CHRIS Study

Blood Pressure

Version 1.1

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1. Introduction

The blood pressure measurements were performed for all participants at the CHRIS study center in Schlanders Hospital by trained study nurses.

Participants book a morning appointment at the CHRIS study center, ranging from 7.45 to 8.45 a.m. Each study participant is assigned a workflow at the reception. If there are ten study participants (maximum capacity), there are ten different workflows, marked with the letters from "A" to "K". The current workflow is as follows: A-B-C-D-E-F-G-H-I-K. All the workflows can be found in the documentation of CHRIS Baseline/General information/Administrative data, in the file named “Workflows at baseline assessment”.

When making the appointment, participants are asked to stay fasting overnight and to drink only water before coming to the study center. They are also requested to avoid wearing jewelry, piercing, and alike. The precise set of instructions are available at CHRIS Baseline/General Information in the files named “Confirmation letter – German version” and “Confirmation letter – Italian version”. The blood pressure measurements always follow the anthropometry assessment (height, weight, body fat). Participants can have breakfast only after their blood pressure has been measured and cannot have smoked or exercised in the previous hour.

OMRON® M10-IT procedure:

The OMRON® M10-IT device measures blood pressure using the oscillometric method. Its measurement range spans from 0 mmHg to 299 mmHg for the pressure and from 40/min to 180/min for the pulse. Its accuracy is of $\pm$3 mmHg for pressure and $\pm$5% for Pulse. Measurements should be taken in a quiet place, not too hot or cold, and the participant should be in a relaxed, seated position. However, in this study it was decided to measure blood pressure while lying, to best accommodate the previous ECG assessment. The participant is asked not to move or talk during measurement, to lie with their back straight, to remove tight fitting clothing from their upper arm, and any thick clothing such as a sweater. The nurse does not place the cuff over thick clothes and does not allow for rolled up sleeves if it is too tight. The arm is preferably the left one, the right one if not possible. The nurse checks that the arm rests on the examination table so that the cuff is at the same level as their heart. The nurse applies the cuff to the upper arm so that the blue strip is centered on the middle of the inner arm and points down the inside of the arm. The air tube should run down the inside of the forearm and be in line with the middle finger. If systolic blood pressure is known to be higher than 220 mmHg, the nurse turns on the device as soon as the cuff begins to inflate, press the Start button until the device inflates the arm cuff 30 to 40 mmHg higher than the suspected systolic blood pressure. However, the cuff cannot be inflated above 299 mmHg. When the cuff is positioned correctly, the fabric fastener is closed firmly, and the assessment can then occur.

The cuff inflates and then deflates. As soon as the air is completely deflated, the first measurement is finished. A timer shows in how many seconds the second measurement starts, namely 120 seconds. The same happens as with the first measurement and the third measurement also starts automatically. Waiting between readings allows the arteries to return to the condition prior to taking the blood pressure measurement.

At the end, the average of all three measurements is displayed on the screen: the first value shows the systolic blood pressure, the second the diastolic blood pressure, the third, the pulse rate.

To increase precision and have an efficient transmission, the blood pressure data is recorded electronically, assigned to the participants, and then transferred to the central database. The readout of the blood pressure data and the assignment of the data to the participants is done with the help of the "Omron Health Management Software". The blood pressure monitor itself stores only raw data without exact user assignment, so it is recommended to reset the memory of the OMRON® M10-IT after every complete assessment, to facilitate the assignment.

The downloaded and assigned blood pressure data are transferred from the individual laptops to the central database using an MS Access application. A check of the data takes place before the transfer.

The complete procedure is as follows:

1. emptying the memory of the OMRON® M10-IT

2. carrying out the blood pressure measurement

3. downloading the data with the "Omron Health Management Software

4. transferring the data to the database immediately afterwards.

CNAP® Monitor 500 procedure:

The CNAP Monitor 500 device is based on the oscillometric method to measure blood pressure. Its measurement range spans 40 mmHg to 250 mmHg for the systolic blood pressure, 30 to 210 mmHg for the diastolic blood pressure, both with an accuracy of ±5 mmHg. The measurement range for the pulse is 30-200/min, whereas its response time is below 3 seconds and its deflation time below 15 seconds. With respect to the previously mentioned device, this is composed by a double finger cuff, that is to be connected with a cable to the NBP (normal blood pressure) cuff. The systolic and diastolic blood pressure come from the arm cuff measured at start, minute 10, and minute 20 of the ECG, whereas the pulse from the finger cuff, as average of the continuous 20 min measurement.

The continuous measurement of systolic and diastolic blood pressure, as well as pulse, are stored in the ECG module of the CHRIS baseline release.

The nurse chooses the correct CNAP® double finger cuff size by means of the graphic on the CNAP® controller. Then the nurse assembles the CNAP® hardware by connecting the CNAP® double finger cuff, the CNAP® controller, the CNAP® cable with the CNAP® Monitor 500. All plugs and connectors are designed to make it impossible to mix them up by accident. The patient is equipped with the CNAP® hardware: The CNAP® double finger cuff is placed on the proximal joints of the index and middle fingers of the left hand, preferably, ensuring that the cuff cables run along the outside of the patient's arm. The CNAP® controller is put into the slide and fastened to the patient's forearm by means of the Velcro fixation strap. No additional force (tension or pressure) is exerted on the CNAP® double finger cuff via the cable connection. The participant should lie on the examination table and avoid moving, as for the OMRON® device.

The correct size of the cuff is given to the patient (Small Adult, Adult, Large Adult). The blood pressure cuff is placed on the patient's upper arm, preferably contra-laterally (i.e., on the opposite side with

respect to the finger cuff), at heart level. The marker on the NBP cuff should be directly above the brachial artery. The NBP cuff is connected with the NBP air connector on the patient side of the CNAP® Monitor 500.

The oscillometric cuff should not be used on patients with vascular prostheses. Furthermore, blood pressure cuffs may not be applied to a limb with intravascular access, intravascular therapy or arteriovenous shunt. A temporary interruption of the blood flow can result in patient injury. Whether a CNAP® measurement should be applied ipsilaterally to a mastectomy, must be evaluated by a physician as regards patient safety.

In rare cases, it might happen that the device is unable to detect a continuous blood pressure signal. Usually, the middle and index fingers are best suited for applying the finger cuffs as their phalanges are the longest. If it is not possible to obtain a continuous blood pressure signal, this is, in most cases, caused by a vasopathy. Warming up the hand, for example in warm water, may solve the problem. If no continuous blood pressure waveform is displayed within a few minutes, the cause is probably an insufficient blood flow in the fingers. In this case, try using another pair of fingers or the other hand. If this is not successful either, please check if the labeling on the CNAP® double fin-ger cuff (symbol) is on the side of the back of the hand.

The CNAP® Monitor is intended for use in adults and in children from the age of 4 years. This includes an application to pregnant women including pre-eclampsia patients. In certain cases, a continuous blood pressure measurement is not reliable and/or not possible:

- Weak signal shown through perfusion indicator (PI): low PI ≤ 1 on the CNAP® Monitor 500
- Reduced peripheral blood flow (peripheral shock, hypothermia, extreme centralization, extreme hypothermia)
- Arterial vascular diseases (arteriosclerosis, Raynaud's syndrome, endarteritis obliterans, collagenosis, extremely advanced vascular diseases PAOD)
- Edema in the fingers
- Normal Blood Pressure limitations.

Under the following conditions there might be a decrease in accuracy of the oscillometric blood pressure measurement:

- weak pulse
- arrhythmia
- patient movement artifacts
- tremor artifacts
- respiratory artifacts

2. History version changes

Version 1

The OMRON Monitor M10-IT protocol involves 3 measurements at 2 min interval at the end of the 20-min ECG assessment. First, the three measurements were performed, but only the mean values of systolic pressure, diastolic pressure, and pulse were stored.

Version 2

Then, beginning with November 11th,2012, also the single assessments were entered manually into the database, the mean was computed manually and compared with the one stored in the database.

Version 3

Starting from March 26th,2013, the single measurements values were automatically transferred to the database. Additionally, the start time for each blood pressure measurement was recorded and stored into the variables x0bp08a, x0bp08b, x0bp08c.

Version 4

Finally, since June 5th, 2015, another instrument substituted the OMRON®: the CNAP® Monitor 500. The protocol involved a continuous BP measurement synchronized with the 20-min ECG on the finger, and 3 calibration measurements at 10 min interval (start, 10 min, 20 min) on the arm. This signifies that pulse is stored as a time series of 20 min and only its mean value is provided in this module.

Between June 5th,2015 and June 15th,2015 no measurements are available. Between August 21st, 2017, and September 7th, 2017, the CNAP® devices were in routine maintenance and the Omron protocol, version 3, was used instead.

Calibration subsample

Between May 2nd,2018, and June 8th,2018, participants had their blood pressure assessed with both the OMRON® and the CNAP® device, in order to enable calibration between the two instruments. For them the version reported is the fourth, since the official measurement was with CNAP®, but the OMRON® assessment followed the third version of the protocol.

Furthermore, the cleaning process resulted in the following variables added:

variables added: x0bp01m x0bp02m x0bp03m x0bp11m x0bp12m

3. Data cleaning

1. A small sample of participants, namely 178 participants, underwent between May 2nd,2018 and June 8th,2018 both measurements to allow a comparison between the two instruments. Their OMRON® measurements were saved in a separate file that was standardized to allow the merge with the entire dataset (same column names, same column types) and saved again.
2. In the main dataset, the assessment of blood pressure (BP) version was stored in a variable named x0bpver, that was:
    a) 1 until December 9th,2012,
    b) 2 between December 10th,2012 and 25th March 2013,

    c) 3 between March 26th,2013 and June 4th,2015, and between August 21st, 2017 and September 7th, 2017 (reparation period);
    d) 4 since 5th June 2015.
3. The variables were renamed so that all measurements with the OMRON device had a name starting with x0bp0*, and those measurements with the CNAP device had a name starting with x0bp1*. Furthermore, the two digits after "bp" of the variables related to the device CNAP (e.g. x0bp11a) were shifted of 10 units with respect to the correspondent variable related to the OMRON device (e.g., x0bp01a).
4. The file with the calibration OMRON measurements for the 178 participants was merged into the main dataset.
5. The participants who had an OMRON device measurement despite their examination date, x0_examd, after the start of the 4th version were assigned version 3 (x0bpver=3).
6. The operator variable, x0bp04a, was split into two variables according to the BP measurement version, x0bpver, resulting in x0bp04a and x0bp14a. For the calibration subsample, both x0bp04a and x0bp14a have the operator reported, as they might differ.
7. The labels of each variable were updated so that also the device name was included.
8. For a participant, the values of the original measurements (before breakfast), could not be inserted in the database because of technical problems, and were therefore inserted manually.
9. For the variables of systolic blood pressure (x0bp01* and x0bp11*), diastolic blood pressure (x0bp02* and x0bp12*), and pulse (x0bp03* and x0bp13*), not feasible values, such as 0 and 1, were converted into "unexpected missing" (-89).
10. The single measurements of systolic and diastolic pressure measured with OMRON, x0bp01a-x0bp01c and x0bp02a-x0bp02c, had their missing values set to:
    a) "Not in use" (-98) for versions 1 and 4,
    b) "Unexpected missing" (-89) for versions 2 and 3.
11. The single measurements of pulse measured with OMRON, x0bp03a-x0bp03c, had their missing values set to:
    a) "Not in use" (-98) for versions 1 and 4,
    b) "Unexpected missing" (-89) for versions 2 and 3.
12. The mean pulse measured with OMRON, x0bp03, had its missing values set to:
    a) "Not in use" (-98) for version 4,
    b) "Unexpected missing" (-89) for versions 1,2, and 3.
13. The mean pulse over 20 minutes measured with CNAP, x0bp13, had its missing values set to:
    a) "Not in use" (-98) for versions 1,2, and 3,
    b) "Unexpected missing" (-89) for version 4.
14. The OMRON device variable, x0bp05, had its missing values set to:
    a) "Unexpected missing" (-89) for versions 1, 2, and 3.
    b) "Not in use" (-98) for version 4.
15. The OMRON device variable, x0bp05, had its missing values set to:
    a) "Not in use" (-98) for versions 1, 2, and 3.
    b) "Unexpected missing" (-89) for version 4.
16. The consistency between the order of the three OMRON measurement was checked, so that the three timestamps, stored in x0bp07a-x0bp07c, occurred on the same day of the examination, x0_examd. If this was not the case, then the wrong timestamp was set to "unexpected missing".

17. It was checked that the time of the three measurements, stored in x0bp08a-x0bp08c, was not the same for each participant. For one participant, the first and third measurement had the same time and day as another participant. The second measurement was saved as the first one, whereas the remainder were set to "unexpected missing".
18. The transmission of the OMRON results to the database sometimes reversed the order of the measurements. Using the time variables, x0bp08a-x0bp08c, the participants were divided into the sequence of measurements they had and reordered appropriately. The first group has 1-2-3 sequence and does not need a correction, the second group 1-3-2, the third group 2-1-3, the fourth group 2-3-1, the fifth group 3-1-2, the last group 3-2-1.
19. It was assessed that the three measurements were performed 2-3 minutes apart from each other. 193 participants had a time between measures (either between the first and the second or between the second and the third) that was above 3 minutes.
20. The fake dates, i.e. dates inserted that were before the start of the recruitment, on 1st August 2011, were set to missing.
21. For the participants who had the blood pressure measured with the CNAP device (version 4), if one of the systolic pressure variables, x0bp11a-x0bp11c, was "unexpected missing", then also the correspondent time variable, x0bp08a-x0bp08c, was set to "unexpected missing".
22. For the variables that are resulting from the mean of three assessments, namely x0bp01, x0bp02, x0bp03, x0bp11, and x0bp12, the mean was calculated and saved if the mean value was not automatically computed. New variables were created to store the number of missing measurements for each blood pressure parameter into x0bp01m, x0bp02m, x0bp03m, x0bp11m, and x0bp12m.
23. It was tested whether there was an effect between the different versions of the BP assessment result. Especially the systolic and diastolic pressure differed substantially between the first three versions and the last one. For this reason, the fourth version assessments are saved into different variables.
24. The variable storing the information on the OMRON device used, x0bp05, was first converted from string to numeric variable. Then its missing and out of range values were set to
    a) "Not in use" after the June 5th,2015,
    b) "Unexpected missing" otherwise.
25. The variable storing the information on the CNAP device used, x0bp15, was first converted from string to numeric variable. Then its missing values were set to
    a) "Not in use" before the June 5th,2015,
    b) "Unexpected missing" otherwise.
26. The variable x0bpnote storing the study nurse's notes are divided into x0bpnote1, notes regarding high and low BP values, and x0bpnote2, regarding deviation from protocol and state of the participant.
27. The two note variables, x0bpnote1 and x0bpnote2, were translated into English and grouped when similar. Only the second one, concerning the deviations from protocol, can be accessed, whereas the first one has no scientifically relevant value and is therefore not available.
28. The variables storing the date and the date plus time of the assessments with OMRON were deleted.

4. Advices for the analysis

The two devices that have been used differ substantially in their measurement range, accuracy, and their protocol, so attempting to merge them into a single variable should be avoided. Furthermore, the three versions of protocol for the OMRON® device influence the distribution of both systolic and diastolic pressure.

The analyst is encouraged to take into account the operator involved in the assessment of the blood pressure, x0bp04 and x0bp14 for the OMRON® and CNAP® devices respectively, since the operator needs to instruct well the participant on their posture and places the cuffs.

5. References

Unger T, Borghi C, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines, *Hypertension,* 2020, 75 (6). DOI: 10.1161/HYPERTENSIONAHA.120.15026