2015•2016
FACULTEIT GENEESKUNDE EN LEVENSWETENSCHAPPEN
master in de biomedische wetenschappen

Masterproef

Remote monitoring to assess the maternal and fetal wellbeing in normal and high-risk pregnancies

Promotor :
Prof. dr. Lars GRIETEN

Anne Van Moerbeke
Scriptie ingediend tot het behalen van de graad van master in de biomedische wetenschappen

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Table of content

List of abbreviations

APGAR	Appearance, Pulse, Grimace, Activity, and Respiratory
BMI	Body Mass Index
BP	Blood Pressure
CTG	Cardiotocography
HELLP	Hemolysis, Elevated Liver Enzymes, and Low Platelets count
IQR	Interquartile Range
MHU	Mobile Health Unit
MIC	Maternal Intensive Care
NIC	Neonatal Intensive Care
PDA	Personal Device Assistant
PE	Preeclampsia
PREMOM	Pregnancy Remote Monitoring
STD	Standard Deviation
ZOL	Ziekenhuis Oost-Limburg

Samenvatting

Inleiding: Gestationele hypertensieve aandoeningen zijn een vaak voorkomend probleem tijdens een zwangerschap en dragen bij aan de maternale mortaliteit wereldwijd. Wanneer deze hypertensieve aandoening niet op tijd behandeld of gediagnosticeerd worden, kunnen zowel de maternale als foetale gevolgen zwaar zijn. Telemonitoring maakt het mogelijk om een dagelijkse follow-up te implementeren in de gezondheidszorg. Door deze techniek worden data die thuis worden gemeten, doorgestuurd naar een online platform. De PREMOM (Pregnancy Remote Monitoring) studie, een interventionele studie, implementeerde telemonitoring binnen de verloskunde en evalueerde de haalbaarheid en de resultaten.

Materiaal en methoden: In totaal werden 33 patiënten geïncludeerd en voltooiden de studie tot bevalling of opname op de Maternal Intensive Care (MIC) afdeling van Ziekenhuis Oost-Limburg (ZOL) tussen 9 November 2015 en 15 April 2016. Elke patiënt kreeg een bloeddrukmeter, een weegschaal, en een stappenteller. Deze toestellen werden verbonden via Bluetooth aan een applicatie geïnstalleerd op de smartphone van de patiënt. De patiënten moesten in totaal twee keer per dag de bloeddruk meten, één keer per dag het gewicht, en gedurende de hele dag en nacht de stappenteller dragen. Tijdens de studie werden in totaal drie vragenlijsten ingevuld, in het begin, tussenin, en op het einde na het voltooien van de studie.

Resultaten: Vijf patiënten werden gediagnosticeerd met preeclampsie (PE) en 12 met gestationele hypertensie. Analyse van de data toonde een sensitiviteit van 72,22% en een specificiteit van 86,67%. In totaal werd er 76,14% van het totaal aantal verwachtte bloeddruk metingen uitgevoerd en van de gewichtsmetingen 62,75%. De gemiddelde compliance bedroeg 76% ± 0,14 en 60% ± 0,15 van respectievelijk de bloeddrukmetingen en gewichtsmetingen. De redenen voor gemiste waarden waren in 66,67% van de bloeddrukmetingen en 76,92% van de gewichtsmetingen persoons-gerelateerd. Andere redenen voor missende waarden waren toestel-gerelateerd.

Conclusie: Uit de resultaten blijkt dat telemonitoring een grote capaciteit heeft om vroege symptomen van PE te voorspellen en te detecteren. Meer data zijn echter nodig om een hogere sensitiviteit en specificiteit te bekomen. Ook is verder onderzoek nodig om de compliantie te verbeteren en de patiënten gemotiveerd te houden.

Abstract

Introduction: Gestational hypertensive disorders (GHDs) are a common feature in pregnancies and still a major cause of maternal mortality worldwide. If not diagnosed or left untreated GHDs could lead to maternal and fetal consequences. Telemonitoring makes it possible to have a close follow-up by transferring data to an online platform in the hospital. This guarantees a daily review of the measured parameters and thus a close follow-up. The PREMOM (Pregnancy Remote Monitoring) study, an interventional study, implemented telemonitoring in obstetrics and evaluated its feasibility and outcomes.

Materials and methods: In total 33 patients were included and completed the study until delivery or admission to the Maternal Intensive Care department of Ziekenhuis Oost-Limburg between 9th November 2015 and 15th April 2016. Every participant received a blood pressure monitor, a weight scale, and an activity tracker, connected to an application on their smartphone via Bluetooth. Participants had to measure their blood pressure twice a day (in the morning and in the evening), weigh themselves once a day, and wear an activity tracker all day and during the night to monitor their sleep pattern. During the course of the study, three questionnaires were filled in, one during inclusion, one interim, and one after completing the study.

Results: Five patients were diagnosed with preeclampsia (PE) and 12 with gestational hypertension. Analysis showed a sensitivity of 72.22% and a specificity of 86.67%. In total 76.14% and 62.75% of the expected blood pressure and weight measurements were performed. Mean compliance was 75% ± 0.14 and 57% ± 0.15 for the blood pressure and weight measurements respectively. Further analysis indicated that 66.67% of the missed blood pressure and 76.92% missed weight measurements were personal-related. Other reasons for missing data were device-related.

Conclusion: Telemonitoring has a high capability of predicting and detecting early signs and symptoms of PE. Further research is necessary to obtain high compliance throughout the study and to keep the patients motivated. More data is needed to increase the sensitivity and specificity of telemonitoring.

1 Introduction

Most pregnancies proceed without any complications. However, in a high-risk pregnancy, both mother and fetus develop a higher than normal risk at complications (1). Approximately, globally 10% develops a high-risk pregnancy (1). There are different categories classifying the risk factors that contribute to the chance of developing problems during the pregnancy (2, 3). Preexisting health conditions, such as diabetes, hypertension, obesity, autoimmune diseases, and kidney or heart disease, enhance the risk of a complication (1-4). But also other physical characteristics, *i.e.* age (first pregnancy after a age of 35), and reproductive abnormalities could contribute (3). Other risk factors include problems during the previous pregnancy (miscarriage, intra-uterine growth retardation (IUGR), preeclampsia (PE), etc.), lifestyle factors (smoking and alcohol usage) and family history (genetic disorders, family history of hypertension, etc.) (1, 3). Not only preexisting conditions magnify the risk of complications, but also conditions arising during the pregnancy, such as hypertension induced by pregnancy, add to the hazard of a high-risk pregnancy (2).

Prenatal care and a good follow-up of high-risk pregnancies are recommended to make it possible to pick up early symptoms of gestational complications and disorders. Telemonitoring, or remote monitoring, offers a possible diagnostic and follow-up tool in the future. In this way, women developing a high-risk pregnancy are monitored daily from a distance, leading to a decrease in adverse outcomes and prenatal visits. A better follow-up could even reduce stress levels in the mother, possibly leading to less hypertensive events induced by stress.

1.1 Hypertensive disorders in pregnancy

Hypertensive disorders are still a remaining leading cause of maternal and infantile morbidity and mortality. This occurs in 6% to 8% of pregnancies (5, 6). Hypertension during pregnancy is defined as a blood pressure of ≥ 140/90 mmHg and it predisposes the mother to complications such as abruptio placentae, cerebral hemorrhage, acute renal failure, and hepatic failure (6). Still unknown are the causes of hypertensive events, in particular PE, during pregnancy.

1.1.1 Classification of hypertensive disorders

Hypertensive disorders during pregnancy are classified into four different categories by the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy: chronic hypertension, preeclampsia-eclampsia, preeclampsia superimposed on chronic hypertension, and gestational hypertension (5, 7) (Table 1).

Chronic hypertension

Chronic hypertension is defined as a blood pressure of ≥ 140/90 mmHg, either preceding pregnancy, diagnosed within the first 20 weeks of pregnancy, or persisting after 12 weeks postpartum (5-7).

Gestational hypertension

Gestational hypertension is the new onset of hypertension after a gestational age of 20 weeks, without the development of proteinuria. Gestational hypertension covers women eventually developing PE and women who do not have PE. The blood pressure returns to normal by 12 weeks postpartum. In total, 50% of the women diagnosed with gestational hypertension between 24 and 35 weeks eventually develop PE. Progression to severe gestational hypertension is accompanied by a worse perinatal outcome than mild PE. Women developing severe gestational hypertension require management similar to those with severe PE. (5-7)

Preeclampsia

Preeclampsia, a multi-organ disease process of unknown etiology, is a pregnancy specific syndrome, characterized by the development of hypertension and proteinuria after 20 weeks of gestation (5-7). Criteria for the diagnosis of PE are: a systolic blood pressure ≥ 140 mmHg and a diastolic blood pressure ≥ 90 mmHg or a diastolic blood pressure ≥ 100 mmHg on two occasions at least six hours apart and proteinuria (300 mg in a 24-hour urine specimen) (5, 7). Edema, affecting the face and hands, is often present but is not a diagnostic criterion (5).

Severity of PE is not only based on the degree of hypertension and proteinuria, but also on the presence of symptoms, such as severe headache, visual disturbances, and hyperreflexia (5). Other possible symptoms include pulmonary edema, epigastric or right-upper quadrant pain, impaired liver function, and thrombocytopenia (7). The Hemolysis, Elevated Liver enzymes, and Low Platelets count (HELLP) syndrome is a manifestation of PE, occurring in up to 20% of pregnancies complicated by severe PE, presented with right upper quadrant pain or epigastric pain, nausea and vomiting (5, 7). Fetal consequences include most commonly intrauterine growth restriction (7). Eclampsia is a rare onset of convulsions in PE, occurring in less than one percent of preeclamptic women (5, 7).

Preeclampsia superimposed on chronic hypertension

Preeclampsia may arise in women already diagnosed with hypertension. The diagnosis of superimposed PE is complicated due to the difficulty of distinguishing superimposed PE from worsening chronic hypertension. (6)

Diagnosis implements the following findings:

- new-onset proteinuria (urinary excretion of ≥ 0.30g protein in a 24-hour specimen) in women with hypertension and no proteinuria before 20 weeks of gestation. (6)
- a sudden increase in proteinuria, in blood pressure (in a woman whose hypertension has been well controlled), thrombocytopenia, or an increase in alanine aminotransferase or aspartate aminotransferase to abnormal levels, in women with hypertension and proteinuria before 20 weeks of gestation. (6)

Table 1: *Classification of the types of hypertensive disorders during pregnancy. Gestational hypertension, preeclampsia, and preeclampsia superimposed on chronic hypertension are also diagnosed with a diastolic blood pressure ≥ 100, independent of the value of the systolic blood pressure.*

Types of hypertensive disorders	Onset (gestational age in weeks)	Maternal systolic blood pressure (mmHg)	Maternal diastolic blood pressure (mmHg)	Proteinuria
Chronic hypertension	Preceding conception, ≤ 20	≥ 140	≥ 90	No
Gestational hypertension	≥ 20	≥ 140	≥ 90	No
Preeclampsia	≥ 20	≥ 140	≥ 90	Yes (≥ 0.30g in a 24 hour specimen)
Preeclampsia superimposed on chronic hypertension	≥ 20	≥ 140	≥ 90	Yes (≥ 0.30g in a 24 hour specimen)

1.1.2 Pathogenesis of preeclampsia

The pathogenesis of PE is still incompletely understood and the only effective treatment is delivery of the placenta (8-10). This fact raises the possibility that the primary cause of PE is abnormal placentation. This hypothesis has led to the two-stage theory, including that PE originates in the placenta, translating in the mother by endothelial dysfunction (9, 10).

The first stage involves the invasion of maternal uterine spiral arteries, supplying the intervillous space, not undergoing vascular remodeling characteristic of normal pregnancy. In normal placental development, trophoblasts transform the maternal spiral arteries, resulting in more dilated arteries and more blood flow to the intervillous space, supporting grow of the fetus. A defective invasion of trophoblasts leads to a limited remodeling and thus spiral arteries remain stiff and undilated. It has been hypothesized that factors released by the placenta are eventually responsible for the effects on the maternal endothelium, stage two of the theory. The second stage causes vasoconstriction and increased vascular resistance. But not only hemodynamic changes are a result of the endothelium dysfunction; also infarction and necrosis in the liver and adrenal, and acute renal failure are consequences of PE. (6, 8-12)

As stated before, delivery is the only curative treatment. The decision of delivery balances the risks of worsening PE and thus the maternal risks of continued pregnancy against the risk of induced preterm delivery (Figure 1). Gestational age at diagnosis and the severity of PE are criteria factors for delivery. After a gestational age of 37 weeks, there are no advantages in continuing the pregnancy. Before a gestational age of 24 weeks, management is not justified concerning the risks of maternal complications and poor neonatal prognosis. At 24-34 weeks of gestational age, management depends on the severity of PE. Between week 34 and 37 of gestation, the risk of preterm delivery is aimed to be limited, depending however on the severity. In all cases of severe

PE, decisions regarding delivery are based on both maternal as fetal factors (*i.e.* evidence of lung maturity, gestational age, and signs of fetal compromise). (8)

Overall, early detection, monitoring, and supportive care are beneficial to both mother and fetus (10).

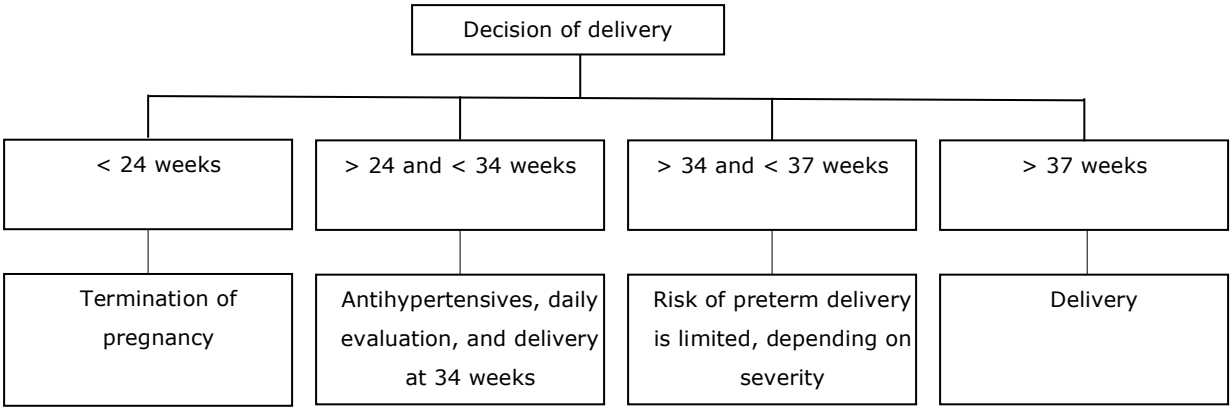

Figure 1: *The decision of delivery is based on specific criteria factors such as gestational age and the severity of preeclampsia. The decision balances the maternal risks against the risk of preterm delivery, thus the fetal risks.*

1.2 Management of high-risk pregnancies

Prenatal care is necessary in every pregnancy, whether being high-risk or not. With regular prenatal care, risks at complications can be reduced, for both mother and fetus. When being diagnosed with a high-risk pregnancy, regular prenatal care could possibly detect early signs of complications. (13)

Mandatory visits normally happen one time a month. From a gestational age of 30 weeks, frequency of prenatal care increases to every two weeks and from a gestational age of 36 weeks, prenatal care takes place every week (14). During these ambulant visits, a cardiotocography (CTG) takes place to evaluate the fetal heart and contractions. Every trimester, at a gestational age of 12, 20, and 30, an ultrasonography is executed to monitor the fetal heart rate, growth and position of the fetus, the placenta, amniotic fluid, and to determine whether problems are present or not (14, 15). During a prenatal visit, health of the mother is controlled by measuring the blood pressure, weight, and analysis of the general wellbeing of the mother. A schedule of the timeline is given in Figure 2.

Management in high-risk pregnancies does not differ from the prenatal care in a normal pregnancy, except that women with high-risk pregnancies are monitored more often. Special care is offered to those with a risk at developing PE at the hospital Ziekenhuis Oost-Limburg (ZOL) (16). These women are monitored to assess different cardiovascular parameters, *e.g.* stiffness of the hepatic and renal veins, and the amount of body fluid. If signs of maladaptation of the maternal cardiovascular system are present, a special PE consultation takes place. When later on in

pregnancy the severity of PE rises, the mother can be administered to the Maternal Intensive Care (MIC). If proteinuria is diagnosed, hospitalization is obliged until labor.

To date, there are multiple problems concerning the management of high-risk pregnancies. Multiple consultations are not only time consuming for the patient but also for the gynecologist. Women eventually diagnosed with a high-risk pregnancy are hospitalized more often due to the fact that monitoring is necessary when complications arise. More hospitalizations days lead to an increased workload and higher costs. However, not only the high cost rate is a current pitfall. Hospitalized women endure a lot of stress, not only affecting the mother's health but also affecting the fetus. The time gap between consultations is another hazard of the management. No measurements are taken in this time gap and possible first signs of complications might be not picked up early enough. (17)

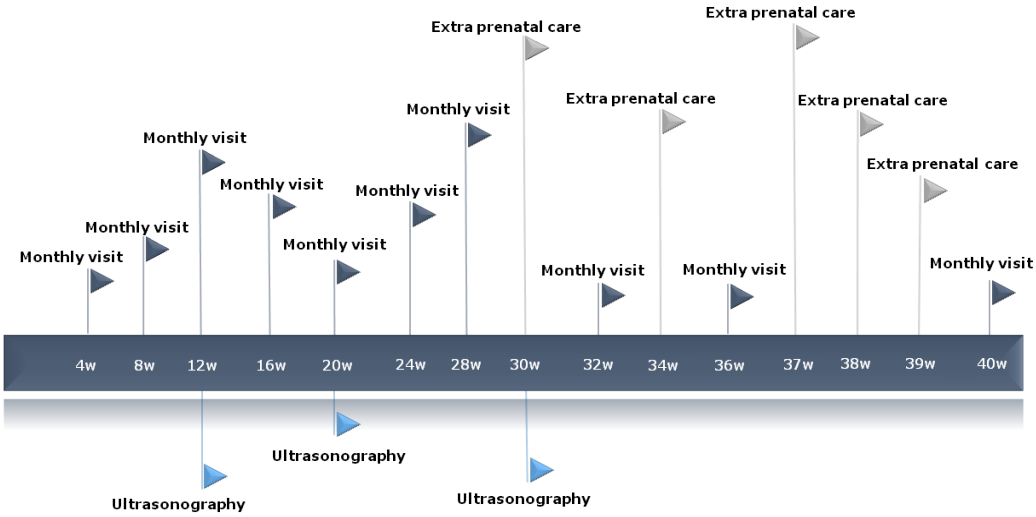

Figure 2:
A timeline schedule of the monthly mandatory visits and extra prenatal care during pregnancy. From week 30, the frequency of prenatal care increases to every two weeks and from week 36 to weekly. Every trimester, gestational age of 12, 20, and 30, ultrasonography is planned.

1.3 Telemonitoring

The technique of telemonitoring, the remote monitoring of patients, is defined as "the use of audio, video, and other telecommunications and electronic information processing technologies to monitor patient status at a distance." (18)

1.3.1 Mobile health

The current high costs of healthcare and the pressure to discharge patients as soon as possible, due to strain on hospital bed occupancy, lead to new measurements for cost reduction, *i.e.* reduction of the number of days in the hospital, number of face-to-face consultations, and reduction of costly treatment programs. Another solution involves the detection of complications in early stage, preventing hospitalization. Telemonitoring contributes to these solutions. It reduces travel time, overall costs, and reduces the use of hospital beds, delivering health care from a distant. (17-19)

Mobile health is a new, undiscovered, and rapidly developing field in healthcare and is defined as "medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices" (20). It technically describes the transmission of data and measured parameters by the patients by means of a mobile phone, coupled via Bluetooth to the measurement device (21). In detail, the patient measures a parameter, *e.g.* blood pressure. The mobile phone of the patient is connected via Bluetooth to the measurement device. When a new measurement is taken, the data of the measurement is sent to the application installed on the mobile phone. These data are then automatically sent to the healthcare provider. In this way, the healthcare provider can evaluate the data from a distance and provide feedback when necessary (Figure 3).

Mobile health increases the effectiveness and quality of the healthcare, and enables a more accurate diagnosis and treatment. It offers the patients the possibility to manage their own health, and, when being in their home situation, living more independently. Mobile health attributes to an enhanced adherence to treatment and lifestyle, leading to a more personalized medication and treatment. Mobile health, however, will not replace the healthcare specialist, but is more seen as an additive tool. It supports the shift towards a healthcare focusing on prevention, leading to a better quality of life, less hospitalizations, and the reduction of complications, avoiding unnecessary treatments. (18, 22)

Figure 3:
The principle of Mobile Health: The patients receive a device for their data measurements. When data are taken with the devices, the data are transferred via Bluetooth to an application on their smartphone. These are then automatically transferred via 3G/4G/Wi-Fi to an online platform, daily controlled by the healthcare team. If necessary, feedback is provided.

1.3.2 Telemonitoring in high-risk pregnancies

There is a growing interest in the use of telemonitoring to reduce high costs of healthcare and to close a spatial distance between patient and practitioner. High-risk pregnant women form one of the target groups of remote monitoring, though the implementation of telemonitoring in high-risk pregnancies is still small. To date, the main focus in research involving telemonitoring in obstetrics was on uterine activity monitoring of women with a high-risk at preterm labor (23-27). The effectiveness of the use of telemonitoring is still not completely proven, although results indicate that the technique may lead to improved neonatal outcomes (18, 19).

Buysse et al. analyzed the cost-effectiveness of telemonitoring in high-risk pregnant women. The study showed that telemonitoring reduces costs but staffing costs, the non-reimbursement of telemonitoring (resulting in unpaid work for the clinicians), and the effective costs of the equipment were not taken into account. No information was given about events or time spend on looking to the transmitted results. (19)

One of the main advantages of the use of telemonitoring in high-risk pregnancies is the time-lapse frame. Data collection at home, *i.e.* blood pressure measurements, are more representative than measurements during a consultation, which are often biased due to factors such as stress. Telemonitoring therefore offers a daily update of the health of the patient without extra hospital visits and the comfort of collecting data in a home situation.

1.4 Aim of the study

The observational pilot study 'PREMOM' (Pregnancy Remote Monitoring) involves the implementation of telemonitoring in obstetrics. The patients themselves monitor parameters as blood pressure, weight, and daily activity. The goal of the study is to determine whether telemonitoring has an added value in the diagnosis of complications related to high-risk pregnancy, more specifically the diagnosis of gestational hypertension and/or PE. Other research questions are whether telemonitoring is beneficial and if it leads to better maternal and neonatal outcomes. Information about missing data is obtained and compliance is assessed. Secondly, the experiences and opinion of the women are gathered, in the beginning, mid-term, and at the end of the study. The overall ultimate goal is the implementation of telemonitoring in the standard healthcare of pregnant women diagnosed with a high-risk pregnancy.

2 Materials and methods

The study PREMOM, an observational feasibility study, was conducted in the hospital ZOL at the department Obstetrics and Gynecology. The study involved the daily monitoring of pregnant women to assess the value of telemonitoring. Parameters collected were blood pressure, weight, and activity by means of devices. Analysis of data reviewed information about missing data and evaluation of the experience of the woman with telemonitoring.

2.1 Ethics

The Committee for Medical Ethics approved the study before start. Every participant gave written informed consent at the moment of inclusion. Standard care of women with a high-risk pregnancy was not changed.

2.2 Patient population

In total, 33 patients were included at ZOL after recommendation by the gynecologist or after the cardiovascular parameters indicated an increased risk for a high-risk pregnancy. The minimal gestational age at inclusion was 11 weeks and 5 days and the maximal gestational age was 39 weeks and 2 days. Exclusion criteria were congenital malformations of the fetus. Further no explicit exclusion criteria were handed because every pregnant woman at risk was included regardless gestational age or absence of other risk factors. Inclusion criteria ranged from preexisting hypertensive disorders, age of the mother (≥ 40 years), and Body Mass index (BMI) higher than 25 kg/m^2 to test results indicating stiff blood vessels. Patients included in the control group were women who voluntary participated.

2.3 Study design

The 33 participants received monitoring devices during their inclusion. The researcher coupled the monitoring devices to an installed application on their smartphone (or a borrowed smartphone), demonstrated how to use them, and filled in a list of questionnaires. At home, the pregnant women measured their blood pressure and heart rate twice a day (in the morning and in the evening), their weight once a day (recommended in the morning), and had to wear an activity tracker all day and night to track their activity and sleep patron. The participants all received a login account made by the Mobile Health Unit (MHU) which was used to login onto the application. These accounts were connected to the online platform and thus measured data were automatically transferred.

The data of the pregnant women were daily reviewed by means of the online platform. When an event, two consecutive blood pressure measurements of ≥ 140/90 mmHg or a diastolic blood pressure ≥ 100 mmHg, measured at least six hours apart, occurred, a specific flowchart was utilized (Figure 4). When an event occurred, the gynecologist was contacted. The next step was to follow the decision of the gynecologist, which was based on the seriousness of the symptoms and the gestational age of the patient at that time point. Either the patient was contacted for a consultation (ambulant CTG), to adjust their medication intake (or start medication intake), a MIC

admission, or no intervention took place. Participants were only contacted at the request of the gynecologist (*i.e.* to change medication intake, to order a CTG consultation, when missed measurements occurred, or for interim questionnaires).

An overview of the blood pressure and weight measurements was sent to the gynecologist when a patient had an interim consultation, independent of whether events were present or not.

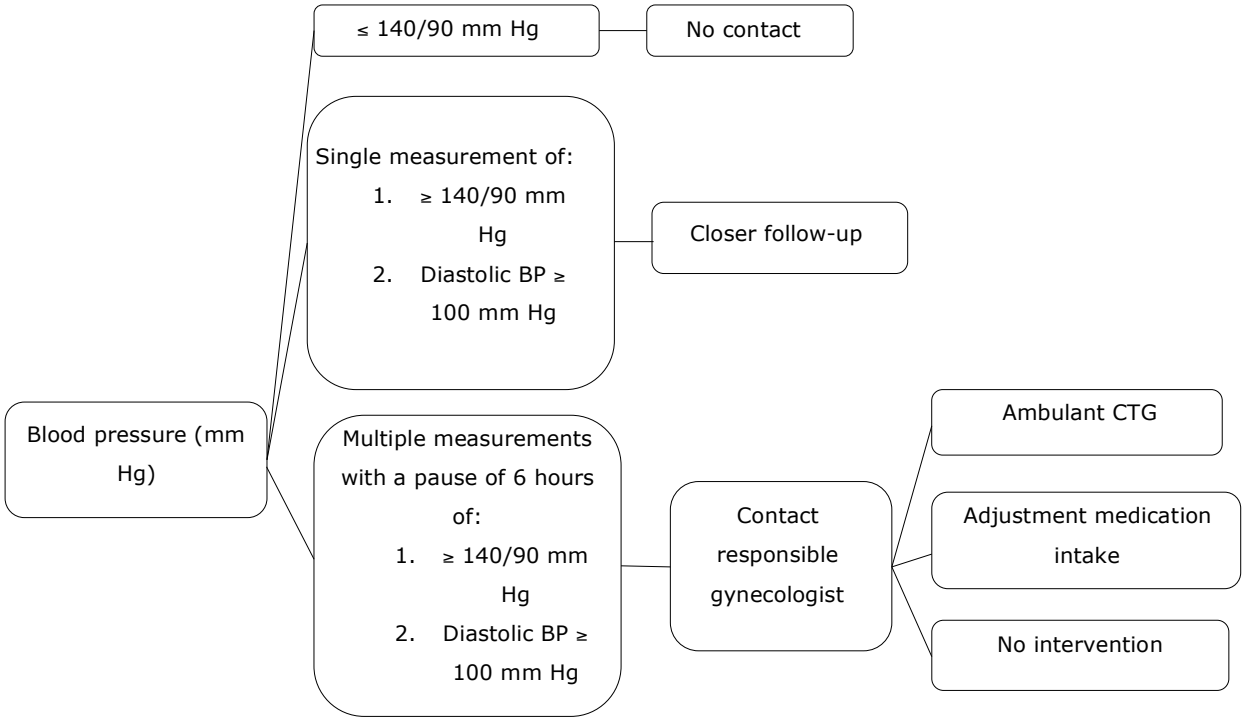

***Figure 4**:*
Flow-chart of actions undertaken when events occurred. When multiple events were stated, the gynecologist was contacted.
BP = blood pressure, CTG = cardiotocography

2.4 Devices

The monitoring devices used were either the Withings (Withings®, Issy-les-Moulineaux, France) devices (Withings Wireless Blood Pressure monitor, the Smart Body Analyzer, and the Pulse O_2) (Figure 5) or the iHealth (iHealth®, U.S.) devices (Wireless Blood Pressure monitor and iHealth Edge) (Figure 6). The Withings devices were installed on the patients their smartphones via the application Withings Health Mate (iOS 7.0 and higher, or Android 4.0 and higher). The iHealth devices were installed on their smartphones via the application iHealth MyVitals (iOS 7.0 and higher, or Android 4.0 and higher, and a compatible smartphone). When a connection was made with the application via Bluetooth, the data measured with the devices were automatically transferred via 3G/4G or Wi-Fi to the online platform.

During the inclusion, the researcher demonstrated how the devices are used correctly in order to obtain valid data. Both Blood Pressure monitors were applied on the upper left arm with the tube

positioned in the extension of the inner side of the forearm. When using the Withings Blood Pressure monitor, it was important that the Withings logo was positioned upwards. It was recommended to measure the blood pressure always in the same posture to overcome bias. The patients had to sit still during measurement and were ordered to be silent and calm. Before measurement, the patient had to be in rest for at least 5 minutes. The Smart Body Analyzer measured not only weight, but also body fat, heart rate, and air quality. The patients had to stand on the weight scale barefoot for a few seconds until all four measurements were done. The patients, who received the iHealth devices, did not receive a weight scale. They were asked to register their weight manually in the application. The Pulse O_2 activity tracker and the iHealth Edge had to be worn all day, either via a wristband or on a clip worn on the body. The activity trackers collected data about the number of steps, distance travelled and calories burned. The trackers also monitored the patients their sleep during night. The Pulse O_2 sleep function had to be activated and the iHealth Edge automatically monitored sleep.

Figure 5:
The devices of Withings used for remote monitoring. A) Withings Wireless Blood Pressure monitor, B) Withings Smart Body Analyzer, C) Withings Pulse O_2.

Figure 6:
The devices of iHealth used for remote monitoring. A) iHealth Blood Pressure monitor, B) iHealth Edge.

2.5 Validation of the monitoring devices

The blood pressure devices used in this study, the Withings Wireless Blood Pressure monitor and the iHealth Blood Pressure monitor, were internally validated and compared to a standard blood pressure monitor. Blood pressures were measured on a total of 150 patients. Before starting the measurements, patients had to be at rest for five minutes. Blood pressures were measured in the same position and at the same arm. Both systolic and diastolic blood pressure, and pulse were collected from the three devices. Agreement was analyzed by means of Bland Altman plots,

assessing agreement between the Withings blood pressure monitor and the standard device, the iHealth blood pressure monitor and the standard device, and eventually between the Withings blood pressure monitor and the iHealth blood pressure monitor.

2.6 Data collection

During inclusion, demographic and sociodemographic data were obtained by means of questionnaires. The demographic information involved age, weight before pregnancy and at the moment of inclusion, length, gestational age, comorbidities, and information about gravida (number of pregnancies), para (number of births of viable offspring, gestational age > 24 weeks), and abortions (abortions and miscarriages < 24 weeks of gestation). Sociodemographic information involved nationality, education, job, and marital status. At the end of the study, information was gathered about mode of delivery, gestational age at delivery, and physical condition of the baby. Parameters which were obtained were weight, length, head circumference, Apgar (appearance, pulse, grimace, activity, and respiratory) score after one, five, and ten minutes, and admission at the Neonatal Intensive Care (NIC). Information about missed blood pressure and weight measurements were gathered by contacting the patients.

The experience of the participants was determined by obtaining information via questionnaires. These questionnaires were filled in at the beginning of the study, during the study, and at the end of the study. Questions were asked about their experience with the devices, the use of the application, and the timing of the measurements. The answers were scaled from one to five, with one being difficult, very unpleasant, or disagreement, and five being easy, very pleasant, or agreement.

2.7 Statistical analysis

Statistical analysis was performed using IBM Statistical Package for Social Sciences release 22 (IBM Corporation, Chicago, United States). Statistical analysis of the validation of the blood pressure monitor devices was performed by means of Bland Altman plots and a paired samples T-test. Normality was assessed with the Shapiro-Wilk test. When normally distributed, data were expressed as mean ± standard deviation (STD). If not normally distributed, data were expressed in terms of median and interquartile range (IQR). The Pearson-Chi square test and Odds ratios were used to test a correlation between demographic characteristics and compliance rate. Values of $p \leq 0.05$ were considered statistically significant.

3 Results

3.1 Validation of the monitoring devices

The monitoring devices implemented in the study (Withings Wireless Blood Pressure monitor and iHealth Blood Pressure monitor) were internally validated with a standard device used in the hospital. In total, systolic and diastolic blood pressure was measured with the three devices on 144 participants. The participants were randomly selected from different departments of the hospital (revalidation and maternity) or were healthy persons. Age varied between 18 and 88 years, with a mean age of 42.4 ± 21 (mean ± STD). In order to obtain a high level of agreement, blood pressure was always first measured with the Withings Wireless Blood Pressure monitor, secondly with the iHealth Blood Pressure monitor, and at last with the standard device.

Mean systolic blood pressure of the Withings Wireless Blood Pressure monitor was 123.50 ± 15.30 (mean ± STD) (Table 2) and mean diastolic blood pressure was 74.40 ± 9.70 (mean ± STD). Mean blood pressures obtained from the iHealth Wireless Blood Pressure monitor were 122.40 ± 17.50 (mean ± STD) and 76.60 ± 10.70 (mean ± STD) for systolic and diastolic blood pressure respectively. Blood pressures obtained from the standard device showed a mean systolic blood pressure of 119 ± 16 (mean ± STD) and a mean diastolic blood pressure of 71.40 ± 10.30 (mean ± STD). Bland-Altman plots were constructed (Appendix 1). A paired samples t-test showed only a non-significant result in systolic blood pressure of the Withings Wireless Blood Pressure monitor compared to the iHealth Blood Pressure monitor ($p > 0.05$). All the other data were significant different ($p < 0.05$). At this point, more data must be collected to analyze an intra difference between measurements with the same device on the same person. Differences between measurements taken with the same blood pressure device must be minimal.

Table 2: *Mean systolic and diastolic blood pressure of the three devices (Withings, iHealth, and standard device). All values are mean ± std.*

	Blood pressure (mmHg)	
Devices	**Systolic**	**Diastolic**
Withings	123.50 ± 15.30	74.40 ± 9.70
iHealth	122.40 ± 17.50	76.60 ± 10.70
Standard device	119 ± 16	71.40 ± 10.30

3.2 Characteristics of the population

In this section the baseline characteristics and demographic characteristics of the population of the PREMOM study, and collection of data and presence of events are analyzed.

3.2.1 Inclusion of participants

In total 35 patients were included between 9th November and 29th February in the PREMOM study and started measurements. One patient stopped before admission to the MIC or delivery because of lack of motivation. One patient was recommended by her gynecologist to stop with the measurements due to hypertension at home but not in a hospital setting.

The remaining 33 patients completed the study until MIC admission or delivery and are included in further data analysis. Three of the 33 patients were considered as low-risk and participated voluntarily out of interest. The other 30 patients were classified as high-risk because of different reasons ranging from PE or HELLP during a previous pregnancy, age, bad maladaptation of the maternal hemodynamics (results of the NICCOMO test), gestational hypertension, high blood pressure during gestation or during a previous gestation, or cardiac dysfunction. In total, six patients were classified as high-risk due to a history of PE, one patient due to HELLP during a previous pregnancy, three because of the diagnosis of gestational hypertension, 11 because of high blood pressure during gestation, one because of her age, one due to the results of the NICCOMO test, two due to high blood pressures during previous gestation, one because of cardiac dysfunction, and finally four for other reasons (Figure 7).

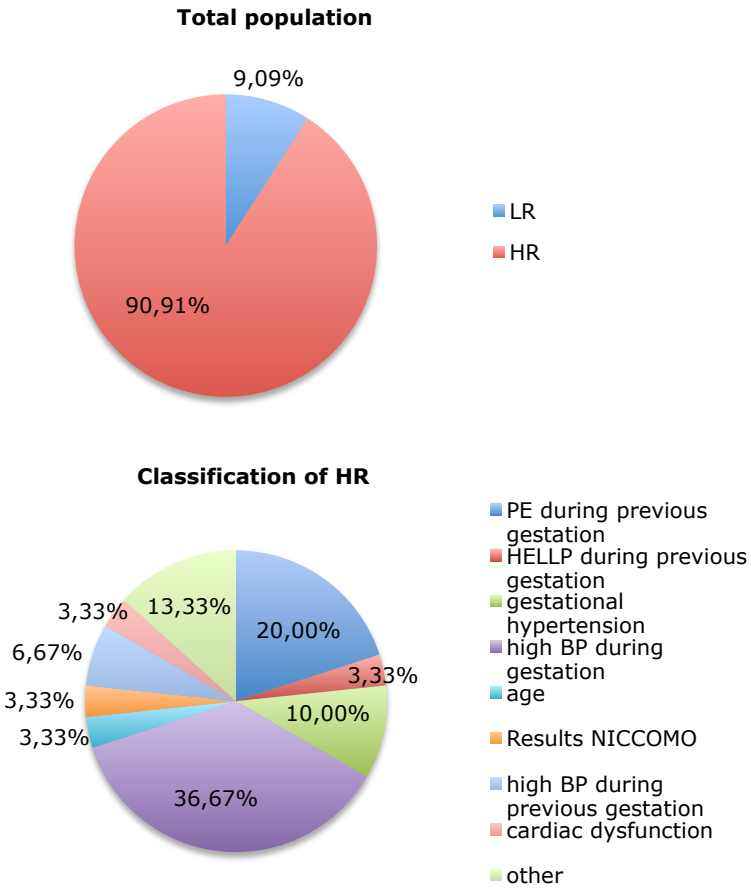

Figure 7:
Representation of the classification of the participants. A) Subdivision of the total population (n=33) in a low-risk and a high-risk group, B) Classification of the different categories of the high-risk group (n=30).
BP = blood pressure, LR = low-risk, HELLP = Hemolysis, Elevated Liver Enzymes, and Low Platelets count; HR = high-risk, PE = preeclampsia

3.2.2 Baseline characteristics

The baseline characteristics of the participants involved age, weight before pregnancy, BMI before pregnancy, weight at the moment of inclusion, gestational age at the moment of inclusion, and GPA score (Table 3). All values are presented as mean ± STD. The mean age of the population was 30.73 years, mean weight before pregnancy 72.08kg weight at moment of inclusion 80.59kg, BMI before pregnancy 26.30kg/m^2, gestational age at moment of inclusion 25 weeks and five days, and most common GPA was G2P0A0. During this analysis and further evaluation of the data, no distinction was made between the low-risk and the high-risk group because of the minimal number of patients in the low-risk group.

Table 3: *Baseline characteristics of the total population (n=33).*
BMI = body mass index

	Population (n=33)
Age (years)	30.73 ± 5.26
Weight before pregnancy (kg)	72.08 ± 14.77
Weight at moment of inclusion (kg)	80.59 ± 14.11
BMI before pregnancy (kg/m^2)	26.30 ± 5.32
Gestational age at moment of inclusion (weeks)	25.83 ± 7.00
Gravida (G)	2 ± 1
Para (P)	0 ± 1
Abortion (A)	0 ± 1

3.2.3 Demographic characteristics

The list of questionnaire regarding the demographic characteristics was filled in during the inclusion process. This survey was assessed to gain a more overall view of the participants and are listed in Table 4 and represented in Figure 8.

Table 4: *Demographic characteristics of the population (n=33).*

	Population (n=33)
Age (years)	
18 – 25	12.12%
26 - 30	45.45%
31 - 35	21.21%
36 - 40	15.15%
> 40	6.06%
BMI (kg/m^2)	
Normal	48.48%
Overweight	30.30%
Obesity	21.21%
Education	
Secondary Education	33.33%
Community College	45.45%
University	21.21%
Marital status	
Married	45.45%
Legal cohabitation	36.36%
Domestic cohabitation	15.15%
Other	3.03%
Profession	
Unemployed	3.03%
Worker	15.15%
Attendant	63.64%
Independent	3.03%
Other	15.15%
Nationality	
Belgian	90.91%
Dutchman	6.06%
Turkish	3.03%
Smoker status	
Yes	6.06%
No	93.94%
Primigravida	
Yes	57.58%
No	42.42%

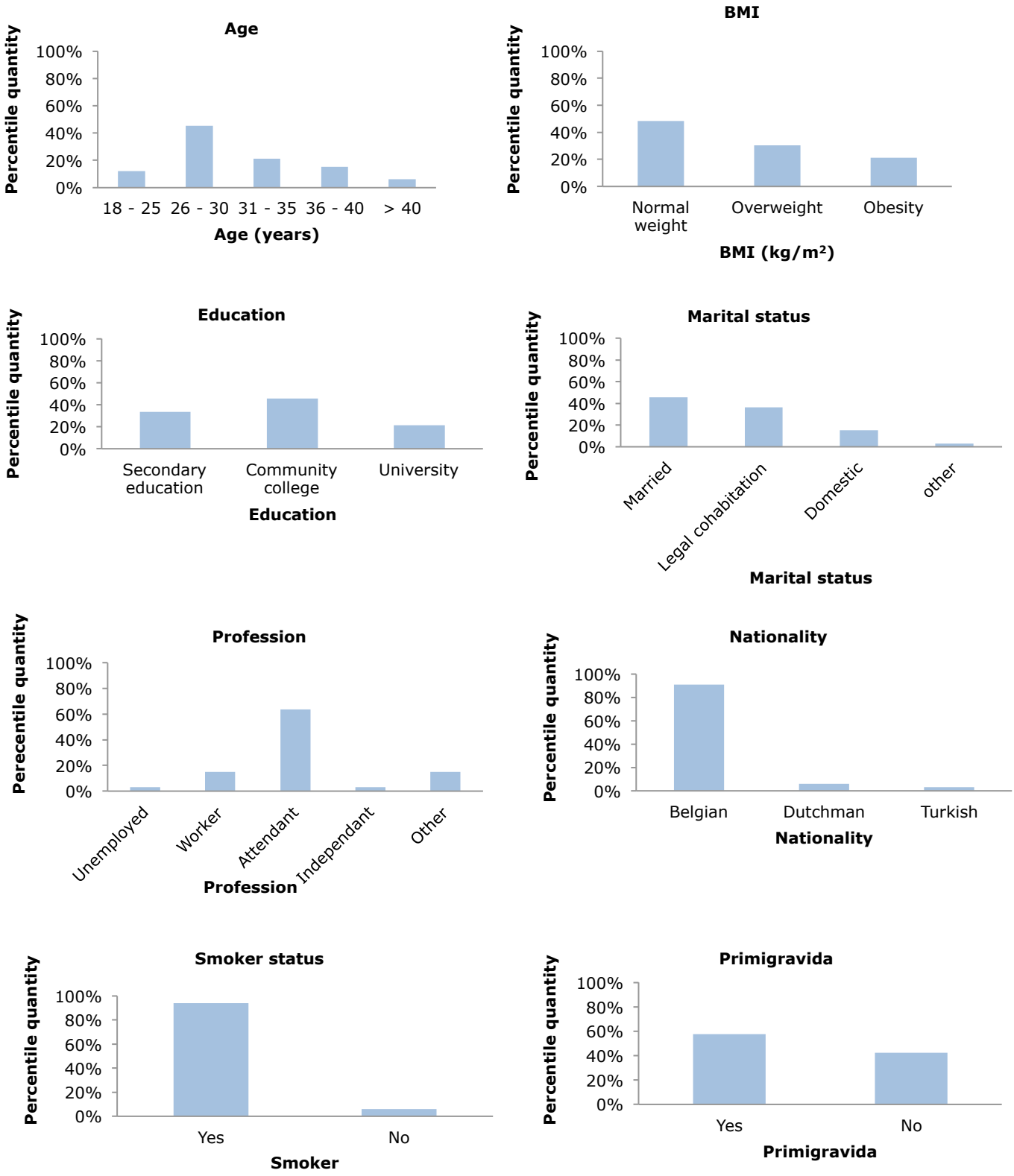

Figure 8:
Representation of the demographic characteristics of the participants (n=33). A) Age, B) BMI, C) Education, D) Marital status, E) Profession, F) Nationality, G) Smoker status, H) Primigravida.
BMI = Body Mass Index.

3.3 Data collection and events

In this section, data about events (consecutive high blood pressure measurements) and consequences of events (start medication, ambulant CTG, 24h urine collection, or MIC admission) are further explained and analyzed.

3.3.1 Events and outcomes

An event is defined as two consecutive blood pressure measurements ≥ 140/90 mmHg or a diastolic blood pressure ≥ 100 mmHg, measured at least six hours apart. During the course of the study, 187 events were stated, divided over 15 patients. Median gestational age at the time of an event was 31 weeks (IQR 25.87 – 37.28 weeks) (Figure 9). These events led to medication intake or adjustments in seven patients, CTG orders in five patients, 24 hours urine collection in four patients, and three MIC admissions, all as a result of telemonitoring. In total, five patients were diagnosed with PE, of which four had events. One patient, who was diagnosed with PE and was admitted to the MIC, thus never had events as defined earlier. However, she had measured multiple times a blood pressure ≥ 140/90 mmHg but not consecutive. Of the other 11 patients with events, eight of them were diagnosed with (gestational) hypertension. Further data analysis of the outcomes of all patients, based on having events or not and the diagnosis of PE, gestational hypertension, or no diagnosis; showed a sensitivity of 72.22% and a specificity of 86.67%. The positive and negative likelihood ratio was 5.42 and 0.32 respectively.

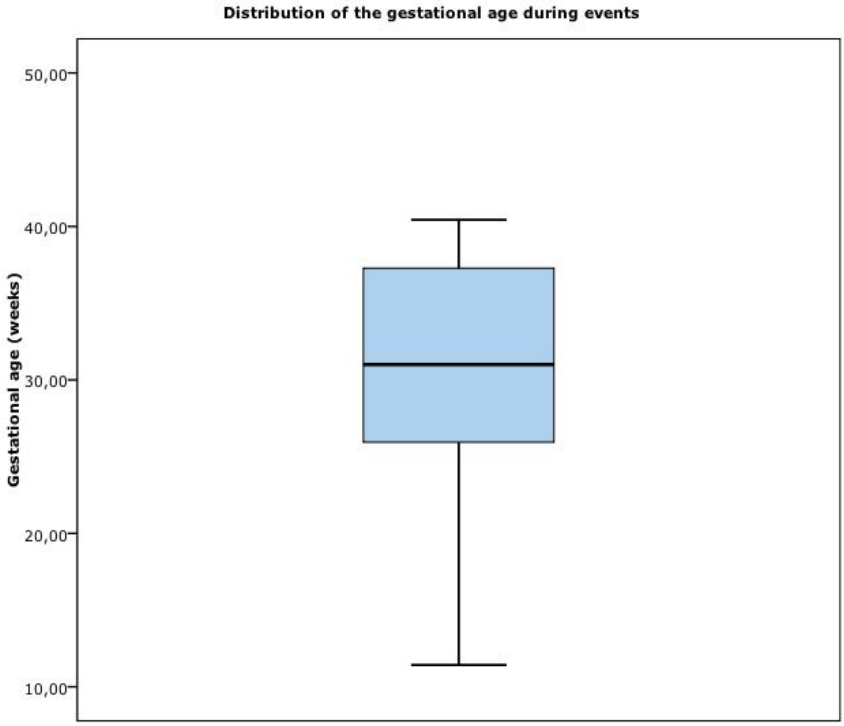

Figure 9:
Distribution of the gestational age at time of an event (n=15). Minimum = 11.43; Maximum = 40.43; Median = 31 (IQR 25.87 - 37.28).

Looking at the outcomes (Table 5), the deliveries of 14 patients (42.42%) out of 33 were induced. Of these 14, 50% was induced as a consequence of hypertension or PE. In 13 patients (39.39%) the delivery started spontaneously. Finally, six patients (18.18%) gave birth by means of a primary caesarian section. Four out of six primary caesarian sections were a result of hypertension or PE. In total, 11 deliveries (33.33%) were induced or happened by means of a planned caesarian section due to hypertension (which may possibly lead to PE) or PE. Other reasons for induced deliveries or caesarian sections were post due date, macrosomia (fetus significantly larger than average), or gestational diabetes.

Table 5: *Means of deliveries in the population (n=33).*

	Population (n=33)
Induction	42.42%
Hypertension/PE	50%
Cesarean section	18.18%
Hypertension/PE	66.67%
Spontaneously	39.39%

3.3.2 Satisfaction surveys

The experience and the satisfaction of the participating women is an important factor in analyzing the implementation of telemonitoring in obstetrics. Eventually, they are the persons who perform the measurements and obtain experience in working with the devices and with the application. The implementation of telemonitoring is of greater success when the patients are satisfied.

In the beginning, during inclusion, the first questionnaire was filled in. This survey handled items as if they ever heard of telemonitoring, what their feelings were when they thought about it, and how they felt knowing that the researcher had a look into their private data. Answers were either scaled from one until five (one meaning very unpleasant/very difficult, and five meaning very pleasant/very easy) or either yes or no (Table 6 and Table 7). In total all 33 participants filled in the first survey. The results showed that 33.33% had ever heard about telemonitoring. In total 81.81% had positive feelings about telemonitoring and gave a score of four or higher. It is even so that 100% would use telemonitoring, 45.45% would voluntarily make us of telemonitoring, 6.06% if benefits are scientifically proven and if it is approved, 60.61% if recommended by the doctor, 36.36% when problems during gestation are present, 6.06% when recommended by friends and/or family, and at last 3.03% for other reasons. Not only were they positive about telemonitoring itself, the majority of the patients (84.84%) was even positive about the fact that the researcher had insight into their data. At last 69.69% thought it would be easy to involve the measurements of their data into their daily routine. Looking at the operation system of their smartphone 66.67% used Android and 33.33% iOS.

Table 6: *Questionnaire filled in during the inclusion moment. Answers are ranged from a scale of one to five (one meaning very difficult/very unpleasant/not satisfied and five meaning very easy/ very pleasant/satisfied) (n=33).*

During inclusion (n=33)	1	2	3	4	5	yes	no
Have you ever heard about telemonitoring?						33.33%	66.67 %
What are your general feelings when you think about telemonitoring?			18.18%	36.36%	45.45%		
How easy do you think it will be to plan the measurements in your daily routine?		3.03%	27.27%	39.39%	30.30%		
How do you feel about the fact that the researcher has insight into your data?			15.15%	36.36%	48.48%		

Table 7: *Additional question asked during inclusion. Multiple answers were possible. A = voluntarily, B = when scientifically proven and approved, C = when recommended by the doctor, D = when problems during gestation are assessed, E = when recommended by friends and/or family, F = other reasons (n=33).*

During inclusion (n=33)	A	B	C	D	E	F	Not
When would you use telemonitoring?	45.45%	6.06%	60.61%	36.36%	6.06%	3.03%	0%

During participation, an interim questionnaire was asked to fill in to evaluate their experience with the monitoring devices and to help to solve the problems associated with the devices (Table 8). In total 29 patients completed the interim survey. The intermediate survey was not conducted in four patients because of short participation time or because of difficulties with contacting the patients. Overall 86.21% was satisfied with the monitoring devices, 86.20% found the devices easy to use, and 89.66% experienced the smartphone application easy in usage. The majority of the participants (72.41%) had no problems with planning the measurements into their daily routine. Only 6.90% had neutral feelings about that the fact that the researcher had insight into their data. The other 93.10% was positive about that and had no problems with it. Finally, only 3.45% was neutral about the possibility to contact the researcher. The score of three was even only given when the participant has never had to contact the researcher because no problems were assessed.

Table 8: *Intermediate survey. Answers are ranged from a scale of one to five (one meaning very difficult/very unpleasant/not satisfied and five meaning very easy/ very pleasant/satisfied) (n=29).*

Interim survey (n=29)	1	2	3	4	5
Are you satisfied with the monitoring devices?			13.79%	62.07%	24.14%
How easy to use are the monitoring devices?			13.79%	34.48%	51.72%
How easy is it to plan the measurements in your daily routine?			27.59%	37.93%	34.48%
How easy to use is the smartphone application?		3.45%	6.90%	41.38%	48.28%
How do you feel about the fact that the researcher have a daily look into your data?			6.90%	31.03%	62.07
How pleased are you with the possibility to contact the researcher?			3.45%	20.69%	75.86%

The last questionnaire was filled in after the participants completed the study, either when admitted to the MIC or after delivery. In total 30 out of 33 patients completed the final survey (Table 9). This last questionnaire handled questions about the patients' experience with the devices and telemonitoring itself, and whether any difficulties were experienced. The grand majority of the patients (93.33%) had the same positive image about telemonitoring as they experienced or even a better experience than they thought. The greater part of the patients experienced telemonitoring as pleasant (90%) and 80% found the devices and the app easy to use. The planning of the measurements into the daily routine was for 63.33% easy, however 26.67% thought that this was neither easy nor difficult, and 10% thought it was rather difficult. Only 23.33% experienced other difficulties, *i.e.* connection problems. In 40% of the patients telemonitoring had an influence on the pregnancy. Half of the patients thought that more access to their data would be an added value but 50% was neutral or did not see more access as an added value. Another question handled was whether the patients would participate again or not and for what reason. In total 56.67% of the patients would participate again voluntarily, 33.33% on recommendation by the doctor, and 20% when complications arise during the pregnancy. An additional question was asked (Table 10) whether the patients would participate again. In total, 56.67% would participate again voluntarily.

Table 9: *Final survey. Answers are ranged from a scale of one to five (one meaning very difficult/very unpleasant/not satisfied and five meaning very easy/ very pleasant/satisfied) or yes or no (n=30).*

Final survey (n=30)	1	2	3	4	5	Yes	No
Was your image about telemonitoring before inclusion the same or better as you have experienced?						93.33%	6.67%
How pleasing did you experience telemonitoring?		3.33%	6.67%	63.33%	26.67%		
How easy were the devices and the app to use?			20%	46.67%	33.33%		
How easy was it to plan the measurements in your daily routine?		10%	26.67%	33.33%	30%		
Did you experience any difficulties?						23.33%	76.67%
Did telemonitoring had an influence on your pregnancy?	40%	10%	10%	16.67%	23.33%		
Would you think of it as an added value if you have more access to your data?	10%	10%	30%	23.33%	26.67%		

Table 10: *Additional question asked during the final survey. Multiple answers were possible. a = yes, voluntarily, b = yes, on recommendation, c = yes, when family and friends recommend it, d= when complications arise during pregnancy, e = no, f = others*

Final survey (n=30)	a	b	c	d	e	f
Would you participate again?	56.67%	33.33%	0%	20%	0%	0%

3.4 Compliance

Telemonitoring and its results depend on the patient's adherence to the number of measurements. The study PREMOM prescribed blood pressure measurements twice a day, weight measurement once a day, and wear an activity tracker all day and night. This section analyses how well the patients adhere to demanded frequency, resulting in compliance per patient, and the reasons for a low compliance (< 66%).

3.4.1 Missing data

In total, data from 33 patients was collected. It was expected that during the study 5546 blood pressure measurements and 2773 weight measurements were performed. In total, 76.14% (a total of 4223) of the expected blood pressure and 62.75% (a total of 1740) of the expected weight measurements were performed. Out of the 33 patients, 12 patients were contacted for missed measurements to increase compliance. Patients were only contacted after two to three days if missing measurements endured. In total, 28 telephone calls (multiple patients were contacted multiple times) were made. Two major reasons for missed measurements were either person-related (no motivation or forgetfulness) or device-related (connectivity problems). Data represented here is only representative for a part of the total population. Reasons for non-adherence summed up here and percentages count only for the part of the population who received phone calls, thus 12 out of 33 patients. Approximately 63.63% of the missed blood pressure measurements were personal-related and 36.36% was device-related. Looking at the missed weight measurements, 75% was personal-related and 25% was device-related (Figure 10).

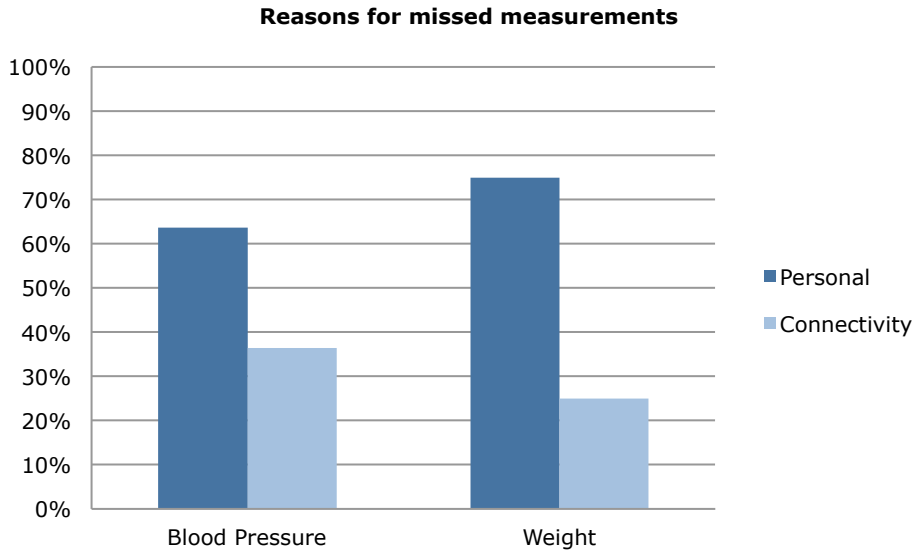

Figure 10:
Graphic representing the distribution of the reasons for missed measurements (n=12). Reasons for missed measurements were either personal-related or device-related connectivity problems.

When analyzing the compliance of every patient and week by week, results showed that the median compliance involving the blood pressure measurements was 76% (IQR 70-83). The median compliance for the weight measurements was 60% (IQR 52-65). Figure 11a shows that there is a trending decrease in compliance rate for the blood pressure measurements. Figure 11b indicates the same trending decrease in compliance rate for the weight measurements as for the blood pressure measurements. These results indicate that as the pregnancy progresses, patients found it harder to adhere to the recommended number of measurements.

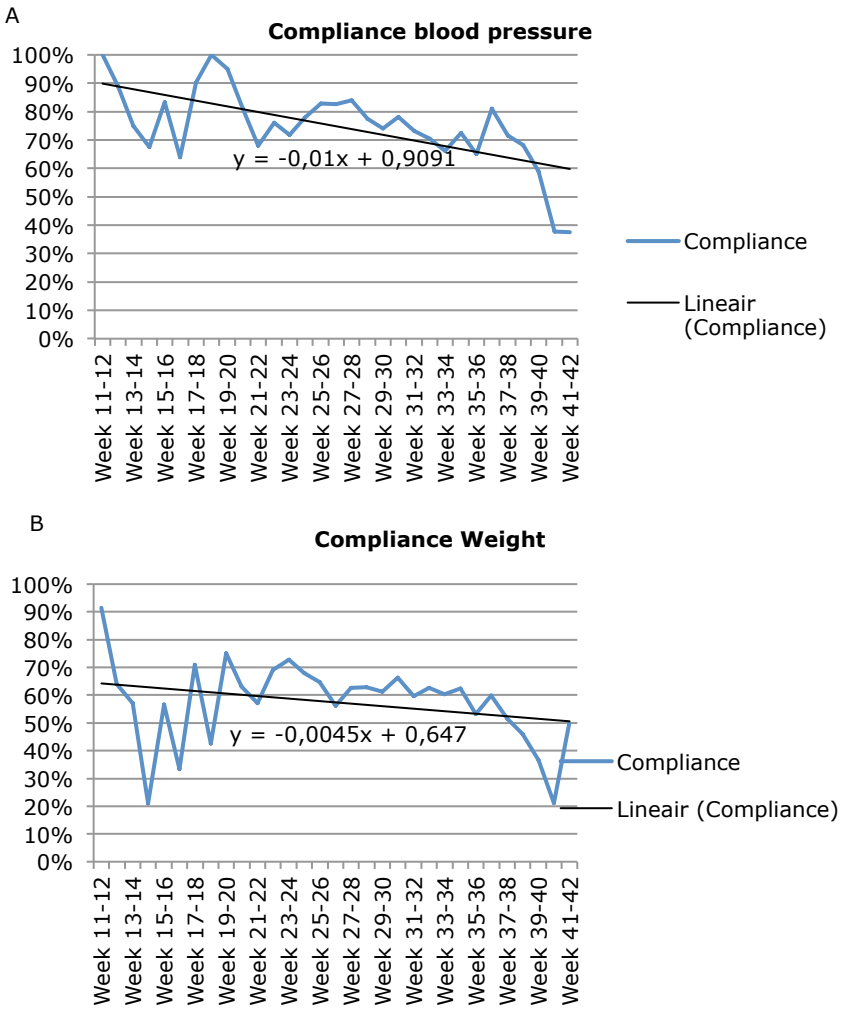

Figure 11:
Compliance week by week. A) Compliance of the blood pressure measurements week by week, B) Compliance of the weight measurements week by week.

When further looking into the data and the results of the compliance and missing data, an analysis was made whether compliance was increased after a contact moment between the researcher and the patient (by a telephone call or after an email). Important to notice here is that one of the 12 patients contacted for missing data had a device-related problem. After the bug was fixed, her measured data was transferred to the online platform and her compliance was throughout her pregnancy high. The change in compliance of this patient after a contact moment is not included in the next analysis. In total, 10 patients were contacted for missed blood pressure measurements (Table 11). Four patients were contacted one time, two patients two times, two patients three times, one patient four times, and one patient five times. Secondly the results of the change in compliance for the weight measurements were analyzed (Table 11). In total, 11 patients were contacted for missing weight measurements. Five of the 11 patients were only contacted once, two patients two times, two patients thrice, one patient four times, and one patient five times. These results indicate that change in compliance after a contact moment is a personal given. Results are represented as a mean compliance until the data of contact and in between contact moments. These data are biased because the number of days before and after a contact moment was not equally distributed.

Table 11: *Analysis of the change in compliance per patient before and after a contact moment.*

	Before	One	Two	Three	Four	Five
Blood Pressure (n=10)						
One contact moment						
Premom 35	76%	66%				
Premom 59	67%	77%				
Premom 74	46%	48%				
Premom 107	50%	60%				
Two contact moments						
Premom 72	46%	36%	72%			
Premom 76	60%	11%	16%			
Three contact moments						
Premom 40	48%	10%	27%	0%		
Premom 68	66%	50%	7%	90%		
Four contact moments						
Premom 89	50%	28%	37%	7%	0%	
Five contact moments						
Premom 73	25%	28%	71%	65%	51%	33%
Weight (n=11)						
One contact moment						
Premom 35	20%	0%				
Premom 59	65%	38%				
Premom 71	50%	24%				
Premom 74	28%	14%				
Premom 107	100%	53%				
Two contact moments						
Premom 72	48%	42%	100%			
Premom 76	81%	35%	19%			
Three contact moments						
Premom 40	25%	20%	34%	0%		
Premom 68	42%	42%	0%	35%		
Four contact moments						
Premom 89	93%	54%	0%	0%	0%	
Five contact moments						
Premom 73	40%	28%	28%	31%	11%	0%

3.4.2 Contact moments

During the study, the researcher made 77 telephone calls to the patient (Table 12). The reason for communication was in 36.36% of the cases involving missing data and missed measurements. Furthermore 19.48% of the telephone contact involved the conduction of a survey (interim or the final survey) and 11.69% of the phone calls were related to medication adjustments or start intake of medication. Other reasons for contacting the patients involved returning of the devices (9.09%),

increased blood pressure (2.60%), to make a CTG appointment (10.39%), to collect 24 hours urine to test for proteinuria (2.60%), explanation about the devices or whether the devices were connected or not (6.49%), or to schedule a PE consultation (1.30%). Remarkably 41.56% of the made phone calls were not answered and thus the message was left on voicemail. In total, the patient contacted the researcher 42 times and in 45.24% of the 42 cases the patient was only calling to return the call of the researcher. Other reasons for the patient to contact the researcher were concerns about an increased blood pressure (19.05%) or technical issues with the devices (35.71%). Not only telephone communication was used to contact the patient or the researcher. In total 9 e-mails were sent, two of them were sent by the researcher about missing data. The other seven e-mails were sent by the patients to contact the researcher about connectivity problems involving the devices (85.71%) or to express their concerns about increased blood pressures (14.29%).

Table 12: *Representation of made telephone calls from the researcher to the patient (n=78) and patient to the researcher (n=42).*

Reasons	Telephone calls
Researcher to patients	**77 phone calls**
Missing data	36.36%
Survey	19.48%
Medication	11.69%
Returning of the devices	9.09%
Increased blood pressure	2.60%
CTG	10.39%
24 hours urine collection	2.60%
Device related	6.49%
PE consultation	1.30%
Patient to researcher	**42 phone calls**
Returned phone calls	45.24%
Increased blood pressure	19.05%
Device related	35.71%

During the course of the study, not only the patients were contacted. In total, 109 e-mails were sent from the researcher to the gynecologists with an update of the blood pressure evolvement of the patient when having a consultation and 27 e-mails concerning increased blood pressure and requesting a policy. Every Friday afternoon a MIC meeting took place. In this meeting the patients were discussed and analyzed for further advice, adjustments, or booking a consultation. In two patients this meeting led to the order of a CTG appointment. This means that two out of eight phone calls made for a CTG consultation was not a consequence of an evaluation sent to the gynecologist by the researcher but as a result of the meeting.

3.4.3 Demographics and compliance

Looking into the psychological side of compliance, the question arose whether certain demographic characteristics could be correlated with a high or a low compliance. The demographic data of all the patients and compliance per patients was analyzed. Compliance was rated high when > 66%. Odds ratios were used to test correlation between the demographic characteristics and the compliance. Results of the compliance of the blood pressure measurements (Table 13) showed a significant correlation between age higher than 40 and a low compliance (Odds ratio = 0.00 and $p < 0.05$), status of unemployment and a low compliance (Odds ratio = 0.00 and $p < 0.05$), HELLP in a previous pregnancy and a low compliance (Odds ratio = 0.00 and $p < 0.05$), high blood pressure during gestation and a high compliance (Odds ratio = 1.44 and $p < 0.05$), and high blood pressure during previous gestation and a low compliance (Odds ratio = 0.00 and $p < 0.05$). However, it must be taken into account that only a small amount of patients (one to two) were classified in these categories, except for the category high blood pressure during gestation (n=11). The other demographic characteristics age, BMI, education, marital status, nationality, primigravida, and smoking status showed no positive significant correlation ($p > 0.05$) (Appendix 2). Analysis of the relation between compliance of the weight measurements and demographics showed no relation between any demographic characteristic and compliance rate ($p < 0.05$) (Appendix 3).

Table 13: *Table representing the relation between compliance of the blood pressure measurements and demographic characteristics. Percentage of compliant and non compliant is given, the Odds ratio, 95% confidence interval (CI), and the p-value. * = p < 0.05, † = no values were calculated due to a small number.*

Blood pressure					
	Compliant (%)	**Non compliant (%)**	**OR**	**95% CI**	**p**
Age					
> 40 (n=2)	0	100	0	†	0.01*
Job					
Unemployed (n=1)	0	100	0	†	0.04*
Reason inclusion					
HELLP previous pregnancy (n=1)	0	100	0	†	0.00*
High blood pressure during gestation (n=11)	100	0	1.44	0.68 – 58.10	0.02*
High blood pressure during previous gestation (n=2)	0	100	0	†	0.01*

3.5 Technical issues in the implementation of the monitoring devices

The implementation of the monitoring devices is dependent on technology. Data measured at home are transferred via Wi-Fi and Bluetooth and the measurement devices are technological devices. Measurements fail when the device is damaged or when no Bluetooth and/or Wi-Fi connection is established. In this section the technological issues concerning the implementation of the monitoring devices is handled.

3.5.1 Installation

During installation of the application on the smartphone of the patient, technological problems came forward. Either the smartphone of the participant was not compatible with the application or no Wi-Fi connection could be made. The usage of 3G/4G could solve this problem however. When these problems arose during the inclusion moment of the patient, not every patient was willingly to use their mobile data. Several reasons were given, *i.e.* battery was too low or usage of 3G/4G cost money.

Other problems during installation were device related. The connection between the devices and the smartphone application failed often, meaning the installation had to start all over again. Even when connection was made, the installation was not always successful. In some cases the patients had to try to install one of the devices at home because of subsequent failed connection.

3.5.2 At home measurements

When performing the measurements at home, several problems were stated. In some cases the connection between the application and one of the devices was lost and reinstallation failed. This problem was often stated with the weight scale, the Smart Body Analyzer. Data measured were not transferred to the application. When this problem arose, the patients were asked to enter their measured weight manually. Not only the weight scale gave problems, but also the Pulse O_2 had often connection problems. Another problem was the fact that after a long time of usage, the Pulse O_2 devices were damaged too hard or disarrayed to use them for another participant.

3.5.3 Transfer to iHealth monitoring devices

Due to the problems analyzed in the previous section, a transfer to the iHealth monitoring devices was considered. The installation of these devices went easier and there were no connectivity problems during the inclusion moment. When the patient received the iHealth monitoring devices, no weight scale was given. This was done because the iHealth weight scale had to be connected to a Wi-Fi network before installation could be completed. The disadvantage of that was that the patients had to reinstall the weight scale at home on their own Wi-Fi network. Another important reason was that most patients have a weight scale at home and thus money spent on the purchase of weight scales could be spend on more blood pressure monitors. The patients then entered their weight, measured with their own weight scale at home, manually in the application. Both the blood

pressure monitor and the activity tracker connected well and there were no problems assessed at home.

Disadvantage of the use of iHealth devices was the fabric of the blood pressure monitor. The fabric of the Withings Blood Pressure monitor was washable and more hygienic compared to the iHealth Blood Pressure monitor. On the other hand, the blood pressure device of iHealth was available in different sizes and easier to apply to the forearm compared to the Withings device. The devices were chargeable by means of an USB cable, and no longer via batteries as was the case with the Withings devices (except for the Pulse O_2).

3.6 Case reports

In the following section four case reports are discussed and analyzed. These four cases are an example of how telemonitoring works and the process behind detected events.

3.6.1 Case report Premom 68

Premom 68, a woman of 41 years old, was included on 14th October 2015 at a gestational age of 11 weeks and one day. Reason for her participation was the diagnosis of gestational hypertension, which is a risk factor for developing preeclampsia. Medication at that point was Nifedipine® (Adalat), a dose of 90 mg one time a day. Nifedipine® is an antihypertensive drug, reducing blood pressure by blocking calcium channels.

Already during the first days of her participation, Premom 68 had events (Figure 12). Her gynecologist was contacted and her medication was adjusted to two times 250mg Aldomet® a day and Nifedipinie® 90mg one time a day. Aldomet® is an antihypertensive drug, which inhibits the sympathetic nervous system and lowering blood pressure. From then on, the hypertension was under control and no more events were stated until 21st November.

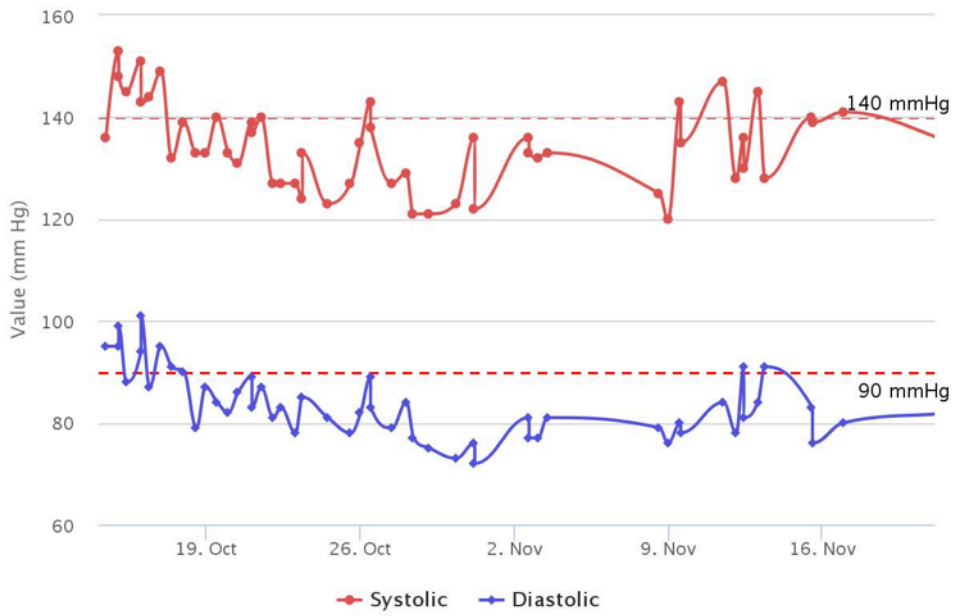

Figure 12:
Blood pressure of Premom 68 of 14th October to 16th November. The red line represents the systolic blood pressure and the blue line the diastolic blood pressure. The red dotted line indicates the limits of both systolic (140 mmHg) and diastolic blood pressure (90 mmHg).

On this day, Premom 68, at that point a gestational age of 16 weeks and four days, was submitted to the MIC on recommendation by her general practitioner to reevaluate her medication because she measured a blood pressure of 181/110 during her consultation. The usage of Nifedipine® was stopped, Trandate® (three times 100 mg a day) was started and Aldomet® was augmented to two times 500mg a day. Trandate® is an antihypertensive drug, reducing vascular resistance. Due to connectivity problems, no data were transferred of 16th November to 24th November. Because of this problem, the events between these dates were missed out. On 24th November, a new update was sent to the gynecologist because of consecutive high blood pressure measurements. The gynecologist decided to augment her medication for one day to Trandate® five times 100mg a day and the same dosage of Aldomet® as usual. The next day, her blood pressure did not show signs of decline and the gynecologist was again contacted. Her medication for that day was adjusted to Trandate® tree times 100mg a day, Aldomet® two times 500mg a day and an extra doses of three times 100mg Aldomet®. At this point, the decision was made to await her blood pressure for a couple of days. On 30th November, the patient contacted the researcher about her blood pressures. Again, an evaluation was sent to the gynecologist because of multiple events. Her medication was augmented to Aldomet® four times 500mg a day, which she had to take on a schedule (08.00h, 12.00h, 16.00h, and 20.00h) and Trandate® two times 100mg a day (at 08.00h and at 20.00h). After this adjustment, her blood pressures kept being high and events were stated everyday (Figure 13).

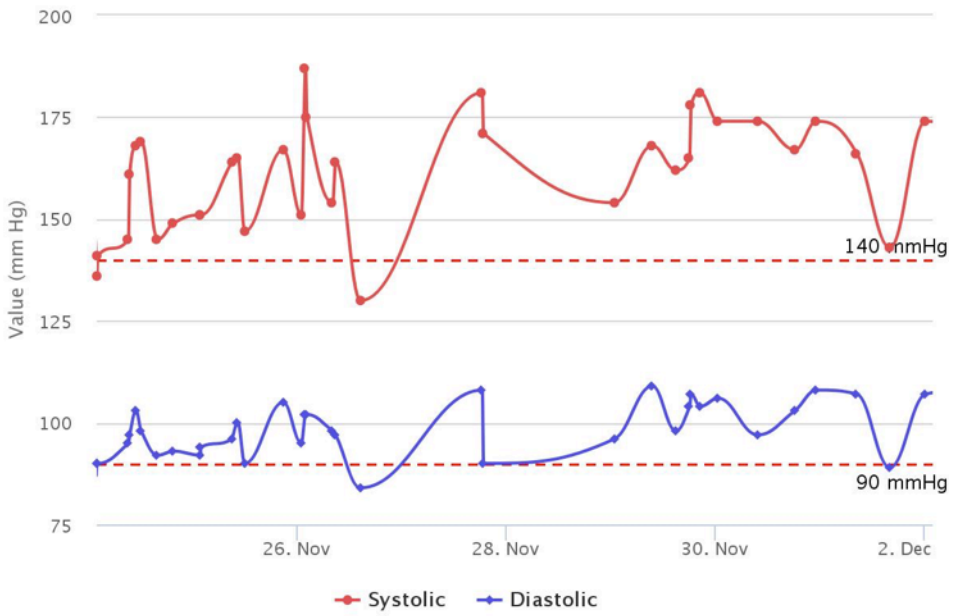

Figure 13:
Blood pressure of Premom 68 of 24th November to 2nd December. The red line represents the systolic blood pressure and the blue line the diastolic blood pressure. The red dotted line indicates the limits of both systolic (140 mmHg) and diastolic blood pressure (90 mmHg). Events are still present and blood pressure does not decrease.

On 3th December, Premom 68, a gestational age of 19 weeks, contacted the researcher and a new policy was requested. From then on, she had to take additionally to her medication one time a day 5mg Amlor®. This medication lowers blood pressure via a mechanism involving calcium. Since the start of Amlor®, fewer events were stated and her blood pressure began to decrease. On 7th December she contacted the researcher because she was suffering from side effects. No adjustments were made to her medication schedule. On 9th December she was submitted to the emergency department at a gestational age of 19 weeks and one day (Figure 14). Premom 68 had a miscarriage and lost her child. Figure 15 shows a schematic timeline of the events and medication adjustments of Premom 68.

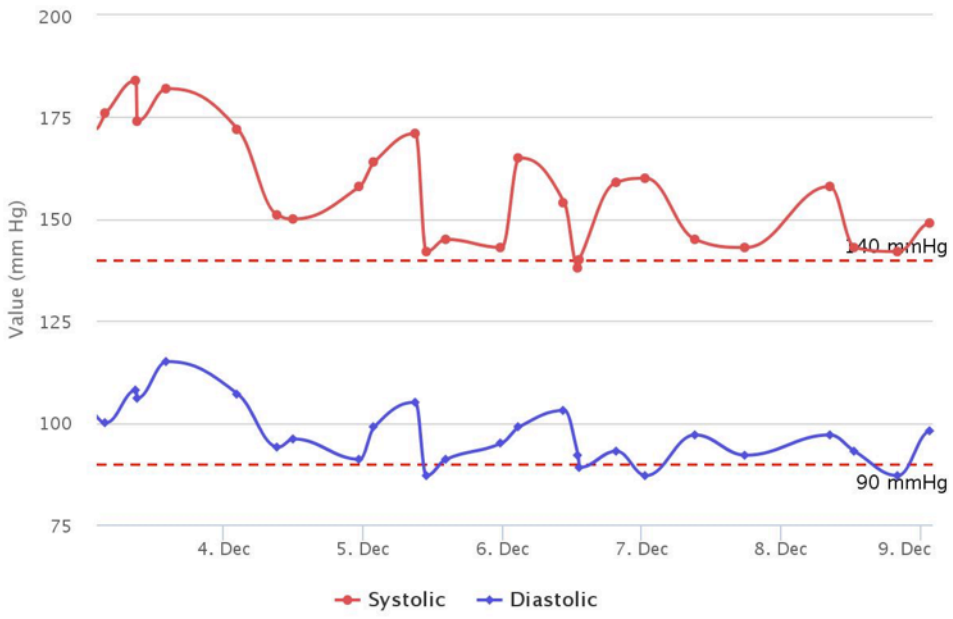

Figure 14:
Blood pressure of Premom 68 from 3th of December until 9th of December. The red line represents the systolic blood pressure and the blue line the diastolic blood pressure. The red dotted line indicates the limits of both systolic (140 mmHg) and diastolic blood pressure (90 mmHg). A decline of the blood pressure can be seen since 4th of December.

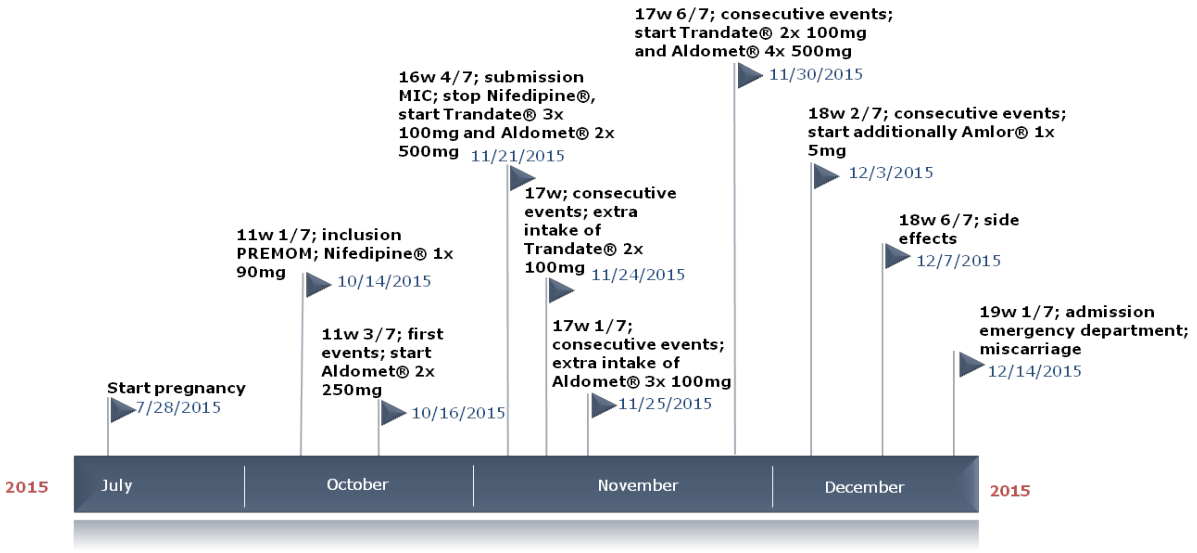

Figure 15:
Schematic timeline of the events and medication adjustments of Premom 68.

This case represents the strengths and a weakness of telemonitoring. All medication adjustments were upon telemonitoring and having a daily picture of the parameters of the patient. However, due to connectivity problems and problems with transferring the data to the online platform, a couple of days and thus important measurements were missing. In this period Premom 68 went to her general practitioner who measured a blood pressure of 181/110 after having a period of controlled blood pressures. Despite medication adjustments and every day control of the parameters of Premom 68, the fetus past away in utero. Anatomopathological examination showed that the fetus had growth retardation but the placenta was well implanted. After the lost of her child, Premom 68 accused the researcher of letting her blood pressure fall to low. The question is

however who was really responsible, the researcher, her gynecologist, although anatomopathological examination showed that her blood pressure was not the cause of death. The problem of liability might occur again in the future and is an important factor to take into account.

3.6.2 Case report Premom 79

Premom 79 was included on 28th November 2015 at a gestational age of 28 weeks and one day. She was 34 years old and this was her first pregnancy. Reason of inclusion was the presence of high blood pressures during gestation. At that point, she did not take antihypertensive medication.

The event on which the researcher contacted the gynecologist for the first time, a blood pressure of 153/102 mmHg, was on 7th December. This was by then her second event. Premom 79 had then a gestational age of 29 weeks and three days. The gynecologist ordered a CTG for 8th December. From that day, medication was started (Aldomet® 2x 250mg) (Figure 16).

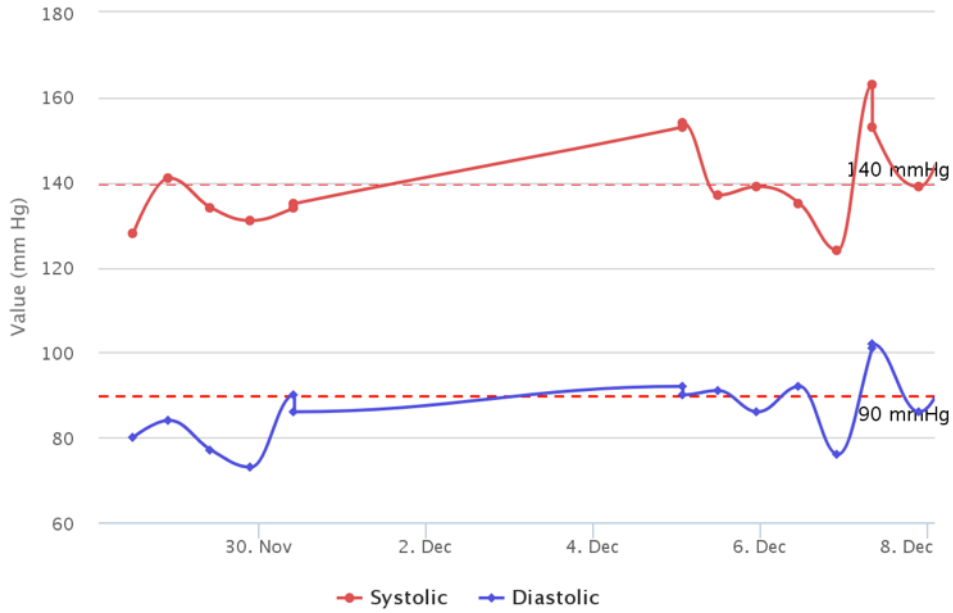

Figure 16:
Blood pressure of Premom 79 of 28th November 2015 to 7th December 2015. The red line represents the systolic blood pressure and the blue line the diastolic blood pressure. The red dotted line indicates the limits of both systolic (140 mmHg) and diastolic blood pressure (90 mmHg).

On 14th December, she was then 30 weeks and three days pregnant, due to consecutive events, the gynecologist was contacted and ordered that the patient should come in that day for a CTG. She was then finally admitted to the MIC on 16th December at a gestational age of 30 weeks and five days, and the diagnosis of PE was made (Figure 17). Figure 18 displays a schematic timeline of the events of Premom 79.

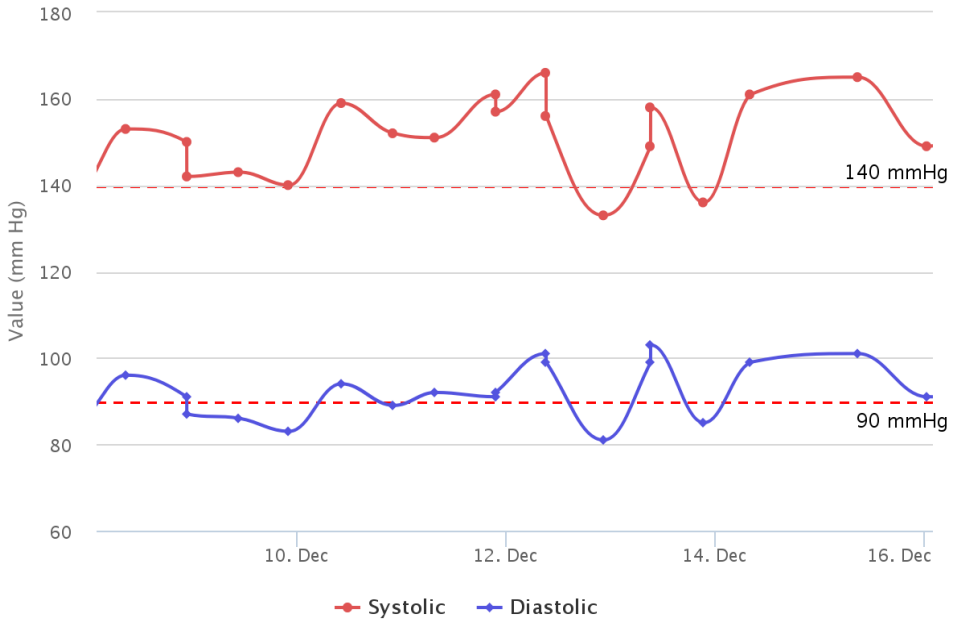

Figure 17:
Blood pressure of Premom 79 of 8th December to 16th December. The red line represents the systolic blood pressure and the blue line the diastolic blood pressure. The red dotted line indicates the limits of both systolic (140 mmHg) and diastolic blood pressure (90 mmHg).

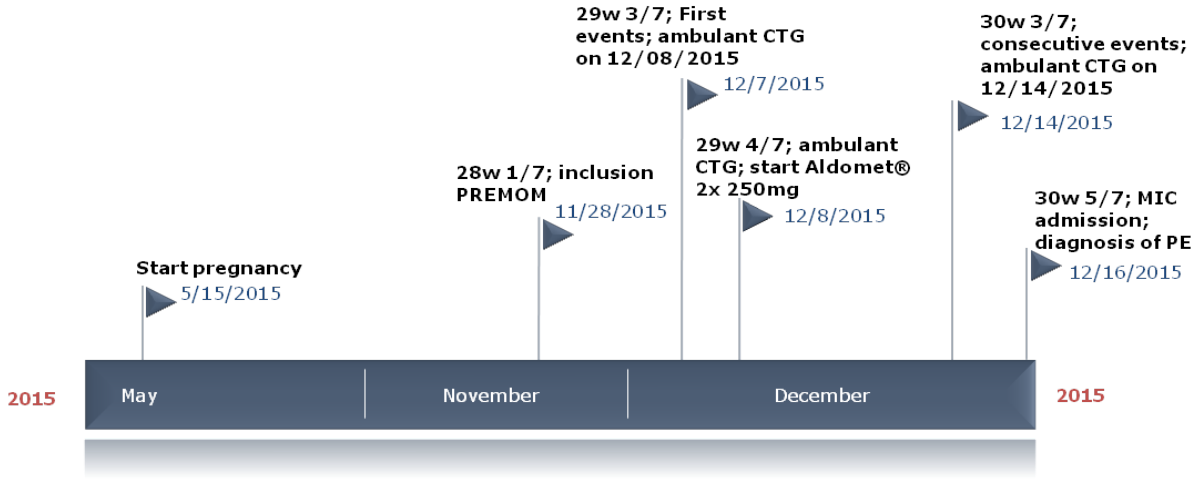

Figure 18:
Schematic timeline of the events and medication start of Premom 79.
CTG = cardiactocography, PE = preeclampsia.

The case report of Premom 79 shows that telemonitoring makes it possible to detect early signs of PE by offering a daily view of the mother's health. Premom 79 was admitted to the MIC as a result of telemonitoring and the daily control of the parameters. Eventually, Premom 79 gave birth to a girl at a gestational age of 31 weeks and four days by means of a cesarean as a consequence of PE. The baby had an Apgar score of 8 and 9 and was admitted at the NIC because of prematurity.

3.6.3 Case report Premom 104

On 17th February 2016, Premom 104 was included at a gestational age of 25 weeks because of hypertension. Premom 104 was 40 years old and smoked 10 cigarettes a day. Her medication at that point was Trandate® 3x 200mg and Adolat® 2x 250mg. An update of Premom 104 was weekly sent to her gynecologist because she was a patient of an external hospital. Events were only stated as a diastolic blood pressure above 100 mmHg because of her already existing high blood pressure before pregnancy.

On 23rd February 2016 the first weekly update was sent to the gynecologist at a gestational age of 25 weeks and six days (Figure 19).

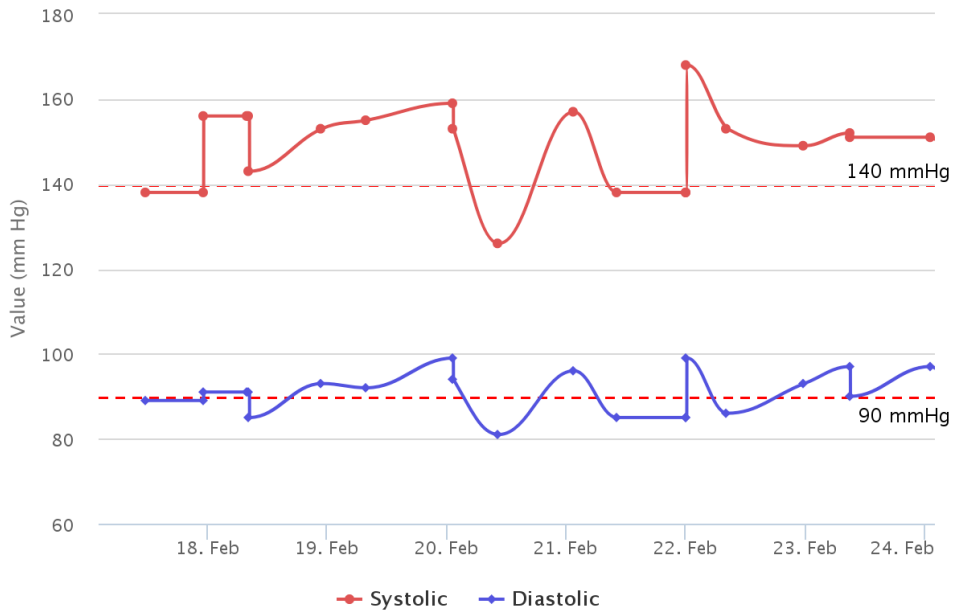

Figure 19:
Weekly update of the blood pressure of Premom 104 of 27th February to 23rd February. The red line represents the systolic blood pressure and the blue line the diastolic blood pressure. The red dotted line indicates the limits of both systolic (140 mmHg) and diastolic blood pressure (90 mmHg).

The next weekly update was 2nd March at a gestational age of 27 weeks (Figure 20) and the third on 8th March at a gestational age of 27 weeks and six days (Figure 21). In these 3 weeks, her blood pressure was under control except for an event on 6th March (159/102 mmHg) at a gestational age of 27 weeks and four days and an event on 8th March (182/108 mmHg) at a gestational age of 27 weeks and six days. On this day, Premom 104 had a consultation and the decision was made to adjust her medication to Trandate® 2x 250mg and Aldomet® 3x 500mg.

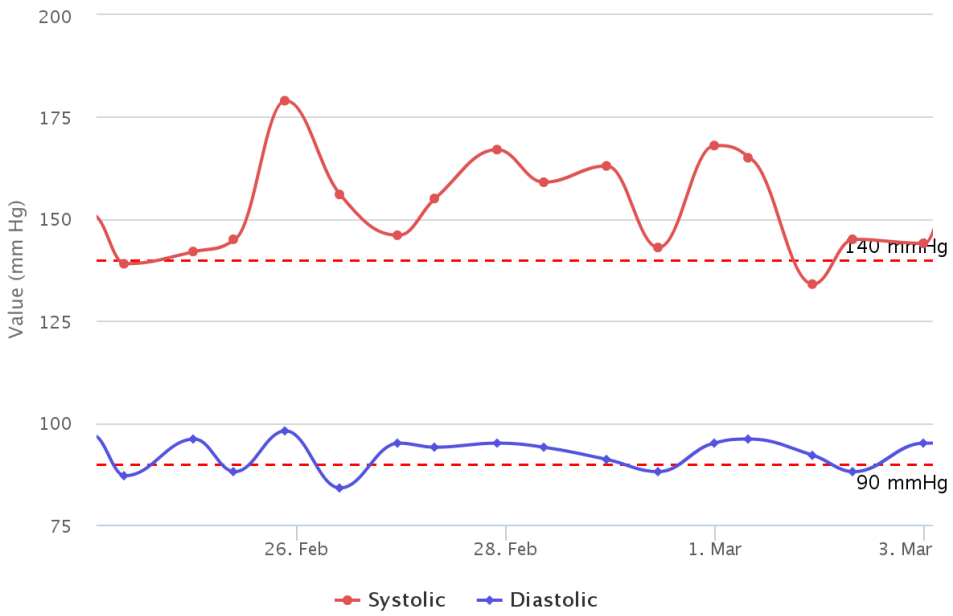

Figure 20:
Weekly update of the blood pressure of Premom 104 of 24th February to 2nd March. The red line represents the systolic blood pressure and the blue line the diastolic blood pressure. The red dotted line indicates the limits of both systolic (140 mmHg) and diastolic blood pressure (90 mmHg).

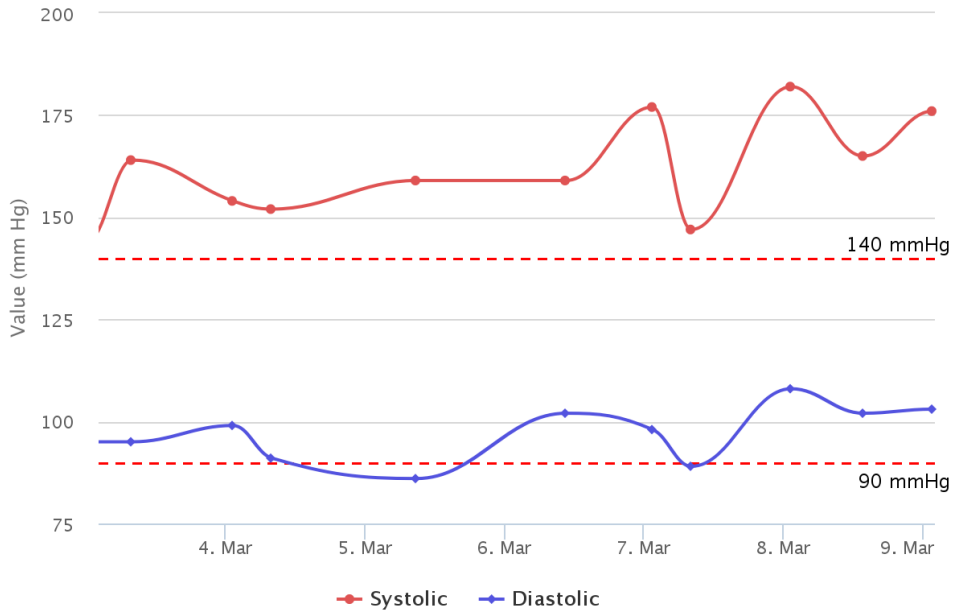

Figure 21:
Weekly update of the blood pressure of Premom 104 of 3rd March to 8th March. The red line represents the systolic blood pressure and the blue line the diastolic blood pressure. The red dotted line indicates the limits of both systolic (140 mmHg) and diastolic blood pressure (90 mmHg).

Between 8th March and 14th March three events were stated one at a gestational age of 27 weeks and six days, one at a gestational age of 28 weeks, and one at a gestational age of 28 weeks and two days. On 14th March a weekly update was sent to the gynecologist (Figure 22). She was then 28 weeks and five days. No medication adjustments were made.

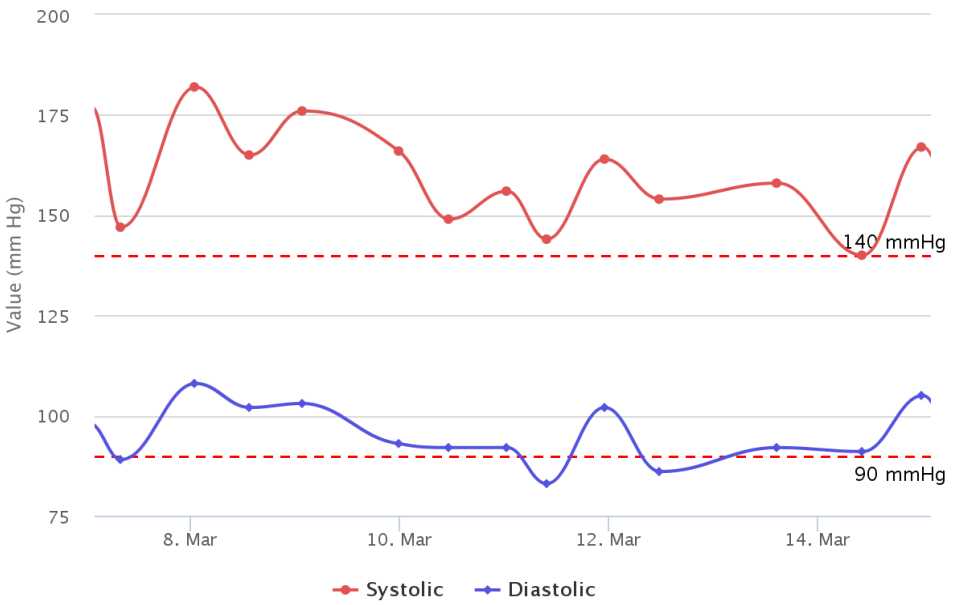

Figure 22:
Weekly update of the blood pressure of Premom 104 of 8th March to 14th March. The red line represents the systolic blood pressure and the blue line the diastolic blood pressure. The red dotted line indicates the limits of both systolic (140 mmHg) and diastolic blood pressure (90 mmHg).

The next weekly update followed 21st March at a gestational age of 29 weeks and five days. Four events were established between 14th March and 21st March (Figure 23). One event was stated at a gestational age of 28 weeks and six days, the second at 29 weeks and one day, the third at 29 weeks and three days, and the last at a gestational age of 29 weeks and five days.

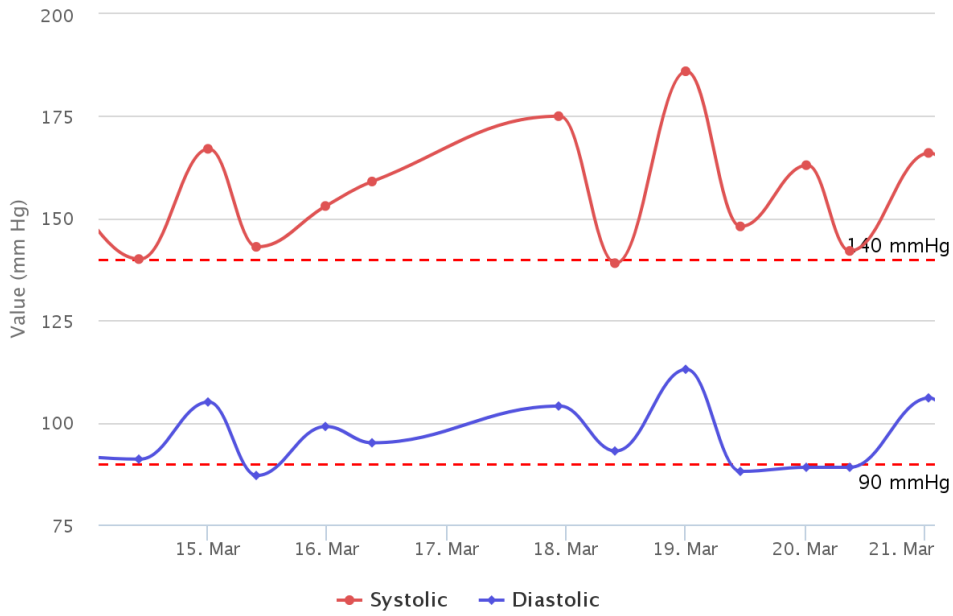

Figure 23:
Weekly update of the blood pressure of Premom 104 of 15th March to 21st March. The red line represents the systolic blood pressure and the blue line the diastolic blood pressure. The red dotted line indicates the limits of both systolic (140 mmHg) and diastolic blood pressure (90 mmHg).

The gynecologist decided on 22nd March to adjust her medication to Trandate® 2x 200mg and Aldomet® 3x 750 mg. Since two more events followed, a new update was sent on 24th March (Figure 24) at a gestational age of 30 weeks and one day. Her medication was not adjusted.

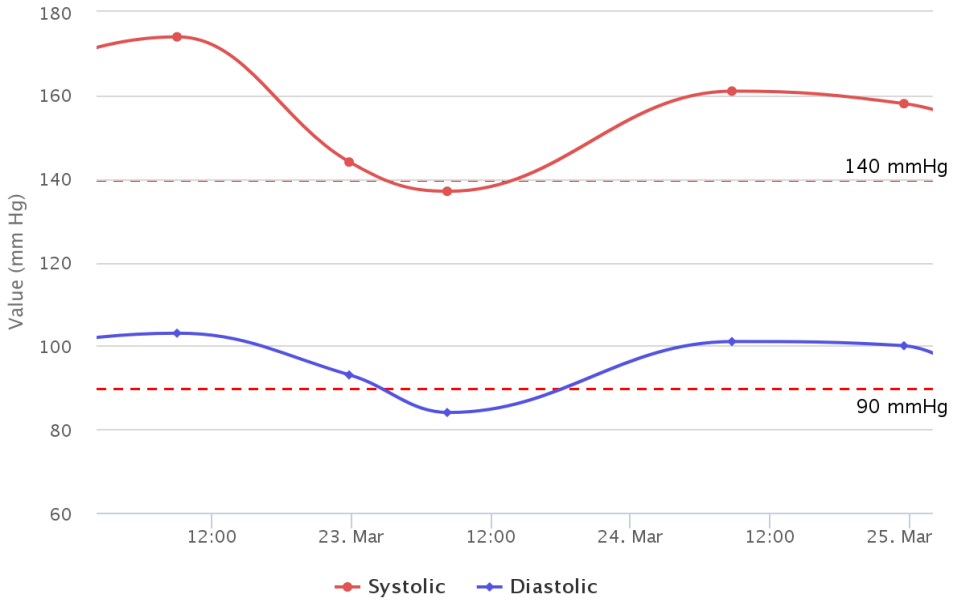

Figure 24:
Blood pressure of Premom 104 of 22nd March to 24th March. The red line represents the systolic blood pressure and the blue line the diastolic blood pressure. The red dotted line indicates the limits of both systolic (140 mmHg) and diastolic blood pressure (90 mmHg).

A new weekly update was sent on 29th March (Figure 25). She was then 30 weeks and six days pregnant.

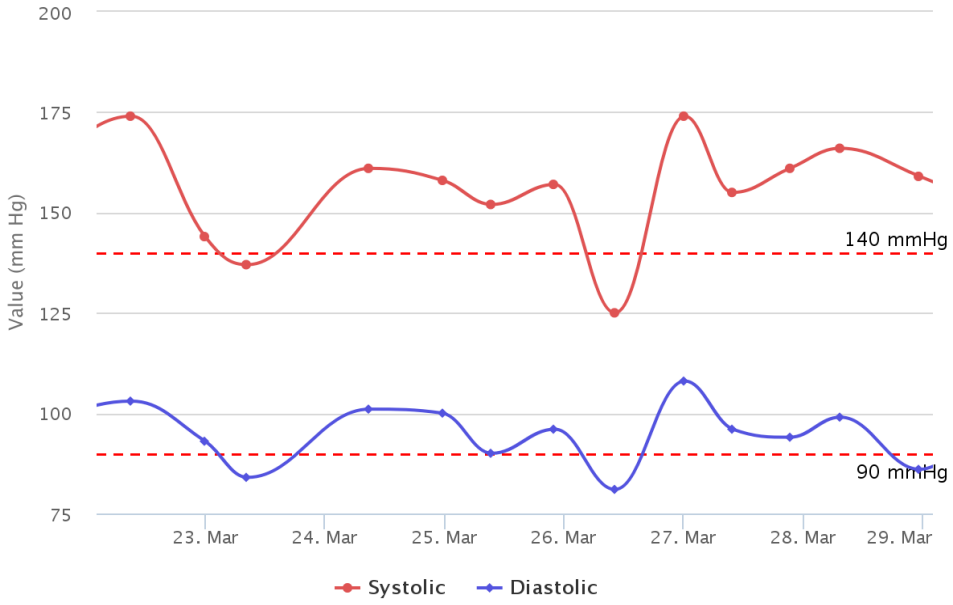

Figure 25:
Weekly update of the blood pressure of Premom 104 of 22nd March to 29th March. The red line represents the systolic blood pressure and the blue line the diastolic blood pressure. The red dotted line indicates the limits of both systolic (140 mmHg) and diastolic blood pressure (90 mmHg).

Finally, on 30th March Premom 104 was admitted to the MIC at a gestational age of 31 weeks as a consequence of Intra-Uterine Growth Retardation (IUGR) of the fetus. Figure 26 illustrates a schematic timeline of the events and reports of Premom 104.

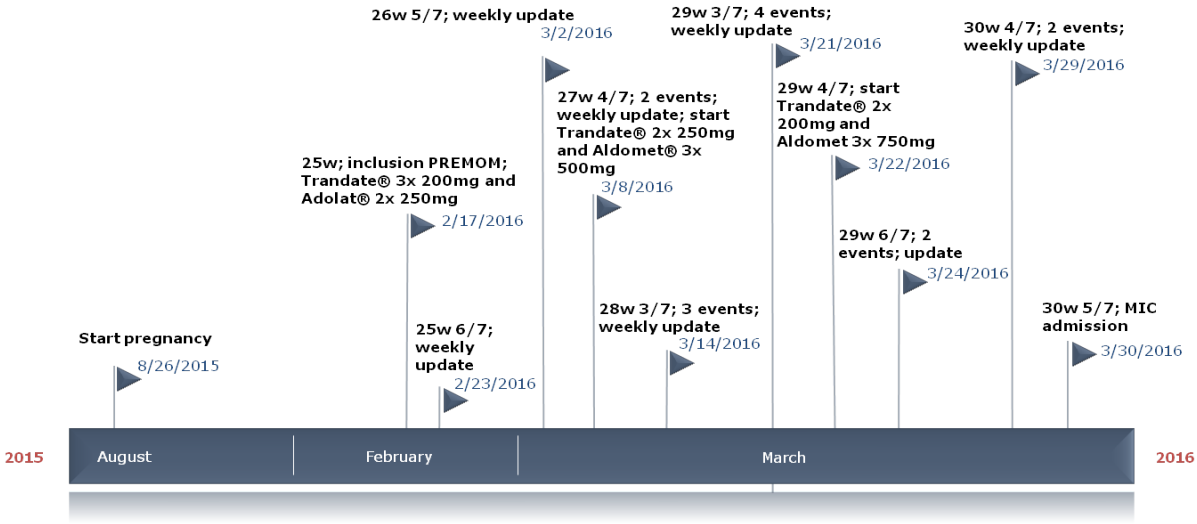

Figure 26:
Schematic timeline of the weekly updates, events, and medication adjustment of Premom 104. MIC = Maternal Intensive Care

Premom 104 was a special case considering her already existing hypertension with consecutive values ≥ 140/90 mmHg. For that reason the gynecologist decided to only state a diastolic blood pressure higher than 100 mmHg as an event. Premom 104 had as a result of that decision only 13 events although her blood pressure was continuously rising above 140/90 mmHg. Telemonitoring in this case was beneficial because weekly updates were sent, keeping the gynecologist up to date. In this way the results of medication adjustments were monitored closely. Eventually, Premom 104 was admitted to the MIC because of IUGR. It is not known whether this was a consequence of the hypertension or not. Premom 104 finally gave birth to a girl at a gestational age of 32 weeks by means of a caesarean. The baby was admitted to the NIC because of prematurity and had an Apgar score of 6 and 7.

3.6.4 Case report Premom 107

Premom 107, 42 years old and primigravida, was included on 29th February 2016 at a gestational age of 30 weeks and six days. Reason for inclusion was a NICCOMO test result showing maladaptation of the vascular system.

Premom 107 had no events until 6th April. However due to connection problems and personal reasons, data were missing of 29th February to 10th March, of 11th March to 15th March, and of 28th March to 6th April (Figure 27).

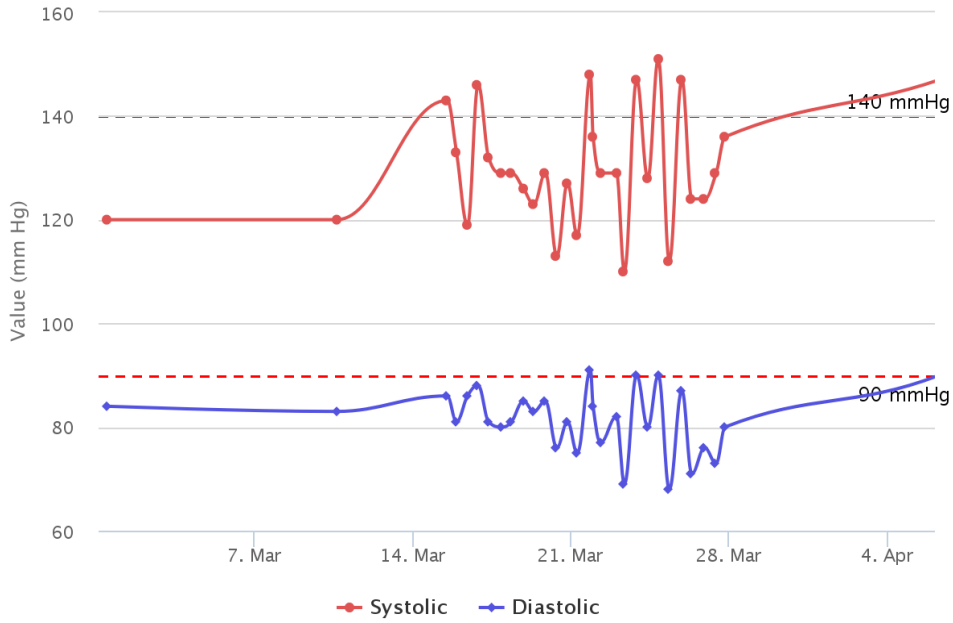

Figure 27:
Blood pressure of Premom 107 of 29th February to 5th April. The red line represents the systolic blood pressure and the blue line the diastolic blood pressure. The red dotted line indicates the limits of both systolic (140 mmHg) and diastolic blood pressure (90 mmHg).

On 6th April the first events were detected at a gestational age of 36 weeks. After a third event was stated, on 7th April an update was sent to the gynecologist at a gestational age of 36 weeks and one day. The order was given to monitor Premom 107 closely and to motivate her to measure adequately. On 11th April Premom 107 contacted the researcher about her measurements and an update was sent to the gynecologist. She was then 36 weeks and five days pregnant. From then on, Premom 107 had to do a 24hours urine collection of 12th April 08.00h to 13th April 08.00h and a PE consultation was scheduled on 13th April. That day the 24hours urine collection showed proteinuria (494 mg) and Premom 107 was admitted to the MIC because of PE at a gestational age of 37 weeks (Figure 28). Figure 29 represents a schematic timeline of the events of Premom 107.

On 15th April Premom 107 gave birth to a healthy girl by means of a secondary cesarean. The decision to deliver the baby was a consequence of the diagnosis of PE. The baby had a birth weight of 2780g, a length of 48cm, and an Apgar score of 9 and 9.

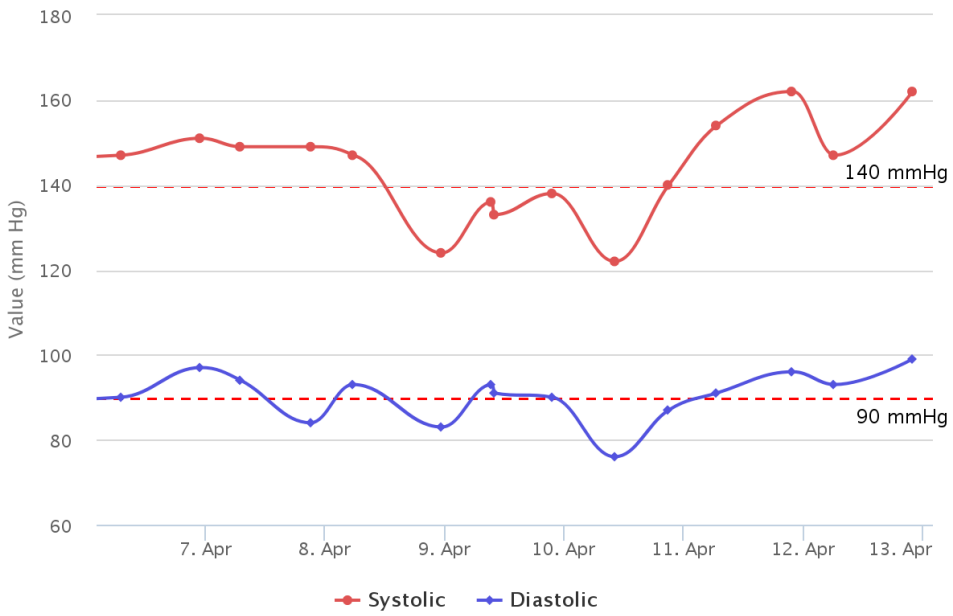

Figure 28:
Blood pressure of Premom 107 of 6th April to 13th April. The red line represents the systolic blood pressure and the blue line the diastolic blood pressure. The red dotted line indicates the limits of both systolic (140 mmHg) and diastolic blood pressure (90 mmHg).

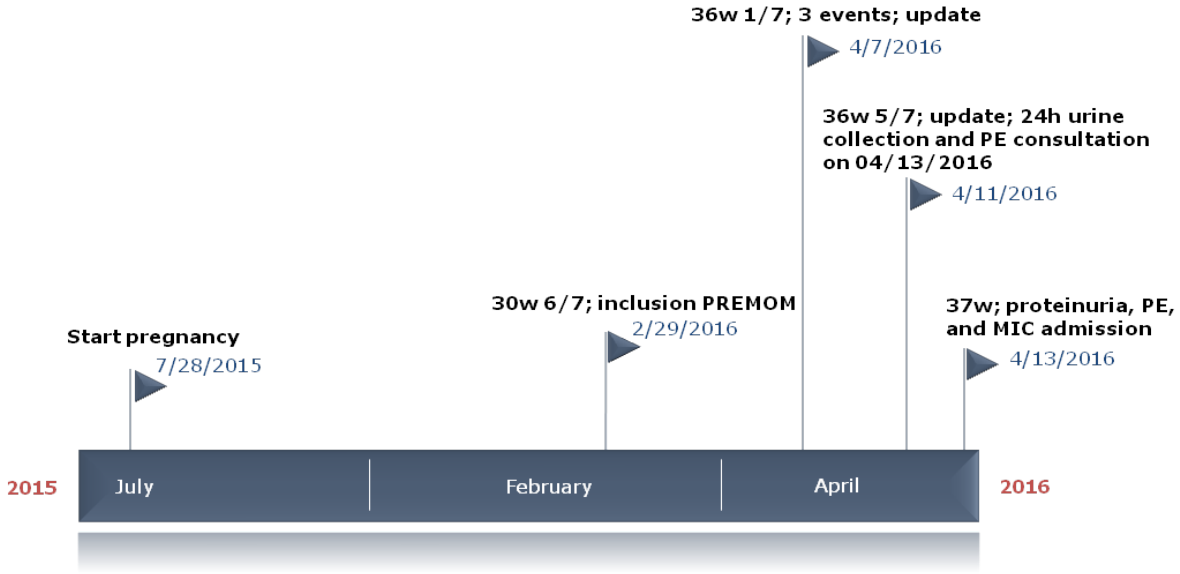

Figure 29:
Schematic timeline of the events and updates sent to the gynecologist of Premom 107. MIC = Maternal Intensive Care, PE = preeclampsia

In the case of Premom 107, both beneficial and detrimental aspects of telemonitoring emerged. Connection problems were stated, leading to missing data and no close follow-up. Relevant events could have been missed. On the other side, telemonitoring and adequately measuring of the blood pressure showed events, leading to the diagnosis of PE and a MIC admission, thus improving both maternal and fetal outcomes.

3.6.5 Conclusion of case reports

The four case reports here discussed all are very different. Two out four were diagnosed with PE thanks to telemonitoring, indicating that this technique of remote monitoring can predict early signs and symptoms of PE. Case report of Premom 68 and Premom 107 showed that telemonitoring is an advantageous tool to adjust medication properly and to observe the effects of medication adjustments on a daily basis. Two out of four were admitted to the MIC as a result of the remote monitoring of the blood pressure, improving both maternal and fetal outcomes.

4 Discussion

The study PREMOM implemented the use of telemonitoring and at home measurements to evaluate its feasibility and its capability in predicting early signs and symptoms of PE and gestational hypertension disorders. In this section the data and results are discussed and further evaluated.

4.1 Data collection, events, and outcomes

The results indicated that telemonitoring has the ability to detect signs of PE but that there are still some pitfalls in its implementation. Not all patients diagnosed with PE were recognized and some patients never had events.

4.1.1 Accuracy and reliability

Looking at the results of the events, only 15 patients out of 33 (45.45%) had events. When realizing that 30 patients were stated as high-risk, 15 is a rather small number of how many patients have got events. One of the five patients who were diagnosed with PE has even never had events, although her blood pressure was high. Thus the question is whether the definition of an event, two consecutive blood pressure measurements of 140/90 mmHg at least six hours apart or a diastolic blood pressure ≥ 100 mmHg, should be adjusted in that way that it also covers high tensions measured not consecutively? The one patient diagnosed with PE but had no events was picked out by means of telemonitoring. Due to her increased tensions, the researcher contacted the gynecologist, and the diagnosis of PE was made. This indicates that the clinician is still valuable behind all the new technologies, and that human thoughts are still important and necessary.

Another problem is that some patients measured at home high tensions but when coming into the hospital for an extra control, the tensions were normal. A discussion point here is whether the patients have had an increased blood pressure at home unconsciously caused by the obligation to measure their blood pressure and having an insight into their own data. This is a plausible explanation for the increased tensions when measured at home. Insight into own data and the obligation of measuring twice a day causes stress and pressure, leading to an increased blood pressure. Telemonitoring might have thus the disadvantage of indirectly causing stress in some patients, increasing the tension and thus have a false-positive classification. Analyzing the reliability of telemonitoring, one must be aware of the fact that the measurements take place without supervision and that the correctness is dependent on the patients performing the measurements. Results can be biased as a consequence of human errors (28). During inclusion, the researcher shows how the measurements are performed correctly, trying to overcome the problem of bias. Bias might thus be that the patients do not take the time for the measurements and measurements fail, or that they could be distracted by for example their other children.

Further data analysis of the outcomes of all patients, based on having events or not and the diagnosis of PE, gestational hypertension, or no diagnosis; showed a sensitivity of 72.22% and a specificity of 86.67%. A total population of 33 might be too small to draw a conclusion of these

values for sensitivity and specificity. A higher number of patients is necessary to obtain a higher sensitivity and specificity.

4.1.2 Satisfaction

Satisfaction surveys were filled in during the study to obtain a better insight into the feelings and opinion of the patients. This is important because telemonitoring is only efficient when performed correctly and accurate. If problems are stated, these should be solved. Overall the patients were satisfied about the devices, the application, and the follow-up by the researcher. Interesting to notice however is that the most problems lay in the planning of the measurements into their daily routine. A discussion point here is that some women might be not that convinced of telemonitoring and make no extra offers to implement the measurements. Other reasons could be that some patients have a busy schedule in the morning and they just simply forget, or that it is difficult to have a quiet moment when having children. Some patients had difficulty with connecting the devices and had connectivity problems. This problem could lead to less measurements and not taking the time to plan the measurements into their routine because of always failing connectivity.

4.2 Compliance

Compliance and adherence to the recommended measurements is important. It could be possible that when a low compliance is stated, signs of PE are missed. Compliance is dependent on personality, medical history, and possible other factors. When identifying the character of the person and motivation behind the measurements, the implementation could become easier when the explanation is based on personality and their motivation.

4.2.1 Missing data

Results showed a compliance of 76% for the blood pressure measurements and a compliance of 60% for the weight measurements. Reasons for missing data were classified in two groups, either personal-related or either device-related. In this specific population, 63.63% of the missed blood pressure measurements and 75% of the missed weight measurements were personal-related. This indicates that the compliance and adherence to the measurements is rather a personal issue.

Results indicated that there is no correlation between the demographic characteristics of the patients and compliance for the blood pressure measurements except for an age > 40 years and a low compliance (n=2) ($p < 0.05$), being unemployed and a low compliance (n=1) ($p < 0.05$), HELLP during a previous pregnancy and a low compliance (n=1) ($p < 0.05$), high blood pressure during previous gestation and a low compliance (n=2) ($p < 0.05$), and high blood pressure during gestation and a high compliance (n=11) ($p > 0.05$). No conclusions can be drawn because of the small sample sizes in these categories. No significant relation was seen between demographic characteristics and compliance of the weight measurements. This means that performing the measurements is based on the personal devotion of the patient and is no further influenced by for example education, marital status, job, and so on. It is interesting that the people who experienced high blood pressure during gestation have a higher compliance. This could be explained by the fact

that already having a high blood pressure makes the patients more aware of the risks engaged with hypertension and are willingly to invest time in their health and the health of the baby. However, drawing conclusions must be done carefully due to a small sample size and only representing here a small part of the population.

The device-related reasons for missing data were due to connectivity problems between the device and the smartphone, Wi-Fi problems, battery problems, or a malfunction of the device itself. When problems with the device came up during the measurements at home, it only became clear that there was a device-problem after the researcher contacted the patient for missing data. This indicates that patients found it hard to call or contact the researcher via email when a problem endures, which indicates either a lack of motivation to try to solve the problem or that they rely on the researcher to contact them when no data are transferred. Connectivity problems of the Smart body Analyzer weight scale were a common problem looking at the missed weight measurements that were device-related. However, during inclusion the patient's attention has been brought to this current problem and they were asked to insert their weight manually in the application. The procedure of transferring their weight manually has been explained during the inclusion moment. For this reason there could be a bias in the results of the missing data correlated to a device or a personal problem. A percentage of the personal-related missing data might be a result of not trying to solve a device-related problem, which means that technically there could be a higher percentage of device-related missing data.

Throughout the study compliance decreased for both the blood pressure and weight measurements. A possible explanation is that towards the end of the pregnancy and when blood pressures are good, patients do not see telemonitoring anymore as a benefit and an extra control. Some patients start to forget to measure when always having a low blood pressure or are just not that interested and motivated as in the beginning of the study. Some might even getting tired off the obliged measurements and just stop. This is a difficult problem to solve because contact moments did not increased compliance during the study.

4.2.2 Reachability

Results indicated that 41.56% of the made phone calls was not answered. This made the collection of missing data and possible reasons why difficult. In the future a possible solution will be implemented in the online platform. If data is missed, the online platform will automatically send the patient a message with questions about her measurements and reasons for missed transmission. This technique reduces the number of phone calls and collects more information about the (missing) data of the patient. However, a disadvantage is that there is no personal contact anymore, which will not be for every patient effective and positive.

4.3 Implementation of telemonitoring: improvement of healthcare?

The implementation of telemonitoring in obstetrics is a new topic within the field of remote monitoring. Because of this, not much is known about the advantages and disadvantages and its cost-effectiveness. Data of the PREMOM study show that telemonitoring makes it possible to detect early signs and symptoms of PE, improving both maternal and fetal outcomes. However to every upside, there are some downsides coupled. Whether telemonitoring is beneficial or detrimental, or a combination of both, and how it contributes to the cost-effectiveness of healthcare is discussed in this section.

4.3.1 Beneficial or detrimental?

The monitoring of the patients at home comes along with advantages but also with disadvantages. A first thing to discuss is the mobility of the patients and whether telemonitoring impairs the patients' mobility and daily activities. The monitoring devices used in this study are transportable and are only used inside the house. However, when the patients went on a holiday, they often did not take the devices with them. Reasons for this could be either that Wi-Fi was not available or that they just do not wanted to measure during their holidays. The patients measure their blood pressure twice a day and transfer their weight once a day. This element makes it possible for the patient to perform their everyday tasks and go out. The activity tracker is a small device worn around the wrist or clipped to a strap, not interfering with daily activities. Another important factor is the experience of the patients and their emotional sensation when measuring parameters at home. Changing their pregnancy into parameters and data might change the way they feel about their pregnancy. Measuring parameters at home and having an insight into their own health might cause feelings of stress. If patients measure a higher than normal blood pressure, they become more tense leading to an even higher blood pressure. If this happens, false-positive data are transferred to the hospital and are analyzed as signs of hypertension. This might lead to an extra control CTG or consultation, where it becomes clear that only in a house setting the patient measures high blood pressures. Circumstances at home present when performing a measurement could also induce a higher blood pressure (noisiness, conversations, etc.). For this reason, the patients are always advised to measure in a silent environment. The opposite of stress by having insight into their data, is the emotional factor of the false feeling of security. Patients are well aware of the fact that the researchers look into their data a couple a times a day. This may give them the feeling that everything is going well when they are not contacted even though they are feeling ill. A solution to this problem is already offered during the inclusion moment namely patients are advised to contact their responsible gynecologist in case of feeling bad even though their blood pressures might still be normal. Some patients could have the constant need of confirmation that the blood pressure is under control, and start to measure more than two times a day. Some then contact the researcher when worried about their blood pressure even though their values did not change. Telemonitoring itself stands or falls by the willingness of the patients. The use of remote monitoring makes the patients responsible and emphasizes them to take care of themselves and of their baby. This leads to the fact that the overall compliance is dependent on the adherence to the prescribed number of measurements. As the results indicated, compliance in

the PREMOM study decreases as the pregnancy progresses for both the blood pressure and weight measurements. It is important to extra motivate those who measure inaccurately. Lynga et al (2013) (29) investigated the experience of the patients in a monitoring study involving transmission of body weight of patients with heart failure. This study showed that the experience of the patients and their perception about telemonitoring is an important factor in analyzing compliance and improving compliance. By means of surveys the experience and their perception was found and optimal care could be provided. The study here also makes use of three consecutive surveys, in the beginning, interim, and after completing the study. Those who are rather negative or do not see the utility and the profits should be motivated and made aware of how important the technique of remote monitoring could be. A disadvantage of this is that if for example information sessions are given about the consequences of PE or how important it is to measure accurately, the patients might get the feeling that they are being lectured, leading to the opposite effect. The motivation and the solution how to motivate them must be handled with the needed cautiousness. At last, system security and privacy of the data must be incorporated. These days the system becomes overloaded with more and more patient data, making the system more vulnerable (30). The data should be protected against third parties. Decoupling the patient's individual data from the monitoring data is a possible solution (31).

4.3.2 Cost-effectiveness

In today's healthcare cost-minimization is a hot topic. Hospital stays should be kept as short as possible and numbers of consultations should be minimalized to the absolute minimum. Telemonitoring can contribute to the cost-effectiveness of healthcare. Several reasons for this are that telemonitoring may lead to lesser hospital visits, a reduction in transportation costs of the patients themselves, and shortening hospital stays because the patient can be further monitored at home (19). The question is whether the remote monitoring of pregnant women with a high-risk pregnancy does reduce the number of hospital visits and consultations. For this to be answered, more research is necessary into this topic. The minister of health of Belgium Maggie De Block wants a legal framework concerning telemonitoring if it can be proven that telemonitoring improves the overall healthcare (32). This would mean that the use of the monitoring devices could be covered by the health insurance.

5 Conclusion and future perspectives

The first question that this study intended to investigate was whether telemonitoring could be implemented in obstetrics and if it helped to predict early signs and symptoms of PE. Results and analysis showed that telemonitoring does have the capabilities of detecting signs of PE or gestational hypertension. The technique helps to evaluate the trend in the evolution of blood pressure throughout the pregnancy. In a total of 15 patients events were stated which led to contacting the gynecologist and thus a faster response. Not only events were stated by telemonitoring, but in addition telemonitoring made it possible to evaluate whether the antihypertensive medication was effective or not and thus if adjustments were needed or not. However, one must be careful with the definition of an event and the increase in tension. The clinicians behind the technologies remain an important aspect.

Another important conclusion that can be drawn from the results is that adherence to telemonitoring and thus the compliance is highly patient-dependent. The motivation of the patient and how willingly they are to perform the measurements is a personal issue. Most of the missed measurements (63.63% of the blood pressure and 75% of the weight measurements) were personal-related. Motivational strategies to obtain a high compliance throughout the study until delivery or MIC admission are an important issue to implement in the use of telemonitoring. However, satisfaction surveys showed that the patients are pleased with the devices and that they do experience the benefits of a daily follow-up. An implemented reminder when missed transmissions occur would be a solution in the future.

The PREMOM study will be implemented in other hospitals in the future, creating a bigger pool of patients. Preeclampsia is not the only medical complication in a high-risk pregnancy, also gestational diabetes is an important health issue. The use of remote monitoring in patients with gestational diabetes could be an extra control with the same benefits as resulted from the PREMOM study.

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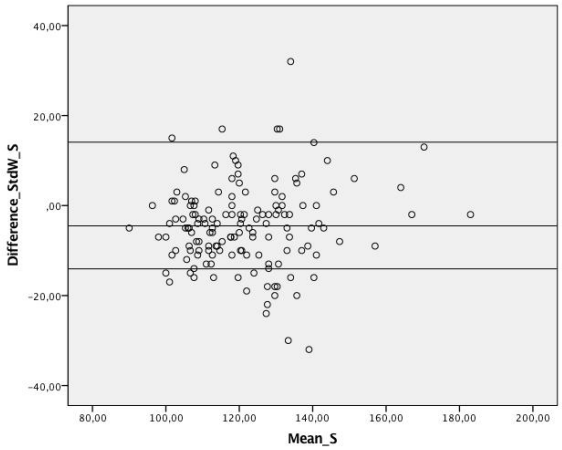
7 Appendix

Appendix 1: *Bland-Altman plots representing the validation of the monitoring devices. A) Standard device compared to the Withings device (systolic), B) Standard device compared to the Withings device (diastolic), C) Standard device compared to the iHealth device (systolic), D) Standard device compared to the iHealth device (diastolic), E) Withings device compared to the iHealth device (systolic), F) Withings device compared to the iHealth device (diastolic).*

A



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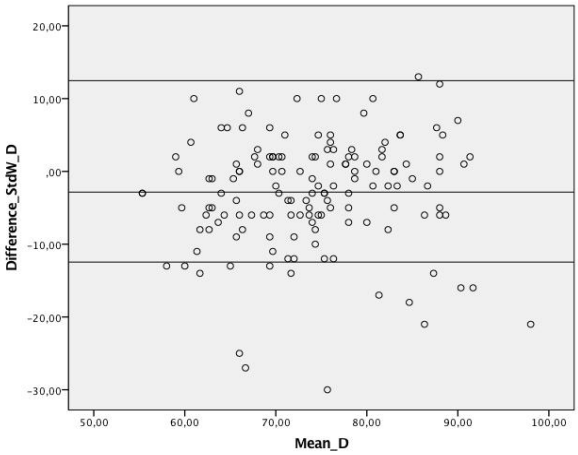

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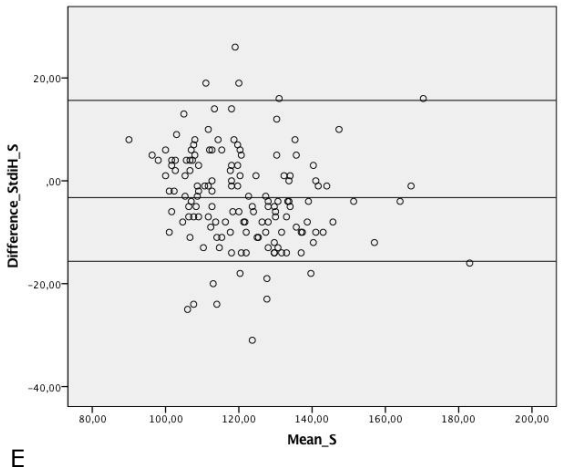

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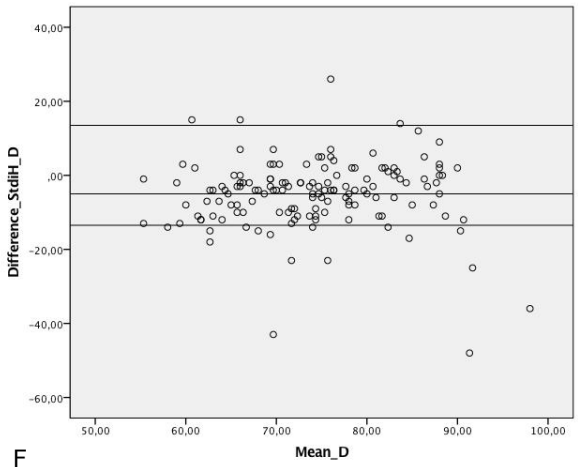

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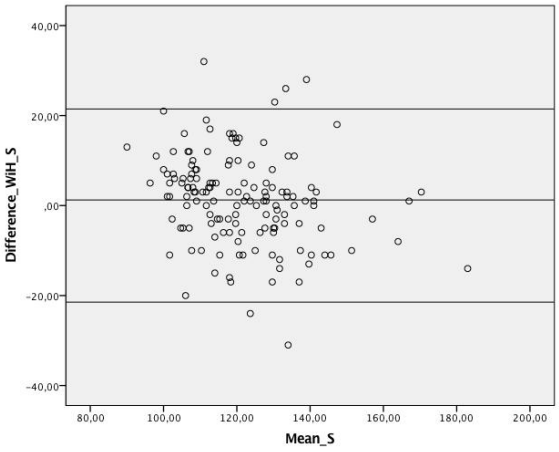
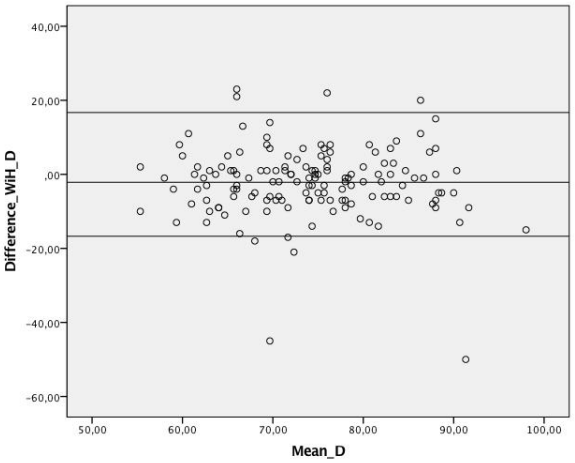


F



Appendix 2: *Table representing the relation between compliance of the blood pressure measurements and demographic characteristics. Percentage of compliant and non compliant is given, the Odds ratio, 95% confidence interval (CI), and the p-value. * = p < 0.05, † = no values were calculated due to a small number.*

Blood pressure					
	Compliant (%)	**Non compliant (%)**	**OR**	**95% CI**	**p**
Age					
18 - 25 (n=4)	75	25	0.99	0.09 – 10.71	0.97
26 - 30 (n=15)	80	20	1.11	0.30 – 7.87	0.60
31 - 35 (n=7)	71.43	28.57	0.93	0.11 – 4.90	0.76
36 - 40 (n=5)	100	0	1.40	†	0.17
> 40 (n=2)	0	100	0	†	0.01*
BMI					
Normal (n=16)	68.75	31.25	0.83	0.09 – 2.42	0.36
Overweight (n=10)	80	20	1.08	0.23 – 8.61	0.71
Obese (n=7)	85.71	14.29	1.17	0.22 – 21.78	0.49
Education					
Secondary (n=11)	81.82	18.18	1.13	0.28 – 10.17	0.57
Community College (n=15)	80	20	1.11	0.30 – 7.87	0.60
University (n=7)	57.14	42.86	0.71	0.05 – 1.90	0.20
Job					
Unemployed (n=1)	0	100	0	†	0.04*
Worker (n=5)	80	20	1.07	0.13 – 14.01	0.81
Attendant (n=21)	76.19	23.81	1.02	0.21 – 5.54	0.94
Independant (n=1)	100	0	1.33	†	0.57
Other (n=5)	80	20	1.07	0.13 – 14.01	0.72
Nationality					
Belgian (n=30)	76.67	23.33	1.15	0.13 – 20.94	0.70
Dutchman (n=2)	50	50	0.65	0.02 – 5.28	0.38
Turkish (n=1)	100	0	1.33	†	0.57
Marital status					
Married (n=15)	66.67	33.33	0.80	0.08 – 2.06	0.27
Legal cohabitiion (n=12)	83.33	16.67	1.17	0.33 – 11.97	0.44
Domestic partnership (n=5)	80	20	1.07	0.13 – 14.01	0.81
Other (n=1)	100	0	1.33	†	0.57
Primigravida					
Yes (n=19)	78.95	21.05	1.11	0.30 – 7.43	0.62
No (n=14)	71.43	28.57	0.90	0.13 – 3.30	0.62
Smoker					
Yes (n=2)	100	0	1.35	†	0.41
No (n=31)	74.19	25.81	0.74	†	0.41
Reason inclusion					

PE previous pregnancy(n=6)	83.33	16.67	1.13	0.10 – 4.01	0.63
HELLP previous pregnancy (n=1)	0	100	0	†	0.00*
Gstational hypertension (n=3)	66.67	33.33	0.87	0.05 – 7.76	0.70
High blood pressure during gestation (n=11)	100	0	1.44	0.68 – 58.10	0.02*
Age (n=1)	100	0	1.33	†	0.57
Results NICCOMO (n=1)	0	100	0	†	0.07
High blood pressure during previous gestation (n=2)	0	100	0	†	0.01*
Cardiac dysfunction (n=1)	100	0	1.33	†	0.57
Other (n=4)	75	25	0.99	0.09 – 10.71	0.97
Low-risk (n=3)	66.67	33.33	0.87	0.05 – 7.76	0.70

Appendix 3: *Table representing the relation between compliance of the weight measurements and demographic characteristics. Percentage of compliant and non compliant is given, the Odds ratio, 95% confidence interval (CI), and the p-value. † = no values were calculated due to a small number.*

	Weight				
	Compliant (%)	**Non compliant (%)**	**OR**	**95% CI**	**p**
Age (years)					
18 - 25 (n=4)	0	100	0	†	0.07
26 - 30 (n=15)	60	40	2.16	0.91 – 16.79	0.06
31 - 35 (n=7)	42.86	57.14	0.74	0.10 – 2.97	0.48
36 - 40 (n=5)	40	60	1.02	0.15 – 7.19	0.98
> 40 (n=2)	0	100	0	†	0.21
BMI					
Normal (n=16)	37.50	62.50	0.80	0.17 – 2.71	0.58
Overweight (n=10)	60	40	1.73	0.61 – 12.97	0.18
Obese (n=7)	28.57	71.53	0.62	0.08 – 2.86	0.40
Education					
Secondary (n=11)	45.45	54.55	1.11	0.28 – 5.18	0.80
Community College (n=15)	46.67	53.33	1.20	0.34 – 5.51	0.65
University (n=7)	28.57	71.53	0.62	0.08 – 2.86	0.40
Job					
Unemployed (n=1)	0	100	0	†	0.38
Worker (n=5)	40	60	0.93	0.13 – 6.18	0.91
Attendant (n=21)	38.10	61.90	0.76	0.15 – 2.58	0.51
Independant (n=1)	0	100	0	†	0.38
Other (n=5)	80	20	2.24	0.70 – 73.54	0.07
Nationality					
Belgian (n=30)	43.33	56.67	1.30	0.12 – 18.76	0.74
Dutchman (n=2)	0	100	0	†	0.21
Turkish (n=1)	100	0	2.46	†	0.24
Marital status					
Married (n=15)	40	60	0.90	0.21 – 3.34	0.80
Legal cohabitiion (n=12)	41.67	58.33	0.97	0.23 – 4.01	0.95
Domestic partnership (n=5)	60	40	1.53	0.33 – 16.19	0.39
Other (n=1)	0	100	0	†	0.38
Primigravida					
Yes (n=19)	52.63	47.37	1.84	0.64 – 12.06	0.17
No (n=14)	28.57	71.43	0.54	0.08 – 1.56	0.17
Smoker					
Yes (n=2)	50	50	1.19	0.08 – 24.23	0.82
No (n=31)	41.94	58.06	0.84	0.04 – 12.64	0.82
Reason inclusion					

PE previous pregnancy(n=6)	33.33	66.67	0.75	0.10 – 4.01	0.62
HELLP previous pregnancy (n=1)	0	100	0	†	0.38
Gstational hypertension (n=3)	0	100	0	†	0.12
High blood pressure during gestation (n=11)	54.55	45.45	1.50	0.48 – 9.14	0.32
Age (n=1)	100	0	2.46	†	0.24
Results NICCOMO (n=1)	0	100	0	†	0.38
High blood pressure during previous gestation (n=2)	0	100	0	†	0.21
Cardiac dysfunction (n=1)	100	0	2.46	†	0.21
Other (n=4)	75	25	1.98	0.45 – 53.27	0.16
Low-risk (n=3)	33.33	66.67	0.77	0.05 – 8.02	0.74

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Remote monitoring to assess the maternal and fetal wellbeing in normal and high-risk pregnancies

Richting: **master in de biomedische wetenschappen-klinische moleculaire wetenschappen**
Jaar: **2016**

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