

Aspects of Home blood pressure: Data collection, analysis, understanding complexity in making and happening, and shift responsibility in clinical practice

In 2020, 33.3 % of the death in the U.S, was directly or indirectly related to cardio-metabolic diseases. (1) Hypertension (HTN) is the leading risk factor for cardiovascular deaths. (2,3,4) The average time delay in initiating treatment of high blood pressure (BP) (> 140/90 mm Hg) from the time of diagnosis seems to be 5 years or more (5). Not being treated even after diagnosis of hypertension (>140/90) is common in up to 80% the population. The proportion of patients not being treated could be higher in younger and other vulnerable subgroups according to new ACC/AHA threshold for HTN (6,7,8,9,10 &11). The net benefit from maintenance of BP systolic and diastolic below 120/ 80 mm Hg seems to keep cardiovascular and renal risks at low level in adult population (12,13,14) The fluctuation in BP is normal hence, guidelines recommend numerous methods to process multiple BP values to ensure accuracy taking time factor in to consideration. Guidelines recommend home blood pressure measurement (HBPM) to help management(22,27,29,30,31,32). The process of gathering BP data directly from patients periodically or continuously adds additional element in profiling BP pattern.

These concerns in general reinforce the need for physicians to consider substitute tools to address valid out-off office data collection and processing to add additional element of making in natural setting and complement with component analysis to more accurately detect clear shift in BP trend in conjunction with other risk factors to influence clinical management of patient. Here we argue gaps in hypertension practice guidelines, practice circumstances, some parallels between ambulatory blood pressure measurement (ABPM) and home blood pressure measurement (HBPM), barriers to adopt recommended standards and patient factors to justify home blood pressure as a basic start up process to exchange information between clinic and patient.

We attempt here to describe required technical platform to facilitate practice to exchange unlimited data on patient's BP, P, blood sugar (BS), weight (WT), Pulse oxygen (PO), temperature (T) and also process additional relevant clinical and supporting activities at frequent intervals to exchange patient's and clinician's need.

Method to improve data collection across home and health care setting;

Here we concentrate on a practical clinical tool to collect validated BP and P data for analysis and explore opportunity to gain deeper insight and improve blood pressure management.

We discuss three-way operation to collect uploaded data, data analytical platform and report interface action in the EMR. The justification in our method aligns with shifting responsibility to end customer with key role to self-monitor principal and routine physiological parameters, introduce critical steps to identify aspects, prioritize challenges and opportunities to rationalize activities to support health needs.

The processing platform assists analyses of components on incoming physiological parameters and designing the weekly report in a customer friendly format for meaningful use. The communication platform helps synchronize interaction and dispatch health or other desired clips. In this report we limit range activity on BP and P and additional components with potential practice implication.

Blood pressure variability

Variability of BP is an intrinsic behavior with fluctuating BP dynamics, and this phenomenon is complex and is affected large number of variables. Hence, detection of magnitude of variability or average real variability (ARV), understanding mean arterial pressure (MAP) around this variability and stiffness index (SI), peak to trough ratio (SI) can be valuable parameters. Thus, a new and operationally easy method may allow better understanding on its added value to routine clinic BP to guide clinicians in risk assessment. Kalman filter process uses linear quadratic equalizer from the past data sets to provides the best estimate on the present state. In time series BP analysis this may aid one to gain insight in to inter current events.

Inference drawn in hypertension is often takes the from aggregation statistics. Distinguishable clinical events and best temporal aggregates on blood pressure is used to infer association in cross sectional and longitudinal data. In this process latent clinical events and time series data on blood pressure may have the potential to help analysis and improve risk allocation than risk attribution. In hypertension, the process of approximation may potentially strengthen significance attached in its temporal changes. Kalman filter data on BP may assist in this process to understand latent clinical factors and change in time series or intercurrent changes in BP.

Discussion

In the clinics BP, T, P, WT, readings are taken routinely during patient's visits by trained medical assistant. The diagnosis of HTN and ongoing treatment is usually made in the office. The value in happening is relevant and to situation it represents. What extent this is accurate reflection to future health risk remains hypothetical. The momentary changes in the blood pressure have demanded clarification of factors in the making. The operational making of this observation could be suboptimal in following the standard guidelines. The details on reporting the estimate/s are limited.

HBPM offers unlimited number of blood pressure readings to support analysis and deeper insight to BP hemodynamics. However, the direction on evidence documentation on HBP is limited. There is no protocol for valuable analysis or characterization of data, running outline on trends, summaries across report groups, sensible, purposive reporting, interfacing in the electronic medical record (EMR), designing the report that appeals for more effective clinical decision and meaningful use to diverse stakeholder's need. Numerous articles on HBP have focused on its potential to detect blood pressure phenotypes, medication titration during management of low and high blood pressure, higher level of achievement of treatment goals in patients and patient empowerment.

BP is a dynamic variable but, assessment in the clinic is a pragmatic to circumstances and reporting in the EMR is random. In the clinics and automated oscillometric blood pressure (AOBPM) is the most common device used for measurement of BP (CBP) for diagnosis and ongoing management of hypertension. The clinical team often, take additional BP readings for validation using aneroid device. In general, it is assumed observations are standardized.

Electronic medical record (EMR) and barriers

The EMR is a used to improve physician's pursuit to improve patient care with quality and quantity of stored information in a crude digital form. Here the required standard underscores validity of patient's presence at the clinical setting to match accuracy of observation and association. The longitudinal biometric parameters (BP and pulse) are assembled in atomic are form. The number of estimates on vital signs allowed during official clinic visit are limited without any additional resolution (order of determination, site consistency, time lapse before and between repeat estimates, remark on taking BP in isolation or quiet setting or with attendant/s presence, diurnal time and concurrent health issues) and informal components are separated. Epidemiological studies across the globe (15,16,17,18) supports small increments in BP from 110 mmHg systolic BP with similar predictive increase in

adverse cardiovascular events in adults above 18 years of age. The existing method of collection of vital signs in the EMR do not support clinicians to detect changes with high resolution and clarity. This requires tools to facilitate processing data for predictive report easy to grasp and visualize for meaningful use.

Guidelines for data extraction and generalizability paradox

Guidelines in hypertension in general are supposed to improve quality of information to support clinical decision. These ideals are very difficult to implement in clinical practice or in real life setting. There are differences between guidelines (19,20,21,22, 23, 24,25,26,27 28) on clinic measurement protocol and conflicting message on BP threshold for intervention. In general home blood pressure (HBP) is accepted as a better measure to guide clinicians and patients during clinical care (29, 30, 31, 32, 33)

The guidelines focus on factor standardization in the clinics to overcome scattered BP measurements and produce better BP size effects. In clinical research studies with objective evaluating clinical outcome, consistency and avoiding error in making and happening across and within setting becomes a key part of evidence synthesis from various studies and supposed impact they make in developing guidelines. These stipulations are critical for comparison in research (evidence-based guidelines) but, not a realistic to routinely practice. This approach to standardize measurement is in conflict with recommendation that also advances out of office setting “Check points” for BP data collection where implementing standard protocol consistently is not practical. These study programs would require additional tools to collect free data for handling and integration in the EMR. Besides, encouraging out-of-office BP monitoring in diverse settings as a routine can pose fidelity issue in a real-world setting.

Ambulatory blood pressure monitoring

Major societies espouse ambulatory blood pressure monitoring (ABPM) in this method frequent collection of additional residuals from outside of clinic adds additional weight and in principle, is comparable to HBPM that is realistic to practice setting and more liberal data collection from those with limited resources. Ambulatory blood pressure measurement (ABPM) is automated easy-going method of taking blood pressure at predefined intervals. The diversity in this method is integral part of both making and happening including blood pressure measured during sleep. The collection 40 – 60 BP readings, is extended over 24 hours in patients natural setting. The only stipulation here is “stay still” during BP estimation.

The standards applied to clinic or home BP measurements (CBPM & HBPM) are not part of this process (meal, watching TV, driving, listening to music, screening e-mail, ambient temperature, break-time, noise factor, back support, bladder factor, status of internal organs or anatomical position). Integration these data sets in the EMR is more complicated with associated cost.

BP has rhythmic and non-rhythmic physiological components. This is included in ABPM thus, inclusion of residuals from diverse making in the aggregate makes it superior to CBP estimate in detection and management of hypertension. CBP realistically, is another singular BP estimate with degree of similarity to random component of ABMP and the idea is also the same in frequent and free HBPM estimates. The question of accuracy and reliability of CBPM is not unique, variation and misclassification are also detected in studies comparing different protocols and in repeated ABPM in research setting. (33,34,35 ,36,37)

Thus, BP assessment protocols are not comparable and variability is intrinsic biological property of BP (37). In addition, in clinical research simultaneous cuff brachial BPM and intrabrachial artery BPM the most sensitive method, is associated with misclassification of BP phenotype in up to 27% in elderly patients (38). Besides, measured BP at any anatomical location represents site specific segmental physiological behavior of the artery (39). Despite all of the above concerns cuff BP measurement will remain the standard method in clinics for routine use. However, the requirement in clinical practice is a tool to collect constantly and reliably patient-centered making of unlimited number of readings to facilitate pattern detection and more synchronized management.

Practice consideration

After the SPRINT trial (40) the major guidelines consider 120 – 129 systolic and 75 – 80 mmHg BP optimal and above 130 mm Hg systolic and 80 mm Hg diastolic is abnormal for age group 18 years of age. It also recognizes doubling of cardiovascular risk associated with a 20-mmHg change in systolic BP from 110 – 130 mm Hg in the middle age population (15) There is also graded association of coronary artery calcification with increase in systolic blood pressure above 90 mmHg (42) and change in integrity of the kidney podocyte (43). Increase in systolic BP above 90-100 mmHg seems to be associated with pathological changes in target organ including left ventricular hypertrophy and brain volume and white matter defects. (44,45) These evolving evidences in the background of epidemiological studies with absent cardiovascular issues and acculturation associated BP change and increase in

vascular problem in special population raises the question what is ideal and threshold blood pressure level that is safe and not associated with significant health risk, qualify for aggressive monitoring and scale intervention with sound scientific support. (46,47,48, 52)

HTN is asymptomatic, many determinants impact acceptance of intervention benefits. In addition, conflict in level of concern (clinical team) and estimate between settings, fear of wrong categorization on marginal BP values, distrust in estimate and its potential reflection on demands in one's personal life such as employability, social stigma, impact on insurance coverage and life policy etc... affect acceptance of diagnosis. Clinical care givers are also equally sensitive to these concerns (49,50,51).

In the clinics evidence for diagnosis of hypertension could be subjective (self-report) or objective measures based on random estimates or association logic such as age, weight, medication often admixed with manifestation of risk factors or report created in other settings with similar unclear definition. The process of extraction of evidence from past medication history with integrity is complicated when there is therapeutic overlap. Acceptance of diagnosis of hypertension and treatment is also affected by patient's age and health literacy.

In clinical practice anchoring to HBPM as is more practical and dependable when collection protocol is more flexible and informal for patients to exercise. Adopting elaborate formalities is less sustainable in routine clinical practice. We believe these observations will make HBPM similar to random ABP estimates.

Acceptance of continuous or intermittent HBP monitoring is an empowerment strategy to detect many underrepresented happening in the natural making. The process of synchronized interaction with robust incoming data is sustainable only through provider interaction beyond problem solving care. Facilitating sustainable involvement in asymptomatic conditions where, checking BP is not a priority as in the majority type ii diabetes patients, integrating active role play by allied health personal is critical to make this sustainable.

Guidance is needed to improve diagnostic method to detect optimum to mild or early elevation or rate of change of BP trajectory. This is only possible with high frequency BP data collection directly or indirectly from patients using capacity building resources. The major challenge is collection and creation of reliable calibrated report on patient's repeated blood pressure holding state, grades and characterize risk adjusted trajectories with other components. The process of

analysis and scale blood pressure in to various categories and monitor changing trend is helpful to determine level of risk and qualify for graded clinical intervention.

Summary

The directive for action in the clinic in general provides graded BP risk burden and outline sample template for data collection and reporting. However, operational complexity and limited time during clinic visit are significant barriers to implementation. The details of these operations are not practical for patients with high risk and limited resources. The larger issue to contend is guidance to implement practice change in the clinics. The method and framework require community alliance that has potential to build data capacity. Platform to facilitate incoming data verification, collaboration to synchronize interaction, system behavior for data processing and linear integration in the EMR. What is now considered ideal may not be really ideal (52,53,) in the future. Besides the vast majority of cardiovascular events are in patients with blood pressure below 140/90 mmHg (54).

The concern about assignment of equivalent BP scale for ages 18 – 75 is a concern in the context our new understanding on cardiovascular risk in young adults (55,56) Hence, approach to detection and management need consideration to adopt substitute methods.

Therefore, information that supports clinicians and patients with the changes in blood pressure requires reliable running estimate on age adjusted upper limit of systolic and diastolic pressure and combine this with attendant risks to equation during shared decision making.

There is no clinical pathway in extant clinical setting to process and detect fine set of BP grades transitioning early from 90 mm Hg and above and track changes. This requires practical and cost-effective patient participatory activity to collect HBP and device enabled platform to collect and structure report to support clinical team The collection of high frequency HBP and other digital data permits estimation of running average, antecedent trend and makings to characterize the information better for clinical decision.

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References

- (1) Ahmad FB, Cisewski JA, Minino A, Anderson RN. Provisional Mortality Data-United States,2020. MMWR Morb Mortal Wkly Rep. Published March 31, 2021 https://www.cdc.gov/mmwr/70/wr/mm7014e1.htm?s_cid=mm7014e1_w)
- (2) Forouzanfar MH, Liu P, Roth GA, Ng M, Biryukov S, Global burden of hypertension and systolic blood pressure of at least 110 to 115 mm hg, 1990- 2015. JAMA 2017; 317:165–182
- (3) Benjamin EJ, Munther P, Alonso A, et al: American Heart Association Council on Epidemiology and prevention Statistics Subcommittee and stroke Statistics Subcommittee. Heart disease and stroke Statistics-2019 Update: A report from the American Heart association. Circulation.2019;139(10):e560-e528.
- (4) Patel SA, Winkel M, Ali MK, Narayan KM, Mehta NK. Cardiovascular mortality associated with 5 leading risk factors: national and state preventable fractions estimated from survey data. Ann Intern MED. 2015;163(4):245-253). Blood pressure (BP) is the leading modifiable risk factor.
- (5) Hassan Imam, Johan Sundström & Lars Lind (2020) Evaluation of time delay between discovery of a high blood pressure in a health screening survey and hypertension diagnosis, Blood Pressure, 29:6, 370-374, DOI: 10.1080/08037051.2020.1782726
- (6) Akira Kuriyama, Yoshimitsu Takahashi, Yuka Tsujimura, Kikuko Miyazaki, Toshihiko Satoh, Shunya Ikeda, Takeo Nakayama, Predicting failure to follow-up screened high blood pressure in Japan: a cohort study, *Journal of Public Health*, Volume 37, Issue 3, September 2015, Pages 498–505,
- (7) Fukuma, S., Ikenoue, T., Saito, Y. *et al.* Lack of a bridge between screening and medical management for hypertension: health screening cohort in Japan. *BMC Public Health* **20**, 1419 (2020). <https://doi.org/10.1186/s12889-020-09532->
- (8) Seshadri S, Wolf PA, Beiser A, et al. Elevated midlife blood pressure increases stroke risk in elderly persons: the Framingham Study. *Arch Intern Med* 2001; 161:2343–50.

(9) Allen NB, Siddique J, Wilkins JT, et al. Blood pressure trajectories in early adulthood and subclinical atherosclerosis in middle age. *JAMA* 2014; 311:490–497.

10) Pletcher MJ, Vittinghoff E, Thanataveerat A, Bibbins-Domingo K, Moran AE. Young adult exposure to cardiovascular risk factors and risk of events later in life: the Framingham Offspring study. *PLoS One* 2016;11:e0154288.

(11) Zhang Y, Vittinghoff E, Pletcher MJ, et al. Associations of Blood Pressure and Cholesterol Levels During Young Adulthood With Later Cardiovascular Events. *J Am Coll Cardiol*. 2019;74(3):330-341. doi:10.1016/j.jacc.2019.03.529

12)Shakia T. Hardy, Swati Sakhuja, Byron C. Jaeger, Suzanne Oparil, Oluwasegun P. Akinyelure, Tanya M. Spruill, Jolaade Kalinowski, Mark Butler, D. Edmund Anstey, Tali Elfassy, Gabriel S. Tajeu, Norrina B. Allen, Orna Reges, Mario Sims, Daichi Shimbo, Paul Muntner Maintaining Normal Blood Pressure Across the life Course Hypertension 2021; 77: 14090 – 1499

13) Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, Chalmers J, Rodgers A, Rahimi K. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet*. 2016 Mar 5;387(10022):957-967. doi: 10.1016/S0140-6736(15)01225-8. Epub 2015 Dec 24. PMID: 26724178.

14) Cheung AK, Chang TI, Cushman WC, Furth SL, Hou F F, JoachimH, Ix JH, Knoll GA, Muntner P, Pecoits-Filho R, Perkovic V, Sarnak MJ, Tobe SW, Tomson CRV, Lytyyn L, Cheung M, Tonelli M, Erly and Mann JFE; Kidney International (2021) 99, 559- 569

15) Lewington S, Clarke R, Quizilbas N, Peto R, Collins R Prilsson, Collaboration PS. Age-specific relevance of usual blood pressure to : a vascular mortality a meta-analysis of individual data for one million adults in 61 prospective studies.*Lancet*.2002;360:1903-13.

16) Lacey B, Lewington S, Clarke R, Kong XL, Chen Y, Guo Y, Yang L, Bennett D, Bragg F, Bian Z, Wang S, Zhang H, Chen J, Walters RG, Collins R, Peto R, Li L, Chen Z; China Kadoorie Biobank collaborative group. Age-specific association between blood pressure and vascular and non-vascular chronic

diseases in 0.5 million adults in China: a prospective cohort study. *Lancet Glob Health*. 2018 Jun;6(6):e641-e649. doi: 10.1016/S2214-109X(18)30217-1. PMID: 29773120; PMCID: PMC5960069.

17) Gajalakshmi V, Lacey B, Kanimozhi V, Sherliker P, Peto R, Lewington S. Body-mass index, blood pressure, and cause-specific mortality in India: a prospective cohort study of 500 810 adults. *Lancet Glob Health*. 2018;6(7):e787-e794. doi:10.1016/S2214-109X(18)30267-5

18) Tapia-Conyer R, Alegre-Díaz J, Gnatiuc L, Wade R, Ramirez-Reyes R, Herrington WG, Lewington S, Clarke R, Collins R, Peto R, Kuri-Morales P, Emberson J. Association of Blood Pressure With Cause-Specific Mortality in Mexican Adults. *JAMA Netw Open*. 2020 Sep 1;3(9):e2018141. doi: 10.1001/jamanetworkopen.2020.18141. PMID: 32975571; PMCID: PMC7519421s in 61 prospective studies *Lancet* 2002; 360: 1903-1913).

19) Umemura S, Arima H, Arima S, Asayama K, Dohi Y, Hirooka Y, Horio T, Hoshide S, Ikeda S, Ishimitsu T, Ito M, Ito S, Iwashima Y, Kai H, Kamide K, Kanno Y, Kashihara N, Kawano Y, Kikuchi T, Kitamura K, Kitazono T, Kohara K, Kudo M, Kumagai H, Matsumura K, Matsuura H, Miura K, Mukoyama M, Nakamura S, Ohkubo T, Ohya Y, Okura T, Rakugi H, Saitoh S, Shibata H, Shimosawa T, Suzuki H, Takahashi S, Tamura K, Tomiyama H, Tsuchihashi T, Ueda S, Uehara Y, Urata H, Hirawa N. The Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2019). *Hypertens Res*. 2019 Sep;42(9):1235-1481. doi: 10.1038/s41440-019-0284-9. PMID: 31375757.

20) Wang JG, Chia YC, Chen CH, Park S, Hoshide S, Tomitani N, Kabutoya T, Shin J, Turana Y, Soenarta AA, Tay JC, Buranakitjaroen P, Nailes J, Van Minh H, Siddique S, Sison J, Sogunuru GP, Sukonthasarn A, Teo BW, Verma N, Zhang YQ, Wang TD, Kario K. What is new in the 2018 Chinese hypertension guideline and the implication for the management of hypertension in Asia? *J Clin Hypertens (Greenwich)*. 2020 Mar;22(3):363-368. doi: 10.1111/jch.13803. Epub 2020 Jan 19. PMID: 31955513

21) The Lancet. NICE hypertension guidelines: a pragmatic compromise. *Lancet*. 2019 Sep 7;394(10201):806. doi: 10.1016/S0140-6736(19)32042-2. PMID: 31498085

22) Whelton PK, Carey RM, Aronow WS, Casey DE, Jr, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure

in adults: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. *J Am Coll Cardiol.* 2018;71:e127–248.

23) Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J.* 2018;39(33):3021–104.

24) 2020 International Society of Hypertension Global Hypertension Practice Guidelines.

Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, Ramirez A, Schlaich M, Stergiou GS, Tomaszewski M, Wainford RD, Williams B, Schutte AE. *Hypertension.* 2020 Jun;75(6):1334-1357. doi: 10.1161/HYPERTENSIONAHA.120.15026. Epub 2020 May 6. PMID: 32370572

25) Leung AA, Daskalopoulou SS, Dasgupta K, McBrien K, Butalia S, Zarnke KB, Nerenberg K, Harris KC, Nakhla M, Cloutier L, Gelfer M, Lamarre-Cliche M, Milot A, Bolli P, Tremblay G, McLean D, Tran KC, Tobe SW, Ruzicka M, Burns KD, Vallée M, Prasad GVR, Gryn SE, Feldman RD, Selby P, Pipe A, Schiffrin EL, McFarlane PA, Oh P, Hegele RA, Khara M, Wilson TW, Penner SB, Burgess E, Sivapalan P, Herman RJ, Bacon SL, Rabkin SW, Gilbert RE, Campbell TS, Grover S, Honos G, Lindsay P, Hill MD, Coutts SB, Gubitza G, Campbell NRC, Moe GW, Howlett JG, Boulanger JM, Prebtani A, Kline G, Leiter LA, Jones C, Côté AM, Woo V, Kaczorowski J, Trudeau L, Tsuyuki RT, Hiremath S, Drouin D, Lavoie KL, Hamet P, Grégoire JC, Lewanczuk R, Dresser GK, Sharma M, Reid D, Lear SA, Moullec G, Gupta M, Magee LA, Logan AG, Dionne J, Fournier A, Benoit G, Feber J, Poirier L, Padwal RS, Rabi DM; Hypertension Canada. *Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults.* *Can J Cardiol.* 2017 May;33(5):557-576. doi: 10.1016/j.cjca.2017.03.005. Epub 2017 Mar 10. Erratum in: *Can J Cardiol.* 2017 Dec;33(12):1733-1734. PMID: 28449828.

26) Lin HJ, Wang TD, Yu-Chih Chen M, Hsu CY, Wang KL, Huang CC, Hsieh MJ, Chiu YW, Chiang LT, Chuang WP, Hsu PF, Wu CH, Hung CS, Chen KC, Wu CC, Wang YC, Chou PC, Yap HY, Cheng HM. 2020 Consensus Statement of the Taiwan Hypertension Society and the Taiwan Society of Cardiology on Home Blood Pressure Monitoring for the Management of Arterial Hypertension. *Acta Cardiol Sin.* 2020 Nov;36(6):537-561. doi: 10.6515/ACS.202011_36(6).20201106A.

27) Muntner P, Shimbo D, Carey RM, Charleston JB, Gaillard T, Misra S, Myers MG, Ogedegbe G, Schwartz JE, Townsend RR, et al. Measurement of blood pressure in humans: a scientific statement from the American Heart Association. **Hypertension**. 2019; 73:e35–e66.
DOI: [10.1161/HYP.0000000000000087](https://doi.org/10.1161/HYP.0000000000000087).Link

28) Paul Muntner, Einhorn PT, Cushman WC, Whelton PK, Bello NA, Drawz PE, Green BB, Jones DW, Juraschek AP, Margolis KL, Miller ER, Navae AM, Osthega Y, Rakotz MK, Rosner B, Schwartz JE, Shimbo D, Stergiou GS, Townsend RR, Williampon JD, Wright Jt & Apple L, Blood Pressure Assessment in adult clinical practice and clinic- based research J Am Coll Cardiol. 2019 Jan; 29: 317-335)

29) 2021 European Society of Hypertension practice guideline for office and out-of-office blood pressure measurement. Stergiou GS, Palatini P, Pararati G, O'Brien E, Januszewicz A, Lurbe E, Persu A, Mancia G, Kreutz R J Hypertension 39 February DOI; 10.1097/HJH.00000000000002843

30) Sharman JE, Howes, F, Head GA, Mcgrath BP, Stowasser M, Schlaich M, Glasziou P, Nelson MR. How to measure home blood pressure: recommendation for health care professionals and patients. Aust family physician. 2016; 45(1)31-34
22) Villar R, Snachez RA, Boggia J, Recommendation for Home blood pressure monitoring in latin American countries: a Latin American Society of Hypertension position paper. J Clin Hypertension(Greenwich) 2020;22(4):544-554

31) Kairo Kpark S, Buranakitjaroen Pet alet al. Guidance on home blood pressure monitoring: a statement of HOPEasia network. J Clin Hypertension. 2018;20(3):456-461.

32) British Hypertension Society. Home Blood pressure monitoring Protocol. <https://bihsoc.org/wp-content/uploads/2017/09/protocol.pdf>

33) McManus RJ, Little P, Stuart B, Morton K, Raftery J, Kelly J, Bradbury K, Zhang J, Zhu S, Murray E, May CR, Mair FS, Michie S, Smith P, Band R, Ogburn E, Allen J, Rice C, Nuttall J, Williams B, Yardley L; HOME BP investigators. Home and Online Management and Evaluation of Blood Pressure (HOME BP)

using a digital intervention in poorly controlled hypertension: randomised controlled trial. *BMJ*. 2021 Jan 19;372:m4858. doi: 10.1136/bmj.m4858. PMID: 33468518; PMCID: PMC7814507

34) Lin H, Pan H, Chen W, Wang T. Variation in Blood Pressure Classification Using 7 Blood Pressure Estimation Protocols Among Adults in Taiwan. *JAMA Netw Open*. 2020;3(11):e2024311. doi:10.1001/jamanetworkopen.2020.24311).

35) The redistribution of patient classification is also seen when ABPM is repeated (Giuseppe Mancia, Rita Facchetti, Cesare Cuspidi, Michele Bombelli, Giovanni Corrao, Guido Grassi, Limited reproducibility of MUCH and WUCH: evidence from the ELSA study, *European Heart Journal*, Volume 41, Issue 16, 21 April 2020, Pages 1565–1571, <https://doi.org/10.1093/eurheartj/ehz651>

36) Moore, Myles N.^a; Atkins, Emily R.^{b,c}; Salam, Abdul^{b,c}; Callisaya, Michele L.^a; Hare, James L.^d; Marwick, Thomas H.^d; Nelson, Mark R.^a; Wright, Leah^d; Sharman, James E.^a; Rodgers, Anthony^{b,c} Regression to the mean of repeated ambulatory blood pressure monitoring in five studies, *Journal of Hypertension*: January 2019 - Volume 37 - Issue 1 - p 24-29 doi: 10.1097/HJH.0000000000001977

37) Salam, Abdul^a; Atkins, Emily^b; Sundström, Johan^c; Hirakawa, Yoichiro^b; Etehad, Dena^d; Emdin, Connor^d; Neal, Bruce^b; Woodward, Mark^e; Chalmers, John^b; Berge, Eivind^f; Yusuf, Salim^g; Rahimi, Kazem^d; Rodgers, Anthony^b on behalf of the Blood Pressure Lowering Treatment Trialists' Collaboration Effects of blood pressure lowering on cardiovascular events, in the context of regression to the mean, *Journal of Hypertension*: January 2019 - Volume 37 - Issue 1 - p 16-23 doi: 10.1097/HJH.0000000000001994

(38) Annina S. Vischer and Thilo Burkard *Diagnostics* 2021,11,235

38) Picone D, Schultz M, Armstrong M, Black J, Bos W, Chen C, Cheng H, Cremer A, Dwyer N, Hughes A, Kim H, Lacy P, Laugesen E, Liang F, Ohte N, Okada S, Omboni S, Ott C, Pereira T, Pucci G, Schmieder R, Sinha M, Stouffer G, Takazawa K, Roberts-Thomson P, Wang J, Weber T, Westerhof B, Williams B and Sharman J (2021) Identifying Isolated Systolic Hypertension From Upper-Arm Cuff Blood Pressure Compared With Invasive Measurements, *Hypertension*, 77:2, (632-639), Online publication date: 1-Feb-2021.

39) Discovery of New Blood Pressure Phenotypes and Relation to Accuracy of Cuff Devices Used in Daily Clinical Practice

Dean S. Picone, Martin G. Schultz, Xiaoqing Peng, J.

Andrew Black, Nathan Dwyer, Philip Roberts-Thomson, Chen-Huan Chen, Hao-Min Cheng, Giacomo Pucci, Ji-Guang Wang, and James E. Sharma

Hypertension Volume 71, Issue 6, June 2018, Pages 1239-1247

<https://doi.org/10.1161/HYPERTENSIONAHA.117.10696>

40) SPRINT Research Group, Wright J.T., Williamson J.D., Whelton P.K., Snyder J.K., Sink K.M., et. al.: A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med* 2015; 373 (36) pp. 2103-2116.)

42) Whelton SP, McEvoy JW, Shaw L, Psaty BM, Lima JC, Budoff M, Nair Khurram, Szklo M, Blumental RS, Blaha MJ. Association of Normal Systolic Blood Pressure Level with Cardiovascular Disease in the Absence of Risk Factors *JAMA Cardiol* 2020;5 (9):1011-1018. doi:10.1001/jamacardio.2020.1731)

43) Naik As, LeD, Aqeel J, et al Podocyte stress and detachment measured in the urine are related to mean arterial pressure in healthy humans. *Kidney Int* 2020; 98:699-707

44) Drukteinis JS, Roman MJ, Fabsitz RR, et al Cardiac and Systemic hemodynamic characteristics of hypertension and prehypertension in adolescents and young adults: the Strong Heart study. *Circulation* 2007;115:221-227,

45) Williamson W, Lewandowski AJ, Forkert ND et al. Association of cardiovascular risk factors and white matter hyperintensities in young adults. *JAMA*. 2018;320:665-673.

46) Hollenberg NK, Martinez G, McCullough M, Meinking T, Passan D, Preston M, Rivera A, Taplin D, Vicaria-Clement M. Aging, acculturation, salt intake, and hypertension in the Kuna of Panama. *Hypertension* 1997;29:171-176.

47) Kaplan H, Thompson RC, Trumble BC, Wann LS, Allam AH, Beheim B, Frohlich B, Sutherland ML, Sutherland JD, Stieglitz J, Rodriguez DE, Michalik

DE, Rowan CJ, Lombardi GP, Bedi R, Garcia AR, Min JK, Narula J, Finch CE, Gurven M, Thomas GS. Coronary atherosclerosis in indigenous South American Tsimane: a cross-sectional cohort study. *Lancet* 2017;389:1730–1739.

48) Mancilha-Carvalho Jde J, Souza e Silva NA. The Yanomami Indians in the INTERSALT Study. *Arq Brasil Cardiol* 2003;80:289–300.

49) Baker R, Wilson A, Nockels K, Agarwal S, Modi P, Bankart J. Levels of detection of hypertension in primary medical care and interventions to improve detection: a systematic review of the evidence since 2000. *BMJ Open*. 2018;8(3):e019965. Published 2018 Mar 22. doi:10.1136/bmjopen-2017-019965

50) Johnson HM, Thorpe CT, Bartels CM, et al. . Antihypertensive medication initiation among young adults with regular primary care use. *J Gen Intern Med* 2014;29:723–31. 10.1007/s11606-014-2790-4

51) Qadi O, Lufumpa N, Adderley N, Bem D, Marshall T, Kokab F. Patients' and health professionals' attitudes and perceptions towards the initiation of preventive drugs for primary prevention of cardiovascular disease: a systematic review of qualitative studies. *BJGP Open*. 2020;4(5):bjgpopen20X101087. Published 2020 Dec 15. doi:10.3399/bjgpopen20X101087

52) Jones DW. What Is a Normal Blood Pressure? *JAMA Cardiol*. 2020;5(9):1018–1019. doi:10.1001/jamacardio.2020.1742

53) Luo D, Cheng Y, Zhang H, Ba M, Chen P, Li H, Chen K, Sha W, Zhang C, Chen H. Association between high blood pressure and long-term cardiovascular events in young adults: systematic review and meta-analysis. *BMJ*. 2020 Sep 9;370:m3222. doi: 10.1136/bmj.m3222. PMID: 32907799; PMCID: PMC7478061.

54) Tajeu GS, Booth JN 3rd, Colantonio LD, Gottesman RF, Howard G, Lackland DT, O'Brien EC, Oparil S, Ravenell J, Safford MM, Seals SR, Shimbo D, Shea S, Spruill TM, Tanner RM, Muntner P. Incident Cardiovascular Disease Among Adults With Blood Pressure <140/90 mm Hg. *Circulation*. 2017 Aug 29;136(9):798-812.)

55) Yano Y, Reis JP, Colangelo LA, Shimbo D, Viera AJ, Allen NB, Gidding SS, Bress AP, Greenland P, Muntner P, Lloyd-Jones DM. Association of Blood Pressure Classification in Young Adults Using the 2017 American College of Cardiology/American Heart Association Blood Pressure Guideline With

Cardiovascular Events Later in Life. JAMA. 2018 Nov 6;320(17):1774-1782. doi: 10.1001/jama.2018.13551. PMID: 30398601; PMCID: PMC6248102.

56) Gerber Y, Rana J, Jacobs D, Yano Y, Levine D, Nguyen-Huynh M, Lima J, Reis J, Zhao L, Liu K, Lewis C and Sidney S (2021) Blood Pressure Levels in Young Adulthood and Midlife Stroke Incidence in a Diverse Cohort, Hypertension, 77:5, (1683-1693), Online publication date: 1-May-2021.

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