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Telemonitoring in hypertension management for patients with chronic kidney disease: a narrative review

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Abstract
Hypertension is a major cause of cardiovascular disease worldwide and a major cause of morbidity and mortality in patients with chronic kidney disease (CKD). The Systolic Blood pressure Intervention Trial (SPRINT) demonstrated that blood pressure (BP) measurement techniques may have an impact on the achievement of outcomes. Home BP monitoring (HBPM) has several advantages over office BP recordings, including avoidance of white-coat reaction, ability to diagnose white-coat and masked hypertension, detection of BP variability, and better ability to predict cardiovascular morbidity and mortality, all of which commonly occur in CKD. The addition of telemonitoring and management support to HBPM allows remote monitoring, especially when close contact is difficult (e.g., patients in remote/rural areas, pandemic, natural disaster, or patients treated with home dialysis). Although there are few studies that have assessed the efficacy of home BP telemonitoring (HBPT) in patients with CKD, these studies suggest the benefits of HBPT for BP control and even limited evidence that it may improve kidney function. This review, using limited available evidence, assesses the roles of HBPT in patients with CKD, barriers to HBPT implementation in the care of patients with CKD, and discusses newer technologies that can be leveraged in the management of hypertension in patients with CKD.

Keywords: Blood pressure measurement, blood pressure variability, chronic kidney disease, home blood pressure, out-of-office blood pressure, telemonitoring

INTRODUCTION

Hypertension is estimated to affect 1.39 billion adults worldwide, with prevalence higher in low- and middle-income countries (LMICs) (31.5%, 1.04 billion people) than in high-income countries (28.5%, 349 million people)[1]. Urbanization, especially unplanned or poorly planned, has been identified as a major driver of the rising burden of high blood pressure (BP) in LMICs as it encourages poor nutrition, a sedentary lifestyle and obesity, increased alcohol and tobacco consumption, and exposure to psychological stressors[2-4]. In a meta-analysis of studies conducted in LMICs[3], hypertension prevalence increased over time with the rate of change greater in rural compared to urban areas[5]. Furthermore, mortality associated with hypertension has also been shown to be higher in the rural than in the urban population. For instance, age-adjusted death rates increased by 72% in rural and 20% in urban populations from 2007 to 2017 in the United States ($P < 0.001$ for time trend)[6]. There is a high prevalence of hypertension in patients with chronic kidney disease (CKD), with prevalence reported to range from 60% to 90%[7] and increasing with rising CKD stages[8,9]. Similarly, the proportion of patients with controlled hypertension is often reported to be lower with advancing stages of CKD while the number of antihypertensives utilized increases[8].

BURDEN OF HYPERTENSION IN CKD

Pathophysiologically, hypertension and CKD are closely related. Sustained elevated blood pressure contributes to worsening kidney function, while a progressive decline in kidney function can lead to worsening BP control[10]. Prevalence of hypertension and CKD is often reported to be higher in rural than urban settings[3,11]. However, access to optimal healthcare delivery, including healthcare interventions and treatment for hypertension and CKD, may be considerably less available for those who reside in rural than urban communities. Patient-level barriers (e.g., remote location with transportation time and duration to health care access, leaving community/family/work/childcare to access health care, potentially lower awareness of current health status and health promotion/illness prevention) and health system-level barriers (e.g., shortages of healthcare professionals, limited coverage of the medication, fragmented referrals pathways to specialists, limited internet connectivity and cellular coverage, and inadequate follow-up care) may contribute to inadequate health services for patients with hypertension and CKD in rural communities[12]. One Chinese study showed that weekly BP measurement in urban elderly was higher than that in rural elderly (63.9% *vs.* 34.3%)[13]. Similarly, hypertension-mediated organ damage is often more prevalent in rural than urban settings[14,15]. Geographically reduced access to healthcare may affect patients in various ways, including the intense psychological impact of rurality, the pressure of extended periods away from home, and suffering from financial losses when attempting to seek healthcare in urban areas[16].

Accurate BP measurement is critical to the diagnosis and management of hypertension in patients with CKD. Various landmark hypertension clinical trials and guidelines reports have detailed various standardized BP measurement techniques/methods for both office and out-of-office BP to define target BP goals[17-21]. Newer out-of-office techniques continue to incorporate digital health technologies (e.g., telemonitoring) into BP measurement via education, monitoring and support, timely feedback, and remote access to health professionals[22-24]. Despite the available options for BP measurement, people with hypertension and CKD in rural populations have limited access to BP measurement. This review, using limited available evidence, assesses the roles of HBPT in patients with CKD, barriers to HBPT implementation in the care of patients with CKD, and discusses newer technologies that can be leveraged in the management of hypertension in patients with CKD.

OVERVIEW OF BP MEASUREMENT TECHNIQUES AND GOALS FROM HYPERTENSION GUIDELINES

The first practical method for the estimation of systolic BP (SBP) was introduced in 1896 through cuff-based sphygmomanometry by Riva-Rocci[25]. Later in 1905, Nikolai Korotkov described his auscultatory measurement method making SBP and diastolic BP (DBP) readings feasible[26]. Although it has since become standardized to report BP using systolic and diastolic values, however, due to variations in measurement techniques[27], professional societies and guideline committees[20,21,28] have repeatedly recommended specific approaches to improve the accuracy of BP measurement [Table 1]. Such recommendations have been made in light of findings from landmark clinical trials[19,29-31] [Figure 1] and in response to transitions from the use of manual aneroid devices (which easily lose calibration) to automated devices capable of measuring BP both in and out of the office[27]. Although BP guideline committees may provide different BP targets based on available evidence, they have been mostly consistent in methods/techniques of BP measurement[20,21,28]. Based on the clinical setting, BP measuring techniques can be broadly categorized into office and out-of-office BP measurements:

Office BP measurement

In clinical practice, the diagnosis and treatment decisions of hypertension are often based on office BP measurements and may be associated with errors related to the device, patient, or measurement process[32]. Types of OBPM include:

Routine (Casual) BP Measurement

Routine (Casual) BP Measurement is the commonly used technique in most clinical practices, especially in resource-limited settings, and is a BP measurement that does not adhere to the standardized BP measurement protocol. Often, only a single measurement is obtained, and errors in BP values (overestimation/elevated BP readings) are related to insufficient rest time, incorrect body position, under-cuffing, and talking during the measurement[33,34].

Standardized BP Measurement

Standardized BP measurement emphasizes the importance of appropriate preparations and measurement techniques. The preparations emphasize the need to be seated with back supported (feet flat on the floor) in a quiet room (no talking by patient or observer), empty bladder, relaxed for > 5 min, and no smoking, caffeine, or exercise for > 30 min before measurement. Although preference for an oscillometric device has been mentioned[20], the process rather than the type of device used is what standardizes the process. Landmark randomized controlled trials (RCTs) such as the Modification of Diet in Renal Disease (MDRD)[29], the African American Study of Kidney Disease and Hypertension (AASK)[30], Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease (REIN-2)[31], The Action to Control Cardiovascular Risk in Diabetes (ACCORD)[18], and The Systolic Blood Pressure Intervention Trial (SPRINT)[19] utilized standardized BP measuring protocol varying from manual sphygmomanometer (MDRD trial)[29] to the automated office BP (AOBP) measurement in the SPRINT trial[19]. Guidelines reported following the publication of SPRINT trial (AHA 2017[28], ESH 2018[21], and KDIGO 2021[20]) have all supported the use of a standardized BP measurement with KDIGO relying heavily on SPRINT measurement methods, achieved targets, and outcomes for making most recommendations. The SPRINT[19] suggested that how BP is measured matters with regards to outcome attainment[35]. In the SPRINT study, BP was measured using standardized methods (proper positioning of participants, measurement of arm circumference and use of proper cuff size, 5-min rest period before obtaining the three seated BPs, participants neither completing questionnaires, talking, nor texting during or between BP measurement)[36]. In addition, over two-thirds of all participants (intensive + standard groups) had their BP measured

Table 1. Checklist for standardized office blood pressure measurement

1. Properly prepare the patient
● Have the patient relax, sitting in a chair (feet on the floor, back supported) for > 5 min ● The patient should avoid caffeine, exercise, and smoking for at least 30 min before measurement ● Ensure the patient has emptied his/her bladder ● Neither the patient nor the observer should talk during the rest period or during the measurement ● Remove all clothing covering the location of cuff placement ● Measurements made while the patient is sitting or lying on an examining table do not fulfill these criteria
2. Use proper technique for BP measurements
● Use a BP measurement device that has been validated and ensure that the device is calibrated periodically ● Support the patient's arm (e.g., resting on a desk) ● Position the middle of the cuff on the patient's upper arm at the level of the right atrium (the midpoint of the sternum) ● Use the correct cuff size, such that the bladder encircles 80% of the arm, and note if a larger- or smaller-than-normal cuff size is used ● Either the stethoscope diaphragm or bell may be used for auscultatory readings
3. Take the proper measurements needed for diagnosis and treatment of elevated BP
● At the first visit, record BP in both arms. Use the arm that gives the higher reading for subsequent readings ● Separate repeated measurements by 1-2 min ● For auscultatory determinations, use a palpated estimate of radial pulse obliteration pressure to estimate SBP. Inflate the cuff 20-30 mmHg above this level for an auscultatory determination of the BP level ● For auscultatory readings, deflate the cuff pressure 2 mmHg per second, and listen for Korotkoff sounds
4. Properly document accurate BP readings
● Record SBP and DBP. If using the auscultatory technique, record SBP and DBP as the onset of the first Korotkoff sound and disappearance of all Korotkoff sounds, respectively, using the nearest even number ● Note the time of most recent BP medication taken before measurements
5. Average the readings
● Use an average of ≥ 2 readings obtained on ≥ 2 occasions to estimate the individual's level of BP
6. Provide BP readings to the patient
● Provide patients with the SBP/DBP readings verbally and in writing

BP: Blood pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure.
Reprinted from the Journal of the American College of Cardiology, Volume 71, Whelton PK, Carey RM, Aronow WS, *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, Pages e127–e248, 2018 with permission from the American College of Cardiology Foundation and the American Heart Association, Inc.[28].

unattended during the assessment, thus reducing the white-coat effect and mimicking out-of-office BP measurements[36].

Out-of-Office BP Measurement

In 2015, the United States Preventive Services Task Force (USPSTF) recommended "obtaining measurements outside of the clinical setting for diagnostic confirmation before starting treatment" of hypertension[37]. This recommendation was made given that about a quarter of patients with elevated office BP have white coat hypertension (normal ambulatory BP or home BP) and are at low risk for adverse outcomes. Although recent guidelines (ESH and ACC/AHA)[21,28] recommend out-of-office monitoring in certain circumstances, including suspected white-coat and masked hypertension, KDIGO recommends that out-of-office BP measurement be used to complement standardized office BP measurement. Types of out-of-office BP measurement includes:

Ambulatory BP Monitoring

Ambulatory BP monitoring (ABPM) has been available since the 1980s and measures BP at intervals (usually every 20 min during the day and every 30 min at night) during the day and night from an appropriately sized cuff applied to the non-dominant arm[38]. ABPM is able to distinguish and identify all

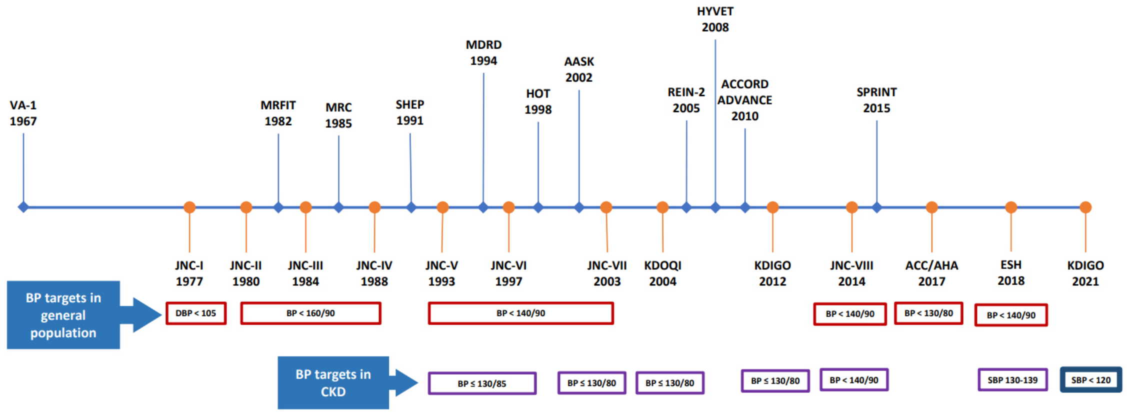

Figure 1. Summary of guideline recommendations and landmark hypertension trials in CKD. AASK: the african american study of kidney disease and hypertension; ACC/AHA: the american college of cardiology/american heart association; ACCORD:the action to control cardiovascular risk in diabetes; ADVANCE :the action in diabetes and vascular disease: preterax and diamicron modified release controlled evaluation; BP:blood pressure; CKD: chronic kidney disease; ESH: european society of hypertension; HOT: the hypertension optimal treatment; HTN: hypertension; HYVET: the hypertension in the very elderly trial; JNC: Joint national committee; KDIGO: kidney disease: improving global outcomes; KDOQI: kidney disease outcomes quality initiative; MDRD: modification of diet in renal disease; MRC: the medical research council; MRFIT: the multiple risk factor intervention trial; REIN-2: blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease; SHEP: the systolic hypertension in the elderly program; SPRINT: the systolic blood pressure intervention trial; VA: veterans affairs.

types of hypertension, including “white-coat”, “masked”, “nocturnal”, and “non-dippers”, all of which are common in patients with CKD[39]. When OBPM and ABPM are available, patients can be classified as controlled (normal office and ambulatory BP), white-coat hypertensive (elevated office and normal ambulatory BP), masked hypertensive (normal office and elevated ambulatory BP), and sustained hypertensive (elevated office and ambulatory BP)[40]. Some limitations to ABPM use include being expensive, cumbersome for the user, and limited availability of the device.

Home BP Monitoring

Using home blood pressure monitoring (HBPM), patients are able to perform measurements of their own BP at home, and it provides information on BP at specific times and under routine conditions over long periods of time. Although ABPM is the gold standard of measurement, HBPM provides a more practical and less expensive alternative, given its usefulness for tracking BP throughout treatment[41]. There are several advantages of using HBPM for BP measurement and monitoring, including the ability to record multiple daily readings over extended periods, extensive availability of HBPM devices, ability to detect masked hypertension and BP variability, avoidance of white-coat effects, improved management of blood pressure from immediate feedback and patient involvement, and relatively low cost[42,43]. ABPM is the ideal method for evaluating true BP variability as it is useful in documenting BP levels during all daily activities, including work and sleep. There is also an agreement between ABPM and HBPM for detecting non-dipping nocturnal BP profiles[41]. Variability in HBPM is a strong predictor of CV events and hypertension-mediated organ damage[44]. Patients with CKD are more likely than patients without CKD to manifest BP variability. In the Jackson heart study, the mean average real variability of systolic BP was 9.2 ± 0.2 and 8.6 ± 0.1 mmHg for those with and without CKD, respectively (each $P \leq 0.001$)[45]. Similarly, long-term (but not short-term) systolic BP variability has demonstrated a significant association with death and CV events in CKD patients[46].

Disadvantages of HBPM use for BP measurement include excessive reliance on patient technique, measurement errors, and lack of funding in some healthcare settings. When compared to routine office BP measurements, it is also observed to be more significantly linked with target organ damage and CKD progression[47,48]. One recent study identified numerous areas of discordance between providers and patients from the perspective of implementing the use of HBPM in CKD patients. This included only a few patients (18%) being aware of BP targets, most patients (89%) not having their upper arm circumference measured for cuff size, providers perceiving patient anxiety as a barrier, and patients reporting expense as a barrier[49]. A variety of interventions have been tested with HBPM, including self-management[50], telemonitoring[51], workplace-linked web-based support with educational materials[52], web communication and monitoring with pharmacist support[53], and behavioral management[54]. The next section will focus on the strength of evidence, barriers, and potential roles of home BP telemonitoring (HBPT) in CKD populations.

Home BP telemonitoring in CKD populations

The effectiveness of HBPM can be improved by the addition of telemonitoring, whereby patients receive feedback from healthcare professionals based on BP readings sent electronically[55]. Home BP telemonitoring (HBPT) is the most common type of BP telemonitoring, with other forms including in-office BP telemonitoring and ambulatory BP telemonitoring[56]. HBPT is performed with an electronic automated oscillometric upper-arm BP monitor with the capacity to store a large number of readings [Figure 2][57]. The readings are asynchronously transmitted to a central monitoring facility through a built-in modem, an access point with a modem router, or a mobile app installed on a smartphone that can transmit data via WiFi or cellular networks. When apps are used, data are typically entered manually or using a Bluetooth-enabled device that pairs with the smartphone. BP is measured at least twice a day (2 measurements at 2-min intervals in the morning and two measurements at 2-min intervals in the evening)[58]. All HBPT activities are usually supervised by a case manager who can interact live with the patient (e.g., through the telephone, a chat, or a video consultation) to obtain feedback on his/her health status and adjust treatment according to the indications of the managing physician (co-intervention or additional support)[56].

Although HBPT has been used extensively in various patient populations with hypertension[59-64], only a few studies have assessed the benefits of HBPT for BP control and other outcomes assessment in patients with CKD. In the Telemonitoring and Self-Management in Hypertension 4 (TASMINH4) trial, after 12 months, adjusted SBP mean differences (self-monitoring and telemonitoring groups) *vs.* usual care was -3.5 mmHg [95%CI: -5.8 to -1.2] and -4.7 mmHg [-7.0 to -2.4]), respectively[64]. Other studies have shown HBPT to be feasible and acceptable[65]. and effective in specific hypertension sub-groups (diabetes[66], high-risk ethnic groups[67], pregnancy[68], cardiovascular (CV) disease)[69], and in specific settings (primary care[64], pharmacy[70]).

Studies of CKD populations assessing the efficacy of HBPT for control have observed reductions in SBP and DBP[71-77] [Table 2]. To date, only two systematic reviews and meta-analyses of HBPT efficacy, specifically in CKD populations, have been reported. Luo *et al.* assessed the effects of telehealth on BP management in patients with stage 3 to 5 CKD[78]. A total of 680 subjects were included and showed decreased SBP [mean difference (MD), -5.10; 95%CI: -11.34, 1.14; $P = 0.11$], increased DBP (MD, 0.45; 95%CI: -4.24, 5.13; $P = 0.85$), and decreased serum creatinine (MD, -0.38; 95%CI: -0.83, 0.07; $P = 0.10$) in the telehealth group. A reason why the study did not identify significant reductions in SBP and DBP includes the low sample size of telehealth studies in CKD patients and the improper study designs of those studies selected. A recent review by Muneer *et al.* that included more studies, a larger sample ($n = 821$), and patients in stages 1 to 5 CKD (but not on dialysis) showed larger and significant MD for SBP (-8.8 mmHg; 95%CI: -16.2 to -1.4; $P = 0.02$), DBP (-2.4 mmHg; 95%CI: -3.8 to -1.0; $P < 0.001$), and eGFR (5.4 mL/min/1.73 m^2; $P < 0.001$) [79]. However, sensitivity analysis showed a non-statistically significant increase in eGFR (5.49 mL/min/1.73 m^2; 95%CI: −1.41 to 12.39; $P = 0.12$). Although most of the studies included in the analysis were not RCTs and the

Table 2. Summary of studies using HBPT in patients with CKD and impact of the intervention

Author	Study design	Country	Sample size	Management support (CKD stage included) [Intervention length]	HBPT device used	Summary of the effects of interventions
Rifkin *et al.*[71]	RCT	USA	43	Physicians or study pharmacists (3 to 5) [6 months]	An automatic oscillometric BP unit and the home health hub receive BP and pulse data via Bluetooth from the BP unit and relay that data through the Internet to a secure website	HBPT and control groups had significant improvement in SBP ($P < 0.05$), which fell a median of 13 mmHg in monitored participants compared with 8.5 mmHg in control participants ($P = 0.31$)
Daelemans *et al.*[72]	Pilot	Belgium	15	General practitioner in consultation with the nephrologist (Not reported) [10 days]	An ESH-validated, automatic upper arm BP monitor paired with a Bluetooth-enabled mobile phone	HBPT use resulted in better and faster BP control
Lin *et al.*[73]	RCT	Taiwan	36	Physicians verified patient BPs (3 to 5) [6 months]	Cloud-based manometers integrated with physician order entry systems	Nighttime SBP and DBP were significantly lower in the HBPT group compared with the control group. There was a significant reduction of serum creatinine in the HBPT group compared to the control group ($P = 0.018$). Lower levels of proteinuria in HBPT compared to the control group ($P = 0.09$)
Sawai *et al.*[74]	Observational	Japan	54	None (Not reported) [23 months]	Device able to measure and transmit BP, pulse, and room temperature	Average SBP and DBP were highest in winter and lowest in summer ($P < 0.01$); only eGFR was significantly correlated with seasonal home BP variation, even after adjustments for age, sex, BMI, DM, room temperature, and baseline SBP ($P < 0.05$)
Ishani *et al.*[75]	RCT	USA	601	Interdisciplinary team (3 to 5) [12 months]	An HBPT device and all the peripherals (BP cuff, scale, glucometer, pulse oximeter, stethoscope, and web camera)	The primary composite outcome in 46.2% of HBPT *vs.* 46.7% ($P = 0.9$). No difference was observed between groups for any component of the primary outcome: all-cause mortality (HR: 1.46; 95%CI: 0.42, 5.11), hospitalization (HR: 1.15; 95%CI: 0.80, 1.63), emergency department visits (HR: 0.92; 95%CI: 0.68, 1.24), or nursing home admission (HR: 3.07; 95%CI: 0.71,13.24)
Ong *et al.*[76]	Pilot	Canada	47	A multidisciplinary team (4 and 5) [6 months]	A smartphone with a preinstalled self-management application and a Bluetooth-enabled home BP monitoring device which was paired to the smartphone for seamless transfer of BP readings	Mean reductions in home BP readings between baseline and exit were statistically significant (SBP: -3.4 mmHg, 95%CI: -5.0, -1.8; DBP: -2.1 mmHg, 95%CI: -2.9, -1.2); 27% of patients with normal clinic BP readings had newly identified masked hypertension
Warner *et al*.[77]	Observational	UK	25	None (3 to 5) [3 months]	An "off-the-shelf" Bluetooth-enabled BP monitor and a tablet computer with custom-developed software	User adherence was high: 13/25 (52%) participants provided > 90% of the expected data, and 18/25 (72%) provided > 80% of the expected data. The usability of the telemonitoring system was rated highly, with mean scores of 84.9/100 after 30 days and 84.2/100 after 90 days

CKD: Chronic kidney disease; RCT: the randomized controlled trial; USA: the United States of America; HBPT: home blood pressure telemonitoring; SBP systolic blood pressure; DBP: diastolic blood pressure; eGFR: estimated glomerular filtration rate; HR: the hazard ratio.

sample size in the sensitivity analysis included data from 79 participants, the improvement in kidney function was thought to be related to significantly improved SBP and DBP[79]. A larger sample size and inclusion of studies with different BP transmission and telemonitoring approaches may have been responsible for differences in results from both studies.

There are no known studies assessing HBPT in patients receiving kidney replacement therapy [KRT - hemodialysis (HD), peritoneal dialysis (PD), or a kidney transplant]; however, data from HBPM studies in this population show home measurement to be a more pragmatic method for assessing control[80], monitoring dry weight[81], and predicting outcomes[82,83]. A study of 140 HD patients found HBPM measurements to be more reproducible and outperformed pre-dialysis and post-dialysis BP in predicting 44-h interdialytic ABPM[81]. Among participants of the Chronic Renal Insufficiency Cohort (CRIC) study[82], a U-shaped association of dialysis-unit-SBP and risk of CV events was observed. In contrast, a linear stepwise association between out-of-dialysis-unit-SBP with risk of CV events was noted, suggesting that out-of-dialysis-unit BP provides key information and may be an important therapeutic target. Hypertension is common after kidney transplant recipients with varied etiology, including pre-transplant volume overload, post-transplant recipient and donor-associated factors, and transplant-specific causes (immunosuppressive medications, allograft dysfunction, and surgical complications such as transplant artery stenosis)[84]. Poor BP control is an independent risk factor for graft failure and has unfavorable CV events for the recipient[84,85]. One study[86] identified HBPM to have a better correlation with ABPM than with OBPM in kidney recipients between 1 and 10 years after transplantation. Put together, these studies support the use of HBPM in patients receiving KRT and suggest benefits if HBPT is utilized, given the additional management support that will be made available. This is in light of other studies that have shown that the use of telehealth services for care can reduce dialysis modality switch, length, and rate of hospitalization[87] as well as other outcomes[88].

POTENTIAL APPLICATIONS OF BP TELEMONITORING IN CKD PATIENTS

Potential benefits of telemedicine (including telemonitoring) for the management of hypertension have been reported across several studies[55,89,90] and include the ability to provide care where face-to-face consultation is not possible, the possibility to reach underserved areas and their population, patient empowerment through self-management and participation, improved patient-caregiver relationship, and assessment of health data in real-time, accelerated delivery of best practice, reduced patient travel time, improved quality of care and the health outcomes, and cost-effectiveness. As hypertension is ubiquitous across all stages of CKD, HBPT can be leveraged to improve BP control and adherence and reduce adverse CV outcomes, including stroke, myocardial infarction, heart failure, and sudden death.

Visit-to-visit BP variability has been associated with CV outcomes and mortality in CKD patients[46,91]. Severe blood volume fluctuations during HD sessions and interdialytic periods may result in higher BP variability in patients undergoing HD than in patients without organ damage. In a large study of 16,546 patients with CKD that examined short-term BP-variability according to kidney function stage, advancing CKD stage was identified as a factor associated with variability[92]. A systematic review that assessed the association between BP variability and clinical outcomes in HD patients reported SBP variability to be associated with higher all-cause [hazard ratio: 1.13; 95%CI: 1.07-1.19; $P < 0.001$] and CV (HR: 1.16; 95%CI: 1.10-1.22; $P < 0.001$) mortality[91]. In the stratified analysis of SBP variability, interdialytic SBP variability, rather than 44-h ambulatory SBP variability or intradialytic SBP variability, was identified to be related to both all-cause (HR: 1.11; 95%CI: 1.05-1.17; $P = 0.001$) and CV (HR: 1.14; 95%CI: 1.06-1.22; $P < 0.001$) mortality[91].

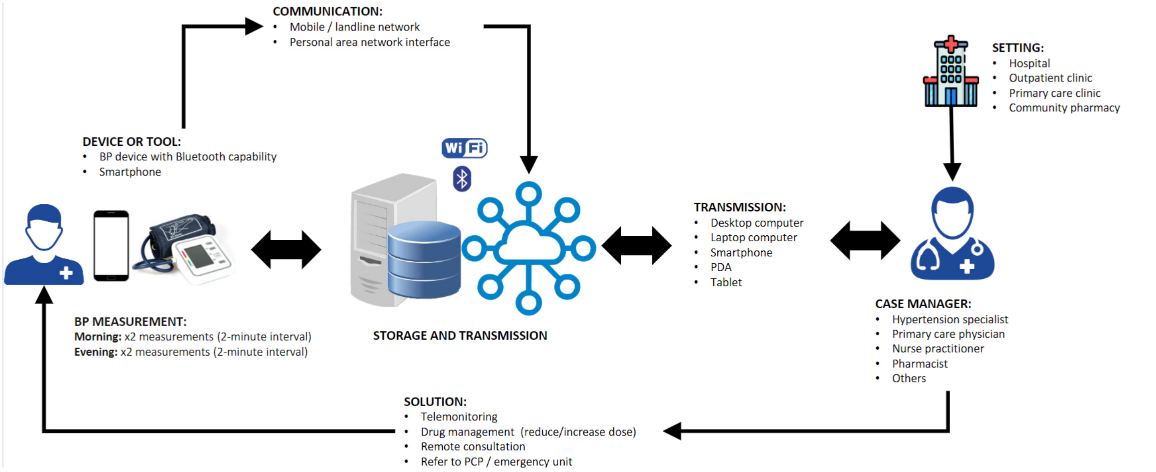

Figure 2. Blood pressure telemonitoring process and workflow. Adapted with permission from Omboni S. 2019[57]. BP: blood pressure; PCPs: primary care physicians; PDAs: personal digital assistants.

BP variability can be difficult to assess given that it covers a wide range spanning from seconds or minutes to occurring between days (best assessed with HBPM)[93]. However, as HBPT is able to gather a large amount of BP data over time, it is able to detect BP variability in patients with CKD. The number of patients requiring treatment for kidney failure continues to increase worldwide, placing a substantial burden on health systems and patients. This has led to increased utilization of home dialysis in many countries - up to 13.1% of kidney failure patients in the United States are treated with home therapies (11.2% PD and 1.9% home HD)[94]. Blood pressures in this large patient population can be relayed in real-time and prompt changes to treatment, including titration of medications and other measures to achieve control. This suggests that intensive monitoring would be useful in the clinical care of CKD patients, particularly those treated with dialysis.

Blood pressure control is challenging in patients with CKD; HBPT has been demonstrated to be associated with improved BP levels which can lead to CV and kidney benefits[78,79]. In a systematic review[95], compared with clinic-based measurements, systolic BP improved with HBPM (-2.63 mmHg; 95%CI: -4.24, -1.02), and diastolic BP also showed improvement (-1.68 mmHg; 95%CI: -2.58, -0.79). HBPM led to more frequent antihypertensive medication reductions [RR: 2.02 (95%CI: 1.32 to 3.11)] and was associated with less therapeutic inertia. Reductions in home BP monitoring-based therapy were greater when telemonitoring was used. However, a more recent systematic review[96] reported that self-monitoring was associated with reduced clinic systolic BP compared to usual care at 12 months [-3.2 mmHg, (95%CI: -4.9, -1.6 mmHg)] and this effect was strongly influenced by the intensity of co-intervention ranging from no effect with self-monitoring alone [-1.0 mmHg (-3.3, 1.2)], to a 6.1 mmHg (-9.0, -3.2) reduction when monitoring was combined with intensive support. The findings of these studies suggest that hypertension control with HBPM can be enhanced further when accompanied by telemonitoring.

Further, CKD patients in rural settings may receive a lower quality of care and experience adverse health outcomes than patients living in urban settings[97,98]. For rural dwellers, practical issues in traveling to healthcare facilities (distance traveled, cost of travel, availability of transportation) make telemedicine attractive and the use of HBPT a potential approach for improving BP outcomes. A study of 120 rural dwellers in the United States using HBPT to assess control reported increased prescribed antihypertensive medications (2.0 to 2.6; $P < 0.001$) and significant lowering of SBP [-14.1 mmHg (95%CI: -16.8 to -11.4 mmHg; $P < 0.001$)] and DBP [-7.9 mmHg (95%CI: -9.5 to -6.4 mmHg; $P < 0.001$)] from baseline to 6-

months of follow-up. It was also reported that among participants with at least one follow-up review, 50% achieved an average BP < 130/80 mmHg, and 80.5% achieved an average goal BP < 140/90 mmHg[99].

In these regards, HBPT can be included within telenephrology services utilized in rural areas to improve outcomes. In one study from Australia, fewer rural CKD patients who received treatment using telenephrology services started dialysis after five years of follow-up compared to patients treated using standard care (5.1% *vs.* 9.9%; $P = 0.02$); fewer deaths were also reported in the telenephrology group (11.1% *vs.* 18.2%; $P = 0.02$)[100]. The application of digital solutions to assess BP control and medication adherence in low-income and lower-middle-income countries suggests that HBPT can be used in these settings to address the challenges of BP control and treatment[101,102]. A Malaysian study has shown that patients found the HBPT service to be easy to use but struggled with the perceived usefulness of doing so[103].The authors concluded that the use of HBPT service must address these issues to maximize the patients' acceptance of HBPT.

The recent coronavirus (COVID-19) pandemic highlighted the need for remote monitoring and treatment strategies for patients unable to access care at a hospital facility. Widespread lockdowns affected the delivery of health care to patients with CKD and have reinforced the need for accessible home-based therapies and remote monitoring technologies. Several reports have also highlighted the importance of remote BP monitoring and management during the pandemic when face-to-face interactions between patients and physicians are not allowed[55,104,105].

POTENTIAL BARRIERS TO USING TELEMONITORING IN CKD

Despite the potential benefits of HBPT use in patients with CKD across various settings, there are several challenges that may limit or hinder the use of HBPT in patients with CKD. These barriers can be categorized into three groups[106,107]: (i) cultural; (ii) structural; and (iii) financial. Cultural barriers[106,107] include poor informatics literacy of healthcare workforces and patients, lack of adequate knowledge and proper implementation of BP monitoring guidelines by doctors, unawareness of the importance of CV risk factors detection and control among people, and need for more robust evidence on the benefit of HBPT in CKD. Although there remains a lack of robust studies of HBPT in CKD populations, available evidence has shown that HBPT is feasible[77], acceptable[71], and effective[79] for BP reduction in this population. Moreover, ongoing RCTs[108,109] are likely to corroborate this evidence and provide evidence to be used in guideline recommendations for BP measurement strategies in CKD. Structural barriers[106,107] to the use of telemonitoring include lack of adequate infrastructures (cellular network, WiFi connectivity), the need for simple and user-friendly devices, possibly integrated into mobile phones, tablets, or home appliances, and the need to ensure data integrity, security, and privacy. Despite the structural barriers, the use of telehealth services has significantly increased, especially during and following the COVID-19 pandemic[110,111]. Moreover, a recent study has shown increasing use of eHealth services worldwide, albeit still reduced in low- and lower-middle-income countries[112]. Finally, financial barriers[106,107] have been noted to include the need for cost-effective systems, the need for inexpensive and integrated devices, and the lack of reimbursement models (device reimbursement for patients and care provider remuneration). Some of the challenges related to financial barriers may relate to health systems and methods of reimbursement. As Wood *et al.* have noted that to overcome financial barriers, there is a need to price HBPT systems competitively in a way that ensures their use is cost-effective and/or cost-saving[106]. This could mean providing HBPT systems to high-risk patients, for whom optimizing BP control is cost-saving, is advisable. Also, although the cost of HBPT systems and case management have been traditionally borne by the patients, consideration could be given to public funding and support for the costs of telemonitoring. Financial barriers are likely to remain a major barrier in LICs and LMICs, where the burden of hypertension continues to increase in the face of existent gaps and major challenges in accessing care[113].

NEWER TECHNOLOGIES FOR BP MEASUREMENT, MONITORING, AND PREDICTION

Following the COVID-19 pandemic, there has been increased interest in the use of cuffless wearable devices for the measurement and monitoring of BP. These devices use different techniques to assess BP levels, including pulse transit time, pulse wave analysis, photoplethysmography, and applanation tonometry[114]. Multiple or continuous BP measurements recorded for days, weeks, or months can be obtained from cuffless BP technologies within wearable devices and smartphones[115]. In CKD patients, these devices can provide detailed information including early detection of hypotensive episodes, thus avoiding complications such as falls and intradialytic complications in patients treated with home dialysis. Continuous HBPM using wearable devices allows for the monitoring of a true average BP, as well as recording variations within the day and night[116]. Although wearable technologies have been postulated to benefit CKD patients, their usefulness has not been tested in RCTs. In a pilot study[117], wearable device-based analysis of heart rate variability and behavioral readouts in patients with CKD from the Chronic Renal Insufficiency Cohort (CRIC) reported that diabetic and non-diabetic CKD patients showed loss of rhythmic organization compared to controls suggesting that such devices can be used to identify complications and improve care.

The continuous data provided by wearable cuffless devices could help inform artificial intelligence (AI) strategies for the prevention and management of hypertension, including predicting the development of hypertension, predicting BP, predicting CV risk in hypertension, and predicting and identifying barriers to BP control[118]. In a Japanese study that used health checkup data from 18,258 individuals, an AI model highly and precisely predicted future hypertension using machine learning methods in a general normotensive population[119]. An AI model developed using 766,000 records of Spanish NephroCare centers to predict the removal of fluid volume, heart rate, BP, and session-specific Kt/V showed good accuracy and precision[120]. AI may not replace the decision-making process for clinicians; it might improve their capacity to deliver optimal personalized therapy.

SUMMARY AND CONCLUSIONS

Evidence continues to strengthen that supports the use of HBPT for BP control in patients with hypertension. Given that BP variability occurs commonly in patients with CKD and that it is associated with mortality, telemonitoring technology offers a useful means of enhancing the accuracy and efficiency of BP data with the added benefit of enabling the recording of BP variability and optimizing control measures, lifestyle, and therapeutic. As recent reviews[78,79] have suggested that HBPT is feasible, acceptable, and effective for BP control and improvement (or stabilization) of kidney function in high-risk patients with CKD, it remains essential to further investigate the usefulness of HBPT in different categories of patients with CKD to assess BP control, CV risk reduction, and mortality. The results of ongoing RCTs[108,109] will likely add strength to existing evidence on HBPT use in CKD patients.

DECLARATIONS

Authors contributions

Contributed to the writing and approved the submission of the final draft: Okpechi IG, Ringrose J, Padwal R, Bello AK

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Conflicts of interest
Padwal R is CEO of mmHg Inc., a digital health company creating guideline-concordant innovations to improve the efficiency of remote patient monitoring. All other authors declare no conflict of interest.

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