**Peer Review File**

Article information: https://dx.doi.org/10.21037/mhealth-23-66

**Reviewer A**

The authors have developed an application (the Hy-Result® system) that helps patients take home blood pressure measurements and understand the results through automated interpretation of readings and a web interface. This is an interesting observational study, but it involves significant problems.

[Major points]
#1. Methods:
The authors described “we excluded 270 reports (1,4 %) with aberrant values defined as follows: DBP < 40 mmHg or > 140 mmHg; SBP < 80 mmHg or > 250 mmHg”. We may experience hypotension as low as 75-79 mmHg, but how did they set the above outlier values? The authors should clarify.

Reply 1 : We understand your comment and are providing the requested clarification. We added the following clarification :

Changes in the text: “These thresholds are arbitrary but mainly based on the technical limitations of some devices. Above these ranges of readings, automatic analysis by the software is questionable without verification of monitor reliability, measurement procedure quality, and clinical information. Since such verification is impossible, we prefer to exclude such extreme values, which constitute a tiny minority of the data, to avoid any hazardous interpretations)

#2. Methods:
What is a "Hypertension Unit"? The authors should explain it.

Reply 2 : Hypertension Unit is a synonym for a Hypertension Department, Hypertension Clinic or Hypertension Center. To simplify, we deleted the term Unit and replaced it by Hypertension Center

Changes in the text: we keep Hypertension Center.

#3. Results:

The authors indicated “Normotensive users are younger with a mean age of 58 (+/-14) and with a lower prevalence of comorbidities”. However, since the "untreated group" generally includes "hypertensive patients," the "untreated group" and "normotensive patients" in Table 3 do not match.

The authors should clarify the classification of these two groups. Also, a t-test should be performed to compare the two groups.

Reply 3: thank you for your comment. we have modified our text by replacing “Normotensive users” with "untreated group". We have also performed the t-test as requested for table 3

Change in the text, we add : In this study, we used the t-test to assess the significance of differences in mean values between two independent groups, while the Pearson correlation coefficient was employed to evaluate the strength and direction of relationships between two continuous variables.

#4. Results:

As in Table 3, statistical analysis (e.g., t-test) should be used for group comparisons in Table 4.

@Nicole : faire un t-test ? et faut qu’on vérifie toutes les tables

Reply 4: thank you for your comment.

Changes in the text: we have performed the t-test as requested for table 4

#5. Results:

The authors set 15 BP measurements as the compliance threshold, but 15 measurements per day would be classified as the "≥15 group". This has nothing to do with compliance with BP measurements. Thus, what does this threshold and subgroup analysis (e.g., Table 5, Figure 4) imply?

Reply 5 : The web application input form does not allow to enter more than 6 readings (3 morning and 3 evening). The threshold of 15 measurements (which could have been 12, as you remark) is discussed below in response to question 8 from reviewer 2. (See above) : "We agree that 12 readings should be correct. But we choose > 12, in the case that a user enters 3 readings according to the French guidelines".

#6. Results:

Page 7, line 4

How does Figure 4 summarize the "patients' characteristics of normal or low BP"? Please clarify.

Reply 6 : Thank you for catching this typo error. It is Tab 4 and not Fig 4.

Changes in text :-Patients' cardiovascular risk factors of normal or low BP (gray color code) are summarized in Tab 4.

#7. Results:

Page 7, line 9

If the authors recognize that the upper arm cuff is the "recommended cuff," why did they include BP measurements with the wrist cuff in their study? At the same time, in the Discussion section, they indicated that the instructions provided through the Hy-Result app advised patients not to use wrist devices. To improve data quality, patients using wrist devices could be excluded. The authors should explain why wrist devices were included.

Reply 7 : ESH guidelines recommend the use of upper-arm cuffs, but do not prohibit the use of wrist cuffs (they "can" use if upper arm cuff are not available guidelines say). Wrist cuffs are authorized for sale and approved by health authorities (FDA and CE). In situations where the use of the arm cuff is difficult (e.g. conical arm, arm circumference > 44 cm, lymphedema, lymph node curage, midline, etc.), the wrist cuff is an alternative. In Europe, it is estimated that the number of arm cuffs sold is comparable to that of wrist cuffs. Since our data are real-world data, we choose to keep them in the analysis. Thus, despite the fact that brachial devices are preferred, we cannot arbitrarily exclude wrist devices because some of these devices have been validated

and their use in recommendations is accepted and, above all, they are widely used by users; their exclusion will be arbitrary.

Changes in the text: none

#8. Results:

Normally, the chapter “strengths and limitations” should be written in the Discussion section.

Reply 8 : OK, thanks for this advice.

Changes in the text: adjustment has been made.

#9. Discussion:

Page 9, line 8

The authors stated “to answer we should consider the patients’ tolerance and orthostatic hypertension”, but how does orthostatic hypertension relate to the outcome? In the protocol, patients have their BP measured after adequate rest, which eliminates the effect of orthostasis.

Reply 9 : In fact, the data obtained by the application do not allow us to know whether orthostatic hypotension is present or not. As we have already said. : « Unfortunately, these data are unavailable in our database » : For greater clarity, we rephrase and correct the typo error (hyp**er** instead of hyp**o**) :

Changes in the text: « To answer this question, we need to consider patient tolerance and orthostatic hypotension. Unfortunately, these data are not available with a sitting measurement. In these cases (gray zone classification), text messages invite users to check their BP with their doctor ».

#10. Discussion:

How do the authors explain the difference in compliance between the Hosp group and the Prim groups in Table 5?

The article note : “This rate reaches 96% for Hosp patients who received instructions from a nurse”.

Reply 10 : For greater clarity, we rephrase :

Changes in the text: “This rate rises to 96% in the Hosp group, which has received specific training from a nurse”.

#11. Conclusion:

The "Conclusion" paragraph is too long. The author should shorten the content.

Reply 11 : OK, We make the adjustment.

Changes in the text: we remove, ~~In conclusion, our study shows that 90% of the HBPM reports include the required minimum number of BP measurements to allow the calculation of a reliable average among whom 40% have uncontrolled BP levels. The self-management Hy-Result software demonstrates significant potential for inclusion in the patient care process, both in primary care settings and tertiary ESH excellence centers. This app rienforces the patient’s engagement to independently monitor their BP, bridging the gap between clinical visits. Whenever the mean BP falls outside the recommended range, the software automatically prompts users with text messages advising them to seek medical guidance. The Hy-Result system represents a valuable tool that not only facilitates patient self-management but also offers healthcare providers a dependable source of data for informed decision-making in both routine and specialized healthcare contexts. Subsequent research should explore the extent to which users adhere to text message recommendations generated by the software.~~

Changes in the text: In conclusion, our real-life study shows that 90% of the HBPM reports include the required minimum number of BP readings to allow the calculation of a reliable average among whom 40% have uncontrolled BP levels. The self-management Hy-Result web app demonstrates significant potential for inclusion in the patient care process and reinforces the patient’s engagement to independently monitor and self-reported their BP.

#12.

In this "digital hypertension" area, feedback systems are essential. The authors have shown that text messages advise patients, but some examples of text message patterns would be better shown in the supplemental material.

Reply 12 : OK

[Minor points]

Tables

The expression "p=0.000" is not common. Usually "p<0.001" is used.

Reply 4: thank you for your comment.

Changes in the text: we replaced "p=0.000" with "p<0.001" in both text and table 6

Table 5:

What is PAS/PAD?

Reply tab 5 : Sorry, PAD and PAD are French abbreviations.

Changes in the text: We correct with SBP and DBP

Figure 1:

What does the number "172279" mean? The author should check that.

Reply Fig 1 : Thank you for seeing this typo on our manuscript, it should read: 17279. We make the adjustment.

Changes in the text: 17279

Figure 3

There are no abbreviation for “PCU” and “TCU”.

Reply 1 : Sorry, this typo mistake. We will correct with Hosp and Prim

Changes in the text: Hosp Prim

The authors should check for spelling errors before sending files (e.g., “This app rienforces…” [in the Conclusion section]).
Changes in the text : app reinforces.

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**Reviewer B**

As someone who treats many patients with hypertension and also designs and uses mHealth interventions, I read this manuscript with great interest. I heartily congratulate the investigators for developing Hy-Result. It is clearly a good program as evidenced by the rather large number of patient users and the list of peer-reviewed publications.
That said, I find the current manuscript does not provide very useful information. Most of the results simply describe differences among population groups and have rather little to do with the application under investigation. What is of greatest interest is how patients interact with the program. The richest data document these interactions -- log-ons, views and submissions of blood pressure data – particularly BP submissions at repeated intervals over time. This manuscript uses much of the results to state how two very different and separate recruited groups differ on BP and demographics instead of focusing on how patients used the app.

1. The introduction and discussion should better note the several primary issues related to the design of patient-facing digital interventions for home blood pressure monitoring – primary technology used (SMS, web-based, smart phone app), primary program features (timed-reminders, an avatar, use of AI, self-management advice, and adaptive messaging), HBPM schedules/data management/BP reports, technology barriers, human supports, and data sharing with providers.

Reply 1 : We understand your comment. We have addressed this in the limitations section of the study and added this precision :

Changes in the text: The data do not provide information on how patients interact with the program over the long term, particularly the submission of BP reports at repeated intervals over time. This information will be made available in a new version of the software.

2. I believe that citations 7 and 8 are a single reference.

Reply 2 : Thank you for pointing out this error. ref 9 was missing :

Changes in the text reference : Groenland EH, Bots ML, Visseren FLJ, McManus RJ, Spiering W. Number of measurement days needed for obtaining a reliable estimate of home blood pressure and hypertension status. Blood Press. 2022 Dec;31(1):100-108. doi: 10.1080/08037051.2022.2071674. PMID: 35574599.

3. Line 79 – Validation can mean many things. Instead of simply saying it is a "validated system", I suggest a separate sentence in this section describing briefly how the device was validated.

Reply 3 : We agree with this remark, so we add details

Changes in the text: "A first study evaluated whether the algorithm classification of the BP status was in accordance with the physician's classification (blinded to the software's results) following a consultation (n=195 patients) and shows that classification by Hy-Result is similar to that of a specialist in current practice (4). A second, study assessed the experience of patients with the functionalities and medical content of Hy-Result, their feelings and expectations, and the impact of Hy-Result on the physician-patient relationship. It concluded that most of the users (n=512) described Hy-Result as an easy-to-use and useful tool (5). Additional study shows that the majority (88%) of pregnant women (n=107) performed HBPM and successfully used the Hy-Result software for self-interpretation of the BP readings" (6).

4. I note that the application is a registered trademark. In that case please clearly state whether the application is proprietary. If so, one or several of the authors likely have a conflict of interest which also should be clearly acknowledged.

Reply 4 : In a disclaimer section we add these details.

changes in the text in the disclaimer section:

The Hy-Result application is certified by the French Society of Hypertension. Its development is supported by 2 non-profit organizations (Association Robert Debré pour la recherche médicale, Fondation de l'Avenir) and university (Faculté de Médecine Paris V); it is free of charge and generates no revenue. Nicolas Postel-Vinay, is one of the academic authors (as already declared), does not receive any remuneration; the scientific advisory board does not receive any remuneration too; the brand name has been registered by the company Thot, which is responsible for IT maintenance and the cost of secure hosting.

5. Without written, signed consent, I do not see how the authors can reliably assert that all participants fully understood and consented to this research study. I am not sure that the stated methods meet the international standards for ethical medical research.

Reply 5 :

Our work is based on the analysis of a totally anonymous database, with no possibility of identifying the application's users. To use the application, users had to give their "agreement to use the application" in a consent screen.

We agree with the reviewers that this is not exactly "signed consent", but from a legal point of view, only the words "do not object to the research" are required. For patients at our hypertension center, Institutional Review Board (regional ethics committee) approval is available for all chart reviews ; but as we did not use this source, we do not mention it.

To ensure complete reporting of our routinely collected health data, we followed the REporting of studies Conducted using Observational Routinely-collected health Data statement (XX).

XX. Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, et al. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD)

Statement. PLOS Medicine [Internet]. 2015 Oct 6 [cited 2022 Jul 12];12(10):e1001885. Available from: https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001885
Change in the text : To ensure complete reporting of our routinely collected health data, we followed the REporting of studies Conducted using Observational Routinely-collected health Data statement.

6. Please clearly state how many days of monitoring were specifically advised. Were they told to do at least three days, at least four days, or were they all told to strive for seven days?
Reply 6 : The exact instructions on the web site is “Measure your blood pressure for 3 to 7 days in a row and fill the table”. We add the precision in the article :
Changes in the text : Webb app instructions are : “Measure your blood pressure for 3 to 7 days in a row and fill the table”.

7. Why were they told to measure blood pressure in triplicate when the ESH guidelines advise measuring blood pressure twice?

Reply 7 : The ESH guidelines advise 2 consecutive measures. However, the French guidelines call for 3 (which is arbitrary of course). In order not to contradict the French guidelines, we ask for 3 consecutive measurements. The guidelines (2000) recommended 3 successive readings (Asmar R, Zanchetti A. Guidelines for the use of self-blood pressure monitoring: a summary report of the First International Consensus Conference. Groupe Evaluation & Measure of the French Society of Hypertension. J Hypertens. 2000 May;18(5):493-508).

8. Why use a minimum threshold of 15 readings? The ESH states the minimum at 3 days of duplicate readings morning and evening, which translates to 12 readings.
Reply 8 : We agree that 12 readings should be correct. But we choose > 12, in the case that a user enters 3 readings according to the French guidelines.
Change in the text : in accordance with the French guidelines recommending 3 measurements morning and evening.

The following comments pertain to how the data were analyzed and what findings are reported. Each revision the authors might undertake could affect several sections (abstract, methods, results, discussion) of the manuscript.

9. The flow chart (Figure 2) is based upon individual blood pressure readings. The convention is that flow charts are based upon individual study participants. Please revise to follow this convention.

Reply 9 : For the methodological reasons described in the limits section, we are unable to make this change.

10. Likewise, the tables use the individual BP reading as the important unit whereas I believe better understanding is created by using the individual patient as the unit of interest. We are far less concerned with a specific BP value than with how regularly a patient interacts with Hy-Result. This would impact the 2nd row in Tables 3 and 4 and all of Table 5.

Reply 10 : We agree with you that the regularity with which a patient interacts with Hy-Result is of great interest. At this time, our database does not allow us to have this information. We have planned to do so for future studies, We have addressed this in the limitations section of the study Changes in the text: The data do not provide information on how patients interact with the program over the long term, particularly the submission of BP reports at repeated intervals over time. This information will be made available in a new version of the software.

11. Were participants asked to do the 3-7 day monitoring once? If they were expected to do the monitoring more than once, on what schedule? Are the data from a single time point in some individuals and reflect several monitoring periods for other individuals?

Reply 11 : See reply 6 : . The exact instructions on the web site is “Measure your blood pressure for 3 to 7 days in a row and fill the table”. We add the precision in the article

12. Table 6 can be moved to an online supplement.

Reply 12 : OK

Change in the text : Table 6 has been removed to the supplementary file

13. The authors firmly conclude that roughly 90% of users submitted at least 15 readings. This is truly remarkable but is based on a denominator that only includes individuals that registered on the website and offered baseline data. So, the value of 90% appears to derive from a select, motivated and willing subset of individuals. Do the authors have data on the number of individuals approached but who did not enter baseline data or otherwise register themselves on Hy-Result?

Reply 13 : We fully agree with your comment. This high percentage was much higher than we expected. We add this clarification with the new reference :

Changes in the text: " The value of 90% derives from a select, motivated and willing subset of individuals. Web site traffic statistics show that of all visitors to the form page, roughly two-thirds enter their BP readings to calculate their average BP (first step). Half of them proceed to the second and final step (by completing their medical profile, entering their BP results, and clicking the “calculate” button). In a previous pilot study, we observed that 54 % (n=304) of the new patients who booked via the Internet an appointment at our Hypertension tertiary center were able to prepare for their visit by going through a digital pathway and following the application's instructions for use. (Postel-Vinay, Nicolas1; Gardini, Margherita2; Nogueira, Lima3; Lorthoir, Aurelien1; Amar, Laurence1. DIGITAL PATH OF THE HYPERTENSIVE PATIENT BEFORE A FIRST VISIT IN A TERTIARY CARE HYPERTENSION UNIT: A REAL-LIFE PILOT STUDY. Journal of Hypertension 39():p e217, April 2021. | DOI: 10.1097/01.hjh.0000746892.08127.a6)

14. I suggest adding analyses that explore sociodemographic predictors on high vs low engagement (based on # of BP readings submitted).

Reply 14 : our database does not allow us to have this information.

15. I do not see much value in Figures 4-6. They demonstrate that the various groups of individuals, in fact, have different blood pressure levels. They do not address the interaction between patients and Hy-Result.

Reply 15 : We understand your comment. We have addressed this in the limitations section of the study. Fig 6 is removed.

16. The Strengths and Limitations section should be moved to the Discussion.

Reply 16 : OK