent respiratory rate measurements; both devices overestimated respiratory rate compared with nurses.[18] Technical issues also differed by device; more than 50% of VitalPatch artefacts 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.[18] For Visi Mobile, almost 70% of all reported artefacts were caused by a connection failure between the mobile device and chest patch sensor. During the study, 1 patient monitored with Visi Mobile had clinical deterioration detected 3 days after elective colorectal surgery. The device alerted the patient's nurse that he developed both tachycardia and tachypnea; this adverse event detection occurred between 2 scheduled nurse vital signs measurements and could otherwise have been missed.[18]

Verrillo et al.[34] 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 vs 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 with the control group, ie, 9.6 vs 34.3 per 1000 patient-days ($P < 0.05$).[34] Clinically significant decreases in transfers to ICU and failure-to-rescue events in the Visi Mobile group were observed as well. By incorporating Visi Mobile data into their patient assessments, nurses reported that they were able to prioritise patient care with greater accuracy, identify signs of clinical deterioration, and facilitate early intervention.[34]

The accuracy and feasibility of the SensiumVital System was assessed in a series of randomized controlled trials (RCTs) in patients undergoing major elective general surgery.[32,33] The reference standard was nurse-recorded vital signs, factored into the National Early Warning Score for adverse event prediction. Participants were individually randomised 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 ($R^2 = 0.13$; $P < 0.001$).[32] 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%, heart rate 59.2%, skin temperature 72.8%) and data losses were attributed to artefacts from patient ambulation.[32] In a follow-up larger feasibility RCT (n = 136),[33] 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: 11.6 days (95% confidence interval [CI] 9.5-13.7 days) vs 16.2 days (95% CI 11.3-21.2 days).[33]

The VitalPatch, SensiumVitals, and Visi Mobile systems have also undergone wearability and usability assessments.[18,35,36] A pilot RCT of 90 postsurgical patients randomised to CM-RAM using Visi Mobile or VitalPatch for 2 to 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.[35] In a feasibility and acceptability study (30 patients, 23 nurses) of SensiumVitals compared with VitalPatch and Visi Mobile in abdominal surgery patients, the majority of patients rated the Sensium sensor patch as comfortable, felt safer, and would choose to wear it again when next in hospital.[36] 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 owing 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.[18]

Large-scale prospective observational studies of other hospital-based CM-RAM systems also have shown positive results. In a before (n = 2139) and after (n = 2263) study of patients admitted to 2 general medicine wards in the United Kingdom, Subbe et al.[37] examined the effect of automated continual vital signs monitoring, with relay of abnormal vital signs to rapid response teams. The Philips Intellivue Guardian solution (Royal Philips, Amsterdam, The Netherlands)—featuring cableless transmittance-based finger SpO_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_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 bronchodialators.[37] Reduction in mortality was also observed from before (n = 173) to after (n = 147) intervention ($P = 0.042$).[37] Bellomo et al.[38] found similar results in a before and after study conducted on a cohort of 18,305 patients across 12 general wards (in 10 hospitals) in Australia, USA, 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%]).[38] The Guardian system was also associated with significantly decreased nurse time required to record vital signs (from 4.1 ± 1.3 min to 2.5 ± 0.5 min, difference 1.6 min [95% CI 1.4 to 1.8]).[38]

Some studies have focused on pilot testing these systems in the home setting, sometimes in combination with environmental ambient sensors. Saner et al.[39] tested a multimodal sensor system in a cohort of 24 community-dwelling seniors over a period of 1 to 2 years. Vital signs and contextual data were collected with the use of integrated sensors including a passive infrared motion-sensing system (Domosafety Ltd, Lausanne, Switzerland) to detect physical activity, toileting, refrigerator use and door openings, as well as an upper armband sensor (Everion; Biovotion, Zurich, Switzerland) to collect heart rate, heart rate variability, respiratory rate and skin temperature. An accelerometer (Axivity, Newcastle, UK) evaluated patient motion.[39] 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 analysis.[39] 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.[39] 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.[39]

More recently, Keogh et al.[40] 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 1 week. Participants thought that lightweight 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 1 week was considered to be ideal. The need to charge systems daily was deemed to be unacceptable and was considered a barrier for extended use of the Everion device.[40] 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.[40]

Some advances are also being made in the use of CM-RAM systems for acuity prediction in trauma and emergency patients. Meizoso et al.[41] used the MiniMedic wireless vital signs monitor (MiniMedic; Athena GTX, Des Moines, IA) to remotely monitor 59 trauma ICU patients to predict shock index, ie, heart rate ÷ systolic BP.[15] 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.[41] The system incorporates an injury acuity algorithm, the Murphy Factor, that summarises overall patient status, accounting for changes in vital signs every 30 seconds. Pulse-wave transit time (PWTT) is used in place of systolic VP.[41] MiniMedic sensors were applied to the forehead and finger of each patient to measure PWTT, temperature, heart rate, and SpO_2, which were recorded and displayed on a standard bedside monitor for 60 minutes. Shock index was calculated with the use of bedside-measured vital signs and compared with the Murphy Factor. The shock index categorised patients equally as "routine," "priority," and "critical," whereas the Murphy Factor overtriaged to "routine" and undertriaged to "critical."[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 noninvasive BP estimation.[41]

Liu et al.[42] pilot tested the Athena Wireless Vital Signs Monitor (WVSM) (Athena GTX) 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 noninvasive BP, and SpO_2; data are transmitted wirelessly to a mobile device or desktop computer. Participants were randomised to either routine vital signs monitoring with a standard bedside monitor or to the WVSM.[42] The WVSM system demonstrated better prediction for life-saving interventions (eg, thoracotomy, cricothyrotomy, pericardiocentesis) performed in the ED compared with standard monitoring (areas under the receiver operating characteristic curve 0.86 vs 0.81, respectively). An identified challenge was increased clinician workload due to lack of integration of the WVSM with the hospital electronic medical record, 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 owing to 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 RCTs 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 noninvasive 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 (ie, 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 utilisation (hospitalisations, length of stay, ED visits) and costs.[43,44] There are important considerations for future economic evaluations of CM-RAM. Analyses may be conducted from the health care system perspective (ie, resource utilisation components and costs from the health care system) or from the societal perspective (ie, all costs and benefits are included regardless of who incurs costs or benefits, eg, savings in patient-related travel).[45] 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 sign parameters monitored.[46] In future evaluations, implementation costs should be subdivided into individual categories (eg, capital costs, software licenses, maintenance, and upgrades) to measure the efficiency of CM-RAM programs.[46] 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 preexisting health system infrastructure (eg, 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,[30,47] using preestablished likelihood thresholds to trigger a warning so that care can be escalated. Although 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.[47] found that all 95 appraised studies were at high risk of bias. In addition to poor reporting, they identified several methodologic weaknesses, including limited sample sizes and event rates, inadequate handling of missing data and regression models, and focus on discrimination (ie, ability of the model to stratify patients according to higher or lower risks of events) rather than on calibration (ie, correspondence between observed and predicted absolute event rates).[47] Moreover, EWSs are static systems, based on the same predictors and cutoffs across populations, which may be neither accurate nor efficient.[30,47]

CM-RAM devices offer a way forward. These systems can generate gigabytes of biophysical and raw physiologic data on patients over a 24-hour period,[48] allowing for the application of machine learning 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 , **V**ascular Events **i**n Noncardiac **S**urgery Patients Cohort Evaluat**ion** (VISION)-2 study, where we will apply the Vitaliti Continuous Vital Signs Monitor[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), SpO_2, continuous noninvasive BP and pulse wave velocity. In addition, the device records multiple continuous high-fidelity biometric raw waveforms underpinning these metrics (eg, photoplethysmography for core temperature and BP) that can be inputted directly into deep learning predictive algorithms. These signals are collected noninvasively at high sampling frequencies (eg, ECG at 1 kHz, or 1000 times per second).[49]

VISION-2 will result in a comprehensive data set suitable for deep predictive modelling research that overcomes challenges (eg, missing data, representation biases) experienced by retrospective machine learning studies that rely on electronic health record data to train models.[50] Moreover, widespread deployment of 5G broadband cellular networks[51] are in progress across most continents. 5G promises increased bandwidths and low latency (ie, minimal lag time) communications to many underserviced 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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Supplementary Material

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