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Home Monitoring of Blood Pressure: Short–Term Changes during Serial Measurements for 56398 Subjects

Giorgio Quer [Senior Member, IEEE],
Scripps Translational Science Institute (in The Scripps Research Institute), La Jolla, CA 92037

Nima Nikzad [Member, IEEE],
Scripps Translational Science Institute (in The Scripps Research Institute), La Jolla, CA 92037

Angela Chieh,
Nokia Digital Health (formerly Withings), Issy-les-Moulineaux, France

Alexis Normand,
Nokia Digital Health (formerly Withings), Issy-les-Moulineaux, France

Matthieu Vegreville,
Nokia Digital Health (formerly Withings), Issy-les-Moulineaux, France

Eric J. Topol, and
Scripps Translational Science Institute (in The Scripps Research Institute), La Jolla, CA 92037

Steven R. Steinhubl
Scripps Translational Science Institute (in The Scripps Research Institute), La Jolla, CA 92037

Abstract

Hypertension is one of the greatest contributors to premature morbidity and mortality worldwide. It has been demonstrated that lowering blood pressure (BP) by just a few mmHg can bring substantial clinical benefits, reducing the risk of stroke and ischemic heart disease. Properly managing high BP is one of the most pressing global health issues, but accurate methods to continuously monitoring BP at home are still under discussion. Indeed, the BP for any given individual can fluctuate significantly during intervals as short as a few minutes. In clinical settings, the guidelines suggest to wait for 5 or 10 minutes in seated rest before taking the measure, in order to alleviate the effect of the stress induced by the clinical environment. Alternatively, BP measured in the home environment is thought to provide a more accurate measure free of the stress of a clinical environment, but there is currently a lack of extensive studies on the trajectory of serial BP measurements over minutes in the home setting.

In this paper, we aim at filling this gap by analyzing a large dataset of more than 16 million BP measurements taken at home with commercial BP monitoring devices. In particular, we propose new techniques to analyze this dataset, taking into account the limitations due to the uncontrolled data collection, and we study the characteristics of the BP trajectory for consecutive measures over several minutes. We show that the BP values significantly decrease after 10 minutes minutes from

Corresponding author: G. Quer (gquer@scripps.edu).

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the initial measurement (4.1 and 6.6 mmHg for the diastolic and systolic BP, respectively), and continue to decrease for about 25 minutes. We also describe statistically the clinical relevance of this change, observing more than 50% misclassifications for measurements in the hypertension region. We then propose a model to study the inter-subject variability, showing significant variations in the expected decrease in systolic BP. These results may provide the initial evidence for future large clinical studies using participant-monitored BP.

I. Introduction

Hypertension is a major cardiovascular risk factor and one of the most important causes of premature death both in developed and underdeveloped countries. According to the World Health Organization, it is responsible for 9.4 million deaths worldwide, as of 2010 [2]. Properly managing hypertension is thus one of the most pressing global health issues. A daily measurement of blood pressure (BP) values outside a clinical setting can help detect early signs of hypertension, leading to early prevention, e.g., with simple life-style changes, before any clinically relevant problem becomes evident.

Daily monitoring the BP is indeed not yet a widespread habit. There are two main complications that slow down the adoption of this important practice: 1) BP measurements are usually done inside a clinic; and 2) BP values vary significantly, depending on body position, mood, time of the day, activity, or food intake, so their clinical interpretation is not straightforward. Regarding the first issue, it is now possible to measure the BP also at home, bringing part of the process of monitoring, decision-making, education and treatment outside of the clinical setting, thanks to wireless devices that measure BP and manage these values in the cloud [3], [4]. In order to be accurate, the device still needs to be equipped with a cuff, but the setup is relatively easy. New techniques for a truly ubiquitous measurement of the BP are being developed, like the estimation of the BP via pulse transit time [5], but they are not yet sufficiently accurate to replace cuff-based measures.

The variability in the BP values [6], [7] is another important aspect. In the past, several methods have been developed to study variability of the heart rate, since large datasets of heart rate data are easy to obtain [8], [9], while limited attention has been given to understanding BP variability and developing new methods to study it. It has been shown that BP variability is an important physiological measure by itself, since it correlates with the occurrence of cardiovascular events, as well as with cardiovascular mortality [10]. An overview about recent findings on BP variability and its clinical implications can be found in the systematic review in [11]. In particular, in this review an increased long-term variability in the systolic BP is shown to be associated with cardiovascular events and mortality. Short-term variability has also been associated with higher mortality in [12].

In the short-term, there is also a decreasing trend in the fluctuations of the BP. It has been shown in [13] that BP values may decrease for up to 10 minutes of seated rest during in-office visits, while after this time the BP value reaches a plateau, and does not decrease further (on average). The decrease is clinically significant, as the number of people with BP readings within the clinical definition of uncontrolled BP (systolic BP higher than 140 or

diastolic higher than 90 mmHg) decreases by 32% when 10 minutes (instead of 5) of seated rest are observed.

A different result is obtained in a recent study [14] that discusses the differences between a single measure of office BP (OBP) and a series of repeated office BP measures during 30 minutes (OBP30), showing a significant decrease when OBP30 was measured. The difference between the mean systolic OBP and OBP30 was 23 mmHg, while the same difference for the diastolic BP was 12 mmHg. The use of OBP30 is very promising, since it may significantly reduce the number of false positives in the diagnosis of hypertension. Unfortunately, the study in [14] can not be generalized, since physicians in that study ordered OBP30 mainly upon observing a high blood pressure reading in the OBP, so the effect of the regression to the mean has played a major role in these measurements.

The BP decrease during in-office visits may be due to a stressful condition of the patient in the office, namely white-coat hypertension, which may not correspond to sustained hypertension. Since the occurrence of most cardiovascular diseases shows a higher correlation with sustained hypertension [15], it is important to measure the value of the BP under normal conditions [16], [17], possibly outside the clinic, and on a daily basis, in order to assess the presence of sustained hypertension.

The general guidelines to interpret measurements taken inside the clinics may not apply at home, where measurements are taken at different times of the day, possibly in different position (not in seated rest), and sometimes as a series of measurements (at intervals of few minutes). In particular, the guidelines from the European Society of Hypertension recommend taking measurements while seated comfortably [18], while it is not specified to wait in seated rest for a certain time before taking the measurement.

There is currently a lack of an extensive study of home BP measurements, and we aim at bridging this gap by analyzing a large dataset of BP measurements from 56398 participants, mostly from US and Europe, that are measuring their BP at home with a personal Withings wireless BP device. The dataset consists of more than 16 million measurements, and it is well suited for our analysis since most measurements are part of series of consecutive measurements.

The goal of this paper is to model the average minute by minute changes in the BP for home measurements, in order to quantify the drop in the BP value if multiple measurements are taken within a small time window. More precisely, the main contributions of this paper are summarized in the following.

- We observe the average (intra-subject) change in the BP for multiple consecutive measurements taken at home, and we approximate the average drop for the systolic and the diastolic BP as a function of the time from the first measurement.
- We classify each BP measurement as one of four classes (normal, prehypertension, hypertension 1 and hypertension 2), and we estimate the probability of misclassification if only the first measurement of a series is considered.

- We propose a model to estimate the expected decrease in systolic BP for a subject in 5 minutes from the first BP measurement. We observe a significant inter-subject variability (expected decrease in systolic BP spans from 2 to 9 mmHg for most subjects), suggesting that the recommended resting time before taking a home BP measurement should be personalized.

The rest of the paper is organized as follows. In Sec. II we present the data available and detail the organization of this data for the subsequent analysis. In Sec. III we detail the processing and analysis we perform on the data, while in Sec. IV we show the main outcomes of our analysis. The results are discussed in Sec. V, which concludes the paper.

II. Processing of home BP data

In this section we first overview the characteristics of the dataset analyzed, then we discuss the pros and cons of performing this study with an existing uncontrolled large dataset as compared to a more standardized clinical trial, and finally we detail how we organize the data in intervals of consecutive measurements for the subsequent analysis.

A. The BP dataset

The data has been collected using the Withings wireless blood pressure monitor (BP-801), approved by the Food and Drug Administration (FDA). The data collected by the device is transferred via Bluetooth to a smartphone device, and is uploaded to the cloud for storage and further analysis. More technical details and a validation study of this device can be found in [19].

We begin the analysis of the general characteristics of the population in our dataset by calculating the distribution per gender and per age of the 56398 participants[1]. For each gender we represent in Fig. 1 the fraction of subjects in each of the age ranges of interest. We observe in particular that the largest fraction of subjects is between 40 and 70 years old, and that the female population is on average older than the male population. In particular, the fraction of females in the dataset who are older than 60 years old is larger than the fraction of males of the same age.

In order to understand the BP characteristics of all the subjects in the dataset, we calculate for each subject the average systolic and diastolic BP, considering the entire measurement duration. Then, we consider intervals of length 2.5 mmHg (e.g., the first interval considered is between 50 and 52.5 mmHg), and we calculate the fraction of subjects whose average systolic (or diastolic) BP lies in any of these intervals. The results are represented in Fig. 2, from which we can observe that there is a huge inter-subject variability among the average systolic and diastolic BP in our dataset. In particular, the average systolic BP for most of the subjects in our dataset ranges between 95 and 162 mmHg, while the average diastolic BP ranges between 57 and 110 mmHg.

[1]All the subjects have agreed to the terms of service and privacy policy upon activating the Withings product, which serves as a consent and includes statements regarding the use of data.

We also found a positive correlation between the average diastolic BP of an individual and the corresponding average heart rate value (Pearson coefficient $\rho = 0.34$). Significant differences in BP measurements have been observed for different location, and for data collected during different days of the week.

B. Issues in the uncontrolled home setting

The dataset analyzed offers a unique opportunity to observe the characteristics of real home measurements of the BP, with minimal or no clinical supervision. Given the large volume of data, it is possible to obtain reliable statistics on the variation, on a minute by minute basis, of the BP values. This may be a starting point for providing new clinical guidelines on monitoring BP at home, like, e.g., what is the most appropriate time to wait in seated rest before measuring the BP.

On the other side, there are several issues that should be considered while interpreting the data. Without control, the measurements are more noisy than in-office BP measurements, e.g., due to a possible incorrect use of the BP device. Comparing across different subjects is also complicated by the fact that there are significant differences in the time of the day for each measurement, the frequency of measurements, or simply the total number of measurements. We observe that some subjects measure their BP only once in a day, while others measure it several times in a short interval. In the latter case, the sampling rate is not constant, and it largely varies between different subjects.

C. Intervals of consecutive measurements (ICMs)

We organize the available data by dividing it into intervals of consecutive measurements (ICMs), i.e., intervals of time in which a single subject is continuously measuring her BP. By definition, two consecutive measures of BP in an ICM can not be separated in time by more than 600 seconds, so for example if an ICM has total length of 30 minutes, it must include at least 4 BP measurements, where two consecutive measurements are separated by no more than 10 minutes[2]. If a BP measurement is taken after more than 600 seconds from the previous measurement, it is considered the first value of a new ICM.

An ICM is indicated by the index $i \in \{1, \dots, I\}$. For the ICM i, each BP measurement k, with $k \in \{0, \dots, K_i\}$, is given by the pair $b_B^{(i,k)} = (b_s^{(i,k)}, b_d^{(i,k)})$, where $b_s^{(i,k)}$ and $b_d^{(i,k)}$ are the measured systolic and diastolic BP values, respectively. We indicate the corresponding time of the measurement, expressed in seconds, with $t^{(i,k)}$, where $t^{(i,k_2)} > t^{(i,k_1)}$ for $k_2 > k_1$. The number of follow-up measurements in a specific ICM (after the initial measurement) is K_i.

For the ICMs with $K_i > 0$, we define for each $k > 0$

$$\delta_B^{(i,k)} = (\delta_s^{(i,k)}, \delta_d^{(i,k)}) = (b_s^{(i,k)} - b_s^{(i,0)}, b_d^{(i,k)} - b_d^{(i,0)}) \quad (1)$$

[2]The choice of the 10 minutes threshold does not significantly affect our results, since the fraction of consecutive measurements separated by more than 10 minutes, but less than 2 hours, is very small.

i.e., the difference in the BP values (systolic and diastolic) from the first measurement of the ICM ($k = 0$). We also define, for each $k > 0$,

$$\delta_T^{(i,k)} = t^{(i,k)} - t^{(i,0)} > 0, \quad (2)$$

which is the corresponding length of the time interval from the first measurement.

In order to clarify how the data has been collected, we represent in Fig. 3 the number of ICMs which have a length equal to τ or longer. In other words, we calculate

$$N(\tau) = \sum_i \mathbb{1}\left\{\delta_T^{(i,K_i)} > \tau\right\}, \quad (3)$$

for all $\tau \in [0, 30]$ minutes, where $\mathbb{1}\{\cdot\}$ is the indicator function, with $\mathbb{1}\{X\} = 1$ if X is true, or $\mathbb{1}\{X\} = 0$ otherwise. We observe that the majority of ICMs have a length of only few minutes; in particular, we have more than 1 million ICMs with a length of at least 3 minutes, while this number is reduced to 14 thousands if we consider the ICMs with a length of at least 20 minutes.

III. Analysis of BP data

A. Minute-by-minute BP changes in a home setting

The aim of this section is to verify if the first measurement of an ICM is an overestimation of the true BP measure. In order to do so, we quantify the absolute differences between the first and the follow-up BP measurements.

We consider a finite set of times, $t_0, t_1, \ldots, t_M$, with $t_M = 1800$ seconds, which identifies M adjacent time intervals, $[t_{j-1}, t_j]$, with $j = 1, \ldots, M$. For each interval, and for each ICM i, we define the set $\mathcal{I}_i(t_j)$ that includes all the data points whose time difference from the first measurement of the corresponding ICM is in the considered interval, i.e.,

$$\mathcal{I}_i(t_j) = \left\{k : t_{j-1} < \delta_T^{(i,k)} \leq t_j\right\}. \quad (4)$$

For each time interval we evaluate the average value of the corresponding $\delta_B^{(i,k)}$. More formally, we define

$$\Delta_B^1(t_j) = E_{i,k}[\delta_B^{(\cdot,\cdot)}(t_j)] = \frac{\sum_i \sum_{k \in \mathcal{I}_i(t_j)} \delta_B^{(i,k)}}{\sum_i |\mathcal{I}_i(t_j)|}, \quad (5)$$

where $|\mathcal{I}_i(t_j)|$ is the total number of measurements in $\mathcal{I}_i(t_j)$.

(5) provides us with a measure of the average BP decrease as a function of time for consecutive home measurements. We notice that only a relatively small fraction of the ICMs have a length at least equal to t_M, as can be verified by observing Fig. 3. This may introduce a statistical bias, as the ICMs considered for larger values of t_j are only a subset of the ICMs considered for smaller values of t_j.

In order to verify that our results hold despite the presence of this bias, we repeat the calculations of above considering the subset $\mathscr{M}_{t_M}$ of ICMs with length at least t_M. In other words, an ICM is included in $\mathscr{M}_{t_M}$ only if its length is greater or equal than t_M. In this way, all the ICMs considered will equally contribute to the estimation of $E_{i,k}[\delta_B^{(\cdot,\cdot)}(t_j)]$ for all the considered values of t_j. For each ICM $i \in \mathscr{M}_{t_M}$, we consider the set $\mathscr{I}_i(t_j)$ defined in (4), and we estimate $E_{i,k}[\delta_B^{(\cdot,\cdot)}(t_j)]$ as follows. If

$$\exists k : t_{j-1} < \delta_T^{(i,k)} \leq t_j, \quad (6)$$

then $|\mathscr{I}_i(t_j)| > 0$ and

$$E_k[\delta_B^{(i,\cdot)}(t_j)] = \frac{\sum_{k \in \mathscr{I}_i(t_j)} \delta_B^{(i,k)}}{|\mathscr{I}_i(t_j)|}. \quad (7)$$

Otherwise, if $|\mathscr{I}_i(t_j)| = 0$, then

$$E_k[\delta_B^{(i,\cdot)}(t_j)] = \delta_B^{(i,k*)}, \quad (8)$$

where

$$k* = \min k \ \text{s.t.} \ \delta_T^{(i,k)} > t_j. \quad (9)$$

Using either (7) or (8), it is guaranteed that we obtain a value of $E_k[\delta_B^{(i,\cdot)}(t_j)]$ for each $i \in \mathscr{M}_{t_M}$ and for each t_j. We can then calculate the equivalent of (5) using the ICMs in $\mathscr{M}_{t_M}$, but this time each point is calculated as the average over the same set of ICMs, i.e.,

$$\Delta_B^2(t_j) = E_i[E_k[\delta_B^{(i,\cdot)}(t_j)] | i \in \mathcal{M}_{t_M}] = \frac{\sum_{i \in \mathcal{M}_{t_M}} E_k[\delta_B^{(i,\cdot)}(t_j)]}{|\mathcal{M}_{t_M}|}, \quad (10)$$

where $|\mathcal{M}_{t_M}|$ is the number of ICMs in $\mathcal{M}_{t_M}$.

B. Change in the Classification of BP

According to the guidelines published in the website of the American Heart Association [20], the BP values can be divided into 4 classes:

1. normal (N): $b_s < 120$ and $b_d < 80$,
2. prehypertension (P): $b_s < 140$ and $b_d < 90$ and ($b_s \geq 120$ or $b_d \geq 80$),
3. hypertension 1 (H_1): $b_s < 160$ and $b_d < 100$ and ($b_s \geq 140$ or $b_d \geq 90$),
4. hypertension 2 (H_2): $b_s \geq 160$ or $b_d \geq 100$.

We denote the classification function that assigns a unique class to each BP measurement as

$$\Gamma(b_s, b_d) \in \{N, P, H_1, H_2\}. \quad (11)$$

For each ICM i, we investigate the probability that the follow-up measurements can lead to a different classification of the BP measure. This conditional probability is particularly interesting, since it gives us an idea of how many misclassifications happen by measuring the BP only once, for home BP measurements. We denote by c_0 the class of the first measurement of an ICM, i.e.,

$$c_0 = \Gamma(b_s^{(i,0)}, b_d^{(i,0)}). \quad (12)$$

Then, for each interval of interest $[t_{j-1}, t_j]$, like e.g., from 0 to 5 minutes, we calculate the class corresponding to the expected values of the follow up values in this interval, i.e.,

$$c_j = \Gamma(E_k[b_s^{(i,\cdot)}], E_k[b_d^{(i,\cdot)}]), \quad (13)$$

for all k such that $t_{j-1} < \delta_T^{(i,k)} \leq t_j$. The conditional probability

$$P[c_j | c_0], \quad (14)$$

is estimated with at maximum likelihood (ML) approach considering all the ICMs with at least one BP value in the corresponding interval $[t_{j-1}, t_j]$, for all $c_0, c_j \in \{N, P, H_1, H_2\}$.

C. Subject variability

In the previous subsections we have described several methods to estimate the average behavior of the BP measurements a few minutes after the first measurement, in a home setting. We now separately analyze each subject in the dataset, in order to quantify the inter-subject variability. This is an initial effort towards more personalized guidelines for BP measurements.

The goal is to obtain a compact measure of the BP decrease for each subject. The main issue lies in the fact that there is a huge difference in the frequency of measurements among the subjects in our dataset, as highlighted in Sec. II-B. To overcome this problem, we define $\mathcal{M}(u)$ as the set of ICMs for each subject u. Among the 56398 subjects in the dataset, we consider in this analysis all the subjects with at least 100 follow-up measurements, i.e., measurements after the first measurement of an ICM, in order to have a significant approximation for each subject. In other words, we include subject u in the analysis if

$$\sum_{i \in \mathcal{M}(u)} K_i \geq 100\,. \quad (15)$$

We selected in this way 12563 subjects with a sufficient number of measurements. We propose an empirical model to fit the decrease in systolic BP as a function of time from the first measurement in our dataset. We tested the goodness of fit for a linear and a logarithmic approximation, and we opted for the latter one, which offers a better approximation of the available data. According to this model, for all $k > 0$ we have

$$\delta_s^{(i,k)} = \beta^{(u)} \ln(1 + \delta_T^{(i,k)}) + \varepsilon, \quad (16)$$

where u is the selected subject, $\beta^{(u)}$ is a scalar parameter to be estimated, and ε represents a noise factor, modeled as a zero mean Gaussian variable with unknown standard deviation. We notice that at the limit for $\delta_T^{(i,k)} \to 0$, we have that $\delta_s^{(i,k)} \to 0$, as expected. On the other hand, in this model the decrease in the BP is very significant during the first minutes after the first measurement, while the additional decrease is much smaller after several minutes from the first measurement, in accordance with the behavior observed in our data.

This model is suitable for our analysis since it represents the behavior of a user with a single scalar parameter, which makes the graphical representation of the inter-subject variability more clear.

Using the model in (16), we can estimate $\beta^{(u)}$ for each subject with a ML approach, which is a simple linear-logarithmic regression without the intercept term, i.e.,

$$\beta^{(u)} = \frac{E^{(u)}\left[\delta_s^{(i,k)}\ln(1+\delta_T^{(i,k)})\right]}{E^{(u)}\left[(\ln(1+\delta_T^{(i,k)}))^2\right]} = \frac{\sum_{i\in\mathcal{M}(u),k>0}\delta_s^{(i,k)}\ln(1+\delta_T^{(i,k)})}{\sum_{i\in\mathcal{M}(u),k>0}(\ln(1+\delta_T^{(i,k)}))^2}, \quad (17)$$

where $E^{(u)}[\cdot]$ is the mean over all the samples for subject u.

We can then calculate $\sigma^{(u)}$, the decreasing rate for subject u, defined as the expected decrease, in mmHg, of the systolic BP after 5 minutes from the initial measurement, i.e.,

$$\sigma^{(u)} = \beta^{(u)}\ln(1+\delta_T) = \beta^{(u)}\ln(301)\,. \quad (18)$$

IV. Results

A. Minute-by-minute BP changes in a home setting

In Fig. 4 we present the average BP decrease obtained considering all the available samples, according to Eq. (5), as a function of the time from the first measurement of the corresponding ICM. In the figure we show also the 95% confidence interval in the estimation of the average. This interval is very small for short intervals from the first measurement, when a lot of samples are available, see Fig. 3, while it is much larger for longer intervals from the first measurement (more than 20 minutes).

We observe that 5 minutes after the first measurement the diastolic BP decreases, on average, of about 3.5 mmHg, while the corresponding decrease for the systolic BP is 6 mmHg. Interestingly, the decrease is larger after 10 minutes (4.1 mmHg for the diastolic, 6.6 for the systolic), and it reaches a maximum after 25 minutes (5.2 mmHg for the diastolic, 7.8 for the systolic). For these values indeed the confidence interval is larger, thus our estimation is less precise. In the same figure, we observe that also the average heart rate (HR) is decreasing of about 2 pulse per minute (PPM) after 20 minutes, supporting the intuition that the subject is in a more relaxed state after a few minutes from the initial BP measurement.

In Fig. 5 we represent the decrease in the systolic and diastolic BP considering all the 4100 ICMs with a length of at least 30 minutes, using $\Delta_B^2(t_j)$ defined in Eq. (10). In this way, we consider the same number of ICMs for each interval represented in the figure. We observe the same trend shown in Fig. 4. The decrease in BP observed after 5 minutes is approximately 2.5 and 4 mmHg for the diastolic and the systolic BP, respectively. After 25 minutes, the average value of the decrease for the same ICMs is approximately 3.5 and 5.5 for the diastolic and the systolic BP, respectively.

Both the results shown in Fig. 4 and 5 have some limitations from a statistical point of view. The former is obtained by considering different ICMs for smaller or larger values of the

interval from the first measurement. Thus, the direct comparison may be unfair. The latter result, in Fig. 5, is obtained by selecting only the ICMs with length 30 minutes or more. So while the comparison among the different intervals is fair, there is an initial bias in the selection of the ICMs. We stress the fact that these approximations are unavoidable given that the data is collected at home, in an uncontrolled setting. Indeed, they provide a starting point for the analysis of large datasets of home BP measurements, towards the goal of developing guidelines which keep into account the fact that, also for home measurements, an interval of time in seated rest may bring to a significant decrease in BP values.

Finally, in Fig. 6 we stratify the results already presented in Fig. 4 depending on the class of the first measurement. We notice that if the first measurement in the ICM is classified as normal ($c_0 = N$), we do not expect any significant change in the BP from the follow-up measurements. On the contrary, if the first measurement of the ICM is classified as hypertension 1 ($c_0 = H_1$), after 20 minutes from the first measurement we expect a decrease of 6 and 10 mmHg for the diastolic and systolic BP, respectively. If $c_0 = H_2$, the expected decrease is even more accentuated, i.e., 9 and 16 for diastolic and systolic BP, respectively.

B. Change in the Classification of BP

In Fig. 7 we plot the conditional probabilities in (14), for the four possible values of the initial class, c_0, and for the different intervals considered in the analysis, i.e., 0–5, 5–10, 10–20, and 20–30 minutes after the first measurement. We observe that if the first measurement for a subject is classified as normal ($c_0 = N$), the probability of remaining in the the same class is about 80%.

For a subject classified as pre-hypertension ($c_0 = P$), the probability of remaining in the same class for measurements in the 0–5 minutes interval is still 80%, but it decreases to 70% for measurements in the 20–30 minutes interval. In this case the probability of being classified as normal in the follow-up measurements is more than 20%.

For a subject classified as hypertension 1 ($c_0 = H_1$), the probability of remaining in the same class spans from 50% (in the 0–5 minutes interval) to 40% (in the 20–30 minutes interval). The probability of falling in hypertension 2 in a follow-up measurement is negligible, while the probability of falling into a better class (normal or pre-hypertension) is more than 60% in the 20–30 minutes interval.

Finally, for a subject classified as hypertension 2 ($c_0 = H_2$) in the first measurement, the probability that the follow-up measurements confirm this class is less than 50% (in the 0–5 minutes interval). In all the other cases, the subject is falling in a better class in the follow-up measurements, and the probability of being classified in a state less dangerous than hypertension 2 is as high as 70% for follow-up measurements taken in the 20–30 minutes interval.

C. Subject variability

In order to describe the high degree of inter-subject variability in our dataset, in Fig. 8 we plot $\sigma^{(u)}$, the expected 5 minutes decrease in BP, or decreasing rate, for each subject u, calculated using (18). For each subject, represented as a point in the figure, it is possible to

read the value of the decreasing rate on the y-axis, while the subject age can be observed in the x-axis. In the figure, we represent subjects with age between 35 and 80 years old.

In the same figure, we also represent the result of a linear regression for the value of $\sigma^{(u)}$ as a function of age. The decreasing rate is higher (in absolute value) for older people, with a difference of 1 mmHg between younger and older people (regression coefficient is 0.02 with $p < 0.01$).

There is indeed a significant difference among subjects in the decreasing rate. Excluding the most extreme cases, we observe that the expected decrease in systolic blood pressure for most of the subjects after 5 minutes from the first measurement spans between 2 and 9 mmHg, as it can be verified by looking at the y-axis in Fig. 8. This observation suggests that general guidelines for the resting time before taking a home BP measurement may not always be appropriate, while a personalized approach may be more effective.

V. Clinical discussion and conclusions

Despite the capability to measure BP for well over a century, high BP remains one of the greatest contributors to premature morbidity and mortality worldwide [21]. It has been demonstrated that lowering BP by just a few mmHg can have substantial clinical benefit. For example, a decrease in blood pressure of 5 mmHg reduces the risk of stroke by an estimated 34% and ischemic heart disease by 21% [22]. Furthermore, the method used to measure the BP and the different placement of the BP device in the body can significantly influence the BP readings, and even small differences in the BP values can make such a big difference clinically. Thus, there remains a good deal of controversy as to the best method for determining a person's "true" blood pressure [23].

Multiple studies comparing BP determined in the office setting versus at home have suggested that home BP is a potentially better measure of the BP [24], meaning that home BP is a better predictor of relevant clinical outcomes, as compared to office BP. The marked difference in BP values in some individuals in these two settings has led to 15–30% of people with elevated office BP as being diagnosed with white-coat hypertension [25], i.e., their in-office BP has value in the hypertension region, while their at home BP is in the normal or pre-hypertension region. This difference is often explained by a higher induced stress in the patient during office visits, so home BP measurements are considered a more stable measure of the true BP. The work described in this paper is the first we are aware of to identify that a single home BP value may still significantly over-estimate the individual's true resting BP.

The analysis and results presented in this paper indeed suggest that a longer period of rest could provide a significantly lower measure of the BP, of almost 8 and 5 mmHg for the systolic and diastolic BP, respectively. More importantly, the classification of the BP can change significantly if we consider follow-up measurements, in particular if the initial measurement of the BP falls in the hypertension 2 class, the most detrimental class considered here.

In the paper, we have highlighted several drawbacks and limitations of the different methods proposed in this analysis. In particular, the dataset is very rich, with more than 16 million BP measurements, but these measurements are taken at home in an uncontrolled settings, and there is no way to verify that these measurements are taken correctly, or that a user in the dataset corresponds to a single or to multiple subjects. There is also no control in the activity performed by the subject between two consecutive measurements. Furthermore, the frequency of BP measurements varies significantly among different subjects, so the comparison is not straightforward.

Despite these limitations, the analysis provides meaningful insights towards the complex task of interpreting this very important physiological measure. It has also the merit of analyzing home measurements, without or with minimal supervision, and finding an interesting decreasing trend. These results, with the support of novel diagnostic algorithms [26], may inform doctors and patients on how to better interpret home BP measurements, keeping into consideration their limitations.

Designing better guidelines for home measurements should be the task of future large studies with a clinical validation, with the goal of estimating a more truthful measure of the BP.

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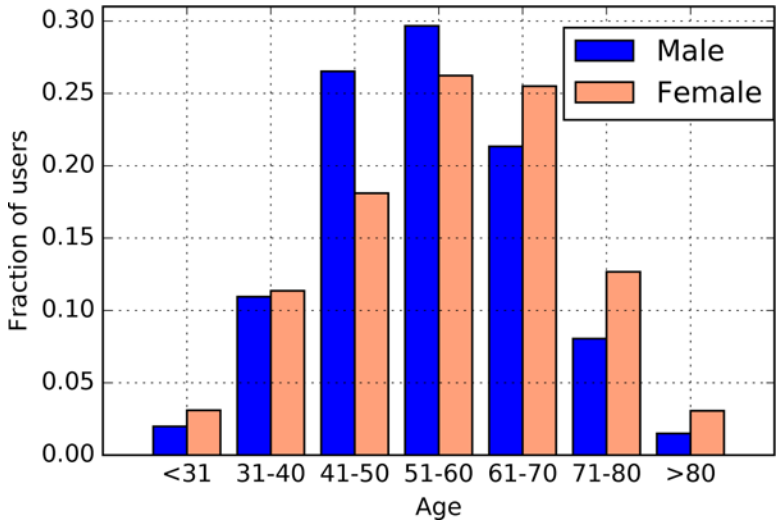

Figure 1.
Fraction of subjects for each age range, divided by gender.

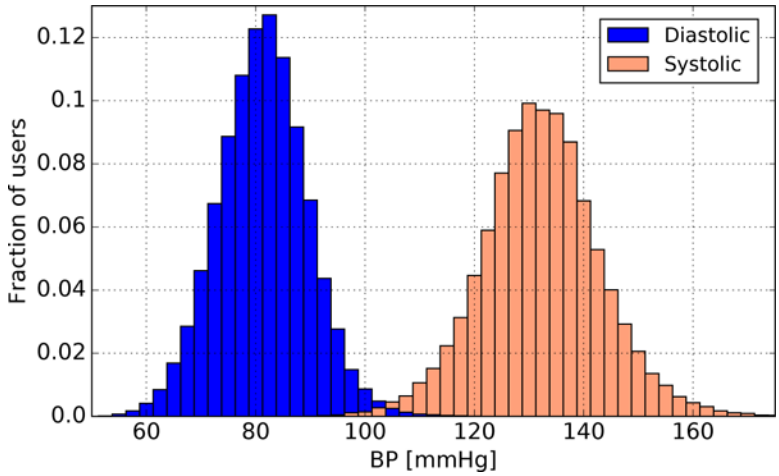

Figure 2.

Fraction of subjects with an average diastolic (systolic) BP for each of the BP ranges considered.

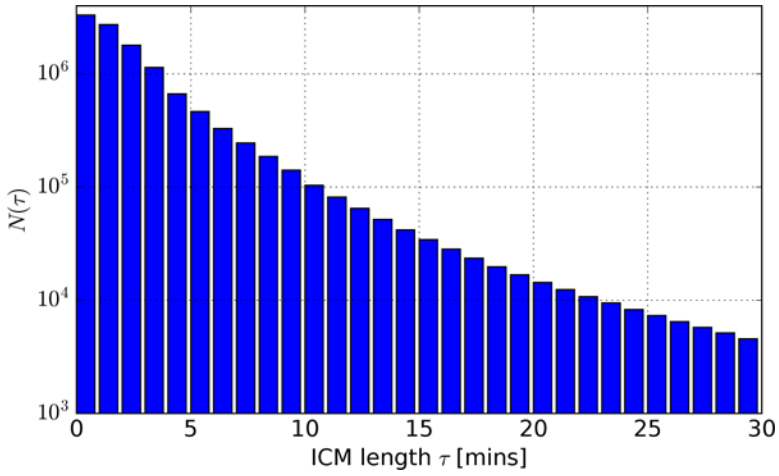

Figure 3.
Number of ICMs analyzed with length (in minutes) greater than τ, as defined in (3).

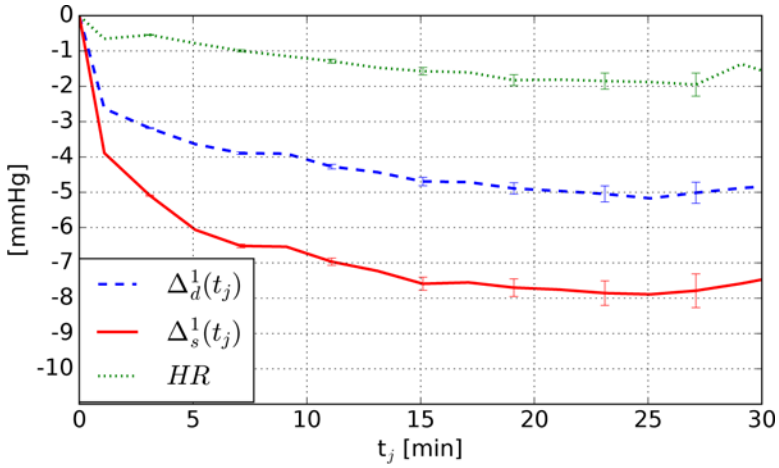

Figure 4.

Average variation, $\Delta_B^1(t_j)$, from the first measurement of an ICM, as a function of the time t_j from the first measurement, for the systolic (in red) and the diastolic (in blue) BP. As a comparison, the corresponding decrease in heart rate (in green), for which the differences are in pulse per minute.

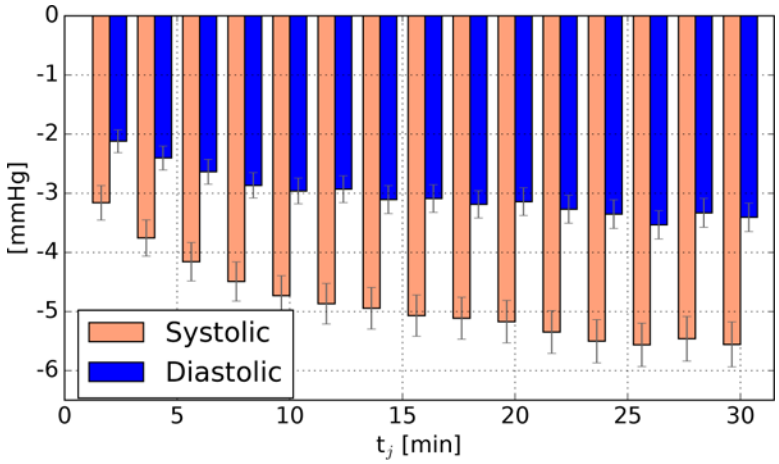

Figure 5.

Average variation, $\Delta^2_B(t_j)$, from the first measurement of an ICM, as a function of the time t_j from the first measurement, for all ICMs with length 30 minutes or more.

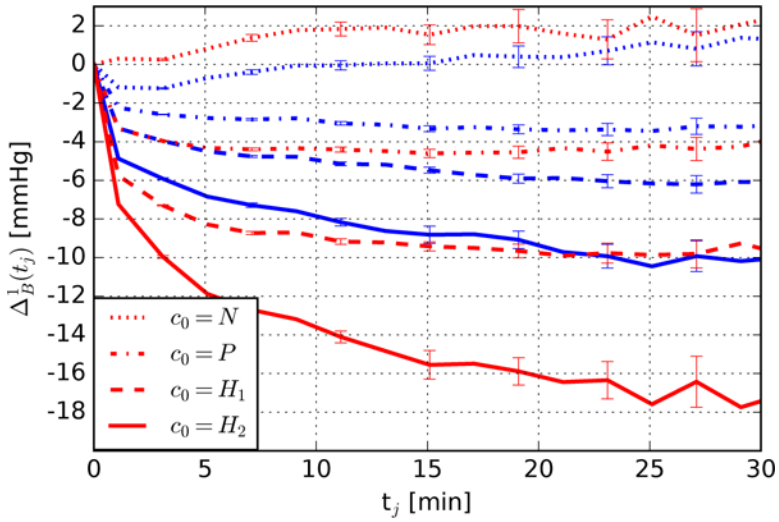

Figure 6.

Average variation, $\Delta_B^1(t_j)$, for the systolic (in red) and the diastolic (in blue) BP from the first measurement of an ICM, as a function of the class c_0 of the first measurement and the time t_j from the first measurement.

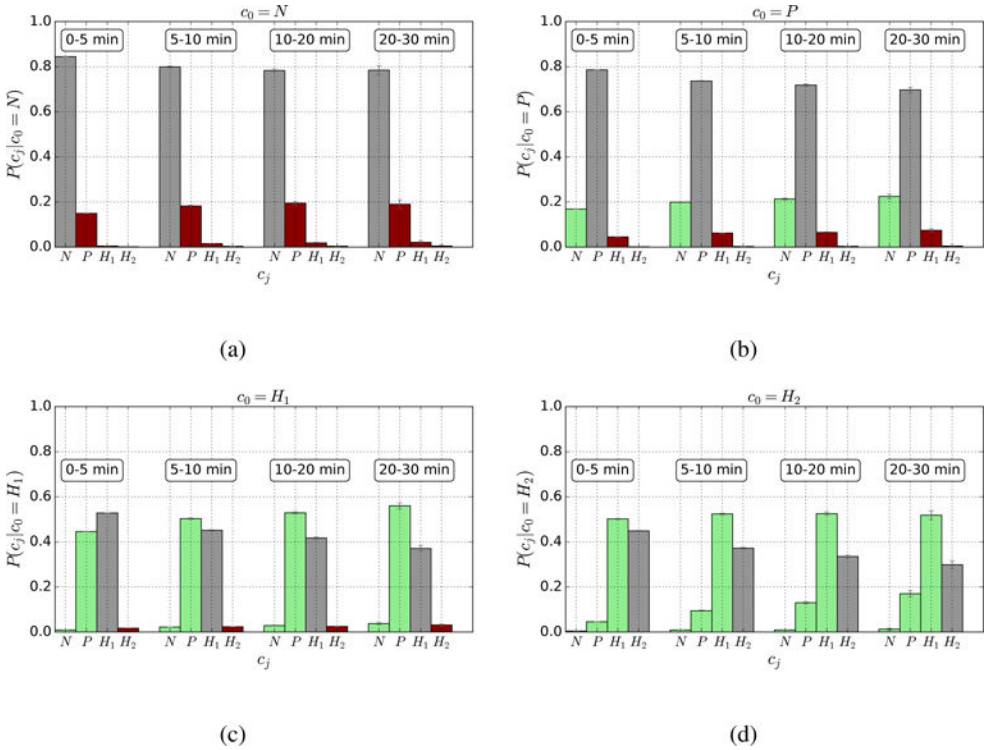

Figure 7.

Conditional probability $P(c_j|c_0)$ for the class $c_j \in \{N, P, H_1, H_2\}$ of the follow-up measure (in the x axis) for 4 cases in each figure: 0–5, 5–10, 10–20, and 20–30 minutes from the first measurement of the corresponding ICM. Each probability is conditioned by the class of the first measurement, which is $c_0 = N$ for subfigure (a), $c_0 = P$ (b), $c_0 = H_1$ (c), or $c_0 = H_2$ (d). The bars are colored in light green for the cases in which c_j is better than c_0, in grey for $c_j = c_0$, and in dark red when c_j is worse than c_0.

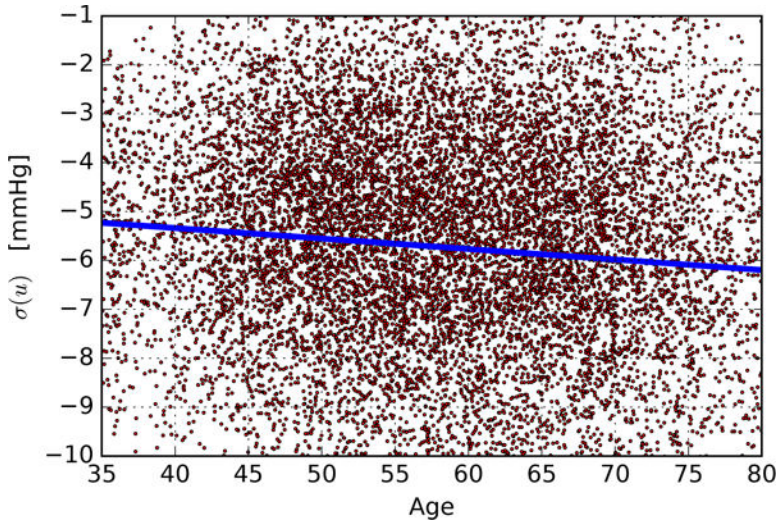

Figure 8.

Estimated parameter $\sigma^{(u)}$ as a function of the age of the subject, and the corresponding simple linear regression