REVIEW





Cardiorespiratory Sensors and Their Implications for Out-of-Hospital Cardiac Arrest Detection: A Systematic Review

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Abstract

Out-of-hospital cardiac arrest (OHCA) is a major health problem, with a poor survival rate of 2–11%. For the roughly 75% of OHCAs that are unwitnessed, survival is approximately 2–4.4%, as there are no bystanders present to provide life-saving interventions and alert Emergency Medical Services. Sensor technologies may reduce the number of unwitnessed OHCAs through automated detection of OHCA-associated physiological changes. However, no technologies are widely available for OHCA detection. This review identifies research and commercial technologies developed for cardiopulmonary monitoring that may be best suited for use in the context of OHCA, and provides recommendations for technology development, testing, and implementation. We conducted a systematic review of published studies along with a search of grey literature to identify technologies that were able to provide cardiopulmonary monitoring, and could be used to detect OHCA. We searched MEDLINE, EMBASE, Web of Science, and Engineering Village using MeSH keywords. Following inclusion, we summarized trends and findings from included studies. Our searches retrieved 6945 unique publications between January, 1950 and May, 2023. 90 studies met the inclusion criteria. In addition, our grey literature search identified 26 commercial technologies. Among included technologies, 52% utilized electrocardiography (ECG) and 40% utilized photoplethysmography (PPG) sensors. Most wearable devices were multi-modal (59%), utilizing more than one sensor simultaneously. Most included devices were wearable technologies (84%), with chest patches (22%), wrist-worn devices (18%), and garments (14%) being the most prevalent. ECG and PPG sensors are heavily utilized in devices for cardiopulmonary monitoring that could be adapted to OHCA detection. Developers seeking to rapidly develop methods for OHCA detection should focus on using ECG- and/or PPG-based multimodal systems as these are most prevalent in existing devices. However, novel sensor technology development could overcome limitations in existing sensors and could serve as potential additions to or replacements for ECG- and PPG-based devices.

Keywords Out-of-hospital cardiac arrest \cdot Wearable sensors \cdot Physiological monitoring \cdot Cardiopulmonary \cdot Electrocardiography \cdot Photoplethysmography

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Introduction

Out-of-hospital cardiac arrest (OHCA) is a major health issue, with a global average incidence of about 111 adults per 100,000 person-years (~ 40 million) [1]. OHCA affects approximately 350,000 individuals in Canada and the United States per year [1-3]. Survival from an OHCA is highly dependent on bystander recognition to provide lifesaving intervention or alert emergency medical services (EMS). Rapid initiation of cardiopulmonary resuscitation (CPR) is critical, with the likelihood of survival decreasing by 13% with each 1-minute delay [4, 5]. A majority (75%) of OHCAs are unwitnessed, which can slow down or prevent the timely initiation of life-saving interventions and activation of EMS. Approximately 50% of unwitnessed OHCAs are not treated at all due to delays in the activation of the chain of care, resulting in a determination of futility death when EMS arrives [5, 6]. While rates of survival from witnessed OHCAs are estimated to be 11%, rates of survival from unwitnessed OHCAs are estimated to be much lower (2-4.4%) [7].

A sudden cardiac arrest results in an abrupt termination of blood circulation in the body that is accompanied and followed by various physiological changes. Cardiac rhythm variations are the most commonly observed physiological changes during/after a cardiac arrest event. For instance, among EMS-treated OHCA patients in residential areas, 7–38% were found in shockable rhythms (e.g., ventricular fibrillation [VF]), with the remainder in nonshockable cardiac rhythms (e.g., pulseless electrical activity [PEA], asystole) [8]. Similarly, data from in-hospital arrests revealed that 23% of the patients were found in shockable rhythms (e.g., VF), while the remainder had non-shockable rhythms (32% PEA; 35% asystole) [9]. Other physiological changes followed by a cardiac arrest event observed in hospital settings include the absence of heart rate (HR) [10, 11], respiratory rate [11], systolic blood pressure [11], and a drop in arterial oxygen saturation (SpO₂) [12] and body temperature [13]. While heart rhythm, HR, and respiratory changes typically occur immediately following the onset of a cardiac arrest event (or even prior to the event), some downstream physiological changes may not be immediately detectable and rather manifest later in response to the primary changes in cardiopulmonary function. Monitoring and characterizing these immediate and downstream parameters are pivotal to OHCA detection.

Various sensor technologies are available for the monitoring of cardiopulmonary physiological parameters. These sensor technologies include (1) electrocardiography (ECG) sensors commonly used for HR [14], heart rhythm [14], and heart rate variability (HRV) monitoring [15]; (2) photoplethysmography (PPG) sensors commonly used for HR, heart rhythm, HRV, SpO₂, and respiration monitoring [16]; (3) near-infrared spectroscopy (NIRS) sensors commonly used for HR [17], respiratory function [18] and tissue oxygenation monitoring [19]; (4) inertial measurement units (IMUs) and accelerometers commonly used for motion tracking [20], HR, and respiratory monitoring [21]; and (5) thermistors/thermometers commonly used for skin temperature monitoring [22]. The application of these sensor technologies into the delivery of health services has been discussed in a diverse range of applications from use in clinical trials to provision of home monitoring for chronic disease management [23, 24].

Consumer devices that leverage these sensor technologies to provide physiological monitoring (e.g., smart watches) have seen considerable commercial success in worldwide consumer markets. A recent estimate suggests that there are roughly 440 million wearable devices in North America, and just over 1 billion worldwide [25, 26]. However, the majority of these commercial devices are designed solely for monitoring healthy individuals, with only a handful FDAapproved to assess conditions such as Atrial Fibrillation. While commercial systems contain sensors that monitor relevant cardiopulmonary parameters, there remains a gap and opportunity in utilizing these devices for OHCA monitoring specifically. A recent review found that, indeed, there currently are no commercially available devices specific to OHCA detection [27]. Thus, the purpose of this systematic review is to assess the landscape of commercial and research health monitoring devices that have sensors that are relevant to OHCA, and to comment on their potential for adaptation to detect OHCA. Specifically, we wanted to identify why there are no OHCA detection devices despite the availability of sensors that could potentially detect physiological signals associated with OHCA, and identify what challenges need to be overcome to achieve broad OHCA detection capabilities in wearable systems. This information can be used to focus efforts in the development of novel OHCA detection technologies.

Methods

Design and Search Strategy

This review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA) checklist. We conducted a literature review of MEDLINE, EMBASE, Web of Science, and Engineering Village for studies that highlighted sensor technologies in cardiopulmonary monitoring. The keywords used were Medical Subject Headings (MeSH) related to device categories (e.g., wearable, implantable, non-contact), cardiopulmonary conditions (e.g., cardiac arrest, cardiac arrhythmia), and associated parameters (e.g., heart rhythm, respiration rate). For the purposes of this review, HR, heart rhythm, and respiration were defined as the "primary parameters" (direct measures of cardiopulmonary function), with the remaining physiological parameters (e.g., blood pressure, skin temperature, body movement) considered as "secondary parameters" (consequences of changes in cardiopulmonary function). These MeSH were combined using *AND* and *OR* logistic operators. The full search strategies and list of MeSH for all included databases can be found in the Appendix. Additionally, reference lists of articles examined were scoped for additional papers meeting the inclusion criteria.

The gray literature search was conducted in addition to the database searches and focused on FDA-approved commercial devices used for cardiopulmonary monitoring. We searched company websites, press release articles, and blogs on the Google search engine. For this search, the terms "cardiac" and "respiratory" were combined with the OR logistic operator, which were further combined with the terms "device" and "monitoring" with the AND logistic operator. Once commercial devices were included, a literature search of validation studies of each device was conducted. The Google Scholar engine was searched by combining each commercial device name with the search terms "heart rate" and "respiration" using the AND logistic operator. Any papers that had been identified as potentially relevant to commercial devices during the initial search for research prototypes were also included at this stage.

Inclusion Criteria

Two searches were conducted for this review; a systematic search of published literature on research prototypes and a gray search of commercialized devices. For the systematic search of research prototypes, we included studies that (1) were conducted with mammalian participants, with no limits on participant age or morbidity; (2) highlighted sensor technologies in primary and/or secondary parameter monitoring, and described its method of operation; (3) had feasible utility in the everyday, out-of-hospital setting; and (4) described a sensor with monitoring that is continuous in nature and did not require user-initiated measurement. We excluded review articles, articles that described purely algorithmic development, articles lacking information relevant to device design, comparative studies, studies that detailed devices that monitored parameters that were not associated with primary function, devices that were not capable of real-time, continuous monitoring, as well as studies that described a commercial, consumer-grade sensor, as these papers were included later in the gray literature review for commercial devices. Full-text case reports, clinical trials,

and technical reports describing cardiopulmonary sensors from January 1, 1950 to May 19, 2023 were eligible. Citations describing the monitoring of secondary parameters only (e.g., body movement) were excluded unless the monitoring was contextualized as cardiopulmonary in nature. Although implantable devices were included, implantable cardiac monitors and defibrillators (ICM & ICD) were not. While ICMs and ICDs are widely used for monitoring and treating aberrant cardiac activity, they are specifically utilized in clinical populations with a known high risk of cardiac arrest. Seeing as our primary objective was to assess the sensor technology landscape for devices that could be used in the everyday, out-of-hospital setting by anyone, including low risk individuals, we did not include these devices in this review.

Study Selection

All identified citations were loaded into the online Covidence systematic review management system [28], and duplicates were removed. Subsequently, title and abstract screening was conducted by two independent reviewers (JH, MK, or SL) for assessment against the inclusion criteria, followed by a full-text screening of passed abstracts. For title and abstract screening, as well as full-text screening, any paper with two inclusion votes was passed to the next phase of the review. At any point in the review process, disagreements were resolved through consensus in reference to the inclusion/exclusion criteria.

Data Extraction

Data were extracted from the appraised studies by two independent reviewers (JH, MK, or SL) using a pre-specified internally developed data extraction framework. Extracted data included information about the sensor technology and design (e.g., sensing modality, form factor), detectable physiological parameters (e.g., HR, heart rhythm, respiration rate), study population, experimental/study settings (e.g., lab vs. clinical), and context of use. Any disagreements were resolved through discussion in reference to the pre-specified extraction tool.

The objective of the review was focused on providing an assessment of the technology landscape in cardiopulmonary monitoring and not comparative in nature. In addition, the extracted data of interest was primarily qualitative in nature, with no reported measures of outcomes, sensor accuracies, or viability of interventions that are subjected to reporter or methodological bias. As such, a risk of bias assessment was not conducted.

Results

Research Prototypes

Our search strategy returned 6945 unique publications, 90 of which met the inclusion criteria and were included in this review. The results of the screening process are detailed in Fig. 1.

Table 1 describes the 90 research prototypes identified in our review, including details of sensor types, sensor modalities, physiological parameters, and form factors.

Physiological Parameters and Sensor Types

Many systems, including single-/multi-modal devices, were capable of monitoring multiple parameters. The 90 prototypes reported a total of 207 measured physiological parameters (Fig. 2, left). Of all measured parameters, HR rate was most prevalent (N=66), followed by respiration (N=28), and heart rhythm (N=25). Other secondary parameters included temperature (N = 21), blood pressure (N=17), body movement (N=17), and blood oxygenation (N=14). ECG, PPG, IMU/Accelerometer, and temperature sensors accounted for the majority of sensor modalities used in the research prototypes (Fig. 2, right). ECG, in particular, was prominent because of its importance in monitoring HR (accounted for 50.0%) and heart rhythm (92.0%) (Fig. 3a and b), while PPG was the secondmost used modality for the primary HR parameter (28.8%) (Fig. 3a). Aside from the primary cardiac parameters, ECG and PPG were also used to monitor secondary parameters such as respiration (7.1% and 3.6%, respectively, Fig. 3c) and blood pressure (21.4% together, 28.6% PPG, Fig. 3d). However, secondary parameters were often captured using other sensing modalities such as the IMU/accelerometer (17.9% respiration, 14.3% blood pressure) and FBG (Fig. 3c, d).

Device Type and Form Factor

For research prototypes, the sensing modalities were integrated into a variety of form factors broadly categorized as wearable (81.1%), non-contact (11.1%), and implantable (7.8%). Certain form factors tended to use different sensing modalities (42.9% of implantable designs had an IMU/accelerometer and 50.0% of non-contact systems had a camera), but the wearable form factor was mostly represented by the ECG and PPG sensing modalities, predominantly used for primary parameter monitoring (Fig. 3a, b). Within wearable devices, various form factors were used, with chest patches (20.8%), garments¹ (18.1%), and wrist-worn devices (15.3%) being the most prevalent designs. Several wearables either



¹ Sensors integrated into clothing

Table 1 Summary of research prototype device types, sensor modalities, form factors, and context of use extracted from reviewed publications

Device type	Sensor (parameter)	Form factor and context of use
Wearable	ECG ^a (HR ^b , HRV ^c); PPG ^d (HR); IMU ^e (Respiration); GSR ^f ; Temperature sensor	A garment for physiological monitoring [29]
	ECG (HR), PPG (Blood oxygenation), Accelerometer (Body movement), Temperature sensor	A wrist-worn device for physiological monitoring of high-risk cardio- pulmonary patients [30]
	ECG (HR, Heart rhythm), PPG (HR, Blood oxygenation), Accelerometer (Body movement), Temperature sensor	A multi-site body worn system for physiological monitoring for space and terrestrial applications [31]
	ECG (HR), PPG (HR), Accelerometer (Body movement), BCG^{g} (HR)	An ear worn device for physiological (cardiovascular) monitoring [32, 33]
	ECG (HR); PPG (Blood oxygenation); Temperature sensor	A multi-site body worn system for remote patient monitoring [34]
	ECG (HR, Respiration), PPG (Blood pressure, Blood oxygenation), Temperature sensor	A multi-site body worn system for physiological monitoring [35]
	ECG (Heart rhythm), PPG (Blood oxygenation), Tem- perature sensor	A garment for physiological monitoring [36]
	ECG (HR, Heart rhythm, Blood pressure); PPG (Blood pressure)	A multi-site body worn system for arrhythmia detection [37]
	ECG (Heart rhythm), PPG (Blood pressure, Blood oxygenation)	A multi-site body worn system for continuous monitoring of cardiovas- cular patients [38]
	ECG (HR, Blood pressure [with PPG]), PPG (HR, Blood oxygenation, Blood pressure [with ECG])	A wrist-worn device for physiological monitoring [39]
	ECG (HR), PPG (HR)	An ear worn device for physiological monitoring [40]
	ECG & PPG (Blood pressure)	A multi-site body worn system for blood pressure monitoring of first responders [41]
	ECG (HR); IMU (Body movement); GSR; Temperature sensor	A wrist-worn device for physiological monitoring [42]
	ECG (HR), IMU (Respiration, Body movement), Temperature sensor	A chest strap system for sudden infant death syndrome monitoring [43]
Wearable	ECG (Heart rhythm), Accelerometer (Body movement), Temperature sensor	A textile-based garment for activity and cardiac monitoring [44]
	ECG (HR, Heart rhythm); Accelerometer (Body move- ment); Piezoresistive sensor (Respiration)	A textile-based garment for physiological monitoring [45]
	ECG (HR), Accelerometer (Body movement), Tempera- ture sensor	An abdominal (strap) device for physiological monitoring [46] A garment (bra) for physiological monitoring [47]
	ECG (HR, Heart rhythm, HRV, Respiration); Accelerometer (Body posture)	A chest patch for cardiopulmonary monitoring [48]
	ECG (HR, Heart rhythm), Accelerometer (Body movement)	A garment for physiological monitoring [49]
	ECG (HR, Heart rhythm), Position sensor (Fall detec- tion), Temperature sensor	A textile-based garment for physiological monitoring [50]
	ECG (Heart rhythm), Bioimpedance sensor (Respiration), Temperature sensor	A multi-site body worn system for physiological monitoring [51] A chest patch for physiological monitoring [52]
	ECG (HR), BCG (HR)	An ear worn device for heart rate monitoring [53]
	ECG (HR, Pulse pressure), Piezoresistive sensor (HR, Pulse pressure)	A wrist-worn device for cardiac monitoring [54]
	ECG (HR), Piezoelectric sensor (Respiration)	A chest strap for cardiopulmonary monitoring [55]
	ECG (HR, HRV), Temperature sensor	A textile-based garment for physiological monitoring [56]
	ECG (HR), Temperature sensor	A chest patch for physiological monitoring [57] A garment for physiological monitoring [58]
	ECG (HR); GSR	A chest strap for physiological monitoring [59]

Table 1 (continued)

Device type	Sensor (parameter)	Form factor and context of use	
	ECG (HR, Heart rhythm)	A chest patch for long-term cardiac monitoring [60] A chest patch for long-term monitoring of cardiac patients [61] A chest patch and abdominal strap for cardiac monitoring [62] A chest vest for cardiac monitoring [63] A chest patch for cardiac monitoring [64] A garment for cardiac monitoring [65, 66]	
	ECG (Heart rhythm)	A chest patch for cardiac monitoring [67] A garment for cardiac monitoring [68] A chest patch for cardiac event monitoring [69] A chest patch for heart beat detection [70]	
	PPG (HR), Accelerometer (Body movement), Tempera- ture sensor	A finger worn device for remote patient monitoring [71]	
	PPG (HR); Accelerometer (Body movement)	An ear worn device for elderly physiological monitoring [72] A headband for remote patient physiological monitoring [73]	
Wearable	PPG (Pulse Rate Variability), Accelerometer (Body movement)	A body worn system for physiological monitoring [74]	
	PPG (HR); GSR; Temperature sensor	An ear and neck worn system for remote physiological monitoring of elderly cardiac patients [75]	
	PPG (HR, HRV, Blood oxygenation, Heart rhythm); GSR	A ring for physiological monitoring [76]	
	PPG (HR), Force sensor (sensor-to-skin contact)	A wrist-worn device for physiological monitoring and pulse detection [77]	
	PPG (HR), Temperature sensor	A chest patch for remote patient physiological monitoring [78]	
	PPG (HR, Blood pressure)	A chest strap for continuous blood pressure monitoring [79]	
	PPG (HR, Blood oxygenation)	A finger worn device for physiological monitoring [80] A hand worn device for physical activity monitoring [81]	
	PPG (HR; Respiration)	A wrist-worn device for cardiopulmonary monitoring [82]	
	PPG (HR)	An ear worn device for heart rate monitoring [83] An ear worn device for driver's physiological monitoring [84]	
	PPG (Blood oxygenation)	A textile-based sleeve for physiological monitoring [85]	
	PPG (Blood pressure)	A wrist-worn device for physiological monitoring [86]	
	NIRS ^h (HR)	A hand worn device for physiological monitoring [87]	
	IMU (Respiration, Body movement)	An abdominal strap for respiration monitoring [88]	
	IMU (Respiration)	A chest strap for respiration monitoring [89]	
	Accelerometer (Respiration)	A chest patch for respiration monitoring [90]	
	Accelerometer (Blood pressure)	A chest patch device for blood pressure monitoring [91]	
	Force Sensitive Resistor (HR)	A wrist-worn device for heart rate monitoring [92]	
	Acoustic sensor (HR, Heart rhythm)	A wrist-worn device for cardiac monitoring [93]	
	Bioimpedance sensor (Respiration), IMU (Motion); Temperature sensor	A chest patch for respiration monitoring [94]	
	Bioimpedance sensor (Blood pressure, Respiration)	A wrist-worn device for blood pressure monitoring [95] A chest patch for respiration monitoring [96]	
	Fiber Bragg Grating (Blood pressure, Respiration)	A textile-based multi-site body worn system for respiration monitoring [97, 98] A wrist-worn device for pulse pressure monitoring [99]	
	Triboelectric sensor	A waist strap for respiration monitoring [100]	
	Strain gauge sensor	A chest/abdominal strap for respiration monitoring [101]	

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Table 1 (continued)

Device type	Sensor (parameter)	Form factor and context of use
Implantable	ECG (HR, Heart rhythm)	A subcutaneous device for cardiac arrest monitoring [102]
	PPG (Blood oxygenation)	A subcutaneous sensor for arterial oxygen saturation monitoring [103, 104]
	NIRS (Blood/Tissue oxygenation, Perfusion)	An implantable device for spinal cord oxygenation monitoring [105]
	Accelerometer (Cardiac motion)	An implantable device to measure endocardial and epicardial accelera- tion [106]
		An implantable device to monitor cardiac contractions [107]
	Accelerometer (Blood pressure)	An implantable device for continuous blood pressure monitoring [108]
Non-contact	RGB camera (HR, Respiration)	A camera-based heart rate monitoring in the neonatal intensive care unit [109]
		A camera-based breathing monitoring system [110] A camera-based respiration monitoring system in infants [111]
	Thermal camera (Respiration)	A camera-based respiration rate monitoring [112]
	Infrared camera (Respiration)	A camera-based respiration monitoring in infants [113]
	Acoustic monitor (Respiration)	An acoustic-based apnea monitoring device in infants [114]
	Acoustic radar (HR, Respiration)	An acoustic-based cardiopulmonary monitoring device for wheelchair users [115]
	Doppler radar (HR, HRV)	A non-contact device for cardiac activity monitoring [116]
	Laser Doppler (HR)	A non-contact device for blood pulse waveform monitoring [117]
	Load cell (HR, Respiration)	A bed-based device for sleep monitoring [118]

^aElectrocardiogram (ECG)

^bHeart Rate (HR)

^cHeart Rate Variability (HRV)

^dPhotoplethysmogram (PPG)

^eInertial Measurement Unit (IMU)

^fGalvanic Skin Response (GSR): Measures the electrical conductance of the skin, which is often used as a measure of physiological/emotional arousal

^gBallistocardiogram (BCG): Measures the mechanical movements of the body as a result of the heart's contractions

^hNear Infrared Spectroscopy (NIRS)

allowed users to place the device at one of several eligible body sites or required application at more than one site (12.5%).

Wearable devices tended to incorporate multiple sensing modalities (multi-modal, 52.8%), compared to non-contact and implantable devices which were always single modality. ECG sensor modalities were most often embedded in form factors localized to the chest (garment, chest straps and patches) and PPG sensor modalities were most often embedded in form factors localized to the extremities (fingers, ears, hand, wrist), with both ECG and PPG being paired with other sensing modalities incorporated into the common form factors, or embedded as a multi-site wearable device (Fig. 4).

Commercial Devices

A list of commercialized devices that met the inclusion criteria is presented in Table 2. The breakdown of sensor types, physiological parameters, form factors, and context of use for these commercialized devices is presented in the remainder of this section.

Physiological Parameters and Sensor Types

Commercial devices tended to monitor multiple parameters, with 102 physiological parameters reported to be measured by the 26 included devices. HR (N=26), heart rhythm (17), body movement (16), temperature (14), and respiration (13) were the most commonly measured. Within the 26 devices, ECG (17 of all 23 devices) were most prevalent, followed by IMU/accelerometer (15), temperature sensors (14), and PPG (10). Other examples of sensors in commercial devices included Impedance Pneumography (IPG), Galvanic Skin Response (GSR), and Acoustic sensors. The breakdown of sensor types and parameters for research prototypes is presented in Fig. 5. HR was most frequently measured by ECG and PPG (Fig. 6a). All commercial devices used ECG and PPG for heart rhythm measurements (Fig. 6b). Similar to



Fig. 2 Prevalence of parameters (left) and all sensors (right) in 90 research prototypes



what was observed in the included research prototypes, the majority (75%) of the included commercial devices were multi-modal, utilizing multiple sensors for cardiopulmonary monitoring. All multi-modal commercial devices used at least one ECG or PPG (multi-modal with ECG: 33.3%; multi-modal with ECG and PPG: 29.2%; and multi-modal with PPG: 12.5%). Among single modality devices, ECG sensors had the highest prevalence (8.3%). 67 total sensors were used throughout the included 26 commercial devices. Within all sensors, ECGs (26.6%) were most prevalent, followed by IMU/accelerometers (23.4%), temperature sensors (20.3%), and PPGs (14.1%).

Device Type and Form Factor

With the exception of 1 mattress-based device and 1 noncontact sensor, all commercial devices were wearable devices. Similar trends were observed in research prototypes, with wearable devices having the highest prevalence. Among wearables, chest patches (26.9%) and wrist-worn



Fig. 4 Breakdown of wearable research prototypes based on sensor modality & form factor

devices (26.9%) were the most prevalent. Similarly, chest patches and wrist-worn devices were among the most prevalent form factors among research prototypes. Multimodal wearables generally utilized ECG and/or PPG with the following order: multi-modal with ECG (32.0%), multi-modal with ECG and PPG (28.0%), and multi-modal with PPG (12.0%) (Fig. 7). The majority of devices that integrated ECG sensors without PPGs were chest patches (70%). Devices that utilized PPG in a multimodal combination tended to be wristbands (Fig. 7). These form factor considerations and design characteristics are in line with extracted data from research prototypes.

Context of Use

The majority (72.0%) of the commercial devices (all FDAapproved) were designed to be used for specific clinical applications (e.g., remote cardiopulmonary patient monitoring). The remainder of the commercial devices (28.0%) were used for fitness tracking or general health monitoring (e.g., Fitbit, Apple watch). However, in conjunction with appropriate software applications, these devices can provide diagnostic capabilities for some cardiac conditions (e.g., AFib detection). Most ECG-based patches were designed in the form of disposable devices with battery life and data storage capabilities of up to 14 days. However, wrist-worn devices used for fitness tracking are rechargeable and use cloud-based apps for data transfer and tracking.

Discussion

Summary

Cardiac arrest is a complex physiological state that is characterized by a cascade of primary (proximate) and secondary (downstream) changes in vital signs. The majority of cardiac arrest cases in the out-of-hospital setting are unwitnessed, and thus have extremely low rates of survival due to a lack of timely response and treatment. Biosensors with continuous monitoring capabilities may be used to address unwitnessed cardiac arrests by identifying these physiological changes and alerting first responders. Although remote cardiopulmonary monitoring devices exist and are being used, there are very

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Name (device or app-specific FDA approval)	Sensor (parameter)	Form factor (placement)	Context of use (population)	Battery life (up to)
BodyGuardian Heart [119]	ECG (HR, Heart rhythm)	Patch (Upper chest)	Clinical (Patients with cardiac arrhythmias)	6 days
Cardea Solo [120]	ECG (HR, Heart rhythm); Temperature	Patch (Upper chest)	Clinical (Patients with heart conditions)	7 days
ZioPatch [121]	ECG (HR, Heart rhythm); Accelerometer (Body movement); Temperature	Patch (Upper chest)	Clinical (Patients with cardiac arrhythmias)	14 days
MBS Vitalpatch [122]	ECG (HR, HRV, Heart rhythm); IPS ^a (Respiration); Accelerometer (Body movement); Temperature	Patch (Upper chest)	Clinical (Patients with cardiac arrhythmias)	7 days
Vivalink [123]	ECG (HR, HRV, Heart rhythm) ; IPS (Respiration); Accelerometer (Body movement)	Patch (Upper chest)	Clinical (Patients with heart conditions)	5 – 7 days
QardioCore [124]	ECG (HR, HRV, Heart rhythm); Accelerometer (Respiration, Body movement); Temperature	Strap (Lower chest)	Clinical (Patients with heart conditions)	12 months
HeartGuide [125]	Oscillometric sensor (HR, Blood pressure)	Wrist worn	Clinical (Patients at risk of developing hypertension)	2 days
RespiraSense [126]	Piezoelectric (Respiration)	Patch (Lower chest)	Clinical (Patients with chronic lung disease)	4 days
Strados RESP [127]	Acoustic (Respiration)	Patch (Lower chest)	Clinical (Patients with respiratory conditions)	8 hours
Embrace2/EmbracePlus [128, 129]	ECG (Heart rhythm); PPG (HR, Blood oxygenation); Electrodermal Activity; Accelerometer (Body movement); Temperature	Wrist worn	Clinical (Patients with epilepsy)	48 hours
Philips Biosensor BX100 [130]	ECG (HR, Heart rhythm); PPG (Blood oxygenation, Blood flow); IPS (Respiration); Accelerometer (Body movement); Temperature	Patch (Upper chest)	Clinical (Remote & real-time patient monitoring)	115 hours
KardiaMobile [131]	ECG (HR, Heart rhythm)	Pad (Fingers)	Clinical (Remote patient monitoring)	NA
BioStamp nPoint [132]	ECG (HR, HRV); Accelerometer/ Gyroscope (Body movement); Temperature	Patch (Multi-site)	Clinical research (Remote patient monitoring)	24 hours
Sensium Patch [133]	ECG (HR, Heart rhythm); IPS (Respiration); Accelerometer (Body movement); Temperature	Patch (Upper chest)	Clinical/hospital (Vital signs monitoring)	5 days

 Table 2
 Summary of device name, sensor types, form factor, context of use, and battery life for commercialized devices

Table 2 (continued)				
Name (device or app-specific FDA approval)	Sensor (parameter)	Form factor (placement)	Context of use (population)	Battery life (up to)
SpireHealth [134]	PPG (HR); Piezoelectric (Respiration); Accelerometer (Body movement); Temperature	Strap (Multi-site)	Remote patient monitoring (Patients with chronic obstructive pulmonary disease)	12 months
EarlySense [135]	NA ^b (HR, Respiration, Body movement)	Mattress-based (non-contact)	Clinical (Vital signs monitoring)	Wired
Fitbit (FDA Clearance for ECG App, AFib detection) [136]	ECG (Heart rhythm), PPG (HR, Heart rhythm); Accelerometer (Body movement); Temperature	Wrist worn	Fitness/Health monitoring (General population)	7 days
Apple Watch (FDA Clearance for ECG App, AFib detection) ^c [137]	ECG (HR, Heart rhythm); PPG (HR, HRV, Blood oxygenation); Accelerometer (Body movement)	Wrist worn	Fitness/Health monitoring (General population)	24 hours
Garmin (FDA Clearance for ECG App, AFib detection) ^d [138]	ECG (HR, Heart rhythm); PPG (Blood oxygenation)	Wrist worn	Fitness/Health monitoring (General population)	2 days
Samsung (FDA Clearance for ECG App, AFib detection) ^e [139]	ECG (HR, Heart rhythm); PPG (HR, Blood oxygenation); Accelerometer (Body movement)	Wrist worn	Fitness/Health monitoring (General population)	AN
CardiacSense Watch [140]	ECG (Heart rhythm), PPG (HR, HRV); Accelerometer (Body movement); Temperature	Wrist worn	Fitness/Health monitoring (General population)	4 days
Oura Ring [141]	PPG (HR, HRV); Accelerometer (Body movement); Temperature	Ring (Finger)	Fitness/Health monitoring (General population)	7 days
Hexoskin [142]	ECG (HR, HRV, Heart rhythm); IPS (Respiration); Accelerometer (Body movement); Temperature	Vest (Thorax)	Fitness/Health monitoring (General population)	36 hours
Vitls [143]	PPG (HR, Respiration); Temperature	Patch (Upper chest)	Clinical (Remote & real-time patient monitoring)	5 days
Neteera [144]	BCG (HR, Respiration)	Non-contact	Clinical (Remote patient monitoring)	NA
Respiree [145]	NA (HR, Respiration)	Patch (Upper chest)	Clinical (Remote & real-time patient monitoring)	2 days

^aImpedance Pneumography Sensor (IPS)

^bInformation not available ^cSeries 4 or later

^dE.g., Venu 2 Plus, Vivosmart 4

eE.g., Galaxy Watch, Gear Watch



Fig. 5 Prevalence of all parameters (left) and sensors (right) in 26 commercial devices.



Fig. 6 Breakdown of sensor types for commercial for **a** heart rate (N=24); **b** heart rhythm (N=17); **c** respiration (N=11) (*BCG* ballistocardiogram, *IPG* impedance pneumography)



few that are specifically designed for OHCA detection. Thus, while there are currently millions of individuals worldwide who wear a wearable device that continuously monitors physiological parameters that may be used to detect OHCA, there are currently few technologies that are specifically designed and validated for this purpose. Our review assesses the current landscape of wearable technologies to better focus efforts on providing continuous OHCA detection capabilities. Specifically, this review was focused on technologies with capabilities for continuous physiological monitoring of parameters associated with changes in cardiopulmonary or associated parameters resulting from a sudden cardiac arrest event.

In our review, HR (30%) and heart rhythm (14%) were among the most commonly reported parameters across both research prototypes and commercial devices for clinical and remote patient monitoring applications. With the high global prevalence and awareness of cardiovascular disease (CVD) [146], and given that HR and heart rhythm are among the main risk predictors of CVDs, it is intuitive that remote cardiovascular monitoring devices should mainly focus on measuring these parameters. We found that many currently available wearable devices marketed for other purposes (e.g., fitness tracking, general health monitoring) also have relevant sensing modalities that monitor these primary parameters. Thus, our review suggests there is great opportunity for developing methodologies (e.g., algorithms) that utilize existing technologies monitoring HR and heart rhythm specifically for OHCA detection that can have a broad and global reach. However, adapting these sensors to inform the design of devices for OHCA detection will require further sensor-specific and system-level considerations.

Adaptation of Current Cardiopulmonary Sensors for OHCA Detection

Sensor-Specific Considerations for ECGs

ECG sensors are capable of highly accurate cardiac monitoring, which was reflected in their prevalence among both research prototypes and commercial devices. ECG-based systems were commonly used for HR and/or heart rhythm monitoring, which is consistent with previous studies investigating sensor technologies in cardiac monitoring applications [24, 147, 148]. Our review revealed that chest patches were the most common form factor incorporating ECGs among both research prototypes and commercial devices. Compared to Holter monitors (i.e., the current gold standard cardiac monitoring device in clinical settings), these ECG patches provide longer-term continuous monitoring capacities (i.e., up to 2-3 weeks), while offering a less intrusive form factor. Compared to Holter monitors, chest patches were perceived to be more comfortable and had higher user adherence [60]. Wrist-worn and garment/textile ECG devices were other common form factors in multimodal ECG-based wearables. Wrist-worn ECGs can offer a more user-friendly alternative to ECG patches for longterm (i.e., months/years) applications (e.g., no adhesives, no interference with clothing). Similarly, garment-based ECGs are other alternatives to patches, avoiding the need for adhesives.

Despite the capabilities of ECG-based devices, they are not practical for OHCA detection in their current form

factors. For instance, chest patches may cause irritation when used long-term [147]. In addition, some patches have limited/no battery charging capacity, and they lack a userfriendly interface [147, 149]. While wristband form factors dominate the consumer market [150], current wristband ECGs necessitate user interaction with the device to obtain a measurement (i.e., intermittent monitoring) [151]. Such user-initiation would not be possible in the event of a cardiac arrest due to a lack of consciousness. Although ECG monitors with at least 2 leads are recommended for accurate HR or heart rhythm monitoring, both patch-based and wristband ECGs are constrained to providing single-lead measurements [152]. Restricting an ECG system to single lead measurements may result in up to 10% increases in measurement error compared to clinical-grade ECGs with more than one lead [151]. In this review, only garments were observed to have sufficient points of body contact (i.e., more than two) to provide multiple lead continuous monitoring capabilities. Despite the benefits of enabling continuous ECG monitoring, the usability of such garmenttype devices for an extended period may be a challenge for many individuals, particularly as these garments require sustained close fit for accurate continuous measurement. Another limitation of ECG-based devices is the inability to detect the presence of PEA - (20% of EMS-treated cardiac arrest cases) [153]. PEA is characterized as a detectable cardiac electrical signal despite the absence of a palpable pulse (i.e., measurable electrical signals during a cardiac arrest).

For those seeking to design OHCA devices that utilize ECG sensors, consideration of how to incorporate multiple points of contact (i.e., multiple-lead measurements) in a form factor that is amenable to long-term continuous use is key. Devices should allow for the acquisition of heart rhythm measurements without requiring user interaction. If garment-style devices such as vests are designed, user comfort and considerations for optimal user adherence should be a priority. Additionally, as ECG-based devices cannot detect PEA arrests, those seeking to design solutions for OHCA should consider the addition of other sensor types in a multi-modal design to complement ECG-based monitoring.

Sensor-Specific Considerations for PPGs

PPGs, capable of monitoring a variety of physiological parameters with high accuracy (e.g., HR, HRV, SpO2), had high prevalence in both research prototypes and commercial devices. Similar trends and capabilities of PPGs in the context of cardiac monitoring were reported in previous studies [24, 148]. The comparison of PPG-derived HR accuracy with ECG-derived HR in clinical settings demonstrated that PPG can produce accurate readings under controlled conditions (e.g., stationary and absence of motion) [154]. Unlike ECGbased devices, PPGs do not require multiple points of contact for accurate monitoring [153]. In addition, PPGs can detect PEA by measuring the lack of volumetric differences in arterial blood due to the cardiac arrest, as opposed to the electrical activity of the heart. One of the major benefits of PPG-based devices is that they can be designed for and used in a variety of locations on the human body (e.g., wrist, finger, ear, chest, etc.), increasing their degree of customizability to be tailored for commercial use. In research and commercial devices, wristbands were the most common form factor incorporating PPGs, representing the second most common form factor overall after chest patches. Comparatively, wrist-based devices are deemed more user-friendly from a convenience and aesthetic value perspective, and have therefore penetrated the non-clinical commercial wearable device sector [150].

Although PPG-based HR and blood oxygenation monitoring has been widely accepted and used in clinical settings, the use of PPG-based devices for HR and heart rhythm monitoring in out-of-hospital settings has limitations. Variable sensor-to-skin contact pressure and the choice of measurement site affect PPG signal quality and accuracy [155]. Measurement sites that tend to be less accurate (e.g., the wrist, compared to the fingertip) also tend to be the locations that users would prefer to wear the device [16]. Body movements at the sensor placement site could result in up to 30% measurement error [156]. Other limitations of PPG arise from its optical methods of detection. Most notably, user-specific characteristics such as skin pigmentation or body weight can cause measurement variations that affect the accuracy of PPG signals [157]. Overall, compared to ECG-based devices, PPG-based devices are expected to be more susceptible to deviation in the real-world setting [158].

For those seeking to design OHCA devices that utilize PPG sensors, it is key to secure and confirm adequate contact with the skin at a body location more conducive to highquality signal acquisition, such as a ring at the base of the finger. In addition, the selected body location would require adequate tissue perfusion, as indicated by the perfusion index. Incorporating several LEDs would aid in the crossvalidation of PPG signals at a single site, while still only requiring a single point of contact. Incorporation of multiple PPG sensors in one form factor, or within form factors that ensure minimal sensor-skin movement, will also help address the vulnerability of PPGs to movement-based errors. Algorithmically, efforts should be undertaken to optimize the signal-noise ratio through the filtering of motion artifacts. Targeted testing and validation on a range of skin pigmentations, body weights, and epidermal thicknesses (which may involve a wider range of PPG light wavelengths) will help address known limitations in accuracy for specific subgroups.

Considerations for Other Wearable Sensing Modalities

Limitations relevant to PPG and ECG (e.g., motion artifacts, form factors, continuous measurement, comfort, time delays) may also apply to other sensor modalities included in this review. However, due to the low number of studies describing such sensors specifically in cardiopulmonary applications, their advantages and limitations are largely speculative. Further development of such sensors for cardiopulmonary applications is necessary to gain a comprehensive understanding of their major advantages and limitations in the potential role of monitoring for both OHCA detection and general cardiopulmonary health monitoring.

Considerations for Multi-modal System Design

Given the limitations inherent to both ECG- and PPGbased devices, as well as the benefits of being able to monitor several different primary and secondary parameters, a multi-modal solution is likely the best approach for OHCA detection.

OHCA sensors require high accuracy, encompassing both sensitivity (i.e., the capability to detect a cardiac arrest when it occurs-minimizing false negatives) and specificity (i.e., the capability not to produce an alert when the user is not in cardiac arrest-minimizing false positives). For every individual, the likelihood of a cardiac arrest is quite low. If one is to make the effort to wear a device for cardiac arrest detection, the user will likely need assurances that it will successfully identify a cardiac arrest if it occurs. On the other hand, it would also be important to users and EMS providers that the device does not produce many faulty alarms, as that would be regarded as a nuisance to users and will risk burdening EMS. A multi-modal approach to cardiac arrest detection may assist in minimizing both false positives and false negatives, improving the system's accuracy overall.

Incorporating multiple sensors can increase the ability of the device to detect cardiac arrest states, particularly through reducing noise artifacts and improving signal quality. An example of such is the utilization of IMUs in an ECG-PPG-based solution to remove motion artifacts. Another such example is using multiple PPG sensors on different body parts, or using high-density PPGs (i.e., PPGs with more than one emitter/detector) [16]. These same solutions work towards minimizing false negatives from a decisionmaking perspective, relying on independent data streams to only produce OHCA alerts when there is a high level of agreement among different sensors above a pre-specified threshold. Examples of such include using both PPG and ECG for HR and heart rhythm monitoring, or incorporating IMUs for the detection of motionlessness. Although the use of several sensor modalities for long continuous periods may reduce battery life, software-level modifications can be made to turn specific sensors on/off as needed (e.g., triggering one sensor after a potential critical state is measured by another sensor) [147].

The utilization of a multi-modal approach for OHCA detection should consider a form factor congruent with longterm use. While multiple points of contact are ideal for monitoring with ECG, developers should target form factors that can incorporate these multiple sensors within one wearable device instead of requiring users to wear multiple devices as part of an integrated system. Such designs will likely lead to higher user comfort and translate to easier adoption for long-term monitoring.

Novel Biosensing Technologies

While multimodal sensing can help bypass some of the issues generated from relying on a single sensor modality, another solution may be given by the development of novel sensor technologies. Our review revealed that there are several upcoming technologies in this category, including textile-based bioimpedance sensors [159], camera-based non-contact sensors [160], and NIRS [161, 162]. However, many of these systems suffer similar issues as ECG and PPG sensors. Textile-based bioimpedance sensors would require adequate continuous physical contact with the user to perform measurements (analogous to garment-based ECGs), camera-based non-contact sensors would necessitate multiple-camera installation to capture continuous measurements (analogous to single-lead ECGs), and NIRS, being an optical based modality, faces similar challenges as PPGs. A novel sensor designed specifically to address OHCA-specific challenges, perhaps one operating on new principles or one adapted for cardiopulmonary monitoring from other existing fields (e.g., non-invasive, continuous biomarker monitoring), could be a strong solution on its own or in a multimodal system.

Considerations Related to Device Type

The similarities between wrist-worn wearable devices and conventional watches or wrist-worn accessories increases the acceptability of such devices among users [163]. However, wrist-worn devices are prone to various artifacts, such as motion or variable sensor-to-skin pressure, which greatly affect measurement quality. While non-contact physiological monitoring devices provide unobtrusive monitoring capabilities, they may impose other challenges, such as a limited range and field of view (e.g., camera-based devices) and scalability issues (e.g., installment in multiple locations, cost). Despite these limitations, a niche may still exist for their use as the majority of OHCA cases occur in the home [6, 153]. Implantable solutions provide limited use cases and are typically only offered to high-risk individuals. The expected benefit of using an implantable device lies in its independence from user-based maintenance (e.g., recharging, ensuring proper attachment, etc.). However, implantable devices may raise other concerns such as risk of infection, replacement issues, and cost [147].

Validation

Although the accuracy of several ECG- and PPG-based devices has been validated previously, the context of use was mainly limited to monitoring healthy or non-immediately life-threatening cardiac states (e.g. AFib) [147]. Many of the reviewed devices described in this paper have a strong foundation of clinical evidence surrounding detection accuracy for physiological monitoring under their conditions of intended use (e.g., Apple Watch and FitBit for AFib) [164, 165]. However, extrapolating this evidence to OHCA is a challenge. For example, a device with high accuracy to detect HR within a normal physiological range does not necessarily retain its accuracy for detecting the absence of a pulse. Indeed, there was a recent reported case study of a FitBit observing an OHCA, where the device continued reported a heartbeat following the OHCA [166]. Thus, technologies for OHCA detection require testing and validation on this specific physiological state.

Laboratory testing is a necessary first step in determining the accuracy of cardiac arrest detection as compared to a gold standard. For devices worn on the extremities that detect HR, standard occlusion tests may provide some indication of device performance (i.e., cardiac arrest detection accuracy) [167]. However, for devices that are worn proximally or on multiple sites, simulating a cardiac arrest with occlusion may not be feasible. For these devices, testing using animal models or during medical procedures that involve inducing cardiac arrest (cardiac surgery, medical assistance in dying) may provide the best estimate of the device performance [168]. In addition, devices developed for OHCA detection should incorporate real-world testing as laboratory testing does fall short of approximating the real-world conditions within which these devices will operate [169]. Ultimately, OHCA sensors will require clinical validation in settings that approximate or mirror the intended conditions of use. Data storage, cloud-based data transmission and processing, and user privacy are among other important features of OHCA detection systems for future exploration [158].

Limitations

We limited the review to include devices that could be adapted to out-of-hospital use for cardiac arrest detection, which required a degree of subjective assessment. Devices that utilized form factors deemed to be non-compatible with long-term, everyday use were excluded from the review (e.g., Holter monitor). Additionally, sensors that appeared in our searches as relevant to OHCA detection were based on the inclusion of our determined list of primary and secondary parameters. However, there may be physiological parameters (and associated sensors capable of detecting such parameters) that were not included in this review that may be potentially relevant to OHCA detection (e.g., biomarkers known to be associated with cardiac arrest).

In the search of commercial devices, we were restricted to devices that are already established and publicly available (FDA-approved). However, some private commercial technologies are still in development, and information on potential utility for OHCA detection is not yet publicly available.

Conclusion

This review revealed that ECG and PPG sensors are heavily utilized in devices for cardiopulmonary monitoring that could be adapted to OHCA detection, but there are several limitations that need to be addressed first. While ECG is a common and familiar sensor type in cardiac monitoring, existing ECG-based devices have a suboptimal use case or form factor for OHCA detection. PPG-based devices offer convenient and continuous monitoring solutions; however, ensuring the maintenance of continuous, high-quality and reliable measurements is a critical consideration relevant to OHCA detection. At the current state of FDA-approved commercial technologies, developers seeking to quickly develop methods taking advantage of existing devices should focus on ECG- and PPG-based multimodal systems. However, there is a potential for novel biosensors (e.g., bioimpedance textiles, NIRS) to address current sensor limitations. Here, we recommend that novel sensors should be designed with a focus on detecting OHCA rather than general cardiopulmonary measures. Although other sensor types (e.g., IMU) did not appear promising on their own for use in cardiac arrest detection, they may be valuable components of a multi-modal approach that could be ECG- and/or PPG-based. Similarly, the addition of sensor modalities to detect the presence and/or absence of primary or secondary parameters (e.g., GSR), may lead to higher specificity. In addition, consideration of end-user input on form factor and usability is essential, as factors related to comfort and usability will be major determinants of the long-term and continuous device use necessary to ensure optimal protection against unwitnessed OHCA. Physiological and contextual differences limit the translation of the robust clinical testing and validation performed for many cardiopulmonary devices to OHCA. Specific testing and validation on patients in cardiac arrest is needed.

Appendix: Search Terms and Search Strategy

The search strategy is provided below. The search databases include MEDLINE, EMBASE, Web of Science, and Engineering Village. The search was restricted to articles in English within the date range of January 1, 1950 to May 19, 2023. Full-text case reports, clinical trials, and technical reports were included in the search.

Search Terms

The terms used in this search fell under four classifying categories: (1) terms for continuous monitoring and detection of physiological parameters, (2) terms for broad categories of sensors, (3) terms for the primary disease

Table 3 Literature search terms

Continuous Monitoring & Detection	Primary Disease State	Sensor	Physiological Parameter
prevent.mp	Exp Heart Arrest/	implant.mp	Heart Rate/
detect.mp	cardiac arrest.mp	Monitoring, Ambulatory/	Respiratory Rate/
monitor.mp	Arrhythmias, Cardiac/	Monitoring, Physiologic/	Respiratory Mechanics/
		Wearable Electronic Devices/	Body Temperature/
			Galvanic Skin Response/
			Motion/
			Blood Pressure/

states associated with cardiac arrest, and (4) terms for cardiac arrest-associated physiological parameters. The exact search terms within each classifying category are listed below (Table 3).

When necessary, keywords were shortened and truncated with an asterisk (e.g. detect*) to retrieve unlimited suffix variations (e.g. detect, detecting, detectable, etc.). The search terms were combined according to the following strategy: Category1AND[(Category2)AND(Category3ORcategory4)]

MEDLINE Example Search

On MEDLINE, all of the search terms used, with the exception of "prevent", "detect", "monitor", "cardiac arrest", and "implant" were Medical Subject Headings (MeSH). Broader MeSH were selected to encompass

#	Search Term	Category
1	prevent.mp	1
2	detect.mp	1
3	monitor.mp	1
4	1 or 2 or 3	1
5	implant.mp	2
6	Monitoring, Ambulatory/	2
7	Monitoring, Physiologic/	2
8	Wearable Electronic Devices/	2
9	5 or 6 or 7 or 8	2
10	Exp Heart Arrest/	3
11	Arrhythmias, Cardiac/	3
12	cardiac arrest.mp	3
13	10 or 11 or 12	3
14	Heart Rate/	4
15	Respiratory Rate/	4
16	Respiratory Mechanics/	4
17	Body Temperature/	4
18	Galvanic Skin Response/	4
19	Motion/	4
20	Blood Pressure/	4
21	14 or 15 or 16 or 17 or 18 or 19 or 20	4
22	13 or 21	3 or 4
23	9 and 22	2 and (3 or 4)
24	4 and 23	1 and (2 and (3 or 4))

Table 4 MEDLINE example search strategy

relevant subcategories when necessary. Below is a more detailed representation of this search strategy (Table 4).

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