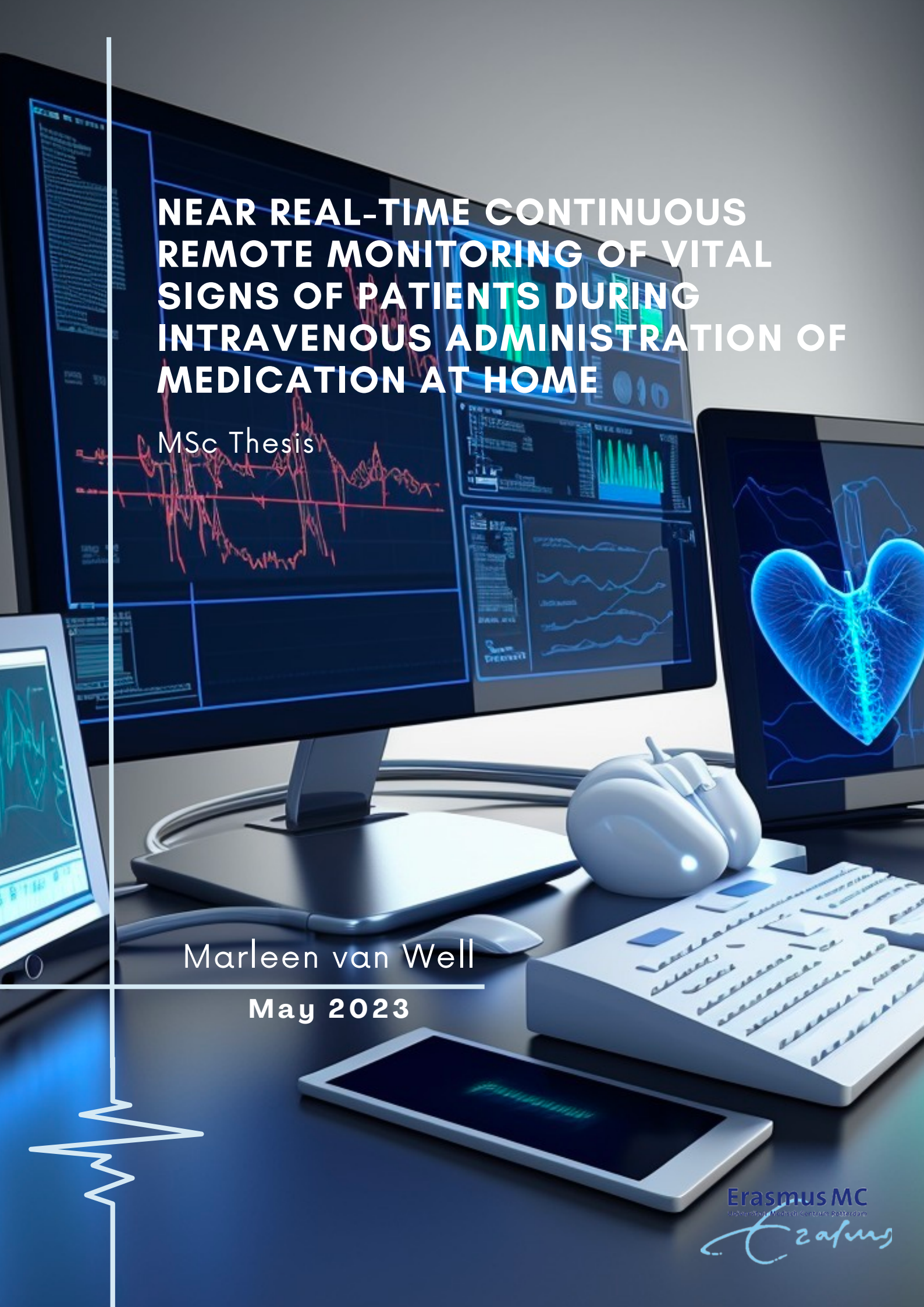

NEAR REAL-TIME CONTINUOUS REMOTE MONITORING OF VITAL SIGNS OF PATIENTS DURING INTRAVENOUS ADMINISTRATION OF MEDICATION AT HOME

MSc Thesis

Marleen van Well

May 2023

Erasmus MC

NEAR REAL-TIME CONTINUOUS REMOTE MONITORING OF VITAL SIGNS OF PATIENTS DURING INTRAVENOUS ADMINISTRATION OF MEDICATION AT HOME

- MSc Thesis -

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Have a good time reading my MSc Thesis!

Marleen van Well
Rotterdam, May 2023

Abstract

Introduction
To cope with the decreasing availability of healthcare personnel, we are in need of a national (and global) transition to make the healthcare system sustainable for the future. Administration of intravenous immunoglobulins (IVIg) at home for patients with immunodeficiencies is an example of a therapy that currently requires a significant amount of nursing staff in relation to the number of patients receiving the treatment. Near real-time continuous remote monitoring (NRCRM) of vital signs of these patients during administration could potentially offer a solution by enabling nurses to treat the same number of patients with fewer staff members. The goal of this pilot study is to test monitoring system functionality, evaluate user experiences and identify challenges and bottlenecks of NRCRM of vital signs of patients during administration of IVIg at home.

Methods
Patients from the department of immunology at Erasmus MC who receive IVIg at home were evaluated for inclusion. During administration, their vital signs were monitored remotely in addition to the usual monitoring procedure performed by the home nurse. Raw data of the vital signs, in combination with an alarm template and observations during administration at home, were used to assess system functionality. User experience was evaluated using custom-made questionnaires. Challenges and bottlenecks for further implementation were identified during execution of the study protocol.

Results
No-data alarms in this study yield an alarm burden of 10.9 ± 4.8 (mean ± SD) alarms per patient per hour with a duration of alarms of 2min59sec ± 13min38sec (mean ± SD).
Threshold alarms in this study yield an alarm burden of 17.1 ± 15.1 (mean ± SD) alarms per patient per hour with a duration of 1min12sec ± 3min (mean ± SD).
Attitudes of both patients and nurses towards the transition to NRCRM are mixed. Most concerns exist around patient safety. 30 challenges and bottlenecks in the transition are identified.

Conclusion
This thesis provides an overview of the actions that need to be taken to overcome associated challenges and bottlenecks. Also, suggestions for implementation were presented. Besides the practical and safety aspect, a challenge lies in addressing the negative attitudes of nurses and patients to ensure smooth adoption.

Content

1. Introduction

1.1 Technical Background

1.1.1 Transition from hospital care to care at home

Globally, the health workforce is suffering from labor shortages. The Global Burden of Disease Study 2019 (GBD 2019)[1], coordinated by the Institute for Health Metrics and Evaluation (IHME), estimated the burden of diseases, injuries, and risk factors for 204 countries and territories and selected subnational locations. The needed national health workforce per 10.000 population to reach 80 out of 100 on the Universal Health Coverage (UHC) index was estimated. This index shows the average coverage of essential health services. In total, the 2019 national health workforce fell short of these minimum thresholds by 6.4 million physicians, 30.6 million nurses and midwives, 3.3 million dentistry personnel and 2.9 million pharmaceutical personnel. Recent research on the Dutch labor market shows that the shortage of healthcare personnel will increase from 48.600 employees in 2022 to 135.000 employees in 2031.[2] Especially in elderly care and hospital care, large deficits are expected. In these two branches, there will be a shortage of 98.000 employees in the near future.
Research has shown significant relationships between the aggregate density of health workers and population-level health outcomes[3] and that investing in health workforces promotes economic growth[4]. Besides the impact of health workforce shortage on patient health outcomes and financial growth, healthcare givers experience increasing workloads, mass traumatization among nurses and a lack of protection against these matters.[5]
It is fair to say that the current healthcare system is not sustainable in providing good quality healthcare services, as the number of trained personnel is not in line with the increasing demand for care. To meet healthcare needs now and in the future, the world is in need of a transition. One transition that has already arisen to address this challenge is the transition from hospital care to care at home.

Among other technologies, the adoption of remote monitoring or telemonitoring has hugely increased this transition. Many telehealthcare systems to date are used for recovery surveillance and disease management at large time intervals.[6-8] However, changes in these parameters are slow and do not generally have to be attended to in (near) real-time.

1.1.2 (Near) real-time continuous remote monitoring

The next step in this transition is (near) real-time continuous remote monitoring (NRCRM) of vital signs of patients at home in combination with real-time alarm handling, e.g. during blood transfusion at home[9], for ill patients in contagious situations like Covid-19[10-12] or during postoperative surveillance at home[13]. In contrast to monitoring at large intervals, this is a continuous process that has to be able to detect the onset of adverse events in (near) real-time and requires readiness for immediate corrective intervention.
This report will focus on NRCRM of vital signs of patients during administration of intravenous immunoglobulins.

1.2 Medical Background

1.2.1 The human immune system

The human immune system is a complex biological system that protects our body against infection and tumors. The system consists of multiple components with different characteristics and functions, operating together to provide an accurate immune response.
There are two main arms of the immune system: innate and adaptive. The innate immune system provides a rapid and unspecific immune response against a wide range of pathogens, including bacteria, viruses, fungi and parasites. The innate immune system includes physical barriers such as skin and mucous membranes, as well as cellular and molecular components such as macrophages,

granulocytes, monocytes and their products. On the other hand, the adaptive immune system provides a slower and specific immune response with the ability to form immunological memory. Immunological memory is the ability to recognize an antigen after it has entered the body for the first time. Key components of the adaptive immune system are T- and B-cells, which become active when their antigen receptors are triggered. The antigenic stimulation and activation of B-cells cause them to proliferate and differentiate. This, in turn, can lead to the formation of immunoglobulin (Ig)-producing plasma cells or memory B-cells.[14]

This thesis report focuses on immunoglobulins (Igs), also known as antibodies, produced by B-cells. Igs are proteins that are involved in the elimination of toxins, pathogens and tumor cells, as well as in the activation of other immune components (e.g. complement proteins). The five main classes are IgA, IgG, IgM, IgD and IgE, differing from each other in structure and function.[15]

1.2.2 Function of immunoglobulins

The general structure of an Ig molecule consists of two identical heavy (H) chains and two identical light (L) chains (*Figure 1*). All chains contain a variable (V) domain that binds antigens and a constant (C) domain that specifies effector functions (the effect the molecule brings about). Five main classes of Igs are identified based on the five different structures of heavy chain C domains, all having different functions (*Figure 1*). The variable component of both the heavy and light chains together form the binding site for antigens, allowing recognition of many different types of antigens.[14]

IgM is the first Ig produced during B-cell development and is involved in the primary immune response, the immune response after a first encounter with an antigen.[16, 17] IgG is the most abundant serum Ig, taking up 80% of the total Ig serum, and is involved in the secondary immune response, the immune response after recognition of a foreign antigen that has encountered the body before.[16, 17] IgA, the second most abundant serum Ig, mainly provides mucosal immunity functioning from within the gastrointestinal, urogenital and respiratory tracts.[16, 18] IgE, only present at low levels, is involved in the response to hypersensitivity, allergic reactions and parasitic infections.[16] Lastly, the role of IgD is not yet entirely understood. Research suggests it may play a role in activating B-cells by binding to bacterial proteins.[16]

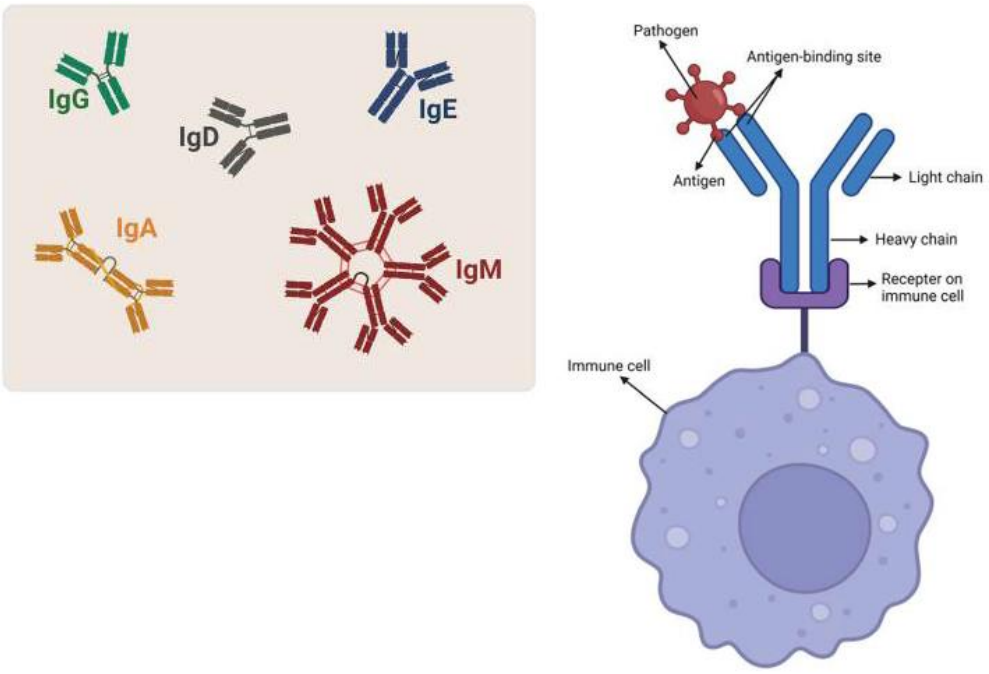


Figure 1 Basic structure and types of immunoglobulins[19]

1.2.3 Immunodeficiencies

The importance of the presence and functionality of serum Igs is illustrated in patients with primary or secondary immunodeficiencies. Primary immunodeficiencies (PIDs) are congenital disorders caused by one or more defects in the functioning of the immune system. PIDs specifically caused by defects in Ig production are called humoral immunodeficiencies. Patients present with recurrent infections, predominantly in the respiratory tract caused by encapsulated bacteria such as *Streptococcus pneumoniae* and *Haemophilus influenzae* and in the gastrointestinal tract caused by *Giardia, Campylobacter, Shigella, Salmonella,* enterovirus and rotavirus.[20] Furthermore, humoral immunodeficiencies are characterized by an increased risk of autoimmune diseases, granulomatous complications, lymphocytic infiltrates in the lungs, lymphoproliferative complications and (hematological) malignancies.[20]
Secondary immunodeficiencies are acquired throughout life, originating outside the immune system. They may be induced for example by the use of corticosteroids, immunomodulating or antiepileptic drugs, and underlying conditions, hematological malignancies or malnutrition and may be transient.[21, 22]

Common Variable Immunodeficiency (CVID) is the most common primary immunodeficiency. There are no precise data on its prevalence, but it has been estimated at between 1:10.000 and 1:100.000 of the global population by the International Union of Immunological Societies (IUIS) Scientific Committee.[23] Even with the highest estimated prevalence, CVID and thus other immune deficiencies are rare. Overall, general practitioners have low suspicion of immune deficiencies upon clinical presentation. This is one of the factors contributing to a 'diagnostic delay' of PIDs. CVID is diagnosed six to eight years after presentation of first symptoms on average.[20] This delay in diagnosing and consequently in initiating adequate treatment can lead to severe and irreversible organ damage, such as the development of bronchiectasis as a result of recurrent respiratory infections.[20]

1.1.4 Medicinal treatment with human normal immunoglobulin at Erasmus MC

An optional choice of treatment for patients with primary or secondary immunodeficiency at Erasmus MC is substitution therapy with human normal immunoglobulins.
Administration of human normal immunoglobulins offers broad-spectrum passive protection to recipients. Besides substitution therapy, another indication for the administration of IVIg is immunomodulation in autoimmune diseases. In autoimmune diseases, the immune system attacks the healthy cells of your body. Immunomodulation can be applied to regulate the immune system's activity and obtain a state of *no evidence of disease activity* (NEDA) for the autoimmune disease.

Patients who receive immunoglobulins for the first time, have switched to a different product or have had a long period since the previous administration are clinically treated at least twice. Provided the clinical treatments proceed without complications, all subsequent treatments take place at home through a specialized home care organization, ZorgFront. Considerations to switch to care at home include making room in the hospital for other patients and minimizing the number of hospital visits for patients with a weak immune system since hospitals are a major source of pathogens.

Optional forms of administration are intravenous or subcutaneous administration. This thesis focuses on the administration of intravenous immunoglobulins (IVIg). The guideline for administering immunoglobulins as maintained at Erasmus MC is 0.4 gram (g) per kilogram (kg) body weight for patients with primary immunodeficiencies and 1 g per kg body weight for patients on immunomodulating therapy every four weeks. Infusion fluid has a concentration of 5 g per 100 milliliter (mL) and a maximum flow rate of 150 mL per hour or a concentration of 10 g per 100 mL and a maximum flow rate of 75 mL per hour, depending on the manufacturer.

To put this in perspective, a patient receiving immunomodulating therapy weighing 70 kg should receive 70 g of immunoglobulins. This will take approximately 9.3 hours to infuse. After four weeks, the donated immune cells no longer provide sufficient protection. This treatment is lifelong.

In rare cases, administration of IVIg can cause anaphylaxis in reaction to the IgE-mediated nature of the medication. Anaphylaxis is a severe, potentially life-threatening allergic reaction. This can also happen in patients who have tolerated previous treatments well. Because of this minor but impactful risk, a home nurse is present during the entire administration. The nurse connects the patient to the infusion line and monitors him/her by measuring his/her vital parameters at every increment of the inflow rate and every bottle change. After all the fluid has been infused, the nurse flushes the infusion line and disconnects it from the patient.
The department of immunology at Erasmus MC has a patient population of approximately 225 patients who receive monthly administration of IVIg at home.

1.3 Thesis Motivation

To cope with the increasing need for care and decreasing availability of healthcare personnel at the same time, we are in need of a national (and global) transition to make the healthcare system sustainable for the future. Administration of IVIg at home for patients with immunodeficiencies is an example of a therapy that currently requires a significant amount of nursing staff in relation to the number of patients receiving the treatment. Patients are 1-on-1 assisted by a home nurse for the total administration duration, where nine hours is more commonly the norm than the exception. NRCRM of vital signs of these patients during administration could potentially offer a solution by allowing home nurses to make better use of their time, thus enabling them to treat the same number of patients with fewer staff members. The goal of this pilot study is to test monitoring system functionality, evaluate user experiences and identify challenges and bottlenecks of NRCRM of vital signs of patients during administration of IVIg at home. As a result, this thesis aims to contribute to the development of best practices for patient care at home in general and for the administration of IVIg at home specifically.

2. Methods

2.1 Study Population

Patients from the department of immunology at Erasmus MC who receive intravenous immunoglobulin (IVIg) at home were evaluated for inclusion. Eligibility criteria for participation were 1) age ≥ 18 years 2) no history of problematic administration of IVIg 3) attendance of a home nurse who is a project participant 4) willing and able to give informed consent to participate. Patients were first contacted by a clinical nurse specialist and were sent a custom-made information folder containing a more detailed description of the study procedure afterward (*Appendix A*).

2.2 Personnel Selection and Training

Other key participants in this study were home nurses from ZorgFront and the telenurses monitoring the patient from within the hospital. The home nurses from ZorgFront have been administering IVIg to the study population for many years. Patients are generally assigned to the same nurse for every administration. Therefore, nurses were automatically selected upon patient inclusion, provided they agreed on participation. Nurses were not asked to take on any action besides their usual activities during the administration but to follow their standard care protocol. The role of telenurse was fulfilled by a nurse specialist and two medical students who took turns. They were located at a remote site at Erasmus MC. Use of the software and study protocols were explained to them and a test simulation was performed before the start of the study.

2.3 Study Protocol

For this study, vital signs of patients receiving IVIg at home were monitored remotely by a telenurse from within the Erasmus MC in addition to the usual monitoring procedure performed by the home nurse. Both patients and home nurses did not have to deviate from their usual way of working and were not subjected to additional actions. Communication between the home front and the telenurse took place via an additional person who was present during administration at home, further referred to as the attendant. Siilo chat was used for communication between the two. No personal information about the patients was used in this study. Hence, data was transmitted and analysed anonymously.

Pre-administration

Upon arrival at the home of a study participant, arrival was confirmed between the attendant and telenurse. Hereafter, the attendant performed various actions. First, the device to collect and transmit vital signs data, further referred to as the DVX Device, was connected to the main power in <10 meters proximity of where the patient would receive the treatment (general range of Bluetooth connection). Then, after the infusion cannula was inserted by the nurse and before the administration had started, the patient was equipped with the wearable sensors. Installation of the equipment was confirmed by the attendant over Siilo.

At the same time, the telenurse set up the software, i.e. connecting the software to the correct DVX Device, creating a new test patient and applying the correct alarm template. Established connection between wearable sensors and the monitor (via the DVX Device) was confirmed between attendant and telenurse over Siilo. Siilo shows time indications (hh:mm) per message, acting as a stopwatch simultaneously.

During administration

As soon as the treatment had started, protocol for the attendant included the registration of time and details in case of the following events:

- Any action performed by the home nurse as a part of their usual working procedure
- Any action performed by the home nurse to solve an infusion-related problem
- Any action performed by the patient other than sitting or lying down

- Disconnection between patient and (one of) the wearable sensors
- Disconnection of the DVX Device from the main power
- Failure of (one of) the wearable sensors
- Failure of the DVX Device

In case of one of the last four types of events, the problem was solved if possible.

Protocol for the telenurse included getting in contact with the attendant in case of the following events:

- Lost connection between one of the wearable sensors and the DVX Device
- Lost connection between the DVX Device and the monitor
- Any alarm

In case of one of the first two types of events, the attendant at home solved the problem, if possible. As nurses were asked to follow their standard care protocol and not take on any action besides their usual activities, alarm generation by the software did not directly lead to an intervention at home. Whether to decrease the infusion rate or discontinue the treatment was at the discretion of the home nurse. In case of an alarm, the attendant would observe at home to find a cause for the event. Details of the alarm and observations at home were described by the telenurse and attendant on Siilo.

Post administration

After the last bottle was completely infused, the infusion line was flushed with 0,9% NaCl to ensure all the medication left in the infusion line would reach the patient. After flushing, the wearable sensors were removed from the patient, the home nurse removed the infusion cannula and the end of treatment was confirmed between attendant and telenurse.

Afterward, a custom-made questionnaire was sent to both patient and home nurse. Questions addressed overall attitude toward the transition to NRCRM and comfort level of the wearable sensors for the patients in specific. Questions and responses are in Dutch (*Appendix C)*. Responses were acquired using LimeSurvey, a tool for digital questionnaires that meets conditions as required by the Erasmus MC.

2.4 Outcome Measurements

Outcomes regarding system functionality include:

- Amount, duration and nature of no data alarms
- Amount and duration of threshold alarms given one alarm template
- Temperature sensor response time

Outcomes regarding user experience of both nurses and patients include overall attitude towards the transition towards NRCRM of vital signs of patients during administration of IVIg at home and additionally for the patients the comfort level of the wearable sensors.

Furthermore, challenges and bottlenecks associated with this transition were identified.

2.5 Monitoring System

The monitoring system used in this study is called Dyna-Vision Version X Telemonitoring System (Techmedic Development International B.V., The Netherlands). The system consists of three components:

1) DVX Device to collect and transmit vital signs data
2) DVX Server to record patient details, alarm settings, vital signs and other information
3) DVX Monitoring software, including an interface to monitor the vital signs in near real-time

An overview of the monitoring system is provided in
*Figure **2***.

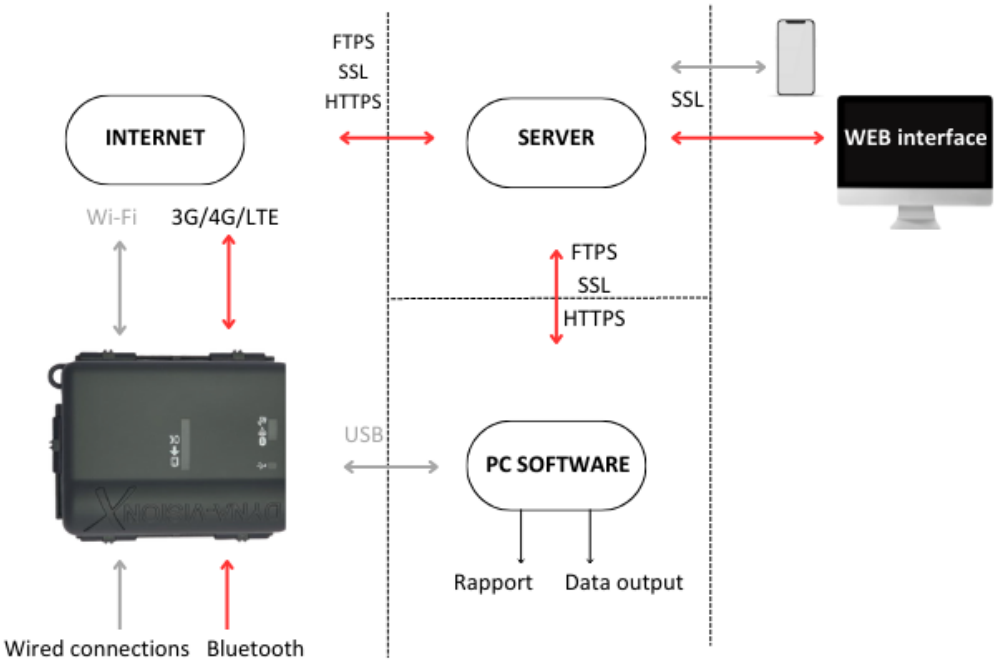


Figure 2 Dyna-Vision Version X Telemonitoring System (Techmedic Development International B.V., The Netherlands) overview. This overview illustrates how patient data is transferred from the patient to the monitoring site via its communication network. FTPS, SSL and HTTPS indicate protocols to ensure connection security. The system used in this study provides multiple options for data transfer. For this study, the system was used as indicated by the red arrows.

2.5.1 DVX Device

The DVX Device acted as a modem between the measured vital sign data and the DVX Server. After vital signs were recorded by third party products, they were transmitted via Bluetooth to the DVX Device collected on the device's SD card. At the same time, the DVX Device transmits the data in near real-time to the DVX Server using cellular transmission. In optimal situations, the data transmission delay is less than one second. The most important specifications of the DVX Device are listed in *Table B* in *Appendix* B.

Vital sign data was recorded with three third party products, referred to as wearable sensors. Vital signs measured in this study include respiratory rate, heart rate (HR), blood oxygen saturation (SpO_2), body temperature and blood pressure (BP). Device characteristics of the wearable sensors are described in *Table B* in *Appendix* B. See *Figure 3* for a photograph of the wearable sensors and the DVX Device. According to the study protocol, patients had to wear the sensors for the entire duration of the administration. However, patients could stop wearing the sensors for any reason if they wished to do so without any consequences.

2.5.2 DVX Server

The server uses a service that receives all the data transmitted by the DVX Device. It uses a database to record (test) patient details, alarm settings and vital signs. The server is an integral part of the monitoring system. When connection between DVX Device and Server is poor, a transmission delay may occur. However, there is no data loss as the device uses internal buffers to store data packages, which are sent when the connection improves.

2.5.3 DVX Monitoring system

The software provides a wireless monitoring system for intermittent and continuous collection of physiological data in home and healthcare settings and for normal daily activities. It includes multiple applications and features. The application used in this study is general patient monitoring with near real-time telemetry to provide vital information about patients of all ages. Relevant features of the monitor for this study include:

- Creating (test) patient records
- Collect data from third party products for display
- Reporting collected data

The software was installed on a computer at Erasmus MC as a web interface (*Figure 4*). The main screen of the monitoring system is divided into four categories: normal, low, medium and high, indicating the level of patient deterioration. Various DVX Devices, which represent patients, could be connected to the software simultaneously. Connected DVX Devices would show up in the software as widgets (*Figure 4*) in the category representing the physical state of the patient. Shifting between categories occurs near real-time, depending on pre-set rules. Pre-set rules for shifting are included in the alarm template. Shifting outside the 'normal' category generates an alarm, including a sound and indication label.
Based on the associated potential risk to patients, the Medical Device Regulation (MDR) classifies this software as class IIb medical software.

Alarm template

The same alarm template was applied to every study participant. Two types of alarms are distinguished, namely 1) when no data is received by the monitor, referred to as a 'no-data alarm', and 2) when pre-set threshold values are transcended, referred to as a 'threshold alarm'. Minimum duration for an alarm to break through was set at 10 seconds.

A no-data alarm is generated when no input data is received by the software. This is caused by a connection failure somewhere in the system. Two types of connection within the system are distinguished, namely 1) the Bluetooth connection between the wearable sensors and the DVX Device and 2) the cellular connection between the DVX Device and the server. Failure of only the first type of connection will generate a no-data alarm and only if the failure persists longer than the minimum duration time. A no-data alarm was automatically categorized as high risk. In case of failure of the second type of connection, the software does not receive any input of vital signs from the server. This does not yield any alarm, because for the system it appears as though no monitoring is taking place. In the software, the patient widget would stop showing the pictogram indicating server connection. During this type of failure, the patient is not monitored and thus left unsupervised.

A threshold alarm is generated when a vital sign parameter, measured with the wearable sensors, transcends a pre-set threshold value. Threshold alarms were generated upon seven different diagnoses:

- Tachycardia (increased heart rate)
- Bradycardia (decreased heart rate)
- Hypoxia (decreased blood oxygen saturation)
- Hypothermia (decreased body temperature)
- Hyperthermia (increased body temperature)
- Systolic hypotension (decreased systolic blood pressure)
- Systolic hypertension (increased systolic blood pressure)

Threshold alarms were categorized as low-, medium- or high-risk, depending on the severity of the diagnosis. As a result, the monitoring system was set to generate a threshold alarm in 21 different situations. Threshold values used in this study are listed in *Table* .

2.6 Data Analysis

Quantitative analysis of the vital sign data was performed using Matlab version R2022b (Mathworks, USA) and Microsoft Excel. Missing values were not imputed. Variables were reported as mean ± standard deviation (SD). Questionnaire responses were reported as numbers.

Table 3 Threshold values

Parameter	*Low*		*Medium*		*High*	
Tachycardia (bpm*)	91	100	101	110	111	200
Bradycardia (bpm*)	53	55	51	52	0	50
Hypoxia (%)	90	93	85	89	0	84
Hypothermia (°C)	33	34	32	32	0	31
Hyperthermia (°C)	36.5	36.9	37	37.5	37.6	42
Systolic hypotension (mmHg)	90	100	80	89	0	79
Systolic hypertension (mmHg)	145	160	161	180	181	250

*bpm = beats per minute

Figure 3
Left: Omron EVOLV HEM-7600T-E (BP)
Middle (upper): Nonin 3150 WristOx2 Pulse Oximeter (HR and SpO_2)
Middle (lower): Temp Pal STP-MB01-1 (Temperature)
Right: DVX Device (also including wire and plug)

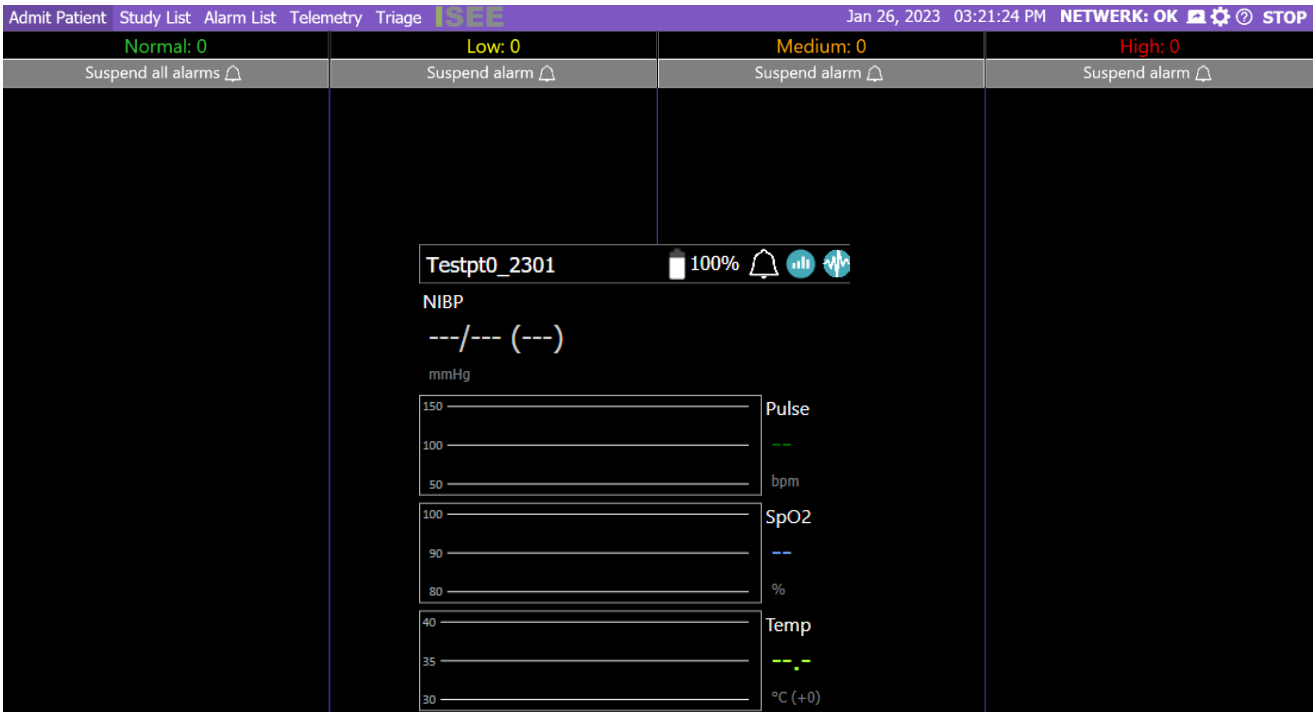


Figure 4 Software user interface (main screen) including patient widget.
The widget is enlarged for visibility in this report. In the actual web interface, the patient widget is smaller compared to the main screen, fitting in the risk category columns.

3. Results

3.1 Patient Characteristics

A total of 10 monitoring sessions were performed on ten patients who provided consent for participation. Baseline characteristics of the study population are shown in *Table 1*. Treatment products for all patients have a concentration of 10 g/100 mL and a maximum infusion rate of 75 mL/h. One patient had a central venous catheter (CVC) and one patient had a port-a-cath (PAC) through which the infusion fluid was administered.

Table 1 Characteristics of the study population

Characteristic	*Value*
Gender	8/10 female
Age (years)	42 ± 12 *(mean ± SD)*
BMI (kg/m^2)	27.2 ± 7 *(mean ± SD)*
Indication for IVIg	7/10 primary humoral immunodeficiency 3/10 immunomodulation
Treatment product	4/10 Kiovig 4/10 Privigen 2/10 Nanogam

3.2 System Functionality

Total monitoring time was 50h17min with a mean administration time of 5h1min per patient. On average, it took 4min6sec to equip the patient with the wearable sensors and establish a two-way connection between patient and monitoring site. An example of representative raw data of the continuously measured vital signs is shown in *Figure 5*. Various events causing the monitoring system to generate an alarm are indicated in the figure. Frequency, duration and nature of both types of alarms are analysed below.

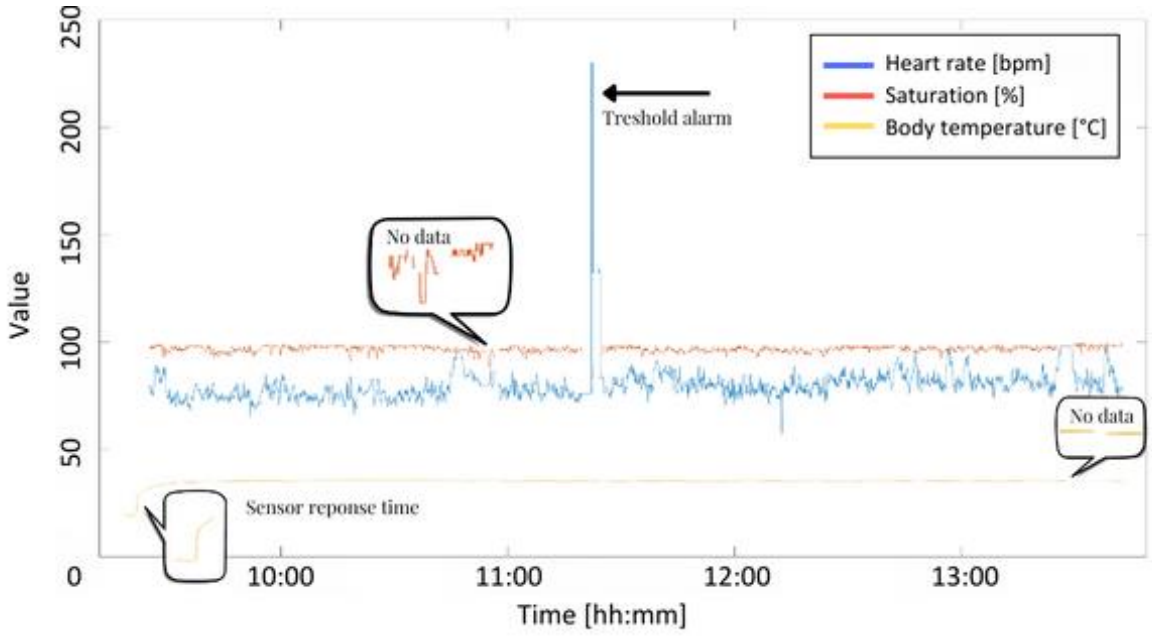


Figure 5 Raw vital sign data of random test patient

3.2.1 No-data alarms

Three cellular connection failures between DVX Device and the DVX Server were observed in total during this study. Nature of all failures was disconnection of the DVX Device from the main power in order to replace the device closer to the patient. No failures with unknown causes were observed.

In total, 546 no-data alarms were generated in this study. Total duration equals 53.9% of the total monitoring time. However, alarms can occur simultaneously. Mean number and duration of no-data alarms per patient per hour are listed in *Table (white columns)*. It was observed that SpO_2 losses occur most frequently and body temperature losses last longest on average.
No-data alarms in this study yield an alarm burden of 10.9 ± 4.8 (mean ± SD) alarms per patient per hour with a duration of alarms of 2min59sec ± 13min38sec (mean ± SD).

A certain type of no-data alarm was marked as non-physiological. These alarms do not reflect the physical condition of the patient. In other words, they do not indicate stagnated vital signs and their origin is explicable. On the other hand, the origin of the remaining no-data alarms could not be confirmed and might be related to stagnated vital signs of the patient. Observed natures and occurrences of non-physiological no-data alarms are listed in *Table .*

Exclusion of the non-physiological no-data alarms results in a total of 493 no-data alarms. Total duration equals 47% of the total monitoring time. Impact on the number and duration of alarms per parameter is listed in the blue columns of *Table .* Analysis suggests that the mean number and duration of alarms are barely impacted when excluding the non-physiological no-data alarms. From *Table* it is observed that temporary disconnection of the *Nonin 3150 WristOx2 Pulse Oximeter* (Nonin Medical B.V., The Netherlands) in order to use the toilet, wash hands or prepare food plays a part in the generation of non-physiological no-data alarms.

No no-data alarms were generated for systolic hypo- or hypertension since this measurement is only a snapshot and data is received nor monitored every second.

Table 5 Number and duration of no-data alarms

Parameter	*Number of alarms per patient per hour (mean ± SD)*		*Duration [mm:ss] (mean ± SD)*	
	All alarms	*Without non-physiological alarms*	*All alarms*	*Without non-physiological alarms*
Heart rate (bpm)	0.6 ± 0.6	0.4 ± 0.6	04:02 ± 06:42	03:05 ± 07:47
Saturation (%)	5.9 ± 2.7	5.2 ± 2.9	00:48 ± 02:28	00:34 ± 02:11
Body temperature (°C)	4.3 ± 3.1	4.3 ± 3.1	05:47 ± 20:56	05:37 ± 20:53
Total	10.9 ± 4.8	9.8 ± 5.3	02:59 ± 13:38	02:52 ± 14:10

Table 6 Non-physiological no-data alarms

	Nature of non-physiological no-data alarms	*Occurrence (/total amount of no-data alarms)*
Heart rate (bpm)		*12/31*
	Sensor temporarily disconnected to use toilet	4
	Sensor temporarily disconnected to wash hands	1
	Sensor temporarily disconnected to eat	2
	Dead battery	3
	DVX Device replacement	2
Saturation (%)		*38/297*
	Sensor temporarily disconnected to switch finger	2
	Sensor temporarily disconnected to use toilet	17
	Sensor temporarily disconnected to wash hands	1
	Sensor temporarily disconnected to eat	11
	Finger is not fully inserted into the case	2
	Dead battery	3
	DVX replacement	2
Body temperature (°C)		*3/218*
	Sensor temporarily disconnected to press the on/off button	1
	Sensor temporarily disconnected to switch to the chest	1
	Dead battery	1
Total		*53/546*

3.2.2 Temperature sensor response time

One concern for the NTC thermistor component of the *Temp Pal STP-MB01-1* (iWEECARE Co., Ltd., Taiwan) is stabilization of the measurement after the first application on the patient's body. The manufacturer states it requires up to 20 minutes to reach stable reading of the actual body temperature without further specification on the definition of stable reading.

A typical course of the sensor observed during monitoring in this study is visualized in *Figure* **6**. In this study, the time to reach stable reading is called the sensor response time and is defined as the time to reach 99.3% of the step change in temperature. The step change is the difference between the measurement of the wearable sensor at baseline ($T_{TempPal,baseline}$) and the full output it should reach eventually. The full output for all patients is considered the tympanic temperature at baseline, $T_{Tymp,baseline}$, measured by the home nurse (accuracy ± 0.2°C).

As seen in *Figure 6*, $T_{TempPal,baseline}$ and $T_{Tymp,baseline}$ are 19.1 ± 0.05°C and 36.7 ± 0.2°C respectively. Step change is computed by:

$$Step\ change = T_{Tymp,baseline} - T_{TempPal,baseline}$$
$$= 36.7 \pm 0.2\ °C - 19.1 \pm 0.05°C$$
$$= 17.6 \pm 0.25\ °C$$

99,3% of the step change is reached at $T_{TempPal,99.3\%}$:

$$T_{TempPal,99.3\%} = T_{TempPal,baseline} + step\ change \times 99{,}3\%$$
$$= 19.1 \pm 0.05°C + (17.6 \pm 0.25°C \times 99.3\%)$$
$$= 36.6 \pm 0.3°C$$

The maximum temperature reached by $T_{TempPal}$ was only 35.7 ± 0.05°C after 1h22min6sec.

For only 3/10 patients $T_{TempPal,99.3\%}$ was reached with a mean sensor response time of 1h28min45sec. This equals 29.6% of the mean administration time per patient.

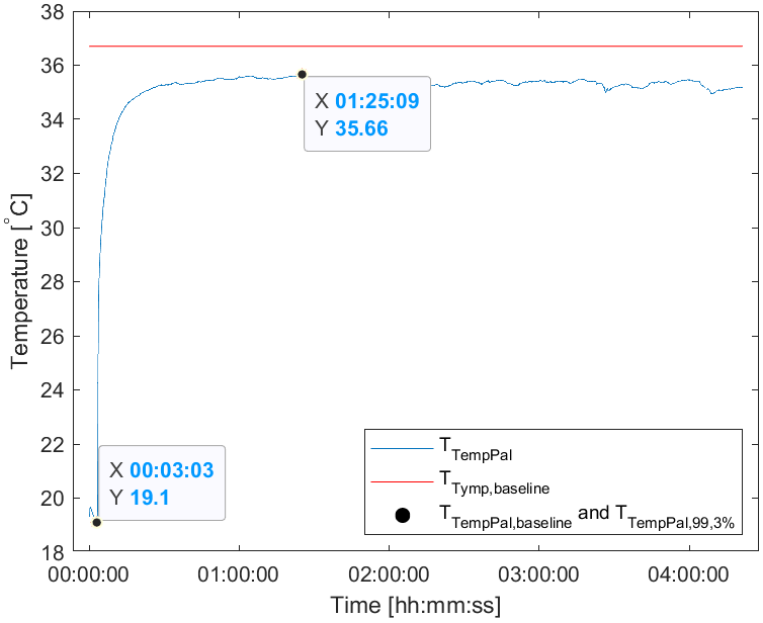


Figure 6 Temp Pal STP-MB01-1 (iWEECARE Co., Ltd., Taiwan) temperature sensor response time

3.2.3 Threshold alarms

In total, 854 threshold alarms were generated in this study, of which 614 low-, 173 medium- and 67 high-risk alarms. This amount is higher than the total no-data alarms. However total duration of threshold alarms covers a lower percentage of the total monitoring time, namely 35.4%. Again, alarms can occur simultaneously. Threshold alarms in this study yield an alarm burden of 17.1 ± 15.1 (mean ± SD) alarms per patient per hour with a duration of 1min12sec ± 3min (mean ± SD).

Mean number and duration of these alarms per patient per hour are listed in *Table 7 (white columns)*. At low-, medium- and high-risk levels, tachycardia, tachycardia and hypoxia alarms occurred most often, respectively. However, hypothermia alarms lasted the longest on average for every risk category. Relatively long duration of hypothermia alarms is most likely due to the time for the temperature sensor to reach stable reading, as described before. Therefore, mean number and duration of hypothermia alarms are also reported with the exclusion of any alarms triggered before the sensor achieved a stable reading *(Table 7 blue columns)*. Still, low hypothermia alarms last the longest on average compared to the durations of other alarms. Tachycardia alarms include one patient with outlying results of 173 low- and 76 medium-risk alarms, respectively.

Furthermore, *Table 8* includes an overview of the total occurrence of high-risk alarms per diagnosis and the percentage resolved within 2 minutes. These data were emphasized since it indicates how often the telenurse should escalate to the patient or emergency workers. A high-risk label could indicate deterioration of the patient. However, 2 minutes is an arbitrary cut-off value.

Three high-risk alarms for tachycardia were not resolved within two minutes. The alarms concern three different patients. One patient with an average HR of 82 bpm yielded an alarm for 2min30sec with an average HR of 113 bpm during this alarm. Another patient with an average HR of 80 bpm yielded an alarm for 2min29sec with an average HR of 142 bpm during this alarm. The last patient with an average HR of 77 bpm yielded an alarm for 2min21sec with an average HR of 138 bpm during this alarm. For all patients, the alarm was generated within the same minute as when the patient went to use the toilet. Furthermore, none of the alarms were preceded by a medium-risk alarm, but originated suddenly in just a few seconds.

Two high-risk alarms for hypothermia were not resolved within two minutes. Both alarms concern the same patient and occurred after stable reading was reached. Duration of the alarms was 3min20sec and 23min40sec. For this patient, not all raw data was successfully retrieved from the software, so severity of the temperature change could not be determined. From the observations from the attendant, there is no non-physiological explanation for the temperature increase. The patient felt well during the whole administration time and no alarm of another vital parameter was observed simultaneously. Both alarms were preceded by low- and medium-risk alarms of multiple minutes.

Table 8 High-risk threshold alarms resolved within two minutes

	Total amount of high-risk alarms	*Resolved within 2 minutes*
Tachycardia (bpm)	20	17/20
Bradycardia (bpm)	2	2/2
Hypoxia (%)	26	26/26
Hypothermia (°C)	6	4/6
Hyperthermia (°C)	0	-
Systolic hypotension (mmHg)	1	N/A
Systolic hypertension (mmHg)	0	N/A

Table 7 Number and duration of threshold alarms

Diagnosis	*Number of alarms per patient per hour (mean ± SD)*		*Duration [mm:ss] (mean ± SD)*	
	All alarms	*After temperature sensor stabilization*	*All alarms*	*After temperature sensor stabilization*
Tachycardia low	6.9 ± 10.3	-	00:32 ± 00:34	-
Tachycardia medium	1.9 ± 4.7	-	00:31 ± 00:34	-
Tachycardia high	0.4 ± 0.6	-	01:00 ± 00:48	-
Total	**9.3 ± 15.1**	**-**	**00:33 ± 00:35**	**-**
Bradycardia low	0.4 ± 1.3	-	00:19 ± 00:15	-
Bradycardia medium	0.0 ± 0.1	-	00:38 ± 00:25	-
Bradycardia high	0.0 ± 0.1	-	00:24 ± 00:03	-
Total	**0.5 ± 1.5**	**-**	**00:21 ± 00:15**	**-**
Hypoxia low	3.0 ± 2.3	-	00:38 ± 01:51	-
Hypoxia medium	0.8 ± 0.9	-	00:24 ± 00:11	-
Hypoxia high	0.5 ± 0.8	-	00:20 ± 00:14	-
Total	**4.3 ± 3.2**	**-**	**00:33 ± 01:32**	**-**
Hypothermia low	1.8 ± 2.4	0.7 ± 0.9	04:44 ± 05:56	05:39 ± 05:54
Hypothermia medium	0.6 ± 1.0	0.3 ± 1.0	04:57 ± 07:03	05:17 ± 08:34
Hypothermia high	0.4 ± 0.4	0.1 ± 0.4	03:48 ± 05:36	04:56 ± 09:15
Total	**2.8 ± 2.9**	**1.2 ± 1.9**	**04:40 ± 06:07**	**05:28 ± 06:59**
Hyperthermia low	0.0*	0.1*	00:41*	00:41*
Hyperthermia medium	0	0	-	-
Hyperthermia high	0	0	-	-
Total	**0.0***	**0.0***	**00:41***	**00:41***
Systolic hypotension low	0.0*	-	-	-
Systolic hypotension medium	0	-	-	-
Systolic hypotension high	0.0*	-	-	-
Total	**0.0 ± 0.1**			
Systolic hypertension low	0.0*	-	-	-
Systolic hypertension medium	0	-	-	-
Systolic hypertension high	0	-	-	-
Total	**0.0***			
Total	**17.1 ± 15.1**	**15.4 ± 14.7**	**01:12 ± 03:00**	**00:54 ± 02:27**

* No SD was reported since only one patient showed a result

3.3 User Experiences

The following question and statement were used to assess the overall attitude of patients (n=7) and home nurses (n=6) regarding the transition towards NRCRM:

Question for patients: Are you open to telemonitoring during administration at home without the attendance of a home nurse?
Response: yes (2x) - maybe (2x) - no (3x)

Statement for nurses: I have a positive attitude towards the potential transition towards NRCRM during administration without the attendance of a home nurse.
Response: strongly disagree (1x) – disagree (2x) – neutral (2x) – agree (0x) – strongly agree (1x)

Additional questions were asked to obtain more insight into the reasoning behind their attitudes (*Figure **7** 7 and Figure **8**8*) and space was left for free speech.
In general, attitudes of both patients and nurses toward the transition to NRCRM are mixed. From *Figure **7**7*, it is possible that patients require more clarification on the societal significance of addressing the labor shortage in healthcare. However, the figure does not provide conclusive evidence to distinguish whether patients do not see an added value for the societal interest due to a lack of knowledge or differing opinions on this topic. Furthermore, amongst both patients and nurses, concerns exist around patient safety in case of complications and emergencies. Two patients added that they highly value the company of an attending home nurse. Additionally, nurses emphasize that some patients are not eligible for unattended treatment.
In addition to the figures, five patients say to be open to being educated on taking on tasks of the home nurse, such as handling the pump and removing the cannula.
Lastly, *Table 9* shows how the patients valued the comfort level of the wearable sensors.

3.4 Identified Challenges and Bottlenecks

A total of 30 challenges and bottlenecks in the transition to NRCRM of vital signs of patients during administration of IVIg at home were identified. Identified items have been divided into pre-, during- and post-administration and not time-dependent on the administration. Furthermore, items were assigned to a category (and subcategory). Categories, including number of identified items, are:

- Monitoring system **subcategories**: software (4) wearable sensors (7)
- Logistics **subcategories**: timing and delay (4), equipment (1), emergency (1)
- Change management **subcategories**: overall attitude (1), working methods (7)
- Information technology (2)
- Patient safety (3)

Furthermore, items were labelled as process, system or people, indicating the type of problem. This could give direction for tackling the challenge or bottleneck in the next phase of implementation.

An overview, including a description of the identified items, is provided in *Appendix D*.

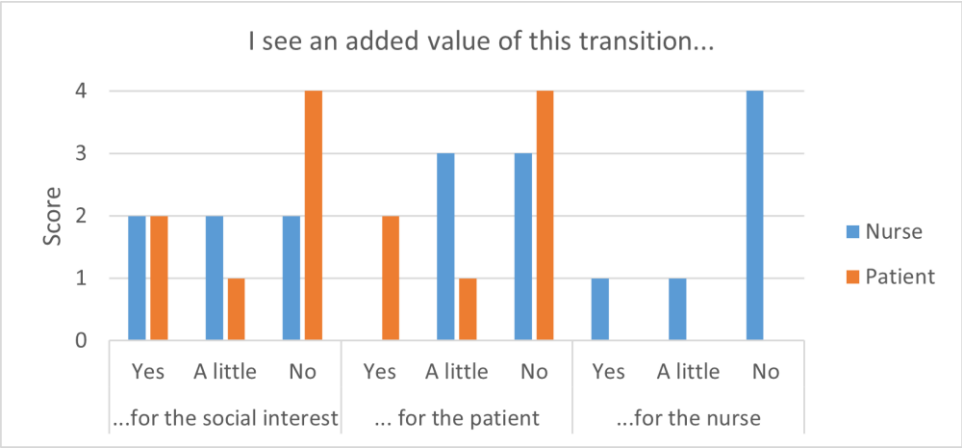


Figure 7 User experiences home nurse and patients - overall attitude

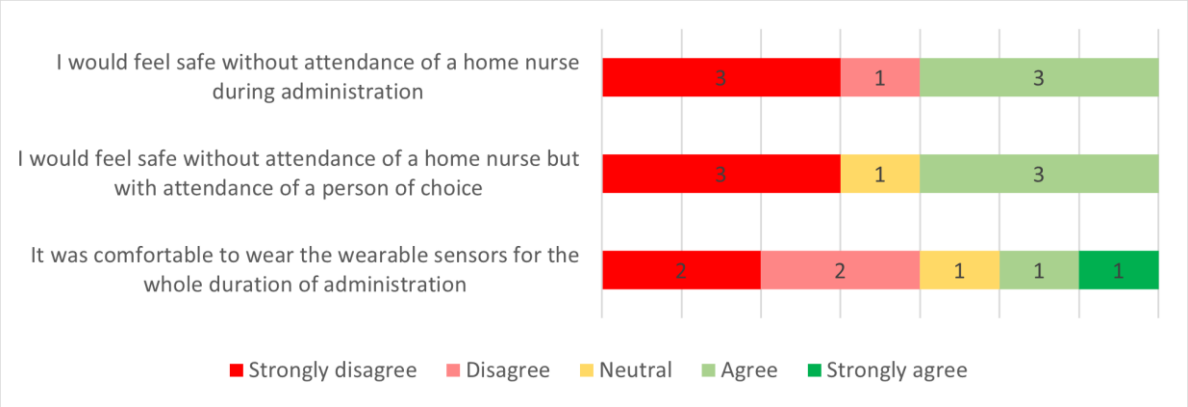


Figure 8 Patient experiences - overall attitude

Table 9 Patient experiences - comfort level wearable sensors

Device	*Comfortable equipment during the total duration of administration*	*Additional Remarks*
Omron EVOLV HEM-7600T-E (OMRON Healthcare Co., Ltd., Japan)	5/7 patients	Two uncomfortable patients found the sensor obtrusive in preparing food, eating, drinking and using the toilet
Nonin 3150 WristOx$_2$ Pulse Oximeter (Nonin Medical B.V., The Netherlands)	2/7 patients	4 uncomfortable patients mentioned that the material of the finger casing was irritating as it caused the finger to sweat quickly 3 uncomfortable patients mentioned it limited them in using their hands for typing and using the toilet
Temp Pal STP-MB01-1 (iWEECARE Co., Ltd., Taiwan)	6/7 patients	One uncomfortable patient mentioned the sensor was not sufficiently adhesive to the body

4. Discussion

4.1 Interpretation of Results

This study aimed to test a specific monitoring system functionality, evaluate user experiences and identify challenges and bottlenecks in near real-time continuous remote monitoring of vital signs of patients during administration of intravenous immunoglobulins at home.

4.1.1 System Functionality

Outcomes on system functionality were divided into no-data alarms, response time of the temperature sensor and threshold alarms. As an example, 5.9 ± 5.2 (mean ± SD) no-data alarms for saturation per patient per hour were observed with a duration of 48sec ± 2min28sec (mean ± SD) per alarm. To put this in perspective, an occupancy of six patients per telenurse would yield 35 alarms per hour with a total duration of 28min on average, resulting in a part-time burden of only this type of alarm. It must be emphasized that alarms of different patients could occur simultaneously. However, this is accompanied by the challenge of escalating to multiple patients at the same moment.

The no-data alarms could partly be explained by non-physiological origin. All sorts of patient activities were observed during administration, e.g. leisure activities such as gaming or crafting, playing with pets or sleeping. These kinds of activities are likely related to the occurrence of no-data alarms, e.g. it allows the *Nonin 3150 WristOx2 Pulse Oximeter* (Nonin Medical B.V., The Netherlands) to get dislocated and disrupted very easily. However, not all remaining no-data alarms could be explained because of these activities and above all, normal daily activities should not interfere with the measurements.

Standard deviations higher than mean values were observed, suggesting the occurrence of no-data alarms is not normally distributed over all patients and includes outliers. This is most likely attributed to patients creating their own routine during administration and thus being little or more active. Accurate monitoring of vital signs during different activities and thereby lowering the burden of alarms is of great importance before further implementation of NRCRM in this field. A suggestion for improvement is using more robust wearable sensors, of which measurements do not interfere when performing normal daily activities. High interference of the measurements might be attributed to the fact that the sensing part of the *Nonin 3150 WristOx2 Pulse Oximeter* (Nonin Medical B.V., The Netherlands) is located around the tip of the index finger and gets dislocated easily since the index finger is a body part involved in many types of activity. Therefore, a device measuring both HR and SpO_2 located at, for example, the earlobe might be considered.[24] At the same time, non-physiological no-data alarms could be avoided since a device at the earlobe does not require temporary disconnection, e.g. to wash hands.

The duration of no temperature data alarms is approximately eight times longer on average than for saturation. Furthermore, the nature of these alarms remains inexplicable. Along with the mean sensor response time covering 29.6% of the total administration time and the occurrence of not reaching full temperature output, this sensor seems unacceptable for NRCRM in the field of this study. In a report by TDK group, a leading electronic components company, it is stated that thermal response time of a NTC thermistor is mainly influenced by its design, mounting configuration and the environment it will be exposed to.[25] Therefore, it is advised to use a sensor with a different design or mounting configuration, which allows stable reading within approximately five minutes. Above all, maintaining a stable Bluetooth connection through clothing is required.

It should be noted that zero burden of no-data alarms is highly unlikely, considering unforeseen patient discomfort, requiring temporary disconnection of a device, or failure of power supply.

A total of 854 threshold alarms were generated in this study. This equals an alarm burden of 17.1 ± 15.1 (mean ± SD) alarms per patient hour with a mean duration of 1min12sec ± 3min (mean ± SD) per alarm.

To put this in perspective, an occupancy of six patients per telenurse would yield 102 alarms per hour with a total duration of 2h2min24sec on average, resulting in an alarm overload of only this type of alarm. The escalation protocol should include rules for whether or not to escalate to the patient or emergency workers in case of a threshold alarm. For example, if protocol demands to escalate to emergency workers for high-risk alarms persisting longer than two minutes, this study would have required escalation five times (*Table*). However, in this study, three of five high-risk alarms persisting longer than two minutes did not reflect patient deterioration in terms of anaphylaxis. The alarms were most likely triggered by using the toilet. Escalation protocols should include clear instructions on when and how to escalate and to whom to prevent escalation to emergency responders in non-life-threatening situations and to enable appropriate care to the patient when necessary.

In addition to an accurate escalation protocol, the alarm burden must remain manageable to guarantee patient safety. Two solutions concerning the design of the alarm template are proposed that may address this challenge. Firstly, set threshold values for alarms as percentages of baseline measurements so that vital sign data are not compared to absolute numbers but serve as their own reference. Secondly, alarm templates could be designed for every patient individually. Standard deviations higher than the mean (*Table 7*) suggest that the occurrence of threshold alarms is not normally distributed and may include outliers. Patient-specific templates are expected to decrease the number of threshold alarms and outliers.

Overall, the outcomes concerning system functionality observed in this study mostly reflect the functionality of the wearable sensors. The amount, duration and nature of alarms were evaluated, as well as the specific functionality of the temperature sensor. However, the wearable sensors are third-party devices and are no integral part of the DVX monitoring system. The preceding interpretation of results suggests room for improvement regarding only these wearable sensors. This suggestion is supported by results from the questionnaire concerning the comfort level of the *Nonin 3150 WristOx$_2$ Pulse Oximeter (Nonin Medical B.V., The Netherlands).* 4/6 patients found the material of the finger casing irritating and 3/6 patients mentioned it limited them in using their hands, e.g. for typing and using the toilet. For financial and durability reasons, it is advised to select wearable sensors that do not have disposable components that require replacement after each administration.

Regarding the DVX Monitoring system, no inexplicable connection failures between the DVX Device and the DVX Server were observed. Therefore, a cellular connection, as applicable in this study, is advised over a Wi-Fi connection. Connection over Wi-Fi is too reliant on the individual situation of a patient. However, ensuring priority on the cellular network is recommended upon further implementation. Any connection failure must be prevented as it is at the expense of patient safety. No errors or signal delays in the software occurred during any of the administrations. Overall, the monitoring system used in this study, regardless of any third-party products, showed flawless performance regarding connectivity, which is a core requirement in the applications of NRCRM in the application of this study.

4.1.2 User Experiences

Questionnaire responses regarding overall attitude towards the transition to NRCRM showed mixed results for nurses and patients. However, regardless of this attitude, almost all responders expressed concerns about patient safety and what would happen if immediate assistance was required at home.

It could be debated whether these results can be generalized with a sample size that does not comprise the total population of nurses. On the other hand, it is expected that the population of home nurses attending during administration of IVIg is homogenous, making it likely that responses are saturated. Three nurses show to have a negative attitude towards the transition. Besides patient

safety concerns, attitude could partially be explained because they do not believe in the added value of the concept. A suggestion to address this issue is to better inform involved employees about the bottlenecks of the current working methods and explain why these are no longer sustainable. This could be done by organizing a real-life event or using online tools.
Regarding the patients, it is expected that the population of patients receiving IVIg at home is a heterogenous group with different ages and comorbidities. With a sample size of seven patients, responses in this study are not saturated. Therefore, the results of the questionnaire are not generalizable. Nevertheless, these results show that patients' attitudes might differ among the total population. The questionnaire of this study can be used to conduct additional research on patient attitudes with a bigger sample size.

4.1.3 Identified Challenges and Bottlenecks

The design and implementation of a NRCRM system and workflow comprise more aspects than just system functionality. After system functionality is improved and considered acceptable, a workflow has to be constructed to monitor patients simultaneously. It is indisputable that the design of a new workflow is accompanied by challenges to overcome and bottlenecks to tackle. Through intensively scanning pre-, during and post-administration in this study, potential challenges and bottlenecks were identified. Identified items apply to a concept of workflow design, visualized in *Figure **9**9.*

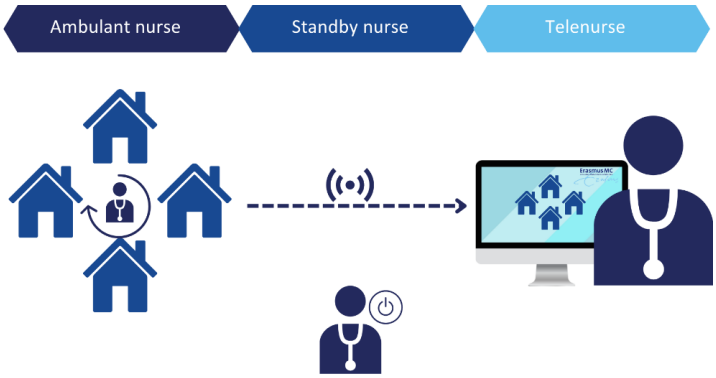


Figure 9 Concept workflow

Identification and tackling of challenges and bottlenecks will contribute to the development of best practices for patient care in the specific field of IVIg at home. The ones which have not yet been addressed are discussed below per category.

Monitoring system
Challenges and bottlenecks concerning the monitoring system apply to the wearable sensors and the software.
In this study, blood pressure was measured intermittently rather than continuously. Detection mechanisms for continuous blood pressure measurement were found in literature[26], but relatively low performance and controversy regarding these techniques are described. Furthermore, an accurate detection mechanism does not directly equal eligibility for unsupervised home monitoring. Altogether, intermittent BP measurement seems the only feasible option at the moment, which does not yield real-time data on this vital parameter. In terms of patient safety, this is not preferred since a drop in blood pressure, possibly indicating anaphylaxis, could occur within minutes of exposure to an allergen.[27] However, it could be debated whether receiving continuous blood pressure data is a hard requirement since anaphylaxis is associated with more symptoms such as skin reactions, tissue swelling, weak and increased pulse rate, nausea, diarrhea and dizziness[28]. NRCRM, in combination with current sensor techniques, can provide continuous real-time heart rate data, offers the

possibility to consult about how the patient is feeling over a (video)call and allows additional snapshot measurement of blood pressure upon request. Whether this is sufficient for safe patient monitoring is to be decided by the team of medical doctors responsible for the patients.
Another point of attention is that the patient has limited freedom of movement when the DVX Device is restricted to main power and proximity of the patient <10 meters from the device is required. It is recommended to switch the DVX Device's power supply to a chargeable internal battery with a battery life of minimally twelve hours. The same recommendation applies for sustainable power consumption of the wearable sensors.
The last challenge concerns the common routine for patients to sleep during administration. However, there is no control of correct equipment of the wearable sensors when the patient is sleeping, which might result in false threshold alarms. This problem is expected to exist regardless of sensor positioning on the body. Another associated problem is that no blood pressure measurements will be performed while sleeping (as the patient should activate the Omron themself) unless the telenurse can operate the device remotely.

Patient safety
Another problem with a sleeping patient concerns alarm handling of the monitoring system and the pump. Communication during alarm handling of the monitoring system between telenurse and patient is of great importance as the telenurse wants to verify if the alarm they receive on the monitor reflects the condition of the patient. Alarm handling nor communication should be obstructed or delayed as it is at the expense of patient safety. Potential way of working could be to sleep with notifications of the communication device turned on so that the patient will be awakened when the telenurse wants to check in. Infusion pumps used in this study generate alarms in case of air molecules in the infusion line, increased pressure somewhere in the infusion line and indicating low battery. Not handling these alarms might jeopardize the patient's safety or cause delays.
When a pump alarm occurs while the patient is asleep, they will most likely not hear the beeping sound of the pump. Certain manufacturers of infusion pumps provide real-time insight into the pump data, including live pump errors, e.g. the BodyGuard 323 (Caesarea Medical Electronics, Israel) and the Mini Rythmic™ PN+ (Micrel Medical Devices SA, Greece). When the telenurse has real-time insight into this type of pump data, they could alarm the patient upon indication.
Two more identified items were categorized as concerning patient safety. An unambiguous and feasible escalation pathway for deteriorating patients should be designed. Earlier research describes a suggestion for such design[11], including clear instructions on when to undertake which action. Actions may include reaching the patient, an emergency contact or a medical doctor to determine a plan of action which may include activating an ambulance. The pathway should consist of multiple scenarios, e.g. when a stakeholder is not able to communicate, and the timing of all subsequent actions should result in timely troubleshooting.
Furthermore, regarding patient safety, control of the infusion rate is given up without an attending home nurse. Maximum rates are set to compromise between speed of infusion and side effects of the medication, as these are partly dependent on the infusion rate. However, patients may individually prioritize a shorter administration over the occurrence of side effects and therefore transcend the maximum infusion rate if they are the only ones in control of the pump.

Logistics
The first subdivision within the logistical challenge concerns timing and delay. This is elucidated with a situational analysis.
To realize NRCRM of patients at home, a team of personnel has to include 1) a telenurse 2) an ambulant nurse to start up infusion at the patient's house and 3) optionally an additional nurse who is stand-by to assist upon request while the ambulant nurse is visiting all patients. The goal of implementation is to shift the current 1-on-1 occupation of medical staff versus patients. In case of a three-member staff team, a minimum of four patients should be treated simultaneously to achieve this goal. Mean administration time per patient is five hours.

Situational analysis:

Assuming a workday lasts till 6 PM, administration of the last patient has to start at 1 PM. Taking the start of a workday at 8 AM, the ambulant nurse has five hours to prepare four patients for administration and travel in between. Equipment of patients with the wearable sensors took 4min6sec on average. Further preparations include inserting the infusion cannula, set-up of the infusion pump and ordering new medication for the patient (the latter task could potentially be handed over, e.g. to the head office of the home care agency). Estimated time for the ambulant nurse to spend per patient is 30 minutes. This does not include presence during the build-up phase of the infusion rate, which would take an additional hour. The build-up phase allows the body to get familiar with the entering fluid and to adjust maximum infusion rate if side effects, like headache, occur.
Considering the inclusion of four patients per monitoring session and 30 minutes of preparation time per patient, this leaves 2.5 hours for the ambulant nurse to travel between patients three times. This restricts the distance between patients to a 50-minute drive, assuming the nurse travels by car. Considering the locations of administration in this study, a 50-minute drive between patients is logistically feasible for certain combinations of patients.

Time indications described above are open to some margin. For example, real-life implementation is not restricted to the working hours used in this example and subgroups of patients living in the same region may have different mean administration times. Also, inserting the infusion cannula can be troubling and therefore time-consuming and traffic is always prone to delay. These factors have to be considered when constructing the logistic workflow. Also, workarounds for scenarios with delay have to be constructed.
In theory, multiple couples of ambulant and stand-by nurses could operate in different regions simultaneously, all connecting patients to the same telenurse. But regarding the burden of alarms resulting from this study, it is not yet advised to give responsibility over more than four patients per telenurse. Whether implementation will be efficient may vary per region.
Two more identified items were categorized as concerning the logistic aspect. The first one concerns home access for emergency responders in case the patient is home alone and not in a position to offer entrance to the house. An option giving most of control to the emergency responders is to invest in a key safe outside of the house of which the code is accessible by the telenurse. It would require strict authentication regulations in the system where this information is kept. The second point concerns storage of the infusion pumps. Currently, all home nurses from ZorgFront working with patients receiving IVIg possess an infusion pump which they bring to the patient for administration. Considering the proposed workflow, home nurses should possess at least four pumps. However, four pumps and casings take up significant space, which might be too much to store in private surroundings. Another suggestion is to attribute a pump to every patient.

Change management
Change management was subdivided into working methods and overall attitude towards the transition.
Currently, various working methods are performed by the attending home nurse during administration. In case of an absent home nurse, these actions must be eliminated or transferred to someone else, e.g. the patient, standby nurse or telenurse. Identified working methods include: increasing the infusion rate of the pump during the build-up phase, bottle change, undertaking action in case of subcutaneous infusion, alarm handling of the pump, flushing of the infusion line and removal of the cannula.
Increasing the infusion rate and changing bottles could be eliminated if applying workarounds. The same pumps as mentioned before, the BodyGuard 323 (Caesarea Medical Electronics, Israel) and the Mini Rythmic^{TM} PN+ (Micrel Medical Devices SA, Greece) (and possibly more), feature the option to

infuse according to a pre-set delivery schedule. This way, the pump does not require manual operation. Another option is to let the patient operate on the pump upon request from the telenurse. Disadvantage of this is that the patient is in control, which may lead to infusion rates that are clinically contraindicated.
Bottle change takes place when the infusion fluid is divided over multiple bottles. At least one bottle change was required for 4/10 of the patients in this study. This action requires some expertise since the entry of air molecules in the line should be avoided. An optional workaround is to work with bigger infusion bags, which no longer require changing. Transferring the infusion liquid from the separate bottles to the infusion bag should be done upon arrival at the patient's house before start of the administration. Additional preparation time is expected to be several minutes. Drawback is that bottles are provided with a number indicating the production badge. If a patient has anaphylaxis using this working method, it is impossible to determine the production badge inducing the anaphylaxis and thus, it is impossible to avoid bottles of this badge for future administrations.
Another point of attention is the complication of subcutaneous infusion. I.e. the cannula has dislocated outside the vein and infusion fluid is administered directly beneath the skin. This is associated with cold skin, pain and swelling around the place of insertion. Causing factors are primarily movement of the patient or tension on the infusion line. Required action is to stop administration and remove the cannula immediately. Patients have to be capable of doing this, even when experiencing pain. Hereafter, a new cannula can be inserted by the standby nurse.
Responsibility concerning alarm handling of the pump, flushing of the infusion line and removing the cannula could be transferred to the telenurse and patient. As mentioned, certain pumps currently on the market provide real-time insight into pump errors. The telenurse could manage error identification and assist the patient in troubleshooting over a (video)call. However, when using the bigger infusion bag instead of separate bottles, the amount of alarms from air molecules in the infusion line is expected to decrease since these bags do not require venting.
Flushing the infusion line withholds to plug the beginning of the infusion line into a new infusion bag containing 0.9% NaCl. This does not require any expertise. Removal of the cannula was already part of the standard procedure for some patients in this study. It withholds removal of the cannula and applying a bandage on the place of insertion, not requiring expertise either. Applying to all three actions described above, the standby nurse could always be requested to visit the patient and help to solve the problem.

Furthermore, (re)training of nursing staff is required upon implementation. Two new job descriptions for telenurse and standby nurse have to be created and the role of home nurse is shifted into the role of ambulatory nurse. The role of standby nurse is not expected to include other working methods than those a trained is already qualified for. The role of telenurse, however, will consist of completely new working methods, including communication and problem-solving with the patient remotely. Furthermore, it should be decided who qualifies for this new role. It is advised to allow trained nurses familiar with patients with immunodeficiencies for this role or retrain nurses with different specializations on how to interpret vital signs of patients during administration of IVIg and how to handle all types of alarms that can occur. The shift from home nurse to ambulatory nurse will most likely not require retraining since the same procedures as before have to be conducted, but the character of the job will change entirely.
Besides the practical challenge of educating patients in skills and (re)training nurses, a challenge also lies in the willingness to change of those involved.

Information Technology
If the Erasmus MC wishes to use applications (i.e. monitoring software) independently, it must take into account security requirements from existing laws and regulations[29].

For the security of personal data, the following laws and regulations are relevant:

1. *The General Data Protection Regulation (GDPR)*
   Measures to ensure a security level tailored to the risk include:
   - the pseudonymization and encryption of personal data;
   - the ability to ensure on a permanent basis the confidentiality, integrity, availability and resilience of processing systems and services;
   - the ability to timely restore the availability of and access to personal data in the event of a physical or technical incident;
   - a procedure for periodically testing, assessing and evaluating the effectiveness of the technical and organizational measures for securing the processing.

   The Dutch Data Protection Authority (AP), which is designated by law as the supervisory authority for the processing of personal data in the Netherlands, has developed a guideline (Guidelines, Security of personal data, February 2013) detailing information security requirements.

2. *The NEN standard 7510:2017, Information security in healthcare*
   This standard describes a large number of management measures for the security of information within healthcare. Some of these management measures are also applicable to the management and security of an application. Based on the aforementioned laws and regulations, several security requirements have been defined, which are classified into three categories. The different categories relate to the parties involved, the cloud provider, and the application itself.

The process to meet security requirements is expected to take up to six months or longer. Parallel to this process, contractual agreements should be discussed between involved parties. Also, internal system architecture should be designed. This includes for example service management and coupling with other applications, such as the electronic health record (EHR), if this is preferred.

For all categories of identified challenges and bottlenecks, more items could potentially be identified in subsequent phases of implementation.

4.2 Strengths and Limitations

Current literature provides limited research on NRCRM of vital signs of patients during administration of IVIg at home. Therefore, this study aimed to test a specific monitoring system functionality, evaluate user experiences and identify challenges and bottlenecks in this field of interest. Results were assessed by monitoring ten IVIg administrations in addition to current working methods of administration carried out by the home nurses of ZorgFront. This resulted in the insight that robust wearable sensors and accurately tailored alarm templates are strict requirements to obtain a manageable alarm burden. Furthermore, it shows that patients and nurses are mostly concerned about patient safety. Lastly, this report indicates the scope of actions that need to be taken to overcome associated challenges and bottlenecks.

A limitation of this study is that the transition towards NRCRM of vital signs of patients during administration of IVIg at home is a point solution to the problem of high labor intensity for this treatment. This point solution may not be optimal for the overall efficiency problem. The eventual implementation should be the optimal combination of costs and patient safety in the administration

of IVIg, needing fewer personnel than the current situation. Implementing a point solution without further analysis and evaluation of alternative solutions may give suboptimal results. Also, this study does not incorporate a financial analysis. Although the study thoroughly examines the challenges and bottlenecks and provides suggestions for solutions, it does not explore associated costs and economic feasibility. However, the financial aspect may be a crucial factor for decision-makers in healthcare organisations. Furthermore, it must be highlighted that patients included in this study are not a hundred percent representative of the whole patient population of patients receiving IVIg at home. Patients with a history of problematic administration were excluded, which may have resulted in unidentified challenges and bottlenecks and unsaturated responses to the questionnaire. Lastly, a questionnaire for the telenurses may have given insight into user experience with the software. Interface usability could have been assessed and subsequently improved in collaboration with the manufacturer or could have led to the decision to switch to a different provider.

4.3 Future Perspectives

In the long term, research could assess the impact of NRCRM on patient outcomes, such as quality of life and clinical outcomes, such as hospitalization rates and medication adherence.

Furthermore, future perspectives comprise the expansion of NRCRM of patients in other applications within health care. Interpretation of results considering the hardware and software might be applicable in different fields, but especially challenges and bottlenecks are to be identified for each application individually. The option to centralize NRCRM within healthcare institutions and include monitoring of patients with different indications might be explored as well. Centralizing care can lead to more efficient use of resources and could potentially create higher expertise in the field of remote monitoring of patients.

5. Conclusion

The goal of this study was to test monitoring system functionality, evaluate user experiences and identify challenges and bottlenecks of NRCRM of vital signs of patients during administration of IVIg at home. As a result, this thesis provides an overview of the scope of actions that need to be taken to overcome associated challenges and bottlenecks. Furthermore, suggestions for implementation were presented. This study has brought up a substantial amount of points of attention that need thoughtful consideration in order to design a safe and efficient monitoring protocol. Besides the practical and safety aspect, a challenge lies in addressing the negative attitudes of nurses and patients and creating a positive culture of change to ensure smooth adoption.

6. Recommendations

This study can be interpreted as a first step in the implementation of NRCRM of vital signs of patients during administration of IVIg at home. Excluding the impact of future financial analysis, this section enlists recommendations for next steps toward successful implementation:

- Start by selecting a definite manufacturer of software and hardware or third-party products in order to start the security requirements process.
- Arrange all security requirements and apply for Medical Research Ethics Committee (MREC) approval since these processes may take up to six months or longer.
- In the meantime, construct alarm templates, escalation pathways and job descriptions. Work out the logistic aspect, recruit and train personnel for the monitoring staff team and arrange other peripheral matters.

Upon arrangement of security requirements and MREC approval:

- A follow-up study should be conducted with the same protocol, monitoring multiple patients simultaneously. A home nurse is still present with every patient but is only operating in case of emergency. The goal is to establish safe working methods.

Once safe working methods have been established, NRCRM could be implemented in home care. Throughout the process, it is advised to pay close attention to stakeholder management and promote a positive culture of change.

Appendices

A. Patient information folder

informatie voor patiënten

Het Erasmus MC gaat starten met telemonitoring (op afstand monitoren) bij patiënten die thuis immunoglobulinen via een infuus krijgen. In deze folder leest u hier meer over.

Achtergrond

U bent onder behandeling bij de afdeling Immunologie in het Erasmus MC vanwege een immuundeficiëntie of een ontstekingsziekte (auto-immuunziekte).
Bij een immuundeficiëntie maakt uw lichaam niet genoeg van een bepaald type antistoffen aan. Hierdoor krijgt u sneller infecties. Om u te beschermen tegen infecties krijgt u antistoffen (immunoglobulinen) van donoren.
Bij ontstekingsziekten krijgt u ook antistoffen (immunoglobulinen) toegediend, vaak in een hoge dosis, om schade aan weefsels en/of achteruitgang van organen tegen te gaan. Dit wordt immunomodulatie genoemd.
De meeste patiënten krijgen deze antistoffen thuis via een infuus toegediend. Tijdens de thuistoediening is er een thuisverpleegkundige aanwezig die u kan ondersteunen bij bijwerkingen en kan ingrijpen als er een (zeldzame) allergische reactie optreedt.

Voordelen van telemonitoring

De toediening van immunoglobulinen via een infuus duurt meestal vier tot acht uur. Het grootste deel van de tijd is er geen actie nodig van de thuisverpleegkundige. De thuisverpleegkundige kan op deze manier slechts één patiënt per dag behandelen, terwijl bijwerkingen en allergische reacties zeer zeldzaam zijn.
Daarom gaat het Erasmus MC starten met het op afstand monitoren van patiënten die thuis via een infuus immunoglobulinen krijgen. Dit noemen we telemonitoring. Met telemonitoring blijft de kwaliteit van de zorg gewaarborgd, maar kan de thuiszorg elders worden ingezet waar dit hoognodig is. Bovendien geeft het u meer vrijheid omdat er niet meer de hele tijd een verpleegkundige bij u thuis aanwezig is.

Hoe werkt telemonitoring?

Volgens het huidige protocol wordt u tijdens de thuistoediening gemonitord door de thuisverpleegkundige. Zij meet ieder uur uw bloeddruk, hartslag en temperatuur om te controleren of uw lichaam goed reageert op de medicatie.
Bij telemonitoring meet de meetapparatuur uw bloeddruk, hartslag en temperatuur continu en stuurt de waarden automatisch door naar een computer in het Erasmus MC. In het ziekenhuis worden uw waarden gedurende de hele tijd van toediening nauwlettend in de gaten gehouden door een zogenoemde telenurse, die op deze manier meerdere personen tegelijkertijd kan monitoren. Het is ook mogelijk om te communiceren met de telenurse via (beeld)bellen.

De rol van de thuisverpleegkundige

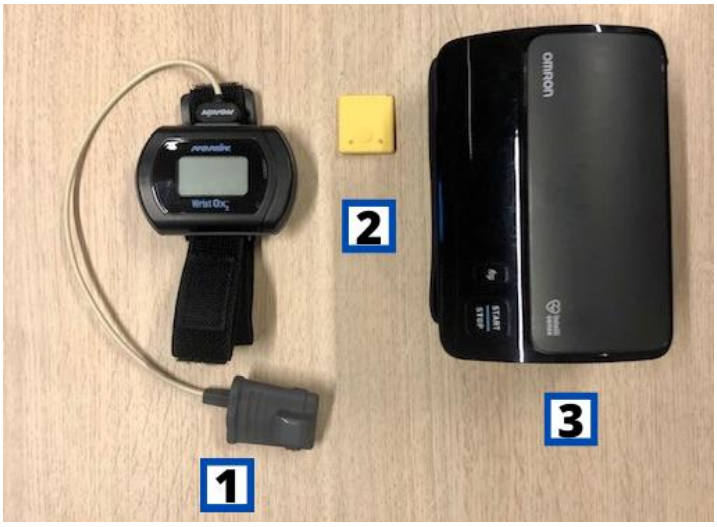
Thuistoediening van immunoglobulinen bestaat uit drie onderdelen, namelijk het inbrengen van het infuus, het inlopen van de medicatie en het afkoppelen van het infuus. Het inbrengen en afkoppelen van het infuus wordt nog steeds gedaan door de thuisverpleegkundige. Tijdens het inlopen zal de thuisverpleegkundige echter uw huis verlaten om andere patiënten te helpen.

Tijdens de afwezigheid van de thuisverpleegkundige bent u de hele tijd aangesloten op de meetapparatuur en houdt de telenurse uw gezondheidstoestand in de gaten. Het is daarbij belangrijk dat u altijd telefonisch bereikbaar bent voor de telenurse.

Meetapparatuur

De meetapparatuur bestaat uit:

- Een pulsoxymeter voor om uw wijsvinger met bijbehorende polsband (1). Deze meet de hartslag en de zuurstofsaturatie van uw bloed.
- Een temperatuursensor (een sticker voor onder de oksel) die uw lichaamstemperatuur meet (2).
- Een manchet die uw bloeddruk meet (3). Deze gaat om de bovenarm waar geen infuus in zit.



Veiligheid

Ook als u al langere tijd probleemloos uw medicijnen ontvangt, blijft er altijd een heel klein risico op een (ernstige) allergische reactie. Als u in aanmerking komt voor telemonitoring tijdens thuistoediening, maken we van tevoren duidelijke afspraken over wat u dan moet doen.
Bij technische of medische problemen tijdens thuistoediening is de telenurse het eerste aanspreekpunt. Wanneer de problemen niet in overleg met de telenurse opgelost kunnen worden, staat er een thuisverpleegkundige in de regio klaar om bij u langs te komen.

Voor wie?

Niet iedereen komt in aanmerking voor telemonitoring tijdens thuistoediening van immunoglobulinen. Ontvangt u al langer thuistoediening? Dan bepaalt uw arts in overleg met uw thuisverpleegkundige of u in aanmerking komt. Heeft u nog niet eerder thuistoediening ontvangen? Dan zal uw arts bepalen of u in aanmerking komt.

Vragen?

Heeft u na het lezen van deze folder nog vragen over telemonitoring bij thuistoediening van immunoglobulinen, dan kunt u terecht bij Marianne van der Ent, verpleegkundig specialist interne geneeskunde - immunologie.

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- E-mail: m.w.vanderent@erasmusmc.nl

B. Hardware specifications

Table B1 DVX Device specifications

Item	*Description*
Dimensions	± 80 x 60 x 20 mm
Weight	± 50 grams (1.76 oz)
Energy supply	Mains power
Memory	32 GB embedded micro SD card
Data transmission mode	Cellular (4G)
Power consumption	± 300 mAh

Table B2 Device characteristics of the wearable sensors (obtained from the operator manuals)

Device	*Vital sign*	*Detection mechanism*	*Performance rate*	*Other relevant specifications*
Omron EVOLV HEM-7600T-E (OMRON Healthcare Co., Ltd., Japan)	Blood pressure	Oscillometry	Accuracy: ±3 mm Hg	Power supply: 4* AAA batteries 1.5V Battery life: 300 measurements Durable period: 5 years
Nonin 3150 WristOx$_2$ Pulse Oximeter (Nonin Medical B.V., The Netherlands)	Heart rate Blood oxygen saturation	Photoplethysmography	-	Power supply: 2*AAA batteries 1.5V Battery life: 53 hours operating
Temp Pal STP-MB01-1 (iWEECARE Co., Ltd., Taiwan)	Body temperature	Negative Temperature Coefficient (NTC) thermistor	Accuracy (in range): ±0.05 °C (32-42 °C) ±0.10 °C (<32 - >42 °C)	Power supply: Rechargeable battery Battery life: 36 hours operating Location: armpit Requires up to 20 minutes to reach stable reading Transmission frequency: Every 10/30/60 seconds

C. Custom-made Questionnaire

-Patients-

1. Overall attitude

Ik zie voor mij persoonlijk een toegevoegde waarde in telemonitoring zonder aanwezigheid van een verpleegkundige
☐Ja
☐Nee
☐Een beetje. Toelichting:

Ik zie voor het maatschappelijk belang een toegevoegde waarde in telemonitoring zonder aanwezigheid van een verpleegkundige
☐Ja
☐Nee
☐Een beetje. Toelichting:

Ik zou me comfortabel voelen om alleen thuis te zijn tijdens toediening
☐Helemaal niet mee eens
☐Overwegend niet mee eens
☐Neutraal
☐Overwegend mee eens
☐Helemaal mee eens
Toelichting bij antwoord:

Ik zou me comfortabel voelen zonder aanwezige verpleegkundige maar met de aanwezigheid van een huisgenoot (partner/kind/iemand anders)
☐Helemaal niet mee eens
☐Overwegend niet mee eens
☐Neutraal
☐Overwegend mee eens
☐Helemaal mee eens
Toelichting bij antwoord:

Zou u eventueel open staan voor telemonitoring tijdens thuistoediening zonder aanwezigheid van een verpleegkundige?
☐Ja
☐Nee
☐Misschien. Dit zijn mijn twijfels:

Indien u hierboven 'Nee' heeft geantwoord. Welke factoren spelen hierbij een rol? Kruis aan:
☐Ik voel me niet veilig zonder aanwezigheid van een verpleegkundige
☐Ik vind het gezelschap van de verpleegkundige prettig
☐Ik vind het handig dat de verpleegkundige mij kan helpen met klusjes in huis
☐Ik zie op tegen de handelingen die dan bij mijzelf komen te liggen
(denk aan: uithalen venflon, omgang met infuuspomp)
☐Andere reden, namelijk:

2. Comfort level wearable sensors

De Omron bloeddrukmeter zat gedurende de gehele toediening comfortabel
☐Ja
☐Nee, want:

Het dragen van dit apparaat was vervelend bij de volgende handelingen:

De pulsoxymeter (armband incl. hoesje om wijsvinger) zat gedurende de gehele toediening comfortabel
☐Ja
☐Nee, want:

Het dragen van dit apparaat was vervelend bij de volgende handelingen:

De temperatuur sensor sticker zat gedurende de gehele toediening comfortabel
☐Ja
☐Nee, want:

Het dragen van dit apparaat was vervelend bij de volgende handelingen:

Ik zie het zitten de meetapparaten, die zijn gebruikt tijdens de pilot, gedurende mijn gehele toediening te dragen:
☐Helemaal niet mee eens
☐Overwegend niet mee eens
☐Neutraal
☐Overwegend mee eens
☐Helemaal mee eens

3. Education
Ik sta er voor open om het oplossen van storingen van de infuuspomp zelf aan te leren (in telefonische overleg):
☐Ja
☐Nee
☐Misschien. Toelichting:

Ik sta er voor open om het uithalen van mijn venflon (canule) zelf aan te leren
☐Ja
☐Nee
☐Misschien. Toelichting:

Ruimte voor algemene extra toelichting:

-Nurses-

Overall attitude
Ik zie een toegevoegde waarde in telemonitoring zonder aanwezigheid van een verpleegkundige…

…voor het maatschappelijk belang:
☐Ja
☐Nee
☐Een beetje. Toelichting:

… voor de patiënt:
☐Ja
☐Nee
☐Een beetje. Toelichting:

… voor mijzelf als thuis verpleegkundigen:
☐Ja
☐Nee
☐Een beetje. Toelichting:

Ik sta positief tegenover een eventuele transitie naar telemonitoring tijdens thuistoediening zonder aanwezigheid van een verpleegkundige:
☐Helemaal niet mee eens
☐Overwegend niet mee eens
☐Neutraal
☐Overwegend mee eens
☐Helemaal mee eens
Toelichting bij antwoord:

Ik maak mij zorgen om een eventuele transitie naar telemonitoring tijdens thuistoediening zonder aanwezigheid van een verpleegkundige:
☐Helemaal niet mee eens
☐Overwegend niet mee eens
☐Neutraal
☐Overwegend mee eens
☐Helemaal mee eens
Toelichting bij antwoord:

Ik sta er voor open als mijn werkwijze tijdens thuistoediening van Ivig verandert:
☐Helemaal niet mee eens
☐Overwegend niet mee eens
☐Neutraal
☐Overwegend mee eens
☐Helemaal mee eens
Toelichting bij antwoord:

Extra ruimte voor toelichting:

D. Overview of Identified Challenges and Bottlenecks

Identified bottleneck	Category	Subcategory	Process/System/People
Pre-administration			
Time limit to temperature sensor response time	Monitoring system	Wearable sensors	System
Time limit to insert IV	Logistics	Timing and delay	Process
Home nurse currently possesses only one infusion pump	Logistics	Equipment	Process
Traffic jam on way to first patient or in between patients	Logistics	Timing and delay	Process
Time limit to do administration and order new medication	Logistics	Timing and delay	Process
During administration			
Alarm fatigue			
-High amount non-physiological no data alarms SpO2	Monitoring system	Software	System
-High amount non-physiological no data alarms Temp	Monitoring system	Software	System
-Duration of all no data alarms	Monitoring system	Software	System
- High occurrence of threshold alarms	Monitoring system	Software	System
- Sensitivity of wearable sensors during normal daily activities	Monitoring system	Wearable sensors	System
Uncomfortable finger casing	Monitoring system	Wearable sensors	System
Non continuous measurement of blood pressure	Monitoring system	Wearable sensors	System
Limit freedom of movement with DVX device restricted to main power	Monitoring system	Wearable sensors	System
Power consumption of wearable sensors	Monitoring system	Wearable sensors	System
Patient monitoring while sleeping			
- Correct equipment of wearable sensors	Monitoring system	Wearable sensors	System
- Alarm handling monitoring system/pump	Patient safety		Process
Home access for emergency responders in case of home alone	Logistics	Emergency	Process
Actions performed by home nurse:			
- Increase infusion rate	Change management	Working methods	Process
- Bottle change	Change management	Working methods	Process
- Alarm handling of infusion pump (air in line,	Change management	Working methods	Process
- Correction in case of subcutaneous infusion	Change management	Working methods	Process
Communication (patient and telenurse) and privacy	Information Technology		Process/System
Escalation protocol	Patient safety		Process
No control of infusion rate by medical staff	Patient safety		Process
Post-administration			
Actions performed by home nurse:			
- Flushing of infusion line	Change management	Working methods	Process
- Removing infusion cannula	Change management	Working methods	Process
Time-independent of administration			
Patient locations	Logistics	Timing and delay	Process
(Re)training of nursing staff (telenurse, ambulatory nurse)	Change management	Working methods	Process
Persuasion of patient of safety	Change management	Overall attitude	People
Security requirements IT EMC	Information Technology		Process

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