Impact of technological innovation on virtual care, monitoring and engagement of patients with uncontrolled hypertension: Hyper2

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Sao Paulo

2022

1.Introduction

Hypertension (AH) is defined by chronic non-transmissible, multifactorial clinical condition and characterized by sustained high levels, often associated with functional and/or structural alterations of the target organs (heart, brain, kidneys and blood vessels) and metabolic changes, with consequent increased risk of fatal and non-fatal cardiovascular events [1].

It is the most prevalent cardiovascular disease, reaching between 30% and 45% of the world's adult population [2]. In Brazil, different epidemiological studies show a prevalence of around 30% [3]. According to the Surveillance System for Risk and Protective Factors for Chronic Diseases by Telephone Survey (SURVETEL) of the year 2017, the prevalence of self-reported AH increased from 22.6% in 2006 to 24.3% in 2017 [4]. The disease tends to increase with age, reaching 60% among adults over 65 years of age, being higher among those with less schooling and among Afro-descendants [3].

AH is responsible for 40% of infarctions, 80% of strokes and 25% of cases of end-stage renal failure in our country [3]. One of the main factors for the occurrence of complications in hypertensive patients is the lack of adequate control. Recent observations have shown that, regardless of which region of the world evaluated, whether from high- or low-income economies, or the level of sophistication of health care delivery, only about 40% of patients with hypertension are under treatment, and of these only 35% are controlled with BP < 140/90 mmHg [2].

Among the main causes of lack of control are the therapeutic inertia of the doctor, effect of the “white coat” and especially the lack of adherence of patients to the correct use of medication and healthy habits of life, especially to the restricted sodium diet and physical activity. Factors that contribute to a low adtake are multiple and at various levels. Barriers to treatment are barriers to the patient (multiple comorbidities, low level of knowledge of the disease, economic restrictions, lack of involvement in the decision-making process of the treatment) - in relation to the doctor (prescription of complex treatment regimens, communication barriers, lack of adequate information of adverse reactions, clinical inertia), and in relation to the health system (limitation of the time of medical consultations, limited access to care, lack of multiprofessional approach and health information technology) [5].

Non-adhering to antihypertensive drugs is highly prevalent in patients with uncontrolled hypertension [6,7]. It is estimated that between 50% and 80% of hypertensive patients receiving

prescription medication demonstrate suboptimal therapeutic adherence [8]. Other studies have shown that a quarter of patients who start newly diagnosed antihypertensive therapy fail to follow the initial prescription [9,10]. During the first year of treatment, most patients take the prescribed antihypertensive medication only 50% of the time, and only 1 in 5 patients have sufficient support to achieve the benefits observed in clinical trials (approximate 80% adherence) [11].

This relatively high proportion of non-adhering is due, at least partially, to the large number of pills to be taken, complexity of doses, presence of adverse reactions with multiple medication regimen, and the little insistence of physicians regarding better support when patients are consistently non-adherent [12].

However, the tendency to improve BP control rates (<140/90 mm Hg) among those on antihypertensive treatment to more than 70% suggests that recent strategies to improve hypertension and care with antihypertensive medication have been successful [13].

In relation to healthy lifestyle habits, adhering to a more restricted sodium diet is one of the most difficult to achieve, despite several efforts to reduce sodium intake in the population. Two-thirds of the salt consumption by the Brazilian population comes from the salt added directly to the meal. The numbers show that Brazilians consume more than twice – almost 12 grams (g) – of the amount recommended by the World Health Organization (WHO) [4]. Data from the Ministry of Health reveal that 90% of men and 70% of women consume more salt than the maximum recommended, 85.1% of adult Brazilians consider their salt consumption adequate [4]. Another important point between life habits is sedentary lifestyle, which can also contribute to the lack of adequate control of BP. There is much evidence that shows the benefit of physical activity to reduce BP, including providing the number of medications needed for control [3].

Therefore, it is essential to help patients adopt healthy measures to assist in the daily control of BP. As the barriers to therapeutic adherence are complex and varied, solutions to improve adherence at the population level should be multifactorial [14,15].

Several systematic reviews and meta-analyses have evaluated the impact of interventions on patients' adhering to antihypertensive medications and their benefits [16, 17].

Most interventions to improve the quality of AH care, medication and healthy habits and BP control are care based on a multidisciplinary team [18]. Different patient-centered models

with a multidisciplinary team showed an increase in the proportion of individuals with better blood pressure support and greater BP control [18,19,20,21,22].

One of the best and most effective models includes decision support systems (treatment algorithms), collaboration between team and patient, medication adherence, home BP monitoring, and patient self-care [23,24].

Recently, support systems such as electronic health records, remote monitoring based on new technologies and self-care support tools, can increase and intensify efforts based on the multidisciplinary team approach [25,26,27,28].

In this sense, some studies are being conducted on the use of mobile technology to control hypertension, aiming at greater access to the patient, education and awareness of the disease, as well as the patient's engagement in their care [29,30,31,32,33]. In a previously developed study, it was seen that virtual distance or face-to-face teaching, through "e-learning", helps to reduce the effect of the white coat and the anxiety of hypertensive patients, with an improvement in adherence to treatment [34].

However, it is not yet known the best technological tools to help hypertensive patients to improve treatment adhering to healthy life habits and, and consequently avoid the complications of AH. In addition, this tool needs to be feasible to be used by patients or caregivers, regardless of social class, preserving their intimacy, privacy and still obtaining the desired health improvement results.

Based on these arguments, the hypothesis of the proposal is that the use of an application developed by artificial intelligence adapted to individual needs and customs can help improve therapeutic adherence and provide better BP control in patients with uncontrolled hypertension.

2. Primary objective

To evaluate the effectiveness of an artificial intelligence application developed for home monitoring compared to institutional standard follow-up in patients with uncontrolled hypertension in the following parameters:

a) To obtain adequate control of blood pressure (< 140/90 mmHg) of the office and of the blood pressure ambulatory monitoring (< 135/85 mmHg at wakefulness)

b) Improving adherence to drug treatment assessed by a validated questionnaire

c) Reduce dietary sodium intake and 24-hour urinary sodium

d) Increase the performance of physical activity evaluated by number of daily steps

e) Reduction of body weight and abdominal circumference

2.1. Secondary objective

a) To evaluate the effects of the use of the monitoring application on: quality of life of patients with uncontrolled hypertension through WHOQOL questionnaire; sleep quality assessed by the Pittsburg questionnaire; anxiety level assessed by the HADS questionnaire; food consumption assessed by consumption questionnaires and food recall:

b) Assess the ability of patients with uncontrolled hypertension to use the application

3. Methodology

3.1. Study design

Randomized study with patients with uncontrolled hypertension followed at the Outpatient Clinic of the Hypertension Unit of the Heart Institute (InCor-HCFMUSP), for the use of an application for monitoring and engagement to antihypertensive treatment - compared to the standard follow-up of the institution in a 12-month follow-up.

The study involves the direct participation of an institutional multidisciplinary team with an international partnership and a national institution of advanced technology in artificial intelligence. The hospital's team includes physicians, nurses, nutritionists, psychologists, physical educators and biomedicals, supported by the institution's own innovation team. The international team includes all members of the Inavya Ventures LTd.

Will be included 100 patients diagnosed with primary arterial hypertension under drug treatment, with at least 3 classes of antihypertensivedrugs in an optimized dose, aged 20 to 65 years, and who present clinic BP ≥ 140 and/or 90 mmHg, and wakefulness BP in ambulatory BP monitoring ≥ 135/85 mmHg. Patients or their caregivers should also be able to use mobile phones and apps.

Patients with stroke sequelae or those with significant cognitive dysfunction will be excluded.

Randomization will be done in the 1:1 form using electronic randomization system, without knowledge by the team involved in the study. There will be two groups in the project,

so that, patients will be randomized to intervention group (application use) or control group (standard follow-up of the institution).

In the intervention group (N= 50), patients will receive a cellular device (by donation consigned by a telephone company) for the exclusive use of the application within 12 months. In this mobile device will be installed, with the guidance of the multidisciplinary team, the AVATR application developed in partnership with the company Inavya Ventures Ltd., where they will be digitized with individualized code for each patient, personal data, including age, gender, behavioral patterns and lifestyle habits (walks, type of diet, quality of sleep, etc.), and daily medications used.

The data will be allocated in a dedicated cloud and protected by cutting edge encryption. All this part of data capture and storage is in accordance with the rules of the General Data Protection Law (GDPL) as well as the General Data Protection Regulation (GDPR), the uk regulation.

Patients will have a 15 days adaptation period to the use of the application, where they will receive virtual guidance by the multidisciplinary team for the correct use. After this period, patients will perform an evaluation by the medical and nursing staff, where clinical data (clinic blood pressure, weight, height and abdominal circumference) will be collected and patients will answer questionnaires on quality of life, anxiety, sleep quality, food intake and therapeutic adherence. In this same consultation, patients will receive an automatic blood pressure measurement device (described in the methods) to make household blood pressure measurement according to nursing guidance. Blood samples will also be collected for biochemical profile (total cholesterol and fractions, triglycerides, fasting glycemia, potassium, serum creatinine) and 24-hour urine sample for urinary sodium dosage, these tests will be collected at the Research Center and the analysis will be performed by the institute's laboratory.

The application automatically receives input data from each patient, such as BP MEASUREMENTS by the device and also the steps walked recorded by own in a third-party application also installed on the mobile phone. This data is safely transferred to the cloud server and analyzed based on an algorithm developed with the help of healthcare professionals to generate a customized lifestyle modification program designed for each patient. The application has automatic messages for the time of medication, in addition to strengthening nutritional guidance, physical activity and emotional order through automatic motivating phrases and also by access to educational videos. Another important tool is speech recognition that allows the patient to send data by voice system when there is difficulty in typing communication.

The multiprofessional team will receive alerts by email or the application platform, according to pre-established limits of blood pressure or symptoms, allowing immediate contact of the team for the necessary guidance. The multidisciplinary team will contact patients in the digital intervention group every 4 weeks for guidance based on the insertions made by patients in the application during the period. The correct use of medication as well as the adoption of healthy life habits will be reinforced in this contact.

The control group (N= 50) will perform the same initial evaluation and answer the same questionnaires as described above for the intervention group. In this evaluation will receive guidance regarding the adoption of life habits by the multidisciplinary team. The control group will receive reinforcement of guidance only in clinic face-to-face visits.

The visits of the study after the pacient's inclusion will take place every 12 weeks (Visits 2, 3, 4 and 5), totaling 4 visits after the initial visit, with the final visit after 12 months. Patients will perform 24-hour ambulatory blood pressure monitoring (ABPM) at visits 2, 3 and 5. In visits 2 to 5, the patient will have the measurement of blood pressure from the office, weight and abdominal circumference, and data on symptoms and events that occurred (hospitalizations, emergency room visits, symptoms) will be collected. In the last visit (12-month), in addition to these measures, the questionnaires performed on the first visit and laboratory dosages will be repeated.

3.2. Blood pressure measurement in the clinic

Determination of systolic (SBP) and diastolic (DBP) blood pressure measured by an automatic sphygmomanometer (Omron HBP 1100 ®), in the right upper limb, with the individual seated, after 10 minutes of rest. Three (3) measurements of systolic and diastolic pressure will be performed, with an interval of 1 minute between them and the average will be calculated later, following the recommendations of the Brazilian Guidelines on Hypertension 2020.[35]

3.3. Measurement of weight and abdominal circumference in the office

For anthropometric evaluation, weight and height will be measured using a Filizola® digital scale, and abdominal circumference will be measured using a standardized measuring tape.

3.4. Ambulatory 24-hour blood pressure monitoring (ABPM**)**

ABPM allows indirect and intermittent bp recording for 24 hours or more while the patient performs his usual activities in wakefulness and during sleep. The Spacelabs® Device will

be used, and the following variables will be obtained: mean systolic, diastolic and pulse blood pressure in the periods of 24 hours, wakefulness and sleep, and considered the normality values according to the Brazilian Guidelines on Hypertension 2020[35].

3.5. Blood Pressure Monitoring at Home

Patients in the intervention group will be instructed to perform blood pressure measurement at home with a validated automatic device (Omron) that will be delivered on the day of the consultation after the training period. Patients will be instructed to take measurements as recommended by the recent guidelines [35], two measurements in the morning and two measurements at night, Monday to Friday, and will enter the values of the 5 days in the application. These values will be evaluated by the medical and nursing team, which will guide the appropriate conduct based on these measures.

3.6. Measurement of capillary glycemia at home

Patients in the intervention group will be instructed to perform capillary glucose measurement at home with a device that will be delivered on the day of the consultation, after the training period. Patients will be instructed to take measurements in the morning fasting, Monday to Sunday, and will enter the values in the application. These values will be evaluated by the medical and nursing team, which will guide the appropriate conduct based on these measures.

3.7. WHOQOL-BREF2 Quality of Life Questionnaire

The WHOQOL-BREF is a questionnaire that tends to evaluate the overall rate of "quality of life" and "satisfaction" with health. Participants answer questions about various aspects of their life in the present and circulate the number that best represents their feeling. The WHOQOL-BREF contains two types of questions: a "positive" where a high number means good quality or satisfactory, a "negative" where a low number or zero means a poor quality of life. Domain scores will be calculated and transformed into a scale ranging from zero to one hundred according to the algorithm.[36]

3.8. Food consumption questionnaires

Two questionnaires will be applied to assess food consumption. A form of food consumption markers for individuals older than 5 years that is proposed by the Food and Nutrition Surveillance System. This tool aims to identify the frequency of pre-established food consumption in the last 7 days. The questionnaire has only ten items that are easy to understand

and apply. From item 1 to 5 are foods where daily consumption is recommended. Items 6 to 10 are foods that should be consumed eventually or should be avoided. The 24-hour Dietary Recall consists of a complete description of the interviewee's eating habits the day before the interview. The data to be obtained by the instrument is the type of food or preparation, quantity consumed, place and time of the meal. The participant will be asked to describe the part in homemade measures that will later be transformed into grams of the food. Nutritional information will be based on the Brazilian Food Composition Table. [3738]

3.9. 8-Stage Moriski Green - Adherence Questionnaire

To evaluate treatment adherence, the Eight-Item Morisky Therapeutic Adherence Scale was used, consisting of eight questions regarding the use of medication. The degree of therapeutic adherence will be determined according to the score resulting from the sum of the answers of the MMAS-8 questionnaire: high adherence (8 points), average adherence (6 or 7 points) and low adherence (<6 points).[39]

3.10. Pittsburg Sleep Quality Questionnaire (PSQI)

The PSQI assesses the quality and sleep disorders during the period of one month, being a standardized questionnaire, simple and well accepted by patients. The instrument consists of 19 questions in self-report and five questions directed to the spouse or companion of room. The 19 questions are categorized into seven components, graduated in scores from zero (no difficulty) to three (severe difficulty). The components of the PSQI are: C1 subjective sleep quality, C2 sleep latency, C3 sleep duration, C4 habitual sleep efficiency, C5 sleep changes, C6 use of sleep medications and C7 sleep day time dysfunction. The sum of the values attributed to the seven components ranges from zero to twenty-one in the total score of the questionnaire indicating that the higher the number, the worse the sleep quality. [40]

3.11. Anxiety Questionnaire - Hospital Anxiety and Depression Scale (HADS)

The HADS scale contains 14 multiple choice questions composed of two subscales, for anxiety and depression, with seven items each. The overall score on each subscale ranges from 0 to 21 and has been applied to patients in general without difficulty, with good clinical relationship.[41]

3.12. Statistical analysis

All analyses will be performed based on the complete population of the set of analyses, and all values of the clinic BP and the mean wakefulness of the ABPM will be included. The

characteristics of the patient at the initial visit will be described using mean ± standard deviation or median deviation (quartiles) for continuous variables, or number (proportion in %) for categorical variables. To compare the main variables before and after using the application, the appropriate tests will be performed according to the type of the variable, that is, whether quantitative or qualitative. Thus, to compare the quantitative variables (blood pressure value, weight, body mass index, abdominal circumference, 24-hour urine sodium and questionnaire score), a comparative analysis of a paired t-test will be performed. For the nonparametric variables, the chi-square and kruskall wallis test will be used to compare them.

4. Expected results

The use of the artificial intelligence application for distance monitoring of patients with uncontrolled hypertension should provide greater engagement of patients and their families in treatment, and thus may lead to better blood pressure control, greater adhering to healthy lifestyle habits (decreased sodium intake, increased physical activity and improved quality of life) when compared to the follow-up currently performed at the institution. Better blood pressure control of these patients, who generally require a high number of medications, may consequently reduce the risks of complications and also the search for emergency services, which can harm the patient, and also encumber the health service. In addition, the integrated participation of a multidisciplinary team more actively ensures greater involvement with patient care, without the need for frequent returns to the Unit for better blood pressure control.

5. Timeline

Month	Activity
1st to 2nd month	Selection of participants
2nd to 3rd month	Signature of the GDPL and training of patients with application
5th to 6th month	Consultation for data collection and delivery of the blood pressure measurement device
7th to 12th month	Monitoring patients by staff through the application
7th to 12th month	Consultation for data collection and delivery of the blood pressure measurement device

****It will be validated after approval by the Ethics Committee****

6. References

1 VI Brazilian Guidelines on Hypertension. Arq Bras Cardiol 2010; 95(1 supl.1): 1-51.

2 Ck Chow, Teo KK, Rangarajan S, et al, PURE Study Investigators. Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. JAMA 2013; 310:959–968.

3 VII Brazilian Hypertension Guidelines. Arq Bras Cardiol 2016; 107(3 supl.3): 1-83.

4 Vigitel Brazil 2017: surveillance of risk and protective factors for chronic diseases by telephone survey: estimates on frequency and sociodemographic distribution of risk and protective factors for chronic diseases in the capitals of the 26 Brazilian states and in the Federal District in 2017.http://bvsms.saude.gov.br/bvs/publicacoes/vigitel_brasil_2017_vigilancia_fatores_risco.pdf.

5 Vigitel Brazil 2017: surveillance of risk and protective factors for chronic diseases by telephone survey: estimates on frequency and sociodemographic distribution of risk and protective factors for chronic diseases in the capitals of the 26 Brazilian states and in the Federal District in 2017.http://bvsms.saude.gov.br/bvs/publicacoes/vigitel_brasil_2017_vigilancia_fatores_risco.pdf.

6 Hameed MA, Tebbit L, Jacques N, Thomas M, Dasgupta I. Non-adherenceto antihypertensive medication is very common among resistant hypertensives: results of a directly observed therapy clinic. J Hum Hypertens.2016;30:83–89.

7 Schulz M, Krueger K, Schuessel K, Friedland K, Laufs U, Mueller WEUde M. Medication adherence and persistence according to different antihypertensivedrug classes: a retrospective cohort study of 255,500 patients. Int J Cardiol. 2016; 220:668–676.

8 Elliott WJ. What factors contribute to the inadequate control of elevated blood pressure? J Clin Hypertens (Greenwich). 2008;10(suppl 1):20–26.

9 Holland N, Segraves D, Nnadi VO, Belletti DA, Wogen J, Arcona S. Identifying barriers to hypertension care: implications for quality improvement initiatives. Dis Manag. 2008; 11:71–77.

10 Gwadry-Sridhar FH, Manias E, Lal L, Salas M, Hughes DA, Ratzki-Leewing A, Grubisic M. Impact of interventions on medication adherence and blood pressure control in patients with essential

hypertension:a systematic review by the ISPOR adherence and persistence special interest group. Value Health. 2013; 16:863–87.

11 Gwadry-Sridhar FH; Petrilla AA, Benner JS, Battleman DS, Tierce JC, Hazard EH. Evidence based interventions to improve patient compliance with antihypertensive and lipid-lowering medications. Int J Clin Pract. 2005; 59:1441–1451.

12 van der Laan DM, Elders PJM, Boons CCLM, Beckeringh JJ, Nijpels G, Hugtenburg JG. Factors associated with antihypertensive medication nonadherence: a systematic review. J Hum Hypertens. 2017; 31:687–694.

13 Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al; on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2016 update: a report from the American Heart Association [published correction appears in Circulation. 2016;133:e599].

14 MT Kim, MN Hill, Bone LR, Levine DM. Development and testing of the Hill-Bone Compliance to High Blood Pressure Therapy Scale. Prog Cardiovasc Nurs. 2000; 15:90–96.

15 Brown MT, Jk Bussell. Medication adherence: WHO cares? Mayo Clin Proc. 2011; 86:304–314; Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keepanasseril A, Agoritsas T, Mistry N, Iorio A, Jack S, Sivaramalingam B, Iserman E, Mustafa RA, Jedraszewski D, Cotoi C, Haynes RB. Interventions for enhancing medication adherence. Cochrane Database Syst Rev. 2014:CD000011.

16 Nieuwlaat; Peacock E, Krousel-Wood M. Adherence to antihypertensive therapy. Med Clin North Am. 2017; 101:229–245.

17 Claxton AJ, J Cramer, Pierce C. A systematic review of the associations between dose regimens and medication compliance. Clin Ther. 2001; 23:1296–1310.

18 Proia KK, Thota AB, Njie GJ, et al; Community Preventive Services Task Force. Team-based care and improved blood pressure control: a community guide systematic review. Am J Prev Med. 2014; 47:86–99.

19 Brownstein JN, Chowdhury FM, Norris SL, Horsley T, Jack L Jr, Zhang X, Satterfield D. Effectiveness of community health workers in the care of people with hypertension. Am J Prev Med. 2007; 32:435–447.

20 Carter BL, Rogers M, Daly J, Zheng S, James PA. The potency of team-based care interventions for hypertension: a meta-analysis. Arch Intern Med. 2009; 169:1748–1755.

21 Clark CE, Smith LF, Taylor RS, Campbell JL. Nurse led interventions to improve control of blood pressure in people with hypertension: systematic review and meta-analysis. BMJ. 2010;341:c3995.

22 Santschi V, Chiolero A, Colosimo AL, Platt RW, Taffé P, Burnier M, Burnand B, Paradis G. Improving blood pressure control through pharmacist interventions: a meta-analysis of randomized controlled trials. 2014 J Am Heart;3: E000718.

23 Brush JE Jr, Handberg EM, Biga C, et al. 2015 ACC health policy statement on cardiovascular team-based care and the role of advanced practice providers. J Am Coll Cardiol. 2015; 65:2118–2136.

24 Thomas KL, Shah BR, Elliot-Bynum S, Thomas KD, Damon K, Allen LaPointe NM, Calhoun S, Thomas L, Breathett K, MathewsR, Anderson M, Califf RM, Peterson ED. Check it, change it: a community-based, multifaceted intervention to improve blood pressure control. Circ Cardiovasc Qual Outcomes. 2014; 7:828–834.

25 Jaffe MG, Lee GA, Young JD, Sidney S, Go AS. Improved blood pressure control associated with a large-scale hypertension program. JAMA. 2013; 310:699–705.

26 Jaffe MG, Jd Young. The Kaiser Permanente Northern California Story: improving hypertension control from 44% to 90% in 13 years (2000 to 2013). J Clin Hypertens (Greenwich). 2016; 18:260–261.

27 Go AS, Bauman MA, Coleman King SM, Fonarow GC, Lawrence W, Williams KA, Sanchez E. An effective approach to high blood pressure control: a science advisory from the American Heart Association, the American College of Cardiology, and the Centers for Disease Control and Prevention Hypertension. 2014; 63:878–885.

28 Omboni S, Ferrari R. The role of telemedicine in hypertension management: focus on blood pressure telemonitoring. Curr Hypertens Rep. 2015; 17:535.

29 Persell SD, Karmali KN, Stein N, Li J, Peprah YA, Lipiszko D, Ciolino JD, Sato H. Design of a randomized controlled trial comparing a mobile phone-based hypertension health coaching application to home blood pressure monitoring alone: The Smart Hypertension Control Study. Contemp Clin Trials. 2018; 73:92-97.

30 Fitzpatrick AL, van Pelt M, Heang H, Steinman L, Ide N, Chhea C, LoGerfo JP. Using Targeted mHealth Messages to Address Hypertension and Diabetes Self-Management in Cambodia: Protocol for a Clustered Randomized Controlled Trial. JMIR Protoc Res. 2019;8(3): E11614.

31 Krittanawong C, Bomback AS, Baber U, Bangalore S, Messerli FH, Wilson Tang WH. Future Direction for Using Artificial Intelligence to Predict and Manage Hypertension. Curr Hypertens Rep. 2018;20(9):75.

32 Morrissey EC, Casey M, LG Glynn, JC Walsh, Molloy GJ. Smartphone apps for improving medication adherence in hypertension: patients' perspectives. Patient Prefer Adherence. 2018; 12:813-822.

33 Blease C, Kaptchuk TJ, Bernstein MH, Mandl KD, Halamka JD, DesRoches CM. Artificial Intelligence and the Future of Primary Care: Exploratory Qualitative Study of UK General Practitioners' Views. J Med Internet Res. 2019;21(3): e12802.

34 War GM, Wen CL, Vieira M, Tsunemi TH, Oliveira JCDE, Fistarol IRB, Giorgi DMA, Rezende CB, Bortolotto LA. E-influence of the embracement versus blended learning/E-learning to improve the anxiety level, white coat effect and blood pressure control in hypertensive patient: A randomized controlled trial. J Cardiovasc Dis Diagn 2018, 06:10.4172/2329-9517-C7-021.

35 Barroso WKS, Rodrigues CIS, Bortolotto LA, Gomes MAM, Brandão A, Feitosa A et al. Brazilian Guidelines on Hypertension 2020. Arq Bras Cardiol 2020;116(3):516-658.

36 Fleck MPA, Louzada S, Xavier M, Chachamovich E, Vieira G, Santos L, Pinzon V. Application of the Portuguese version of the abbreviated instrument for quality of life evaluation "WHOQOL-bref". Rev. Public Health, 34 (2): 178-83, 2000.

37 Geometry R, Analysis G. Protocols of the Food and Nutrition Surveillance System - SISVAN in health care [Internet]. 2008. 61 p. Available from: http://189.28.128.100/dab/docs/portaldab/publicacoes/protocolo_sisvan.pdf.

38 NEPA/UNICAMP. Brazilian Table of Food Composition. Center for Food Studies and Research. 2011. 161 p.

39 Morisky DE, Ang A, Krousel-Wood M et al. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens (Greenwich). 2008; 10(5):348-54.

40 Bertolazi AN, Fagondes SC, Hoff LS, Dartora EG, da Silva Miozzo IC, de Barba ME, et al. Validation of the Brazilian Portuguese version of the Pittsburgh Sleep Quality Index. Sleep Med. 2011; 12:70-5.

41 Zigmond AS, Snatih RP. The hospital anxiety and depression scale. Acta Psychiat. Scand. 1983, 67: 361-70.