

Continuous vital sign monitoring in COVID-19 patients

E.M. BIEL, BSc

Graduate Intern Technical Medicine

University of Twente

University Medical Centre Utrecht

Division Vital functions

Department of Anaesthesiology and the COVID-19 cohort ward

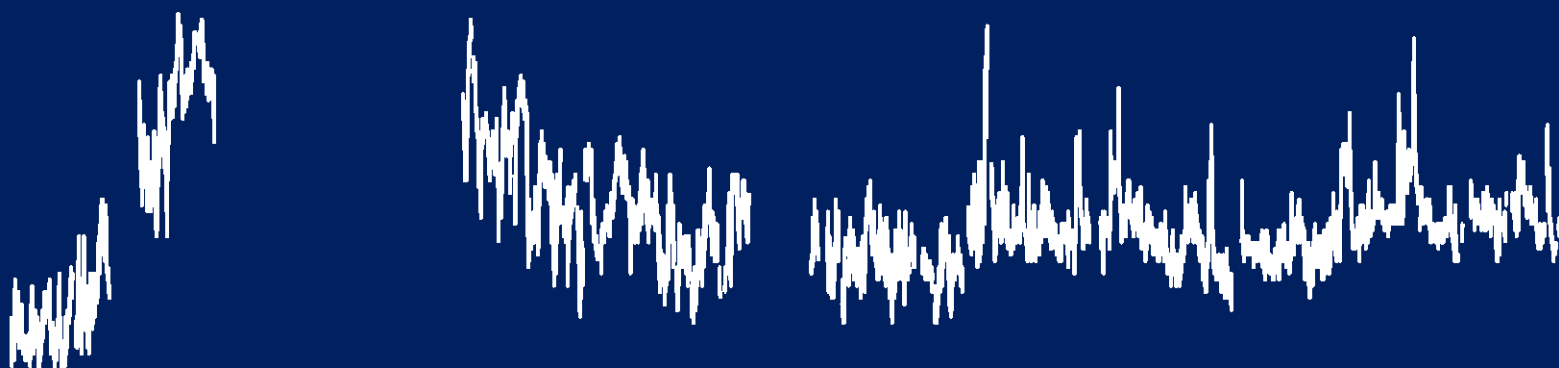
SUPERVISORS:

Medical supervisors: Prof. dr. C.J. Kalkman and M.J.M. Breteler, MSc

Technical supervisors: Prof. dr. ir. H.J. Hermens and M.C. van Rossum, MSc

Process supervisor: R.J. Haarman, MSc

External member: dr. ir. B.E. Westerhof



Author's information

Author: E.M. (Elin) Biel
Email: elinbiel@gmail.com
Tel: +31 6 46666073

Study programme

Technical Medicine (TM), master's track: Medical Sensing and Stimulation (MSS)
Faculty of Science and Technology
University of Twente, Enschede, the Netherlands

Institution and department of graduation

Department of anaesthesiology and the COVID-19 cohort ward
Division of Vital Functions
University Medical Centre Utrecht (UMCU), Utrecht, the Netherlands

Graduation committee

Prof. dr. ir. H.J. Hermens
Professor Neuromuscular control & Telemedicine
Biomedical Signals and Systems, University of Twente, Enschede, the Netherlands

Chairman and technical supervisor I

Prof. dr. C.J. Kalkman
Professor of anaesthesiology
University Medical Centre Utrecht, Utrecht, the Netherlands

Medical supervisor

M.J.M. Breteler (MSc)
Technical Physician & PhD Candidate
University Medical Centre Utrecht, Utrecht, the Netherlands
And
Clinical research specialist
Luscii Healthtech BV, Amsterdam, the Netherlands

Daily supervisor

M.C. van Rossum (MSc)
Technical Physician & PhD Candidate
Biomedical Signals and Systems and Cardiovascular and Respiratory Physiology, University of Twente, Enschede, the Netherlands

Technical supervisor II

R.J. Haarman (MSc)
Teacher 'vaardig communiceren en professioneel gedrag' (skillfull communication and professional behaviour)
Psychologist, supervisor and coach
Technical Medicine, University of Twente, Enschede, the Netherlands

Process supervisor

Dr. ir. B.E. Westerhof
Senior researcher
Cardiovascular and Respiratory Physiology, University of Twente, Enschede, the Netherlands

External member

ABSTRACT

Introduction The ongoing pandemic of the coronavirus disease 2019 (COVID-19) has put a huge pressure on all aspects of modern-day society. Healthcare systems are being faced with enormous challenges when it comes to managing capacity and dealing with high admission rates of critically ill patients. Hospitals have quickly adapted, for example by accelerating implementation processes of healthcare innovations. At the University Medical Centre of Utrecht a system for continuous vital sign monitoring was implemented at the COVID-19 cohort ward to support healthcare professionals and improve insight into continuous vital sign data of COVID-19 patients. This research focuses on evaluating the implementation process at the COVID-19 ward and analysing the acquired data to assess the possibilities of quantitatively detecting patient deterioration.

Methods The first component of this research concerns the evaluation of the implementation process of the continuous monitoring system, which was done by distributing two different questionnaires (among nurses and members of the monitoring team who were responsible for monitoring the data and operating the system). The second component concerns a case series report in which the continuous heart rate (HR) and respiratory rate (RR) data of eight selected patients was visually and quantitatively analysed along with patient specific context information. The third component concerns the exploration of quantitatively detecting patient deterioration by means of trend detection. This was done by developing a set of moving linear regression algorithms that were evaluated by applying them to the continuous HR and RR data of patients that experienced a severe case of deterioration.

Results The nurses and the monitoring team showed a positive attitude towards the monitoring system. Short-term implementation processes can be optimised by focussing on adequate integration of the monitoring system into the workflow of nurses. Long-term implementation processes can be optimised by developing and upgrading both hardware and software components of monitoring systems. Continuous monitoring at the COVID-19 ward can be used to visually detect clinical deterioration as well as recovery by respectively observing a steadily increasing trend and a sinusoidal pattern that matches the circadian rhythm. Quantitative methods that were proposed to explore the feasibility of detecting patient deterioration by means of trend detection showed moderate results.

Conclusion Continuous vital sign monitoring is a valuable tool at the COVID-19 cohort ward, and implementation of continuous monitoring systems at other wards is recommended. Future work is needed to optimise continuous monitoring systems in terms of improving implementation processes and upgrading both hardware and software components (e.g. improving notification systems).

LIST OF ABBREVIATIONS

(+)ssRNA	positive-sense single stranded RNA
2019-nCoV	first, temporary name of SARS-CoV-2
ABCDE	airway, breathing, circulation, disability, environment/exposure
ACE	angiotensin-converting enzyme
ARDS	acute respiratory distress syndrome
AVPU	alert, reaction to voice, reaction to pain, unconsciousness
BP	blood pressure
bpm	beats per minute
brpm	breaths per minute
CCI	charlson comorbidity index
CE	conformité européenne
CoV	coronavirus
COVID-19	coronavirus disease 2019
ECG	electrocardiogram
EPR	electronic patient record
EWS	early warning score
FDA	food and drug administration
FiO ₂	fraction of inspired oxygen
HR	heart rate
ICU	intensive care unit
IGS	intellivue guardian software - by Philips
IQR	interquartile range
MCU	medium care unit
MERS-CoV	middle east respiratory syndrome coronavirus
MET	medical emergency team
MEWS	modified early warning score
NRB	non-rebreating mask
OLS	ordinary least squares
OR	operating room
PPG	photoplethysmogram
R ²	coefficient of determination
RF	respiratory failure
RR	respiratory rate
SARS	severe acute respiratory distress syndrome
SARS-CoV	severe acute respiratory distress syndrome coronavirus
SARS-CoV-2	severe acute respiratory distress syndrome coronavirus 2
Slice _{step}	slice steps for time slicing
Slice _{window}	window length for time slicing
Slope _{ols}	estimated slope of the OLS regression model
SpO ₂	oxygen saturation
UMCU	university medical centre utrecht
WHO	world health organisation

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1 INTRODUCTION

The rise of the ongoing pandemic

After a series of pneumonia cases in the city of Wuhan (capital of the province Hubei in China) in December 2019, a new type of human-infecting virus was found. On the 9th of January, the World Health Organisation (WHO) reported that the ongoing outbreak was caused by a novel coronavirus (at that point referenced to as '2019-nCoV'). On the 11th of January, the first death due to the consequences of an infection with 2019-nCoV was reported. Shortly after, on the 13th of January, the first infection outside China, was reported in Thailand. [1, 2]

On the 30th of January, the WHO declared its highest level of alarm: a '*public health emergency of international concern*', defining the situation as 'an extraordinary event which is determined to constitute a public health risk to other states through the international spread of disease and to potentially require a coordinated international response'. On the 11th of February, the WHO officially named the disease that was caused by the novel coronavirus the 'coronavirus disease 2019' – abbreviated as 'COVID-19'. In addition, the Coronavirus Study Group of the International Committee on Taxonomy of Viruses renamed the virus based on phylogenetic analyses. The virus was renamed to the 'severe acute respiratory syndrome coronavirus 2' (abbreviated as 'SARS-CoV-2') based on its genetic relations to SARS-CoV. [2–7]

On the 8th of March 2020, the total number of confirmed infections with the SARS-CoV-2 virus, surpassed the number of a 100,000 cases. Shortly after, on the 11th of March, the WHO expressed the severity of their concerns, stating that the ongoing situation could be defined as a *pandemic: a worldwide spread of a new disease*. [2, 8, 9]

On the 13th of March, Europe had become the new epicentre of the pandemic instead of the Western Pacific. A few weeks later, on the 4th of April, the WHO reported that the number of confirmed infections with the SARS-CoV-2 virus had surpassed a 1,000,000 cases. Since then, numbers have kept increasing, and multiple guidance strategies on how to deal with this critical situation have been published by the WHO. Updates on these strategies include advice on the use of facemasks, advice on movement restrictive measures such as the nowadays commonly known 'lockdowns', and reports on clinical trials on the use of medication such as hydroxychloroquine and dexamethasone. The truth is, that the pandemic is still very much ongoing, and that SARS-CoV-2 is still dominating society as we know it. [2]

The epidemic curves

Figure 1 depicts the epidemic curve (version 14/01/2021) of the ongoing COVID-19 pandemic. Since the first contamination at 'ground zero' in Wuhan, the SARS-CoV-2 virus has rapidly spread on a global level [8, 9]. From China, the virus spread throughout more countries in Asia, after which it was carried to other continents. A new epicentre arose in Lombardy, a popular winter sports region in Italy. Through this new epicentre, the virus quickly spread to all European countries. Simultaneously, the SARS-CoV-2 virus was carried to other continents, especially affecting the Americas. The epidemic curve depicted in figure 1 and the curve regarding the number of deaths as a consequence of COVID-19 in figure 2 clearly show the high rate at which the SARS-CoV-2 virus spread from the Western Pacific to the entire world, inevitably resulting in a pandemic in March 2020. [10–13]

After the formal declaration of the situation being a pandemic, the daily reports of confirmed infections kept increasing. As of now (14/01/2021), a total of 90,759,370 cases have been confirmed since the first set of cases in December 2019. Following the number of confirmed cases, a total of 1,963,169 deaths have been reported. Note that these number only include *confirmed* cases or deaths that have been reported as a consequence of COVID-19; the *actual* number of cases and deaths due to COVID-19 will be even higher. [12]

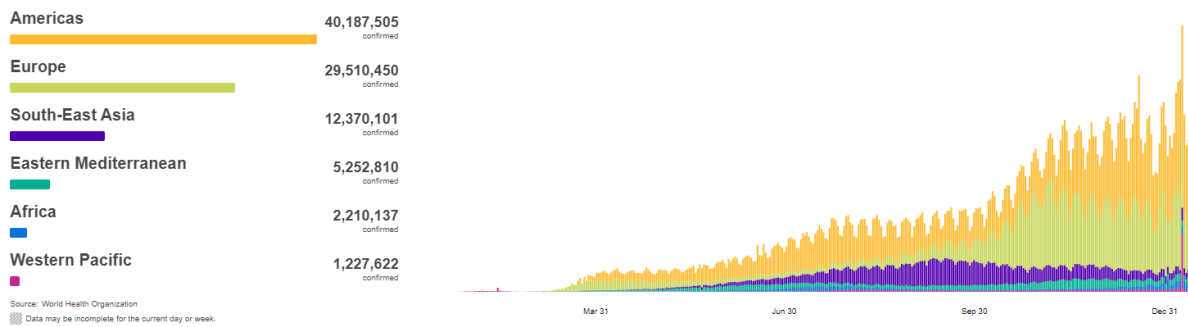


Figure 1: This figure depicts the epidemic curve of COVID-19 infections on a global scale per WHO region. The numbers that are stated on the left side of the curve represent the number of confirmed cases per WHO region. [12]

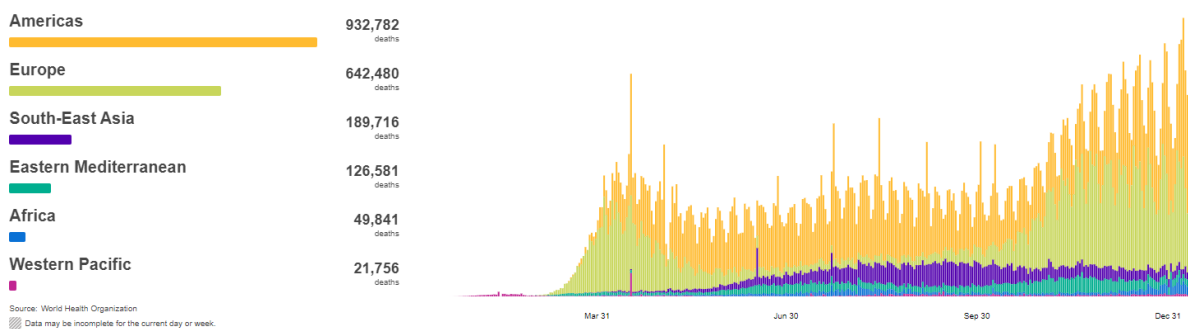


Figure 2: This figure depicts the number of deaths as a consequence of COVID-19 infections on a global scale per WHO region. The numbers that are stated on the left side of the curve represent the number of deaths as a consequence of COVID-19 infections per WHO region. [12]

When studying figures 1 and 2, it can be deduced that the situation in Europe is characterised by two waves: the first from around the start of March until the end of May, and the second wave initiating in September, still ongoing (14/01/2021). This phenomenon of two distinct waves is also applicable to the Netherlands – the country in which this research was executed. The epidemic curve and the curve regarding the number of deaths as a consequence of COVID-19 for the Netherlands specifically, is included in figures 3 and 4. Once again, note that these numbers only include *confirmed* cases or deaths that have been reported as a consequence of COVID-19; the *actual* number of cases and deaths due to COVID-19 will be higher (mainly due to the substantial increase in testing capacity).

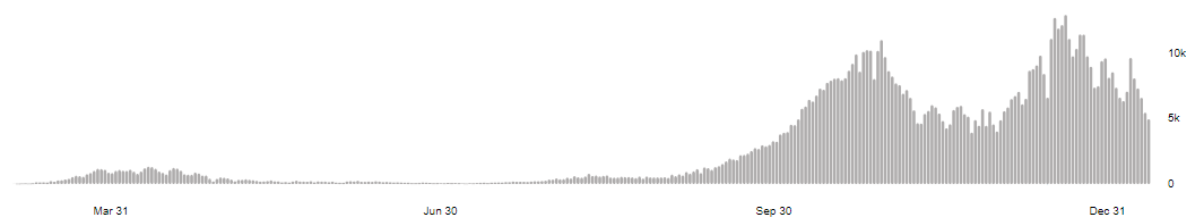


Figure 3: This figure depicts the epidemic curve of COVID-19 infections in the Netherlands. [12]



Figure 4: This figure depicts the number of deaths as a consequence of COVID-19 infections in the Netherlands. [12]

For the remainder of this report, when referring to the 'waves', we refer to the 'waves' of COVID-19 infections in the Netherlands. When referring to the 'first wave', we refer to the series of COVID-19 infections from the start of March until mid-May. When referring to the 'second wave', we refer to the series of COVID-19 infections from the start of September until now (14/01/2021).

The effect of the pandemic on society

Since the formal declaration of the COVID-19 outbreak being a pandemic, the world as we know it has changed. The pandemic has put enormous pressure on healthcare institutions, governments, and society in general. As a response to the COVID-19 pandemic, countries have taken various measures, depending on the severity of the situation. Some countries have enforced temporary lockdowns, meaning that the movement of the population is restricted. On the other hand, some countries have (had) less strict measures, allowing their citizens to move around freely, provided that they keep their distance of for instance 1.5m from one another and stay at home as much as they can. Most countries have a varying set of measures, which are flexibly strengthened or eased, based on the severity of the situation at that moment. In the end, all measures are implemented to flatten the epidemic curve, while hospitals simultaneously raise their capacity when the number of COVID-19 cases increases.

As do all medical interventions, the measures that are being taken to flatten the epidemic curve, come with side effects. The ongoing pandemic has resulted in an increase of mental health problems due to multiple reasons. For example: increased loneliness as a consequence of social distancing and (self-)isolation, the anxiety of getting infected, concerns for the health of loved ones or the financial uncertainty and possibility of losing a job. [14–17] This last concern is realistic, as the economy has been affected by the impact of the pandemic [18]. In addition, movement restriction for the population is having its effect on the environment. Through multiple routes, such as less travelling for work or recreation, the measures have indirectly resulted in a decrease of air and water pollution (especially in big, overpopulated cities) [19–21]. Last, but definitely not least important, the COVID-19 pandemic is having an effect on healthcare itself.

The disease characteristics of COVID-19

COVID-19 symptoms are reported to range from asymptomatic, to mild, and to severe with progression to acute respiratory distress syndrome (ARDS). In a research in China on 44,672 COVID-19 patients, 81% had mild manifestations, 14% had severe manifestations and 5% has critical manifestations (defined as respiratory failure, septic shock and/or multiple organ dysfunction). Additionally, a study of 20,133 COVID-19 patients in the United Kingdom reported that 17,1% of hospitalised individuals were admitted to high-dependency or intensive care units (ICUs). [22–24]

The incubation period has been reported to be approximately 5 days (median with an interquartile range – IQR – of 2-7) [25, 26]. Most patients who develop symptoms, will do so within 11.5 days after the initial infection [25]. For COVID-19 patients in need of hospital care, the median (IQR) number of days from symptom onset to hospital admission is 7 (3-9) [27]. Hospitalised patients comprise for 60% of male adults, and the median age of patients in need of hospitalisation varies from 43 to 73 years in different publications [22, 23, 26]. Most hospitalised patients are over 50 years old [23, 27]. [24]

Approximately 60 to 90% of hospitalised COVID-19 patients are reported to have comorbidities, whereas 25% of the total group of infected patients has comorbidities, suggesting that patients with comorbidities are more at risk for hospitalisation [22, 23, 27, 28]. Predominant comorbidities are hypertension (reported to be present in 48%-57%), diabetes (reported to be present in 17%-34%), cardiovascular disease (reported to be present in 21%-28%), chronic pulmonary disease (reported to be present in 4-10%), chronic kidney disease (reported to be present in 3%-13%), malignancy (reported to be present in 6%-8%) and chronic liver disease (reported to be present in <5%) [22, 23, 27]. [24]

The predominant symptoms are fever (reported to be present in up to 90%), dry cough (reported to be present in 60%-85%), dyspnoea (reported to be present in 53%-80%), fatigue (reported to be present in 38%), nausea/vomiting and/or diarrhoea (reported to be present in 15%-39%) and myalgia (reported to be present in 15%-44%). Other, less prevalent symptoms are isolated gastrointestinal symptoms, olfactory and/or gustatory dysfunction, headache, productive cough, and haemoptysis. [22–24, 26–33]

Complications of COVID-19 include impaired function of the heart, brain, lungs, liver, kidney and the coagulation system. Venous and arterial thromboembolic events occur in 10-25% of hospitalised COVID-19 patients. At the ICU, these events may occur in up to 59% of COVID-19 patients. A predominant thrombo-embolic event is the development of a pulmonary embolism, which often results in sudden and severe clinical deterioration. It is vital to timely detect such acute events to provide adequate and rapid treatment. [24, 34–38]

In short, the severity of the disease pattern differs per individual. Hospitalised COVID-19 patients are generally very sick and require a lot of attention and support in order to recover, while being nursed in isolation. Patient monitoring is vital to detect clinical deterioration: both 'long-term' deterioration due to respiratory failure and rapid deterioration due to prevalent thrombo-embolic events. Therefore, healthcare is faced with a two-faced challenge: significantly increasing hospital capacity in order to keep up with the high influx of COVID-19 patients, and optimising nursing care while dealing with the difficulties that come with nursing in an isolation setting.

The effect of the pandemic on healthcare (and our creative responses)

During the two COVID-19 waves in the Netherlands, regular healthcare has been downsized or postponed to increase capacity for COVID-19 patients. A huge burden has been put on healthcare professionals, quickly shifting from their usual working activities, to work at designated COVID-19 departments. Changes in healthcare that have been initiated in these two waves of COVID-19 infections, or accelerated implementation processes of healthcare innovations, will undoubtedly affect healthcare as we know it in the long run. [15–17, 39]

With regard to the accelerated implementation of promising healthcare innovations, the University Medical Centre of Utrecht (UMCU) – the centre at which this research takes place – has been no exception. The UMCU has creatively adapted to the situation and has shown to be flexible and quick with respect to up- and downscaling the hospital's capacity. In addition, one of the COVID-19 cohort wards, was rapidly equipped with innovative technology for the continuous monitoring of hospitalised COVID-19 patients.

Prior to the first wave in the Netherlands, continuous monitoring at the UMCU was limited to advanced clinical environments, such as the operating room (OR) and the intensive care unit (ICU). At a regular nursing ward, patients were monitored based on intermittently performed vital sign measurements by nurses (every four to eight hours) [40]. As a result of these infrequent vital sign assessments, chances are that clinical deterioration may go unnoticed, which in a worst-case-scenario may result in failure-to-rescue [40, 41]. Research has shown that frequent assessment of vital signs and other basic physiological parameters at the ward, improves healthcare quality and reduces the number of adverse events [40, 42]. Moreover, studies have suggested or shown that trend monitoring through continuous measurement of vital signs and other physiological parameters at the ward is of prognostic value and possesses the ability to recognise abnormal parameter patterns preceding severe deterioration [41–46]. As the disease pattern of COVID-19 remains unpredictable and acute changes can occur, continuous trend monitoring of physiological data may be a valuable tool to recognise deterioration in COVID-19 patients at an early stage. In addition, continuous trend monitoring can be performed remotely, therefore preventing unnecessary physical contact between COVID-19 patients and healthcare workers. [40–46]

This innovative technology that is implemented at the UMCU concerns a chest-worn patch – the Philips Biosensor – which measures heart rate (HR) and respiratory rate (RR) continuously. In addition, each patient bed was equipped with an innovative 'spot check' monitor (Philips EarlyVue VS30) that synchronises nurses' measurements into the electronic patient record (EPR) and is capable of continuous oxygen saturation (SpO₂) measurements. All continuously measured parameters are uploaded into a software system – the Philips IntelliVue 'Guardian' Software – that enables healthcare professionals to monitor their patients from outside the room. More information on these systems is provided in the background section.

This research focuses on the evaluation of the implementation process and data-analysis of the data that were acquired through the implemented monitoring technology. In short, this research aims to formulate an advice on the improvement of continuous patient monitoring by evaluating the implementation process at the COVID-19 cohort ward and quantitatively analysing the acquired data to assess the possibilities of continuous monitoring in early detection and prediction of patient deterioration. This aim is focussed on the population of COVID-19 patients hospitalised at the COVID-19 cohort ward at the UMCU.

2 OBJECTIVES

The main research question of this thesis corresponds to the qualitative and quantitative evaluation of a continuous monitoring system that was implemented at the COVID-19 cohort ward, as well as the exploration of trend detection methods for detection and prediction of deterioration within this patient group:

Main research question

How can continuous vital sign monitoring at the COVID-19 cohort ward be improved in terms of optimising the implementation process, providing valuable insight into the data-based clinical condition of the patients, and to quantitatively detect patient deterioration in COVID-19 patients?

An answer to this research question is formulated by exploring three sub-questions, all serving as a component of the main research question. These research questions are formulated below, with the corresponding chapter titles.

Sub-question 1 : The implementation of continuous monitoring (Chapter 5)

How can the implementation of continuous ward monitoring be optimised, with a focus on improving patient care, reducing workload for healthcare workers and improving working experience?

Sub-question 2: Vital signs trends in COVID-19 patients (Chapter 6)

How can continuously monitored heart rate and respiratory rate data be used to visually detect and predict clinical deterioration or recovery in COVID-19 patients, and what are characteristic trend patterns indicating deterioration or recovery?

Sub-question 3: Detection of deterioration in COVID-19 patients (Chapter 7)

How can continuously monitored heart rate and respiratory rate data be used to quantitatively detect clinical deterioration in COVID-19 patients by means of trend detection?

3 READING GUIDE

In order to provide the reader with some guidance in navigating through this thesis, a textual overview on 'what to find in which chapter' is provided here:

- Chapter 4 – Background. This chapter provides elaborate background information on all relevant topics regarding the title of this report ('Continuous vital sign monitoring in COVID-19 patients'). This roughly concerns three topics:
 - 4.1 – SARS-CoV-2 and COVID-19. An elaborate description on 'the path of infection: from a SARS-CoV-2 virion to a severe case of COVID-19'. By walking this path with the reader, a description on the effect of an infection on the human body and the consequential symptoms is generated.
 - 4.2 – Continuous monitoring. This background section provides insights into present-day patient monitoring at general wards, and the possibilities that wearables offer by enabling for continuous patient monitoring at the wards.
 - 4.3 – Continuous monitoring at the COVID-19 cohort ward at the UMCU. This background section presents information on the set-up of the continuous monitoring system at the COVID-19 cohort ward at the UMCU. This background information is of importance, as this thesis was written on the qualitative and quantitative evaluation of this continuous monitoring system.
- Chapter 5 – The implementation of continuous monitoring. This chapter corresponds to sub-question 1, focusing on the evaluation of the continuous monitoring system by means of two evaluation-questionnaires and discussing general observations.
- Chapter 6 – Vital sign trends in COVID-19 patients. This chapter corresponds to sub-question 2, by means of executing a case series study, in order to visually study the continuous data of a representative selection of cases, as well as performing quantitative analyses of data segments prior to events of deterioration.
- Chapter 7 – Detection of deterioration in COVID-19 patients. This chapter corresponds to sub-question 3, focusing on developing methods for detection of deterioration in COVID-19 patients.
- Chapter 8 – General discussion. General discussion on the entire thesis.
- Chapter 9 – General conclusion. General conclusion on the entire thesis.

4 BACKGROUND

4.1 SARS-CoV-2 and COVID-19

Human coronaviruses (CoVs) were first isolated in the 1960s. Most of the known CoVs are associated with common colds and do not pose a direct threat on public health. However, in 2002, a new viral disease – the ‘severe acute respiratory syndrome’ (SARS) – caused by a novel CoV (SARS-CoV) occurred in China and rapidly spread across multiple countries and continents. SARS became an epidemic, causing severe pneumonia cases and reportedly contaminating 8,422 individuals and causing 916 reported deaths in a few months. In 2012, another novel human-infecting CoV – the ‘middle east respiratory syndrome’ CoV (MERS-CoV) – was identified in the middle east. MERS-CoV also caused severe respiratory problems in the reportedly 1,401 infected individuals of whom 543 died of the disease, reportedly. In December 2019, a new CoV (SARS-CoV-2), emerged in China. At this moment in time (14/11/2021), the novel CoV ‘SARS-CoV-2’ has resulted in a pandemic (officially declared on the 11th of March 2020) resulting in 90,759,370 confirmed cases and 1,963,169 consequential deaths. [2, 12, 13, 47–50]

Path of infection: from a SARS-CoV-2 virion to a severe case of COVID-19

In order to improve understanding of the symptoms and clinical problems in COVID-19 patients, this section will briefly discuss the characteristics of SARS-CoV-2 and the path of infection through the respiratory tract. This is done through strongly simplified schematic illustrations, figures 5 and 6.

Coronaviruses (CoVs) are large, enveloped, positive sense single-stranded RNA viruses. Figure 5 shows a schematic illustration of a SARS-CoV-2 virion (an entire, individual virus particle). The S-protein depicted in this illustration is the spike glycoprotein, which is important for cellular entry of the virion. The (+)ssRNA indicates the enveloped the viral genome, which is packaged in nucleocapsid proteins. The genome size ranges from 26 to 32 kilobases, making it the largest viral genome known to mankind. In reality, the SARS-CoV-2 virion is a much more complex structure, for example including a more elaborate set of surface membrane proteins. Further description of the viral structure is however outside the scope of this research. [48, 51]

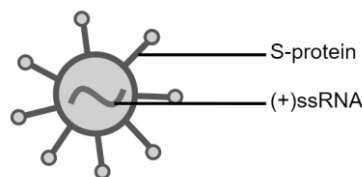


Figure 5: a simplified schematic illustration of a SARS-CoV-2 virion. S-protein = spike glycoprotein, (+)ssRNA = positive-sense single stranded RNA [48, 51]

Figure 6 depicts a schematic illustration of the path of infection via the respiratory tract. The steps that are indicated in this figure are explained in this section.

(1) A virion (or a set of virions) enters the respiratory tract and travels to an alveolus. An alveolus consists of two different types of pneumocytes: type I and type II. The type I pneumocytes form the epithelial lining of the alveolus. Type I pneumocytes have a very thin cytoplasmic layer, enabling for gas exchange from the alveolar space to the surrounding capillaries. Type II pneumocytes are more numerous yet cover less epithelial lining. Type II pneumocytes secrete surfactant, which reduces surface tension and prevents alveolar collapse. [51–53]

(2) The virion approaches a pneumocyte type II cell. (3) To enter the cell, the S-protein binds to a cellular receptor on a pneumocyte type II cell: the angiotensin-converting enzyme 2 (ACE2). ACE2 can be found in cells of the lungs, arteries, heart and intestines [54]. It catalyses the conversion of angiotensin-II (a vasoconstrictor) into angiotensin-(1-7) (a vasodilator), therefore decreasing blood pressure (BP) and countering the activity of the related angiotensin-converting enzyme (ACE) [55]. In the situation depicted in figure 6, ACE2 has a different function: it serves as a ‘door’ for the virion to enter the host cell. [50, 51, 53]

(4) As the S-protein binds to the ACE2 receptor, the membrane fuses and allows for the virion to enter the cell through endocytosis. (5) Shortly after, the membrane breaks down and the virion enters the cytoplasm of the host cell. (6) As the virion enters the cytoplasm of the host cell, the RNA genome is released from its envelope into the cell. (7) The (+)ssRNA then binds onto a ribosome which translates the genome into proteins. (8) These polypeptides are converted into proteins that make up the virion. Also, some of the translated proteins are needed for RNA replication. (9) Inside the cell, the proteins and new (+)ssRNA strings are used to create new virions. (10) These new virions are then released from the cell through exocytosis. (11) In this process of viral replication, the host cell gets damaged and cell death is inevitable. [51, 53, 56]

(12) As a consequence, proinflammatory factors, such as a wide variation of cytokines, are released into the alveolus. These proinflammatory factors have multiple effects on the surrounding tissue. The most important effects are indicated in the schematic illustration in figure 6. (13) One of these effects is that surrounding (healthy) pneumocytes are alerted on the presence of a virulent particle. As a response, these pneumocytes will start producing antiviral factors. [51, 53]

(14) The proinflammatory factors also alert and activate alveolar macrophages. (15) These alveolar macrophages then start secreting more proinflammatory factors, which also have multiple effects. (16) One of these effects is that these molecules move out of the alveolus into the capillary area and cause the capillary to become more porous. (17) This will result in capillary leakage into the interstitium, leading to interstitial and alveolar oedema. The oedema will increase the diffusion barrier and therefore decrease gas exchange. This will result in hypoxemia and hypercapnia and can therefore result in respiratory acidosis. At this advanced stage of infection, the patient will start showing shortness of breath symptoms. [51, 53, 57]

(18) The proinflammatory factors also act on the vascular endothelium and increase the expression of vascular cell adhesion molecules. An increase of these molecules will result in an increase of white blood cell migration (macrophages and neutrophils) into the alveolus. This attributes to the increase of the diffusion barrier, further decreasing gas exchange. [51, 53, 57, 58]

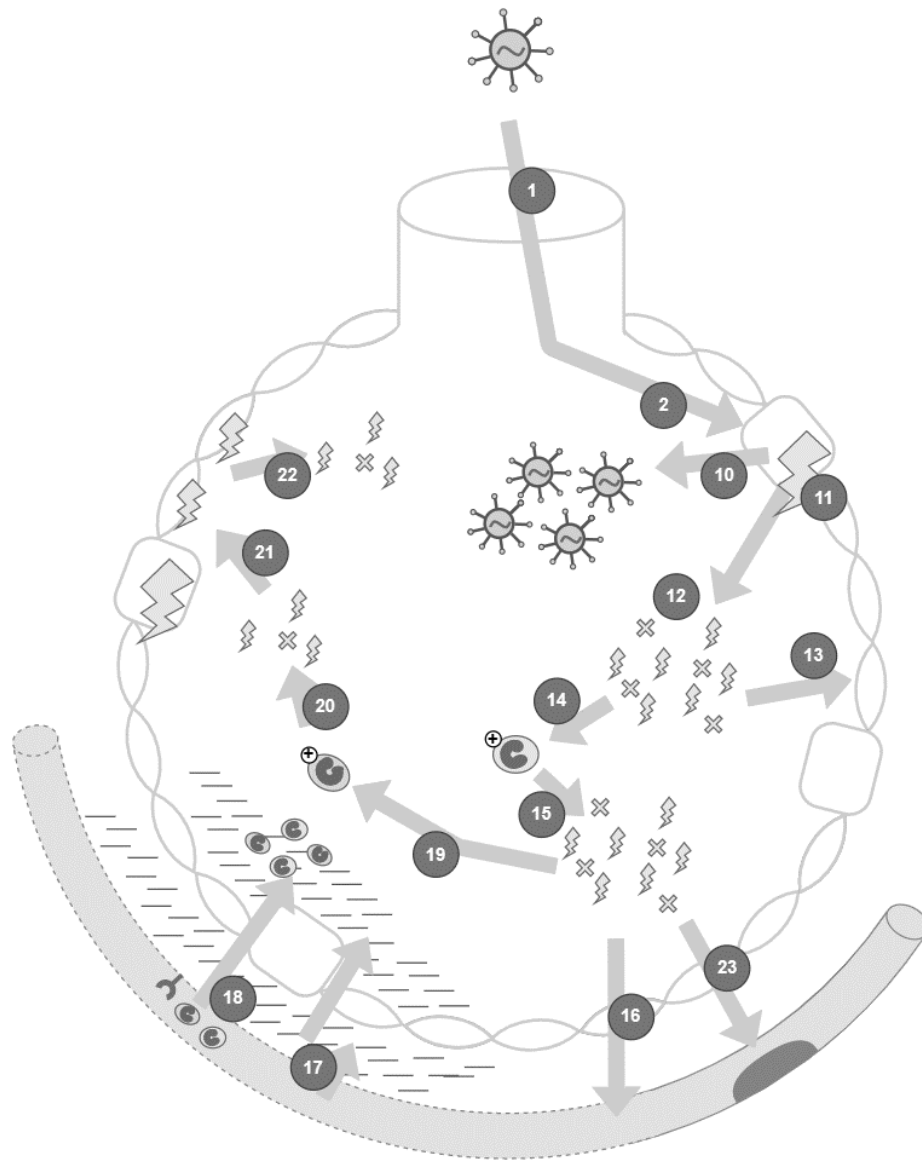
(19) The cytokines present at this moment can activate the neutrophils that entered the alveolus. (20) The activation of the neutrophils by these cytokines cause the neutrophils to secrete reactive oxygen species and proteases. (21) These molecules start to fight the cause of the inflammation yet also damage other pneumocytes in the process. If this process damages the type I pneumocytes, gas exchange decreases, resulting in hypoxemia and shortness of breath symptoms. If pneumocyte type II cells get damaged in this process, the amount of surfactant decreases, therefore increasing alveolar collapse, which ultimately leads to hypoxemia and shortness of breath symptoms. (22) The damaged cells will also result in an increase of the proinflammatory factors in the alveolus. [51, 53, 58]

(23) Another effect of the proinflammatory factors is that the cytokines increase the activity of procoagulants while decreasing the anticoagulant activity, resulting in clot formation and potentially pulmonary embolisms (PEs). [35, 51, 58]

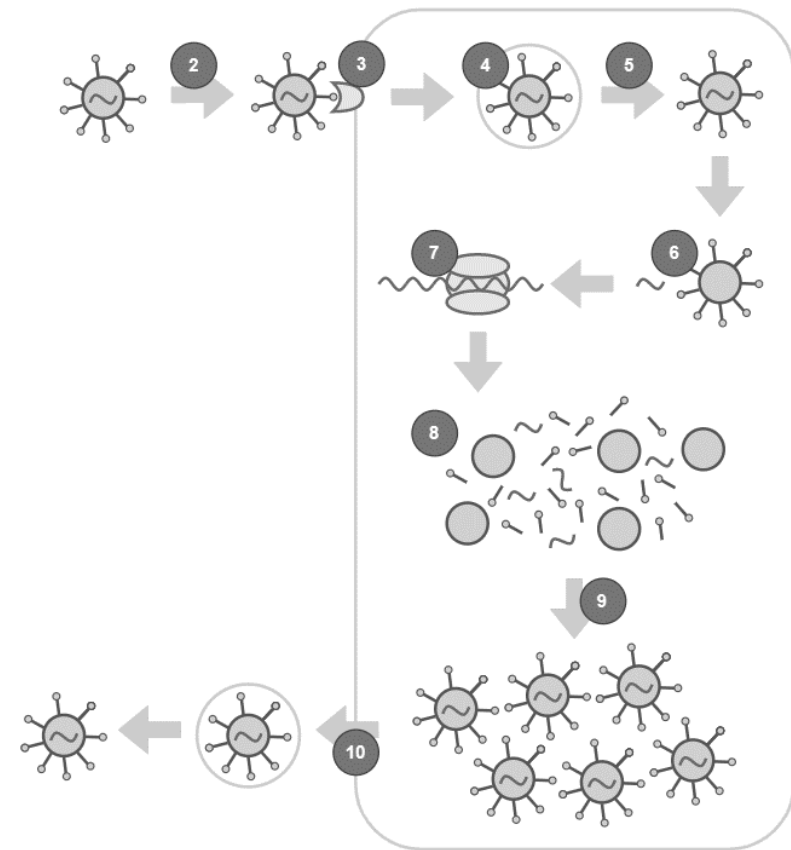
In addition to the aforementioned effects of the proinflammatory factors, the cytokine storm also affects other systems and induces other symptoms. By acting on the nervous system, a cough reflex can be generated, which will most often result in a non-productive, dry cough. By acting on the respiratory smooth bronchial muscles, bronchoconstriction can be induced, contributing to shortness of breath symptoms. Lastly, by acting on the central nervous system, particularly the hypothalamus, the body thermostat can be increased, resulting in a fever. [51, 53, 59]

This simplified explanation on the path of infection of the SARS-CoV-2 virus, provides insight in the underlying mechanisms that cause severe COVID-19 symptoms. Figure 7 provides an overview of the direct effects of an infection with SARS-CoV-2 in terms of consequential symptoms [24, 35, 50–59]. In short, these symptoms are hypoxemia, (which leads to) shortness of breath and fever. Of course, more complications may arise based on the damage that the virus does to the body.

More epidemiological background on the characteristics of the disease of COVID-19 has been provided in the introduction, section 'The disease characteristics of COVID-19'. [24]



(a) – alveolus



(b) – pneumocyte type II cell

Figure 6: a simplified schematic illustration of the path of infection of a SARS-CoV-2 virion through the respiratory tract. (a) depicts a concise illustration of the path of infection within an alveolus. (b) depicts a concise illustration of the infiltration of a virion in a pneumocyte type II host cell. [24, 35, 50–59]

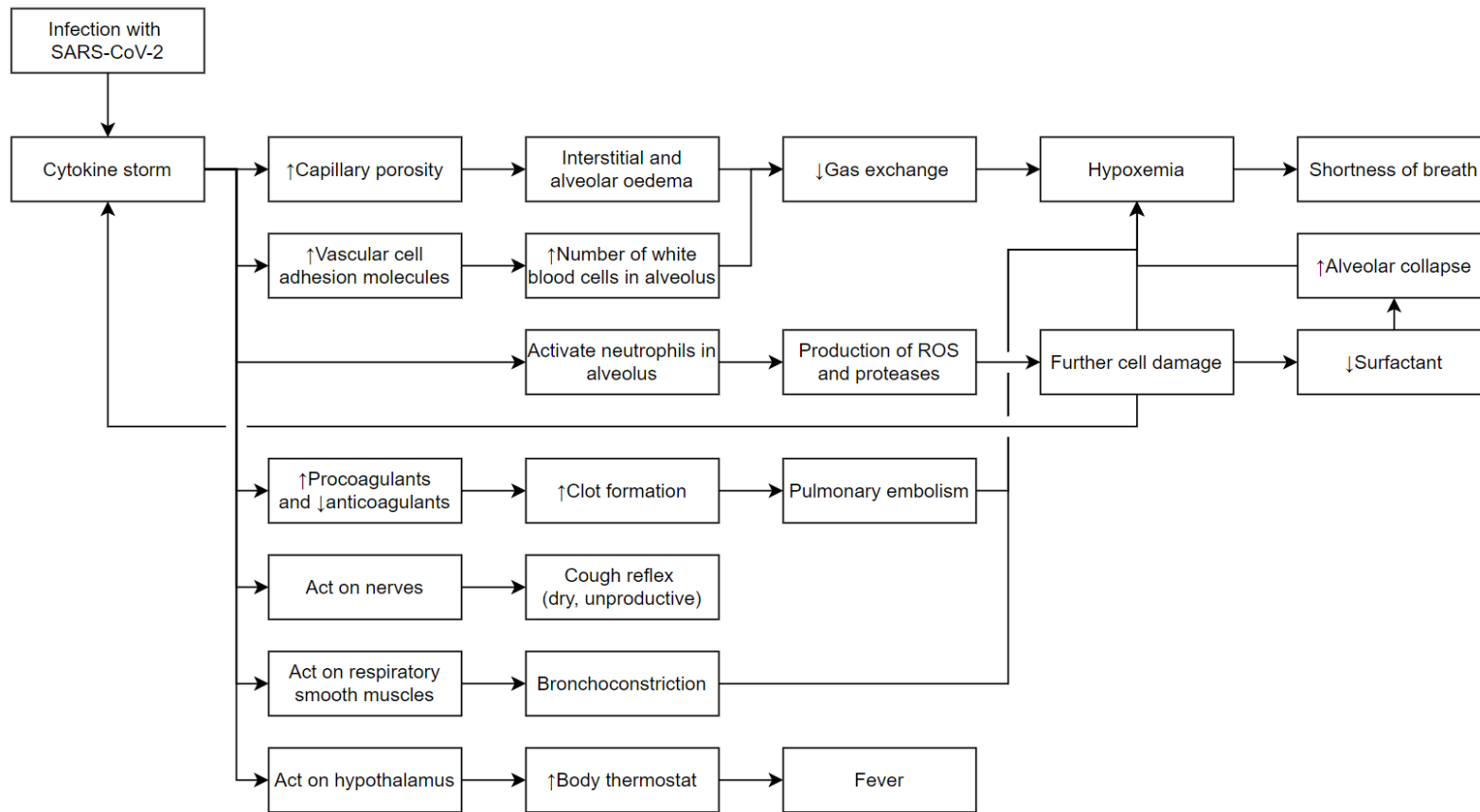


Figure 7: Summary of direct clinical consequences of an infection with SARS-CoV-2. Note that not all of these effects and symptoms apply to all COVID-19 positive patients, since the intensity of illness varies per individual [24, 35, 50–59]

4.2 Continuous monitoring

Early interception of clinical deterioration is important to prevent (re-)admission to the intensive care unit (ICU) or even death [40, 42, 60, 61]. COVID-19 patients are known to have a high likelihood of rapid deterioration up to the point that intensive care and intubation is the only remaining treatment option. Vital signs have shown to be accurate predictors of patient deterioration, as subtle or rigorous abnormalities in basic vital sign values can be observed minutes to hours (and sometimes even days) before life-threatening complications [40–42, 44, 60, 62, 63]. At the OR and ICU, vital signs such as heart rate (HR) are measured continuously. In such settings, trends in vital signs or other physiological data are well monitored by nurses and physicians, enabling early detection of clinical deterioration. [42]

At the nursing ward, intensity of care is lower and vital signs are measured intermittently rather than continuously [41, 64–66]. These intermittent measurements are generally performed with an interval of 4 to 8 hours. [40]. While nursing COVID-19 patients, the need for donning and doffing with personal protective equipment creates an extra barrier to check up on the patient. Frequent assessment of the patient's vital signs values is therefore difficult, in some cases resulting in an incomplete or situational perception of the patient's clinical condition. As a result, chances are that clinical deterioration may go unnoticed, which in a worst-case-scenario may result in failure-to-rescue [40, 41].

Research has shown that frequent assessment of vital signs and other basic physiological parameters at the ward, improves healthcare quality and reduces the number of adverse events [40, 42]. Moreover, studies have suggested or shown that trend monitoring through continuous measurement of vital signs and other physiological parameters at the ward is of prognostic value and possesses the ability to recognise abnormal parameter patterns preceding severe deterioration [41–46].

As the disease pattern of COVID-19 patients remains highly unpredictable and acute, continuous trend monitoring of physiological data may be a valuable tool to recognise deterioration in COVID-19 patients at an early stage. In addition, continuous trend monitoring can be performed remotely, therefore preventing unnecessary physical contact between COVID-19 patients and healthcare workers.

The following subsections provide additional information on conventional patient monitoring, novel methods for continuous patient monitoring and the challenges that come with the implementation of novel continuous monitoring techniques.

Conventional methods of patient monitoring

Vital signs

In current clinical practice, ward nurses intermittently measure vital sign values to assess the condition of their patients [40]. A *vital sign* can be defined as any patient specific feature that either predicts clinical outcome, indicates the need for a specific treatment or could be used to monitor clinical developments [67]. Vital signs are the simplest, cheapest and probably most clinically relevant parameters in patient monitoring [41, 67].

As vital signs reflect the most fundamental aspects of health and survival, a significant abnormality in any vital sign parameter indicates that emergent care is required [52]. A study of over 1.15 million vital signs obtained in 42,430 admissions of 27,722 patients, showed that patients with a solitary abnormal vital sign value had an in-hospital mortality of 0.92%, whereas those with three simultaneous abnormal vital sign values had an in-hospital mortality of 23.6% [68]. These results, and other findings in literature, demonstrate the ability of vital signs to predict clinical deterioration [40–42, 44, 60, 62, 63, 67, 68].

Classical vital signs

Although a wide range of physiological parameters are considered helpful in assessing the vitality of a patient, only four specific physiological parameters are considered to be a *classical vital sign*. These four classical vital signs are:

- *respiratory rate* – RR ;
- *heart rate* – HR ;
- *blood pressure* – BP ;
- *and temperature* – T [52, 67].

Physicians have been aware of the relation between vital signs and the clinical condition of their patient's for centuries, such as the association between fever ($T\uparrow$) and an increased pulse ($HR\uparrow$). However, vital signs have not been a part of routine medical care up until the mid-nineteenth century. Moreover, BP was adopted even more recently, during the twentieth century. [41]

Alternative vital signs

Besides the four classical vital signs, *other physiological parameters* could also serve as valuable signs of patient deterioration. In literature, pain is often suggested as a fifth vital sign by means of intermittent pain screening through numeric rating scales [69–72]. The accuracy of pain assessment through numeric rating scales is however moderate [69]. Although that pain assessment is helpful in assessing the general vitality of the patient, it cannot be used for continuous patient monitoring. This also applies to other additional parameters that have been suggested, such as level of consciousness, nutritional status, smoking status, spirometry, urine output, breathlessness and mobility [41, 72, 73]. A newer physiological parameter – available since the early 1990's – that shows more promise as an additional vital sign is *oxygen saturation*, measured noninvasively using *pulse oximetry* (SpO_2) [73]. However, SpO_2 also has its downsides as it requires adequate peripheral blood flow and may be distorted in anaemic or vasoconstrictive patients [72].

Vital signs in current clinical practice

In current clinical practice, vital signs are assessed in a structured way. Rapid response systems (RRS) are used to recognise clinical deterioration, respond to prevent further deterioration and ultimately improve the patient's clinical condition. Formally, the term RRS refers to the entire system for responding to all patients with a critical medical problem [67]. This system is composed of an afferent and efferent limb. The afferent limb focusses on early recognition of clinical deterioration. The efferent limb focusses on responding to the clinical deterioration by means of interventions, varying from a simple intervention as increasing the FiO_2 (by on-duty healthcare workers) to a more profound intervention such as the activation of a medical emergency team (MET). In short, the goal of RRS's is early detection of clinical deterioration (afferent limb), resulting in rapid response in order to prevent deterioration and improve the clinical condition of the patient (efferent limb). A schematic overview of the general structure of rapid response systems is provided in figure 8.

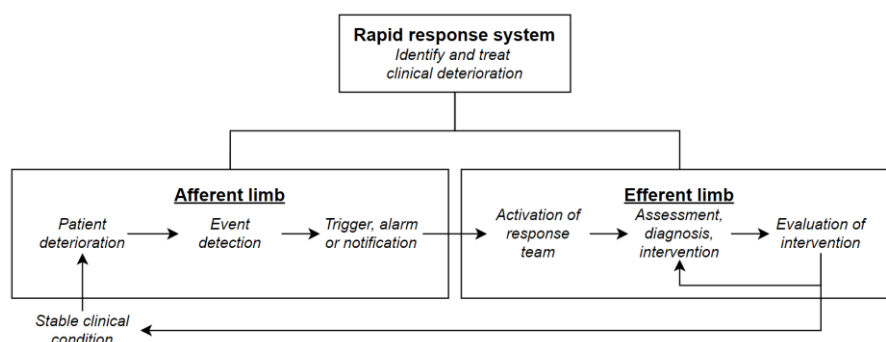


Figure 8: schematic overview of the general structure of rapid response systems.

Within the afferent limb, many hospitals use validated systems that are based on vital signs abnormalities, as vital signs possess the ability to predict clinical deterioration. One of the most frequently used systems is the *early warning score* (EWS) where points are allocated depending on the degree of abnormality for each vital sign. EWS systems may differ slightly by country or even by institution, resulting in several 'modified' EWS's (MEWS). The MEWS currently used at the UMCU is depicted in table 1. Once the MEWS reaches the pre-agreed cut-off value, the efferent limb is activated by means of first notifying the ward physician, or in case of rapidly worsening MEWS, by directly calling the MET. [40–42, 44, 60, 62, 63, 67, 68, 74–76]

Table 1: System for calculation of modified early warning score that is used at the University Medical Centre Utrecht. A-E represent the category of the parameter (A = airway, B = breathing, C = circulation, D = disability, E = environment). In determining the score for 'level of consciousness': A = alert, V = reaction to voice, P = reaction to pain, U = unconsciousness. [75]

Score	3	2	1	0	1	2	3
A O ₂ administration (L O ₂ /min)				Normal air	≤5	≥5	Optiflow
B SpO ₂ (%)	≤90%	91% - 93%	94% - 95%	≥96%			
RR (breaths/min)	≤8		9 - 11	12 - 20		21 - 24	≥25
C HR (beats/min)		≤40	41 - 50	51 - 100	101 - 110	111 - 129	≥130
BP (mmHg)	≤70	71 - 80	81 - 100	101 - 200		≥201	
D Level of consciousness				A	V	P	U
E T (°C)	≤35.0		35.1 - 38.0	36.1 - 38.0	38.1 - 39.0	≥39.1	
other Concerned?				No	Yes		
Urine output (mL/4h)			<75				

The (M)EWS is a well-performing and widely implemented form of the afferent limb of RSS's [40, 77]. However, computation of the (M)EWS can only be done intermittently, as computation is dependent on a full set of nurses' observations (such as 'D – level of consciousness'). Unfortunately, respiratory rate is not always measured.

In terms of continuous patient monitoring, the current and future developments of wireless wearables will allow for the (pseudo)continuous measurement of current and additional vital signs in patients (both bed-ridden as well as mobilising) at the ward. Such additional features could possibly contribute to the improvement of ward monitoring by means of intercepting clinical deterioration at an early stage.

Novel methods for continuous patient monitoring

Wireless wearable devices

Developments in technology have allowed manufacturers in healthcare to design *wireless wearable devices*, intended for continuous patient monitoring. Various devices for continuous vital sign monitoring exist, but have not yet been fully implemented for medical purposes [42, 43, 46, 78, 79]. These devices are based on diverse measurement methods and come in different shapes and sizes, such as chest-worn patches, patient-worn monitors around the wrist, or contactless mattress sensors [43, 78, 80]. Some devices are 'single-use' disposables, while others are reusable. Currently, an increasing number of wireless wearable sensors have reached the market. Most of these devices are developed by start-up companies within the medical device sector; clinical validation data is often limited and not always publicly available.

Previously published research on wireless wearable sensors has focused on the potential of these devices in the early recognition of clinical deterioration at the ward by means of continuous vital sign monitoring. These researches are encouraging, as they have demonstrated that validated wireless wearables are able to detect abnormal parameter patterns and are therefore expected to be advantageous in reducing unnoticed deterioration at the ward [78]. Still, additional work is necessary to continue product validation and software optimisation, as well as research on the effect of implementation of such devices on the workload of staff members and quality of care.

At the time of writing (January 2021), most of these wearables have received the 'Conformité Européenne' (CE) mark, indicating that the product conforms with health, safety and environmental protection standard for products sold within the European Economic Area. In addition, some of these devices have been approved by the American Food and Drug Administration (FDA).

While these devices may have been found safe and adequate enough for healthy subjects by receiving a CE mark and/or FDA approval, very few devices have been validated for patients with medical risks of underlying diseases that may affect the data. Validation of such products on patients with medical risks is essential to assess the opportunities that these devices have to offer in clinically compromised patients. To what extent is the device able to adequately detect deterioration? Are the notifications generated by the device appropriate for patient care? How many false positive and false negative notifications are generated? Does the device work properly in a highly diverse patient population (age, weight, co-morbidities)? Hence, before implementation of such devices, it is extremely important that wireless wearable sensor devices are researched within a clinical setting.

Challenges in continuous patient monitoring

The implementation process of continuous wireless monitoring technology faces many challenges. To ensure high quality care, the wireless wearable sensors need to be reliable and accurate. Therefore, meticulous unbiased validation in clinical settings (i.e., without undue commercial interference) is necessary. Through evaluation and product assessment, products should be optimised to serve as valuable adjuncts to healthcare, without limiting healthcare professionals during the process of implementation. [46, 67, 81]

To accomplish this, artifacts and false alarms need to be minimised as much as possible. A major risk in the implementation of continuous patient monitoring, is the risk of *alarm fatigue* in healthcare professionals. Alarm fatigue refers to the situation in which healthcare workers encounter an abundance of false alarms and no longer respond to these alarms. Healthcare workers may start to ignore alarms if there are simply too many to keep up with or will start to consider them as 'non-valid'. This makes alarm fatigue a dangerous phenomenon, as it may occur that very relevant alarms (such as serious oxygen saturation dips) are ignored. Increased alarm fatigue may therefore result in life-threatening situations if continuous monitoring is implemented insufficiently. Coping with alarm fatigue and preventing false alarms is therefore an important challenge to overcome in the coming years, as more wireless monitoring systems will be implemented on general patient wards. [46, 67, 82]

Related to overcoming alarm fatigue, another challenge in the implementation of continuous monitoring is to improve the generation of notifications. The number of false positives and false negatives should be minimised in order to prevent invalid notifications. A system that only generates true positive alarms will be more trustworthy to healthcare workers, therefore preventing alarm fatigue. This is a formidable challenge, as the back-end system has to be intelligent enough to distinguish between indecisive cases. Ideally, a notification system should relate the data to patient specific thresholds before generating a notification, while taking context information into account. [46, 67, 82]

In addition, the implementation of continuous patient monitoring will be accompanied by a large increase in data streams in the hospital. This will pose a logistical challenge on the in-hospital IT infrastructure (e.g., wireless bandwidth) and services. In addition, the continuously acquired data should be accessible to healthcare workers through simple software, preferably accessible through the electronic patient record (EPR). These technological challenges of the implementation may come with economic consequences for the hospital. [46, 67, 81]

Lastly, one of the most important aspects in the process of implementing continuous monitoring is the positive engagement of healthcare workers. Dealing with continuous data – let alone acting on them – is new for most nurses, and even for physicians outside the ICU and OR environment. This therefore requires adequate training and direct involvement of the implementation project supervisor. The culture regarding patient monitoring must change from tolerating 'unsafe' monitoring practices (intermittent monitoring with large intervals) to a culture that seeks to eliminate preventable harm by the use of continuous monitoring. In addition, the general opinion on innovation and the flexibility of healthcare workers may affect the success of the implementation of a wireless wearable sensor. Implementation should be done very carefully, to prevent negativity and bad experiences with the monitoring technology. The technique should be well integrated with the current workflow and support healthcare workers without limiting them. [46, 67]

4.3 Continuous monitoring at the COVID-19 ward in the UMCU

This report is written in relation to a pragmatic implementation project concerning: continuous monitoring of COVID-19 patients hospitalised at the cohort ward at the UMCU. In order to elaborate on the objective and methods of this research, the project at the COVID-19 cohort ward in the UMCU is briefly described in this section of the report.

Rationale

Halfway through March, when the first 'intelligent lockdown' in the Netherlands was in effect, an idea arose to continuously monitor COVID-19 patients who were hospitalised at the COVID-19 cohort ward of the UMCU. The two project supervisors (M.J.M. Breteker MSc and H.M.R. van Goor MSc) started a project to implement a wireless wearable sensor for continuous monitoring of vital signs for COVID-19 patients. The reason for the implementation of continuous monitoring at the COVID-19 cohort ward was two-folded:

- The primary reason was to closely monitor the patient's vital sign values and therefore possibly facilitate early detection of patient deterioration.
- The secondary reason was to facilitate healthcare workers by monitoring the isolated patients from outside the room, hopefully protecting healthcare workers by reducing redundant physical contact with infectious patients.

During the first wave of COVID-19 patients in the Netherlands, the monitoring system was implemented from the beginning of April until mid-May. During the second wave of COVID-19 patients in the Netherlands, the monitoring system was once again implemented from mid-October, and is still ongoing at the time of writing (January 2021).

Devices

The monitoring system at the COVID-19 cohort ward comprises of multiple components. To adequately describe this monitoring system, the individual components are described first, after which the integration of these components into the overall monitoring system is illustrated.

The Philips biosensor

Multiple options regarding the choice of wearable were investigated, after which the *Philips biosensor* was selected – referred to as the ‘biosensor’. The biosensor is a battery-operated chest-worn patch with integrated sensors and a wireless transceiver. This wearable was originally developed by VitalConnect, a company that was founded in 2011 and is currently based in Silicon valley, CA. The biosensor was adopted by Philips; firmware was rewritten and the sensor was integrated into their cloud-based monitoring system. [78, 83–86]

The biosensor continuously registers physiological data parameters: HR, RR, skin temperature and body position. Within this current research, only HR and RR are studied. The HR is estimated based on the single lead ECG. The reciprocals of the R-R intervals are computed from the automatically detected QRS complexes in the single lead ECG. These reciprocals are used to determine an instantaneous HR, which is then passed through a 10-beat low pass filter to obtain a smooth HR. [78, 83–87]

The RR is estimated through a combination of ECG derived respiratory signals (the respiratory sinus arrhythmia and the amplitude of the QRS complex) and the signal registered by the 3-axis micro-mechanical system accelerometer. The RR is computed from each of the three signals independently, after which the quality of the individual computations is assessed to determine an adequate weighted average for the RR. [78, 83–87]

Figure 9 shows the biosensor, as depicted in the instructions folder of VitalConnect. The top view shows the power button of the biosensor. Once this power button is pushed (for a few seconds), the biosensor is activated until the moment that the battery is empty. The battery life lasts from 120 up to 168 hours. The bottom view shows the adhesive backings. Once removed and placed on the patient’s chest, the ECG electrodes will come into contact with the patient’s skin and register the ECG, which is then translated into HR and components of the RR computation. The Bluetooth ID label depicted in the bottom view in figure 9, is used to digitally link the biosensor to the patient’s record. Figure 10 shows the area of the chest where the biosensor should be placed. For the biosensor to work properly, excessive hair should be removed, and the skin should be clean before application. [78, 83–86]

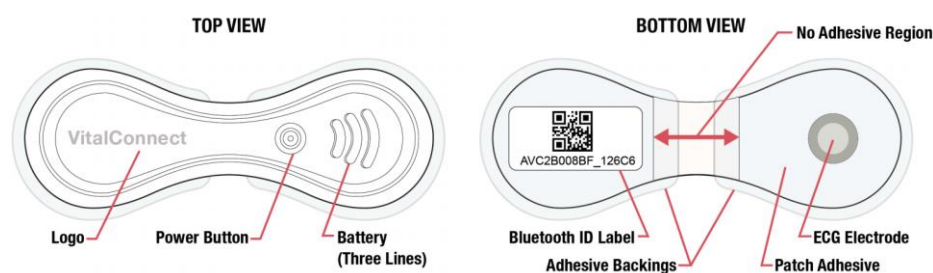


Figure 9: top and bottom view of the biosensor. [83]

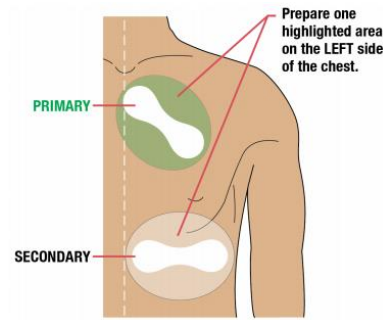


Figure 10: placement of the biosensor on the patient's chest. [83]

The Philips EarlyVue VS30 monitor

In addition to the biosensor, each bed at the COVID-19 cohort ward is equipped with a dedicated bedside monitor (Philips EarlyVue VS30) further referred to as 'VS30 monitor'. The VS30 monitor is a compact bedside monitor that enables nurses and other healthcare professionals to perform all measurements that are necessary to compute a complete MEWS. The VS30 monitor is equipped with software that encourages healthcare workers to perform a complete set of measurements to automatically compute the MEWS of the patient. To compute a complete MEWS with the VS30 monitor, all required values are acquired and should be entered as follows:

- O₂ administration – manually entered into the VS30 monitor
- SpO₂ – automatically and continuously measured by the pulse oximeter of the VS30 monitor
- RR – manually entered into the VS30 monitor*
- HR – automatically and continuously measured by deducing pulse rate from the photoplethysmogram (PPG) signal*
- BP – automatically entered by measurement of BP cuff measurement
- Level of consciousness – manually entered into the VS30 monitor
- T – automatically entered after manual measurement using the built-in temperature sensor
- Concerned? – manually entered into the VS30 monitor
- Urine output – manually entered into the VS30 monitor

* Note that the HR and RR are respectively deduced from the PPG signal of the pulse oximeter and manually entered into the VS30 after nurse observations. Values of HR and RR that were measured by the Philips biosensor are *not* used for MEWS computation by the VS30 monitor.

The VS30 monitor allows for connection to the cloud-based monitoring system of Philips, meaning that the measurements of the VS30 monitor are stored and can be synchronised into the EPR. Also, as long as the patient wears the pulse oximeter (finger) probe, SpO₂ can be measured continuously, providing important additional information on the clinical condition of the patient, while the patient can be monitored remotely from outside the room. Figure 11 shows the VS30 monitor.



Figure 11: The Philips EarlyVue VS30 monitor [88]

The Philips IntelliVue Guardian Software

The Philips IntelliVue Guardian Software (IGS) – referred to as 'IGS system' – brings the measured signals together and generates an insightful interface for its users to monitor their patients. The IGS system is intended for collection, storage and management of the data that is generated by Philips' data acquisition systems, such as the biosensor and the VS30 monitor.

In addition to visualisation of the generated data, the IGS system is equipped with a notification system – referred to as the Guardian EWS – which is based on the MEWS. In contrast to the 'spot check MEWS' that nurses compute with the VS30 monitor, the IGS software uses HR and RR measurements by the biosensor as an input to MEWS computation. If the MEWS of a patient was increased, the system re-evaluated the MEWS twice during the following twenty minutes. If the MEWS remained increased, a notification was generated. This system did not require all MEWS components to be known, in other words: a 'MEWS notification' could also be generated based on increasing MEWS values for only the HR and/or RR. Note that, based solely on continuous HR and RR data, the calculated MEWS should be interpreted as a 'sub-score'. [84, 89, 90]

Philips specifically states that the IGS system is not an alarming system and not a replacement for real-time monitoring. It merely provides basic assessment of the data in relation to the clinical condition of the patient and helps healthcare workers to recognise the early signs of deterioration in their patients. [84, 89, 90]

The overall monitoring system at the COVID-19 cohort ward

Integration of all components into a complete monitoring system

All of these products were integrated in the monitoring system at the COVID-19 cohort ward. Figure 12 shows a schematic illustration of the monitoring system, as it was operated and put to use.

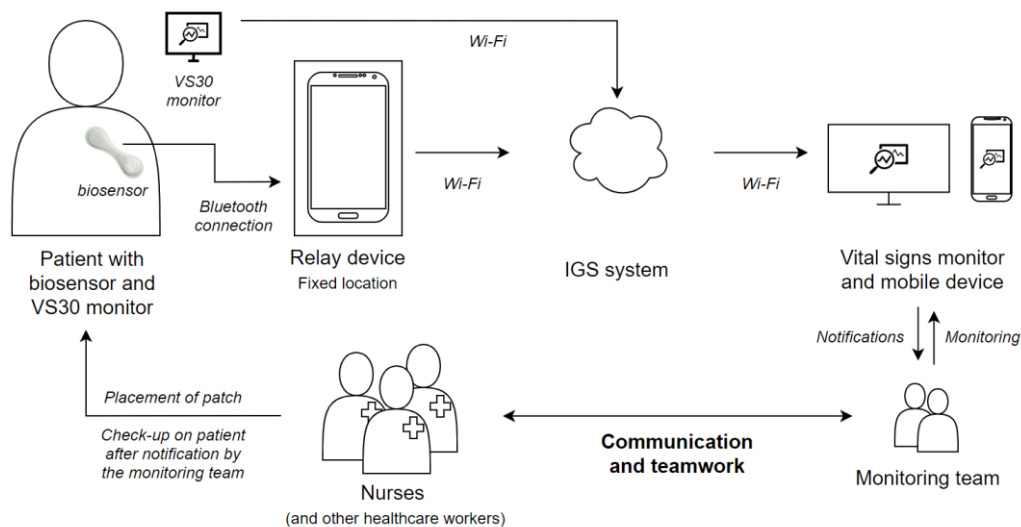


Figure 12: Schematic illustration of the monitoring system, as it was operated and put to use at the COVID-19 cohort ward.

Patients are patched with a biosensor and each bed is equipped with a VS30 monitor. Patients are patched with a biosensor by the nurses after receiving directions from the monitoring team to do so. Once activated, the biosensor continuously registers HR and RR. To transfer the data to the cloud-based IGS monitoring system, the biosensor first transfers the data to a nearby relay device via Bluetooth. This relay device is a phone-like device that is placed at a fixed location, near the bed of the patient. Each bed at the COVID-19 cohort ward therefore has its own, fixed relay device that is coupled to the patient that is assigned to that specific bed. Similarly, each bed at the COVID-19 cohort ward is equipped with a VS30 monitor. The relay device and the VS30 monitor both transfer the acquired data to the cloud-based IGS system. This system provides healthcare workers with insight into the continuous HR, RR and SpO₂ data. Both the vital signs monitor and the mobile device were equipped with the IGS application. This application enabled the healthcare workers with the tools to visualise the data, and operate the monitoring system (in terms of coupling relays to new patients, or coupling a new patch to a patient by scanning the Bluetooth ID label). Both the monitoring team and on-duty nurses had access to the IGS application.

Responsibilities of the monitoring team

The monitoring team is responsible for monitoring the continuous data that is provided via the vital signs monitor and the mobile device. The monitoring team consists of experienced medical master students and young medical professionals. Also, the monitoring team interprets the notifications that were generated by the Guardian EWS system. The most important task of the monitoring team is, however, to support nurses in their work. Therefore, teamwork and communication was an essential aspect of the working activities of the monitoring team. Contact between the monitoring team and the nursing staff comprised of morning briefings with the entire staff of the ward, and communication throughout the day on patient's conditions. More specifically, the communication and teamwork between the monitoring team and nurses comprises of the following tasks for the monitoring team:

- *Requesting nurses to perform logistical actions.*
Such as applying a new patch when the battery is exhausted.
- *Notifying the nurses of possible patient deterioration in an adequate and timely fashion.*
The monitoring team used the notifications of IGS to determine whether notification of the nurses was necessary. In principle, each notification triggered the monitoring team to visually assess the trend data. Note that an increased MEWS may be a consequence of (sudden) mobilisation, and therefore does not necessarily require nurse notification. In addition to acting on the notifications, the monitoring team monitored the continuously vital sign values visually and monitored trends of instable patients throughout the entire day.
- *Discussing individualised target SpO_2 levels for each patient in order to provide early intervention if the SpO_2 level drops.*
- *Educating nurses on the interpretation of continuously monitored vital signs data.*
- *Educating nurses on operating the monitoring system.*

The monitoring team as a rapid response system

In background section '4.2 Continuous monitoring', rapid response systems were discussed and described as tools for (early) recognition of clinical deterioration, in order to respond to prevent further deterioration and ultimately improve the patient's clinical condition. The described continuous monitoring system that was implemented at the COVID-19 cohort ward, can be interpreted as a RRS. Below, figure 13 (an adjusted version of figure 8 from background section '4.2 Continuous monitoring'), shows how the implemented continuous monitoring system can be interpreted as a RRS, by dividing the 7 'steps' in the afferent and efferent limb into three components:

- 1) The clinical condition of the *patient* (grey);
- 2) An action of the *monitoring team* as a consequence to the use of the IGS system (blue);
- 3) An action of the *nurse* (orange).

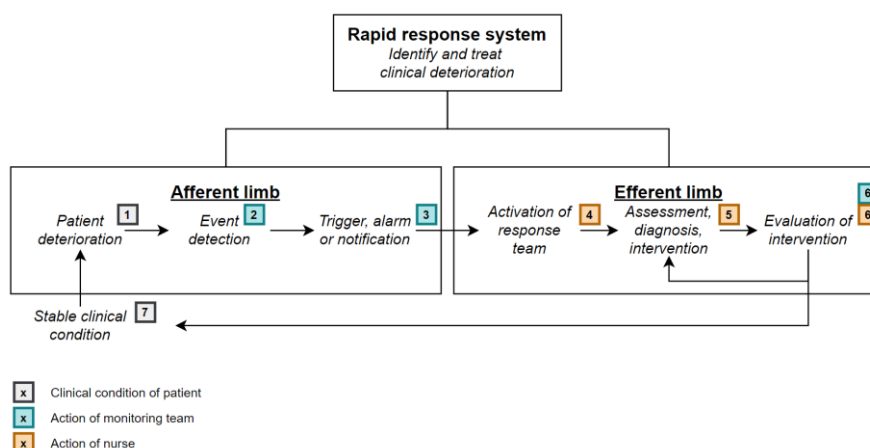


Figure 13: An adjusted version of figure 8 of background section '4.2 Continuous monitoring', to explain how the implemented continuous monitoring system can be viewed as a RRS.

Data acquisition while monitoring

The data that were (and still are) acquired during this project provide opportunities for researchers to study the patterns of continuously measured vital signs in COVID-19 patients with different clinical outcomes. Research regarding these data may contribute to improved insight in the disease and may help healthcare workers in future crises.

5 THE IMPLEMENTATION OF CONTINUOUS MONITORING

5.1 Introduction and objective

Even today, continuous wireless vital signs monitoring at general wards is still rare. Most healthcare workers at the ward are not familiar with observing and interpreting continuous vital signs data. Implementation of continuous monitoring on a general patient ward and adopting this into the daily nursing routines is a major challenge. It is of great importance to implement continuous monitoring in a sustainable way, in order to accomplish lasting success.

This chapter focusses on the evaluation of the implementation processes of the continuous monitoring technique at the COVID-19 cohort ward. The technique was implemented twice: during the first COVID-19 wave (start April until mid-May of 2020) and again during the second COVID-19 wave (mid-October 2020 until now, 14/1/2021). Both implementation processes will be included in this chapter. A conclusion to this chapter and advice for future implementation processes will be formulated in relation to the following research question:

How can the implementation of continuous ward monitoring be optimised, with a focus on improving patient care, reducing workload for healthcare workers and improving working experience?

5.2 Methods

The original plan was to organise retrospective, in-depth, individual interviews, in order to perform qualitative research. Unfortunately, this original plan was subjected to multiple setbacks. Once the second COVID-19 wave hit healthcare facilities in the Netherlands, and the second implementation process of continuous monitoring was on-going, the original plan was rejected and a new plan was introduced. Appendix 11.1 includes the original plan, with the original interview guide. This is included, as this interview guide was composed with great care, and may be used by other researchers in future projects. For the remainder of this chapter, only the executed plan is discussed.

Study design

This study concerns an observational study on the evaluation of the implementation processes of the continuous monitoring system at the COVID-19 cohort ward. This will be done through multiple ways, discussed below.

Evaluation questionnaire for the student monitoring team – first COVID-19 wave

The researcher included results from the evaluation questionnaire that was sent to the student monitoring team after the first COVID-19 wave. The student monitoring team was closely involved in the implementation process of the continuous monitoring team as this team was responsible for data acquisition (by making sure that the patients were patched), data interpretation and the consequential notification of deterioration towards ward nurses. The evaluation questionnaire was composed by the two supervisors of the implementation project at the COVID-19 cohort ward (M.J.M. Breteler MSc and H.M.R. van Goor MSc) and can be found in appendix 11.2.

'Coffee break room'-questionnaire for nurses – second COVID-19 wave

The experiences of nurses with the continuous monitoring technique were assessed by the use of a so-called 'coffee break room'-questionnaire. This questionnaire was planted in the coffee break room at the COVID-19 cohort ward during the second COVID-19 wave in the Netherlands, more specifically: from the 27th of October until the 11th of December. This questionnaire can be found in appendix 11.3. The questionnaire was purposely formulated to be concise and easy to complete in-between working activities.

General observations

Lastly, the researcher will objectively discuss some general observations regarding the implementation process of the continuous monitoring technique. These observations, for example, include observations regarding the logistics of the system, the interest of nurses towards the monitoring system, and topics that came up during casual conversations.

Study population

Study population: evaluation questionnaire for the student monitoring team – first COVID-19 wave

The student monitoring team consisted of nineteen medical master students. Two of these students were trained as super users, meaning that they received a more elaborate training by Philips. All students were asked to complete the questionnaire. There were no additional exclusion criteria.

Study population: 'coffee break room'-questionnaire for nurses – second COVID-19 wave

The study population for the questionnaire covers all nurses who worked at the COVID-19 cohort ward during the second COVID-19 wave. No exact sample size calculation has been performed since the nursing staff at this particular department is not unlimited and all input is relevant to improve future implementation processes. As an inclusion criterium, the nurse should have worked at the COVID-19 cohort ward during the second COVID-19 wave, while the continuous monitoring technique was implemented. There are no exclusion criteria.

Analysis

The results of both the evaluation questionnaire and the 'coffee break room'-questionnaire were extensively analysed and described to ensure that no results were missed. The elaborate descriptions of the results are included in appendices 11.4 and 11.5 The results section of this chapter was written as a global and structured summary of all of the results. The results were categorised and presented in a concise overview to prevent a wordy results section. Findings are assorted to one of the four main categories of interest. These categories are:

- *Technology*
Referring to the quality hardware and software of the monitoring system
- *Communication and teamwork*
Referring to contact and teamwork between all involved parties: ward nurses, ward physicians, the monitoring team and the project supervisors
- *Experience*
Referring to the experience that all involved parties expressed, varying from (dis)trust in the monitoring system, to (dis)comfort towards the technology, to enthusiasm that was expressed.
- *Effect*
Referring to the effect that was realised by the implementation of the technology (e.g. whether nurses thought if the monitoring system resulted in a decrease of donning and doffing to enter the room)

Component-specific methods for analyses are as follows. Note that these component specific methods resulted in the elaborate descriptions that are included in appendix 11.4 and 11.5.

- *Analysis: evaluation questionnaire for the student monitoring team – first COVID-19 wave*
The evaluation questionnaire for the student monitoring team was studied for recurring themes, observations and suggestions. These themes, observations and suggestions are discussed by the researcher.
- *Analysis: 'coffee break room'-questionnaire for nurses – second COVID-19 wave*
The questionnaire results were analysed by calculating the percentage of agreement for every statement, scores from 'strongly disagree' to 'strongly agree'. Results that were acquired by the 'open box' in which nurses could answer the question 'Do you have any additional comments about the continuous monitoring?' were transcribed and studied for recurring themes, observations and suggestions. These themes, observations and suggestions are discussed by the researcher.
- *General observations*
The general observations by the researcher were not elaborately described when compared to the results of the evaluation questionnaire and the 'coffee break room'-questionnaire. The general observations are intertwined in the results and discussions section. In case the researcher makes a specific statement on a perceived observation, this is clearly indicated in the text.

5.3 Results

Study population

Study population: evaluation questionnaire for the student monitoring team – first COVID-19 wave

The student monitoring team of the first COVID-19 wave consisted of nineteen medical master students. Fourteen out of nineteen students completed the evaluation questionnaire. The evaluation questionnaire was anonymous; hence no additional population characteristics are provided.

Study population: 'coffee break room'-questionnaire

Table 2: contains the population characteristics of the nurse respondents to the 'coffee break room'-questionnaire

Characteristic	N	Value
		Median (IQR) or # (%)
Gender	17	
Male		3 (18%)
Female		14 (82%)
Age	17	32 (26-36)
Experience as a nurse ^a	14	
≤ 5 years		6 (35%)
> 5 years, yet ≤ 10 years		2 (12%)
> 10 years		6 (35%)
Number of shifts ^b	11	
≤ 5		4 (24%)
> 5, yet ≤ 10		5 (29%)
> 10		2 (12%)

^a Not all respondents were nurses: the population of n=17 included two 'verzorgenden individuele gezondheidszorg' (loosely translated as *assistant nurses*) and one obstetrician

^b Two respondents did not provide an answer, two provided a non-serious answer, and two respondents answered wordily: 'a lot'.

Combined results of both questionnaires

The responses on both the evaluation questionnaire for the student monitoring team (first wave) and the 'coffee break room'-questionnaire (second wave) have been elaborately described. The elaborate description of the results of the evaluation questionnaire for the student monitoring team can be found in appendix 11.5. The elaborate description of the results of the coffee break room'-questionnaire can be found in appendix 11.6.

Here, the results of both questionnaires, are combined with the general observations of the researcher. Findings are assorted to one of the four main categories of interest. These categories are – as described in the methods section – technology, communication and teamwork, experience and effect. At the end of this result section, table 3 provides a structured and summarised overview of the results.

Technology

The biosensor (including the HR and RR trend data)

All respondents of the student monitoring team were convinced of the added value of the biosensor and the HR and RR trend data. Respondents stated that the data that was acquired by the biosensor allowed for early recognition of clinical deterioration and generated more insight into the overall condition of the patients present at the COVID-19 cohort ward.

Most nurses stated that it was easy to adequately apply the patch to the patient's chest. Results are varying on whether nurses did or did not look at the trend data by themselves during the shifts. Slightly more than half of the nurse respondents stated that they did use the available continuous trend data (especially during night shifts), and agreed that the data provided additional insight into the clinical condition of the patient. Remaining nurse respondents were neutral on the subject or stated that they did not use the trend data and/or did not think that the data provided additional insight into the patients' conditions. One nurse

respondent stated that, in terms of future projects, the UMCU should invest in more elaborate wearables that are able to measure a wider range of continuous data. This nurse stated that he/she would especially appreciate it if continuous non-invasive BP would be available.

A general observation by the researcher regarding the biosensor, is that the data always seemed valid with respect to the clinical condition and degree of mobilisation (resulting in 'peakiness' in the data) of the patient. Some problems were experienced with sensors that did not attach properly to the patient's skin. In such cases, the patient was often male, with a relatively large amount of chest hair. No other notable problems were experienced with the biosensor in terms of measurement performance.

The VS30 monitor (including the SpO₂ trend data and the synchronisation of MEWS measurements into the EPR)

Most respondents of the student monitoring team were convinced of the added value of the VS30 monitor. Students did however state that most of its value was in the continuous measurement of SpO₂, as this enabled the monitoring team to notify nurses on acute SpO₂ dips or silent hypoxemia. In addition to this, students also stated that they often heard that patients experienced the pulse oximeter as uncomfortable, which led to missing data when patients removed the pulse oximeter. Also, students valued the possibility for nurses to have the monitor automatically compute a complete MEWS. Students suggested that it would be even more valuable if these measurements were automatically transferred to the EPR. Therefore, this functionality was implemented during the second wave of COVID-19 patients.

Nurse respondents valued the possibility of being able to compute a complete MEWS that could be automatically transferred to the EPR. This was however not always possible due to some technological difficulties, yet mostly due to misunderstandings by the nurses on how to adequately assign a bedside VS30 monitor the patient (making it impossible to establish the connection to the EPR). This resulted in some annoyances for some of the nurses.

Other technological aspects of the monitoring system in general

Respondents of the student monitoring team emphasized multiple times that they thought that the technology provided valuable additional insight into the condition of the patients, and that they especially appreciated the continuously available SpO₂ data. In addition, the student respondents stated that the monitoring system did have some technological aspects that should be improved. *First*, they stated that the MEWS notification system was sub-optimal, as the students experienced some notifications as unnecessary, whereas at some moments they felt that they really needed to notify the nurse based on a trend, while the MEWS notification system did not generate a notification. For example, a MEWS notification was often generated in mobilising patients who showed mobilisation-induced tachycardia or tachypnoea. Contrarily, if the monitoring team noticed a slow but steady increase in HR and RR, which did not affect the MEWS (the MEWS thresholds were not surpassed), the monitoring team was likely to discuss the trend with the nurse, prior to an IGS notification. *Second*, some students were annoyed by the variable quality of the UMCU Wi-Fi signal, necessary for the relay devices to connect to the IGS system. *Lastly*, the IGS system did not generate a notification if a patient had died – it simply did not publish any more measurements.

One nurse respondent emphasised that he/she found the MEWS notifications in the IGS system difficult to understand, not knowing what to do when a specific notification was generated. Other than that, nurse responses did not provide additional commentary on the technological aspects of the monitoring system.

The researcher's observations suggest that the logistics around this specific monitoring system may be somewhat too complex. When looking at figure 12 (the schematic illustration of the monitoring system), one can deduce that the system consists of a lot of components: a biosensor (with a limited battery life), a VS30 monitor (which needs continuous power), a relay device (which also needs continuous power to prevent an empty battery), an IGS system, the notification component of the IGS system, a monitoring team, a nursing team with inconsistent knowledge of the system, et cetera. Obviously, the more individual components there are, the more the system will be prone to errors.

Communication and teamwork

Contact between the disciplines (monitoring team, nurses, physicians, project supervisors)

Respondents of the student monitoring team experienced contact with the nurses and the teamwork as pleasant and sufficient. Sometimes it was difficult for the students to find the nurse who they needed to speak to. Students suggested that this process should be improved, perhaps by creating more planned contact moments or a low-key phone connection with the nurses. Student respondents stated that there was none to very little communication and teamwork with the ward's physicians. Also, some students noted that not all physicians were interested in the continuous monitoring system. These students emphasised that communication

and teamwork with physicians should be improved in order to optimise the system. Lastly, all student respondents were positive about contact with and involvement of the project supervisors.

Most of the nurses stated that they appreciated the monitoring team and valued the low-key contact. In addition, one nurse stated that physicians should be more involved in the monitoring system.

As a general observation, the researcher emphasises that the fact that the monitoring team could sometimes not find the nurse, was limiting with respect to the efficacy of the monitoring system. In addition, the researcher emphasises that the physicians were only involved and used the continuous data when patients severely deteriorated. Lastly, the researcher adds that the efficacy of the monitoring system is dependent on the quality of contact and teamwork between the monitoring team and the ward nurses. If the student had an approachable attitude and actively made a connection with the nurses, this resulted in an improved collaboration and an increased efficacy of the monitoring system.

The presence of the monitoring team

Almost all respondents of the monitoring team stated that they felt useful, and felt that they sometimes were able to 'make a difference', for example by affecting treatment policy when detecting clinical deterioration. Most of the team felt appreciated. One respondent specifically stated that he/she often felt useless, and that the tasks that came with being a part of the monitoring team should be assigned to the nurses and/or physicians. In terms of improving the monitoring team in the long run, most of the students agreed with this and suggested that the tasks should be transferred to the nurses, by integrated the monitoring tasks into the workflow of the nurses. Other students suggested that the monitoring team should receive more tasks, should be able to access more background medical information on the patients, more meetings with the staff to support clinical decision making, and should be responsible for more patients (e.g., remotely observing patients from other departments).

Most nurse respondents stated that they found it reassuring that the monitoring team was present to monitor their patients from outside the room. In addition, nurses stated that they valued that the monitoring team was present so nurses could come and ask for explanation on the system.

As a general observation, the researcher adds that the situation was (and still is, in this second wave) very hectic: a high admission rate of new patients, patients who are very sick and in need of high-intensity nursing care, and a lot of impressions and emotions for patients and healthcare workers. The continuous monitoring system has provided additional support for nurses to monitor their patients from outside the room, providing reassurance and extra insights. The integration of such a system into the workflow of nurses is a long-term project that should be executed with great care. This was not possible within this pragmatic approach of the implementation of this monitoring system. The most appropriate solution was to mobilise a monitoring team to unburden the nurses of the logistics and monitoring tasks that come with the implementation process. Thus, for this specific and critical situation, the presence of the monitoring team was considered convenient and successful.

Experiences

All of the student respondents of the monitoring team felt that the monitoring system was of added value to the clinical process at the COVID-19 cohort ward. Some of the students stated that they learned more and more on the topic of continuous monitoring and everything that comes with being a part of a monitoring team (communication, teamwork, et cetera) while on the job. The students expressed some annoyances that were experienced, summarised as: insufficient information transfers by colleagues, not being able to find a nurse, monitoring team members who showed less initiative in the monitoring team, disinterest of the ward physicians, too little communication by the nurses towards the monitoring team on new admissions or discharges of patients, and an insufficient amount of work during shifts in the last weeks of the first wave.

In the open section on the 'coffee break room'-questionnaire, slightly less than half of the nurse respondents emphasised their enthusiasm on the monitoring system. Most of these nurses added that the monitoring system is of great added value to the nurses' own clinical view, but that it is definitely no replacement of the intermittent nurses' measurements. Some of the nurses stated that they would like this innovation to be implemented on other nursing wards in the UMCU. One nurse specifically emphasised that the he/she appreciated the presence and help of the monitoring team. Two of the nurses mentioned that they did not fully trust the technology.

As a general observation, the researcher adds that most of the nurses were very positive towards the monitoring system. The level of interest and positivity however varied per individual, with some nurses expressing negative prejudice before gaining any experience with the innovation.

Effect

In terms of the effect of the monitoring system at the COVID-19 cohort ward, the student respondents stated multiple things. The student respondents mentioned that the acquired data allowed early detection of patient deterioration, sometimes affecting treatment policy. In addition, the continuously available SpO₂ data facilitated early detection of silent hypoxemia or sudden desaturations. Technological and logistical aspects sometimes resulted in annoyances, limiting the effect of the monitoring system.

Most of the nurse respondents experienced the monitoring system as a valuable tool to their own clinical intuition, stating that they felt reassured that the patients could be monitored from outside the room. Likely, most nurses felt reassured that a monitoring team was present to support the nurses in the monitoring process. Nurses' opinions and experiences on whether the technology provided additional insight into the clinical condition or whether the data influenced clinical decisions were divided, yet most of the nurses did agree with these statements. Also, it varied strongly whether nurses assessed the trends of the data themselves. To correctly interpret this result, note that the 'coffee break room'-questionnaires were mainly completed at the start of the second implementation process, meaning that most of the nurses had little to no experience with the technology and still required training on the system and interpretation of the data. Finally, most nurses stated that the monitoring system did not notably reduce the number of times that the nurses had to entered the isolation rooms in order to check on their patients.

In terms of general observations, the researcher adds that as time goes by (considering that the innovation is still implemented), nurses are becoming more and more involved and autonomous with respect to including a patient into the monitoring system or keeping an eye on the trend data.

Table 3: Structured summarised overview of key findings of evaluation questionnaire for the student monitoring team (first COVID-19 wave), 'coffee break room'-questionnaire for nurses (second COVID-19 wave) and the general observations

Technology		
Biosensor	Monitoring team	- All convinced by added value - Most convinced by ability of HR and RR data to detect clinical deterioration
	Nurse respondents	- Most find application of biosensor to patient's chest easy - Varying results on: - Whether the nurses studied the trend data during shifts, most did - Whether the HR and RR data provided additional insights, most agreed - One nurse asked for more elaborate technologies (more vital signs, e.g. BP)
	General observations	- Data always seemed valid regarding severity of disease and degree of mobilisation - Some attachment problems for patients with excessive chest hair
VS30 monitor	Monitoring team	- Most convinced of added value, especially the continuous SpO₂ measurement - Some observed/heard that the pulse oximeter was uncomfortable for patients - Most valued the possibility for nurses of computing MEWS on the monitor
	Nurse respondents	- Most valued the possibility of computing MEWS and automatic data transfer into the EPR - Some expressed annoyances concerning technological issues regarding synchronisation of MEWS into EPR
Other	Monitoring team	- Some mentioned that logistic and technological aspects should be improved - Improve and optimise MEWS notification system - Improve UMCU Wi-Fi signal to improve connection of relay devices - Add notifications to notify patient's death
	Nurse respondents	One mentioned that MEWS notifications are difficult to interpret
	General observations	System consists of many components. The more individual components, the more prone the system is to errors
Communication and teamwork		
Contact between disciplines	Monitoring team	- Most respondents experienced contact with nurses as pleasant - Most mentioned that it was often difficult to find the nurse they needed at the ward - Most respondents had no to little contact with physicians; most imply this should be improved - Most experiences contact with project supervisors as very pleasant
	Nurse respondents	- Most expressed that they valued the pleasant contact with the monitoring team - Some expressed that physicians should be more involved
	General observations	- Adds that the monitoring team not being able to find nurses limited the efficacy of the monitoring system - Adds that efficacy of monitoring system is dependent on quality of teamwork between disciplines

Presence of monitoring team	Monitoring team	• Most felt useful, some felt able to 'make a difference'; one felt useless • In terms of improvement: ○ Either no monitoring team, all monitoring tasks transferred to nurses; ○ Or monitoring team with more tasks and responsibilities
	Nurse respondents	• Most felt reassured that the monitoring team was present for extra support
	General observations	• Adds that in this particular, hectic and critical situation, the presence and support of the team is of added value
<i>Experiences</i>		
	Monitoring team	• Most felt appreciated by other staff • Annoyances: ○ Insufficient information transfers from colleagues ○ Not being able to find a nurse ○ Colleagues who showed less effort on the job ○ Disinterest of some physicians ○ Too little communications from nurses towards monitoring team
	Nurse respondents	• Slightly less than half of the nurses expressed their enthusiasm • Most felt that the monitoring system was of added value to the nurses' own clinical intuition, yet that it is definitely not a replacement • Two nurses felt that they could not fully trust the technology based on their experiences
	General observations	• Deduced from many conversations, most nurses were positive towards the monitoring system • Some nurses had negative prejudices before gaining any experience with the innovation
<i>Effect</i>		
	Monitoring team	• Most mentioned the ability for early detection of patient deterioration • Some mentioned the ability for detection of silent hypoxemia or sudden desaturations • Some mentioned that technological and logistic problems limited the effects of the monitoring system
	Nurse respondents	• Most felt reassured by the presence of the monitoring system • Most felt reassured by the presence of the monitoring team • Varying results on the use of the monitoring system by the nurses • Most nurses stated that there was no notable reduction in the number of times that they entered the isolation room
	General observations	• Over time nurses seem to get more and more involved and autonomous with respect to including patients into the monitoring the system and monitoring the trend by themselves

5.4 Discussion

The described continuous monitoring system was successfully implemented at the COVID-19 cohort ward, during both the first and second wave of COVID-19 patients in the Netherlands. This chapter of this report focused on evaluating these implementation processes in order to formulate an advice for future implementation of continuous monitoring systems at nursing wards. Key findings that were acquired via the evaluation questionnaire for the student monitoring team (first wave), the 'coffee break room'-questionnaire and general observations by the researcher are presented and discussed here.

Key findings

The continuous HR and RR data that was acquired by the use of the biosensor was of added value to the clinical process, according to all members of the monitoring team and the majority of nurse respondents. The involvement of nurses in the operating and using the monitoring system varied per nurse, with some being very enthusiastic, and others being more conservative with respect to the innovation. Opinions on the availability of the continuous SpO₂ data (acquired by the VS30 monitor) were similar, yet received even more appreciation from the monitoring team as the data allowed for detection of silent hypoxemia and sudden SpO₂ dips. Regarding other opinions on the VS30 monitor, nurses appreciated the possibility to compute and store a complete MEWS, yet were sometimes annoyed by a poor connection between the VS30 monitor and the EPR, limiting the efficacy of the system. All parties noted other technological difficulties (which especially occurred at the start of the implementation process during the first wave). Related to this, a general observation was that the monitoring system consisted of many individual components, making the system more prone to errors.

Considering how the monitoring system was set up, communication and teamwork between the different disciplines was key. All parties mostly agreed that the contact between nurses, the monitoring team, and the project supervisors was pleasant. Also, all parties agreed that the involvement of physicians in the interpretation of the continuous data could have been better, in order to optimise the efficacy of the monitoring system. In this particularly hectic and critical situation at the COVID-19 cohort ward, the presence of the monitoring team was favorable, to unburden nurses of operating the system and interpreting the data without any guidance. However, in future projects these tasks should be either transferred to the nursing staff completely, or expanded with more tasks and responsibility to extend the role of the monitoring team.

According to the results, the monitoring system affected care at the COVID-19 cohort ward in terms of providing extra insight into the global clinical condition of the patient, providing the possibility for early detection of patient deterioration and reassurance for the nurses that their patients were adequately monitored. Importantly, according to the nurse respondents, the implementation of the monitoring system did not reduce the amount of times that the nurses entered the isolation room. [91]

Interpretation of results

The overall effect of the continuous monitoring system on healthcare at the COVID-19 cohort ward was/is of a positive influence on patient care, according to the respondents and the general observations. The continuous data provided additional insights into the clinical condition of the patients, sometimes resulting in changes in treatment policy to optimise patient specific care. This is in accordance with previously published literature, stating that continuous monitoring contributed to a decreased amount of adverse events [40–46].

No evident conclusions on the effect of the continuous monitoring system on the workload of healthcare workers are formulated. This effect is not completely clear, as the implementation of the monitoring system created some additional tasks, yet also provided a sense of reassurance, as patients were monitored from outside the room. Also, the implementation of continuous monitoring did not reduce the number times a nurse entered the isolation room, which is in accordance with another recent study on this topic [91]. Nurse respondents did however state that they felt supported by the presence of the monitoring team and availability of the continuous trend data. Previously published researches also report varying results with respect to the effect of continuous monitoring on nursing workload. These results vary from continuous monitoring resulting in a reduced nursing workload [92], to vital sign monitoring being overly time consuming and overwhelming [64]. In the end, the current methods of continuous vital sign monitoring have shown to be of added value, but have also shown to not be perfect yet: methods should be further optimised in order to affect nursing workload in a positive way.

Limitations

This research has its limitations. The original plan – included in appendix 11.1 – was to perform in-depth interviews with nurses who had worked with the monitoring system during the first wave of COVID-19 patients. This would have been the optimal method for researching the topic, as the opinions, prejudices and perhaps even emotions of nursing staff regarding the continuous monitoring system and its effects could have been better intercepted through such an in-depth conversation. The eventual method of data acquisition, through questionnaires and casual conversations in the coffee break room or at the ward may have limited the quality of information that respondents provided. In addition, most nurses had no intrinsic motivation to fill in the 'coffee break room'-questionnaire. The researcher had to actively remind nurses of the questionnaire, sometimes distributing the questionnaire at quiet hours during the evening shifts.

The student respondents to the evaluation questionnaire of the student monitoring team that was in active during the first wave of COVID-19 patients, may have been positively influenced by the project supervisors. Of course, the project supervisors (who were both a PhD candidate on the topic of continuous monitoring) were enthusiastic about continuous monitoring and convinced of the added value of the monitoring system. This may have affected the monitoring team in being positive-minded on the performance of the monitoring system. In addition, this also applies to the general observations that were made by the main researcher. These general observations may also have been affected by the researcher's positive view on continuous monitoring in general.

In addition to the limitations with respect to the use of questionnaires, the evaluation questionnaire for the student monitoring team was distributed shortly after the first wave of COVID-19 patients, while the 'coffee break room'-questionnaire was distributed during the second wave of COVID-19 patients. Therefore, the results need to be interpreted carefully, as the situation (especially the 'acuteness' and 'criticality' of the situation) differed for these two periods.

Within this research, patients have not been questioned on their experiences with the continuous monitoring system. The researcher did sometimes get information from nurses on the patients' experiences with the biosensor, such as the feeling of reassurance, or on the other hand confusion about the biosensor for patients with delirium. To fully evaluate the continuous monitoring system, the experiences of patients should have been included.

Recommendations

Future research should focus on improving the technological aspects of continuous patient monitoring (e.g. further innovation of wireless wearables and the development of improved notification systems), as well as optimising the effect of continuous monitoring on workload and working experience of healthcare workers. The short-term and long-term recommendations for optimisation of implementation processes of continuous monitoring systems at (COVID-19) nursing wards are formulated in a 'recommendation overview', formulated in subsection '5.5 recommendation overview' on the following page. The recommendations can be summarised as follows:

- Short-term (<1 year):
 - Focus should remain on positive engagement of healthcare workers
 - Involvement of physicians should be increased
 - Re-evaluate the involvement of a monitoring team (for each implementation situation)
 - Develop simple, short and regularly updated training methods which should be promoted by ward coordinators
- Long-term (>1 year):
 - Hardware optimisation: simplify logistics, improve wireless wearable (enable for measurement of additional physiological parameters), improve pulse oximeter.
 - Software optimisation: develop well-designed user interface with adequate notification system, and integrate this into the EPR.

5.5 Recommendation overview

Research on the optimisation of the implementation of continuous monitoring at (COVID-19) nursing wards concludes with the following short-term and long-term recommendations.

Short-term (<1 year)

- Positive engagement of healthcare workers is key to accomplish lasting success. The main focus of optimising the implementation process should therefore always be on the positive engagement of both nurses *and* physicians.
- Increase (positive) engagement of physicians in order to increase the support that the technology provides for the clinical process.
- Re-evaluate the involvement of the monitoring team. This comes with multiple options, which are recommended in different types of situations:
 - Option 1: No monitoring team involved, and complete integration of the monitoring tasks into the workflow of nurses and physicians. This is advised in a situation where the group of healthcare workers at the ward of interest is 'rigid', meaning that little change within the nurse and physician population will occur. This option is preferred over option 2, as it will result in the highest possible integration of the continuously available data into the clinical process of the patient.
 - Option 2: Monitoring team involved. Advised in a situation where the group of healthcare workers at the ward of interest is 'flexible', meaning that a lot of personnel changes will occur within the nurse population. In this situation, the monitoring team could be a 'stable factor' in supporting the flexible group of healthcare workers. If project supervisors choose to involve a monitoring team, the tasks of the monitoring team should also be re-evaluated and clearly described, mainly focussing on providing the monitoring team with more clinical context information on the hospitalised patients (such as access to the EPR). Also, it should be considered whether a monitoring team should be installed per nursing ward, per group of nursing wards (e.g. per hospital division), or for an entire hospital (i.e. installing a hospital-wide observation centre). All of these options are feasible and should be decided on based on the preferences of healthcare workers and hospital policy.
- Develop simple and short (e-learning) training methods that are regularly updated and easily accessible for all involved healthcare workers. Ward coordinators should always be updated on changes in the monitoring system and consecutively transfer knowledge and experience to other healthcare workers as well as to motivate colleagues to follow the (e-learning) training methods.

Long-term (>1 year)

- Hardware optimisation: improving and further developing the hardware components of the system
 - Simplify the logistics around the technology of the monitoring system (e.g. less components: biosensor *and* relay device *and* spot-check monitor et cetera) to make the system more solid and less prone to errors.
 - Improve wireless wearable by adding more features, such as continuous non-invasive BP for extra medical insight and accelerometry measurements in order to detect movement, indicating active patient mobilisation
 - Develop a mobile and comfortable pulse oximeter for continuous monitoring of SpO₂
- Software optimisation: improving and further developing the software component of the system
 - Develop an intuitive, yet transparent and straightforward user interface for healthcare workers, including a straightforward notification system. This notification system should be both intuitive to understand, but also provide straightforward actions for the healthcare workers to undertake when receiving a notification.
 - Integrate this software system into the EPR, enabling for displaying the continuous trend data and notifications with just a few 'clicks' while clinical context information is at hand.

5.6 Conclusion

To briefly answer the research question corresponding to this chapter:

How can the implementation of continuous ward monitoring be optimised, with a focus on improving patient care, reducing workload for healthcare workers and improving working experience?

The implementation process of continuous ward monitoring should be optimised by:

- Short-term (<1 year): focus on positive engagement of healthcare workers, increase the involvement of physicians, re-evaluate the involvement of a monitoring team for each implementation situation, and lastly, develop simple, short and regularly updated (e-learning) training methods in consultation with ward coordinators.
- Long-term (>1 year) comprises of hardware and software optimisation. Hardware optimisation: simplify logistics of the system, improve wireless wearable (enable for measurement of additional physiological parameters such as BP and accelerometry) and improve pulse oximeter (improve mobility and comfort while wearing). Software optimisation: develop well-designed user interface with adequate notification system, and integrate this into the EPR.

6 VITAL SIGNS TRENDS IN COVID-19 PATIENTS

6.1 Introduction and objective

The outbreak of the novel SARS-CoV-2, causing the COVID-19, has quickly resulted in a true pandemic, affecting healthcare systems and society on a global scale [6, 7, 9]. The disease has various clinical manifestations, varying from asymptomatic to critical manifestations, which in some cases result in long-term intensive care unit (ICU) admissions, or death [93].

The number of COVID-19 patients in need of in-hospital care, has put a serious pressure on healthcare capacity and workload. Hospitals have come up with innovative solutions for capacity problems or have sped up implementation processes of innovative technologies. This study focusses on the unique data that was collected due to the implementation of one of these innovative technologies during the first wave of COVID-19 patients (spring 2020) in the Netherlands.

At the COVID-19 cohort ward of the UMCU, a technology for continuous monitoring was implemented: the biosensor, in combination with the VS30 monitor and the IGS system. Every patient admitted to the cohort ward received a chest-worn patch that measured HR and RR. The primary goal of this implementation was early detection of patient deterioration by monitoring the HR and RR trend of patients. The secondary goal was to facilitate healthcare workers in monitoring the isolated patients from outside the room.

The data that were acquired during this project provide opportunities for researchers to study the patterns of continuously measured vital signs in COVID-19 patients with different clinical outcomes. Research regarding these data may contribute to improved insight in the disease and may help healthcare workers in future crises. In this observational study we report on the continuously recorded vital signs data of suspected COVID-19 patients in the form of a case series report. We describe the continuous HR and RR patterns that were registered in COVID-19 patients who were hospitalised at the COVID-19 cohort ward. A conclusion to this chapter and advice for future implementation processes will be formulated in relation to the following research question:

How can continuously monitored heart rate and respiratory rate data be used to visually detect and predict clinical deterioration or recovery in COVID-19 patients, and what are characteristic trend patterns indicating deterioration or recovery?

6.2 Methods

Study design

This study concerns an observational retrospective cohort study of all suspected COVID-19 patients admitted to the cohort ward of the UMCU equipped with the continuous monitoring technology. A case series was performed to describe the HR and RR patterns that were registered in COVID-19 patients who were hospitalised at the COVID-19 cohort ward during the first wave of COVID-19 patients in the Netherlands. In addition, general description of the data is formulated, describing data characteristics within the entire included study population.

Study population

Overall in- and exclusion criteria

The overall study population covers all adult patients diagnostically confirmed with COVID-19, admitted to the COVID-19 cohort ward during the first wave of COVID-19 patients in the Netherlands, and equipped with the continuous monitoring technology. Since this is a retrospective observational study in order to gain insight in the added value of continuous vital signs measurements in COVID-19 patients, no exact sample size calculation has been performed. The in- and exclusion criteria are formulated below in table 4.

Table 4: in- and exclusion criteria for the entire population of COVID-19 patients monitored at the COVID-19 cohort ward

Inclusion

- Age > 18 years
- Patient is diagnosed with COVID-19
- Patient was continuously monitored using a wireless wearable sensor

Exclusion

- Patients with a pacemaker or implantable cardioverter defibrillator

Selection for case series

The selection of cases from the overall population for the case series, was done in such a way that an as complete and representative as possible depiction of the HR and RR trends of the overall study population was generated. To do so, the following aspects were taken into account:

- The selection of cases should contain at least one case of every possible clinical outcome (which were 'discharged to home', 'discharged to home with care', 'discharged to revalidation centre', 'discharged to care hotel', and lastly 'death');
- The selection of cases should contain both patients who experienced both 'recovery' *and* 'deterioration';
- The selection of cases should contain representative trends regarding the amount of missing data points.

Data acquisition

All data that is used in this chapter was acquired at one of the COVID-19 cohort wards at the UMCU. The set-up of the monitoring system at the COVID-19 cohort ward is elaborately described in the background section '2.3 Continuous monitoring at the COVID-19 ward in the UMCU'. Figure 12 provides a schematic illustration of the continuous monitoring system set-up. The data that is included in this chapter were acquired during the first wave of COVID-19 patients in the Netherlands, from the start of April, until mid-May.

Data analysis

All data were visualised and quantitatively analysed using Matlab R2020a. To describe population characteristics, descriptive statistical analyses are performed. Variables are expressed as medians (with IQR) and discrete variables are expressed as numbers (with percentages).

Data processing

The continuous HR and RR trend data does not have a constant sample frequency. The time difference between two datapoints is variable, yet datapoints are generated once or twice per minute – excluding large time gaps due to other, logistic reasons (e.g. an empty biosensor battery). This was purposely not corrected for, as all datapoints are realistic and relevant for data analyses and visualisation for trend assessment.

Continuous HR and RR trend data was cleaned and processed in Matlab in order to remove erroneous data. After structurally storing the data in Matlab, the first three and last three datapoints of each individual case were removed. Likewise, all data was searched for time gaps that were longer than four minutes, after which the three datapoints preceding and following these timegaps were removed. This was done as these datapoints are prone to error, for example due to patch removal, or other motion artifacts.

Case series report

The COVID-19 cases with that were selected are described to match context information regarding the clinical course of the patient according to nurses' observations to the continuously measured HR and RR data. All COVID-19 cases are discussed individually by stating the patient characteristics, presenting the entire clinical course during admission at the UMCU, and discussing the continuous data that was registered at the COVID-19 cohort ward.

In addition to the case descriptions, 'events' that occurred during the period of continuous monitoring are quantitatively described. These events are defined as:

- Type 1: The need for oxygen therapy with an $\text{FiO}_2 \geq 40\%$ at the start of continuous monitoring;
- Type 2: The need for oxygen therapy with an $\text{FiO}_2 \geq 40\%$ after at least 12h of continuous monitoring;
- Type 3: An ICU admission;
- Type 4: Death.

For patients who experience an event, the period during which the event was ongoing is indicated in the data visualisations by the use of colour blocks.

Feature computation per event per case study

Features of the vital signs trend data are computed during specific periods of time (0.5h, 1h, 2h, 4h, 6h, 12h and 24h) prior to these events. The computed features (for both HR and RR) are: mean, SD, netto increase over the selected segment (computed by subtracting the average of the first 10% of HR or RR values of the last 10% of HR or RR values), mean slope, SD of slope, slope of linear regression model fitted to the selected segment, coefficient of determination (R^2) of linear regression model fitted to

the selected segment and p-value of the R^2 of linear regression model fitted to the selected segment. Also, the HR and RR trend during these periods of time prior to the events are visualised – along with the fitted linear regression models.

As type 1 events start approximately when continuous monitoring of the patient starts, none to little data is available of the period prior to type 1 events. Therefore, it is not possible to elaborately study the period of continuous data prior to type 1 events. For this reason, to feature computation was only performed for type 2, type 3 and type 4 events.

Interpretation of computed features per event per case study – when is a trend ‘detected’?

Linear regression models were studied in order to explore whether trends were present prior to the defined type 2, type 3 and type 4 events. This was done by following three steps:

- 1) Interpretation of the coefficient of determination (R^2):
 - a. Is $R^2 \geq 0.5$?
 - b. Is the p-value of $R^2 \leq 0.05$?
- 2) Interpretation of the slope of the linear regression model:
 - a. For HR: Is the slope of the linear regression model ≥ 10 bpm $\uparrow$ /day?
 - b. For RR: Is the slope of the linear regression model ≥ 5 brpm $\uparrow$ /day?
- 3) And lastly, visual assessment: does the visualisation of the period prior to the event show a trend? In this subjective assessment, ‘trend’ was detected as ‘a steady increase of the parameter over the entire period of interest’.

General descriptive overview of the data

Lastly, a general descriptive overview of the data was created for the study population. This descriptive overview was generated by visually assessing data characteristics per patient, in order to provide insight into the general data characteristics. Data characteristics that were visually assessed are: total amount of data in hours, whether or not a sinusoidal pattern was present in the data, presence of data gaps, periods of tachycardia, presence of bradycardia and the presence of tachypnoea.

6.3 Results

Population characteristics

Figure 14 shows a schematic illustration of the inclusion of the monitored patients for trend analysis. During the period that the continuous monitoring technique was implemented at the COVID-19 cohort ward, 64 patients were continuously monitored. Thirty out of these 64 patients tested positive for COVID-19 in the period of continuous monitoring, excluding 34 of the monitored patients for this research.

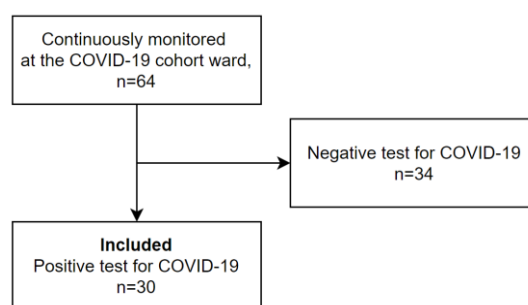


Figure 14: schematic illustration of the included population for trend analysis.

Table 5 depicts the baseline characteristics table of the entire included study population. Subgroups were constructed based on the diagnosis with RF (defined as the need for invasive or non-invasive mechanical ventilation, the need for high flow nasal oxygen therapy or the need for $FiO_2 > 0.4$) and the reason for admission to the COVID-19 cohort ward (primary admission versus post-ICU care).

Table 5: Baseline characteristics table of the included study population. RF = respiratory failure, BMI = body mass index, ICU = intensive care unit, MCU = medium care unit, CCI = Charlson comorbidity index.

		All patients (n=30, 100%)	RF ^a (n=25, 83%)	No RF ^a (n=5, 17%)	Primary admission to COVID-19 cohort ward (n=15, 50%)	Post-ICU care at COVID-19 cohort ward (n=15, 50%)
Patient characteristics at admission						
Age (years)		64 [54 ; 73]	64 [48; 73]	59 [59; 77]	60 [51.5; 76.5]	64 [54.5; 72]
Gender	Male	17 (57%)	14 (56%)	3 (60%)	7 (47%)	10 (67%)
	Female	13 (43%)	11 (44%)	2 (40%)	8 (53%)	5 (33%)
BMI (kg/cm ²)		27.3 [24.8; 29.9]	27.5 [25.5; 30.4]	24.1 [21.3; 26.1]	26.4 [24.5; 29.7]	27.5 [25.0; 30.8]
Hospitalisation details ^b						
Length of stay (days)		19 [9; 30]	23 [13; 21]	6 [4; 10]	9 [4.5; 14.5]	28 [20.5; 32.5]
ICU admission		16 (53%)	16 (64%)	0	1 (7%)	15 (100%)
Length of stay (days)		15 [9.8; 18.5]	15 [9.8; 18.5]	-	33 [-; -]	14 [9.5; 16]
MCU admission		7 (23%)	7 (28%)	0	4 (27%)	3 (20%)
Treatment restrictions during entire hospitalisation ^c						
No resuscitation		14 (47%)	12 (48%)	2 (40%)	11 (73%)	3 (20%)
No invasive ventilation		12 (40%)	10 (40%)	2 (40%)	10 (67%)	2 (13%)
No ICU admission		9 (30%)	8 (32%)	1 (20%)	8 (53%)	1 (7%)
Comorbidities prior to hospitalisation						
Comorbidities	None	8 (27%)	8 (32%)	0	0	8 (53%)
	Total	3 [0.25; 4]	3 [0; 4]	2 [2; 3]	3 [2.5; 4.5]	0 [0; 2.5]
	CCI	1 [0; 2]	0 [0; 2]	1 [0; 2]	2 [0.5; 2.5]	0 [0; 0.5]
Chronic pulmonary disease		4 (13%)	4 (16%)	0	2 (13%)	2 (13%)
Chronic cardiac disease		6 (20%)	5 (20%)	1 (20%)	4 (27%)	2 (13%)
Hypertension		11 (37%)	10 (40%)	1 (20%)	7 (47%)	4 (27%)
Obesity	BMI ≥ 30	6 (20%)	6 (24%)	0	2 (13%)	4 (27%)
	BMI ≥ 35	2 (7%)	2 (8%)	0	1 (7%)	1 (7%)
Diabetes		10 (33%)	9 (36%)	1 (20%)	7 (47%)	3 (20%)
Complications during entire hospitalisation stay at the ward ^d						
Thrombotic event		11 (37%)	11 (44%)	0	2 (13%)	9 (60%)
Pulmonary embolism		7 (23%)	7 (28%)	0	1 (7%)	6 (40%)
Other		6 (20%)	6 (24%)	0	1 (7%)	5 (33%)
Cardiac arrhythmia		4 (13%)	4 (16%)	0	1 (7%)	3 (20%)
Patient outcome						
Discharged to home		5 (17%)	2 (8%)	3 (60%)	3 (20%)	2 (13%)
Discharged to home with care		2 (7%)	2 (8%)	0	1 (7%)	1 (7%)
Rehabilitation centre		12 (40%)	10 (10%)	2 (40%)	3 (20%)	9 (60%)
Care hotel		3 (10%)	5 (20%)	0	2 (13%)	3 (20%)
Death		8 (27%)	8 (32%)	0	6 (40%)	2 (13%)
Outcome different situation prior to hospitalisation?		23 (77%)	22 (88%)	1 (20%)	10 (67%)	13 (87%)

Data is presented as median (IQR) and n(%).

^a RF = respiratory failure is defined as the need for invasive or non-invasive mechanical ventilation, the need for high flow nasal oxygen therapy or the need for FiO₂ > 0.4.

^b Denotes hospitalisation details concerning the entire period of admission to the UMCU.

^c Denotes treatment restrictions at any point during hospitalisations. For some of the patients, treatment restrictions were added during their stay at the UMCU, for example at admission or during hospitalisation at the ICU or COVID-19 cohort ward.

^d Denotes complications that occurred during the entire period of admission to the UMCU

^e Denotes complications that occurred during the period of continuous monitoring at the COVID-19 cohort ward.

Case series: eight cases of COVID-19

The following section of this report consists of a case series report in which the clinical course and the continuous data of eight cases is described. Table 6 depicts an overview of the eight selected cases. This table indicates the clinical outcome of the patient and the 'types of event(s)' (and how many of these events occurred) that the patient experienced during the period of continuous monitoring. These event types are defined as:

- Type 1: The need for oxygen therapy with an $\text{FiO}_2 \geq 40\%$ at the start of continuous monitoring*;
- Type 2: The need for oxygen therapy with an $\text{FiO}_2 \geq 40\%$ after at least 24h of continuous monitoring;
- Type 3: An ICU admission;
- Type 4: Death.

* As type 1 events start approximately when continuous monitoring of the patient starts, none to little data is available of the period prior to the event. Therefore, it is not possible to elaborately study the period of continuous data prior to type 1 events. For this reason, to feature computation was performed for type 1 events.

The eight selected patients are a good representation of the overall study population of $n=30$, except for the fact that the selected patients have been monitored for over 48 hours. In reality, three patients were monitored for less than 24 hours, one patient was monitored for less than 48 hours and one patient was monitored for just over 48 hours. Short periods of continuous monitoring are mostly the consequence of two completely opposite situations: 1) patients that are quickly recovering and no longer need hospital care, and 2) patients that are quickly deteriorating and transferred to the ICU or die. For research purposes, a set of continuous data of less than 48 hours limits the possibilities to define clinical processes in relation to the trend. Therefore, data sets with a duration of > 48 hours were preferred for case selection. For completeness, two figures of continuous data of patients who were monitored for less than 48 hours are included in appendix 11.6.

Table 6: overview of the eight selected cases for the case series report

Case	Events				Patient outcome
	Type 1	Type 2	Type 3	Type 4	
Case 1					Discharged to home
Case 2					Discharged to home with care
Case 3	1				Discharged to revalidation centre
Case 4	1	1			Discharged to care hotel
Case 5	2				Discharged to revalidation centre
Case 6	1	1	1		Discharged to revalidation centre
Case 7	1	1		1	Death
Case 8	1			1	Death

Reading guide of case series report

Each case description consists of the multiple components. These components are summarised here in order to provide guidance in reading the case series report.

- *Table – Patient overview*
Provides the reader with baseline characteristics of the patient, such as age, BMI and co-morbidities.
- *Figure – Clinical course of the case throughout the entire period of hospitalisation*
Provides the reader with a summary on the clinical course of the patient, which offers context information on the severity of the effects of COVID-19 for that specific case.
- *Figure – Continuous data that was acquired during the period of continuous monitoring at the COVID-19 cohort ward*
Depicts the actual continuous data that was acquired during the period of continuous monitoring. These figures contain four subplots:
 - Subplot 1: Continuous HR data
 - Subplot 2: Continuous RR data
 - Subplot 3: SpO₂ measurements, registered by nurses
 - Subplot 4: O₂ therapy, registered by nurses
- *Table – Description of the vital sign trend*
Provides the reader with a concise description of the trend: what is visually apparent from the data within the four subplots?
- *Optional: Table – IF a type 2, 3 or 4 event occurred during the period of continuous monitoring, a table is added for each event*
Features are calculated during periods of time (0.5h, 1h, 2h, 4h, 6h, 12h and 24h) prior to these events. The computed features (for both HR and RR) are: mean, SD, net increase over the selected segment (computed by subtracting the average of the first ten HR or RR values of the last ten HR or RR values), mean slope, sd slope, slope of linear regression model fitted to the selected segment (in HRT/day), R² of linear regression model fitted to the selected segment and p-value of the R² of linear regression model fitted to the selected segment. Also, the HR and RR trend during these periods of time prior to the events are visualised – along with the linear regression models – in order to explore patterns in features prior to the occurrence of an event.

Case 1

Table 7 provides an overview of the patient's characteristics. Figure 15 provides an overview of the clinical course of case 1 throughout hospitalisation.

Table 7: patient characteristics of case 1

Age	47
Gender	Male
BMI	29.9
Patient outcome	Discharged to home
Comorbidities/medical history	None
Thrombotic event	Yes, pulmonary embolism
Treatment restrictions	None
Reason for admission to COVID-19 cohort ward	Post-ICU care
Events	None

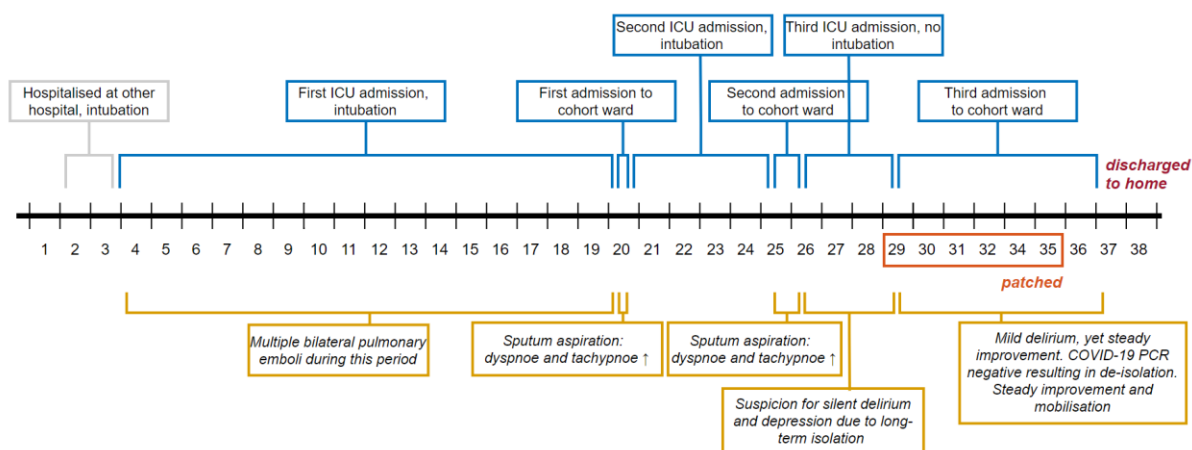


Figure 15: clinical course of case 1 throughout hospitalisation. Blue text boxes above the timeline indicate the hospitalisation details of the patient. Orange text boxes below the timeline indicate other clinical aspects or events.

Figure 16 shows the continuous data that was measured during the period that the patient was patched with the Philips Biosensor. Table 8 contains the description of the vital sign trends. The patient was continuously monitored at the ward during a period of approximately six days. Note that for this patient, this was during a period of recovery from COVID-19.

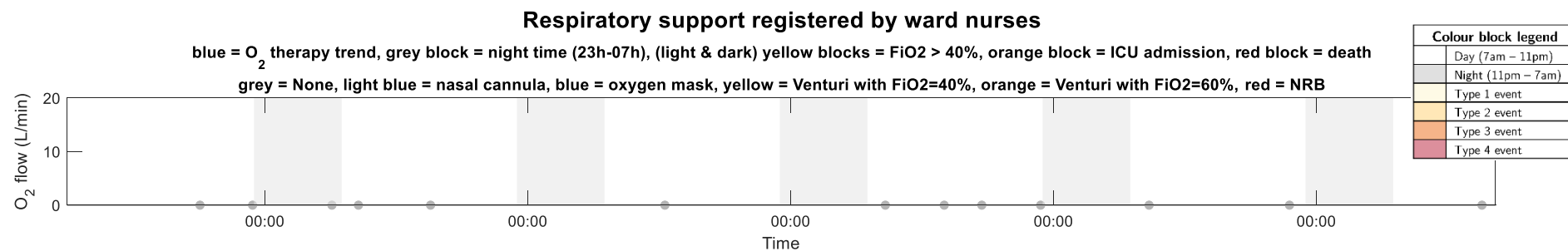
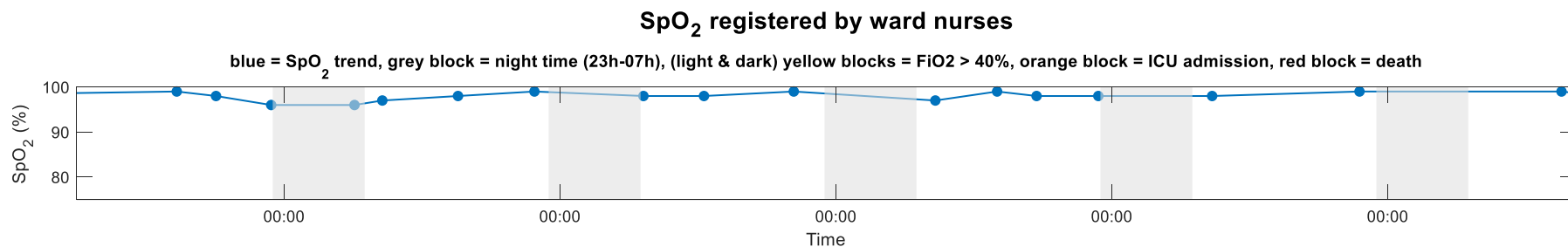
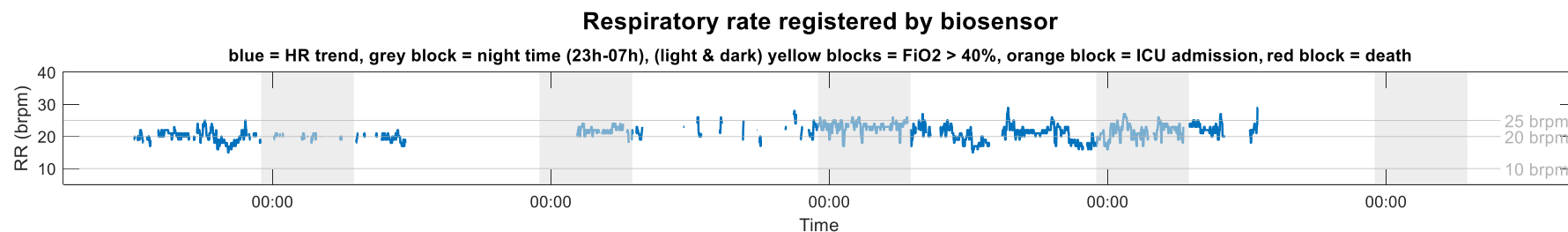
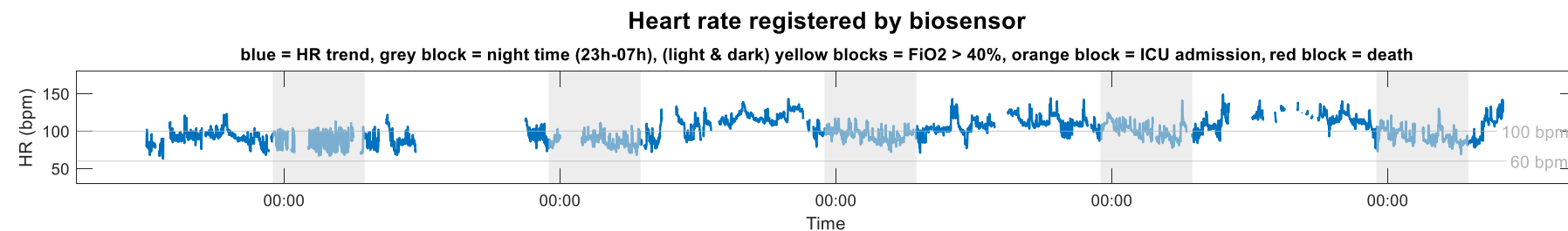


Figure 16: case 1 – Patient outcome = discharged to home.

Table 8: Description of vital sign trend (which is depicted in figure 16) for case 1

	Timeframe	Comment
HR trend	Start – day 2	Somewhat 'chaotic' and unstable HR of approximately 80 to 120 bpm. This matches nurses' observations in the EPR, which stated that the respiratory condition was still improving, that the patient was not comfortable and that the patient has some trouble sleeping due to restlessness.
	Day 2 – end	Patient was steadily improving according to nurses' observations. The HR trend shows a <i>sinusoidal pattern</i> with the HR decreasing overnight (varying from 60 bpm to 120 bpm, mostly around 90 bpm) and increasing during the day (between 60 and 140 bpm, mostly over 100 bpm).
RR trend	Start – end	The RR data contains a predominantly large amount of data gaps. When studying the entire set of continuous data, the RR data still provides an indication of the RR: stable tachypnoea of ± 22 brpm. If the data were to be studied on a 'real-time' basis, the data gaps would limit the healthcare worker from obtaining a complete interpretation of the patient's continuous vital signs within a limited timeframe
SpO ₂ data	Start – end	The SpO ₂ was registered about four times a day. The SpO ₂ varied from 96 to 99%. The SpO ₂ seems to increase – therefore improve – towards the end of the continuous data.
Oxygen therapy	Start – end	The patient did not receive any respiratory support while patched at the COVID-19 cohort ward.

Event(s)

This patient did not experience a type 2, 3 or 4 event during the period of continuous monitoring. Therefore, no quantitative assessment of the period prior an event has been performed.

Summary of the case study of case 1 – discharged to home

The continuous vital sign trends of case 1 match up with the documented nurses' observations. The RR data shows a predominantly large amount of data gaps, limiting real-time observers in obtaining a complete interpretation of the data. A sinusoidal pattern can be observed in the HR data during the period of recovery: increasing HR during the day, decreasing HR during the night.

Case 2

Table 9 provides an overview of the patient's characteristics. Figure 17 provides an overview of the clinical course of case 2 throughout hospitalisation.

Table 9: patient characteristics of case 2

Age	72
Gender	Female
BMI	28.1
Patient outcome	Discharged to home with care
Comorbidities/medical history	Hypertension, asthma, paroxysmal atrial fibrillation and diabetes without complications.
Thrombotic event	None
Treatment restrictions	None
Reason for admission to COVID-19 cohort ward	Post-ICU care
Events	None

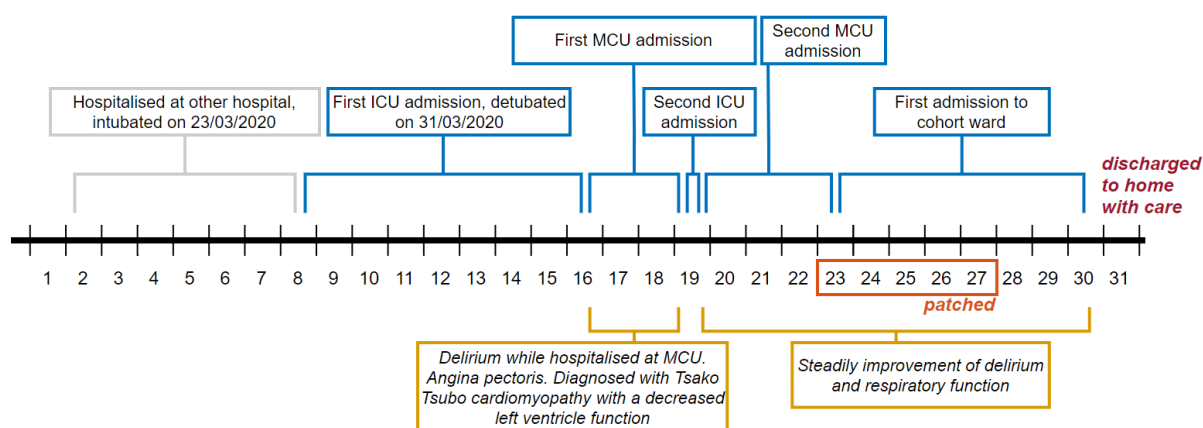


Figure 17: clinical course of case 2 throughout hospitalisation. Blue text boxes above the timeline indicate the hospitalisation details of the patient. Orange text boxes below the timeline indicate other clinical aspects or events.

Figure 18 shows the continuous data that was measured during the period that the patient was patched with the Philips Biosensor. Table 10 contains the description of the vital sign trends. The patient was continuously monitored at the ward during a period of approximately four days. Note that for this patient, this was during a period of recovery from COVID-19.

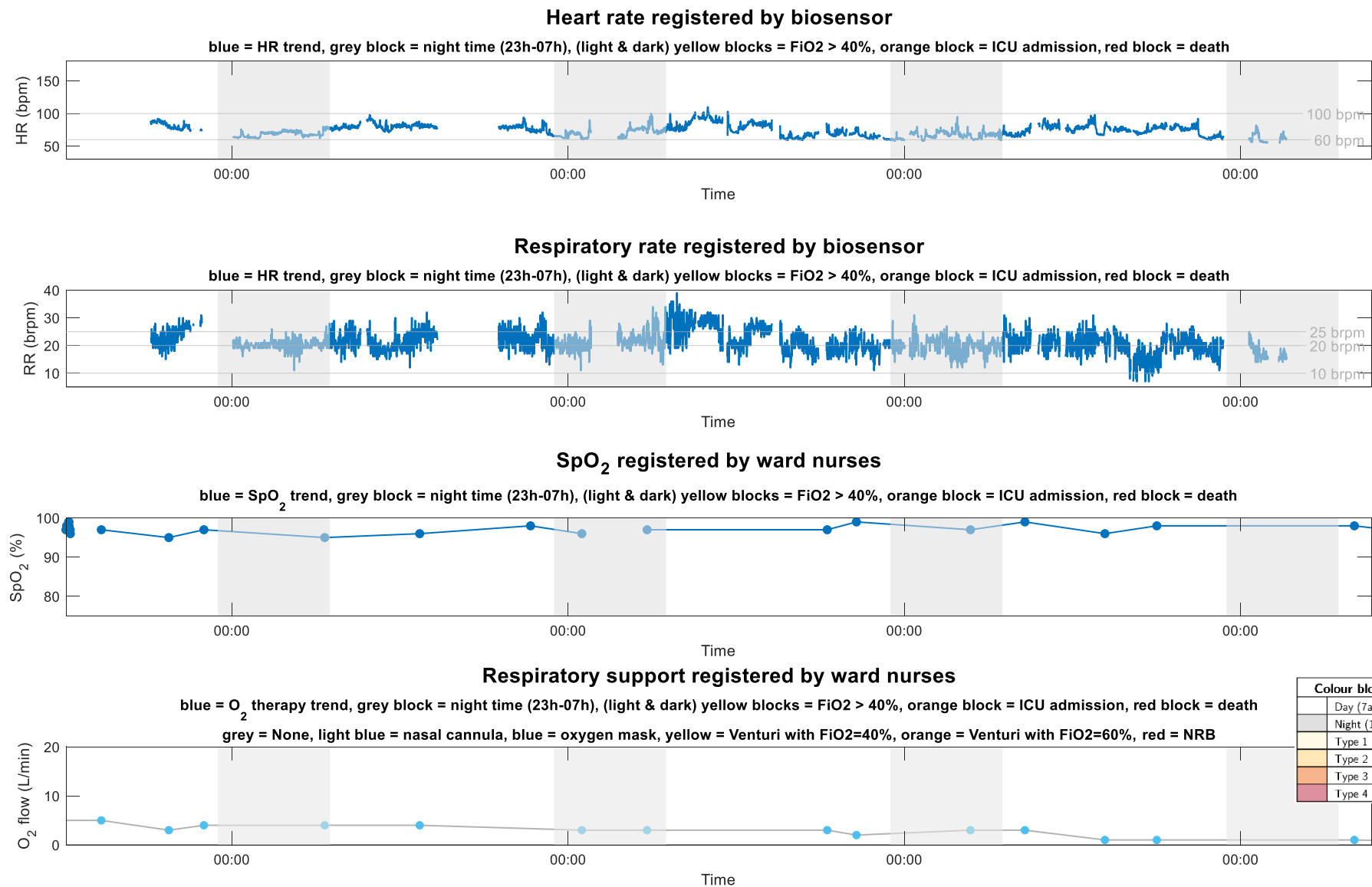


Figure 18: case 2 – Patient outcome = discharged to home with care.

Table 10: Description of vital sign trend (which is depicted in figure 18) for case 2

	Timeframe	Comment
HR trend	Start – end	The HR shows a <i>sinusoidal pattern</i> , with the HR decreasing overnight (varying from 60 to 90 bpm, mostly around 75 bpm), and increasing during the day (between 60 and 100 bpm, mostly around 80 bpm).
RR trend	Start – end	The patient was notably tachypnoeic, with a RR mostly around 22 brpm, varying from 8 to over 30 brpm. Documented nurses' observations in the EPR stated that the patient was very keen on improving, resulting in high efforts of mobilisation. Also, nurses' observations stated that the patient's nights were still somewhat restless as the patient was experiencing some mild delirium complaints. These factors may have contributed (on top of the moderate respiratory condition of the patient) to this unsteady and tachypnoeic pattern.
SpO ₂ data	Start – end	The SpO ₂ was registered about three times a day. The SpO ₂ varied from 95 to 99%. The SpO ₂ seems to increase – therefore improve – towards the end of the continuous data.
Oxygen therapy	Start – end	The patient was supported by the use of a nasal cannula, of which the flow was steadily decreased. By the time of 22:30 shortly after the patch was removed, the patient did no longer need a nasal cannula to maintain a steady level of SpO ₂ .

Event(s)

This patient did not experience a type 2, 3 or 4 event during the period of continuous monitoring. Therefore, no quantitative assessment of the period prior an event has been performed.

Summary of the case study of case 2 – discharged to home with care

The continuous vital sign trends of case 2 match up with the documented nurses' observations. A sinusoidal pattern can be observed in the HR data during the period of recovery: increasing HR during the day, decreasing HR during the night. The patients RR is notably unstable and increased.

Case 3

Table 11 provides an overview of the patient's characteristics. Figure 19 provides an overview of the clinical course of case 3 throughout hospitalisation.

Table 11: patient characteristics of case 3

Age	73
Gender	Male
BMI	25.6
Patient outcome	Discharged to revalidation centre
Comorbidities/medical history	Hypertension and diabetes without complications
Thrombotic event	None
Treatment restrictions	None
Reason for admission to COVID-19 cohort ward	Primary admission to COVID-19 cohort ward
Events	Type 1

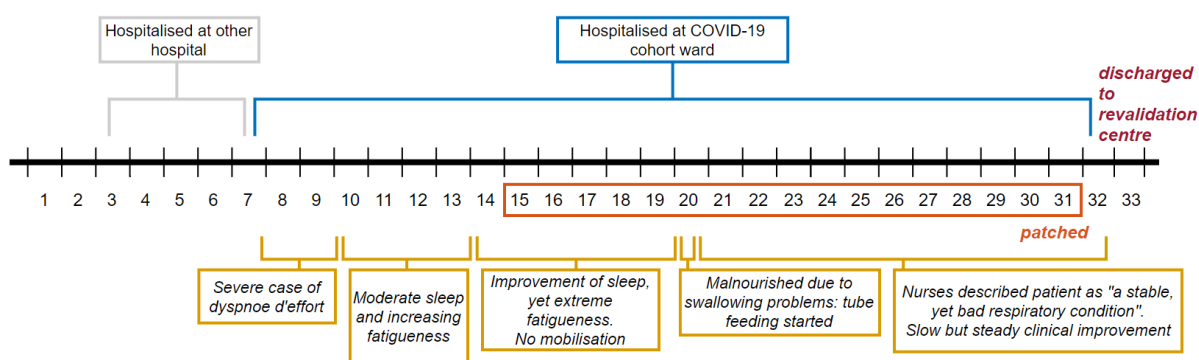


Figure 19: clinical course of case 3 throughout hospitalisation. Blue text boxes above the timeline indicate the hospitalisation details of the patient. Orange text boxes below the timeline indicate other clinical aspects or events.

Figure 20 shows the continuous data that was measured during the period that the patient was patched with the Philips Biosensor. Table 12 contains the description of the vital sign trends. The patient was continuously monitored at the ward during a period of approximately seventeen days. Note that for this patient, this was during a period of recovery from COVID-19.

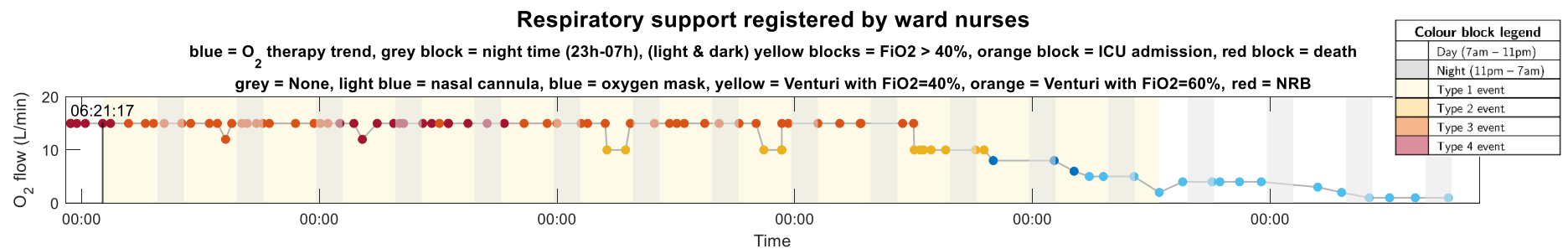
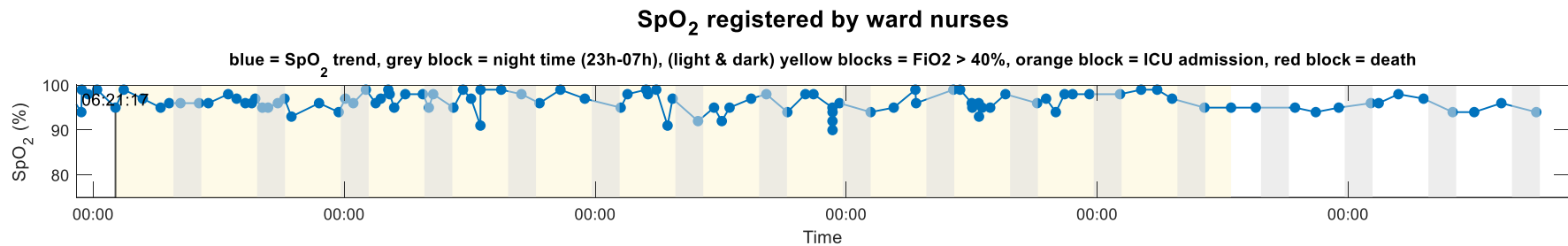
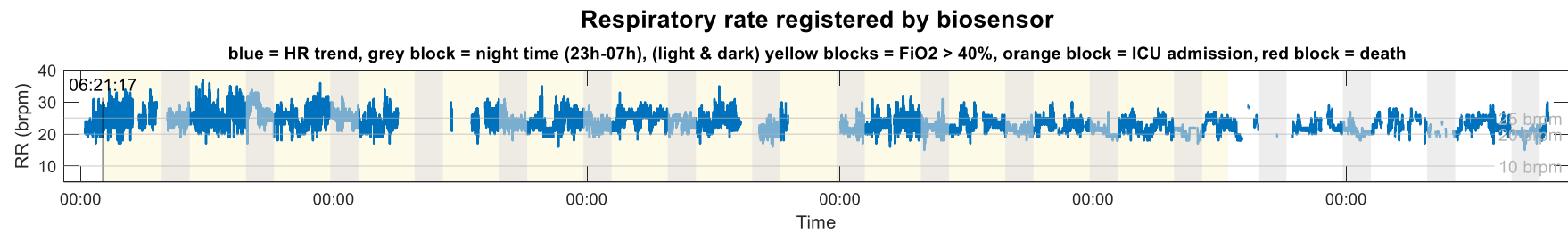
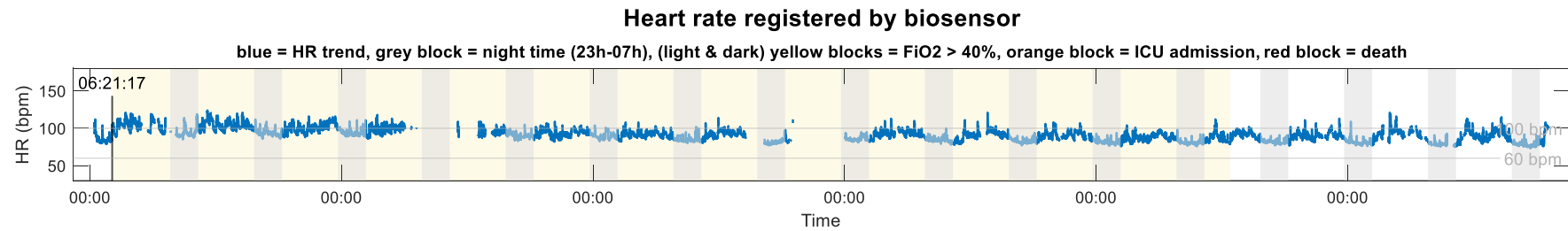


Figure 20: case 3 – Patient outcome = rehabilitation centre.

Table 12: Description of vital sign trend (which is depicted in figure 20) for case 3

	Timeframe	Comment
HR trend	Start – end	During the entire period of continuous monitoring, the HR trend shows a <i>sinusoidal pattern</i> .
	Start – day 4	During night-time, the HR varies from 80 to 110 bpm, mostly around 85 bpm. During day-time, the HR varies from 90 to 120 bpm, mostly around 110 bpm.
	Day 5 – day 8	During night-time, the HR varies from 80 to 100 bpm, mostly around 85 bpm. During day-time, the HR varies from 85 to 110 bpm, mostly around 95 bpm. The amplitude of the <i>sinusoidal pattern</i> slightly decreases.
	Day 9 – end	During night-time, the HR varies mostly around 80 bpm. During day-time, the HR varies from 80 to 120 bpm, mostly around 85 bpm.
RR trend	Start – end	The patient was notably tachypnoeic during the entire period of continuous monitoring. The degree of tachypnoea however decreased over time.
	Start – day 4	During this period, the RR is very unstable, varying from 18 to 35 brpm. The RR seems less variable during night-time than during day-time.
	Day 5 – day 8	With respect to the previous period, the overall RR slightly decreased. Also, the RR was slightly lower during night-time (around 23 brpm) than during day-time (varying from 20 to 30 brpm).
	Day 9 – end	In this period, the RR is stabilising, with a RR down to around 20 brpm at night-time and 23 brpm at day-time. However, at the point of discharge, the patient is still tachypnoeic.
SpO ₂ data	Start – end	The SpO ₂ was registered about seven times a day. The SpO ₂ varied from 90 to 99%. The SpO ₂ of this patient was unstable during the first period of continuous monitoring, as the patient was highly dependent on oxygen therapy. This stabilised towards the end of hospitalisation, yet the SpO ₂ never reached the optimal value of 100%, and the patient was still in need of respiratory support at the moment of discharge.
Oxygen therapy	Start – end	The patient was supported by the use of a wide variation of respiratory supportive techniques while patched at the ward: a NRB mask, Venturi mask (of both 40% and 60%), an oxygen mask and a nasal cannula. The respiratory support was slowly decreased over time. At the point of discharge to a revalidation centre, the patient was still in need of minor respiratory support through a nasal cannula.

Event(s)

This patient did not experience a type 2, 3 or 4 event during the period of continuous monitoring. Therefore, no quantitative assessment of the period prior an event has been performed.

Summary of the case study of case 3 – discharged to revalidation centre

The continuous vital sign trends of case 3 match up with the documented nurses' observations. A sinusoidal pattern can be observed in the HR and the RR data during the period of recovery: increasing (variability of) HR and RR during the day, decreasing (variability of) HR and RR during the night. Note that this sinusoidal pattern becomes more apparent over time, as the patient steadily recovers and the dependency on oxygen therapy decreases. At the start of continuous monitoring, this patient is notably tachycardic and tachypnoeic. HR and RR slowly decrease over time, yet remain increased compared to normal values in healthy individuals.

Case 4

Table 13 provides an overview of the patient's characteristics. Figure 21 provides an overview of the clinical course of case 4 throughout hospitalisation.

Table 13: patient characteristics of case 2

Age	43
Gender	Female
BMI	21.0
Patient outcome	Discharged to care hotel
Comorbidities/medical history	Depression, complex regional pain syndrome (leg and wrist), obstructive sleep apnoea syndrome, allergic rhinitis, mental disability (IQ 63), somatisation disorder, fibromyalgia, diabetes without complications, asthma
Thrombotic event	Yes, pulmonary embolism
Treatment restrictions	Yes, <i>do not resuscitate</i> and <i>do not perform invasive ventilation</i> added at admission to UMCU for medical reasons.
Reason for admission to COVID-19 cohort ward	Primary admission to COVID-19 cohort ward and post MCU-care
Events	Type 1 and type 2

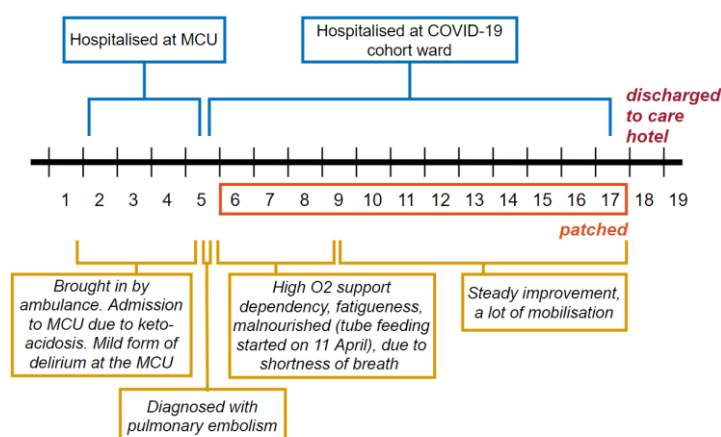


Figure 21: clinical course of case 4 throughout hospitalisation. Blue text boxes above the timeline indicate the hospitalisation details of the patient. Orange text boxes below the timeline indicate other clinical aspects or events.

Figure 22 shows the continuous data that was measured during the period that the patient was patched with the Philips Biosensor. Table 14 contains the description of the vital sign trends. The patient was continuously monitored at the ward during a period of approximately seventeen days. Note that for this patient, this was during a period of recovery from COVID-19.

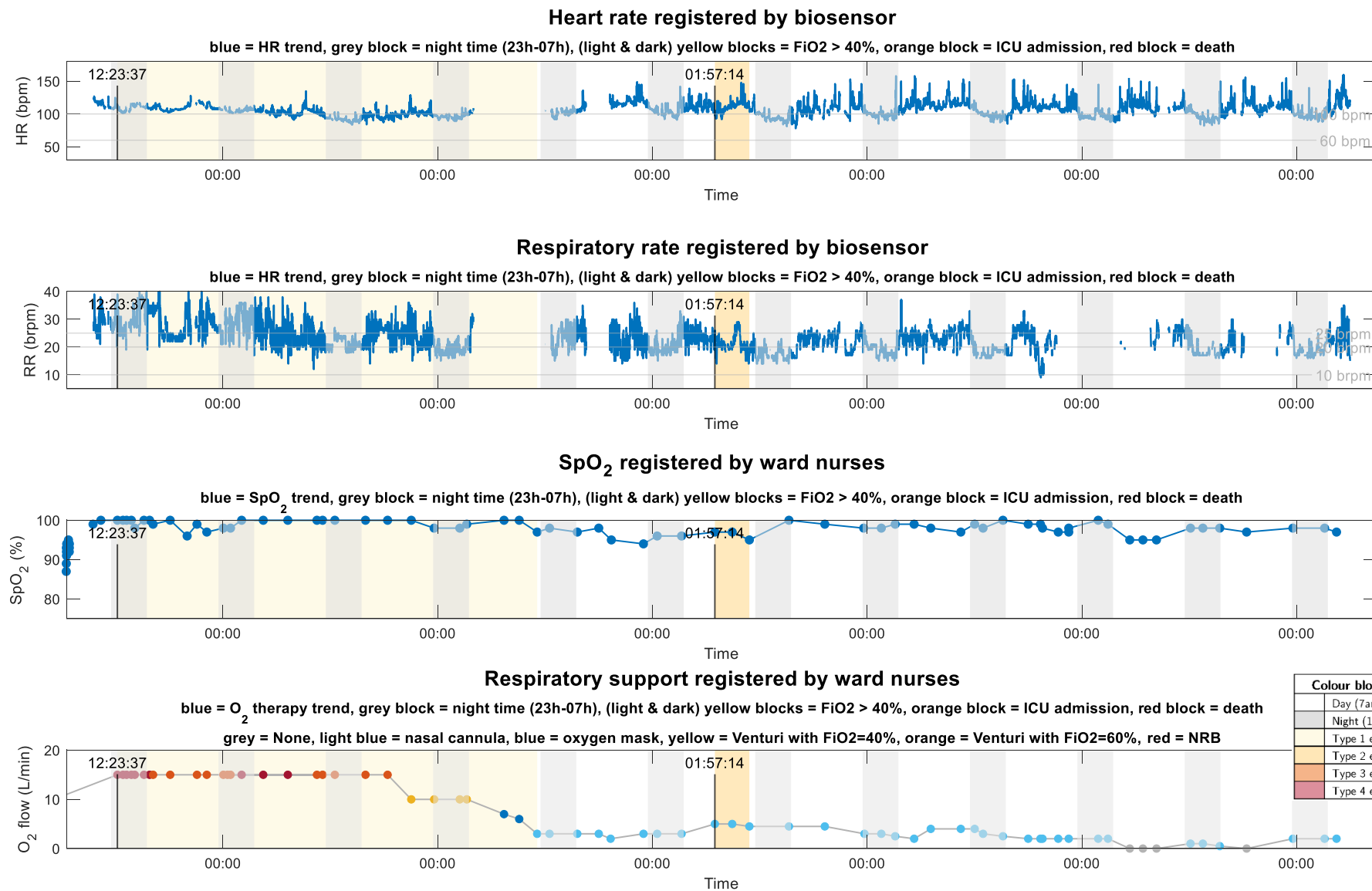


Figure 22: case 4 – Patient outcome = care hotel.

Table 14: Description of vital sign trend (which is depicted in figure 22) for case 4

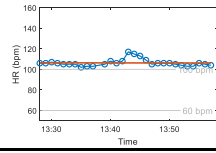
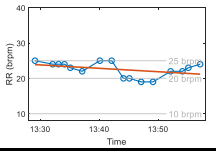
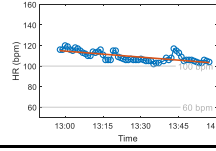
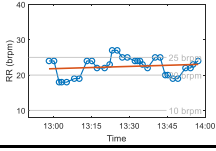
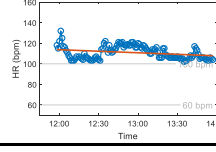
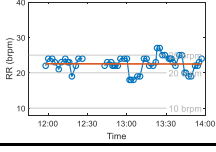
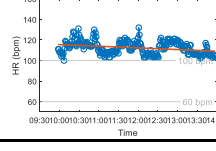
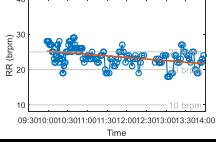
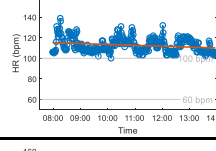
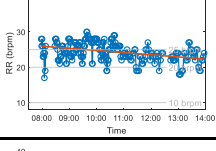
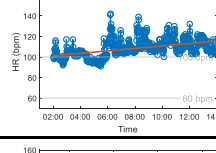
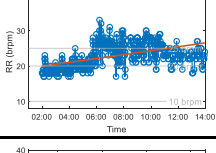
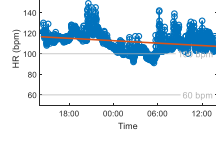
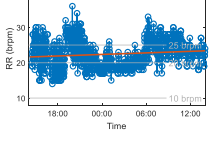
	Timeframe	Comment
HR trend	Start – day 4	A slight downward trend is visible as the HR decreases from around 125 bpm to around 100 bpm. The documented nurses' observations in the EPR, that during this period of continuous monitoring, the patient was extremely tired, not mobilising and sleeping badly due to shortness of breath complaints.
	Day 5 – end	During this period, the HR shows a <i>sinusoidal pattern</i> . During night-time, the HR varies mostly around 100 bpm. During day-time, the HR varies from 80 to 150 bpm, mostly around 120 bpm. This patient in particular shows a lot of 'peakiness' in the HR data during the day. This matches information in the nurses' observations, which stated that the patient was quickly tachycardic after mobilisation.
RR trend	Start – end	The patient was notably tachypnoeic during the entire period of continuous monitoring. The degree of tachypnoea however decreased over time. Also, the RR is unstable, showing a high variation in the data.
	Start – day 4	During this period, the RR is very unstable, varying from 12 to over 35 brpm. The RR shows a somewhat downward trend, decreasing down to around 20 brpm at night and 25 to 30 brpm during the day.
	Day 5 – end	In this period, the RR is stabilising, showing a 'turbulent' <i>sinusoidal pattern</i> . During night-time the RR is around 17 brpm. During day-time the RR is around 23 brpm. The word "turbulent" refers to the fact that the RR data is not very stable, especially during the day: the RR highly fluctuates between 19 brpm and 28 brpm.
SpO ₂ data	Start – end	This subplot shows that the SpO ₂ was registered about five times a day. The values of the SpO ₂ vary from 95 to 100% during the period of continuous monitoring. The SpO ₂ of this patient was unstable, as the patient was highly dependent on oxygen therapy.
Oxygen therapy	Start – end	The patient was supported by the use of a wide variation of respiratory supportive techniques while patched at the ward: a NRB mask, Venturi mask (of both 40% and 60%), an oxygen mask, and a nasal cannula. The respiratory support was slowly decreased over time. At the point of discharge to a care hotel, the patient was still in need of minor respiratory support through a nasal cannula.

Event(s)

This patient experienced one type 2 event. Table 15 contains the quantitative assessment of the period prior to the type 2.

- Type 2: Based on the three steps for assessment whether trends were present prior to the event...
 - ... it can be concluded that a no HR trend is present in the periods prior to the event.
 - ... it can be concluded that a no RR trend is present in the periods prior to the event.

Table 15: quantitative assessment of the period prior to the type 2 event in case 4. For interpretation, note that the unit of the slope of the linear regression model is in HR $\uparrow$ /day.

Segment length (hours)	Mean HR	Mean RR	Standard deviation HR	Standard deviation RR	Netto increase HR	Netto increase RR	Mean slope HR	Mean slope RR	Standard deviation slope HR	Standard deviation slope RR	Slope linear regression model HR	Slope linear regression model RR	R ² linear regression model HR	R ² linear regression model RR	p-value linear regression model HR	p-value linear regression model RR	HR trend during specified segment prior to event	RR trend during specified segment prior to event
0.5	106.3	22.6	3.5	2.1	-1.8	-1.5	-0.1	-0.1	2.5	1.9	-9.9	-138.8	0.00	0.2	0.9	0.1		
1	109.2	22.4	4.9	2.6	-12.7	1.0	-0.2	0.0	2.7	2.2	-282.4	30.6	0.5	0.02	<0.01	0.4		
2	110.9	22.5	4.3	2.2	-9.7	-1.5	-0.1	0.1	3.3	1.9	-72.0	-0.8	0.08	<0.01	<0.01	0.9		
4	112.4	23.7	6.4	2.6	-6.5	-3.2	-0.03	-0.01	3.5	1.8	-38.9	-21.4	0.09	0.2	<0.01	<0.01		
6	112.6	24.4	6.8	2.7	-9.9	-2.2	-0.01	-0.01	3.6	1.9	-20.6	-15.6	0.05	0.1	<0.01	<0.01		
12	108.3	22.8	8.5	3.4	10.0	4.1	0.01	0.01	3.5	1.9	28.6	13.2	0.2	0.3	<0.01	<0.01		
24	111.7	22.5	8.9	3.8	-3.8	0.2	-0.01	0.01	3.1	2.6	-9.4	1.7	0.09	0.01	<0.01	<0.01		

Summary of the case study of case 4 – discharged to care hotel

The continuous vital sign trends of case 4 match up with the documented nurses' observations. An increasingly apparent sinusoidal pattern in the HR and RR data is visible: HR decreases overnight and increases as mobilisation increases during the day. Note that the sinusoidal pattern is more apparent in the HR data than the RR data. During the entire period of continuous monitoring, the patient is notably tachycardic and tachypnoeic. In addition, the SpO₂ of this patient was unstable, as the patient was highly dependent on oxygen therapy. This patient experienced one type 2 event. Quantitative assessment does not show an apparent trend in either HR or RR prior to the event.

Case 5

Table 16 provides an overview of the patient's characteristics. Figure 23 provides an overview of the clinical course of case 5 throughout hospitalisation.

Table 16: patient characteristics of case 5

Age	60
Gender	Male
BMI	26.6
Patient outcome	Discharged to revalidation centre
Comorbidities	None
Thrombotic event	Yes, pulmonary embolism
Treatment restrictions	None
Reason for admission to COVID-19 cohort ward	Post ICU care
Events	Type 1

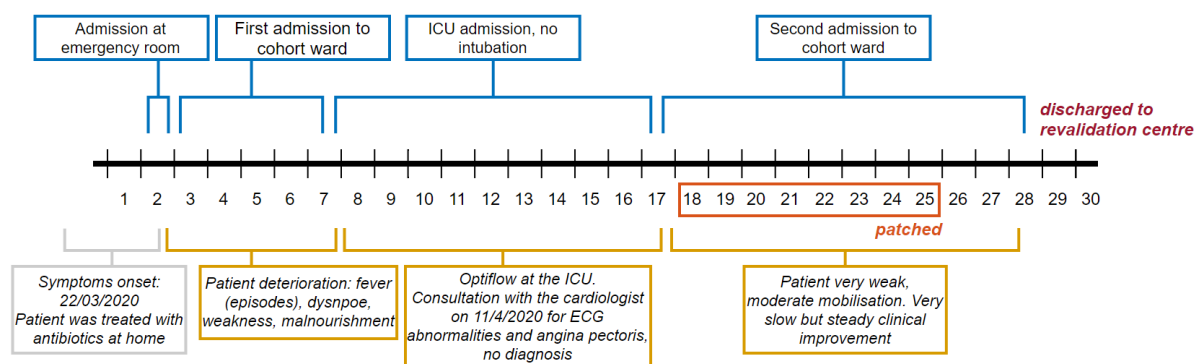


Figure 23: clinical course of case 5 throughout hospitalisation. Blue text boxes above the timeline indicate the hospitalisation details of the patient. Orange text boxes below the timeline indicate other clinical aspects or events.

Figure 24 shows the continuous data that was measured during the period that the patient was patched with the Philips Biosensor. Table 17 contains the description of the vital sign trends. The patient was continuously monitored at the ward during a period of approximately seventeen days. Note that for this patient, this was during a period of recovery from COVID-19.

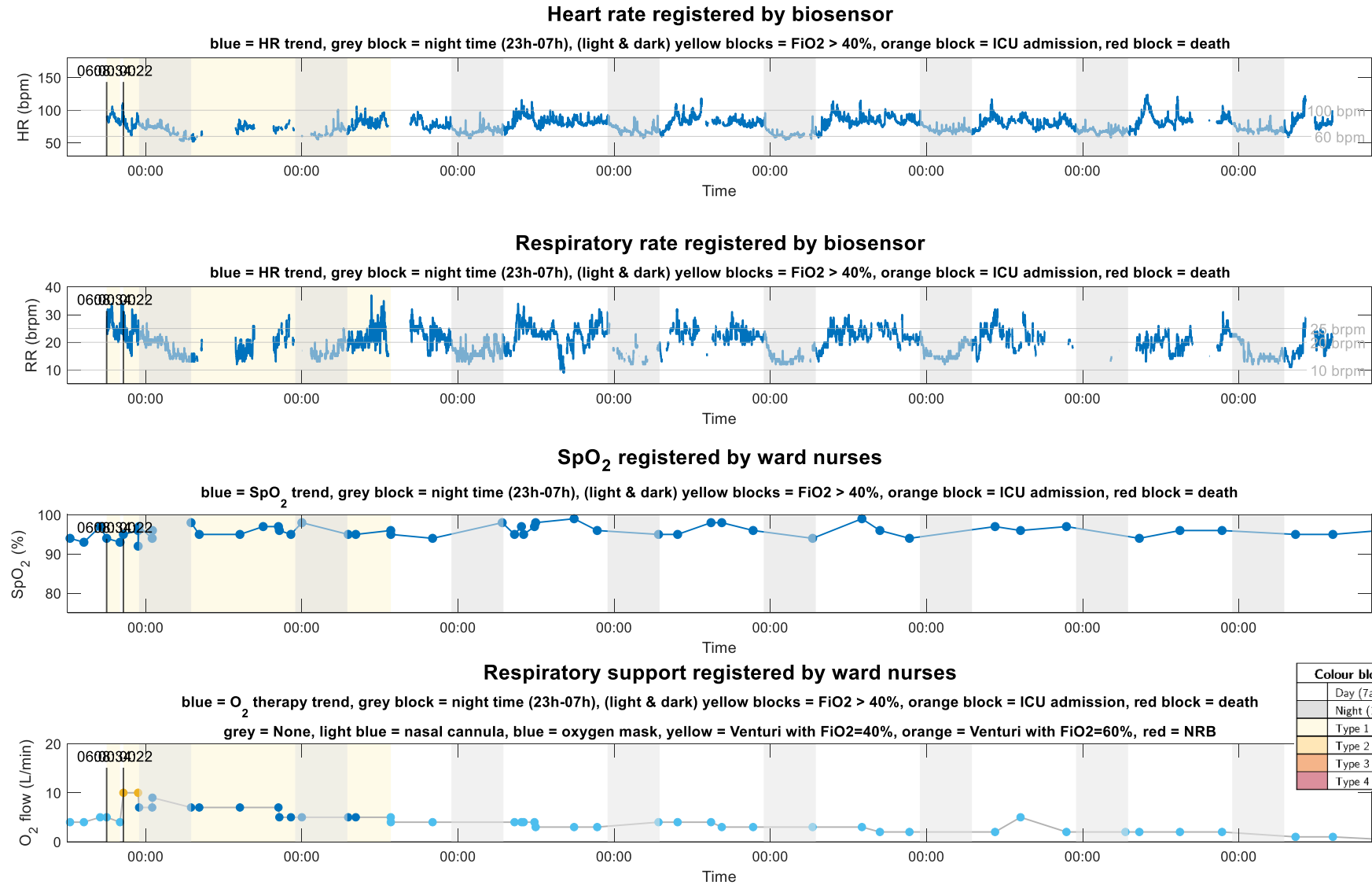


Figure 24: case 5 – Patient outcome = discharged to revalidation centre.

Table 17: Description of vital sign trend (which is depicted in figure 24) for case 5

	Timeframe	Comment
HR trend	Start – end	During the entire period of continuous monitoring, the HR shows a <i>sinusoidal pattern</i> . During night-time, the HR varies mostly around 70 bpm. During day-time, the HR varies from 70 to 110 bpm, mostly around 85 bpm. This patient in particular shows a lot of 'peakiness' in the HR data during the day, more specifically in the morning. This matches information in the nurses' observations, which stated that the patient was quickly tachycardic after mobilisation.
RR trend	Start – end	During the entire period of continuous monitoring, the RR shows a <i>sinusoidal pattern</i> . During night-time, the RR decreases down to around 12 brpm. During day-time, the RR varies from 20 to over 30 brpm, mostly around 25 brpm. The patch was placed shortly after the patient returned from the ICU. The first few days after return from the ICU, the continuous RR data shows tachypnoea during the day, up to a maximum of 35 brpm. Although that the patient remains tachypnoeic for the remainder of his stay at the cohort ward, the RR stabilises, and is only increased during the day. This matches the nurses' observations, as the patients was trying to mobilise, which resulted in increasing tachypnea.
SpO ₂ data	Start – end	This subplot shows that the SpO ₂ was registered more (five to eleven times a day) during the first four days of continuous monitoring, and less (four or three times a day) as the patient recovered during last few days of continuous monitoring. The values of the SpO ₂ vary from 92 to 100% during the period of continuous monitoring.
Oxygen therapy	Start - end	The patient was supported by the use of a wide variation of respiratory supportive techniques at the ward: Venturi mask (of 40%), an oxygen mask and a nasal cannula. The respiratory support was slowly decreased over time. At the point of discharge to a revalidation centre, the patient was no longer in need of oxygen support

Event(s)

This patient did not experience a type 2, 3 or 4 event during the period of continuous monitoring. Therefore, no quantitative assessment of the period prior an event has been performed.

Summary of the case study of case 5 – discharged to revalidation centre

The continuous vital sign trends of case 5 match up with the documented nurses' observations. An increasingly apparent sinusoidal pattern in the HR and RR data is visible: HR and RR decrease overnight and increase as mobilisation increases during the day. During the entire period of continuous monitoring, the patient is notably tachypnoeic during the day.

Case 6

Table 18 provides an overview of the patient's characteristics. Figure 25 provides an overview of the clinical course of case 6 throughout hospitalisation.

Table 18: patient characteristics of case 6

Age	72
Gender	Female
BMI	31.6
Patient outcome	Discharged to revalidation centre
Comorbidities	Chronic pulmonary disease
Thrombotic event	None
Treatment restrictions	Yes, no resuscitation
Reason for admission to COVID-19 cohort ward	Post ICU care
Events	Type 1, type 2 and type 3

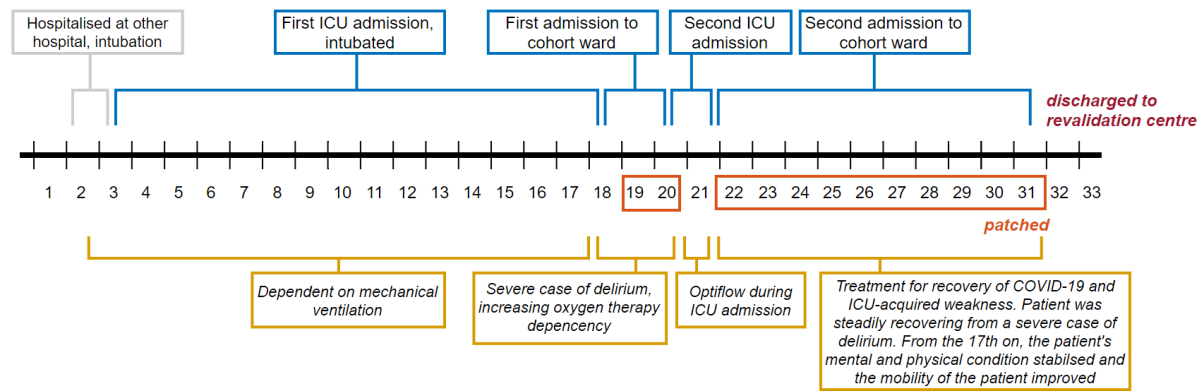


Figure 25: clinical course of case 6 throughout hospitalisation. Blue text boxes above the timeline indicate the hospitalisation details of the patient. Orange text boxes below the timeline indicate other clinical aspects or events.

Figure 26 shows the continuous data that was measured during the period that the patient was patched with the Philips Biosensor. Table 19 contains the description of the vital sign trends. The patient was continuously monitored at the ward during a period of approximately six days. Note that for this patient, this was during a period of recovery from COVID-19.

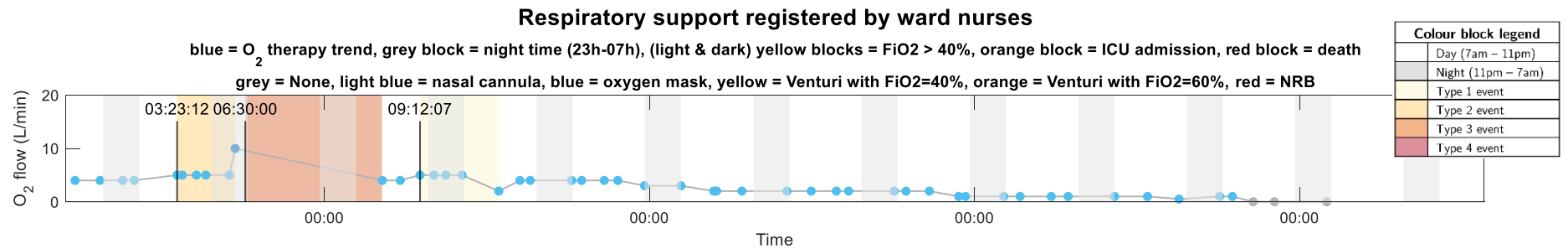
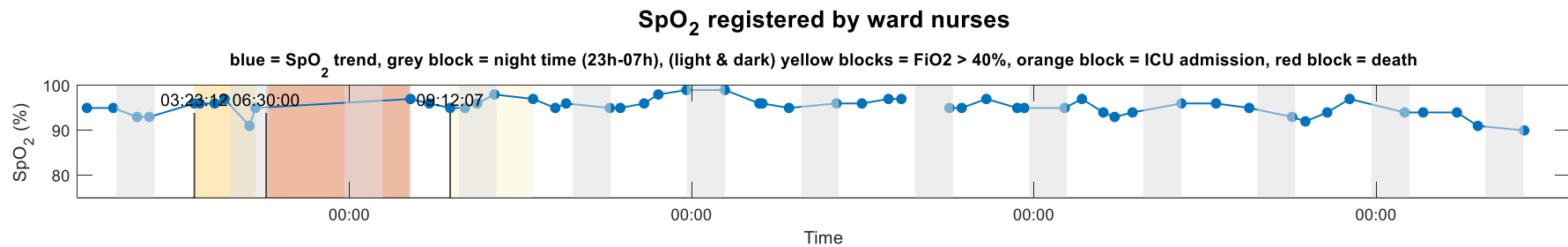
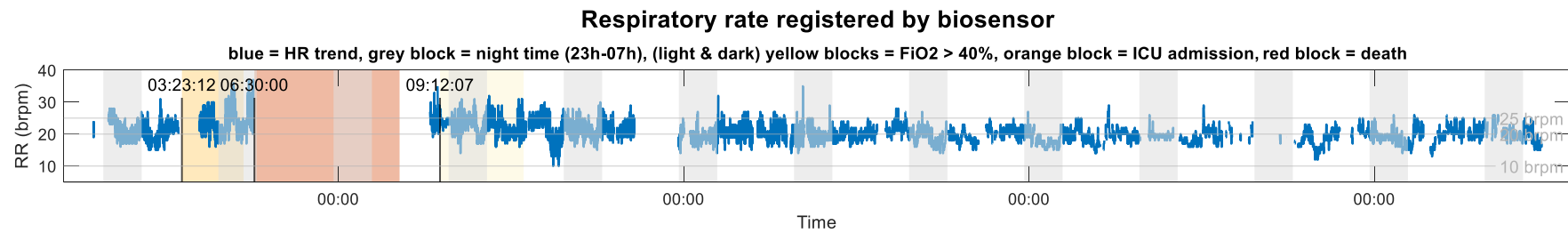
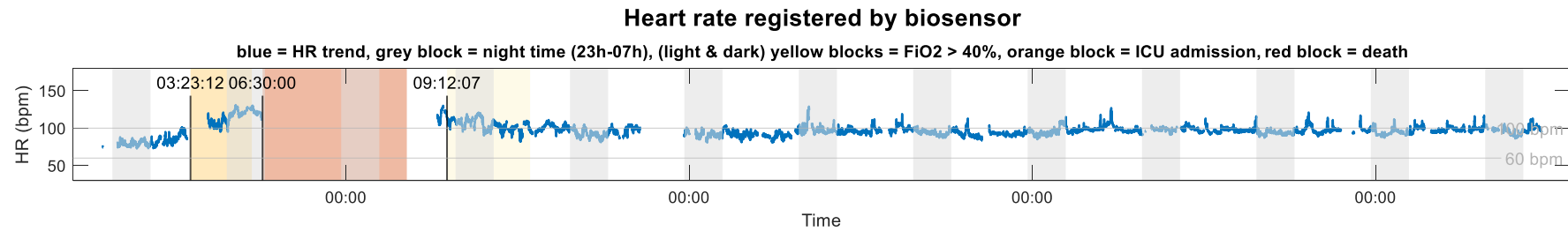


Figure 26: case 6 – Patient outcome = discharged to revalidation centre.

Table 19: Description of vital sign trend (which is depicted in figure 26) for case 6

	Timeframe	Comment
HR trend	Start – end of the night day 2	An apparent upward HR trend is visible up until the point of readmission to the ICU. During this period of approximately thirty hours, the HR increases from about 80 bpm to 130 bpm. Nurses' observations report that the HR and RR trends stimulated nurses and physicians to re-evaluate the treatment policy of the patient which ultimately resulted in ICU readmission.
	Evening day 3 – afternoon day 5	A slightly downward trend in HR can be seen during these two days. The HR decreases from around 13 bpm to around 90 bpm. Nurses' observations state that the patient was still suffering from a severe case of delirium, which improved over time.
	Night day 6 – end	The HR trend seems stable, around 90 to 100 bpm, with relatively little peakiness and no sinusoidal pattern. According to nurses' observations, the patient was recovering (very) slowly, yet still remained extremely weak up until the point of discharge. This matched the observed HR pattern, as no mobilisation-related peakiness can be seen.
RR trend	Start – end of the night day 2	A slightly chaotic upward RR trend is visible up until the point of readmission to the ICU. During this period of approximately thirty hours, the RR varies from 15 to 35 brpm. Nurses' observations report that the HR and RR trends stimulated nurses and physicians to re-evaluate the treatment policy of the patient which ultimately resulted in ICU readmission.
	Evening day 3 – afternoon day 5	A slightly downward trend in RR can be seen during these two days. The RR decreases from around 25 brpm to around 20 brpm. Nurses' observations state that the patient was still suffering from a severe case of delirium, which improved over time.
	Night day 6 – end	The RR trend stabilises over time, with variations between 12 to 25 bpm, with relatively little peakiness and no sinusoidal pattern. According to nurses' observations, the patient was recovering (very) slowly, yet still remained extremely weak up until the point of discharge. This matched the observed HR pattern, as no mobilisation-related peakiness can be seen.
SpO ₂ data	Start – end	This subplot shows that the SpO ₂ was registered around five times a day. The values of the SpO ₂ vary from 90 to 99% during the period of continuous monitoring.
Oxygen therapy	Start - end	The patient was supported received respiratory support through an oxygen mask and a nasal cannula. The respiratory support was slowly decreased over time. At the point of discharge to a revalidation centre, the patient was no longer in need of oxygen support.

Event(s)

This patient experienced three events in the following order: type 2 – type 3 – type 1. Tables 20 and 21 contain the quantitative assessment of the period prior to the type 2 and type 3 events, respectively.

- Type 2: Based on the three steps for assessment whether trends were present prior to the event...
 - ... it can be concluded that a HR trend is present in the periods of 4 and 6 hours prior to the event.
 - ... it can be concluded that no RR trend is present in the periods prior to the event.
- Type 3: Based on the three steps for assessment whether trends were present prior to the event...
 - ... it can be concluded that a HR trend is present in the periods of 12 and 24 hours prior to the event.
 - ... it can be concluded that no RR trend is present in the periods prior to the event.

Table 20: quantitative assessment of the period prior to the first type 2 event in case 6. For interpretation, note that the unit of the slope of the linear regression model is in HR $\uparrow$ /day.

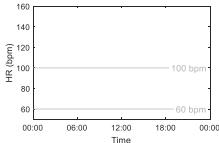
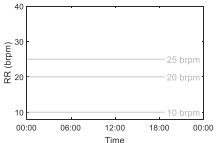
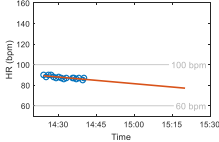
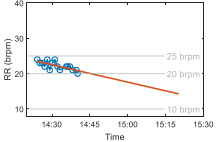
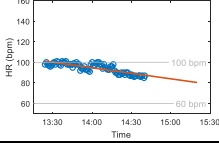
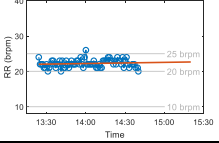
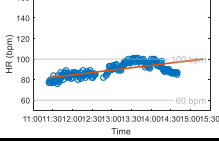
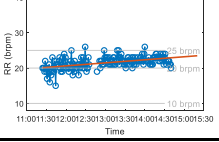
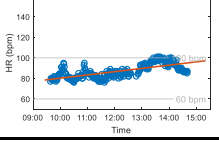
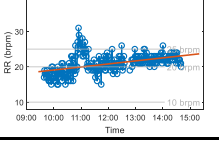
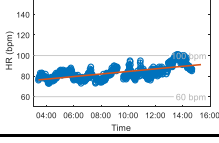
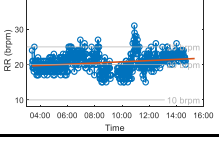
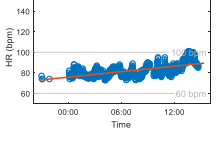
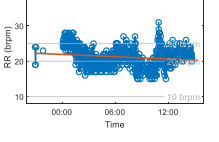
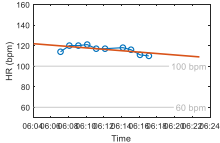
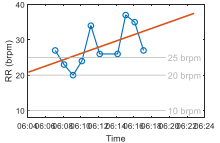
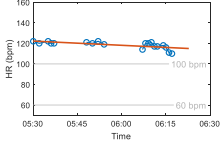
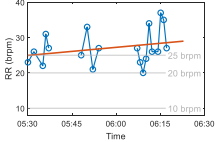
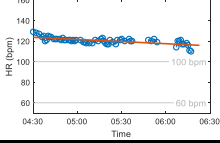
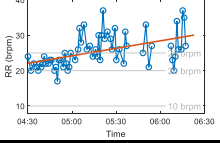
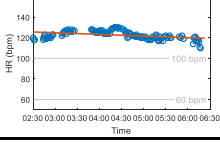
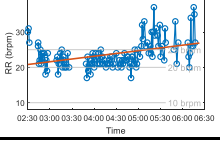
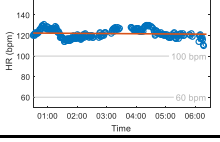
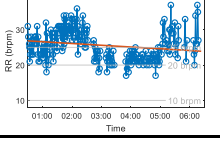
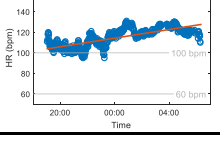
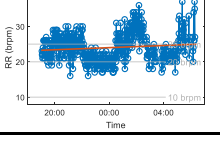
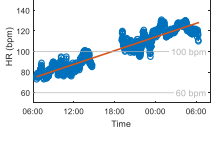
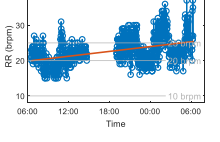
Segment length (hours)	Mean HR	Mean RR	Standard deviation HR	Standard deviation RR	Netto increase HR	Netto increase RR	Mean slope HR	Mean slope RR	Standard deviation slope HR	Standard deviation slope RR	Slope linear regression model HR	Slope linear regression model RR	R ² linear regression model HR	R ² linear regression model RR	p-value linear regression model HR	p-value linear regression model RR	HR trend during specified segment prior to event	RR trend during specified segment prior to event
0.5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
1	87.5	22.2	1.5	1.2	-	-	-0.2	-0.3	1.4	1.4	-311.1	-237.2	0.6	0.5	<0.01	<0.01		
2	94.4	22.2	4.8	1.1	-11.9	-0.7	-0.15	-0.05	2.2	1.3	-257.6	7.9	0.7	0.01	<0.01	0.3		
4	89.5	21.5	6.6	1.7	7.8	2.4	0.06	-0.006	2.7	1.9	111.2	20.6	0.5	0.2	<0.01	<0.01		
6	87.0	20.9	6.7	2.6	7.1	4.9	0.04	0.007	2.5	2.3	76.1	20.6	0.5	0.2	<0.01	<0.01		
12	83.2	20.6	6.4	2.5	15.2	2.9	0.05	-0.01	2.2	2.2	29.8	4.1	0.4	0.06	<0.01	<0.01		
24	82.3	21.2	6.0	2.7	15.8	-2.8	0.03	-0.01	2.1	2.2	21.2	-2.6	0.4	0.03	<0.01	<0.01		

Table 21: quantitative assessment of the period prior to the type 3 event in case 6. For interpretation, note that the unit of the slope of the linear regression model is in HR $\uparrow$ /day.

Segment length (hours)	Mean HR	Mean RR	Standard deviation HR	Standard deviation RR	Netto increase HR	Netto increase RR	Mean slope HR	Mean slope RR	Standard deviation slope HR	Standard deviation slope RR	Slope linear regressionmodel HR	Slope linear regressionmodel RR	R ² linear regression model HR	R ² linear regression model RR	p-value linear regression model HR	p-value linear regression model RR	HR trend during specified segment prior to event	RR trend during specified segment prior to event
0.5	116.4	27.9	3.7	5.6	-	-	-0.4	0.0	3.2	7.0	-984.9	1,279.9	0.4	0.3	0.05	0.1		
1	118.4	27.1	3.5	4.8	-10.5	5.5	-0.5	-0.5	2.7	7.1	-197.5	110.2	0.4	0.07	<0.01	0.3		
2	120.4	25.4	3.3	4.5	-10.0	9.3	-0.3	0.08	2.1	5.0	-99.1	101.9	0.5	0.3	<0.01	<0.01		
4	122.6	23.8	4.0	4.0	-3.3	2.5	-0.05	0.008	1.8	4.1	-38.3	37.5	0.2	0.2	<0.01	<0.01		
6	121.9	25.6	4.2	4.3	-7.5	1.9	-0.03	0.0	1.7	4.2	-4.5	-11.9	0.01	0.04	0.3	<0.01		
12	114.8	24.0	8.7	4.0	-10.8	3.2	0.007	0.01	2.1	3.6	50.3	3.6	0.6	0.01	<0.01	0.01		
24	101.5	22.0	16.7	3.8	44.3	2.5	0.04	-0.001	2.2	3.1	53.1	5.5	0.9	0.2	0	<0.01		

Summary of the case study of case 6 – discharged to revalidation centre

The continuous vital sign trends of case 5 match up with the documented nurses' observations. As clinical deterioration occurs on the 9th and 10th of April, the patient's HR and RR trend increase. When the patient returns to the cohort ward, after readmission to the ICU, the HR and RR stabilise over time. This patient experienced both a type 2 as a type 3 event. Quantitative assessment of the segments prior to the events point out that an apparent trend for the HR data is visible for both events (for the type 2 event in the periods of 4 and 6 hours prior to the event, and for the type 3 event in the periods of 12 and 24 hours prior to the event).

Case 7

Table 22 provides an overview of the patient's characteristics. Figure 27 provides an overview of the clinical course of case 7 throughout hospitalisation.

Table 22: patient characteristics of case 7

Age	76
Gender	Male
BMI	27.5
Patient outcome	Death
Comorbidities	Hypertension, chronic obstructive pulmonary disease, diabetes without complications, rheumatologic disorder, chronic pancreatitis (since 01-2020), recently diagnosed atrial fibrillation (since 02-2020), smoker, clinical frailty score of 6
Thrombotic event	None
Treatment restrictions	Yes, <i>do not resuscitate</i> and <i>do not perform invasive ventilation</i> were registered prior to admission. <i>No ICU admission</i> was registered during the admission at the UMCU, based on medical reasons and the patient's wishes.
Reason for admission to COVID-19 cohort ward	Primary admission to COVID-19 cohort ward
Events	Type 1, type 2 and type 4

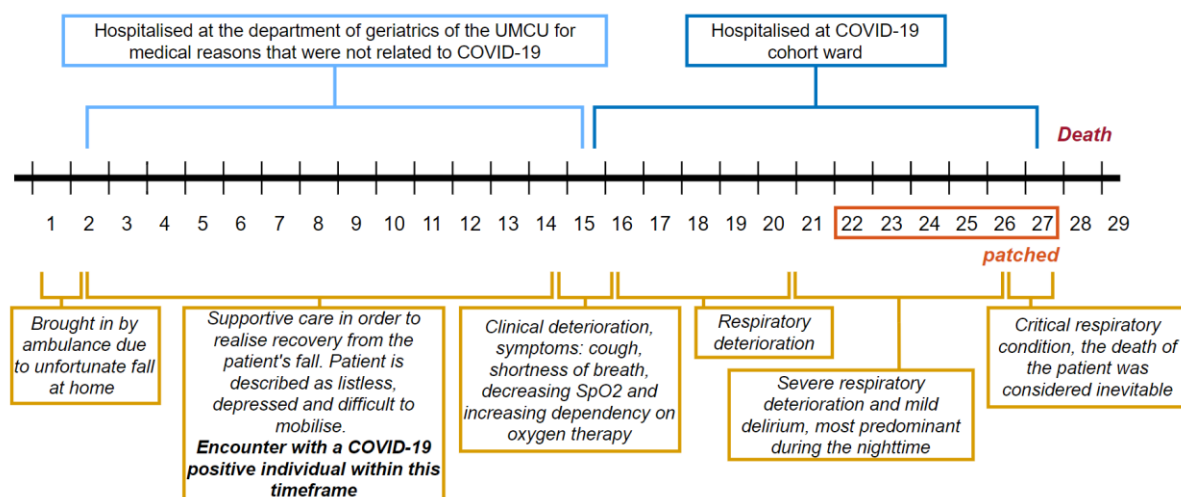


Figure 27: clinical course of case 7 throughout hospitalisation. Blue text boxes above the timeline indicate the hospitalisation details of the patient. Orange text boxes below the timeline indicate other clinical aspects or events.

Figure 28 shows the continuous data that was measured during the period that the patient was patched with the Philips Biosensor. Table 23 contains the description of the vital sign trends. The patient was continuously monitored at the ward during a period of approximately six days. Note that for this patient, this was during a period of severe deterioration from COVID-19 and other pre-existing medical problems.

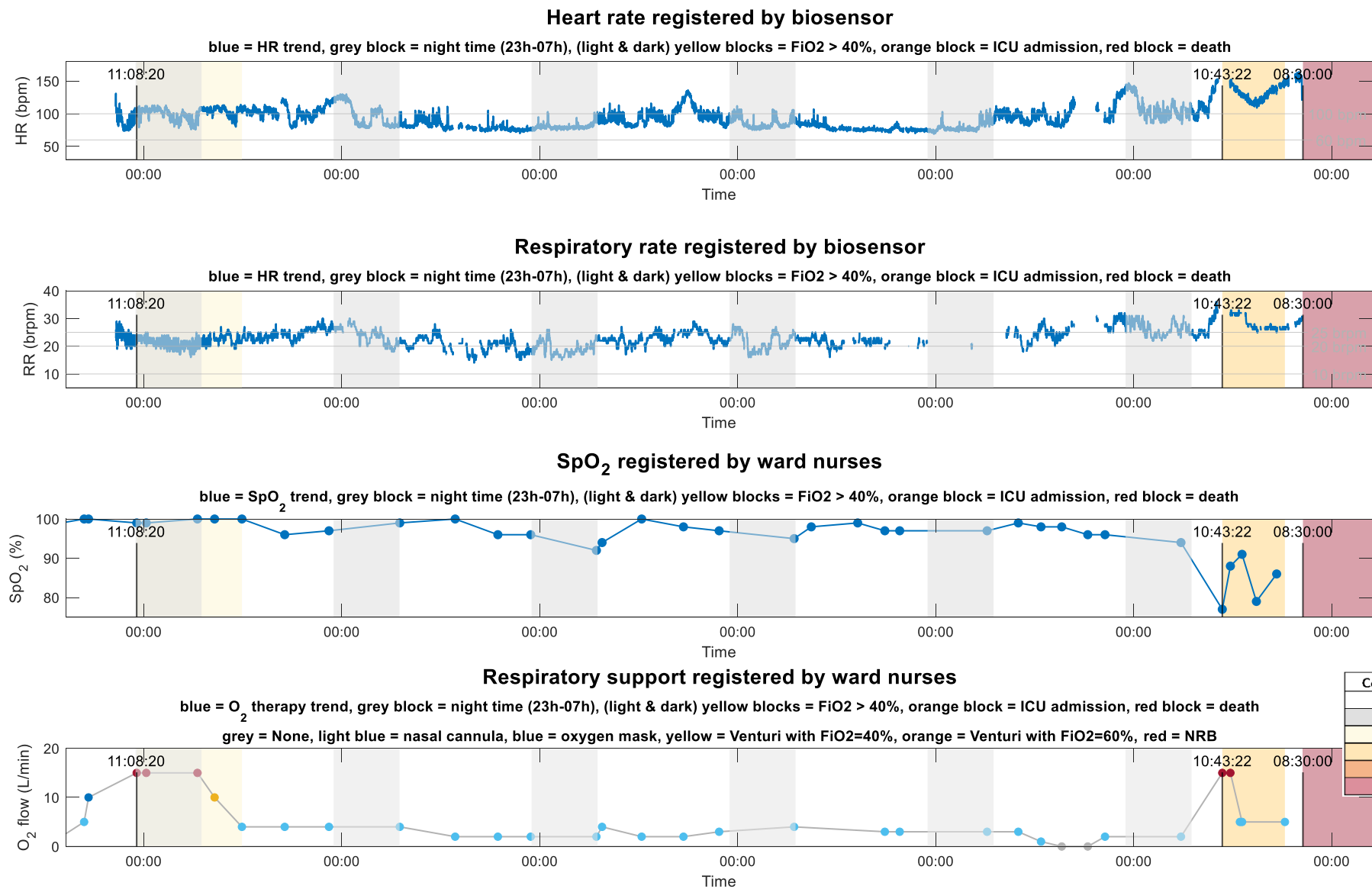


Figure 28: case 7 – Patient outcome = death.

Table 23: Description of vital sign trend (which is depicted in figure 28) for case 5. For interpretation, note that the unit of the slope of the linear regression model is in HR↑/day.

	Timeframe	Comment
HR trend	Start – end	The HR trend shows an unsteady pattern, matching the clinical description of events in the documentation of nurses' observation in the EPR. This patient is diagnosed with atrial fibrillation, which may explain some of the prolonged tachycardic episodes of the patient. The inconstant parts of the HR trend match up to periods of delirium or clinical deterioration that are described in the nurses' observation. The more constant parts of the HR trend (such as the 18th of April) match up with periods of exhaustion and rest (no mobilisation). The nurses' observations describe that the patient acutely deteriorated on the 6th day of continuous monitoring. The HR trend shows an upward trend in HR (from a 'resting' HR of 75 bpm up to a HR of 150 bpm), up until the time of death.
RR trend	Start – end	The RR data matches the pattern of the HR data, being increased in similar timeframes. The patient is tachypnoeic most of the time, especially at the time of acute deterioration. The RR increases from a 'resting' RR of 22 brpm up to a RR of over 30 brpm at the time of death..
SpO ₂ data	Start – end	This subplot shows that the SpO₂ was registered about five times a day. The SpO₂ values vary between 90 and 100%, decreasing to below 80% during acute deterioration
Oxygen therapy	Start – end	The patient was supported by the use of a wide variation of respiratory supportive techniques at the ward: a NRB mask, Venturi mask (of 40%), an oxygen mask, and a nasal cannula. The degree of respiratory support was decreased from a NRB to a nasal cannula within a short period of time on the first day of continuous monitoring. The following days the patient only received supplementary oxygen via a nasal cannula. The SpO₂ of the patient remained acceptable while receiving a relatively limited amount of oxygen support. On the day 6, the need for oxygen support increased, resulting in short-term treatment with an NRB.

Event(s)

This patient experienced three events in the following order: type 1 – type 2 – type 4. Tables 24 and 25 contain the quantitative assessment of the period prior to the type 2 and type 4 events, respectively.

- Type 2: Based on the three steps for assessment whether trends were present prior to the event...
 - ... it can be concluded that a HR trend is present in the periods of 1, 2 and 4 hours prior to the event.
 - ... it can be concluded that a RR trend is present in the periods of 2 and 4 hours prior to the event.
- Type 4: Based on the three steps for assessment whether trends were present prior to the event...
 - ... it can be concluded that a HR trend is present in the periods of 4 and 6 hours prior to the event.
 - ... it can be concluded that a RR trend is present in the periods of 1, 2 and 4 hours prior to the event.

Table 24: quantitative assessment of the period prior to the type 2 event in case 7. For interpretation, note that the unit of the slope of the linear regression model is in HR $\uparrow$ /day.

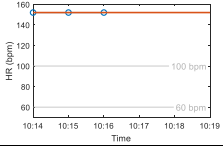
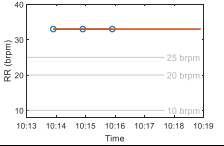
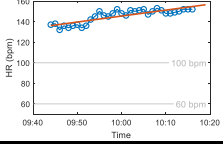
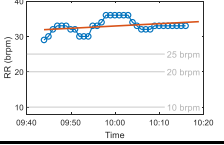
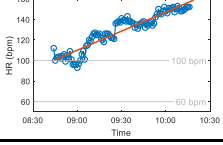
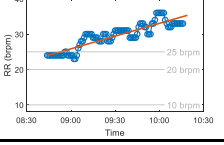
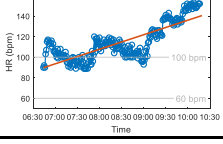
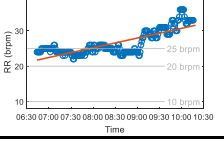
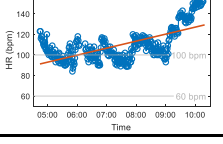
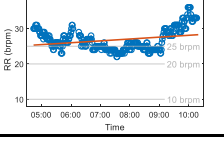
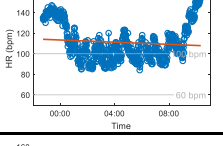
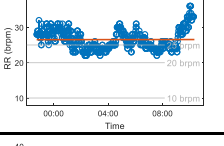
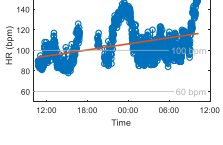
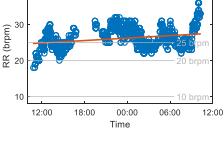
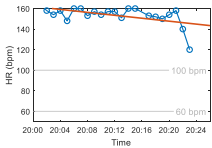
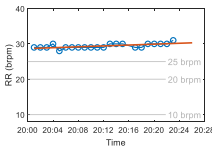
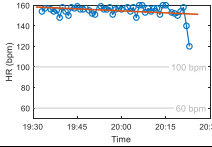
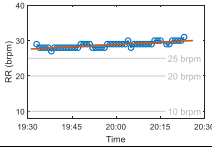
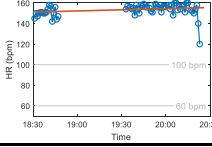
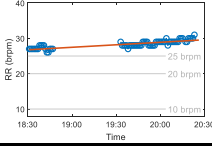
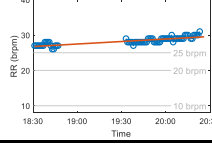
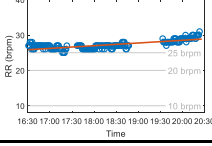
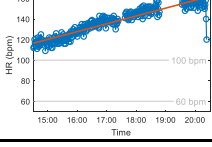
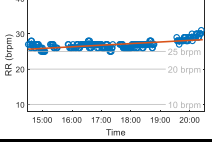
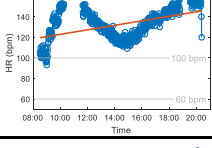
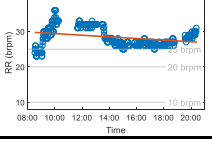
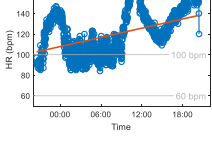
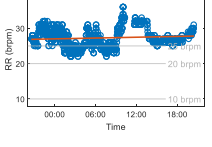
Segment length (hours)	Mean HR	Mean RR	Standard deviation HR	Standard deviation RR	Netto increase HR	Netto increase RR	Mean slope HR	Mean slope RR	Standard deviation slope HR	Standard deviation slope RR	Slope linear regressionmodel HR	Slope linear regressionmodel RR	R ² linear regression model HR	R ² linear regression model RR	p-value linear regression model HR	p-value linear regression model RR	HR trend during specified segment prior to event	RR trend during specified segment prior to event
0.5	152.0	33.0	0.0	0.0	-	-	0.0	0.0	0.0	0.0	<0.01	<0.01	1.0	1.0	0	0		
1	145.4	32.9	6.6	1.9	16.3	2.0	0.5	0.13	3.1	1.0	835.5	93.4	0.7	0.1	<0.01	0.06		
2	128.5	29.4	17.8	3.6	46.5	9.0	0.4	0.1	4.0	0.8	889.7	173.0	0.9	0.8	<0.01	<0.01		
4	114.9	26.6	18.1	3.5	43.9	9.2	0.3	0.04	5.1	0.7	339.5	66.1	0.6	0.6	<0.01	<0.01		
6	110.4	26.8	16.7	3.1	39.0	4.3	0.08	0.01	5.3	0.8	163.4	12.7	0.08	0.08	<0.01	<0.01		
12	110.9	26.0	17.8	2.8	-0.84	3.0	0.02	0.009	5.4	0.9	-12.8	0.08	0.01	<0.01	0.01	0.9		
24	105.5	26.2	17.8	2.9	31.2	4.2	0.06	0.01	5.2	0.84	23.6	2.7	0.2	0.07	<0.01	<0.01		

Table 25: quantitative assessment of the period prior to the type 4 event in case 7. For interpretation, note that the unit of the slope of the linear regression model is in HR $\uparrow$ /day.

Segment length (hours)	Mean HR	Mean RR	Standard deviation HR	Standard deviation RR	Netto increase HR	Netto increase RR	Mean slope HR	Mean slope RR	Standard deviation slope HR	Standard deviation slope RR	Slope linear regression model HR	Slope linear regression model RR	R ² linear regression model HR	R ² linear regression model RR	p-value linear regression model HR	p-value linear regression model RR	HR trend during specified segment prior to event	RR trend during specified segment prior to event
0.5	153.5	29.4	9.1	0.7	-38.7	2.0	-2.1	0.1	7.8	0.7	1029.9	90.6	0.3	0.4	0.01	<0.01		
1	154.8	28.8	6.6	0.8	-14.0	2.0	-0.7	0.04	6.4	0.6	-185.4	62.9	0.08	0.6	0.04	<0.01		
2	153.7	28.4	6.4	1.1	-2.7	2.6	-0.5	0.03	6.3	0.6	53.1	34.1	0.05	0.7	0.08	<0.01		
4	146.3	27.2	8.3	1.2	16.8	2.5	-0.1	0.01	5.0	0.6	134.6	18.4	0.7	0.6	<0.01	<0.01		
6	136.7	27.0	13.9	1.1	37.6	3.0	-0.007	-0.004	4.9	0.6	182.8	11.0	0.9	0.4	<0.01	<0.01		
12	132.8	28.4	14.6	2.7	42.1	2.9	0.009	0.008	4.5	0.6	52.6	-5.5	0.2	0.09	<0.01	<0.01		
24	119.6	27.3	19.7	2.7	38.0	-0.80	0.01	0.003	5.0	0.8	35.7	0.9	0.3	0.01	<0.01	<0.01		

Summary of the case study of case 7 – death

The continuous vital sign trends of case 5 match up with the documented nurses' observations. This patient's vital sign trends do not show the sinusoidal pattern that is visible in the recovering cases. This patient's vital sign trends do not show a repeating pattern, yet an inconsistent series of increasing and decreasing HR and RR values. Note that this patient was diagnosed with atrial fibrillation, which may explain the temporary increases in HR. About 30 hours prior to the patient's death, the HR and RR trends started to increase gradually. This patient experienced both a type 2 and a type 4 event. Quantitative assessment of the segments prior to the events point out that an apparent trend for the HR data is visible for both events (for the type 2 event in the periods of 1, 2 and 4 hours prior to the event, and for the type 4 event in the periods of 4 and 6 hours prior to the event). Quantitative assessment of the segments prior to the events point out that an apparent trend for the RR data is visible for both events (for the type 2 event in the periods of 2 and 4 hours prior to the event, and for the type 4 event in the periods of 1, 2, and 4 hours prior to the event).

Case 8

Table 26 provides an overview of the patient's characteristics. Figure 29 provides an overview of the clinical course of case 8 throughout hospitalisation.

Table 26: patient characteristics of case 8

Age	75
Gender	Male
BMI	27.5
Patient outcome	Death
Comorbidities	Hypertension, Chronic cardiac disease, chronic pulmonary disease, chronic neurological disease, other risks
Thrombotic event	None
Treatment restrictions	Yes, <i>do not resuscitate</i> and <i>do not perform invasive ventilation</i> were registered prior to admission. <i>No ICU admission</i> was registered during the admission at the UMCU, based on medical reasons.
Reason for admission to COVID-19 cohort ward	Post ICU care
Events	Type 1 and type 4

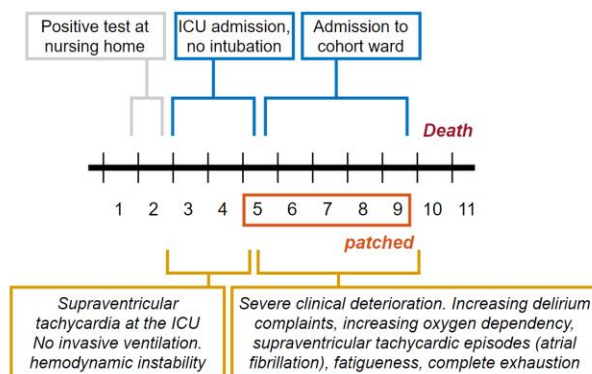


Figure 29: clinical course of case 8 throughout hospitalisation. Blue text boxes above the timeline indicate the hospitalisation details of the patient. Orange text boxes below the timeline indicate other clinical aspects or events.

Figure 30 shows the continuous data that was measured during the period that the patient was patched with the Philips Biosensor. Table 27 contains the description of the vital sign trends. The patient was continuously monitored at the ward during a period of approximately six days. Note that for this patient, this was during a period of severe deterioration from COVID-19 and other pre-existing medical problems.

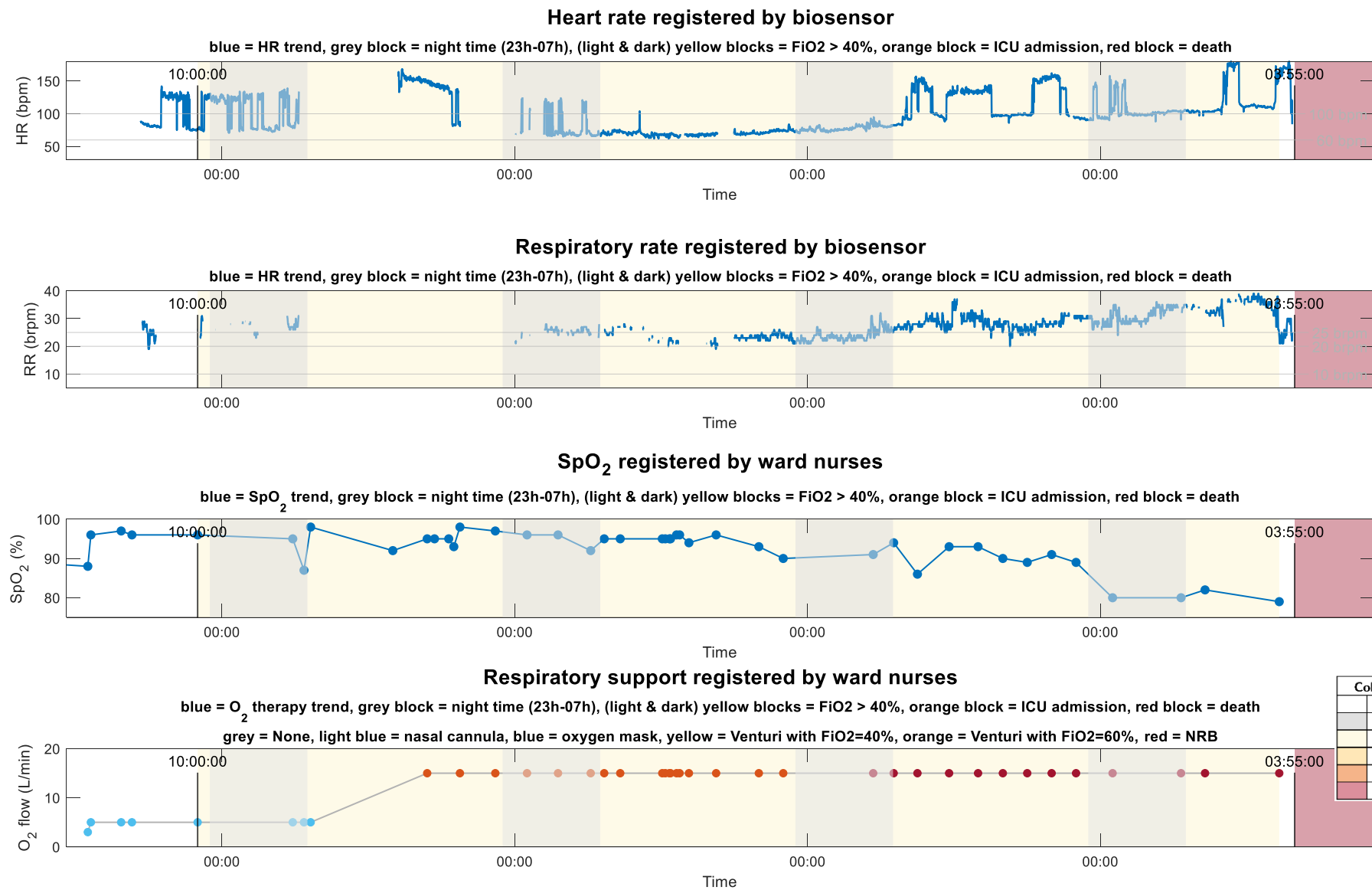


Figure 30: case 7 – Patient outcome = death.

Table 27: Description of vital sign trend (which is depicted in figure 30) for case 7

	Timeframe	Comment
HR trend	Start – end	The HR trend of this patient shows prevalent supraventricular tachycardic episodes, due to atrial fibrillation. These episodes are 'block-like' increases in the HR trend. The 'normal' HR is around 75 bpm at the start of continuous monitoring, yet increases slowly over the entire monitoring period (of four days), up to 110 bpm. The 'supraventricular tachycardia' HR is around 130 bpm and also increases over the entire monitoring period, up to around 170 bpm. Just before the time of death, the HR decreases to about 90 bpm. These measurements comply with the nurses' and physicians' observations. For this patient, the physicians often consulted the continuous data and reported measurements in the EPR.
RR trend	Start – end	The first half of the RR data (start – 03/05/2020) of this patient contains an excessive amount of data gaps. The second half of the RR data (04/05/2020 – end) shows a slightly a increasing trend in RR. The RR increases from about 22 to 40 brpm. Just before the time of death, the RR decreases to about 22 brpm. These measurements comply with the nurses' and physicians' observations.
SpO ₂ data	Start – end	This subplot shows that the SpO ₂ was registered about ten times a day. The SpO ₂ values decrease over time, from around 95% to around 80%. This matches nurses' observations, which state decreasing SpO ₂ and complaints of an increasing shortness of breath.
Oxygen therapy	Start – end	The patient was supported by in increasingly intensive oxygen therapy, from a nasal cannula, to a Venturi mask (of 60%), to a NRB. At the time of death, the patient was supported by a NRB, while the SpO ₂ was no higher than 80%.

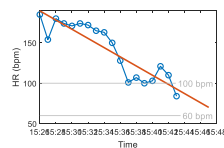
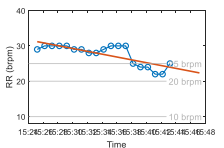
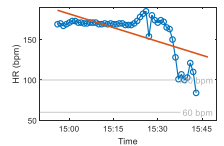
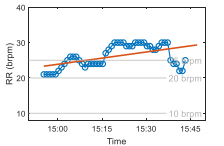
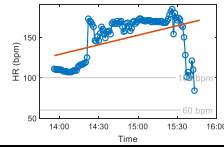
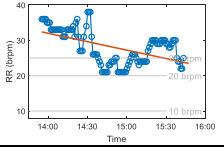
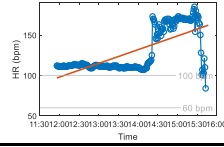
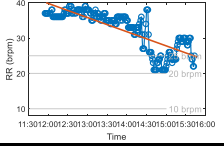
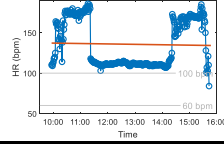
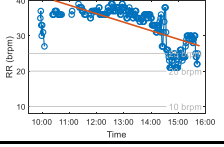
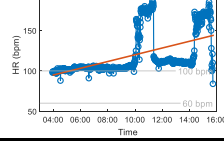
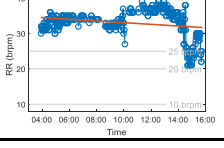
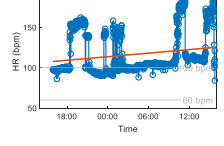
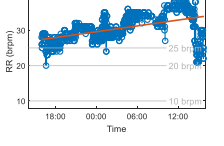
Event(s)

This patient experienced one type 4 event. Table 28 contains the quantitative assessment of the period prior to the type 4 event.

- Type 4: Based on the three steps for assessment whether trends were present prior to the event...
 - ... it can be concluded that no HR trend is present in the periods prior to the event.
 - ... it can be concluded that no RR trend is present in the periods prior to the event.

Context information for interpretation: this patient suffered from atrial fibrillation, which lead to episodes of supraventricular tachycardia. These episodes can be perceived as *'plateau'-like tachycardic episodes*. Note, that these 'plateau'-like tachycardic episodes hinder the process of fitting linear regression models to the period of data. Therefore, quantitative assessment of the periods prior to the events does not reliably show a trend. Subjective visual assessment does however show that the HR and RR slowly and steadily increase over time, up until the moment of death.

Table 28: quantitative assessment of the period prior to the type 4 event in case 8. For interpretation, note that the unit of the slope of the linear regression model is in HR $\uparrow$ /day.

Segment length (hours)	Mean HR	Mean RR	Standard deviation HR	Standard deviation RR	Netto increase HR	Netto increase RR	Mean slope HR	Mean slope RR	Standard deviation slope HR	Standard deviation slope RR	Slope linear regression model HR	Slope linear regression model RR	R ² linear regression model HR	R ² linear regression model RR	p-value linear regression model HR	p-value linear regression model RR	HR trend during specified segment prior to event	RR trend during specified segment prior to event
0.5	141.2	27.6	33.8	2.9	-89.0	-4.7	-5.9	-0.2	15.3	1.6	-8,191.2	-578.5	0.8	0.6	<0.01	<0.01		
1	159.6	26.1	25.0	3.2	-65.3	2.1	-1.8	0.08	9.7	1.2	-1,636.6	166.8	0.4	0.3	<0.01	<0.01		
2	148.5	28.1	27.2	4.8	7.7	-8.4	-0.3	-0.1	8.7	1.7	569.6	-114.4	0.2	0.3	<0.01	<0.01		
4	129.0	32.2	26.4	5.5	35.0	-8.9	-0.1	-0.06	6.0	1.3	407.0	-96.0	0.5	0.6	<0.01	<0.01		
6	135.8	32.8	28.9	5.3	-10.1	-6.8	-0.08	-0.08	7.2	1.3	-12.2	-57.7	<0.01	0.5	0.6	<0.01		
12	119.4	33.0	26.4	4.1	60.3	-6.7	-0.02	-0.02	5.3	1.1	100.2	-5.7	0.3	0.05	<0.01	<0.01		
24	116.4	30.4	25.7	3.7	42.0	2.4	-0.01	-0.004	6.4	1.0	17.6	6.6	0.04	0.3	<0.01	<0.01		

Summary of the case study of case 8 – death

This patient was extremely weakened due to the consequences of the COVID-19 infection in combination with existing impairments. This patient's HR trend shows prevalent supraventricular tachycardic episodes. Both the HR and RR trend show an increasing pattern during the three days prior to the moment of death. Both the HR and RR reach extreme values of respectively tachycardia (~170 bpm) and tachypnoea (~40 brpm). SpO₂ drops down to 80% during the last three days prior to death, while the patient is still supported by a NRB. Quantitative assessment does not show an apparent trend in either HR or RR prior to the event, as reliable quantitative assessment of the data is hindered by the presence of the 'plateau'-like supraventricular tachycardic episodes.

Overview results case series

Table 29 provides a summary on whether events that occurred within the selected cases, could be quantitatively recognised using linear regression.

Table 29: Summary on whether the defined events that occurred within the selected cases could be quantitatively recognised using linear regression models

Case	Events		
	Type 2	Type 3	Type 4
Case 1	-	-	-
Case 2	-	-	-
Case 3	-	-	-
Case 4	No quantitative detection of trend	-	-
Case 5	-	-	-
Case 6	Quantitative detection of trend in HR data 4 and 6 hours prior to event. No quantitative detection of trend in RR data.	Quantitative detection of trend in HR data 12 and 24 hours prior to event. No quantitative detection of trend in RR data.	-
Case 7	Quantitative detection of trend in HR data 1, 2 and 4 hours prior to event. Quantitative detection of trend in RR data 2 and 4 hours prior to event.	-	Quantitative detection of trend in HR data 4 and 6 hours prior to event. Quantitative detection of trend in RR data 1, 2 and 4 hours prior to event.
Case 8	-	-	No quantitative detection of trend in HR and RR data. Subjective visual assessment by researcher does show a very slow yet steady increase of HR and RR over a period of ~ 30 hours.

Table 30 (on the following page) provides a summary of the continuous monitoring data that was acquired for the included population ($n = 30$). This descriptive overview was generated by visually assessing data characteristics per patient, in order to provide insight into the general data characteristics.

Table 30: Overview of biosensor data characteristics. Subgroups were constructed based on the development of respiratory failure and the reason for admission to the COVID-ward (primary admission versus post-ICU care).

RF = Respiratory failure, ICU = intensive care unit, HR = Heart rate, RR = Respiratory rate.

	All patients (n=30, 100%)	RF (n=25, 83%)	No RF (n=5, 17%)	Primary admission to COVID-19 cohort ward (n=15, 50%)	Post-ICU care at COVID-19 cohort ward (n=15, 50%)
Biosensor data overview					
Total amount of data (hours)	141 [81.5; 279]	188 [95; 283]	83 [78; 112]	96 [41; 195]	203 [109; 293]
Sinusoidal pattern in HR data	14 (47%)	12 (48%)	2 (40%)	4 (27%)	10 (67%)
Data gaps > 1h ^a HR	25 (83%)	21 (84%)	4 (80%)	10 (67%)	15 (100%)
RR	26 (87%)	22 (88%)	4 (80%)	11 (73%)	15 (100%)
Data gaps > 6h ^a HR	17 (57%)	15 (60%)	2 (40%)	6 (40%)	11 (73%)
RR	19 (63%)	17 (68%)	2 (40%)	7 (47%)	12 (80%)
Data gaps > 24h ^a HR	6 (20%)	5 (20%)	1 (20%)	1 (7%)	5 (%)
RR	9 (30%)	8 (32%)	1 (20%)	2 (13%)	7 (47%)
Tachycardia > 100 bpm for > 1h ^b	19 (63%)	17 (68%)	2 (40%)	6 (40%)	13 (87%)
Tachycardia > 100 bpm for > 6h ^b	17 (57%)	16 (64%)	1 (20%)	5 (33%)	12 (80%)
Tachycardia > 100 bpm for > 24h ^b	5 (17%)	5 (20%)	0	1 (7%)	4 (27%)
'Plateau'-like tachycardic episodes ^c	3 (10%)	3 (12%)	0	2 (13%)	1 (7%)
Bradycardia < 60 bpm for > 1h ^b	4 (13%)	3 (12%)	1 (20%)	2 (13%)	2 (13%)
Bradycardia < 60 bpm for > 6h ^b	1 (3%)	0	1 (20%)	1 (7%)	0
Bradycardia < 60 bpm for > 24h ^b	1 (3%)	0	1 (20%)	1 (7%)	0
Tachypnoea > 20 brpm for > 1h ^b	27 (90%)	25 (100%)	2 (40%)	12 (80%)	15 (100%)
Tachypnoea > 20 brpm for > 6h ^b	27 (90%)	25 (100%)	2 (40%)	12 (80%)	15 (100%)
Tachypnoea > 20 brpm for > 24h ^b	17 (57%)	16 (64%)	1 (20%)	6 (40%)	11 (73%)
Tachypnoea > 25 brpm for > 1h ^b	25 (83%)	23 (92%)	2 (40%)	12 (80%)	13 (87%)
Tachypnoea > 25 brpm for > 6h ^b	17 (57%)	16 (64%)	1 (20%)	8 (53%)	9 (60%)
Tachypnoea > 25 brpm for > 24h ^b	3 (10%)	3 (12%)	0	1 (7%)	2 (13%)
^a Data gaps are generally caused by logistic challenges, such as empty biosensor batteries, a short ICU or MCU admission, or a inadequately placed biosensor.					
^b Tachycardia/bradycardia/tachypnoea during the <i>entire</i> period, for example: a HR of > 100 for an entire period of 6 hours					
^c 'Plateau'-like tachycardic episodes were observed in multiple patients and were perceived as a 'rectangular function', the trend data in figure 30 of case 8 shows an example of a 'plateau'-like tachycardic episode					

Note from table 30 that the HR data of 14 out of 30 continuously monitored COVID-19 positive patients showed the sinusoidal pattern that is described in the case studies. 22 out of the 30 continuously monitored COVID-19 positive patients are survivors, 8 out of 30 died due to the consequences of COVID-19. Therefore 64% (14 out of 22) of the survivors showed the sinusoidal pattern and 36% (6 out of 22) did not show the sinusoidal pattern. For the surviving group that did not show the sinusoidal pattern, two patients were hospitalised for over two weeks after the patch was removed, meaning that the patients were not yet in recovery during the period of continuous monitoring. For the remaining six patients within this group, the patch was removed on the day of discharge or a maximum of two days prior to discharge.

6.4 Discussion

Key findings

This case series illustrates that continuous HR and RR trend data can be used to visually recognise patient deterioration, as well as patient recovery.

Visual recognition of patient deterioration

Patient deterioration was recognised by visually assessing the HR and RR trends, while taking context information into account (e.g., the comorbidities of the patient or the type of oxygen therapy). In case of deterioration, we observed that the HR trend steadily increased over time. The RR trend also increased for most of these cases. The RR trend was however a more variable signal (more 'peakiness' and less steady), therefore resulting in less clear-cut trends of progressive tachypnoea.

Please note, that 'mild deterioration', can often not be deduced from the continuous data. For example: a moderate increase in shortness of breath complaints resulting in a slight increase in O₂ therapy (for example 2L nasal cannula to 3L cannula) may not have a notable effect on the continuous data. In such cases, the continuous data may however be of use to get an indication of the global condition of the patient or to check whether the HR and RR (and if available the SpO₂) positively respond to the intervention of slightly increasing the O₂ therapy.

In accordance to the above, visual assessment of the continuous data does not necessarily allow for 'prediction' of a type 2 event (= the need for oxygen therapy with an FiO₂ ≥ 40% after at least 24h of continuous monitoring) in terms of trend recognition. In contrast, visual assessment of the continuous data does allow for trend recognition prior to type 3 and type 4 events (respectively, ICU admission and death). The increases that were observed in relation to these more *severe cases of patient deterioration*, were often perceived as linear increases over a period of time (1-24 hours). Of course, these linear increases are subjected to 'imperfections', resulting from either physiological processes that may be related to the process of deterioration (e.g., periods of atrial fibrillation in cases 7 and 8) or simply by movement (e.g. 'peakiness' in HR trends). Partially due to these 'imperfections', the quantification of these linear trends by means of linear regressions, resulted in moderately convincing results. The ability of a dynamically computed linear regression model (e.g. in the form of a rolling linear regression model) over the entire HR and RR trends to detect significant and apparent trends is to be further explored.

Visual recognition of patient recovery

In addition, two thirds of the recovering patients showed a diurnal 'sinusoidal pattern' in either the HR trend, or both the HR and RR trend. In short, this 'sinusoidal pattern' entails a relatively decreased HR (and often also RR) during the night, and a relatively increased HR (and often also RR) during the day. This matches the circadian rhythm of a healthy individual of sleep during the night and activity and mobilisation during the day. None of the deteriorating patients showed this 'sinusoidal pattern' or circadian rhythm, meaning that observing this pattern might help in recognising early signs of recovery. Further exploration on the value of the 'sinusoidal pattern' for classifying patients as 'recovering' or 'deteriorating' is needed. In addition, feasibility of automated quantification of the sinusoidal pattern should be explored. In this process, other features related to the circadian rhythm should be explored, such as the ratio of HR and RR variance during the day and during the night (hypothesising that HR and RR variance is increased during the day in recovering patients, due to mobilisation and cognitive activity).

Insight into the COVID-19 disease pattern

Lastly, this case series report provides valuable insight into the capricious clinical course of hospitalised COVID-19 patients: severely affected individuals with notably increased RR values (a RR of 25 is almost 'the normal value' in these patients), sudden desaturations or long-term decreased SpO₂ values while receiving extensive O₂ therapy for support. Case specific clinical symptoms, match previously published literature on the clinical aspects of the disease [22–31]. Contrarily to these previously published literature on the *overall* aspects of COVID-19, the described case series report provides new insights into patient specific clinical courses, concerning both deterioration (slow but steady increase of trend) and recovery (sinusoidal pattern). These findings should be used in future monitoring of severely affected (COVID-19) patients, in order to promote early detection of patient deterioration.

Interpretation of results

The detailed continuous vital signs observations in this case series illustrate how HR and RR trend data can be used to visually recognise patient deterioration (potentially leading to ICU admission or death), as well as recognising patient recovery. Previously published literature on the possibility of continuous monitoring with wearables to detect deterioration is in accordance with these findings [40–46]. The results of this ongoing observational research in COVID-19 patients suggests that it may be worthwhile to further explore the possibility of automated trend analysis for detection and prediction of severe cases of patient deterioration. The added value of trend recognition in notification systems should be further explored.

While intuitively logical, the relationship between the presence of a circadian HR and RR rhythm in recovering patients and the absence of such a pattern in severely ill COVID-19 patients, has not been described before. The potential value of (visually) assessing whether a circadian pattern is present, or possibly the automated quantification of such a pattern is to be further explored.

In addition, the described key findings mostly confirm that continuous data is a valuable tool for monitoring the clinical condition of the patient [40–46]. Please note, however, that it is very important to add 'context information' in order to adequately interpret the continuous vital signs data, and to determine whether actions are needed (e.g. increase of O₂ therapy). Some examples:

- A morning walk on the ward with physiotherapist will in most COVID-19 cases result in tachycardia and tachypnoea (and possibly a decreased SpO₂).
- If a patient uses beta blockers, the HR data has to be interpreted differently as some types of beta blockers slow down the patients HR.
- If a patient is known to have certain comorbidities, data should be interpreted while considering the effect of the comorbidities. For example, the data of case 7 and case 8 in this chapter show episodes of tachycardia, for case 8 even the mentioned 'plateau'-like tachycardic episodes. In both cases these episodes are the result of the comorbidity of atrial fibrillation.

Limitations

While the data was acquired, the data was meticulously monitored by a student monitoring team, resulting in consequential actions to improve the patients' condition. These data driven actions may have resulted in alterations in the data, as the patients' condition is likely have improved based on these actions (for example, the monitoring team notifying the nurses of a sudden desaturation or long-term increasing RR trend). This is not necessarily a limitation, yet it influences the interpretation of the data, as no data from a 'control' patient series is available (where no data driven actions were undertaken).

The data registered by nurses of the SpO₂ and O₂ therapy, as well as the starting and ending times of the events and the general context information on the condition of the patient, were manually extracted from nurses' observations documented in the EPR. The times at which the SpO₂ and O₂ therapy was reported in the EPR, are registered with the report. These 'times of report' are not in accordance with the actual times at which the measurement of oxygen therapy adjustments were performed. The same applies to the starting and ending times of the events and the general context information that was extracted from nurses' and physician's observations. Also, as data extraction was done manually, this process might have resulted to some errors.

Lastly, the cases that are discussed are all COVID-19 patients who were hospitalised during the first wave in the Netherlands. Since then, treatment policies regarding COVID-19 patients have been optimised, for example the administration of dexamethasone. Therefore, the observed clinical processes of COVID-19 patients in the continuous data may be somewhat outdated by now.

Recommendations

This case series illustrates that continuous HR and RR trend monitoring is a valuable tool to assess the clinical condition of the patient and disease development. In order to facilitate healthcare workers at the general ward or the COVID-19 cohort ward, the data should be presented as clear and simple as possible, yet be substantiated with context information. Relating the continuous HR and RR trends to context information of the patient is key to adequate interpretation of the continuous vital signs data, as was done in this case series report. Therefore, future research and development should focus on optimising the integration of continuous data with context information, such as patient activity, patient symptoms, the administered O₂ therapy, comorbidities, current medications, and a summary of the clinical condition according the physician.

Optimising the visual presentation of the continuous data for the various groups of users is important, but our data also suggest that quantification of the data in order to further develop adequate notification systems is another potentially valuable avenue of exploration. As described, it was possible to visually detect the more severe cases of patient deterioration (by a long-term linear trend) and patient recovery (a circadian pattern). Future research should focus on the quantification of these detection methods,

to explore the possibility that these findings offer in optimising notification systems. In order to do so, future studies should also explore optimised methods to 'explain' the data (e.g., automated detection of atrial fibrillation, or using accelerometer data for automated detection of ECG or PPG movement artifacts). This will be necessary to adequately develop the suggested methods of deterioration or recovery detection.

6.5 Conclusion

To briefly answer the research question corresponding to this chapter:

How can continuously monitored heart rate and respiratory rate data be used to visually detect and predict clinical deterioration or recovery in COVID-19 patients, and what are characteristic trend patterns indicating deterioration or recovery?

Continuously monitored HR and RR data can be used to visually detect (the more severe cases) of clinical deterioration or recovery in COVID-19 patients. This can be done by visual trend assessment on the presence of respectively a long-term linear increase in HR (and often also RR), or a sinusoidal pattern in HR (and often also RR) that matches the circadian rhythm. These conclusions should be incorporated into the training of healthcare workers (nurses, physicians and the monitoring team) at the COVID-19 cohort ward, who are currently working with the implemented continuous monitoring system.

7 DETECTION OF DETERIORATION IN COVID-19 PATIENTS

7.1 Introduction and objective

Recapitulation of the results of chapter 6

Detection of patient deterioration

Chapter 6 (a case series report on a selection of eight continuously monitored COVID-19 patients) has reported that visual assessment of continuously monitored HR and RR data in COVID-19 patients, allows for visual recognition of severe cases of patient deterioration. Such cases of deterioration were preceded by 'linear' trends, showing a steadily increasing HR (and often also RR) prior to ICU admission or death of the patient. These so-called 'linear' trends were, of course, subjected to 'imperfections' (e.g. due to episodes of atrial fibrillation or the effect of movement on the data) which compromised the steadiness of the linearity of the trend. Still, findings in chapter 6 suggest that quantitative detection of patient deterioration by means of trend detection may be of added value in continuous monitoring systems. Therefore, quantitative methods for trend detection are explored within this current chapter.

Introducing the objective of chapter 7

Previously published studies have described that vital sign trends are of added value in continuous monitoring, in terms of detecting patient deterioration and supporting clinical decision making [40–46, 94]. The conclusion of the case series report that was executed within the previous chapter, complies with these published studies. As an extension to the findings in chapter 6, the research that is presented in this current chapter focusses on exploring the feasibility of quantitatively detecting patient deterioration by means of trend detection. A conclusion to this chapter will be formulated in relation to the following research question:

How can continuously monitored heart rate and respiratory rate data be used to quantitatively detect clinical deterioration in COVID-19 patients by means of trend detection?

7.2 Methods

Study design

This study concerns an observational retrospective cohort study of all COVID-19 patients admitted to the COVID-19 cohort ward of the UMCU, that were equipped with the continuous monitoring technology. As described in the introduction to this chapter, this research is an extension to the findings that are presented in chapter 6. This current chapter explores the feasibility of automated quantitative detection of patient deterioration by means of trend detection.

Study population

In- and exclusion criteria

The overall study population for the continuous monitoring project covers: all adult patients diagnosed with COVID-19, admitted to the COVID-19 cohort ward, and equipped with the continuous monitoring technology, who experienced a serious case of deterioration (defined as ICU admission or death) *while being monitored*. The only exclusion criteria for the overall study population for the continuous monitoring project, was: patients with a pacemaker or implantable cardioverter defibrillator. In addition to these criteria, one inclusion and one exclusion criterium were added for the research that is presented within this chapter. The overall in- and exclusion criteria are formulated below, in table 31.

Table 31: in- and exclusion criteria for the entire population of COVID-19 patients monitored at the COVID-19 cohort ward

<i>Inclusion</i>	<i>Exclusion</i>
• Age > 18 years • Patient is diagnosed with COVID-19 • Patient was continuously monitored using a wireless wearable sensor • Patients who <i>did</i> experience a serious case of deterioration (defined as ICU admission or death) <i>while being monitored</i>	• Patients with a pacemaker or implantable cardioverter defibrillator • Patients with a duration of continuous monitoring of ≤ 24 hours

Data acquisition

All data that is used in this chapter were acquired at one of the COVID-19 cohort wards at the UMCU. The set-up of the monitoring system at the COVID-19 cohort ward is described in detail in the background section '2.3 Continuous monitoring at the COVID-19 cohort ward in the UMCU'. Figure 12 provides a schematic illustration of the continuous monitoring system set-up. The data that is used, were acquired during the first (start of April 2020 until mid-May 2020) and the second (mid-October until the mid-December) wave of COVID-19 patients in the Netherlands.

Data processing

All data were visualised and quantitatively analysed using Matlab R2020a. The continuous HR and RR trend data does not have a constant sampling frequency. The time difference between two datapoints is variable, yet datapoints are generated approximately once or twice per minute – excluding large time gaps due to other, logistic reasons (e.g. an empty biosensor battery). This was purposely not corrected for, as all datapoints are realistic and relevant for data analyses and visualisation for trend assessment.

Continuous HR and RR trend data was cleaned and processed in Matlab in order to remove erroneous data. This was done in the following way. After structurally storing the data in Matlab, the first three and last three datapoints of each individual case were removed. Likewise, all data were searched for time gaps that were longer than four minutes, after which the three datapoints preceding and following these data gaps were removed. This was done as these datapoints are prone to error, for example due to patch removal, or other motion artifacts.

Algorithm design: 'moving linear regression algorithm'

As described, this chapter focuses on exploring the feasibility of quantitatively detecting patient deterioration by means of trend detection. This was done, by developing a '*moving linear regression algorithm*' and exploring its abilities to adequately detect trends in HR and RR data. In short, this moving linear regression algorithm moves a window (with a predetermined window length, and predetermined step length) along the continuous HR and RR data, and fits a linear trend to each data window. Based on predetermined cut-off values for the characteristics of the linear fit, the algorithm assesses whether a trend is or is not detected. Figure 31 (following page) provides an overview of the structure of the moving linear regression algorithm. On the following pages, the working mechanism of the moving linear regression algorithm is meticulously described by discussing each algorithm component.

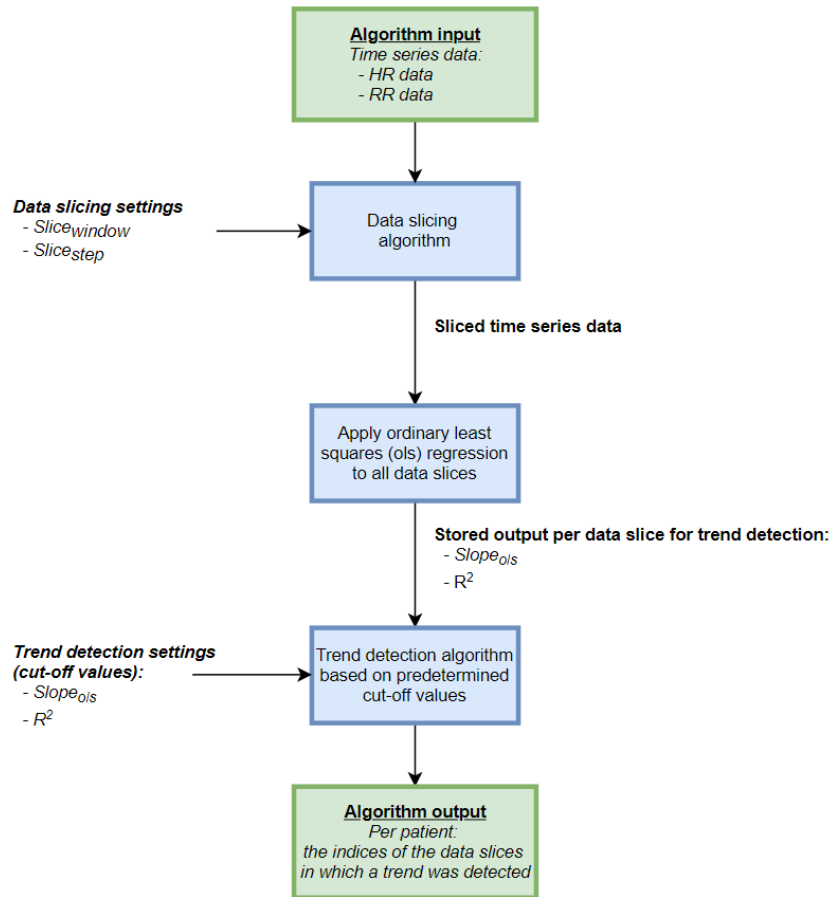


Figure 31: overview of the moving linear regression algorithm showing all components of which it is comprised. The green blocks show the algorithm input (top) and the algorithm output (bottom). The blue blocks show the algorithm components (elaborately described in the text following this figure). The text on the left-side of this figure, shows the settings of the moving linear regression algorithm (two types: data slicing settings and trend detection settings). The data slicing settings comprise of $slice_{window}$ (the predetermined window length that is moved along the continuous data) and $slice_{step}$ (the predetermined step length with which $slice_{window}$ is moved along the continuous data). The trend detection settings comprise of cut-off values for the linear regression data slice characteristics: $slope_{ols}$ (the slope of the linear fit to the data slice) and R^2 (the coefficient of determination of the fit).

Algorithm input

The algorithm input comprises of time series data: continuous HR and RR data.

Data slicing algorithm

The first blue block in figure 31, hence the first component of the moving linear regression algorithm concerns the 'data slicing algorithm'. This algorithm component creates data slices by moving a predetermined window length ($slice_{window}$, in hours) along the continuous data, with a predetermined step length ($slice_{step}$, in hours). Both $slice_{window}$ and $slice_{step}$ are data slicing settings that can be varied by the researcher (e.g. $slice_{window}$ can be either 1 hour, or 24 hours, depending on the period over which we want to detect a trend). A schematic example of this 'data slicing'-approach is depicted in figure 32. This example concerns a $slice_{window}$ of 24 hours and slicing steps of 8 hours.

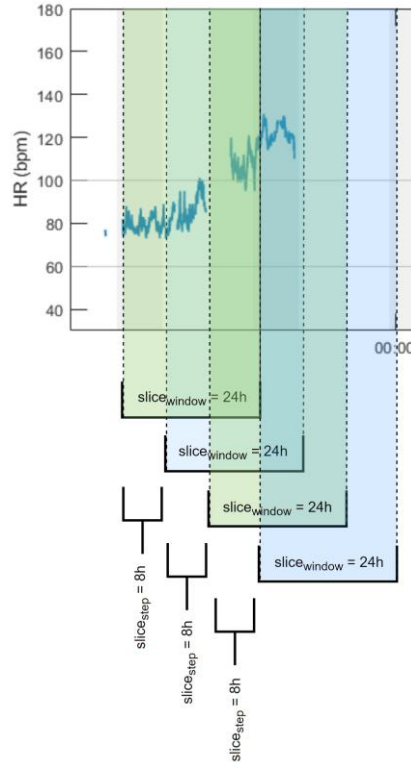


Figure 32: Schematic illustration of the working mechanism of the data slicing algorithm. The data slicing settings comprise of $slice_{window}$ (the predetermined window length that is moved along the continuous data, in this case 24h) and $slice_{step}$ (the predetermined step length with which $slice_{window}$ is moved along the continuous data, in this case 8h). This example concerns a patient who was transferred to the ICU, just after the ending of the second data slice.

Ordinary least squares regression model, applied to all data slices

After slicing the time series data of the HR and RR data, ordinary least squares (OLS) regression was performed on all data slices. By applying OLS to the data slices, the linear fit that is chosen, should have the minimum (with respect to all other possible linear fits) sum of the squares of the differences between the data and the fitted line.

Per data slice, three outputs of the linear fit were stored for further use. Two of these outputs were used within the algorithm for trend detection. The remaining linear fit characteristic – the estimated y-axis intercept of the linear fit – was not used within the moving linear regression algorithm, yet was stored in order to visualise the linear fits alongside the continuous data. The two linear fit characteristics that were used within the moving linear regression algorithm for trend detection are:

- $Slope_{ols}$ – estimated slope of the linear fit (for HR in bpm $\uparrow$ /day, and for RR in brpm $\uparrow$ /day).
- R^2 – the coefficient of determination, a statistical measure that indicates the proportion of the variance in the dependent variable (in this case the fitted line to HR and RR) that is predictable from the independent variable (in this case time), therefore a R^2 of 1 indicates that the linear fit explains the data perfectly.

Trend detection algorithm

These linear fit characteristics – $\text{slope}_{\text{ols}}$ and R^2 – serve as data input for the third and last component of the moving linear regression algorithm: the trend detection algorithm. In short, the trend detection algorithm evaluates per data slice whether the $\text{slope}_{\text{ols}}$ and R^2 of the linear fit are in accordance with predetermined cut-off values. If both $\text{slope}_{\text{ols}}$ and R^2 comply with the cut-off values, the trend detection algorithm indicates that a trend was detected. Figure 33 shows a flowchart, providing insight into the working mechanism of the trend detection algorithm.

As is depicted in the flowchart in figure 33, the algorithm works differently for R^2 and $\text{slope}_{\text{ols}}$. For R^2 of the linear fit, the algorithm simply assesses whether the R^2 of the linear fit is equal to or greater than the chosen cut-off value. For $\text{slope}_{\text{ols}}$ of the linear fit, the algorithm first assesses in which MEWS level the linear fit ends. Depending on the MEWS level in which the fitted line ends, the cut-off value is multiplied with:

- $0.75^{\text{MEWS level}}$, therefore:
 - $0.75^0 = 1$ for ending in MEWS level 0);
 - $0.75^1 = 0.75$ for ending in MEWS level 1);
 - $0.75^2 \approx 0.56$ for ending in MEWS level 2);
 - or $0.75^3 \approx 0.42$ for ending in MEWS level 3).

In other words, if the linear fit ends in a high MEWS level (e.g. 3), the algorithm is less 'strict' as the linear fit can be identified as a '*trend*' even though the $\text{slope}_{\text{ols}}$ is lower than the predetermined cut-off value (e.g. for MEWS level 3, between a factor 0.75^3 and 0.75^0 lower). The algorithm was designed this way, as critical clinical situations (where MEWS scores are generally increased), should be accompanied by more cautious monitoring (in this case by decreasing cut-off values and being more easily inclined to generate a notification).

Please note, that the trend detection algorithm *only* decreases the cut-off value for $\text{slope}_{\text{ols}}$, when the linear trend ends in a higher MEWS score that is associated with an *increased* HR or RR. Of course, MEWS levels are also increased when HR and RR fall *below* a certain threshold, as can be seen in table 1 on the MEWS levels in the background section of this thesis. This was not incorporated into the trend detection algorithm, as results in chapter 6 suggest that COVID-19 patients rarely show HR and RR values below MEWS level 0 (51-100 bpm and 12-20 brpm, respectively). Results of chapter 6 also suggest that deterioration of COVID-19 patients is often observed as an *upward* trend in the HR and RR data. Therefore, chances of HR and RR in deteriorating patients being lower than the lower threshold values of MEWS level 0 (51 bpm and 12 brpm, respectively), are limited. For these reasons, all values below 100 bpm for HR and 20 brpm for RR were multiplied by the factor 0.75^0 (thus, multiplied with 1).

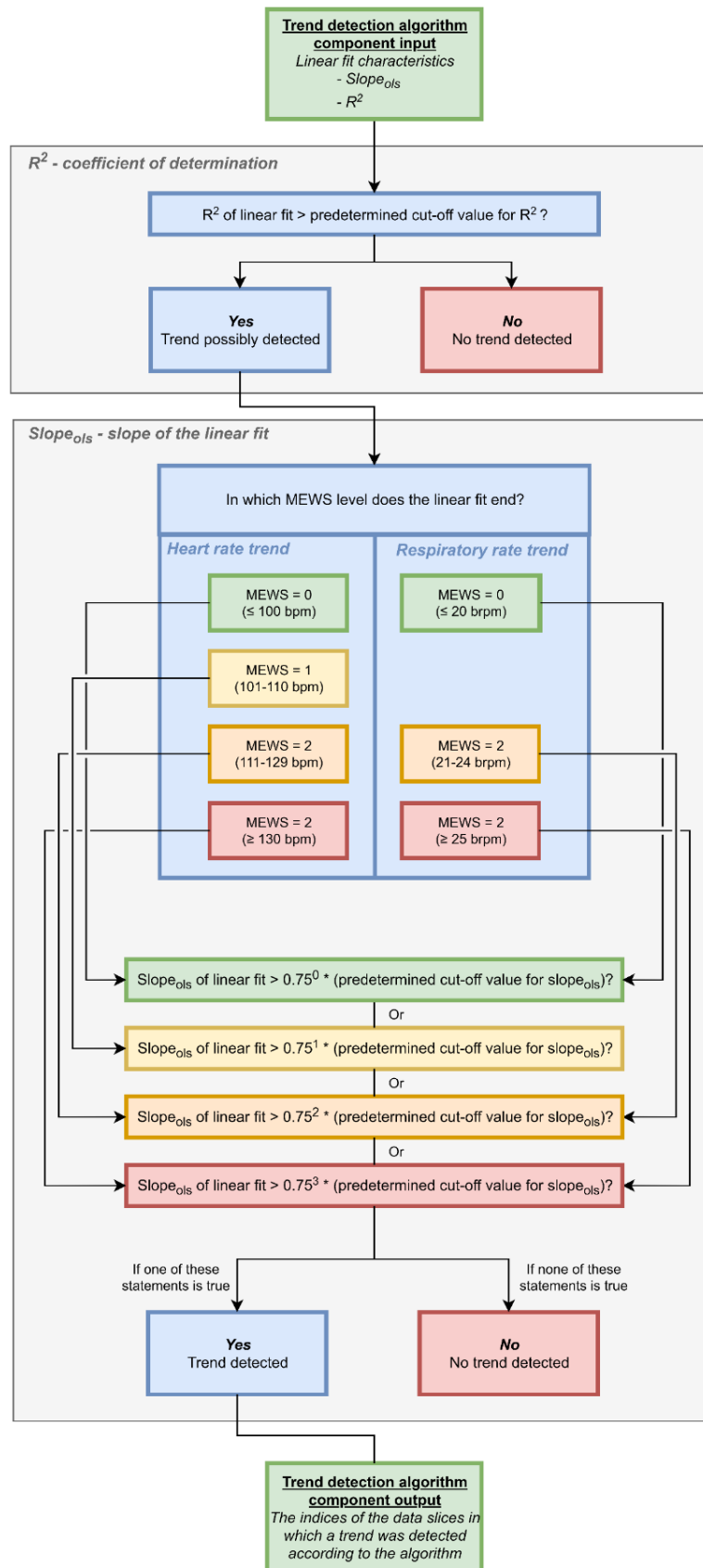


Figure 33: overview of trend detection component of the moving linear regression algorithm showing all components of which is it comprised. The trend detection settings comprise of cut-off values for the linear regression data slice characteristics: $slope_{ols}$ (the slope of the linear fit to the data slice) and R^2 (the coefficient of determination of the fit).

Algorithm output

After applying the trend detection algorithm to the data slices, the output of the moving linear regression algorithm entails the data slices (per patient) in which a trend was detected.

Algorithm design: choosing settings for the moving linear regression algorithm

As described in the previous pages on the structure of the moving linear regression algorithm, the algorithm comes with two different types of settings: *data slicing settings* and *trend detection settings*. The values for these settings were chosen (and varied) by the researcher, in order to formulate candidate algorithms that were tested on the available continuous data of COVID-19 patients. The values for these settings were chosen as follows:

- *Data slicing settings*
 - $slice_{window}$

A set of values for $slice_{window}$ were chosen by the researcher, based on the findings in chapter 6 on quantitative trend detection prior to ICU admission and death. These findings suggested that linear trends could be observed during periods of 1, 2, 4, 6, 12 and 24 hours prior to ICU admission and death. Therefore, settings for $slice_{window}$ were varied within this scope of window length:

 - 2h
 - 4h
 - 8h
 - 12h
 - 24h
 - $slice_{step}$

The value for $slice_{step}$ was set to be proportional to the value for $slice_{window}$. This was done, as the settings for $slice_{window}$ were varied strongly (2h-24h), requiring for adapted settings for $slice_{step}$. For example, if a rigid number of $slice_{step} = 1h$ were to be used, the steps would possibly be 'too large' for a $slice_{window}$ setting of 2h, possibly resulting in 'missed trends'. The value for $slice_{step}$ was set proportional to the value for $slice_{window}$, by the use of the following formula:

$$slice_{step} = \frac{1}{8} * slice_{window}$$
- *Trend detection settings*
 - Cut-off value for R^2

As described, R^2 represents the coefficient of determination of the linear fit, a statistical measure that indicates the proportion of the variance in the dependent variable (in this case the fitted line to HR and RR) that is predictable from the independent variable (in this case time). In other words: 'how well does the linear fit estimate the data?'. Results in chapter 6 suggest that the HR data is a more 'steady' signal, and the RR data is a more 'turbulent' and 'peaky' signal. Therefore the cut-off value of R^2 for HR and RR were set at different values. These cut-off values were not varied.

 - Cut-off value of R^2 for HR was set at 0.65
 - Cut-off value of R^2 for RR was set at 0.50
 - Cut-off value for $slope_{ols}$

The cut-off values for $slope_{ols}$ were chosen and varied by the researcher. The cut-off values were initially based on the observations that were done within the case series report of chapter 6: how strongly did the HR values increase during a process of deterioration? In addition, these settings were varied strongly, in order to study the results of algorithms that used a relatively small cut-off value for $slope_{ols}$ (e.g. 15 bpm↑ within 24 hours is relatively small increase) opposed to algorithms that used a relatively large cut-off value for $slope_{ols}$ (e.g. 45 bpm↑ within 24 hours).

 - Cut-off value for $slope_{ols}$ for HR
 - 15 bpm↑/day
 - 30 bpm↑/day
 - 45 bpm↑/day
 - Cut-off value for $slope_{ols}$ for RR
 - 10 brpm↑/day
 - 12.5 brpm↑/day
 - 15 brpm↑/day

As described, the cut-off values of $slope_{ols}$ for HR and RR were to be set by the researcher, yet will decrease with factor of $0.75^{MEWS \text{ level}}$, if the linear fit of the data ends in an increased MEWS level. Table 32 shows the cut-off values within different MEWS levels.

Table 32: cut-off values for $slope_{ols}$ per MEWS level in which the linear fit to the data slice ends

Cut-off value	In which MEWS level does the linear fit end?			
	0 (* 0.75 ⁰)	1 (* 0.75 ¹)	2 (* 0.75 ²)	3 (* 0.75 ³)
Cut-off value HR				
15 (bpm↑/day)	15.00	11.25	8.44	6.33
25 (bpm↑/day)	30.00	22.5	16.88	12.66
35 (bpm↑/day)	45.00	33.75	25.3	18.98
Cut-off value RR	0 (* 0.75 ⁰)		2 (* 0.75 ²)	3 (* 0.75 ³)
10 (brpm↑/day)	10.00		5.63	4.22
12.5 (brpm↑/day)	15.00		8.44	6.33
15 (brpm↑/day)	20.00		11.25	8.44

Altogether, these settings result in a set of candidate models. Tables 33 and 34 provide an overview of the different combinations of settings, resulting in 15 candidate models for both HR and RR data.

Table 33: overview of the 15 moving linear regression algorithms for trend detection in the HR data slices. The table only includes the settings that were varied. $slice_{step}$ and R^2 were not varied, and were respectively set at $1/8 * slice_{window}$ and 0.65.

Name of the candidate algorithm	Data slicing setting	Trend detection setting
	$slice_{window}$ (in hours)	$slope_{ols}$ for HR (in bpm↑/day)
HRalgorithm1.1	2	15
HRalgorithm1.2	2	30
HRalgorithm1.3	2	45
HRalgorithm2.1	4	15
HRalgorithm2.2	4	30
HRalgorithm2.3	4	45
HRalgorithm3.1	8	15
HRalgorithm3.2	8	30
HRalgorithm3.3	8	45
HRalgorithm4.1	12	15
HRalgorithm4.2	12	30
HRalgorithm4.3	12	45
HRalgorithm5.1	24	15
HRalgorithm5.2	24	30
HRalgorithm5.3	24	45

Table 34: overview of the 15 moving linear regression algorithms for trend detection in the RR data slices. The table only includes the settings that were varied. $Slice_{step}$ and R^2 were not varied, and were respectively set at $1/8 * slice_{window}$ and 0.65.

Name of the candidate algorithm	Data slicing setting	Trend detection setting
	$Slice_{window}$ (in hours)	$Slope_{ols}$ for RR (in brpm $\uparrow$ /day)
RRalgorithm1.1	2	10
RRalgorithm1.2	2	15
RRalgorithm1.3	2	20
RRalgorithm2.1	4	10
RRalgorithm2.2	4	15
RRalgorithm2.3	4	20
RRalgorithm3.1	8	10
RRalgorithm3.2	8	15
RRalgorithm3.3	8	20
RRalgorithm4.1	12	10
RRalgorithm4.2	12	15
RRalgorithm4.3	12	20
RRalgorithm5.1	24	10
RRalgorithm5.2	24	15
RRalgorithm5.3	24	20

Evaluating the performance of the algorithms

As described in the introduction to this chapter, the goal of this research is to explore the feasibility of quantitatively detecting patient deterioration by means of trend detection. The ability of the candidate algorithms to adequately detect trends, was therefore evaluated, by applying the candidate algorithms to data of patients who experienced a severe case of deterioration while being monitored (leading up to ICU admission or death). By applying the candidate algorithms to this relatively small group of severely affected patients, it was assessed whether trends could be detected within data where trends are most likely to occur: during processes of deterioration.

After applying the candidate algorithms to the continuous data of the included patient group, the number of detected trends within the data sets were counted. Based on this count, it was assessed whether some of the algorithms functioned inadequately by detecting too many or, contrarily, no trends at all. Consecutively, visualisations of the detected trends were made for a set of patients from the included patient group. This was done, to provide insight into the trends that were detected by the different candidate algorithms and to consider the advantages and disadvantages of the different settings within the candidate algorithm. Ultimately, a conclusion was formulated on the feasibility of detecting clinical deterioration by means of trend detection.

This method will reveal whether continuously monitored HR and RR data can be used to quantitatively detect clinical deterioration in COVID-19 patients by means of trend detection. In other words: by evaluating the performance of the candidate algorithms within a patient group that did in fact deteriorate while being monitored, we are exploring the feasibility of detecting clinical deterioration by the use of trend detection.

Note, that this research focusses on the ‘*exploration*’ of using trend detection in order to recognise and predict clinical deterioration, and does not attempt to propose a complete and optimal functioning ‘trend detection’-based notification system. In other words, this research *does not* aim to accomplish complete validation of the moving linear regression algorithm, yet *does* aim to assess whether these algorithm could be of added value to detect and/or predict deterioration. Also, please note, that no adequate validation data was available during this research. All data on the clinical conditions of the patient was retrieved manually from the EPR – therefore being prone to errors (e.g. due to inadequate time specification of events). For algorithm validation, complete and consistent data on whether the patient can be classified as recovering, stable or deteriorating (based on unambiguous definitions) should be available throughout the entire period of monitoring. As this data was not at hand, it was not possible to meticulously validate the results of the candidate algorithms.

7.3 Results

Study population

Figure 34 shows a schematic illustration of the inclusion of the continuously monitored patients. A total of $n=160$ COVID-19 patients was continuously monitored at the COVID-19 cohort ward at the UMCU. A group of fifteen patients was monitored for less than 24 hours. Within the remaining population of $n=145$, fourteen patients did experience a severe case of deterioration (defined as ICU admission or death) *while being monitored*, whereas 131 did not experience such an event *while being monitored*. Table 35 provides a concise baseline characteristics overview of the study population total population of continuously monitored patients ($n=160$) and the included population for the evaluation of the algorithms ($n=14$).

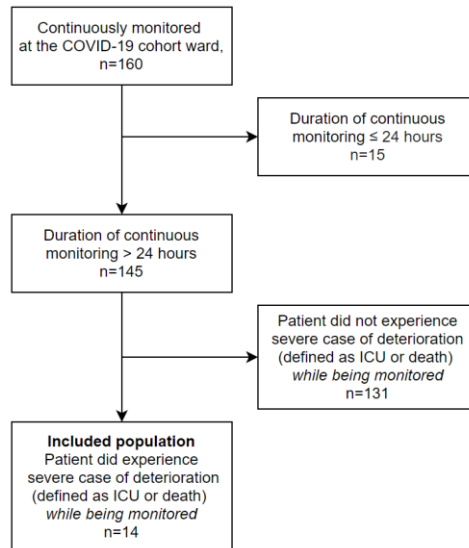


Figure 34: Schematic illustration of the inclusion and exclusion patients

Table 35: Baseline characteristics table of the study population

		Entire population of continuously monitored COVID-19 patients ($n=160$, 100%)	Included population ($n=14$, 8.8%)
Patient characteristics			
Age (years)		65.0 [55.0; 74.0]	69.0 [57.0; 74.8]
Gender	Male	100 (62.5%)	7 (50.0%)
	Female	60 (37.5%)	7 (50.0%)
Patient outcome	Survival	143 (89.4%)	8 (57.1%)
	Death due to COVID-19	17 (10.6%)	6 (43.9%)

Evaluating the performance of the candidate algorithms

The designed candidate moving linear regression algorithms were applied to HR and RR data of patients that did experience a severe case of deterioration (defined as ICU admission or death). This was done in order to assess whether these candidate algorithms were able to detect the processes of deterioration that occurred in these continuously monitored patients. In order to provide an overview on the amount of trends that the candidate algorithm detected within the included patient group, table 36 and 37 provide the number of detected trends that the candidate algorithms detected for each included patient. These tables also include the total number of data slices that were generated by the setting for $\text{slice}_{\text{window}}$ that was applied. Following these tables, visualisations of the outcomes of some of the algorithms are provided and discussed in order to consider the advantages and disadvantages of the different sets of candidate algorithms. In addition, visualisations of all outcomes of candidate algorithms for three selected patients are included in appendices 11.8 and 11.10 in order to ensure an as complete as possible view on the outcomes of the candidate algorithms.

Number of detected trends by the HR candidate algorithms

Based on table 36, it can be concluded that no trends in HR data were detected for patient 1, 3 and 11 by any of the algorithms. In order to provide insight into their data, appendix 11.7 contains the HR trends of these patients. Based on visual assessment of these data sets (concise description is included in appendix 11.7), no visually apparent trends were observed, which is in agreement with the fact that the algorithms did not detect a HR trend for these patients.

All HR candidate algorithms detected trends within the continuously monitoring data of the included patient group. The amount of detected trends differs, which can be explained by two reasons: 1) as $\text{slice}_{\text{window}}$ increases per algorithm (left-right), less data slices are generated by the data slicing algorithm component, resulting in less detected trends (e.g. HRalgorithm5.1 only detects trends for two out of fourteen patients); 2) within a smaller window length, it is more likely detect a trend, due to slight fluctuations in the HR data (e.g. due to physical activity such as showering). HRalgorithm5.1 and HRalgorithm5.2 only detect trends for two patients (8 and 9). Moreover, HRalgorithm5.3 only detected trends for one patient (8). This suggests that the $\text{slice}_{\text{window}}$ setting of 24h may be too large to adequately detect HR trends in most patients. Contrarily, HRalgorithm1.1-3 detect a lot of trends within some of the patients (5, 6, 9, 10 and 14), suggesting that the $\text{slice}_{\text{window}}$ setting of 2h may be too small and consequently results in detection of trends that are not related to deterioration, yet for example caused by mobilisation. These findings are further elaborated on by visually assessing the outcomes of the candidate algorithms, on the following pages

Table 36: Overview of the number of trends that were detected by the candidate algorithms within the continuous HR data of the included patient group. '#slices' indicates the total number of data slices that resulted from the data slicing settings that were used within the data slicing algorithm. Note: this number indicates the number of data slices that contained data; data slices that did not contain data (e.g. due to large data gaps due to ICU admissions) were not counted. '#trends' indicates the number of data slices in which a trend was detected based on the trend detection settings that were used within the trend detection algorithm.

Patient	#slices = total number of data slices #trends = total number of detected trends	HRalgorithm1.1	HRalgorithm1.2	HRalgorithm1.3	HRalgorithm2.1	HRalgorithm2.2	HRalgorithm2.3	HRalgorithm3.1	HRalgorithm3.2	HRalgorithm3.3	HRalgorithm4.1	HRalgorithm4.2	HRalgorithm4.3	HRalgorithm5.1	HRalgorithm5.2	HRalgorithm5.3
1	#slices	359			177			83			49			7		
	#trends	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	#slices	541			275			136			87			29		
	#trends	12	12	12	0	0	0	0	0	0	0	0	0	0	0	0
3	#slices	131			63			26			11			0		
	#trends	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	#slices	593			297			147			94			34		
	#trends	8	8	8	4	4	4	6	6	6	4	4	4	0	0	0
5	#slices	973			488			242			158			63		
	#trends	47	47	47	24	24	22	18	18	15	8	6	4	0	0	0
6	#slices	378			198			99			63			18		
	#trends	24	24	24	6	5	5	0	0	0	3	2	2	0	0	0
7	#slices	107			51			20			7			0		
	#trends	5	5	5	1	1	1	0	0	0	0	0	0	0	0	0
8	#slices	1048			531			266			174			73		
	#trends	41	41	41	8	8	8	3	3	3	3	3	3	6	6	4
9	#slices	1619			815			408			269			121		
	#trends	49	49	49	28	28	28	18	18	18	10	10	10	1	1	0
10	#slices	361			178			83			49			7		
	#trends	25	25	25	9	9	9	11	11	11	4	4	4	0	0	0
11	#slices	185			90			39			20			0		
	#trends	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	#slices	192			93			41			21			0		
	#trends	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0
13	#slices	418			211			104			65			17		
	#trends	4	4	4	5	5	5	3	3	3	0	0	0	0	0	0
14	#slices	584			289			139			86			25		
	#trends	47	47	47	21	21	21	2	2	2	0	0	0	0	0	0

Visual assessment of the performance of the HR candidate algorithms

All visualisations comprise of a similar lay-out. To prevent wordy figure descriptions, figure 35 provides explanation on the lay-out of the figures that are included in this section (and appendix 11.8).

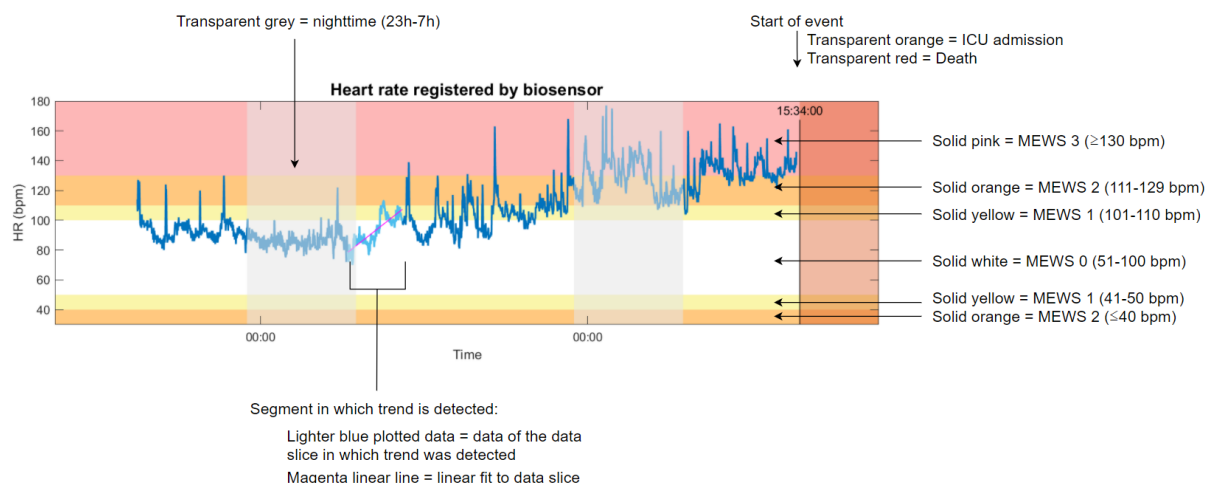


Figure 35: explanation on the lay-out of the visualisations of the outcomes of the algorithm. Detected trends are plotted as magenta lines, along the continuously monitored HR data. In addition, the data slice in which a trend was detected is plotted a lighter blue in order to show within which period the trend was detected

Appendix 11.8 contains visualisations of the outcomes of all candidate algorithms for three selected patients. These three patients were selected based on their differences from one another (type of event and amount of detected trends), yet representativeness with respect to the entire population. Patient 8, 12 and 14 were selected for visualisation (readers may request the remaining visualisations of other patients). Patient 8 and 12 were transferred to the ICU admission while being monitored and patient 14 passed away while being continuously monitored.

By counting the number of trends that were detected per candidate algorithm for each patient (see table 36), it was found that the trend detection setting that was varied ($slope_{ols}$) did not notably affect the amount of detected trends. This is confirmed when studying the visualisations in appendix 11.8.

Below, the visualisations of the outcomes of the HR candidate algorithms for patients 8, 12 and 14 are concisely discussed. Some examples of the visualisations are included within this results section.

Patient 8

- *HRalgorithm1.1-3 and HRalgorithm2.1-3*

A lot of trends were detected within the 2h and 4h data slices. These trends were detected prior to the event, as well as during the recovering period of the patient. For this patient, the trends that were detected were often based on short-term increases of HR, which may have been due to physical or cognitive activity. Therefore, detection of these trends may be irrelevant, as they may not necessarily raise concern or result in data-driven medical interventions. Figure 36 shows the outcomes of HRalgorithm1.2, showing the large amount of detected trends.

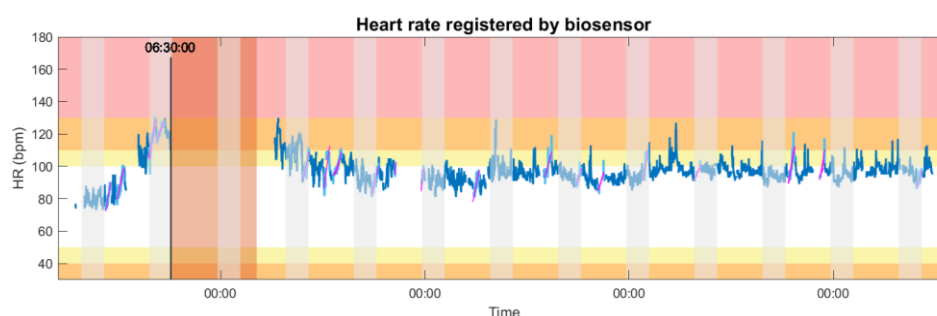


Figure 36: trends detected by HRalgorithm1.2 for patient 8. See figure 35 for explanation on the lay-out of this figure.

- *HRalgorithm3.1-3*
Trends prior to the event (ICU admission) were adequately detected within the data slices of 8h. One 'false' trend was detected in a data slice that comprised of little data as it followed a data gap of approximately 8 hours.
- *HRalgorithm4.1-3 and HRalgorithm5.1-3*
Trends prior to the event were adequately detected within the data slices of 12 and 24 hours. Both algorithms only resulted in detected trends prior to the event; no trends were detected during the period of recovery after ICU admission. Especially HRalgorithm5.1-3 performed well in detecting the visually apparent trend prior to ICU admission. Figure 37 shows the outcomes of HRalgorithm5.2, showing the detected trends prior to the event.

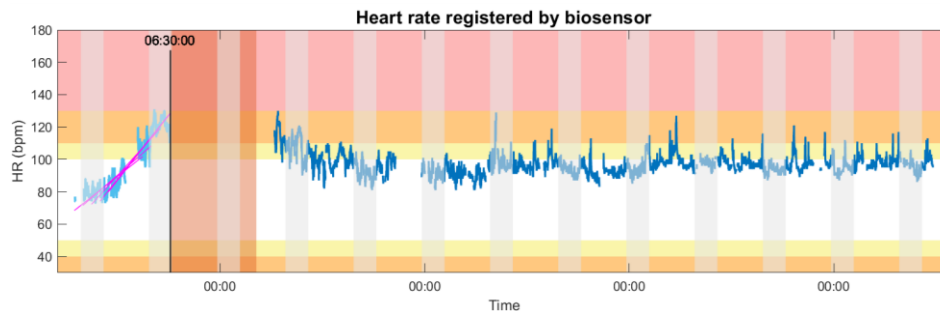


Figure 37: trends detected by HRalgorithm5.2 for patient 8. See figure 35 for explanation on the lay-out of this figure.

Patient 12

- *HRalgorithm1.1-3 and HRalgorithm2.1-3*
These algorithms all detected merely 1 trend within the data slices of 2h or 4h. Figure 38 shows the outcomes of HRalgorithm2.2. This patient shows a trend that steadily increases from ± 90 bpm up to ± 135 bpm. Note that the HR data shows 'peakiness', meaning that the HR values suddenly and shortly increase (from for example 90 bpm to 160 bpm) after which the HR value stabilises relatively quickly. This 'peakiness' within the HR data may have resulted in a limited amount of detected trends within the relatively short data slices of 2h and 4h.

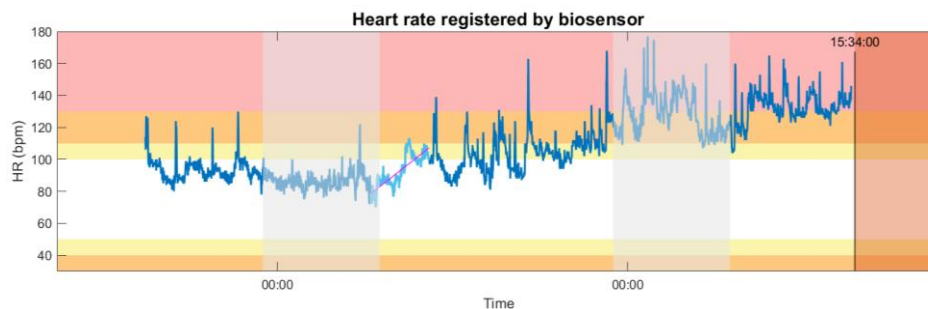


Figure 38: trends detected by HRalgorithm2.2 for patient 12. See figure 35 for explanation on the lay-out of this figure.

- *HRalgorithm3.1-3, HRalgorithm4.1-3 and HRalgorithm5.1-3*
These algorithms did not detect a trend within the HR data of the patient, while visual assessment of the data of patient 12 suggests that an increasing HR trend is present: the data shows a HR trend that steadily increases from ± 90 bpm up to ± 135 bpm. This may have been due to the aforementioned 'peakiness' of the signal, illustrating that the algorithms are not capable of detecting trends in such 'peaky' data.

Patient 14

- *HRalgorithm1.1-3 and HRalgorithm2.1-3*
These algorithms adequately detected the short-term yet evident increases of the HR throughout the entire period of monitoring. This patient concerns case 7 from chapter 6. This patient was diagnosed with atrial fibrillation. These short-term yet evident increases in HR may therefore be related to the consequences of atrial fibrillation. Figure 39 shows the outcomes of HRalgorithm2.2 for this patient, clearly showing that this algorithm is capable of detecting the visually apparent HR increases.

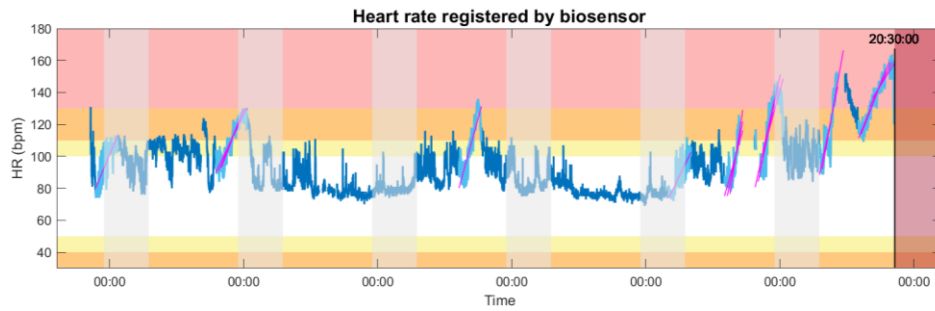


Figure 39: trends detected by HRalgorithm2.2 for patient 14. See figure 35 for explanation on the lay-out of this figure.

- *HRalgorithm3.1-3*
These algorithms only detected two trends within the very last increase in HR leading up to the death of this patient. This suggests that a $\text{slice}_{\text{window}}$ of 8h may have been slightly too large to detect all increasing HR trends within this patient.
- *HRalgorithm4.1-3 and HRalgorithm5.1-3*
These algorithms did not detect a trend within the HR data of the patient.

Summary of the results for the HR candidate algorithms outcomes

These visualisations of the outcomes of the HR candidate algorithms illustrate that the developed algorithms are able to detect trends during processes of deterioration. However, a trend *was not* always detected adequately, even if visual assessment of the data implies that a HR trend was present (as was seen in the visualisations for patient 12). This indicates that visual assessment cannot be completely replaced by a trend detection algorithm. However, the detected trends did not per se serve as adequate detectors/predictors of patient deterioration, as trends were also detected during periods of recovery (e.g. for patient 8). In addition, trends were not always detected prior to an event (defined as ICU admission or death).

In addition, no 'optimal' candidate algorithm can be appointed from the table 36 and the visualisations that were made for the study population as all included models have their advantages and disadvantages. For example: for patient 8, algorithms with $\text{slice}_{\text{window}}$ of 12 and 24h were the most optimal in order to (fully) detect the process of deterioration in terms of long-term increase in HR prior to ICU admission. However, these settings of $\text{slice}_{\text{window}}$ of 12 and 24h showed no results in terms of detecting trends for patient 12 and 14. Contrarily, algorithms with $\text{slice}_{\text{window}}$ of 2h and 4h were the most optimal in order to detect the increasing HR 'episodes' in patient 14, whereas this setting resulted in a lot of seemingly 'irrelevant' detected trends in patient 8. Therefore, it is dependent on the data characteristics of the patient if a model does or does not adequately detect trends.

Number of detected trends by the RR candidate algorithms

Based on table 37, it can be concluded that the RR candidate algorithms detected trends for all patients. However, for patient 7, trends were only detected by algorithms RRalgorithm1.1-3. To provide insight into RR data of this patient, appendix 11.9 contains a visualisation of the outcome of the application of RRalgorithm1.1 to the RR data of patient 7. The outcome of RRalgorithm1.1 was identical to the outcome of RRalgorithm1.2 and RRalgorithm1.3.

All RR candidate algorithms detected trends within the continuously monitoring data of the included patient group. The amount of detected trends differs, which can be explained by two reasons: 1) as $\text{slice}_{\text{window}}$ increases per algorithm (left-right), less data slices are generated by the data slicing algorithm component, resulting in less detected trends (e.g. RRalgorithm5.1 only detects trends for two out of fourteen patients); 2) within a small window length, it is more likely detect a trend, due to slight fluctuations in the RR data (e.g. due to physical activity such as showering). RRalgorithm5.1 and RR algorithm5.2 only detected trends for two patients (8 and 9), which suggests that the $\text{slice}_{\text{window}}$ setting of 24h may be too large to adequately detect RR trends. Contrarily, RRalgorithm1.1-3 detected a lot of trends within some of the patients (1, 5, 6, 8, 9, and 14), suggesting that the $\text{slice}_{\text{window}}$ setting of 2h may be too small and consequently results in detection of trends that are not related to deterioration, yet for example caused by mobilisation. These findings are further elaborated on by visually assessing the outcomes of the candidate algorithms, on the pages following table 37.

Table 37: Overview of the number of trends that were detected by the candidate algorithms within the continuous RR data of the included patient group. '#slices' indicates the total number of data slices that resulted from the data slicing settings that were used within the data slicing algorithm. Note: this number indicates the number of data slices that contained data; data slices that did not contain data (e.g. due to large data gaps due to ICU admissions) were not counted. '#trends' indicates the number of data slices in which a trend was detected based on the trend detection settings that were used within the trend detection algorithm.

Patient	#slices = total number of data slices #trends = total number of detected trends	RRalgorithm1.1	RRalgorithm1.2	RRalgorithm1.3	RRalgorithm2.1	RRalgorithm2.2	RRalgorithm2.3	RRalgorithm3.1	RRalgorithm3.2	RRalgorithm3.3	RRalgorithm4.1	RRalgorithm4.2	RRalgorithm4.3	RRalgorithm5.1	RRalgorithm5.2	RRalgorithm5.3
1	#slices	346			173			81			47			6		
	#trends	25	25	25	9	9	8	5	1	0	0	0	0	0	0	0
2	#slices	402			206			105			69			21		
	#trends	11	11	11	12	12	12	1	1	1	0	0	0	0	0	0
3	#slices	129			62			25			10			0		
	#trends	10	10	10	4	4	4	1	1	1	0	0	0	0	0	0
4	#slices	483			246			125			83			29		
	#trends	17	17	17	7	7	7	6	5	2	8	4	2	1	1	1
5	#slices	868			443			227			153			63		
	#trends	34	34	34	22	22	22	8	6	6	3	2	2	0	0	0
6	#slices	356			187			97			62			18		
	#trends	24	24	23	22	22	20	3	2	1	6	5	2	0	0	0
7	#slices	107			51			20			7			0		
	#trends	6	6	6	0	0	0	0	0	0	0	0	0	0	0	0
8	#slices	1047			530			266			174			73		
	#trends	33	33	33	18	18	18	1	1	1	0	0	0	0	0	0
9	#slices	1584			803			404			268			121		
	#trends	87	87	84	39	38	31	9	8	5	6	6	2	3	3	1
10	#slices	361			178			83			49			7		
	#trends	15	14	12	8	4	1	4	0	0	0	0	0	0	0	0
11	#slices	184			89			39			19			0		
	#trends	6	6	6	1	1	1	0	0	0	0	0	0	0	0	0
12	#slices	190			92			40			20			0		
	#trends	3	3	3	0	0	0	1	1	1	0	0	0	0	0	0
13	#slices	413			208			102			64			17		
	#trends	7	7	7	3	3	3	1	1	1	0	0	0	0	0	0
14	#slices	574			284			136			84			24		
	#trends	71	71	71	26	26	23	6	6	3	2	0	0	0	0	0

Visual assessment of the performance of the RR candidate algorithms

All visualisations comprise of a similar lay-out. To prevent wordy figure descriptions, figure 40 provides explanation on the lay-out of the figures that are included in this section (and appendix 11.10).

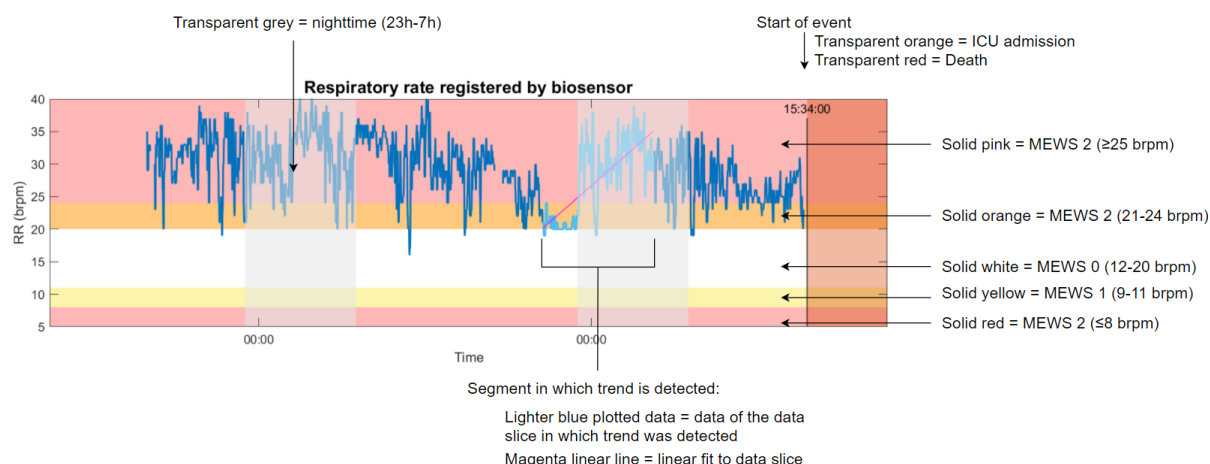


Figure 40: explanation on the lay-out of the visualisations of the outcomes of the algorithm. Detected trends are plotted as magenta lines, along the continuously monitored RR data. In addition, the data slice in which a trend was detected is plotted a lighter blue in order to show within which period the trend was detected

Appendix 11.10 contains visualisations of the outcomes of all candidate algorithms for three selected patients. These three patients concern: patients 8, 12 and 14 (the same patients for whom the visualisations of the HR candidate algorithms are included in appendix 11.8). Patients 8 and 12 were transferred to the ICU while being monitored and patient 14 passed away while being continuously monitored.

By counting the number of trends that were detected per candidate algorithm for each patient (see table 37), it was found that the trend detection setting that was varied ($slope_{ols}$) did not notably affect the amount of detected trends. This is confirmed when studying the visualisations in appendix 11.10.

Below, the visualisations of the outcomes of the HR candidate algorithms for patients 8, 12 and 14 are concisely discussed. Some examples of the visualisations are included within this results section.

Patient 8

- *RRalgorithm1.1-3 and RRalgorithm2.1-3*

A lot of trends were detected within the 2h and 4h data slices. Some of these trends were detected prior to the ICU admission of the patient, yet mostly during the consecutive recovering period of the patient. For this patient, the trends that were detected were often based on short-term increases of RR, which may have been due to physical activity. Therefore, detection of these trends may be irrelevant, as they may not necessarily raise concern or result in data-driven medical interventions. Figure 41 shows the outcomes of RRalgorithm1.2, showing the large amount of detected trends. In addition, this figure also shows two 'false' trends that were detected in data slices that comprised of little data as these data slices followed a data gap of approximately 8 hours.

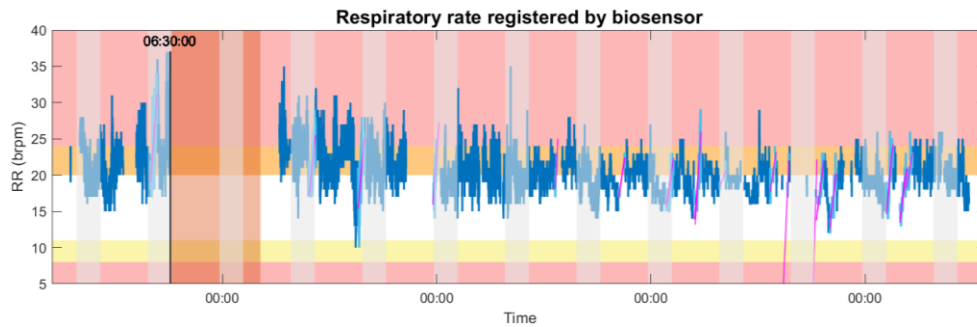


Figure 41: trends detected by *RRalgorithm1.2* for patient 8. See figure 40 for explanation on the lay-out of this figure.

- *RRalgorithm3.1-3*
Within these algorithms, in which 8h was used for the $\text{slice}_{\text{window}}$ data slicing setting, only one trend was detected. This concerned a trend within a data slice that comprised of little data as it followed a data gap of approximately 8 hours.
- *RRalgorithm4.1-3* and *RRalgorithm5.1-3*
These algorithms did not detect a trend within the RR data of the patient.

Patient 12

- *RRalgorithm1.1-3*
These candidate algorithms detected three trends, which can be seen in figure 42. The detected trends concerns an evident increase in RR at the beginning of the night prior ICU admission (which might be a sign of acute deterioration).

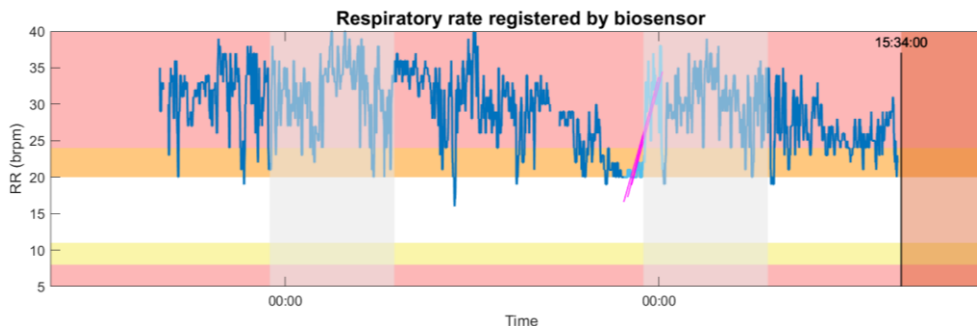


Figure 42: trends detected by *RRalgorithm1.2* for patient 8. See figure 40 for explanation on the lay-out of this figure.

- *RRalgorithm2.1-3*
These algorithms did not detect a trend within the RR data of the patient.
- *RRalgorithm3.1-3*
These candidate algorithms all detected one trend. The detected trends were detected around the same time as where the trends were detected by the *RRalgorithm1.1-3* (see figure 42). The detected trends concern an evident increase in RR at the beginning of the night prior ICU admission (which might be a sign of acute deterioration).
- *RRalgorithm4.1-3* and *RRalgorithm5.1-3*
These algorithms did not detect a trend within the RR data of the patient.

Patient 14

- *RRalgorithm1.1-3 and RRalgorithm2.1-3*

A lot of trends were detected within the 2h and 4h data slices. For this patient (case 7 in chapter 6), the trends that were detected were often based on short-term increases of RR, which may have been due to physical or cognitive activity. However, this may also have been caused by the severely deteriorating condition of the patient. Figure 43 shows the outcomes of RRalgorithm1.2, showing the large amount of detected trends.

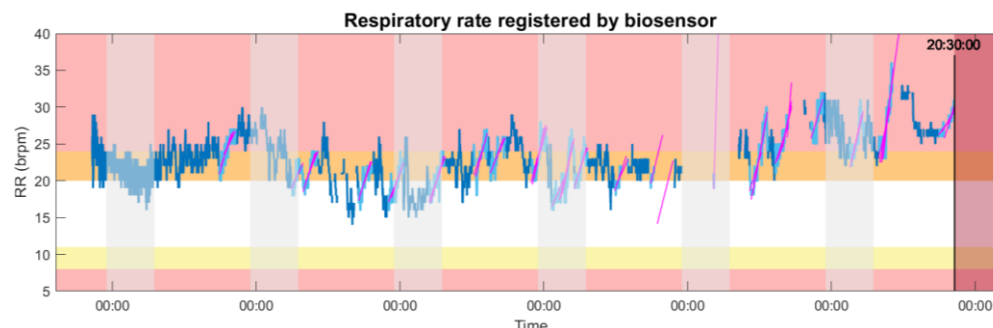


Figure 43: trends detected by RRalgorithm1.2 for patient 14. See figure 40 for explanation on the lay-out of this figure.

- *RRalgorithm3.1-3 and RRalgorithm4.1*

These algorithms detected less trends than the other candidate algorithms as $\text{slice}_{\text{window}}$ was longer (8h and 12h). Figure 44 shows the outcomes of RRalgorithm3.2, showing the detected trends within data slices with a window length of 8h. Within the 48 hours prior the death of the patient, the multiple trends were detected.

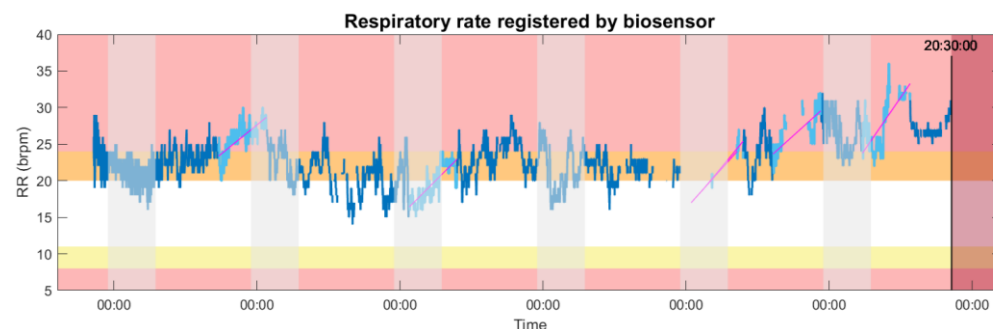


Figure 44: trends detected by RRalgorithm3.2 for patient 14. See figure 40 for explanation on the lay-out of this figure.

- *RRalgorithm4.2-3 and RRalgorithm5.1-3*

These algorithms did not detect a trend within the RR data of the patient.

Summary of the results for the RR candidate algorithms outcomes

Compared to the HR data, the RR data is more 'turbulent' and 'peaky'. This makes it more difficult to quantitatively detect trends that are visually observed as a trend. Still, the candidate algorithms for RR trend detection were able to detect trends during processes of deterioration. However, the detected trends did not per se serve as adequate detectors/predictors of patient deterioration, as trends were also detected during periods of recovery (e.g. for patient 8). In addition, trends were not always detected prior to an event (defined as ICU admission or death).

Also, no 'optimal' candidate algorithm can be appointed from the table 37 and the visualisations that were made for the study population as all included models have their advantages and disadvantages. This is similar to the examples that are provided within the summary of the results for the HR candidate algorithms outcomes. Data characteristics are different for each patient. Therefore, it is dependent on the data characteristics of the patient it a model does or does not adequately detect trends.

7.4 Discussion

Key findings

A moving linear regression algorithm was developed in order to explore the feasibility of quantitatively detecting patient deterioration by means of trend detection. A total number of 15 candidate algorithms for both HR and RR data were composed by varying the input settings of $\text{slice}_{\text{window}}$ and $\text{slope}_{\text{cols}}$. Although the algorithms were successfully developed, the results on the ability of the algorithms to detect trends within the data of deteriorating patients were moderate.

The developed HR and RR candidate algorithms were able to detect trends within the continuously monitored data of the included population of COVID-19 patients. In some observed cases, the detected trends adequately fit the data during a process of deterioration prior to ICU admission or death (e.g. in figures 37 and 44). However, in most cases, the developed algorithms for trend detection did not serve as an adequate method for the detection of patient deterioration. This statement was made based on several observations that are described in the results section, for example: in some cases, 'too many' trends were detected which was likely due to physical or cognitive activity (e.g. visible in figure 36 and 41), and in other cases, visually apparent trends were 'missed' (e.g. visible in figure 38).

Interpretation of results

Findings in chapter 6 and previously published literature describe that trend detection in vital sign data may be of added value in terms of detecting patient deterioration [41, 44, 94]. For example, Churpek et al found that adding trends of vital signs significantly increased the accuracy of models that were designed to detect critical illness at the ward [44]. However, these previously published studies focused on trends that could be (quantitatively) observed in intermittently measured vital signs. Within this current research, we focused on continuously acquired HR and RR data, exploring the feasibility of quantitatively detecting patient deterioration by means of trend detection within *continuous* HR and RR data.

This research has shown that quantitative detection of trends in HR and RR data is possible, but is not (yet) suitable for adequate and sensitive detection of patient deterioration. This is mainly due to the fact that data characteristics (such as 'peakiness' or the rate of deterioration) varied strongly among the included patient population. Of course, this is intuitively logical, as the data of each patient is unique. However, this makes it extremely difficult to develop algorithms or models that can quantitatively detect clinical deterioration based on continuously monitored vital sign data. By improving the integration of context information (for example by integrating accelerometry to identify mobilisation) it could be pursued to tackle this issue and develop more adequate systems for the quantitative detection of patient deterioration based continuously monitored data.

For now, it can be concluded that quantitative detection of patient deterioration by means of trend detection is possible, yet that the proposed method is not reliable and cannot be used as a notification system on itself. However, if the proposed trend detection algorithms are improved adequately and perhaps combined with other relevant notification systems (e.g. a MEWS-threshold based notification system), quantitative detection of patient deterioration by means of trend detection may be of added value. In addition, the value of trend detection does not only lie in the generation of trend-based notifications, yet also in the visualisation of trends to support healthcare workers in interpreting the continuous data.

Limitations

A limited amount of patients was included ($n=14$ out of 160 continuously monitored patients) as a limited amount of patients experienced a severe case of clinical deterioration while being monitored. If more patients would have been included, a more diverse set of results may have been found and other conclusions may have been drawn. As we were interested in exploring the feasibility of quantitatively detecting patient deterioration, we only studied the results of the candidate algorithms for patients who severely deteriorated while being continuously monitored. Therefore, the results of the developed algorithms on the data of the remaining 146 patients has not been studied.

All context information on the clinical conditions of the patients were retrieved manually from the EPR – therefore being prone to errors (e.g. due to inadequate time specification of events). In addition, information from the EPR does not provide a complete and consistent view on whether the patient could have been classified as 'stable' or 'deteriorating' throughout the period of continuous monitoring. Therefore, this data could not be used in terms of validation of the developed algorithms. For meticulous algorithm validation, complete and consistent data on whether the patient can be classified as stable or deteriorating (based on unambiguous definitions) should be available throughout the entire period of monitoring. As this data was not at hand, it was not possible to validate the results of the candidate algorithms.

In relation to this limitation, little context information on the clinical condition of the patient was integrated into the design of the candidate algorithms. Increased integration of context information – for example on the level of oxygen therapy dependency or level of mobilisation – would possibly improve the performance of the candidate algorithm.

Lastly, a limitation that was mentioned in the discussion for chapter 6 also applies here: while the data was acquired, the data was meticulously monitored by a student monitoring team, resulting in consequential actions to improve the patients' condition. These data driven actions may have resulted in alterations in the data. This is not necessarily a limitation, yet it influences the interpretation of the data, as no data from a 'control' patient group is available, where no data driven actions were undertaken.

Recommendations

Improvement of the algorithm for trend detection

The proposed method for quantitative detection of patient deterioration showed to be able to sometimes detect patient deterioration, yet in most cases, the method was not reliable and could not reliably be used in order to adequately detect trends. The developed method for trend detection for the detection of deterioration could be further improved in multiple ways. Future research should focus on the following aspects of algorithm improvement:

- Explore the possibilities of integrating more context information into the algorithm by including additional parameters, such as continuous oxygen saturation, accelerometry or the oxygen dependency of the patient.
- Explore other input values for the data slicing settings ($\text{slice}_{\text{window}}$ and $\text{slice}_{\text{step}}$) and the trend detection settings (cut-off values for $\text{slope}_{\text{ols}}$ and R^2).
- Explore other input parameters for the trend detection component of the algorithm such as the variance within a data slice. Results from chapter 6 suggested that variance increases as the patient recovers and starts to mobilise. Variance could therefore be a valuable input parameter to distinguish between deteriorating and recovering patients.
- Study the effects that the method of decreasing the cut-off value for $\text{slope}_{\text{ols}}$ (with a factor of $0.75^{\text{MEWS level}}$) had on the detection of trends (see figure 33 for explanation), and explore if it would be beneficial to extend this method and also integrate the MEWS level at the start of the linear fit to the data slice.
- Explore the added value of the detection of *downward* trends.
- Explore the performance of the candidate algorithm if the continuous data is first smoothened by for example subjecting the data to a moving average filter.
- Explore the added value of combining the outcomes of different candidate algorithms. In that way, 'short-term' and 'long-term' detected trends could be evaluated and compared.

Quantitative detection of patient recovery

In addition to detecting patient deterioration, it should be studied whether such trend detection algorithms could also be used to quantify the 'sinusoidal' pattern that was observed in recovering patients in chapter 6. Within this chapter it was found that recovering patients show decreased HR (and RR) values during nighttime, whereas HR (and RR) values remained increased during nighttime for patients who were severely ill. By assessing whether upward 'waking up' trends and downward 'going to sleep' trends are present, the visually observed 'sinusoidal' pattern could possibly be quantified.

Short-term future research

The developed algorithms showed moderate results. Of course, it remains interesting to further research and develop such algorithms for the detection of either deterioration or recovery. However, the most essential developments in order to improve continuous monitoring at the wards, lies within less technical and more pragmatical levels. Pragmatical improvements have been elaborately described in chapter 5. This current chapter has shown that (with the proposed methods) it is not yet possible to reliably detect patient deterioration by means of trend detection in continuously monitored HR and RR data. Therefore, quantitative methods for trend assessment are not yet suitable for detecting patient deterioration, and cannot replace the clinical view of healthcare professionals. However, visualisations of detected trends could help healthcare professionals in interpreting the continuous data. Further research should therefore focus on using technical analyses of the data to support healthcare professionals in their visual assessments of continuously monitored vital sign data.

7.5 Conclusion

To briefly answer the research question corresponding to this chapter:

How can continuously monitored heart rate and respiratory rate data be used to quantitatively detect clinical deterioration in COVID-19 patients by means of trend detection?

This research has shown that – for several of the included patients – it is possible to detect clinical deterioration by means of using a moving linear regression algorithm for trend detection. However, in most cases, the developed algorithms for trend detection did not serve as a reliable method for detecting patient deterioration. Future researches should focus on further developing algorithms that aim to quantitatively detect patient deterioration. More importantly, future work regarding technical analyses of continuous vital sign data should always remain focused on developing ways to use the continuous data to optimally support healthcare professionals in their daily tasks.

8 GENERAL DISCUSSION

This study aimed to evaluate the continuous vital sign monitoring system that was implemented at the COVID-19 ward in the UMCU, and to explore how the continuously monitored data could be used in order to detect patient deterioration. This was done by 1) evaluating the implementation process of the continuous monitoring system (chapter 5), 2) formulating a case series report in order to assess how the continuous data can be used to visually detect patient deterioration and recovery (chapter 6), and lastly 3) exploring quantitative methods for trend detection in deteriorating patients (chapter 7).

Key findings and interpretation of results

In general, the results of this thesis demonstrate that continuous monitoring is of added value in improving healthcare at the wards by enabling for additional insight into the patient's clinical condition, creating reassurance and being of support for ward nurses, and enabling for (early) visual detection of patient deterioration. These demonstrated results are in accordance with previously published literature on the added value of continuous monitoring. [40–46, 64, 92]

Future implementation processes of continuous monitoring should be further optimised, based on findings in chapter 5. Optimisation in *short-term* future implementation processes should focus on optimising the integration of the monitoring system into the workflow of the nursing staff. Continuous monitoring systems should be logistically simple to operate and should comply (as much as realistically possible) to the wishes and needs of nursing staff, in order to create positive engagement among the nursing staff. In addition, adequate training of ward nurses as well as ward physicians is essential to accomplish lasting success. To do so, it is advised to train permanent and respected ward nurses and ward supervisors who can then coach other nurses and ward physicians in using the system. Optimisation in *long-term* future implementation processes concerns a more elaborate advice. In terms of this long-term advice, continuous monitoring systems should be improved by adding additional parameters (e.g. continuous BP and movement registration), developing a comfortable pulse oximeter, simplifying the logistics around the system, creating a simple, intuitive, yet straightforward user interface, integrating context information (e.g. current O₂ therapy, comorbidities) into this user interface and lastly provide an (again, intuitive, yet straightforward) improved notification system that is adapted to the wishes of the nurses.

The case series report that was formulated in chapter 6, showed that continuously monitored HR and RR data can be used to visually detect clinical deterioration as well as clinical recovery in COVID-19 patients, which is in accordance with previously published literature [40–46]. In addition, case specific clinical symptoms of COVID-19, matched previously published literature on the clinical aspects of the disease [22–31]. Clinical deterioration was visually recognised by increasing trends over a period of 1 to 24 hours. In some cases, the trends of deterioration increased linearly over these periods of time, allowing to quantitatively assess the trend prior to deterioration events. In other cases, the trends prior to deterioration events increased less linearly due to physiologically explainable reasons (e.g. tachycardic episodes/plateaus due to atrial fibrillation). In these cases, the deterioration of the patients could still be visually recognised based on overall increases in the trend data. Lastly, most of the recovering patients (64%) showed a sinusoidal pattern in the continuously monitored data. These sinusoidal patterns matched the circadian rhythm, suggesting that the circadian rhythm may be used to visually distinguish between deterioration and recovery.

Findings in chapter 6 and previously published literature describe that trend detection in vital sign data may be of added value in terms of detecting patient deterioration [41, 44, 94]. These previously published studies focused on the trends that were based on intermittently measured vital sign data. Within chapter 7, we focused on *continuously* acquired data, by exploring the feasibility of quantitatively detecting patient deterioration by means of trend detection within *continuous* HR and RR data. This research has shown that the proposed method for quantitative detection of trends in HR and RR data is possible, but is not suitable for adequate and sensitive detection of clinical deterioration. This is mainly due to the fact that data characteristics (such as 'peakiness' or the rate of deterioration) varied strongly among the included patient population. This makes it extremely difficult to develop a 'one size fits all' algorithm that can quantitatively detect clinical deterioration based on continuously monitored vital sign data. By improving the integration of context information (for example by integrating accelerometry to identify mobilisation) it could be pursued to develop more adequate systems for the quantitative detection of patient deterioration based on continuously monitored data. More importantly, future work regarding technical analyses of continuous vital sign data should always remain focused on developing ways to use the continuous data in order to optimally support healthcare professionals.

Limitations

The main limitation of the studies that were executed in relation to this thesis are the small study populations. For chapter 5, fourteen nurses responded to the 'coffee break room'-questionnaire and fourteen students responded to the evaluation questionnaire that was sent out to the monitoring team. If more nurses would have responded to the questionnaire, conclusions could have been further substantiated, and possibly, additional conclusions would have been drawn. Especially for chapter 7, the small population size limited evaluation of the developed candidate algorithms for trend detection, as a small number of patients (n=14 out of 160) developed a serious case of deterioration while being continuously monitored.

In addition, all analyses were performed retrospectively. Therefore, all context information varying from the administered O₂ therapy, to nurses' observations, to the occurrence and time specification of an event, was manually extracted from the EPR. This makes the context information prone to error, for two reasons: 1) the researcher may have misread or misinterpreted nurses' or physician's observations, and 2) registration of information into the EPR may have been subjected to some human errors. This may have had an effect on the retrospective interpretation of the clinical condition of the patients, affecting the results of both chapter 6 and 7. In addition, information from the EPR does not provide a complete and consistent view on whether the patient could have been classified as 'stable' or 'deteriorating' throughout the period of continuous monitoring. Therefore, this information from the EPR could not be used in terms of validation of the developed algorithms in chapter 7.

Recommendations

Improvement of continuous monitoring systems

To summarise the recommendations of improving continuous monitoring systems, this research recommends focusing on complying monitoring systems to the wishes and needs of nursing staff. According to the researcher, focus should be put on *robust* implementation processes, not on selecting complex and revolutionary devices. In short-term implementation processes, focus should be put on adequate integration of the monitoring system into workflow of nurses, and positive engagement of nursing staff by sustainable training. In long-term optimisation of implementation processes, focus should be put on developing and upgrading wearables, simplifying operation of the monitoring systems and creating a simple, intuitive yet straightforward user interface which is integrated with context information of the patient and an adequate notification system. In other words: plenty of work to get done!

Future research

In terms of the recommendations for future research, each implementation process of a continuous monitoring system at a general ward should be meticulously evaluated in order to improve consecutive implementation processes. In order to get an as complete as possible view on the wishes, needs, experiences and opinions of ward nurses, semi-structured in-depth individual interviews should be executed with ward nurses, as well as ward physicians. Also, focus groups with healthcare workers could be of added value in getting more insight into the optimal integration of continuous monitoring systems in nurses' and physician's workflows. Most importantly, the generated insights regarding optimisation of continuous monitoring systems should be shared with other hospitals that pursue to implement continuous monitoring at general wards.

The research corresponding to chapter 6 of this thesis has concluded that visual assessment of continuous HR and RR data enables for visual recognition of patient deterioration (steadily increasing trend) and recovery (sinusoidal pattern that matches the circadian rhythm). Further research is needed on how these 'visual assessments' can be quantified in order to support interpreters with informative visualisations and adequate notifications of deterioration. Also, future research should focus on continuously monitoring a larger study population, in order to substantiate the conclusions of chapter 6. In such research, focus should not only be put on detecting deterioration, yet also on whether continuous monitoring can be used in order to detect patient recovery.

In chapter 7, a method was proposed for quantitative detection of patient deterioration. The developed algorithms showed to be able to sometimes detect patient deterioration, yet in most cases, the method was not reliable and could not reliably be used in order to adequately detect trends. Future research should be done on improving the proposed model. The discussion of chapter 7 described multiple ways to do so, for example by improving the integration of context information into the algorithms. In addition to improvement of the proposed methods for quantitative detection of patient deterioration, future research should focus on using technical analyses of the data to support healthcare professionals in their visual assessments of continuously monitored vital sign data.

9 GENERAL CONCLUSION

This thesis concludes that continuous vital sign monitoring is a valuable tool for improving healthcare at the COVID-19 ward, and recommends implementation of continuous monitoring systems at other general wards.

To briefly answer the research question corresponding to this thesis:

How can continuous vital sign monitoring at the COVID-19 cohort ward be improved in terms of optimising the implementation process, providing valuable insight into the data-based clinical condition of the patients, and to quantitatively detect patient deterioration in COVID-19 patients?

In terms of optimising the implementation process, short-term and long-term optimisations are formulated. Short-term implementation processes of continuous vital sign monitoring at the COVID-19 cohort ward can be optimised by focussing on adequate integration of the monitoring system into the workflow of nurses, and positive engagement of nursing staff, for example by sustainable training. Long-term implementation processes of continuous vital sign monitoring at the COVID-19 cohort ward can be optimised by putting focus on developing and upgrading wearables, simplifying operation of the monitoring systems and creating a simple, intuitive yet straightforward user interface which is integrated with context information of the patient and an adequate notification system.

Continuous vital sign monitoring at the COVID-19 cohort ward can be used to visually detect clinical deterioration as well as patient recovery, by visual detection of respectively a steadily increasing (linear) trend and a sinusoidal pattern that matches the circadian rhythm.

Quantitative methods that were proposed for detecting patient deterioration by means of trend detection showed moderate results. In most cases, the developed algorithms for trend detection did not serve as a reliable method for detecting patient deterioration. Future researches should focus on further development and improvement of algorithms that aim to quantitatively detect patient deterioration. More importantly, future work regarding technical analyses of continuous vital sign data should always remain focused on developing ways to use continuous data to optimally support healthcare professionals in their daily tasks.

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11 APPENDICES

Appendix 11.1: Methods for interviews with nurses

This appendix comprises of the original plan that was formulated to answer the first research question:

How should the implementation of continuous ward monitoring be optimised in order to improve patient care, reduce workload on healthcare workers and improve working experience?

This original plan, was subjected to multiple setbacks. Once the second COVID-19 wave hit healthcare facilities in the Netherlands, and the second implementation process of continuous monitoring was on-going, the original plan was rejected and a new plan was introduced. As the original plan and the corresponding interview guide were composed with great care and attention, both the original methods and the interview guide are included in this appendix. The interview guide may be valuable and useful for future research projects. The interview guide is included both in Dutch (as the interviews would have taken place in Dutch) and English (loosely translated).

Methods

Study design

Retrospective, in-depth, individual interviews will be executed to perform qualitative research. The interview questions will be formulated open-ended, starting mainly with 'why' and 'how'. The interview guide will be semi-structured, to enable the researcher to ask additional questions if necessary.

Interviews will mainly focus on the opinions and experiences of the nurses. In addition, specific questions will be formulated in relation to the other research questions of this research proposal. For example, a research question will be formulated to assess nurses' opinions and expectations of individualised notification thresholds. Outcomes will be used in the designing process of the algorithms that will be composed based on research questions 2 to 4.

In addition to the nurse interviews, the monitoring team has already filled in a survey on the process of implementation of the continuous monitoring technique. The results of this survey will be consulted to gain insight into the experiences and value of the monitoring team.

Study population

The study population covers nurses that worked at the COVID-19 cohort ward while the continuous monitoring technique was implemented. Since this is a retrospective study, no exact sample size calculation has been performed. In order to get an adequate representation of the overall opinion of the ward nurses, nurses with varying backgrounds, educational levels and working experience will be interviewed. At least eight interviews will be performed. However, interviews will have to be continued if the researcher concludes that data saturation has not yet been reached. This will be assessed by evaluating the amount of new input the researcher receives from new interviewees. The in- and exclusion criteria for the interviewees are as follows:

Inclusion

- Nurse worked at the COVID-19 cohort ward while the continuous monitoring technique was implemented

Exclusion

- Nurse worked less than five shifts while the continuous monitoring technique was implemented

Analysis

The interview results will be analysed by completely transcribing the interviews, along with the notes made during the interview by the researcher. Transcriptions will be re-read to identify recurring themes. These themes will be used to organise the results of the interviews for analysis.

Feedback interviews

All nurses will be asked whether they would be interested to be contacted for a second interview in a later phase of the research. During such an interview, the researcher may present results that were found or algorithms that were designed during data analysis. Feedback of these nurses will be used for further product development and optimisation.

Interview guide – Dutch version

Interview guide COVID-19 verpleegkundigen betreffende de implementatie van continue monitoring op de cohortafdeling.

	Vragen/te bespreken punten	Notities
Opening	Voorstellen, uitleg onderzoek en interview	

Naam verpleegkundige	
Leeftijd verpleegkundige	
Werkervaring als verpleegkundige - Hoeveel werkjaren? - Werkzaam geweest op welke afdelingen in welke ziekenhuizen? - Ervaring met continue data? - Ervaring met EWS?	
Diensten op de D2WEST - Hoeveel diensten op de D2WEST gedaan? - Wanneer diensten op de D2WEST gedaan?	
Overige aantekeningen over omstandigheden interview (face-to-face/digitaal, huidige situatie omtrent COVID-19 in NL)	

	Vragen/te bespreken punten	Notities
Ervaringen	- Hoe kijk je terug op je werkzaamheden op de COVID-19 afdeling? <i>Klinisch beeld van de patiënten</i> <i>Obstakels in de zorg voor COVID-19 patiënten</i> <i>Manier van werken en werkdruk</i>	
Continue monitoring op de D2WEST	- Hoe heb je de implementatie van de continue monitoring op de cohortafdeling ervaren? <i>Wat ging er goed?</i> <i>Wat kon er beter?</i> <i>Effect op werkzaamheden</i> <i>Effect op werklust</i> <i>Effect op beslissingen</i> <i>Had je het gevoel dat je op de technologie kon vertrouwen?</i>	
Toekomstige implementatie van continue monitoring op verpleegafdelingen	- Wat zou jij belangrijk vinden bij toekomstige implementatie van continue monitoring op de verpleegafdeling waar jij werkt? <i>Waarom?</i> <i>Hoe kunnen we het beste werkzaamheden ondersteunen en werklust verminderen?</i> - Wat is jouw mening over de betrokkenheid van een monitoringsteam? <i>Liever een monitoringsteam als tussenpersoon of liever alle monitoring bij de verpleegkundigen leggen?</i> - In het geval dat er geen monitoringsteam zou zijn, zou je het dan prettig vinden om een groot monitoringsdashboard met de	

	trends op de verpleegkundige post te hebben? ○ <i>Waarom?</i> ○ <i>(Uit eerdere focusgroepen is gebleken dat verpleegkundigen die liever niet wilden)</i>	
Specifieke vragen	• Denk jij dat gepersonaliseerde drempelwaardes wel/niet van toegevoegde waarde zouden zijn bij de continue monitoring van patiënten op de verpleegafdeling? ○ <i>Waarom?</i> ○ <i>Waar zouden deze op gebaseerd moeten zijn?</i> • Welke parameters (zoals vitale parameters of patiëntgeschiedenis) zouden op basis van jouw ervaring, de mate van achteruitgang in COVID-19 patiënten het beste kunnen voorspellen? ○ <i>Waarom?</i>	
Afsluiting	• Heb je nog opmerkingen of vragen? Of wil je nog iets kwijt? ○ <i>Zorgen?</i> • Zou ik je later (na de zomer) in mijn afstudeeronderzoek nogmaals mogen benaderen voor een nieuw interview? ○ <i>Om inhoudelijke bevindingen te bespreken en input te vergaren.</i> • Bedanken!	
Afsluitende opmerkingen na interview door onderzoeker		

Interview guide – English version (loosely translated)

Interview guide COVID-19 nurses on the implementation of continuous monitoring at the cohort ward

	Questions/points to discuss	Notes
Opening	• Introduction, explanation on research and interview	

Name nurse	
Age nurse	
Working experience as a nurse 5. How many years? 6. In which (hospital) departments? And which hospitals? 7. Any experience with continuous data? 8. Any experience with the EWS?	
Shifts at the D2WEST 3. How many shifts at the D2WEST? 4. During which period?	
Other notes on the circumstances of the interview (such as face-to-face versus digital, current situation concerning COVID-19 in the Netherlands)	

	Questions/points to discuss	Notes
Experiences	• How do you look back at your working activities at the COVID-19 cohort ward? ○ <i>Clinical depiction of the patients</i> ○ <i>Obstacles in caring for the patients</i> ○ <i>Working methods and workload</i>	
Continuous monitoring at the D2WEST	• How did you experience the implementation process of the continuous monitoring technique at the COVID-19 cohort ward? ○ <i>What went well?</i> ○ <i>What could have gone better?</i> ○ <i>Effect on working activities</i> ○ <i>Effect on workload</i> ○ <i>Effect on decisions</i> ○ <i>Did you feel that you could trust the continuous monitoring techniques?</i>	
Future implementation of continuous monitoring at the general wards	• What would you consider important in future implementation of continuous monitoring at the nursing wards where you normally work? ○ <i>Why?</i> ○ <i>How can we best support you in your working activities and decrease your workload?</i> • What is your opinion on the involvement of a monitoring team? ○ <i>Would you rather have a monitoring team as an</i>	

	<i>intermediary, or rather take on the responsibilities of monitoring the patients by yourself?</i> • In the case that there would be no monitoring team at all, would you like to have a big monitoring dashboard with the vital sign trends at the nurse station? ○ <i>Why?</i> ○ <i>(Previous focus groups revealed that the nurses did not want this)</i>	
Specifieke vragen	• Do you think that personalised thresholds will or will not be of added value in continuous monitoring of patients at the general wards? ○ <i>Why?</i> ○ <i>On what should these thresholds be based?</i> • According to your experience, which parameters (such as vital parameters or medical history) should be adequate predictors of clinical deterioration in COVID-19 patients? ○ <i>Why?</i>	
Afsluiting	• Do you have any remaining comments or questions? ○ <i>Any concerns?</i> • Is it okay if I contact you again (after the summer) to interview you a second time, in relation to my graduation research? ○ <i>To discuss research findings and gather new input.</i> • Give thanks!	
Concluding comments after the interview by the researcher		

Appendix 11.2: Evaluation questionnaire for the student monitoring team

The questions for the evaluation questionnaire for the student monitoring team that worked at the COVID-19 cohort department during the first COVID-19 wave are depicted below. The questions are included both in Dutch (as the evaluation questionnaire was executed in Dutch) and English (loosely translated).

In order to establish a clear overview of the results, the questions are categorised in the following way: question 1-5 – devices, question 6-8 – the monitoring team, question 9-12 – contact with other disciplines, question 13-15 – the monitoring system in general, question 16 – future monitoring projects and question 18 – other comments.

Evaluatie-enquête voor het studentenmonitoringsteam – 1^e COVID-19 golf (Dutch)

Devices

1. Heb je het idee dat monitoring met de biosensor pleister van toegevoegde waarde is voor COVID-19 patiënten? – open vraag
2. Waarom was de biosensor wel/niet nuttig? – open vraag
3. Heb je het idee dat monitoring met de VS30 monitor van toegevoegde waarde is voor COVID-19 patiënten? – open vraag
4. Waarom was de VS30 monitor wel/niet nuttig?
5. Voor welke patiëntengroep denk je dat de biosensor+VS30 monitor in de toekomst van nut zou kunnen zijn? – open vraag

The monitoring team

6. Heb je het idee dat jullie als monitoringsteam nuttig waren op de D2West? – open vraag
7. Waarom denk je dat jullie wel/niet nuttig waren? – open vraag
8. Hoe zouden we het monitoringsteam kunnen verbeteren? – open vraag

Contact with other disciplines

9. Hoe was het contact met de verpleegkundigen op D2West? – score van 1-5
10. Hoe was het contact met de artsen op D2West? – score van 1-5
11. Hoe was het contact met Martine en Harriët (de projectleiders)? – score van 1-5
12. Hoe zouden we het contact tussen het monitoringsteam en de verpleegkundigen, artsen en onderzoekers kunnen verbeteren? – open vraag

The monitoring system in general

13. Wat waren de sterke punten van het monitoringssysteem zoals we dat hadden ingericht op de D2West? – open vraag
14. Wat waren de zwakke punten van het monitoringssysteem zoals het dat hadden ingericht op de D2West? – open vraag
15. Wat was je allergrootste ergernis tijdens diensten op de D2West? – open vraag

Future monitoring projects

16. Hoe denk jij (als alles mogelijk is) dat we de continue monitoring van patiënten op de verpleegafdeling zouden moeten inrichten? – open vraag
17. (Als er een tweede golf van coronapatiënten komt, zou je dan weer als trendwatcher ingezet willen worden? – open vraag)

Other comments

18. Heb je nog andere ideeën/opmerkingen/vragen? – open vraag

Evaluation questionnaire for the student monitoring team – 1st COVID-19 wave (English)

Devices

1. Do you feel that monitoring with the biosensor patch is of added value in COVID-19 patients? – open question
2. Why was the biosensor patch useful/not useful? – open question
3. Do you feel that monitoring with the VS30 monitor is of added value in COVID-19 patients?? – open question
4. Why was the VS30 monitor useful/not useful? – open question
5. For which patient group do you think the biosensor + VS30 monitor could be useful in the future? – open question

The monitoring team

6. Do you feel that as a monitoring team you were useful on the D2West? – open question
7. Why do you think that you were/were not useful? – open question
8. How could we improve the monitoring team? – open question

Contact with other disciplines

9. How was the contact with the nurses at D2West?– score of 1-5
10. How was the contact with the physicians at D2West? – score of 1-5
11. How was the contact with Martine and Harriët (the project supervisors)? – score of 1-5
12. How could we improve contact between the monitoring team and the nurses, doctors and researchers?– open question

The monitoring system in general

13. What were the strengths of the monitoring system on the D2West? – open question
14. What were the weaknesses of the monitoring system on the D2West? – open question
15. What was your biggest annoyance during shifts on the D2West?– open question

Future monitoring projects

16. How do you think (if everything is possible) that we should organize the continuous monitoring of patients in the nursing ward? – open question
17. (If there is a second wave of corona patients, would you want to be a trend watcher again? – open question)

(Other comments)

18. (Do you have any other ideas/comments/questions? – open questions)

Appendix 11.3: 'Coffee break room'-questionnaire

This appendix comprises of the so-called 'coffee break room'-questionnaire that was composed in relation to the following research question:

How should the implementation of continuous ward monitoring be optimised in order to improve patient care, reduce workload on healthcare workers and improve working experience?

The 'coffee break room'-questionnaire was composed in such a way that it was brief and that the nurses needed little time to answer all questions in de questionnaire.

The interview guide is included both in Dutch (as the questionnaire was officially formulated in Dutch) and English (loosely translated). The following pages contain the Dutch 'koffiekamer-enquête' and the loosely translated English 'coffee break room'-questionnaire.

Koffiekamer-enquête COVID-19 verpleegkundigen: 'continue monitoring van COVID-19 patiënten'

De onderstaande enquête is bedoeld voor verpleegkundigen die tijdens de tweede golf COVID-19 patiënten op de D2West in het UMCU werkzaam zijn of zijn geweest. Op deze afdeling is een technologie (Philips biosensor, zie figuur 1) geïmplementeerd voor continue monitoring van de hartslag en ademhalingsfrequentie van COVID-19 patiënten. De ervaringen en meningen van verpleegkundigen over deze technologie zijn essentieel om de technologie en de implementatie hiervan in de toekomst te optimaliseren!

Alle ingevulde enquêteformulieren zullen door de onderzoeker (Elin Biel, masterstudent technische geneeskunde) geanonimiseerd worden. Na het anonimiseren zullen de antwoorden geanalyseerd worden om te onderzoeken hoe toekomstige implementatie van dit soort technieken vormgegeven moet worden.

Algemeen – enkele algemene vragen die context bieden tijdens het onderzoeken van de antwoorden	
Voor- en achternaam	
Leeftijd	
Datum van invullen	
Aantal jaren werkzaam als verpleegkundige	
Op welke afdelingen ben je tot nu toe werkzaam geweest?	
Hoe veel diensten heb je tot nu toe op de D2West gedraaid?	

Continue monitoring – geef per stelling aan in welke mate je het eens of oneens bent					
	1 <i>Zeer oneens</i>	2 <i>Oneens</i>	3 <i>Neutraal</i>	4 <i>Eens</i>	5 <i>Zeer eens</i>
Ik vind het aanbrengen en aanzetten van de patch eenvoudig	0	0	0	0	0
Ik denk dat continue monitoring ook op andere verpleegafdelingen van toegevoegde waarde zou zijn	0	0	0	0	0
Ik vind het een geruststellende gedachte dat de patiënten op afstand in de gaten gehouden kunnen worden	0	0	0	0	0
Ik kijk meerdere keren per dienst naar de trend van de hartslag en ademhalingsfrequentie van mijn patiënten	0	0	0	0	0
De trend van de hartslag en ademhalingsfrequentie geven mij extra inzicht in de klinische conditie van de patiënt	0	0	0	0	0
Ik merk dat de trends van de hartslag en ademhalingsfrequentie invloed hebben op klinische beslissingen	0	0	0	0	0
Ik vind het prettig dat er een medisch student aanwezig is om de trend van de hartslag en ademhalingsfrequentie in de gaten te houden	0	0	0	0	0
Ik merk dat ik minder vaak de patiëntenkamer in loop om te controleren hoe het met de patiënt gaat nu de patiënt continu gemonitord wordt	0	0	0	0	0
In de toekomst zou ik graag zelf de beoordeling van de trend van de hartslag en ademhalingsfrequentie willen doen (bijvoorbeeld via HiX)	0	0	0	0	0

Heb je nog aanvullende opmerkingen over de continue monitoring?

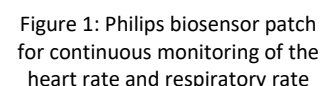


Figuur 1: Philips biosensor patch voor continue monitoring van hartslag en ademhalingsfrequentie

This questionnaire is intended for nurses who work(ed) at the D2West at the UMCU during the second wave of COVID-19 patients. At this department, a new technology (the Philips biosensor, figure 1), was implemented to continuously monitor the heart rate and respiratory rate of COVID-19 patients. The experiences and opinions of nurses on this technology are essential to optimise future implementations of continuous monitoring techniques!

General – some general questions to get context information	
First and last name	
Age	
Date	
Nursing experience in years	
At which departments have you worked up until now?	
How many shifts have you done at the D2West up until now?	

Do you have any additional comments about the continuous monitoring?



Appendix 11.4: Elaborate results description of the evaluation questionnaire for the student monitoring team

The evaluation questionnaire can be found in appendix 11.2. Here, the results are elaborately described per category: devices, monitoring team, contact with other disciplines, the monitoring system in general and other comments.

Devices

The biosensor

All respondents (100%) felt that the biosensor was of added value for COVID-19 patients. All respondents shared their view on *why* they felt that the biosensor was of added value.

- Six respondents stated that the data that was acquired by the patch enabled for early recognition of clinical deterioration. One of the respondents specifically emphasised that the HR and RR *trend* was of added value in determining stability versus deterioration.
- Four respondents commented that they noticed that the biosensor gave the nurses reassurance and support: their (deteriorating) patients were monitored from a distance.
- Four respondents emphasised that the biosensor very useful, as it was difficult to check up on the patients due to the isolation nursing.
- Three respondents mentioned that they felt that the continuous monitoring of the patients provided more insight into the overall clinical condition of the patient.
- Two respondent commented that they spoke with nurses who had noticed that the biosensor reassured the patients that their clinical condition was closely monitored.
- One respondent mentioned that the continuous data sometimes helped the physician in deciding whether the patient did or did not need more oxygen therapy.
- Lastly, one respondent commented that the biosensor helped in the early detection of a fall of the patient (at times that no nurses were in the isolation room of the patient).

VS30 monitor

Twelve respondents (86%) felt that the VS30 monitor was of added value for COVID-19 patients. One respondent (7%) felt that the monitor was only of added value if the pulse oximeter was connected. One respondent (7%) did not have any experience with the VS30 monitor. Twelve respondents (86%) shared their view on *why* they felt that the VS30 monitor was of added value.

- Six of the respondents felt that the continuous SpO₂ measurements that were possible through the VS30 monitor were of great added value for this specific patient population as COVID-19 patients have shown to possible develop sudden or silent hypoxemia.
- Four of the respondents noticed that the continuous SpO₂ were helpful for nurses and physicians in deciding on the adequate type of oxygen therapy. One respondent added that it was also used in deciding whether a patient should be transferred to the ICU.
- Two of the respondents noted that it was very useful that the nurses could determine the MEWS on the VS30 monitor. These respondents also mentioned that it would be even more useful if these measurements could automatically be synchronised into the EPR. One respondent mentioned that this may improve early detection of patient deterioration.
- One respondent mentioned he/she noticed that the pulse oximeter was not comfortable and that patients often took it off of their fingers.
- One respondent commented that the information that could be acquired through the VS30 monitor was of support to the nurses and physicians.
- One respondent noted that VS30 monitor was easy and intuitively to use.

Future use of the biosensor and VS30 monitor in other patient groups

Respondents were asked for which patient group continuous monitoring with the biosensor and/or the VS30 monitor would be useful, with respect to future implementation projects. Nine respondents (64%) mentioned that they saw great value of continuous monitoring for instable and vulnerable patient groups, such as post-surgery, post-ICU care, elderly, immunocompromised and patients with respiratory or cardiac problems. Six respondents (43%) stated that they felt that the monitoring technique would help to care for patients in that are nursed in isolation. One respondent (7%) emphasized that he/she felt that the continuous monitoring of the SpO₂ had the most added value.

Monitoring team

Evaluation of the monitoring team

Twelve respondents (86%) felt that the presence of the monitoring team at the COVID-19 cohort ward was useful. One respondent (7%) felt that the presence of the team was not useful and of no added value. One respondent (7%) did not comment on whether the presence of the team was useful. All respondents (100%) shared their view on *why* they felt /did not feel that the monitoring team was of added value.

The respondents that experienced the presence of the monitoring team as useful mentioned multiple arguments for *why* the presence of the team was useful. Some respondents felt that they sometimes 'made a difference' as the continuous data provided early recognition of deterioration. This difference sometimes affected treatment policy, such as the (type of) administration of oxygen therapy. Most of these respondents mentioned that they felt very appreciated by the nurses and the physicians; the monitoring team relieved the workload of healthcare workers by facilitating easy assessment of the patients' conditions.

The respondent who did not think that the presence of the team was of added value stated that he/she thought that it would be better if the monitoring system would be operated and used only by the nurses. The respondent stated that he/she thought that this would be possible with proper training. The respondent stated that he/she often felt useless.

Improvement of the monitoring team

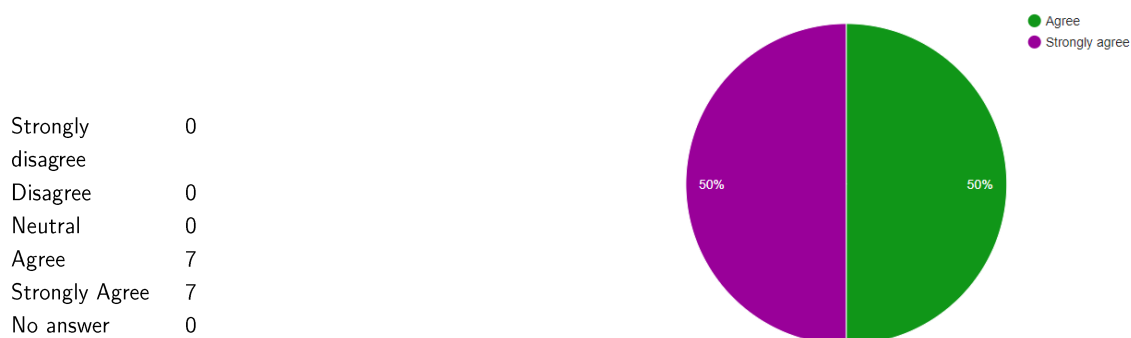
Nine of the respondents (64%) suggested ideas for the improvement of the monitoring team. Three team members (21%) suggested that the nurses should be trained to operate the system monitor the patients by themselves, without the presence of a monitoring team. Two respondents (14%) felt that the monitoring team could be improved by formulated more, and more clearly tasks. In addition, two respondents (14%) felt that the monitoring could be made easier and more insightful if more elaborate medical background information on the patients would have been provided. Lastly, one respondent mentioned that the information transfers inbetween shifts could have been better if a general system for an adequate information transfers would have been in place. One respondent (7%) felt that a more frequent general meeting for updates and questions from the team for the supervisors would have been useful. Lastly, one respondent (7%) felt that more direct contact with the patients through for example a video connection would have been of added value.

Contact with other disciplines

Contact with nurses

Seven out of 14 respondents (50%) scored the contact with the nurses with a 4 out of 5. The other seven respondents (50%) scored the contact with the nurses with a 5 out of 5.

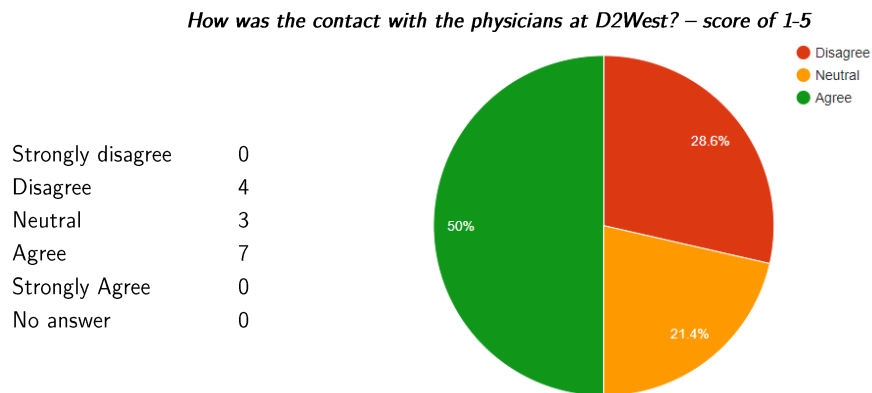
How was the contact with the nurses at D2West?– score of 1-5



Two respondents (14%) emphasised that the contact with nurses in general was good and adequate. Two respondents (14%) stated that it sometimes was difficult to find a nurse, which hindered adequate notification of for example patient deterioration. Two respondents (14%) mentioned that the 'day start' and 'day evaluation' were valuable moments to mention the presence of the monitoring team and explain the goal of the continuous monitoring technique. One respondent (7%) suggested that it would be beneficial if the monitoring team would join the information transfers of the nurses and physicians to gain additional insight into the clinical conditions of the patients. Another respondent (7%) suggested that it helpful if the monitoring team could approach the nurses via a phone call to inform the nurses on abnormalities in the trend.

Contact with ward physicians

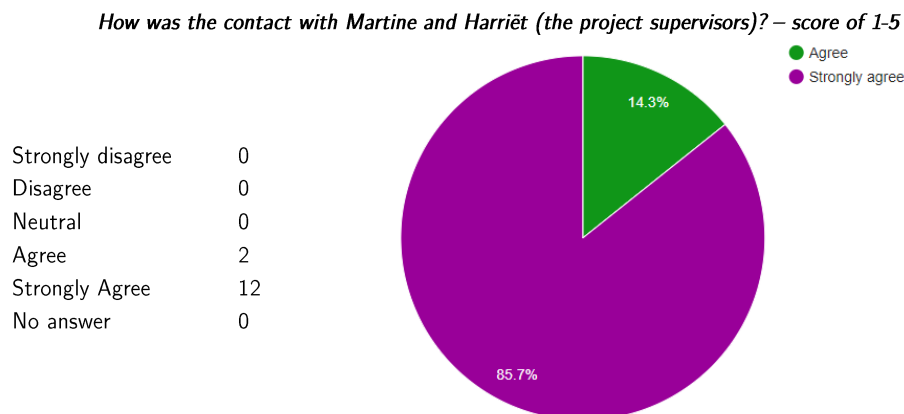
Four out of 14 respondents (29%) scored the contact with the ward physicians with a 2 out of 5. Three respondents (21%) scored the contact with the physicians with a 3 out of 5. Seven out of 14 respondents (50%) scored the contact with the nurses with a 4 out of 5.



Three respondents (21%) stated that they had had no to little contact with ward physicians. Two respondents (14%) stated that they felt that ward physicians should be trained in operating the monitoring system and interpreting the continuous data. Two respondents (7%) mentioned that they appreciated that they could be a part of the daily meeting of the ward physicians and that this helped in creating awareness and insight into the continuous monitoring technique among the physicians. Contrarily, two of the respondents (7%) stated that the meeting was often forgotten by the physicians and did not take place. Remaining comments concerned: increasing involvement of ward physicians and creating a better connection and 'more teamwork' between the monitoring team and the physicians, for example in processes like the assessment of the adequate type of oxygen therapy.

Contact with project supervisors

Two of the respondents (14%) scored the contact with the project supervisors with a 4 out of 5. The other twelve respondents scored the contact with the physicians with a 5 out of 5.



No elaborate suggestions on the improvement with the project supervisors were made. One respondent (7%) suggested that weekly evaluation moments with the entire team and the project supervisors may have been of added value to the process.

The monitoring system in general

The following strengths of the monitoring system in general were mentioned:

- Early recognition of clinical deterioration and an adequate global overview of the clinical condition of the patient (mentioned by four respondents, 29%)
- Pleasant contact with nurses (four respondents, 29%)

- Pleasant contact with the project supervisors, who were very approachable and provided guidance if necessary (four respondents, 29%)
- Clear manual, job description and schedule (three respondents, 21%)
- The monitoring room was nice (three respondents, 21%)
- The training for nurses was sufficient (two respondents, 14%)
- As the monitoring team initially started voluntarily, everyone was motivated (one respondent, 7%)
- The monitoring system provided a good method for evaluated changes in treatment policy (such as increasing oxygen therapy) (one respondent, 7%)
- The monitoring system was realised very quickly (one respondent, 7%)
- The fact that the patients were monitored 24 hours of the day (one respondent, 7%)
- Two respondents (14%) did not provide comments on the strengths of the monitoring system.

The following weaknesses of the monitoring system in general were mentioned:

- Some start-up problems, such as technical issues, connection issues between the relay and the Biosensor patch, or the inconsistency in knowledge of nurses (e.g. an enthusiastic nurse may have developed more knowledge quickly than a less enthusiastic/involved nurse) (mentioned by three respondents, 21%)
- Communication on specific events (e.g. the removal of a relay) could have been better (one respondent, 7%)
- The notification system worked well, considering the MEWS system, yet sometimes the monitoring team saw increasing and alarming abnormalities in the trends, which did not generate a notification (one respondent, 7%)
- The death of a patient could not be recognised in the monitoring system as no specific notification was generated. The system merely showed the 'no sensor connection' notification (one respondent, 7%)
- The Wi-Fi sometimes was insufficient (one respondent, 7%)
- The monitoring team learnt 'while on the job', which sometimes resulted in situation where the team member did not quite know what to do (one respondent, 7%)
- The nurses sometimes questioned the reliability of the data. The respondent who mentioned this, stated that he/she him-/herself had also sometimes doubted the reliability (one respondent, 7%)
- Four respondents (29%) did not provide comments on the strengths of the monitoring system.

Biggest annoyances during monitoring shifts

- Technical issues that were complex, not easy to solve or vague to the monitoring team (five respondents, 36%)
- Insufficient information transfers (two respondents, 14%)
- When the monitoring team member could not find the nurse (one respondent, 7%)
- Colleagues who did not tackle technical problems during their shifts (one respondent, 7%)
- When physicians did not show interest in the monitoring system (one respondent, 7%)
- When there were just a few patients to monitor, making the monitoring shift less challenging and less useful (one respondent, 7%)
- When the nurses saw you as an 'intruder' to their work (respondent stated that this happened a few times, but not necessarily often) (one respondent, 7%)
- When the nurses and/or did not notify the monitoring team of patients that were discharged (one respondent, 7%)
- To little knowledge of the patient's clinical condition and medical history (one respondent, 7%)
- Two respondents (14%) did not provide comments on the strengths of the monitoring system.

Future monitoring projects

The results regarding the question on *how* the monitoring team members visualised future implementations of continuous monitoring was oriented in the same direction. The monitoring team described a setting in which the nurses (and physicians) would be trained to operate the monitoring system by themselves, and that the acquired data would be easily accessible through the EPR. Some respondents suggested that one person could be present as a 'monitor' for the entire department or even hospital. This monitor should call/notify the nursing department of apparent abnormalities. Also, most respondents suggested a large 'airport' screen on the nursing ward, to easily view the real-time vitals of the patients. One respondent added that a video (or speech) connection would be a valuable tool to monitor whether the notifications were caused by deterioration or mobilisation. Lastly, some of the respondents stated that they felt that the notification system should be further improved and simplified for a more easily interpretation.

Appendix 11.5: Elaborate results description of the 'coffee break room'-questionnaire for COVID-19 nurses

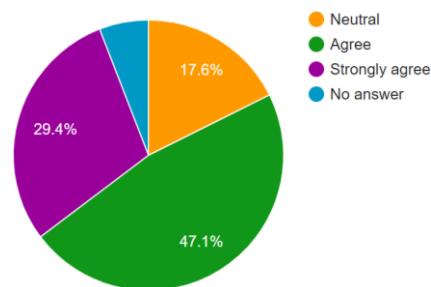
The 'coffee break room'-questionnaire can be found in appendix 11.3. Here, the results are elaborately described (n=17).

First, the categorical questions for which the nurses could choose from 'strongly disagree' to 'strongly agree' are presented by depicting the number of nurses that chose a certain category and presenting this numbers in a percentual fashion in a pie chart.

Second, the answers to the open question 'Do you have any additional comments about the continuous monitoring?' were analysed for recurring themes, observations and suggestions. The findings in this analysis are described.

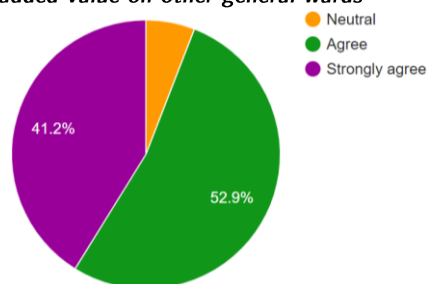
I find it easy to apply and turn on the patch

Strongly disagree	0
Disagree	0
Neutral	3
Agree	8
Strongly Agree	5
No answer	1



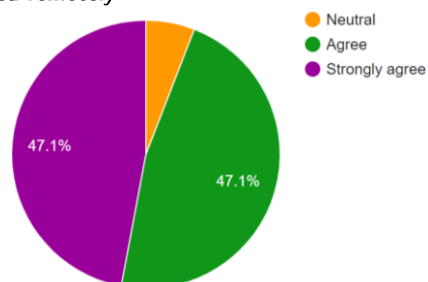
I think that continuous monitoring could also be of added value on other general wards

Strongly disagree	0
Disagree	0
Neutral	1
Agree	9
Strongly Agree	7
No answer	0



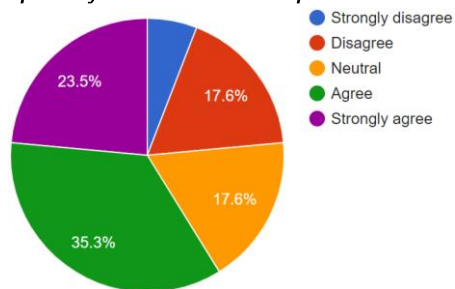
I find it reassuring that the patients can be monitored remotely

Strongly disagree	0
Disagree	0
Neutral	1
Agree	8
Strongly Agree	8
No answer	0



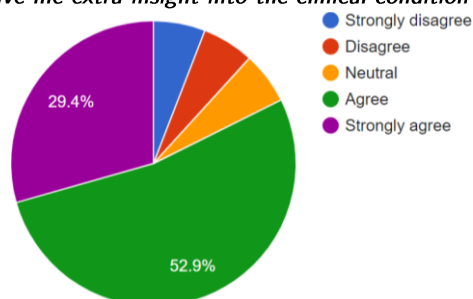
I look at the trend of my patients' heart rate and respiratory rate several times per shift

Strongly disagree	1
Disagree	3
Neutral	3
Agree	6
Strongly Agree	4
No answer	0



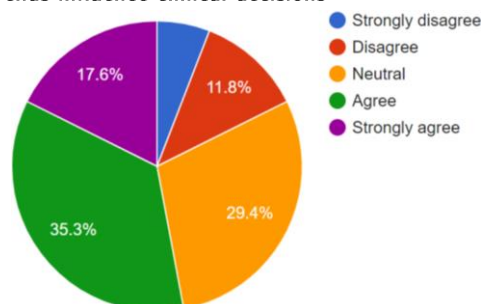
The trend of the heart rate and respiratory rate give me extra insight into the clinical condition of the patient

Strongly disagree	1
Disagree	1
Neutral	1
Agree	9
Strongly Agree	5
No answer	0



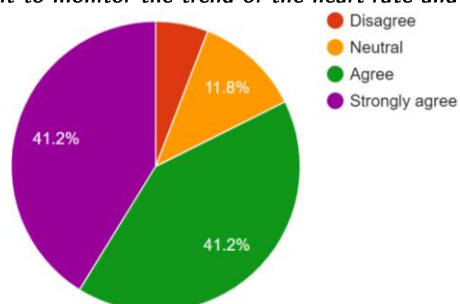
I notice that the heart rate and respiratory rate trends influence clinical decisions

Strongly disagree	1
Disagree	2
Neutral	5
Agree	6
Strongly Agree	3
No answer	0

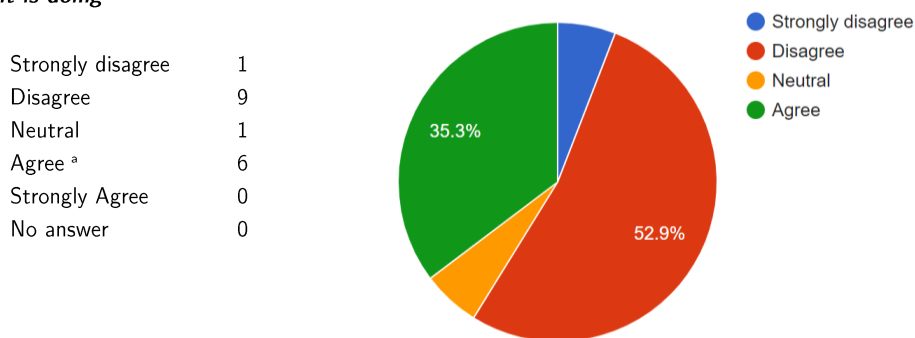


I find it reassuring that a medical student is present to monitor the trend of the heart rate and respiratory rate

Strongly disagree	0
Disagree	1
Neutral	2
Agree	7
Strongly Agree	7
No answer	0

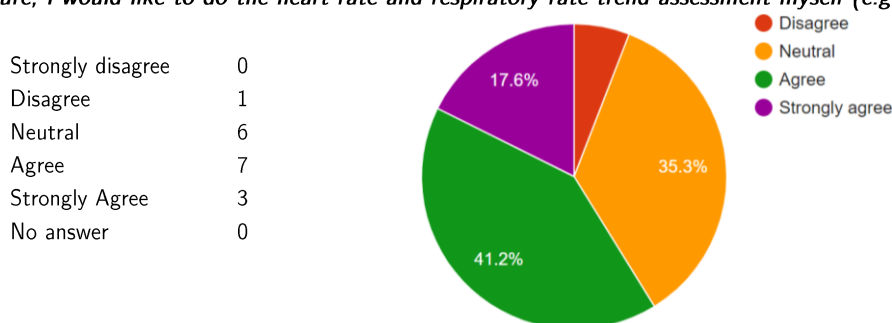


Now that the patient is continuously monitored, I notice that I enter the patient's room less often to check on how the patient is doing



^a One respondent put their answer between 'neutral' and 'agree'. This answer is put under category 'agree'

In the future, I would like to do the heart rate and respiratory rate trend assessment myself (e.g. via HiX)



Do you have any additional comments about the continuous monitoring?

The following themes, observations and suggestions were made by the nurse respondents to this open question.

- Eight nurse respondents (47%) expressed their enthusiasm on the continuous monitoring system. These nurses stated that the technology was a welcome addition to their own clinical view.
- Four nurse respondents (24%) mentioned that the monitoring system did not always work adequately. Nurses in particular mentioned the troublesome synchronising of the nurse MEWS measurements on the VS30 monitor into EPR.
- Two nurse respondents (12%) mentioned that they felt that they could not fully trust the data of the continuous monitoring system.
- Two nurse respondents (12%) stated that they do not think that the continuous monitoring system can replace nurse measurements and nurse observations.
- One nurse respondent (6%) stated that he/she especially appreciated the possibility to monitor the patients from outside the room during his/her night shifts.
- One nurse respondent (6%) suggested that the trend data should be discussed with the ward physician during the visitations.
- One nurse respondent (6%) stated that he/she appreciated that the MEWS measurements on the VS30 monitor were automatically synchronised into the EPR and that he/she did not need to carry loose notes with measurements.
- One nurse respondent (6%) suggested that the UMCU should invest in more elaborate technologies (that measure more parameters, such as BP) for future implementation processes of continuous monitoring system. This nurse suggested the VisiMobile, as the nurse had worked with this technology at the Radboudumc in Nijmegen.
- One nurse respondent (6%) stated that he/she would appreciate implementation at other nursing wards in the UMCU.
- One nurse respondent (6%) stated that the MEWS notifications were confusing and difficult to understand.
- One nurse respondent (6%) stated that the presence of the monitoring team was nice, especially if the monitoring team was involved with the nurses and took the time to time to fully explain the system.
- Four nurse respondents (24%) did not answer this open question.

Appendix 11.6: data of patients who were monitored for < 48 hours

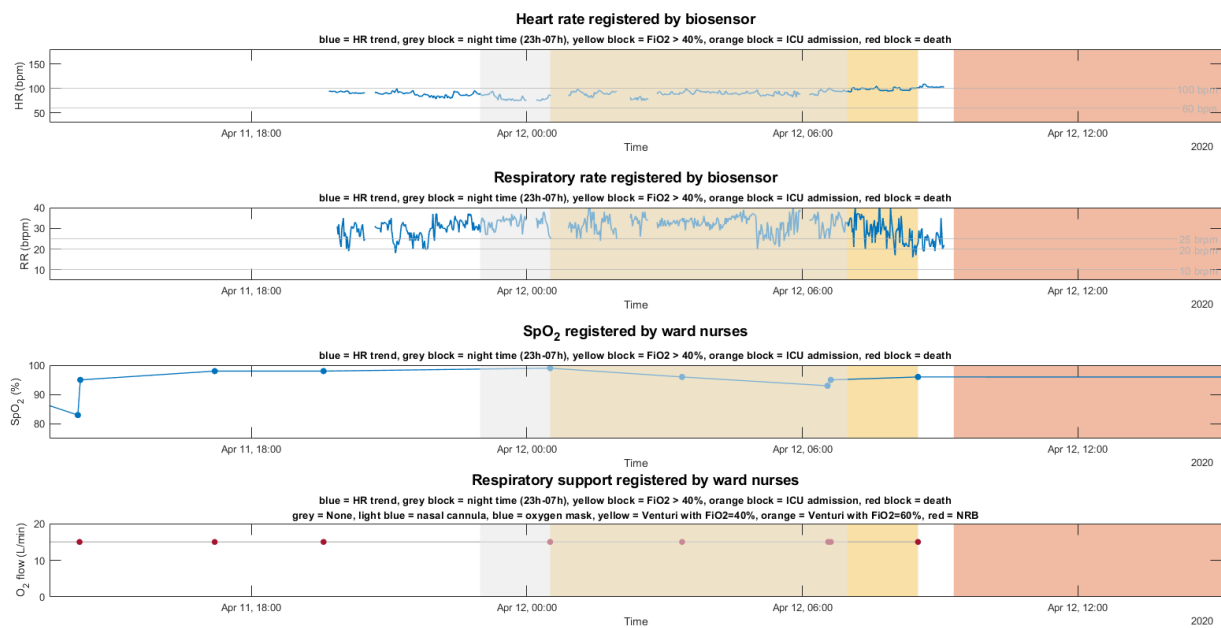


Figure 45: Continuous data of patient who was monitored for 13 hours and 30 minutes. Clinical outcome of this patient: death



Figure 46: Continuous data of patient who was monitored for 48 hours and 18 minutes. Clinical outcome of this patient: discharged to home.

Appendix 11.7: HR data of deteriorating patients where no trends were detected

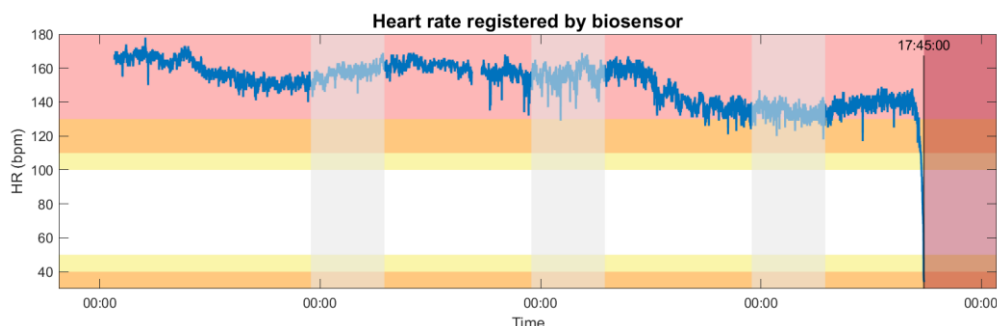


Figure 47: Patient 1 – no trend detected by any of the candidate algorithms. Serious deterioration event while being monitored: death. Horizontal color blocks indicate the MEWS levels being (bottom-top): 2 – ≤ 40 bpm (orange), 1 – 41-50 bpm (yellow), 0 – 51-100 bpm (white), 1 – 101-110 bpm (yellow), 2 – 111-129 bpm (orange), 3 – ≥ 130 bpm (red). Note that this patient was extremely tachycardic from the start of monitoring, up until the moment of death: this suggests that the patient was already severely deteriorated prior to the start of monitoring. Therefore, it is likely that the process of deterioration did not happen while being monitored (yet prior to monitoring).

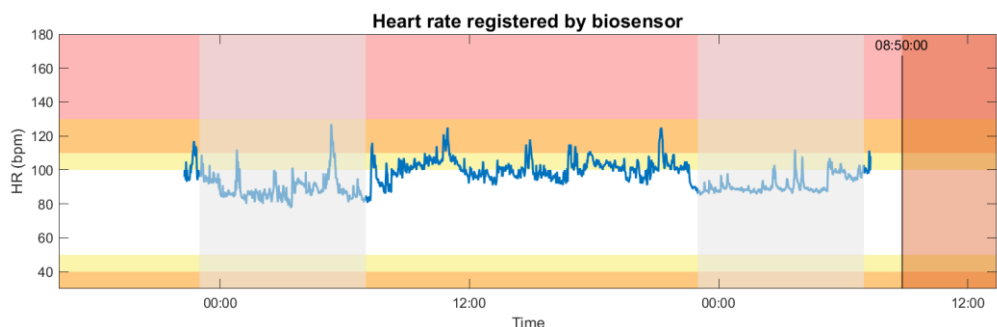


Figure 48: Patient 3 – no trend detected by any of the candidate algorithms. Serious deterioration event while being monitored: ICU admission. Horizontal color blocks indicate the MEWS levels being (bottom-top): 2 – ≤ 40 bpm (orange), 1 – 41-50 bpm (yellow), 0 – 51-100 bpm (white), 1 – 101-110 bpm (yellow), 2 – 111-129 bpm (orange), 3 – ≥ 130 bpm (red). Note that this patient showed some mild tachycardic peaks (sometimes reaching MEWS level 2 of 111-129 bpm), yet no increasing HR trend.

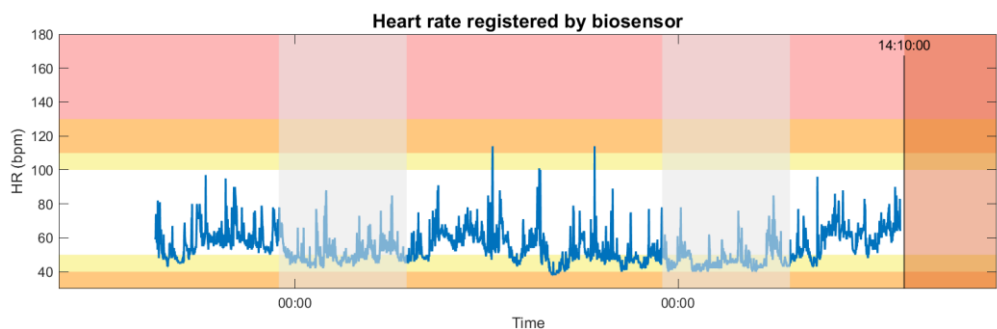


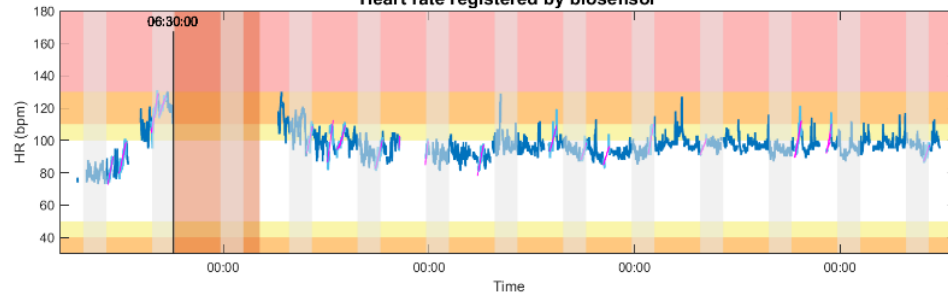
Figure 49: Patient 11 – no trend detected by any of the candidate algorithms. Serious deterioration event while being monitored: ICU admission. Horizontal color blocks indicate the MEWS levels being (bottom-top): 2 – ≤ 40 bpm (orange), 1 – 41-50 bpm (yellow), 0 – 51-100 bpm (white), 1 – 101-110 bpm (yellow), 2 – 111-129 bpm (orange), 3 – ≥ 130 bpm (red). Note that this patient had a low yet peaky HR. Prior to ICU admission, a slightly increasing HR appears to be present (within an acceptable HR range, based on the MEWS thresholds), yet no HR trends were detected.

Appendix 11.8: visualisations of the outcomes of all HR candidate algorithms for patients 8, 12 and 14

HRalgorithm1.1

Patient 8

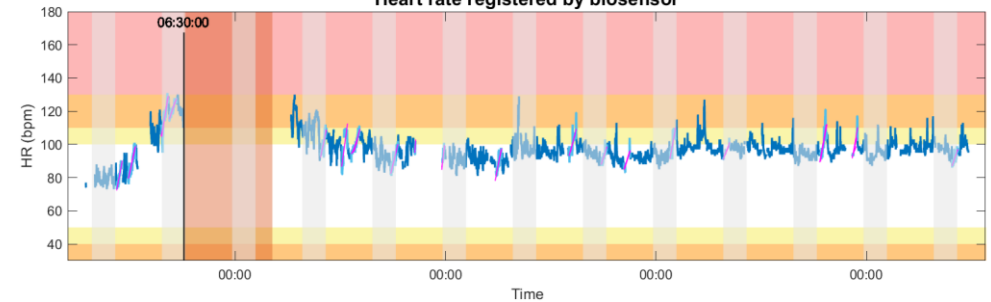
Heart rate registered by biosensor



HRalgorithm1.2

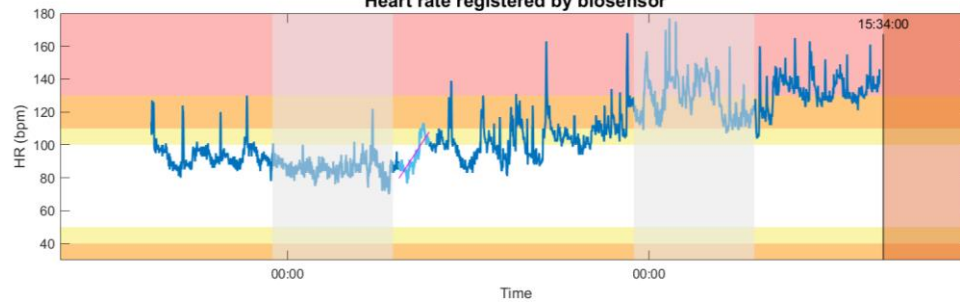
Patient 8

Heart rate registered by biosensor



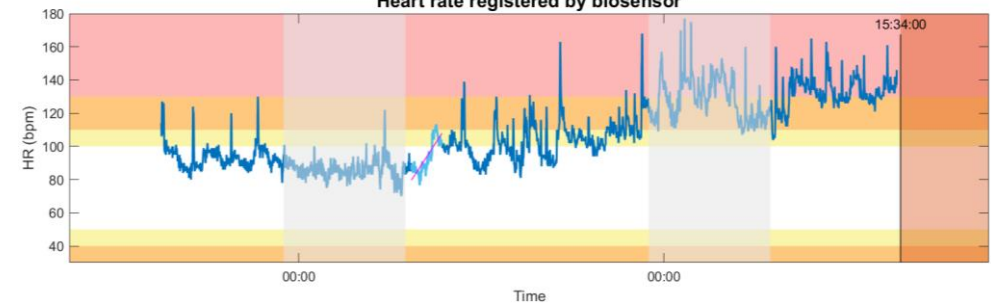
Patient 12

Heart rate registered by biosensor



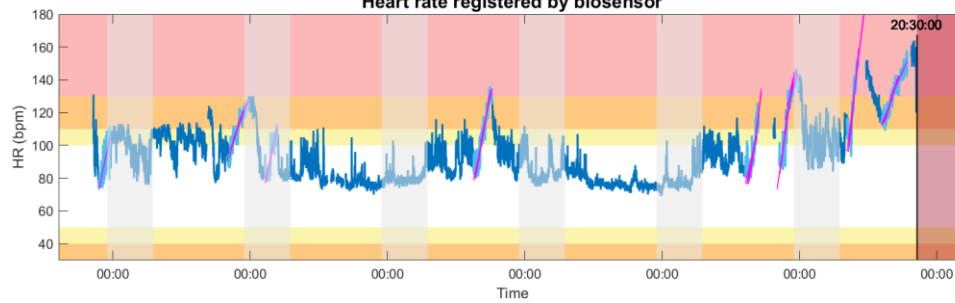
Patient 12

Heart rate registered by biosensor



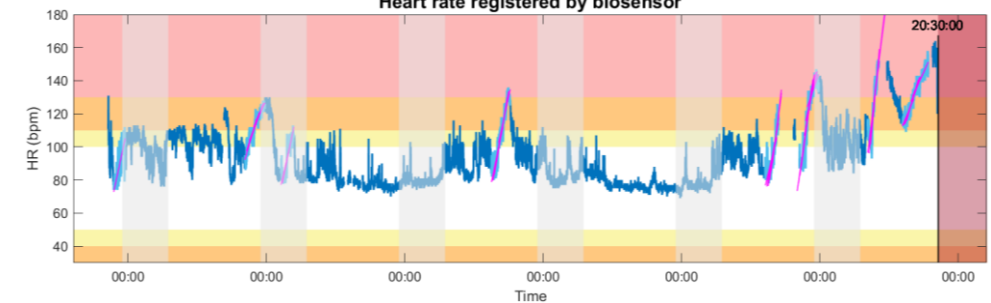
Patient 14

Heart rate registered by biosensor



Patient 14

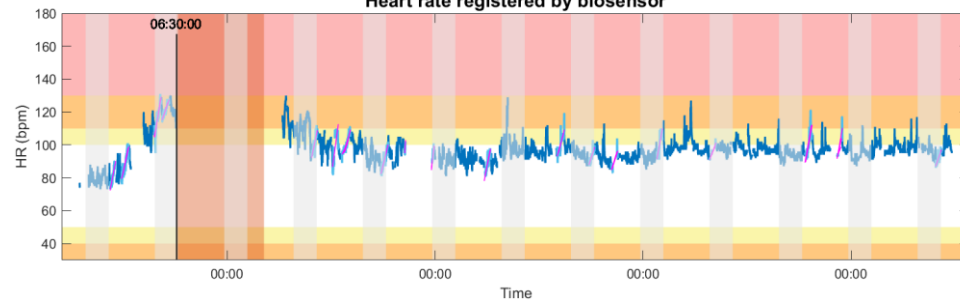
Heart rate registered by biosensor



HRalgorithm1.3

Patient 8

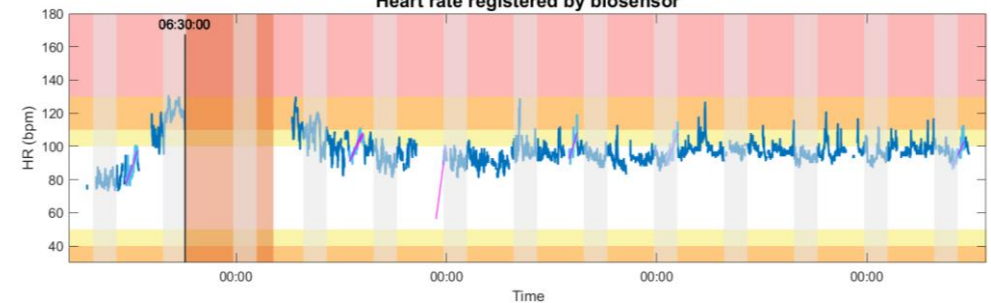
Heart rate registered by biosensor



HRalgorithm2.1

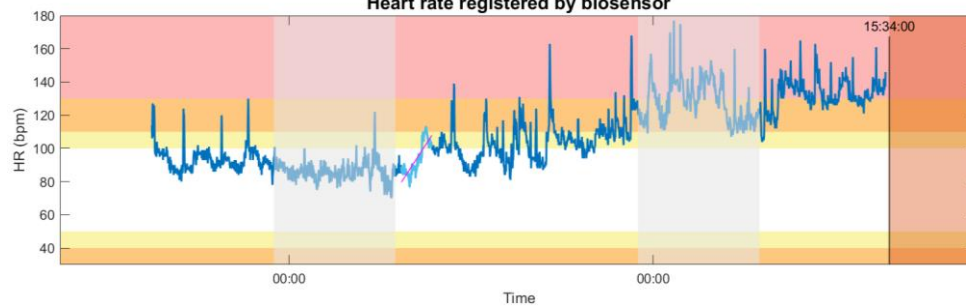
Patient 8

Heart rate registered by biosensor



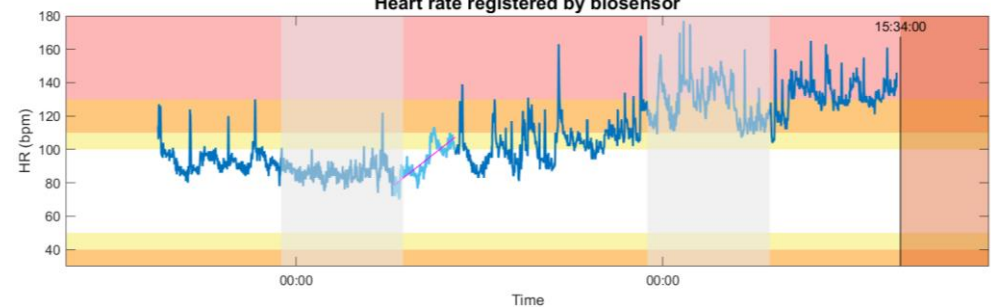
Patient 12

Heart rate registered by biosensor



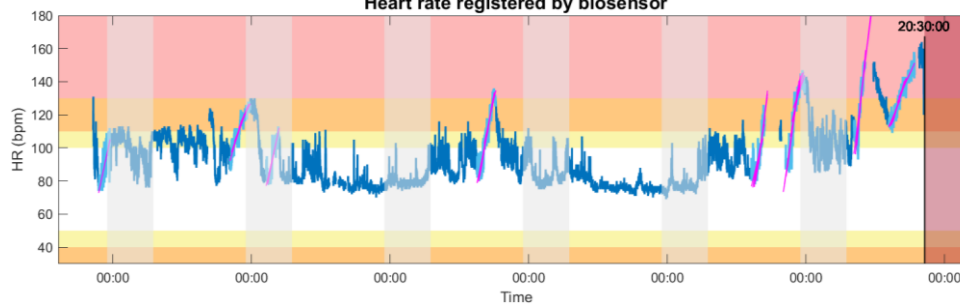
Patient 12

Heart rate registered by biosensor



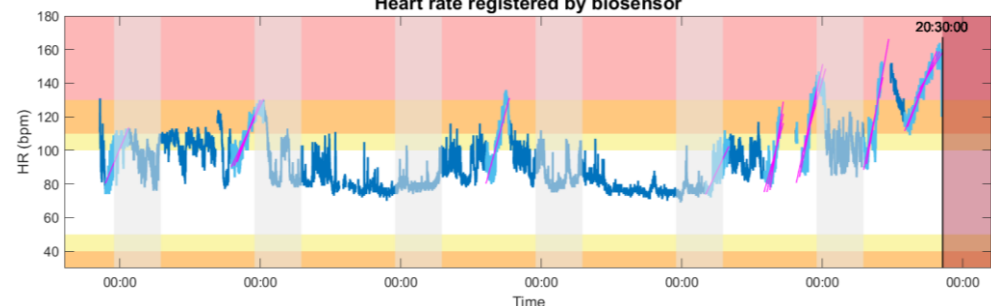
Patient 14

Heart rate registered by biosensor



Patient 14

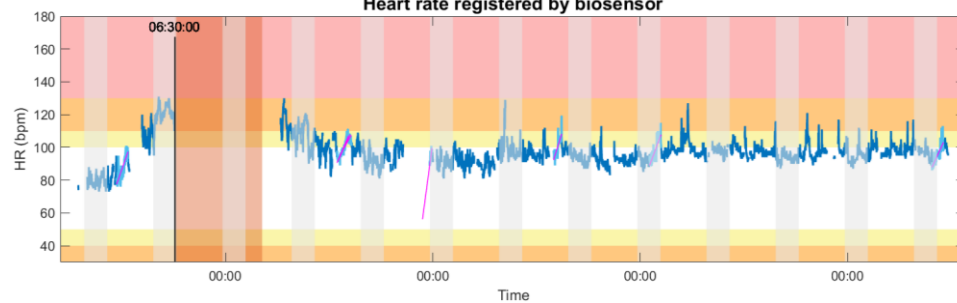
Heart rate registered by biosensor



HRalgorithm2.2

Patient 8

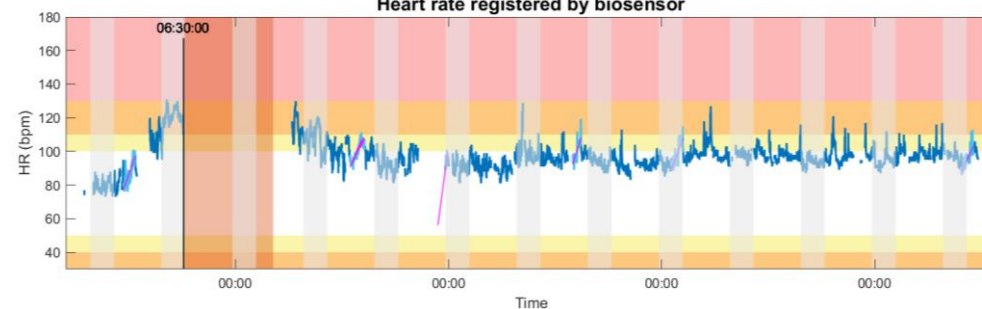
Heart rate registered by biosensor



HRalgorithm2.3

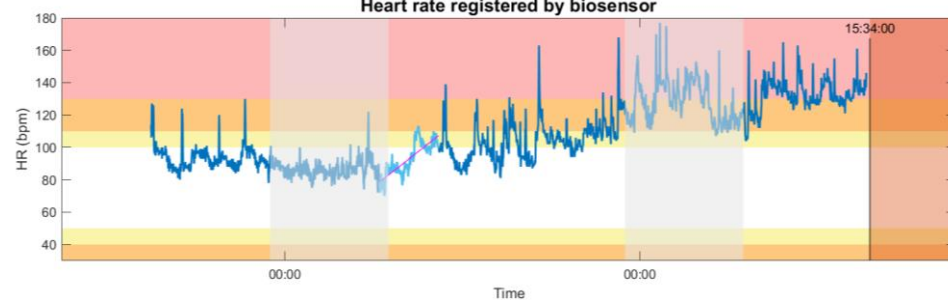
Patient 8

Heart rate registered by biosensor



Patient 12

Heart rate registered by biosensor



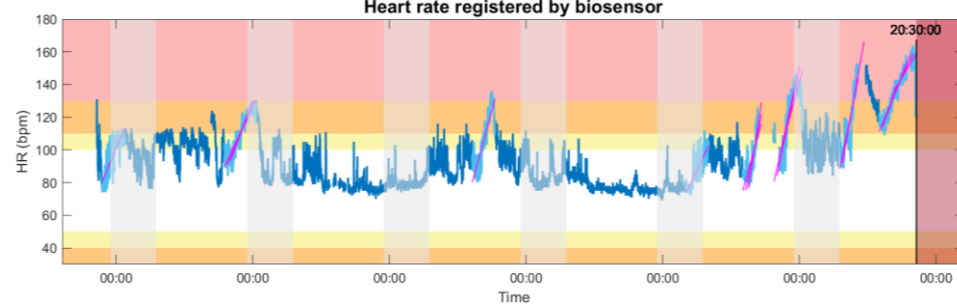
Patient 12

Heart rate registered by biosensor



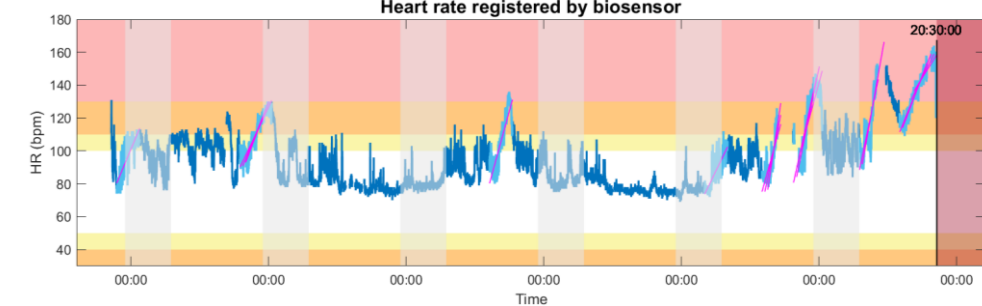
Patient 14

Heart rate registered by biosensor



Patient 14

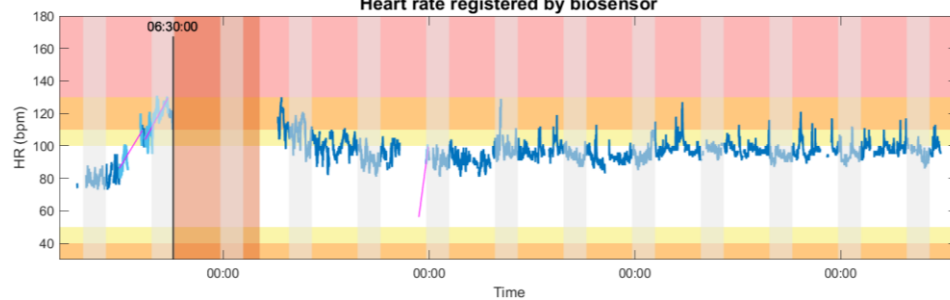
Heart rate registered by biosensor



HRalgorithm3.1

Patient 8

Heart rate registered by biosensor



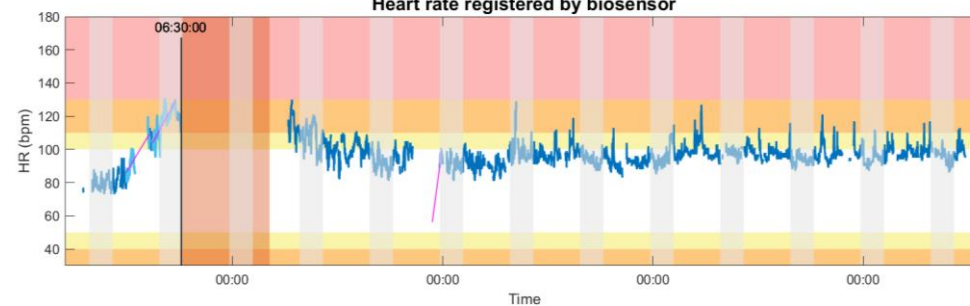
Patient 12

No trends detected

HRalgorithm3.2

Patient 8

Heart rate registered by biosensor

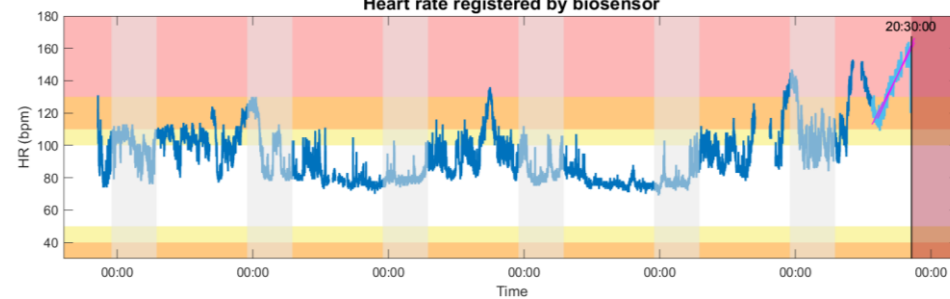


Patient 12

No trends detected

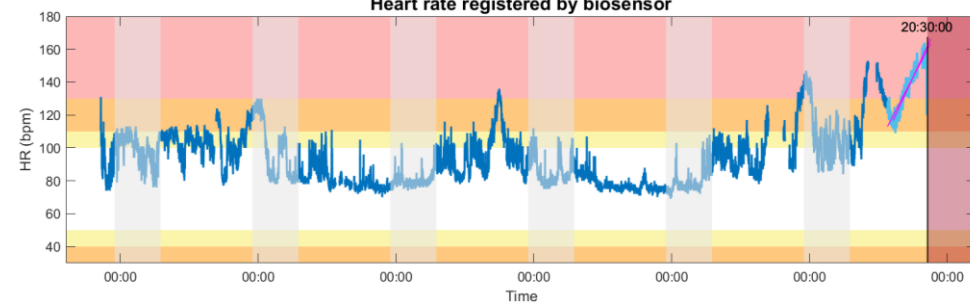
Patient 14

Heart rate registered by biosensor



Patient 14

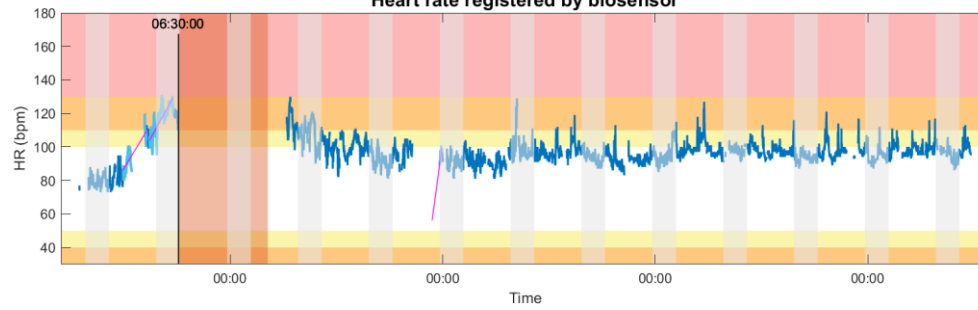
Heart rate registered by biosensor



HRalgorithm3.3

Patient 8

Heart rate registered by biosensor



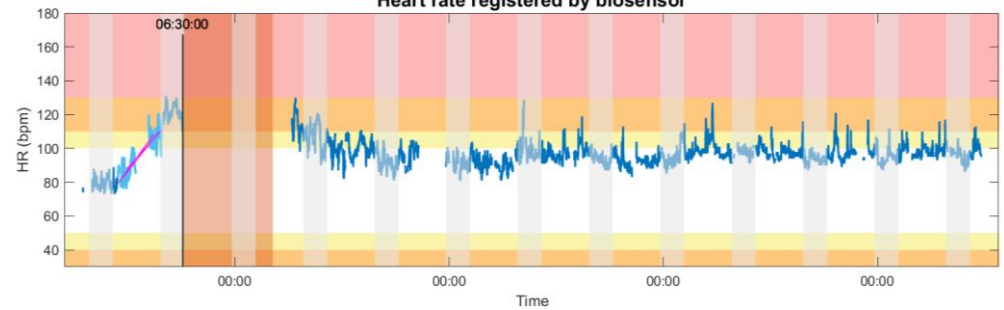
Patient 12

No trends detected

HRalgorithm4.1

Patient 8

Heart rate registered by biosensor

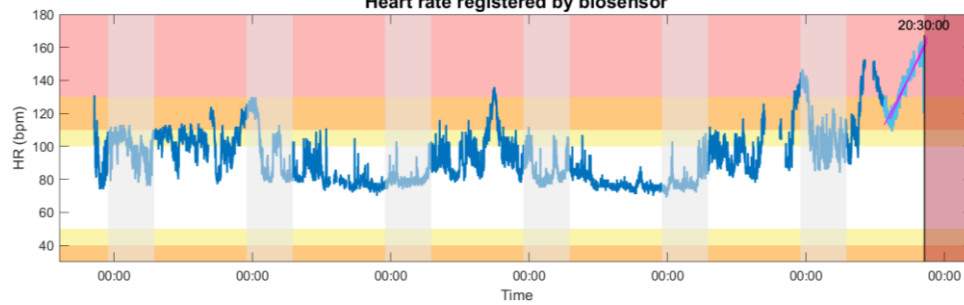


Patient 12

No trends detected

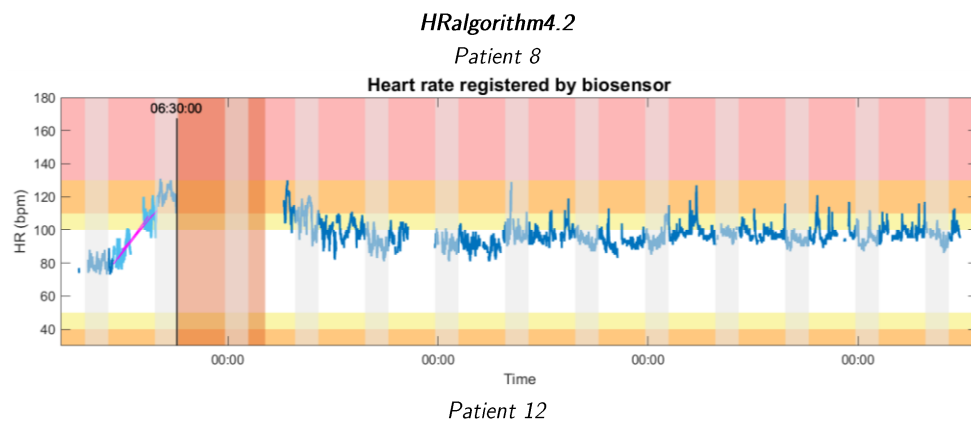
Patient 14

Heart rate registered by biosensor



Patient 14

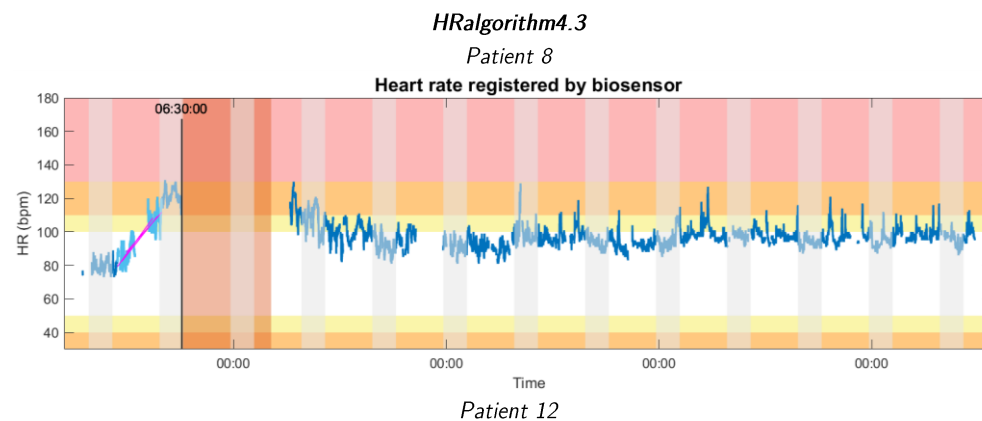
No trends detected



No trends detected

Patient 14

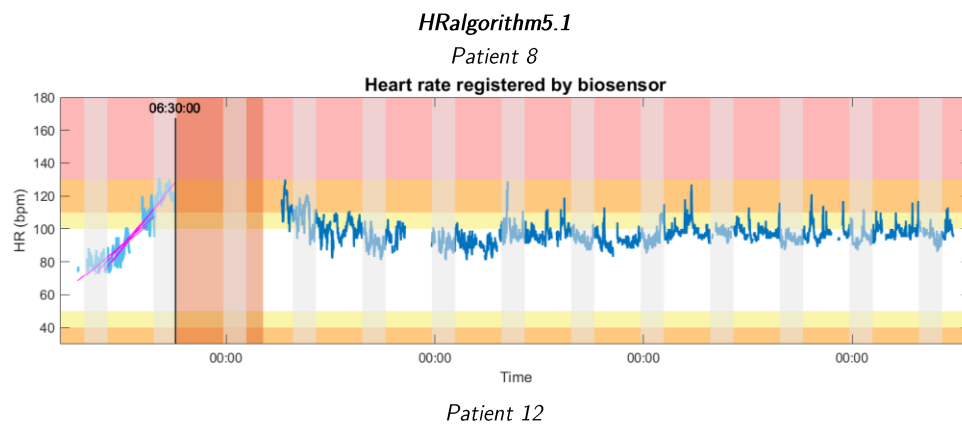
No trends detected



No trends detected

Patient 14

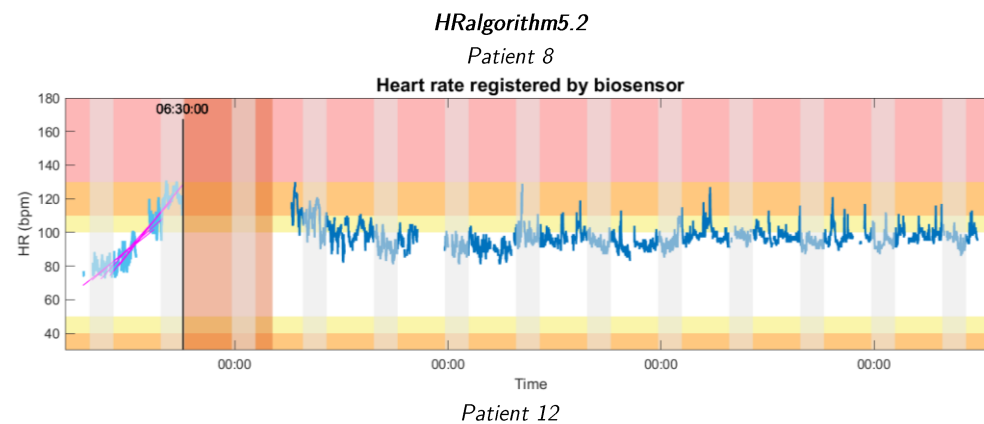
No trends detected



No trends detected

Patient 14

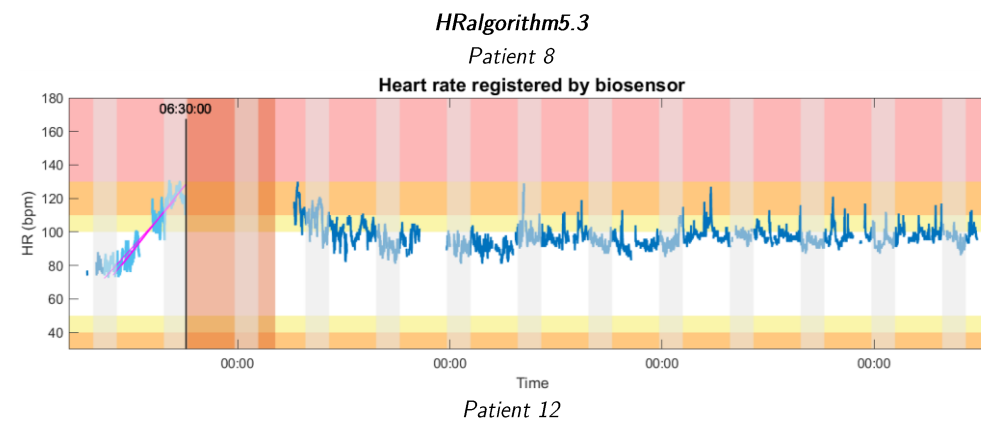
No trends detected



No trends detected

Patient 14

No trends detected



No trends detected

Patient 14

No trends detected

Appendix 11.9: RR data of deteriorating patient where trends were only detected in algorithms RRAgorithm1.1-3

For this patient ('patient 7'), trends in the RR data were only detected by algorithms RRAgorithm1.1-3 (with slicewindow = 2h). When looking at the continuous RR data of patient 7, no visually apparent trends are observed, matching the fact that no trends were detected by the other algorithms. The RR data of this patient shows that the RR fluctuates between MEWS levels 2 (21-24 brpm) and 3 (≥ 25 brpm) from the start of continuous monitoring up until ICU admission. This suggests that the patient was already severely deteriorated prior to the start of monitoring. Therefore, it is likely that the process of deterioration did not happen while being monitored (yet prior to monitoring). Note that the patient was only monitored for just over 24h, suggesting that it is highly possible that the process of deterioration occurred prior to the start of continuous monitoring.

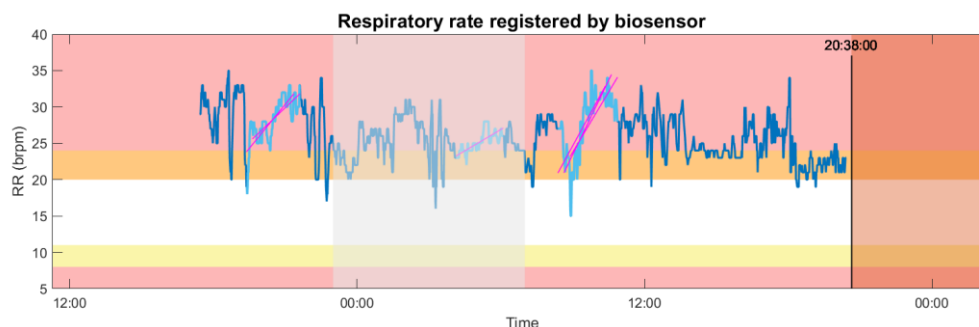


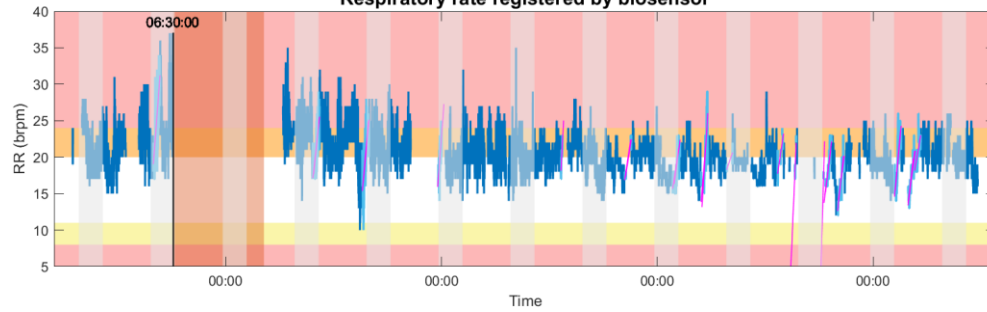
Figure 50: Patient 7 – trends were only detected by RRAgorithm1.1-3. Outcomes of these algorithms are identical for this patient. Serious deterioration event while being monitored: ICU admission. The magenta lines are visualisations of the linear fits. The parts of the data that is a lighter shade of blue represent the data slices in which a trend was detected. Horizontal color blocks indicate the MEWS levels being (bottom-top): 3 – ≤ 8 brpm (red), 1 – 9-11 brpm (yellow), 0 – 12-20 brpm (white), 2 – 21-24 brpm (orange), 3 – ≥ 25 brpm (red). The grey color blocks symbolise the

Appendix 11.10: visualisations of the outcomes of all RR candidate algorithms for patients 8, 12 and 14

RRalgorithm1.1

Patient 8

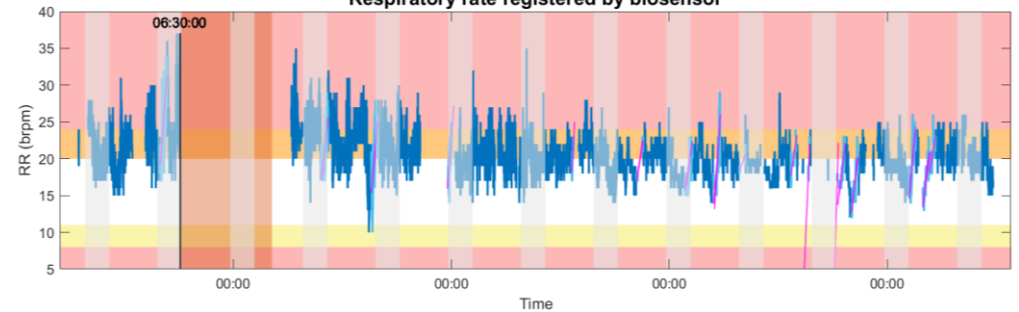
Respiratory rate registered by biosensor



RRalgorithm1.2

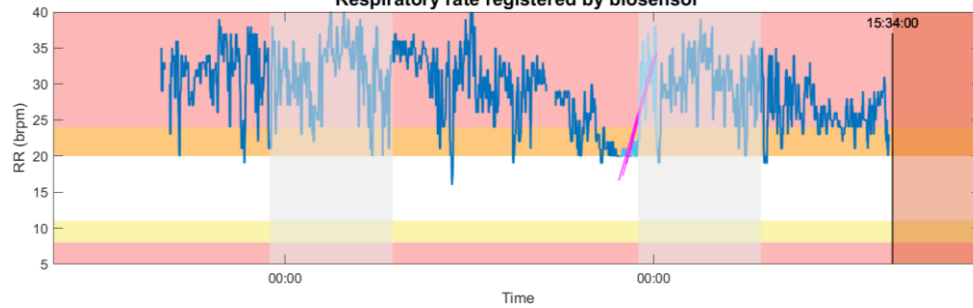
Patient 8

Respiratory rate registered by biosensor



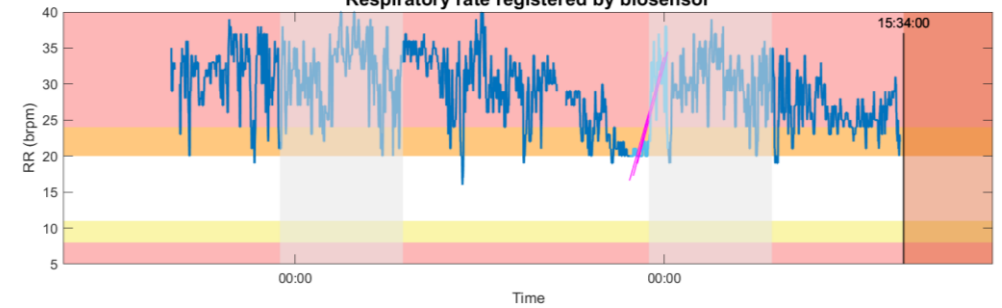
Patient 12

Respiratory rate registered by biosensor



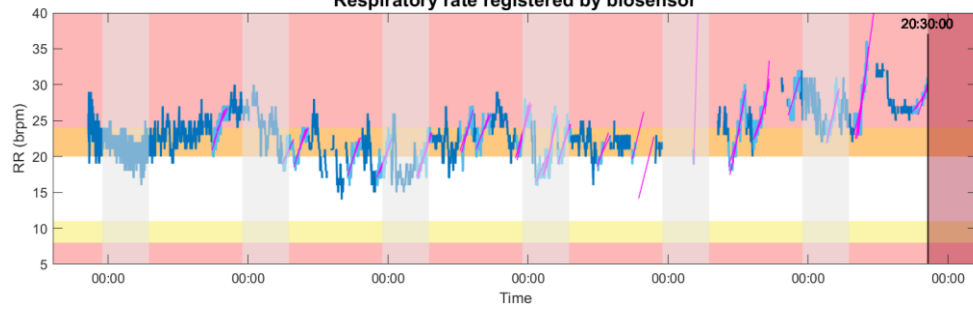
Patient 12

Respiratory rate registered by biosensor



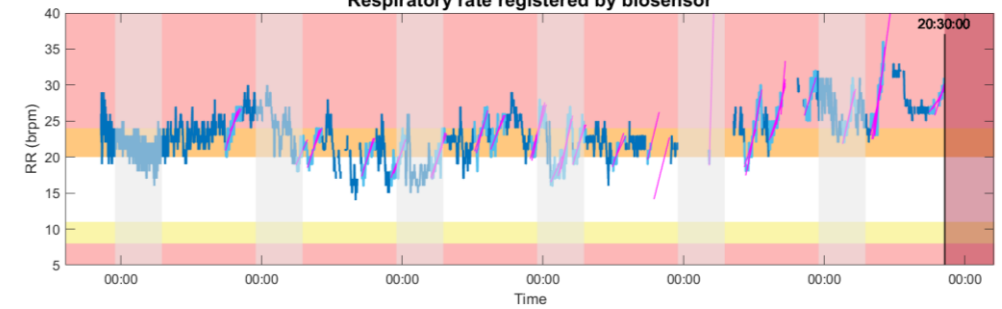
Patient 14

Respiratory rate registered by biosensor



Patient 14

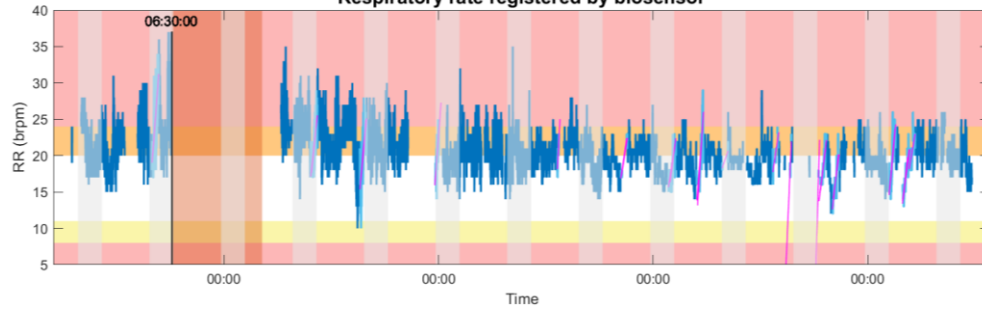
Respiratory rate registered by biosensor



RRalgorithm1.3

Patient 8

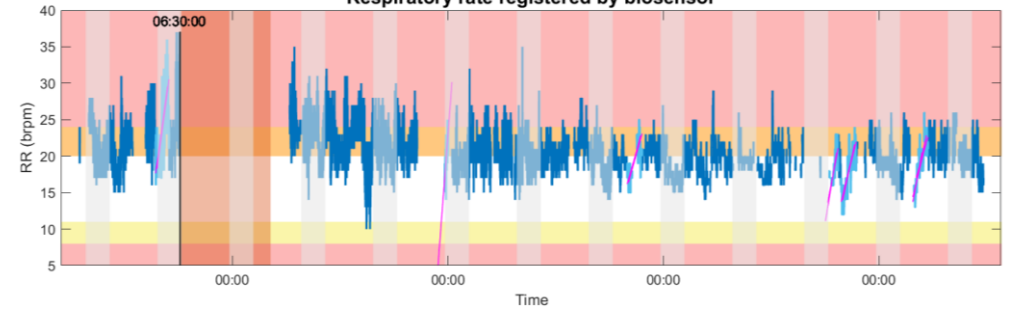
Respiratory rate registered by biosensor



RRalgorithm2.1

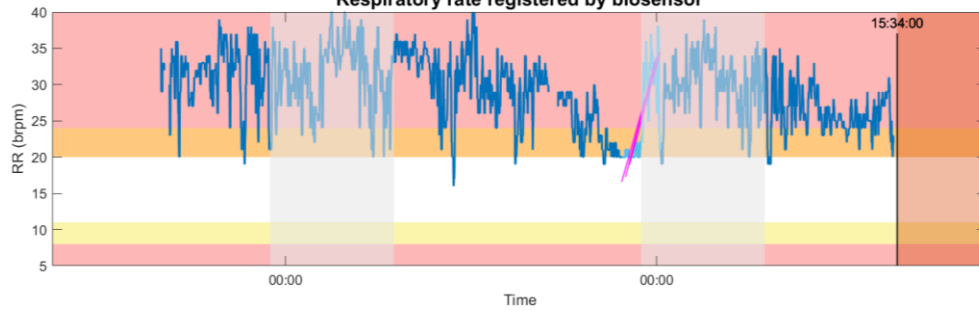
Patient 8

Respiratory rate registered by biosensor



Patient 12

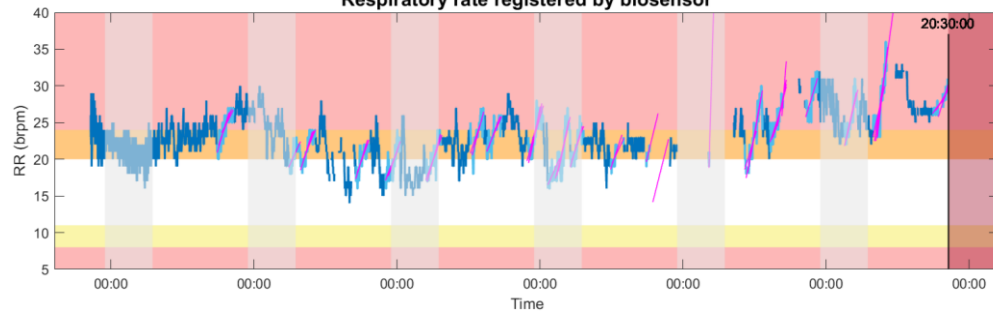
Respiratory rate registered by biosensor



No trends detected

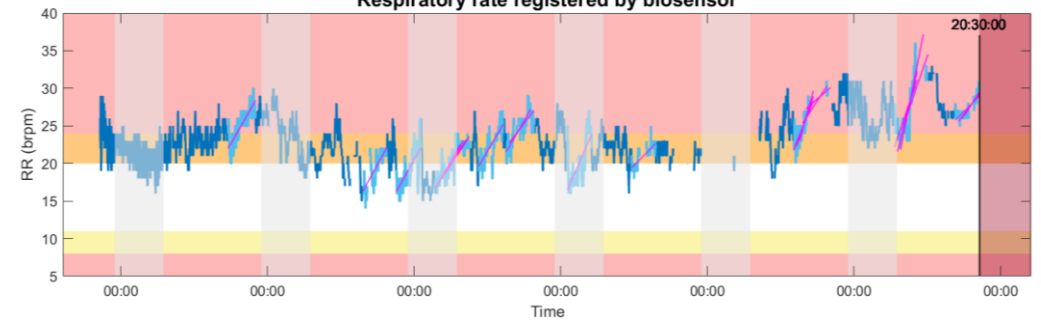
Patient 14

Respiratory rate registered by biosensor



Patient 14

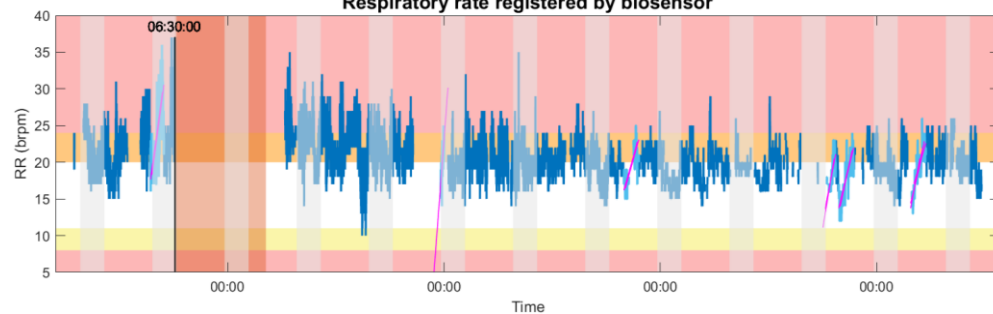
Respiratory rate registered by biosensor



RRalgorithm2.2

Patient 8

Respiratory rate registered by biosensor



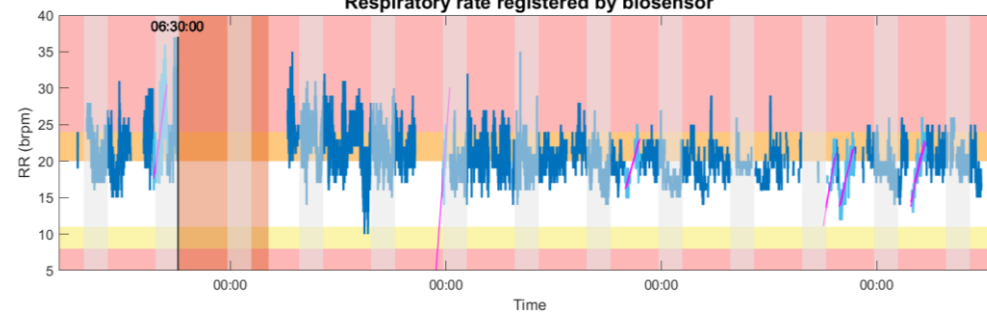
Patient 12

No trends detected

RRalgorithm2.3

Patient 8

Respiratory rate registered by biosensor

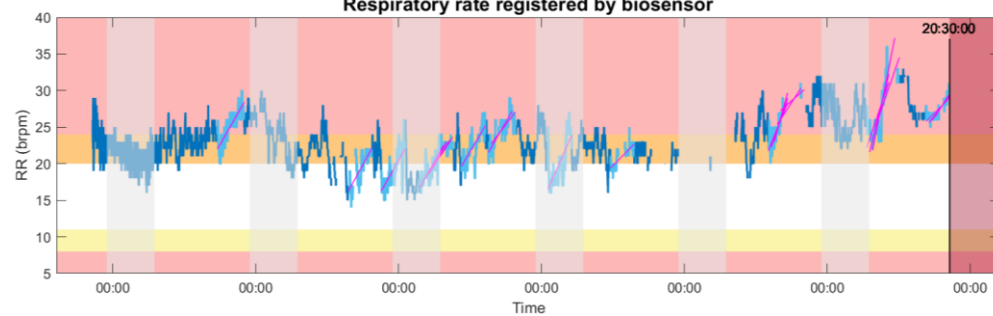


Patient 12

No trends detected

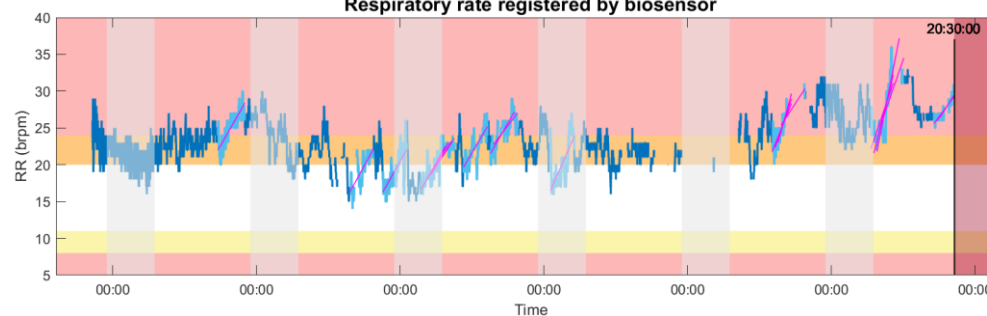
Patient 14

Respiratory rate registered by biosensor



Patient 14

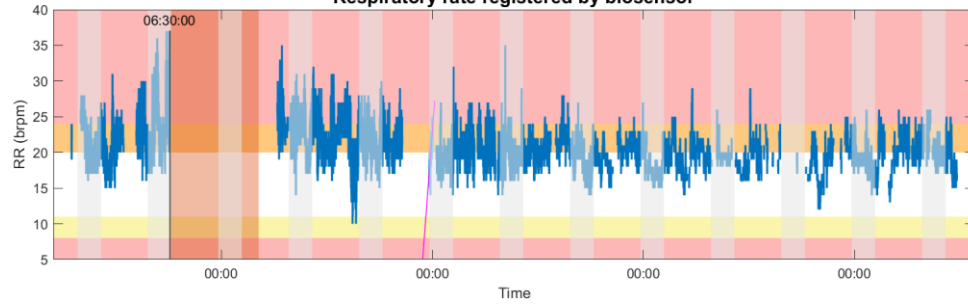
Respiratory rate registered by biosensor



RRalgorithm3.1

Patient 8

Respiratory rate registered by biosensor



RRalgorithm3.2

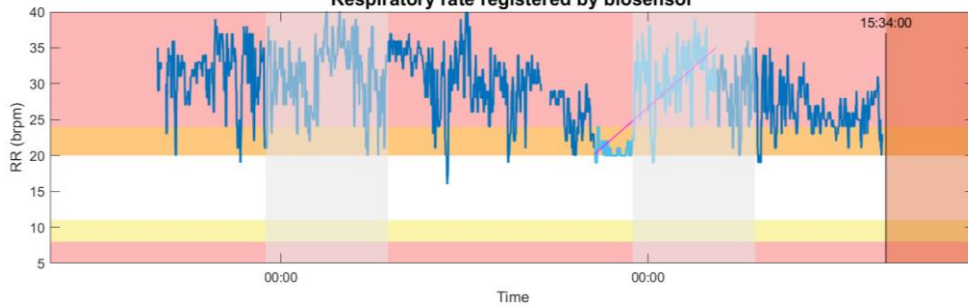
Patient 8

Respiratory rate registered by biosensor



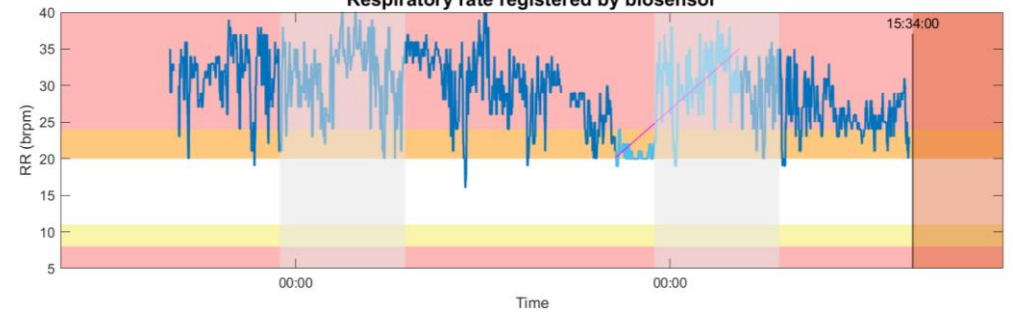
Patient 12

Respiratory rate registered by biosensor



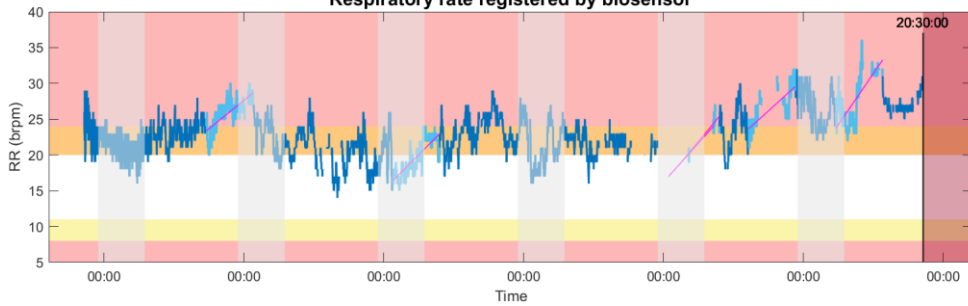
Patient 12

Respiratory rate registered by biosensor



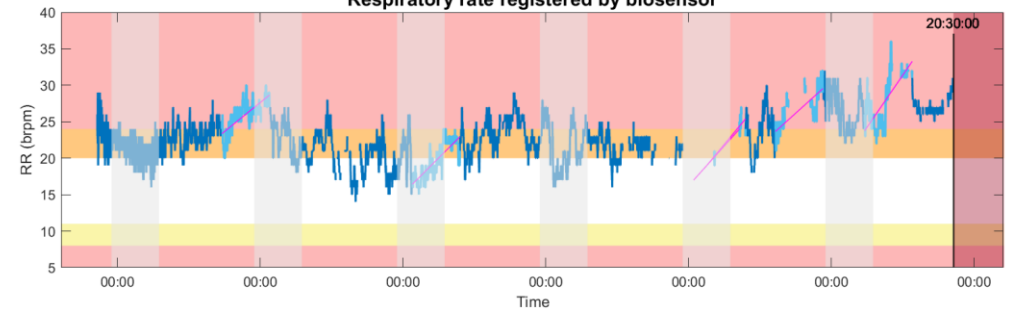
Patient 14

Respiratory rate registered by biosensor



Patient 14

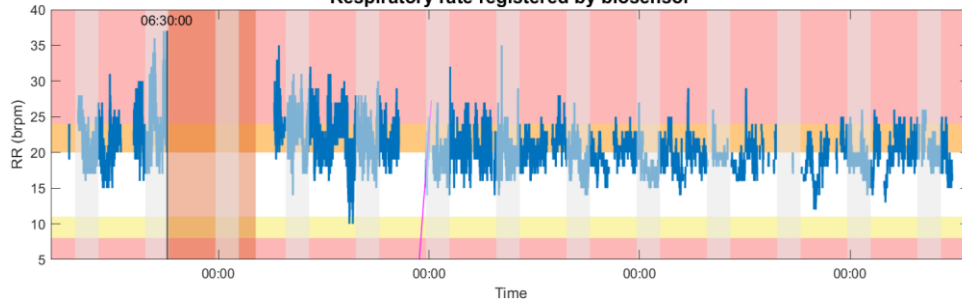
Respiratory rate registered by biosensor



RRalgorithm3.3

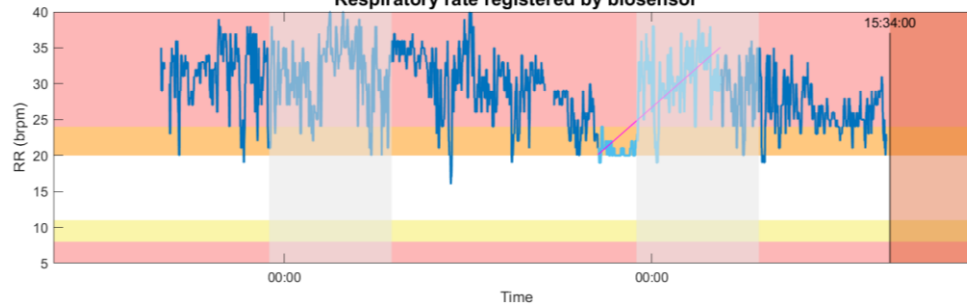
Patient 8

Respiratory rate registered by biosensor



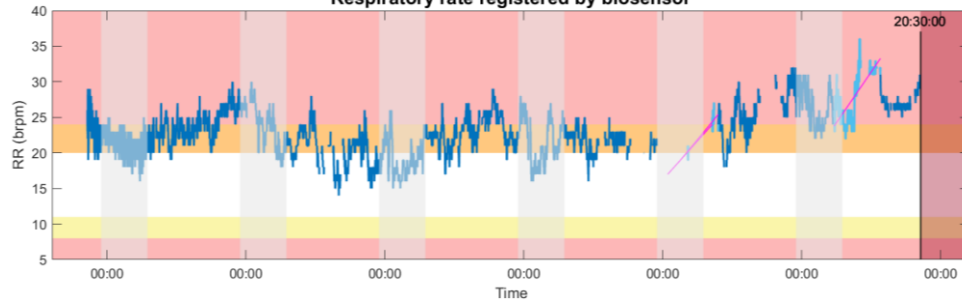
Patient 12

Respiratory rate registered by biosensor



Patient 14

Respiratory rate registered by biosensor



RRalgorithm4.1

Patient 8

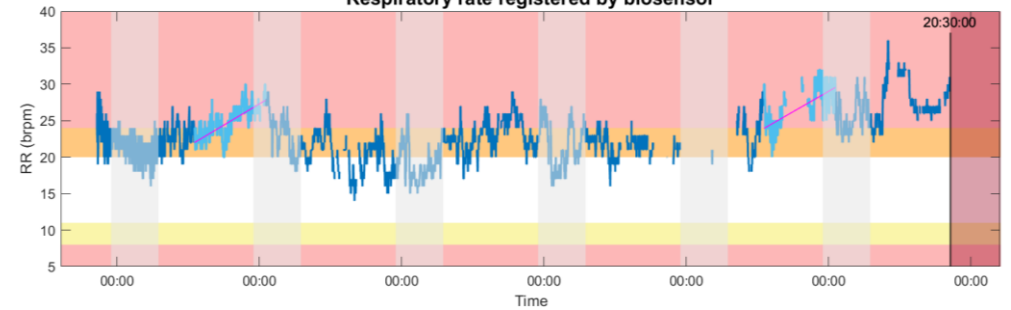
No trends detected

Patient 12

No trends detected

Patient 14

Respiratory rate registered by biosensor



For the remaining candidate algorithms (HRRalgorithm4.2-3 and HRRalgorithm5.1-3) no trends were detected for patient 8, 12 and 14. Therefore, no visualisations of detected trends are included.

