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Recent Advances in eHealth Smart Solutions

MonEco: a Novel Health Monitoring Ecosystem to Predict Respiratory and Cardiovascular Disorders



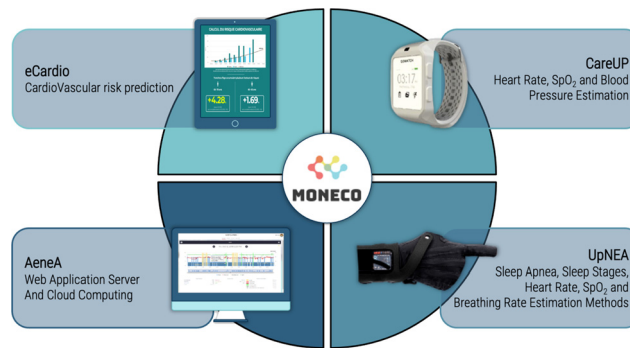
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HIGHLIGHTS

- MonEco is a health monitoring ecosystem that employs eCardio, CareUp, and UpNEA.
- eCardio is an application available for iOS devices that predicts cardiovascular risk.
- CareUp is a smartwatch for blood pressure estimation and fitness tracking.
- UpNEA is a smart glove for sleep monitoring, detecting sleep disruptive breathing events.
- MonEco transforms the doctor-patient relationship by monitoring user's illnesses.

GRAPHICAL ABSTRACT



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ABSTRACT

Objectives: the present manuscript introduces a health monitoring ecosystem called MonEco, to monitor and predict respiratory and cardiovascular disorders.

Material and methods: the system comprehends a tablet application called eCardio and two smart devices named CareUp and UpNEA. eCardio is an application available for iOS devices that predicts cardiovascular risk based on user' data and habits. CareUp is a smartwatch for blood pressure estimation and fitness tracking. UpNEA is a smart glove for sleep monitoring, detecting sleep disruptive breathing events.

Results: MonEco smart devices embed novel algorithms and top-notch home health care monitoring technologies. The user can access data collected via a web application hosted by a remote server (AeneA), allowing clinicians to follow up on a patient's health.

Conclusion: MonEco wants to inspire and disclose the architecture of a connected health monitoring ecosystem.

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1. Introduction

The rise of well-being or home automation-oriented connected objects will renew the relationship with our daily environment,

passing most objects from a passive mode to that of active, connected, and intelligent terminals. In all Western countries, it is possible to observe that the progress of medicine and the development of new technologies allow life expectancy to increase [1,2]. The population also expresses its desire to maintain its autonomy and be kept at home in the event of loss of autonomy [3–6].

In this context, it is possible to note the need for solutions to satisfy the desire to continue living at home while retaining their autonomy. Even if many products have been placed on the market,

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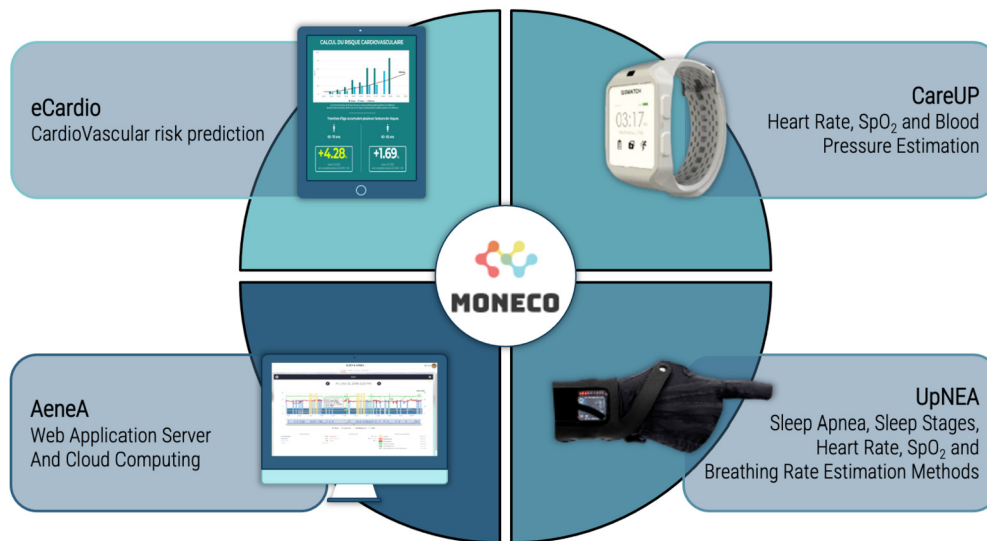


Fig. 1. Moneco: a monitoring ecosystem.

it is still not easy for a physician to follow the patient's physiological activity outside the clinic.

The exponential growth of connected objects [7] and their democratization allow the general public to self-monitor by measuring physiological parameters. These data can then be transmitted to the attending physician. The doctor-patient relationship is being transformed since the patient is starting to play a crucial role in his health, notably improving his lifestyle or monitoring illnesses. Also, the exchange of data between several health systems is gaining importance. A consequence of this is the implementation and use of standard protocols well established in the hospital system (such as DICOM or HL7 protocols) and taking place also in the field of home support and more generally in personal connected health objects (such as in Bluetooth and ANT+).

The present paper aims to integrate the different proposed devices into a unique ecosystem to monitor users' health daily. The main property of this ecosystem is the interoperability of all of its products. All the connected devices had access to writing on the same shared database, allowing the user to access all his data from the same application.

1.1. Description of MonEco

The present manuscript proposes MonEco: a health monitoring solution that allows the user to measure its physiological parameters and exchange this information with a physician. In this way, the doctor can directly analyze the impact of treatment on the patient, check if it is well adapted to his pathology, and prevent certain risks of incompatibility or adverse effects.

The MonEco ecosystem, as shown in Fig. 1, is based on different e-health care solutions:

- A web application, where each user could visualize the information collected by his smart devices; the website recalls all user's information from a dedicated SQL database. This information can be shared with a third user, typically a physician, to investigate the possibility of an eventual cure or follow the treatment.
- eCardio: a cardiovascular disease risk prediction platform based on the Framingham and SCORE studies [8]. This platform is available in two formats: a web application (integrated into the user web dashboard) and an electronic stand installed in some pharmacies that applied to the initial experimentation.

- CareUp: a smartwatch with health-care functionalities [9]. The smartwatch can estimate blood pressure (BP), oxygen desaturation (SpO₂), and heart rate from photoplethysmogram (PPG) signals; sleep stages are instead detected from accelerometers data. The smartwatch allows the user to input his medical information, follow treatment, and eventual physician meetings. Finally, an alert button is implemented to send a rescue message (SMS alert) to some specific contacts predefined by the user.
- UpNEA: a connected glove that monitors the user's sleep [10]. The smart glove acquires PPG, SpO₂ and 3-axis accelerometer data for this task. It sends them to a mobile application that redirects this information to a remote server (AeneA) for signal processing.
- AeneA: the remote server collects data sent from the connected devices and then performs the signal processing task on acquired records storing results in a dedicated SQL database. AeneA also hosts a web application that can access the SQL database to allow the user to visualize his health tracking results.

The authors of the present manuscript developed and conceived CareUp and UpNEA. The smartwatch technology and performances were discussed in [9]. The UpNEA architecture instead was proposed in [10]. The sleep monitoring algorithms embedded in AeneA were introduced in two papers: [11] for sleep apnea-related methods and [12] for breathing rate estimation processes.

2. Proposed system and methods

2.1. eCardio: a cardiovascular disease risk forecasting application

eCardio is a cardiovascular disease (CVD) risk prediction platform [8]. This platform is available in two versions: one in the online user dashboard and another embedded in a floor standing tablet. The two versions work the same way and share the same code and user interface.

When a new session is started, the application visualizes a series of questions about his habits and physiological parameters. The list of inputs introduced by the user is presented in Table 1. Once all this information is collected, it is recorded in the AeneA SQL database. Finally, a report containing the ten-year CVD risk prediction is sent to the user by email. The client can repeat the



Fig. 2. eCardio floor standing tablet, installed in a pharmacy.

Table 1

Table of eCardio entries.

eCardio user collected data
Sex, age, weight, height, ethnicity, nationality, total cholesterol, HDL cholesterol, systolic blood pressure, anti-hypertension, diabetes, chronic kidney disease, rheumatoid arthritis, atrial fibrillation, smoke, precedents of cardiovascular diseases, family history involving people with CVD.

test over a certain period to track the effects of his habits upon his health.

A prototype of the floor standing tablet is depicted in Fig. 2. It can be installed in pharmacies, medical clinics, hospitals, or companies. The additional functionality of this system is to provide a statistic about the population that used it. For example, an IT company with eCardio installed could get the information that 30% of its male employees suffer from cholesterol. This averaged information can drive the company to create a prevention (or treatment) program. A big issue in this example concerns privacy requirements for employees' data. Data should be kept inaccessible to third-party users as health insurance partners, protecting personal data from being sold for commercial purposes.

Several models of cardiovascular risk, described in the ANAES report [13], have been proposed. For example, the Procarn model [14] assesses mortality and the occurrence of a heart attack. However, the two most conventionally used models are D'Agostino corresponding to the latest statistics from Framingham and SCORE.

The main feature of eCardio is cardiovascular risk forecasting. This probability is computed using the Framingham [15], and SCORE [16] algorithms. Also, the heart age calculator published by the United Kingdom National Health Service (NHS) was implemented. The equations for these risk functions are based on the Cox statistical model.

2.1.1. Framingham heart study

The Framingham Heart Study [17,18,15] is a long-term research project that began in 1948 in Framingham, a town in eastern Massachusetts, USA. The project aimed to identify risk factors of CVD. The study tracked the effects of smoking, diet, and exercise on

heart diseases. Its findings further emphasized the need to prevent, detect, and treat risk factors in their earliest stages. The study was carried out in collaboration between the National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH) and the Boston University School of Medicine. It was designed to track health information on persons who initially did not show signs of heart disease. Two-thirds of Framingham's adult population (more than 5200 residents), ranging from 30 to 62 years, were included in the original study group. Every two years, these people answered detailed questions about their lifestyle. Throughout the study, researchers kept track of which participants experienced heart disease and which did not. It was possible to study the relations between disease and collected data in this way. In 1971, 5120 recruits (first generation cohort) were added to the study. From the 1990s, the study also included new persons (second-generation cohort) [18] and finally, in 2001, a third-generation cohort [15] was added. The Framingham algorithm embedded in eCardio, was transposed from the work in [15].

2.1.2. Systematic coronary risk evaluation

The Systematic Coronary Risk Evaluation (SCORE) [16] project assembled a pool of datasets from 12 European cohort studies, mainly carried out in general population settings. This project was supported by the European Society of Cardiology (ESC) through the European Association of Preventive Cardiology (EAPC). There were 205178 persons (88080 women and 117098 men) involved in the project, and a ten-year risk of fatal CVD was calculated for high-risk and low-risk regions of Europe. The risk charts are based on gender, age, total cholesterol, systolic blood pressure, and smoking status, with relative risk chart, qualifiers, and instructions. The SCORE algorithm embedded in eCardio, was transposed from the work in [16].

2.1.3. NHS heart age tool

The NHS Heart Age tool [19] is an implementation of the JBS3 Cardiovascular Risk Assessment [20] and is the product of a collaboration among the National Health Service (United Kingdom), Public Health England, University College London, and the British Heart Foundation. This JBS3 cardiovascular risk assessment tool has



Fig. 3. CareUp performing blood pressure estimation.

already been used for many years in Great Britain [21] to estimate the patient's 10-year risk of developing CVD, and to identify high-risk people for primary prevention. This tool can be applied to all individuals except those with established CVD, familial hypercholesterolemia or other inherited dyslipidaemias, chronic renal dysfunction, or type 1 or 2 diabetes mellitus [20]. The heart age tool embedded in eCardio, was transposed from the source code made available online in [22].

Among the others, the choice of these CVD risk tools was based on the geographic area the eCardio product could have been used: the USA and Europe. The ten-year temporal period accounted for all three selected CVD risk predictors.

2.2. CareUp: a smart watch for estimating blood pressure

Raised blood pressure (BP) is the leading cause of death and disability worldwide [23]. Increased pressure in the arteries is common, leading to hypertensive heart disease and CVD. Therefore, accurate BP measurement is vital in preventing and treating such disorders, especially in hypertensive patients. In the USA, about 30% of the population suffers from hypertension and less than 50% of them, monitor their BP [24].

The most common technique in medicine for estimating blood pressure involves using a sphygmomanometer; after that, a non-invasive blood pressure measurement is possible by hearing the Korotkoff sounds (K-sound) [25]. This method is not automatic and requires a person performing the measurement, such as a doctor or a nurse. Automatic devices continue to use a cuff that wraps around the arm: They estimate the BP by detecting pressure oscillations during cuff deflation using a built-in pressure sensor.

The present manuscript unveils a cuff-less method for BP estimation that requires two PPG signals as input. The algorithm is embedded in the CareUp smartwatch [9] and is based on the time delay the blood volume (pulse) takes to travel from the heart to peripheral organs. This time delay is called pulse transit time (PTT) [26–28] and is inversely related to BP [29].

The PTT can be estimated using two PPGs: one obtained close to the heart and one obtained at a distal place. CareUp is made up of two pulse oximeters: one on the back and one on the front. The acquisition of two PPGs is initiated by placing the index finger on the front oximeter. Fig. 3 depicts the BP estimation procedure. The PTT is then calculated by filtering and cross-correlating the signals.

BP is affected by a variety of factors, including vasomotor tones, neural control, and HR [30,31]. As a result, the BP estimation model in CareUp employs two variables: the heart rate (HR) estimated from one of the two PPG signals and the PTT. Manlises et al. initially implemented the model in [32] and adopted a linear regression analysis to produce an estimated systolic and diastolic BP as output.

This approach seems to be dependent on temporal trials, as well as on motion activities [33,34]. For this reason, CareUp

requires a specific calibration to tune the center of the model's constants according to the user's physiological characteristics.

2.3. UpNEA: a smart glove for sleep monitoring

Sleep is a physiological process that has a variety of effects on daily life and is essential for maintaining one's health and well-being throughout one's lifetime [35]. The USA National Institutes of Health acknowledges that chronic sleep deprivation and circadian disruption are new aspects of contemporary urban lifestyles and are linked to decreased public safety and higher disease risk in all age groups [36]. In order to improve the prevention, diagnosis, and treatment of such disturbances, the Congress and the Department of Health and Human Services in the USA have designated sleep and circadian disturbance disorders as high-priority targets for basic and clinical scientific investigation [37].

Sleep quality is primarily influenced by a person's habits and physio-pathological state. As a result, monitoring vital signs while sleeping can aid in preventing, diagnosing, and treating sleep disorders.

The clinically acceptable sleep stages are determined by reading the recorded electroencephalogram (EEG) based on the R&K criteria. These criteria were standardized in 1968 by Rechtschaffen and Kales [38] and further developed by the American Academy of Sleep Medicine in 2007 (AASM 2007) [39].

The gold standard for identifying any sleep disorder is polysomnography (PSG). Various electrophysiological signals, including EEG, electromyogram, electrooculogram, electrocardiogram (ECG), airflow, SpO₂, and PPG, are recorded throughout the night. Because acquiring and analyzing these signals require human expertise and specialized equipment, it is primarily done in medical clinics. Due to the uncomfortable and expensive nature of the diagnostic process, sleep disorders are frequently not adequately diagnosed.

Polygraphy is a less restrictive examination conducted at home for the most straightforward cases to diagnose. Usually, it requires using a nasal cannula to detect the nasal pressure airflow, which could interfere with natural sleep. However, it does not record EEG and thus is not helpful for sleep staging.

For the easiest cases to diagnose, a less stringent examination called polygraphy is performed at home. To detect the nasal pressure airflow, it typically requires using a nasal cannula, which is uncomfortable to wear and frequently disrupts restful sleep. However, because it does not record EEG, it is ineffective for sleep staging.

To investigate the presence of HR abnormalities during sleep, the golden standard methods are the 24-h Holter monitor or the 30-day event recorder [40], employing ECG electrodes adhered to the person's chest. In recent years, wearable solutions for long-term HR monitoring have implemented wrist-wearable PPG sensors to measure HR in free-living conditions continuously [41].



Fig. 4. The UpNEA device and its prototype.

In MonEco, the authors proposed the integration of a smart glove called UpNEA as a less invasive alternative to the PSG and polygraphy. This solution has already been presented by the authors in [10] and integrated into the present ecosystem. The device and its prototype, interfacing with the mobile app, are shown in Fig. 4. The solution aims to keep track of two vital parameters: respiration and heartbeat, using PPG and SpO₂ sensors. Furthermore, the proposed system incorporates some previously validated algorithms for detecting heart rate and breathing rhythm irregularities.

UpNEA acquires PPG, SpO₂ and 3-axis accelerometer signals. For signal processing, it sends them to a mobile application that stores this information into a remote bucket in AeneA. The smart glove implements a zero data loss encoding method, avoiding signals corruption but compressing the transmitted information.

In particular UpNEA is able to perform the following overnight tasks:

- heart rate estimation,
- tachycardia and bradycardia detection,
- atrial fibrillation and premature ventricular contraction detection,
- estimation of breathing rate,
- identification and classification of apnea and hypopnea, and
- overnight segmentation in sleep stages.

The time difference between two successive pulses was used to calculate the beat time duration. To detect and handle ectopic pulses, the method in [42,43] was implemented. The methodology proposed by Bonomi et al. in [44] was included to detect episodes of bradycardia and tachycardia. AF and PVC are detected using Rademeyer's method [45], which was embedded in a wireless device designed to monitor psychiatric patients' heart. The sleep stages detector based on accelerometer data was integrated as described in [10].

In previous works, the authors published a method to detect and classify sleep apnea/hypopnea syndrome from PPG signals [11] and compared the performances of different algorithms for BR estimation in [12]. These methods have been integrated into a sleep monitoring platform called UpNEA, published in [10]. In the present manuscript, the authors want to integrate UpNEA into an ecosystem of smart devices called MonEco, comprehensive of a blood pressure monitor device (CareUp, [9]) and a heart risk predictor app (eCardio, [8]).

2.3.1. Methods for apnea and hypopnea detection and classification

In contrast to hypopnea, which is marked by abnormally low respiratory flow, sleep apnea refers to the cessation of breathing while asleep [46]. Both conditions can be obstructive or central: obstructive when breathing effort is maintained despite an airway obstruction that interrupts airflow; central when neither breathing

effort nor airflow is present. More than 15% of the U.S.A. population suffers from sleep apnea, which increases the risk of heart attack, stroke, and mortality, as well as daytime sleepiness, injuries, hypertension, cognitive impairment, and mortality [37,47–49]. PSG or polygraphy is the gold standard tool for diagnosing these disturbances, but numerous noninvasive techniques have been developed in recent years [50].

As demonstrated in [51] during tilt table tests, the pulse rate time series, which is derived from PPG, serves as a surrogate for the heart rate time series and, consequently, the pulse rate variability (PRV) with regard to the heart rate variability (HRV). HRV represents variations in heart rate related to autonomic nervous system control: the vagal tone is represented by the high-frequency components of HRV, which range in frequency between 0.15 and 0.4 Hz. Low-frequency (LF) components, on the other hand, exhibit the activation of both the parasympathetic and sympathetic nervous systems (from 0.04 to 0.15 Hz). The PRV and the ratio of LF to HF, which is known as the sympathovagal balance [52], have both been used to distinguish between different sleep breathing disorders [53,11].

The designed and published new methods for detecting and classifying sleep apnea and hypopnea [11]. In summary, the detection and classification methods are based on a decrease in amplitude fluctuation (DAP) of the PPG signal, which is usually associated with a sleep-disordered breathing event, as shown in [54–59].

PRV-based features were extracted from 65 seconds PPG temporal windows, centered on the DAP, to differentiate between sleep-disordered breathing event types to account for sympathovagal arousals. Finally, a Fine Gaussian Support Vector Machines (SVM) classifier with a Gaussian kernel was used to distinguish between apneic or hypopneic, obstructive, or central DAP events.

2.3.2. Derive respiratory rate from PPG

Breathing rate (BR) is an essential physiological indicator to diagnose various chronic diseases such as pneumonia and, eventually, cardiac arrest [60]. Capnography is the gold standard measurement technique for BR, but it requires cumbersome equipment that is uncomfortable for long-term monitoring. To reduce the discomfort, recent publications have explored how to derive the respiration signal from the ECG and PPG signals [61–63]. Respiration activity modulates both ECG and PPG signals [64]. Respiratory sinus arrhythmia is the term for the condition where the heart rate rises during inspiration and falls during expiration [65,66]. Due to ventricular filling, the decreased stroke volume in cardiac output causes respiration-induced amplitude variation in the PPG signal [67,68]. The amplitude, frequency, and baseline wander modulations of ECG and PPG signals are used to estimate BR indirectly [62,69,70].

Khreis et al. in [63], implemented the embedded algorithm for breathing rate estimation.



Fig. 5. MonEco web application showing the eCardio report.

The authors chose the best respiration rate estimation method in a comparative study published in [12]. Several techniques were used for comparison, including empirical mode decomposition (EMD), EMD combined with principal component analysis, wavelets analysis, respiratory-induced intensity variation analysis, respiratory-induced amplitude variation analysis, respiratory-induced frequency variation analysis, and data fusion's Kalman Smoother method.

2.4. AeneA web application

A dedicated internet web page hosted by AeneA allows the user to access his data.

In Fig. 5, the web application shows the user the eCardio report based on his daily habits and physiological data.

The customer can also navigate, for example, through the recorded nights and select the one to display. The server imports data from the SQL database and displays them using the Highcharts JavaScript charting engine from Highsoft. Fig. 6 shows a generic overnight plot with no clinical significance. The chart is made up of a zoomable time series, a range selector bar at the bottom, and a legend. The range selector only shows the overnight sleep stages, and a legend is an active tool that allows to show/hide information on the plot. HR, SpO₂, BR signals, apnea and hypopnea detections, and tachycardia and bradycardia events are depicted in colored bands on the chart. Sleep stages are represented in various blue tonalities in the background. When the mouse pointer passes over the yellow bands, each SDBE detection is labeled as apneic or hypopneic, central or obstructive. To avoid overexpression, the red bands of tachycardia and bradycardia have been removed from the figure. Finally, overnight statistics are provided below the graph.

3. System validation

3.1. eCardio validation

Table 2 presents the main differences between the Framingham model and the SCORE index. The table references the work published in [71].

The main risk factors currently identified cannot be modified for age, sex and inheritance but can be modified for hypertension, cholesterol, tobacco, diabetes, and lifestyle (diet and physical activities). Other indicators such as risk factors, such as menopause in women, metabolic syndrome (including the body mass index), physical inactivity, and unfavorable socio-economic conditions are also recognized. Nevertheless, they have not been integrated into the conventionally used risk models, either because they have not been taken into account in the studies or because they prove to be non-significant for the performance of the risk model.

The accuracy of these models is analyzed by comparing the predicted risk with the reality observed in large numbers of patients followed for several years. Under these conditions, the Framingham model underestimates the risk in high-risk populations and overestimates the risk in low-risk populations [74]. This last point is particularly marked in the countries of southern Europe like in Spain [75] and in France, where corrections are necessary, compared to the original Framingham model. The work of Laurier in 1994 [76], Vergnaud in 2008 [77] (3440 men aged 45 to 60), and Empana in 2003 [78] (9750 men followed for five years) converge to show an overestimation of risk according to Framingham by a factor of 2 to 2.3 for the French population.

The value of the Score index (for low-risk countries) is 7 to 10 times lower than the Framingham index. It is because only one part is reduced by all the events considered in Framingham. On

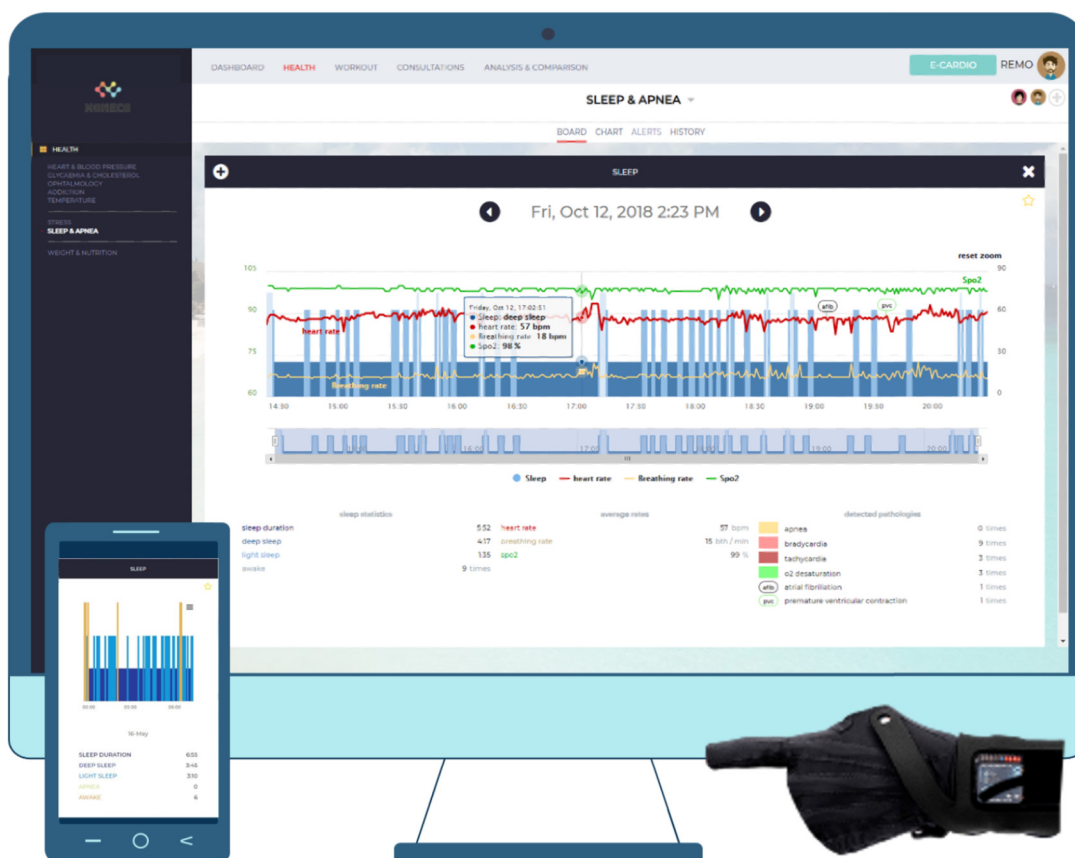


Fig. 6. MonEco web application plotting overnight sleep monitoring. For interpretation of the colors in the figure, the reader is referred to the web version of this article.

Table 2
Comparison table between the Framingham and SCORE study.

Model	Framingham	SCORE
Promoter Program	American: NIH [72] Extensive permanent research program, since 1948.	European: ESC [73] Group of studies was carried out in 12 European countries in 2003.
Population	8491 participants followed over 12 years, with 1174 cardiovascular events.	12 national cohorts totaling more than 200000 patients with 7934 deaths.
Type of risk	Composite morbidity and mortality: coronary, cerebral events, lower limbs arteritis, and heart failure.	Cardiovascular mortality only.
Reference risk	Patients of the same age whose risk factors would be ideal: Total cholesterol 1.8 g/l, HDL-cholesterol 0.45 g/l, SBP 125 mmHg, tobacco and diabetes-free.	
High/Low risk	High risk if >20% Intermediate between 10 and 20% Low risk if <10%	High risk if >5%
Remarks	The risk is lower for a population in Western Europe. For France, the risk must be divided by approximately 2.	Diabetes is not considered in the equations because these patients are considered a priori at high risk (it is necessary to multiply the SCORE index by two at least).

the other hand, it could be since the Framingham index practically overestimates the occurrence of events in France by a factor of 2 compared to what is observed in the USA [71].

The National Institute for Health and Care Excellence (NICE, UK) guidance (2010) does not recommend any particular risk calculator [79]: the Framingham risk equation may overestimate risk in UK populations as much as 5% for UK men [80].

3.2. CareUp validation

The validation was performed on 44 subjects in a clinical context, in the Institut Coeur Paris Centre Turin (ICPC) in Paris. Patient characteristics were heterogeneous: males and females with an age of 67 ± 13 years, with European, Caucasian and African skin color; some of them were in health status, while others had car-

Table 3

Results comparison for SBP and DBP estimation on 126 measures from 44 subjects, taken in the Institut Coeur Paris Centre Turin (ICPC) in Paris. The acquisitions were performed using a sphygmomanometer as a reference device and CareUp.

	CareUp	
	SBP	DBP
\bar{e}_{dev}	-1.52	0.39
σ_e^{dev}	9.45	4.93
p_{dev}	0.6338	0.7249

Table 4

Table showing the results comparison for SBP and DBP pressure estimation on 78 measurements from 44 subjects, acquired in the ICPC clinic in Paris. The acquisitions were performed using a sphygmomanometer as a reference device, Magnien® and CareUp.

	Magnien		CareUp	
	SBP	DBP	SBP	DBP
\bar{e}_{dev}	-3.44	-0.94	-1.97	0.31
σ_e^{dev}	15.08	12.00	10.56	3.57
p_{dev}	0.2328	0.8928	0.6952	0.7725

diac arrhythmia, coronary occlusion, or a pacemaker implant. Each acquisition consisted of different measurements performed with different devices: the reference device was a sphygmomanometer mechanically inflated using a manual pump, and the comparison devices were CareUp and two oscillometry-based devices already available on the market: Thuasne® and Magnien®. A total of 126 measurements were taken using the sphygmomanometer and CareUp, with a mean of three acquisitions per patient; of the 126 measures, 78 were also performed using Magnien® and 76 also using Thuasne®. A professional conducted acquisitions and all devices were always worn on the same wrist. The reader can find more information about the trial in [9].

The mean and standard deviation of the errors (calculated as the measurement difference between the reference and the device) were computed, and the Wilcoxon rank-sum test was conducted.

As a reference for the reader, the AAMI standard for non-automated sphygmomanometers authorizes a mean error difference of less than five mmHg and an error standard deviation within 8 mmHg [81]. The Wilcoxon rank-sum test compares whether or not two independent samples come from identical continuous distributions with equal medians.

The comparison on 126 measures between the sphygmomanometer and CareUp is reported in Table 3. Table 4, on the other hand, reports the results for the comparison, on 78 measurements, between the reference, CareUp, and Magnien®. Finally, Table 5 presents a comparison of the sphygmomanometer, CareUp, and Thuasne®, on 76 measures. The mean error, standard deviation error, and p-value of the Wilcoxon rank sum test performed on the device acquisitions are shown in these tables.

The results demonstrate the method's robustness to a variety of physiological characteristics and pathologies. They also prove that there is no statistically significant difference in SBP measurement between market-available devices and CareUp. Furthermore, the smartwatch outperformed the other devices in DBP estimation. Based on the p_{dev} -values, the Wilcoxon tests confirmed that the measures taken with the reference and those taken with the CareUp smartwatch share the same median: the CareUp data distribution was the closest to the reference. Finally, thanks to several experiments, it is possible to claim that the CareUp measurements met AAMI standards.

Table 5

Results comparison for SBP and DBP pressure estimation on 76 measures from 44 subjects, taken in the ICPC clinic in Paris. The acquisitions were performed using a sphygmomanometer as a reference device, Thuasne® and CareUp.

	Thuasne		CareUp	
	SBP	DBP	SBP	DBP
\bar{e}_{dev}	-3.86	-5.42	-2.08	0.17
σ_e^{dev}	15.34	16.16	11.67	4.45
p_{dev}	0.0397	0.0296	0.6409	0.9222

Table 6

Total number of sleep disordered breathing events, per category, in the database.

	CA	CH	OA	OH	MA
Number of events	765	689	4984	14,140	750
Percentage of events	3.6%	3.2%	23.4%	66.3%	3.5%

Table 7

Apnea and hypopnea detection results.

	CA	CH	OA	OH
Se [%]	86.6	73.3	86.4	76.2
Sp [%]	55.3	57.4	57.2	68.2
Acc [%]	70.9	65.4	71.8	72.2

3.3. UpNEA validation

3.3.1. Methods for apnea and hypopnea detection and classification

The methods were tested on 96 overnight signals from patients with sleep apnea/hypopnea syndrome and no collateral morbidity at the UZ Leuven hospital. Each record included a PPG and a SpO₂ signal sampled at 500 Hz, and the apnea-hypopnea index (AHI) was calculated using the AASM 2012 rules [82]s. In the UZ Leuven hospital dataset, the average AHI is 31.3, and 39 percent of the subjects had an AHI greater than 30; 53 percent had an AHI between 5 and 30, and the remaining 8 percent had an AHI less or equal to 5. The start and end times of central apnea (CA), central hypopnea (CH), obstructive apnea (OA), and obstructive hypopnea (OH) are all annotated. The total number of annotations in the database per sleep-disruptive breathing event (SDBE) category is shown in Table 6.

For overnight sleep apnea/hypopnea detection, each PPG recording was divided into one-minute segments. Then, 3-fold cross-validation (CV) was performed: two-thirds of the patients in the database trained the detector parameters and one-third tested the trained detector at each fold. The 3-fold CV was performed on each patient separately, with no re-substitution. Because PPG features can be patient-specific, it was decided that each patient should be included in either the detection test set or the detection training set to ensure proper generalization to new subjects.

The authors published the algorithms for apnea and hypopnea detection in [11] and embedded them in UpNEA [10]. Those methods had a 75.1 percent accuracy (Acc) for detecting apneic/hypopneic events in one-minute segments, with 76.9 percent sensitivity (Se) and 73.2 percent specificity (Sp). The detection Se, Sp, and Acc values of the different sleep-disordered breathing events are reported in Table 7. To build the table, a criterion was adopted to compute the metrics: e.g., considering central apnea detection, a sleep-disruptive breathing event was considered FP when it did not correspond to a central apnea annotation, even if other apnea types were present.

Furthermore, those algorithms were tested on patients with a low AHI index ($AHI \leq 5$), and their results are shown in Table 8.

Table 8Apnea/Hypopnea Detection results on patients with AHI ≤ 5 .

Event Type	Se [%]	Sp [%]	Acc [%]
All	79.9	75.8	76.1
Central Apnea	100	72.0	72.2
Central Hypopnea	83.6	72.4	72.6
Obstructive Apnea	88.9	63.6	63.8
Obstructive Hypopnea	76.8	74.2	74.3

Table 9

Respiratory events classification performances for Fine Gaussian SVM.

		TPr [%]	FPr [%]	Acc [%]	AUC
C-O	C	95	10	93	0.97
	O	90	5		
CA-CH	CA	86	19	84	0.91
	CH	82	14		
OA-OHA	OA	85	20	83	0.89
	OHA	81	14		

When we compare the apnea and hypopnea detector results from the comprehensive database to those from patients with low AHI, we see no significant difference, confirming the detector's robustness. Finally, those methods produced comparable results to those found in the literature when tested on the same database, [83–85].

In order to classify SDBEs in CA, OA, CH, and OH, 37 features were extracted from the PPG and SpO₂ signals corresponding to the SDBE time frame. Because of the heterogeneous distribution of SDBE types among patients, a dataset containing labeled extracted features was created without implementing a Leave One Subject Out (LOSO) procedure. A subsequent step involved balancing data so that the same amount of information represented each class. The dimensionality problem was then addressed by implementing a feature selection algorithm. A 10-fold CV was then used to train and test the Fine Gaussian Support Vector Machine model.

Additionally, in [11], authors also published the classification method designed on the detected DAP events to discriminate between central and obstructive, apneic and hypopneic events. The classification was performed with a Fine Gaussian SVM classifier and yielded 92.6 percent Acc in distinguishing central from obstructive apnea, 83.7 percent in distinguishing central apnea from central hypopnea, and 82.7 percent in distinguishing obstructive apnea from obstructive hypopnea. Table 9 displays the True Positive (TPr = Se) and False Positive (FPr = 1 - Sp) rates, as well as the Acc and ROC area under the curve (AUC) obtained with the classification. In comparison, no other work on the same database was done to classify the SDBE subtypes.

It should be noted that these results were obtained using signals acquired by devices available at the UZ Leuven clinic rather than from the proposed UpNEA device. To simulate the UpNEA acquisition, the database signals were downsampled at 100 Hz before processing. Due to cost and time constraints, launching a clinical protocol for the presented device was not possible. Nonetheless, because the proposed platform transmits lossless data by design, the authors conclude that hardware validation is unnecessary.

3.3.2. Derive respiratory rate from PPG

The public CAPNOBASE database [86], which contains 42 subjects (29 children and 13 adults) with simultaneous ECG and PPG recordings, was used to validate different respiratory rate estimation algorithms. For each subject, eight minutes of high-quality data were collected during elective surgery or routine anesthesia. The capnography waveforms were manually labeled by the study's

Table 10

Results comparison in [bpm], of methods tested on the same CAPNOBASE database.

	Khreis (2019)	Pimentel (2016)	Karlen (2013)	Flemming (2007)	Shelly (2006)	Nilsson (2000)
	32 s					
Median	0,50	1,50	1,20	1,40	4,50	10,50
IQR	0,90	3,00	2,90	3,30	9,70	7,80
Q1	0,20	0,30	0,50	0,50	0,80	4,90
Q3	1,10	3,30	3,40	3,80	10,50	12,70
	64 s					
Median	0,20	1,90	0,80	1,10	2,20	10,20
IQR	0,80	3,10	2,40	3,10	8,10	7,60
Q1	0,10	0,30	0,30	0,40	0,20	4,80
Q3	0,90	3,40	2,70	3,50	8,30	12,40

authors, and the annotations of BR were used as reference; methods comparison was performed by segmenting the PPG signal in 32 s and 64 s windows.

Khreis developed the PPG breathing rate estimation algorithm [63], integrated into the proposed sleep monitoring solution [10]. By segmenting the signal in 32 s windows, the absolute median error was 0.5 breath per minute (0.2–1.1 interquartile range 25th–75th) and 0.2 breath per minute (0.1–0.9) for the 64 s windowing. These results outperformed others proposed by Pimentel in 2016 [87], Karlen in 2013 [69], Flemming in 2007 [88], Shelly in 2006 [89], and Nilson in 2000 [90].

For an exhaustive comparison of the breathing rate estimation algorithms, the reader can find more information in [12]. In the present manuscript, Table 10 reports the performances of methods tested on the same CAPNOBASE database and proposed by the following authors: Khreis in [63], Pimentel in [91], Karlen [92], Flemming [88], Shelly [89] and Nilson [90]. The Table shows the absolute errors expressed as the median, mean, interquartile range (IQR), 25th (Q1), and 75th (Q3) percentile. These values are obtained by evaluating breathing segments from 0–0.5 Hz.

Finally, the best performing algorithm was implemented by Khreis et al. in [63], that tracks the respiration signal, using the Kalman smoother, to fuse modulation signals with the highest respiratory quality indices.

3.3.3. UpNEA performances

Finally, UpNEA was employed in [10] to monitor four nights of sleep on a 30 years old healthy male subject not suspected to have apnea or hypopnea syndrome. The subject voluntarily wore the UpNEA smart glove for four nights and reported no sleep discomfort while wearing the acquisition device. The apnea and hypopnea detection and classification analysis was performed by segmenting the entire night recording into one-minute segments and running the algorithm through the remote server AeneA. Even though even a completely healthy person could have some apneic/hypopneic episodes, it was supposed that no apneas or hypopneas were present for testing purposes. The tests results showed a detection specificity of 96.2%. The specificity value obtained on the four nights' recordings were most likely due to the absence of desaturation in correspondence to the detected DAP event. In conclusion, the authors proposed this test as support for a proof-of-concept of UpNEA.

4. Discussion

4.1. eCardio

The awareness of the importance of risk factors has already led to a significant reduction in myocardial infarcts and mortality linked to a heart attacks in Europe and the United States. For example, in Ontario (USA), the 35% drop in heart attack mortality

observed between 1994 and 2005 is explained half by the effect of therapeutics and half by preventive measures against the main risk factors [93].

In order to maintain good cardiovascular health, the ESC recommends [94] to control all the main risk factors: no tobacco, healthy food, at least half an hour of physical activity per day, body mass index (BMI) < 25, BP < 140/90 mmHg, Total cholesterol < 5 mmol (1.9 g/l), LDL-cholesterol < 3 mmol/l (1.15 g/l) and blood sugar < 6 mmol/l (1.1 g/l).

eCardio aims to make its user aware of their cardiovascular risk. Different factors can play a role in lowering the risks: new treatments, sports, and alimentary habits changes can influence the overall risk report. For this reason, the eCardio questionnaire, if performed with a certain regularity (e.g., every three or six months), can allow the user to assess if his new habits or treatment affected his cardiovascular risk.

4.2. CareUp

The smartwatch's BP estimation performance was validated at the Institut Coeur Paris Centre Turin (ICPC) using a sphygmomanometer on 44 subjects. During the validation, the CareUp measures were compared to those of two existing oscillometry-based devices on the market: Thuasne® and Magnien®. The CareUp results were comparable to oscillometry-based devices measurements in terms of accuracy; additionally, they met the American Association for the Advancement of Medical Instrumentation standard for non-automated sphygmomanometers.

In this way, CareUp becomes an easy-to-use, wearable device for monitoring blood pressure in real-time by incorporating the BP estimation task into a smartwatch. The user can register HR, SpO₂ and BP at different times in a day, and all those values will be registered into the AeneA SQL database to be available for the user upon request. During sleep, CareUp can also detect sleep stages from accelerometer data, using the same algorithm embedded in UpNEA.

4.3. UpNEA

UpNEA is a proof-of-concept system for non-invasive sleep monitoring. This platform's strength is its flexibility and scalability, and it is aimed at individuals and clinics that perform polysomnography. The zero data loss encoding method built into the system's hardware enables it to communicate and transfer data without degrading signal quality. Different studies published in the literature put the algorithms integrated into the smart glove to the test. Continued validation of the proposed sleep monitoring platform as a medical solution complementary to polysomnography will be of great interest.

5. Conclusion

The manuscript proposes an ecosystem that integrates different connected devices. The authors developed and tested them in separate works. MonEco aims to transform the doctor-patient relationship, letting the patient become a player in his health, particularly in improving his lifestyle or monitoring illnesses. The proposed system presents a smartwatch for blood pressure estimation (CareUp, [9]), a smart glove for sleep monitoring (UpNEA, [10]) and a cardiovascular risk prediction platform (eCardio, [8]). Performances of blood pressure estimation performed by the smartwatch have been evaluated in a clinical study and are comparable to those reported by commercially available devices [9]. The presented sleep monitoring activity provides sleep apnea and hypopnea detection and classification tasks, heart rate variability assessment, and sleep stages recognition [10]. All these methods

have been validated on annotated clinical datasets showing the feasibility of the solution [11,12]. The authors are convinced that similar ecosystems of health monitoring devices will continue to spread in the future; for this reason, the present paper wants to inspire and suggest new ideas about this future technology challenge.

Human and animal rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans as well as in accordance with the EU Directive 2010/63/EU for animal experiments.

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Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

Declaration of competing interest

The authors declare that they have no known competing financial or personal relationships that could be viewed as influencing the work reported in this paper.

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