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E-Pertension Study: Proof of Concept of an Enablement Suite for the Self-Measurement of Blood Pressure in Hypertensive Patients

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Abstract

Background: *hypertension is a major health concern worldwide and is known as a "silent killer". Patient's therapeutic adherence is known to be low, thus its efficiency. A potential way to improve it, is to use blood pressure self-measurement in combination with "m-health" (mobile health: a combination of electronic systems and processes in healthcare with the smartphone technology [1]).*

Aim: *the study aimed at developing and evaluating, in terms of functionality, feasibility and performance, a digital platform to improve self-management of hypertensive patients.*

Methods: *the platform was developed in collaboration with Nokia Belgium. 8 hypertensive patients were recruited. Patients received a connected blood pressure monitor device in order to perform their self-measurements. The devices were synchronised with a smartphone application, the "Nokia Health Mate", and the data collected in the smartphone application were transferred to the platform. The patients had to measure blood pressure twice a week during 8 weeks. They received reminders, warnings and/or encouraging messages according to the frequency of measurements and level of blood pressure.*

Analysis: *patients' compliance to the protocol was relatively high with 223 out of 252 measures performed (88,5%). The platform was shown to be functional and efficient with 187 out of 223 measures correctly transferred (83,85%). Regarding blood pressure control, some trend to improvement could be observed. Regarding feasibility, 7 out of 8 patients found this system very helpful and were ready to extend this practice.*

Conclusion: *adherence to the protocol was high. Patients' satisfaction was high or very high in terms of functionality and usefulness. The platform needs further development in order to prevent some issues encountered.*

Keywords: *arterial hypertension, adherence, self-measurement, connected device, home blood pressure monitoring, m-health*

Abbreviation

ABPM - Ambulatory Blood Pressure Monitoring, ACC - American College of Cardiology, ACE - Angiotens in Conversion Enzyme, ACTO - Access to Care and Therapy Optimization, AHA - American Heart Association, BMI - Body Mass Index, BP - Blood Pressure, ESC - European Society of Cardiology, ESH - European Society of Hypertension, HBPM - Home Blood Pressure Monitoring

Introduction

Arterial Hypertension

Hypertension is defined by a systolic blood pressure (BP) ≥ 140 mmHg and/or a diastolic BP ≥ 90 mmHg [2]. When suspected based upon office measurements, hypertension should ideally be confirmed by ambulatory measurements.

The total number of hypertensive people reaches one billion worldwide; hypertension is more prevalent in African countries (46%) than in high income countries (35%) [3].

The diagnosis should include the blood pressure degree, searching for secondary forms of hypertension and assessing global cardiovascular risks [2]. Blood pressure measurements in the office is performed with auscultatory or oscillometric semiautomatic sphygmomanometers placed on the upper arm [2]. Beside office' measurements, it is also possible to perform ambulatory blood pressure monitoring (ABPM) or home blood pressure monitoring (HBPM). These techniques allow for multiple measurements away from the medical environment [2]. ABPM provides the average of several BP measures over a defined period, usually 24h. The patient is equipped with a device measuring BP regularly, usually every 15 to 30 minutes and is asked to register his activities and sleep period in a diary. Average values are provided based on daytime, night-time and 24-hours basis. HBPM consists of self-measurement of blood pressure at home during at least 3 consecutive days according to the European guidelines [2]. Measurements should be done at least twice a day (in the morning and in the evening). In the long-term follow-up, less frequent measurements can be performed aimed at reinforcing treatment adherence [3].

Diagnostic thresholds for mean ambulatory BP values are 130/80 mmHg for 24-hours ABPM, 135/85mmHg for HBPM and daytime ABPM, and 120/70 mmHg for night-time ABPM [3].

Digital Health and Telemonitoring

E-health, m-Health and connected medical devices appeared recently in health care [4]. With billions of mobile phone users, such a way to enhance healthy behaviours has to be considered [5]. Telemedicine trials show encouraging results with improvement of patients' condition [4]. Indeed, Kim et al. (2016) [6] performed a trial on hypertensive patients comparing a monitored and a control group in order to evaluate the influence of a self- monitoring program on health behaviours, therapeutic adherence and control of blood pressure. The monitoring group had an improvement in health condition, showing that hypertensive patients were receptive to this type of program. There was no difference in therapeutic adherence [6].

Objectives

The current study is a proof of concept trial aimed to evaluate the feasibility, usability and performance of a digital platform, the « Enablement Suite » in view of future clinical trials to be conducted to evaluate the benefit in non-adherent patients.

Materials & Methods

Design and Study Sample

The web platform "Suite" was developed by Nokia Belgium with the collaboration of the promotors from the University of Namur. After approval by the ethics committee of Ambroise Paré University Hospital (Mons, Belgium), 8 hypertensive patients were recruited, based on inclusion and exclusion criteria (Table 1), in order to test the platform in combination with the connected device (Withings BP-801). Patients had to self-measure blood pressure during 2 months. In accordance with the AHA recommendations, hypertensive patients with cardiac arrhythmia were excluded due to the risk of the device not giving accurate measures in this setting [7].

Table 1. *Inclusion and exclusion criteria*

Inclusion criteria	Exclusion criteria
- Patients older than 18 years - Patients possessing a smartphone able to run the platform and that allows access to Internet - Patients treated with at leastone antihypertensive drug	- Patients with cognitivedisorders - Patients unable to follow a 2 months protocol - Patients who do not understand French - Patients unable to understand informed consent - Patients included in another trial - Patients with blood pressureabove 200/110 mHg - Patients presenting significant arrhythmia

Platform Development

The BPM devices (Withings BP-801) were to be used with a smartphone application, the "Nokia Health Mate" (available on both Apple and Android smart phones), allowing patients to register the measurements. During the follow-up period, patients were also given access to the digital platform developed by Nokia and the Access to Care and Therapeutic Optimisation Research Unit (ACTO) of the Faculty of Medicine, University of Namur, in order to follow their blood pressure values and received regular comments or advices (Figure1). This platform contained a questionnaire at the inclusion in the study to collect socio-demographic factors (gender, age, social status…), clinical data (comorbidities, treatments…) and a satisfaction survey to be filled by the patients at the end of the trial.

4 types of warnings for patients were developed:

- Absence of measure registered
- Technical error
- Abnormal BP values defined as < 90/50 mm Hg or >200/110 mmHg
- Non-adherence to the protocol

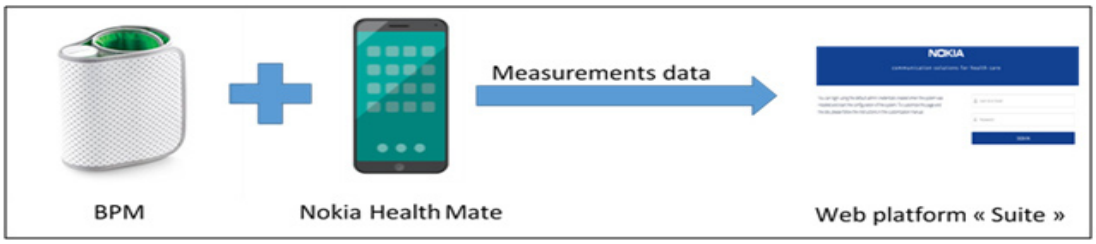

Fig 1. *Organization of the system developed*

Patient Inclusion and Follow-Up

Hypertensive, treated patients presenting at the hypertension outpatient clinic of Ambroise Paré University Hospital were invited to participate. Patients were duly informed about the trial and signed an informed consent form, then were trained to use the device along with the app and how to answer the general information questionnaire. Patients were contacted by phone during the trial period. These phone calls to the patients happened during the first week, at the end of the first month and at the end of the second month. These calls were done by the research team in order to identify if patients faced any issue with the use of the device or the suite. Patients were also able to contact the research team at any time in case of problems. Patients' feedback was collected at the end of the trial.

Blood Pressure Measurement

Patients were instructed to perform self-measurements at home, atleast 2 days a week, 2 times in the morning and 2 times in the evening. This schedule is in accordance with the guidelines from the ESH that recommend a minimum of 3 days a week of measurements or 1 or 2 measurements a week in case of a long term follow-up [8]. A third measurement was requested if the second one differed significantly from the first one (> 20mmHg difference in systolic blood pressure). Patients were instructed to perform their self-measurements in a seated position, after 5 minutes of relaxing and to abstain from talking during cuff inflation.

Privacy and Confidentiality

Patients' data were collected only if the informed consent was signed at the inclusion.

These data remained confidential and were fully anonymised. Individual data were not accessible to the promotor or to Nokia Company.

End Points

The primary endpoint of this study was to evaluate the convenience (feasibility, usability, and performance) of the suite.

Secondary endpoints were:

- Patients' feedback at the end of the 2 months period (level of satisfaction, perception of usefulness and willingness to eventually continue this self-measurement practice)
- Compliance with the protocol
- Percentage of measurements performed correctly
- Systolic and diastolic blood pressure evolution during the 8weeks
- Technological reliability

Results

Patients' Characteristics

10 patients were screened. One patient refused to participate because of the time requirement to participate in the study. The other patient didn't make the necessary proceedings to be added in the platform. In total, 8 patients (50% men) were included in the study. Mean age was 66.12±12.37 years (range 46-81) and mean BMI was 31.83± 6.14.

A majority of the patients (75%) were retired. Half of the patients had a university or high school level as the highest degree obtained.

The majority (87.5%) of patients had been diagnosed for more than 3 years, one was treated since only 1 year. The most used antihypertensive class of medication was angiotens in conversion enzyme inhibitors (ACE-i), taken by 7 out of 8 patients (87.5%). Four patients were on a monotherapy with an ACE inhibitor, four on polytherapy.

No patients had a history of myocardial infarction or stroke, two patients (25%) had a history of renal impairment. Patients took an average of 5.1±2.8 tablets a day, including antihypertensive medication(s). The majority of patients (87.5%) owned a HBPM device before the start of the study, using arm (57%) or wrist (43%) devices. Despite that, they didnot take their blood pressure on a regular basis: 3 patients never took their blood pressure and four patients took their blood pressure only very few times a month (Table2).

Table 2. *Patients' characteristics and clinical features*

n	8
Gender (males)	4 (50%)
Age (years)	66.12 ± 12.37
Professional situation (active)	2 (25%)
Professional situation (inactive)	6 (75%)
Highestdegree (Highereducation)	4 (50%)
Highestdegree (High school)	4 (50%)
Weight (kg)	92.1 ± 25.5
Height (cm)	170 ± 8.8
BMI	31.8 ± 6.1
BMI < 25	3 (37.5%)
BMI 25-29.9	1 (12.5%)
BMI > 30	4 (50%)
ACE inhibitors	7 (87.5%)
Diuretics	3 (37.5%)
Calcium antagonists	2 (25%)
Central antihypertensivedrugs	2 (25%)
Hypertension since 1 to 3 years	1 (12.5%)
Hypertension for more than 3 years	7 (87.5%)
Treated for HTN since 1 to 3 years	2 (25%)
Treated for HTN for more than 3 years	6 (75%)
Diabetes	2 (25%)
Hypercholesterolemia	4 (50%)
Tablets per day	5.1 ± 2.8
Previous history of myocardial infarction	0
Previoushistory of stroke	0
Previous history of renal impairment	2 (25%)
Previoushistory of HBPM	7 (87.5%)
Previous device for HBPM (arm)	4 (57%)
Previous device for HBPM (wrist)	3 (43%)
Previous HBPM frequency (never)	3 (43%)
Previous HBPM frequency (few times a month)	4 (57%)

Platform Functionality and Convenience

A few issues were encountered during the two first weeks of operation: the addition of some patients in the system was not correctly performed, resulting in the appearance of duplicates in the database. During the last week of the study another issue occurred which prevented the data to be transferred from the smartphone application to the platform. This issue was due to a slowdown in the smartphone application which caused delays. The latest data that had not been transferred were retrieved directly from the patients with their authorizations. The last phone call at the end of the study was replaced by a face-to-face session to collect the patients' feedback more indetails.

83,85% (187 out of 223) of the data were treated correctly by the platform. Beside the first and last week issues, only 8 measures (4,28%) were not treated correctly by the platform.

80 cases (which are alerts sent to the healthcare professionals according to the alerts received by the patient and which are classified according to their importance by a colour code) were created in the expert account among which 16,25% (13 out of 80) were "red" cases (out of range values); 48,75% (39 out of 80) were "yellow" cases (incomplete measures, missing one day of measurement in a week or no measures done at all during the week) and 35% (28 out of 80) were "green" cases (no measures done before mid-week evening or too much measurements in a week). 11,25% (9 out of 80) of these cases came from duplicated data during the two first weeks issue.

Compliance to Protocol

Patients' compliance to the protocol was high: 88,5% (223 out of 252 measurements done) (Figure 2). Despite this high compliance, the timing of measurements was relatively irregular (Figure 3). Only one patient had a lower compliance with 43,75% of measures done (14 out of 32) due to late initiation of the protocol. Two patients demonstrated an adherence level above 100% due to extra measures performed during the study.

No difference in compliance was observed, whether depending on the time of the day or the time of the studyperiod.

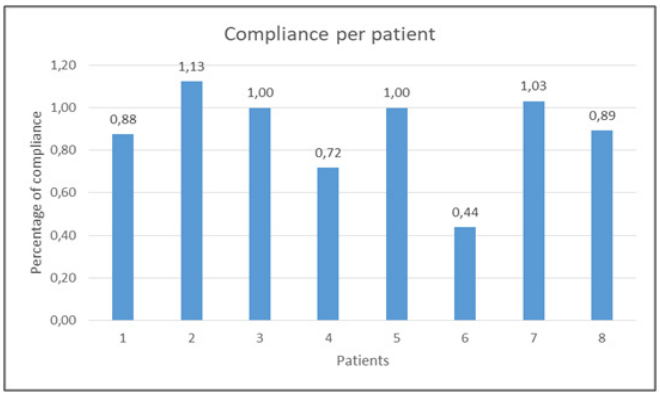

Fig 2. *Percentage of compliance per patient.*

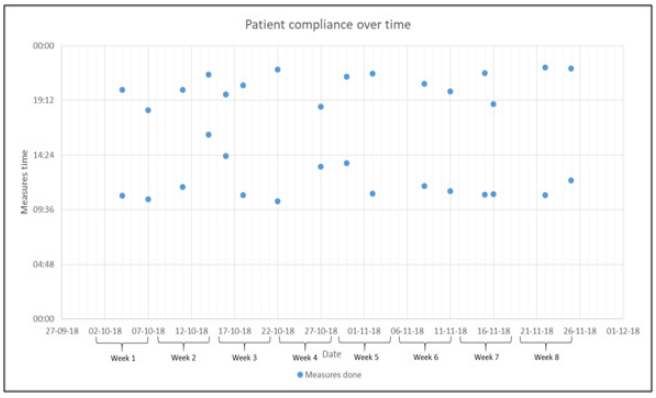

Fig 3. *An example of patient compliance over time. The blue dots represent each measure.*

Blood Pressure Measurements

A third measure was only requested in a limited number of cases (1,79%), showing high concordance between the 2 initial measures. This demonstrates reliability of the devices used and potentially absence of stress generated by home blood pressure measurements.

There was a trend to a decrease in both systolic and diastolic blood pressure after the first month (37 vs 25 measures above the limits for the systolic blood pressure and 40 vs 35 measures above the limits for the diastolic blood pressure). However the sample size was too small to determine significance.

Patients' Feedback

Patients were seen face-to-face at the end of the trial for a feedback interview. 7 out of 8 patients found the study very useful and were also ready to extend this practice. 5 out of 8 of patients were very confident in the system while three were only moderately confident. The device was perceived as easy to use. All patients found the smartphone application convenient.

Four patients shared their data with their general practitioner and, in two of them, the practitioner confirmed a white coat effect thanks to the HBPM. Seven patients agreed that self-measurements with the help of the smartphone application and the platform might improve the control of their blood pressure. All patients would recommend this system to a relative and five patients (62,5%) declared being willing to pay up to 10€ per month to continue using this system. As other remarks, one patient found the device bulky and thus difficult to transport if going on holiday. Another patient reported that some messages received in case of problem might be stressful for the patients and should be adapted.

Discussion

This proof of concept study demonstrates that performing HBPM monitoring in hypertension is well accepted by patients, who consider this practice as helpful to the management of their condition. A further study is planned to evaluate the benefit of such system in non- or poorly adherent hypertensive patients. This might avoid escalation in the treatment and reduce the risk of a false diagnosis of resistant hypertension.

Inparallel, Yatabe et al. (2018) [9] are conducting a study in which they compare traditional care to telemedicine in hypertensive patients using HBPM. They will compare a control group (traditional care with office visit) to a telemonitoring group (HBPM with office visits) and to a telemedicine group (HBPM without office visits and physician assessment by e-mail) [9]. The effect on the way hypertensive patients are managed and on the medical costs of hypertension might be influenced by the results of further studies. Based on our observed patient satisfaction, we believe pharmacists might also have a role in blood pressure control in hypertensive patients. Indeed, the HyperLink study [10] assessed whether a pharmacist case management in combination with home telemonitoring of blood pressure improved blood pressure control compared to usual care in uncontrolled hypertensive patients [10]. This study was a two-arm randomized trial. The intervention arm consisted in HBPM in combination with a pharmacist case management. The pharmacist first reviewed the medical history of the patients before informing them about hypertension and eventually instructed them on how to use the telemonitoring device [10]. The pharmacist would then receive all the measures from the patients and was allowed to make changes in their medication, to adjust dosage, to order refills or to order lab tests in case of adverse effects from the therapy according to the data received [10]. They would also discuss blood pressure goals with the patients. Phone visits were performed by the pharmacist, during which they would emphasize adherence to therapy and the patient's lifestyle. Change in medication was only performed when there were less than 75% of blood pressure readings that achieved the goal that was set up. The usual care arm consisted in patients managed by their healthcare providers as usual[10].

At the end of the study, the intervention group showed a significant improvement in blood pressure control and a decrease in blood pressure over 12 months [11]. The intervention group also had an increase in medication and a better therapeutic adherence. These benefits persisted for 6 months after the intervention [11]. An economic evaluation was done in this study [12]. The intervention cost 7337$ per person in average with 139$ and 265$ per decreased mmHg for the systolic and diastolic blood pressure respectively. There was a non-statistically significant decrease of medical care costs in the intervention group, but the authors (Dehmer et al. about the *Hyperlink* study)

concluded that a significant cost reduction might be realised over a long term period [12]. A pharmacist intervention might then be effective and implemented without increasing overall medical care costs [12].

Another study by Green et al. [13] showed the effectiveness of telemonitoring in combination with pharmacist care on blood pressure control. In this study, patients with uncontrolled hypertension were divided into three groups: usual care, HBPM with web training and HBPM with web training plus a pharmacist care delivered through webcommunication [13]. The pharmacist had to collect medical data from the patients and then decide on an "action plan" with them. Patients were then contacted on a regular basis by the pharmacist to discuss the goals achieved by the patients and their concerns about their treatment. The follow-up lasted twelve months [13]. The results showed no significant difference between the usual care and HBPM with web training but there was a significant improvement in blood pressure control in the intervention group applying pharmacist care. Indeed, there were 25% and 20% more patients with controlled blood pressure in this intervention group compared to usual care and HBPM with web training respectively [13].

An extension to this study was performed to assess the effectiveness of the intervention one year after completion [14]. All three groups achieved better blood pressure control but the pharmacist care group maintained a better blood pressure control than the two other groups (usual care and HBPM with web training) [14]. The results of these two studies [13, 14] were retranscripted by Omboni et al. (Figure 4) [15].

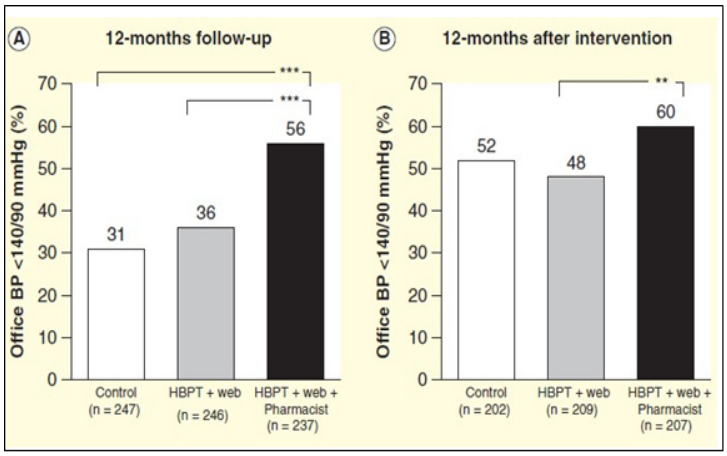

Fig 4. *Retranscipted results from Green et al. studies [14, 15] by Omboni et al. [16] showing the percentage of patients with controlled blood pressure (<140/90mmHg) among the three study arms after 12 months follow-up (A) and 12 months after the intervention (B). The pharmacist care group (HBPT + web + Pharmacist) shows a greater percentage of patients with controlled blood pressure*

Omboni et al. Also emphasized the role of the pharmacist in managing chronic diseases such as hypertension [15]. They bring a useful clinical expertise and recommendations about medications to support physicians. They are involved in long term monitoring of the patients and can help them with adherence issues [15]. This brings improvementto patients' health and well-being, education and satisfaction. As seen in the *Hyper Link* study [10], pharmacists can improve patients' education about hypertension, can change their medication and manage the refills. The benefits of this relationship between patients and their pharmacist(s) tend to improve if the pharmacist intervention is performed on a regular basis (at least monthly) [15]. White coat effect was also reduced with successive and regular visits to the pharmacists compared to the physician's office visits. Collaboration between pharmacists and physicians seems to be a good approach for a better management of hypertension and is a way to move to a patient- centered model[15].

Conclusion

The primary endpoint of the platform's convenience in terms of functionality, feasibility and performance was achieved. Indeed, besides the first week's issue (which was rapidly corrected), a large majority of the data were well treated and patients didn't report any

serious further issue. The platform still needs some improvements and adaptations to be more robust and to correspond more to the patient's demand.

Patients' compliance with the protocol was high during the study. Some patients even made more measurements than required. The level of compliance was not different between morning and evening measures. However, some patients didn't take their blood pressure on regular moments; a routine should then be implemented via some adaptations in the schedule of measurements and reminders sent to the patients. No differences were seen in compliance between the first and second month nor in patients with a different degree ofeducation.

Blood pressure seems to be better controlled after 1 month of self-measurement with a slight decrease in systolic and diastolic blood pressure.

Patients found this system very useful and helpful. They were ready to continue this practice and found that this system might help reach and maintain better blood pressure control.

A further study is then envisaged to evaluate the benefit of such system in non or poor adherent hypertensive patients.

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