Baseline Antihypertensive Drug Count and Patient Response to Hypertension Medication Management

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Telemedicine-based medication management improves hypertension control, but has been evaluated primarily in patients with low antihypertensive drug counts. Its impact on patients taking three or more antihypertensive agents is not well-established. To address this evidence gap, the authors conducted an exploratory analysis of an 18-month, 591-patient trial of telemedicine-based hypertension medication management. Using general linear models, the effect of medication management on blood pressure for patients taking two or fewer antihypertensive agents at study baseline vs those taking three or more was compared. While patients taking two or fewer antihypertensive agents had a significant reduction in systolic blood pressure with medication management, those taking three or more had no such response. The between-subgroup effect difference was statistically significant at 6 months (−6.4 mm Hg [95% confidence interval, −12.2 to −0.6]) and near significant at 18 months (−6.0 mm Hg [95% confidence interval, −12.2 to 0.2]). These findings suggest that baseline antihypertensive drug count may impact how patients respond to hypertension medication management and emphasize the need to study management strategies specifically in patients taking three or more antihypertensive medications. *J Clin Hypertens (Greenwich).* 2016;18:322–328. Published 2015. This article is a U.S. Government work and is in the public domain in the USA.

Despite widespread recognition that hypertension is a modifiable cardiovascular risk factor, up to half of hypertensive patients have inadequate blood pressure (BP) control.[1] Because hypertension causes tremendous morbidity and costs,[2,3] care redesign strategies that can improve BP control are urgently needed. Trials have demonstrated that medication management, which utilizes telemedicine or other strategies to enhance treatment intensification outside the traditional clinic visit, can effectively lower BP vs usual care.[4–8] Medication management approaches therefore hold substantial promise as a means of increasing rates of BP control.

Many trials of telemedicine-based medication management, however, have focused on patients taking relatively few antihypertensive medications, including two particularly high-impact trials in which patients averaged fewer than two antihypertensive agents at study baseline.[4,8] A recent meta-analysis indicated that, among telemedicine trials reporting the number of prescribed antihypertensive agents, patients took an average of only 1.8 baseline BP medications.[9] Therefore, while the value of telemedicine-based medication management for patients with low antihypertensive drug counts is clear, this approach's impact among higher-count patients is not established. This evidence gap is problematic, because antihypertensive use continues to increase and the proportion of patients with hypertension requiring three or more BP medications is rising.[10–12] This high-count group includes the particularly challenging population meeting criteria for resistant hypertension,[12] a condition strongly associated with negative cardiovascular outcomes.[13–15]

In order to explore the uncertain impact of telemedicine-based medication management for patients with high medication counts, we analyzed data from the Hypertension Intervention Nurse Telemedicine Study (HINTS), a trial of telemedicine-based medication management for hypertension.[5] Based on previous studies,[4,8] we hypothesized that patients taking two or fewer antihypertensive medications at study baseline would respond to medication management, but those taking three or more antihypertensive medications would not. We also examined whether differences in treatment intensification might explain any observed variations in the impact of medication management.

MATERIALS AND METHODS

HINTS Design and Population

HINTS (ClinicalTrials.gov NCT00237692) has been described elsewhere.[5,16] Briefly, this was an 18-month, single-center, randomized controlled trial that allocated 591 veterans into one of three telephone-delivered intervention arms or usual care. The three intervention arms included: (1) nurse-administered, physician-directed medication management; (2) nurse-administered behavioral management; and (3) combined medication and behavioral management. For this exploratory analysis, we sought to assess the impact of baseline

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antihypertensive drug count on patients' BP response to medication management. We therefore grouped patients based on whether they were randomized to a study arm receiving the HINTS medication management intervention (Figure 1).

All study participants had medication-treated hypertension with evidence of inadequate control based on the previous year's electronic health record (EHR)–derived BP measurements (average BP >140/90 mm Hg). Exclusion criteria included advanced chronic kidney disease; recent hospitalization for cardiovascular causes; metastatic cancer, prior organ transplantation, or dementia; inability to use a telephone; or receipt of skilled nursing or home health care. HINTS received approval from the institutional review board of the Durham Veterans Affairs Medical Center and all patients provided informed consent.

Patients in the intervention arm measured their BP every other day using a wireless home BP monitor (A&D Medical, model UA-767PC; Tokyo, Japan) and telemedicine device (Carematix Inc, model 102; Chicago, IL). BP data automatically uploaded to a secure server for review by study personnel. A patient's assigned intervention was triggered if their 2-week mean home BP exceeded the activation threshold. Because home-measured BP runs consistently lower than clinic-measured values,[17] the chosen BP threshold was >135/85 mm Hg (135/80 mm Hg for diabetic patients). Once activated, the intervention could not be triggered again for 6 weeks. Patients maintaining adequate BP control did not activate their intervention, but received a phone call every 6 months to reinforce their self-management.

In the main HINTS analysis, neither medication management nor behavioral management significantly improved mean systolic BP (SBP) relative to usual care at 18 months.[5] Of note, although poor BP control based on the prior year's EHR values was required for study inclusion, a higher-than-expected proportion of the enrolled population had well-controlled BP at in-person baseline study assessment. Among patients with inadequate baseline BP control, mean SBP did improve relative to usual care for all three intervention groups at 12 months and for the combined group at 18 months.[5]

HINTS Intervention

Activation of the medication management intervention prompted the study nurse to send the study physician a report containing summary information on BP and treatment adherence, along with medication change recommendations generated by decision support software. The study physician reviewed this report, and in cases where an alternative explanation for the BP elevation (eg, treatment nonadherence) was not present, electronically prescribed medication changes as indicated. The study physician then generated a note in the patient's medical record, while the study nurse communicated any changes to the patient by phone. The study nurse called patients following medication changes to inquire about adverse effects and address questions.

The nurse-administered behavioral management intervention consisted of 11 sequential, phone-delivered modules addressing topics including memory, knowledge and risk perception, health care access, and others.[16] Patients in the combined intervention arm received full doses of both the medication and behavioral management interventions; upon identification of an elevated 2-week BP, the study nurse first provided medication management and then delivered behavioral management. Patients in all study arms continued management of hypertension and other conditions per their primary care provider. Patients randomized to usual care received neither a home BP monitor nor telemedicine device and had no study nurse contact.

Defining Antihypertensive Medication Count at Baseline

We utilized EHR-derived medication data to create a variable for each patient reflecting the number of

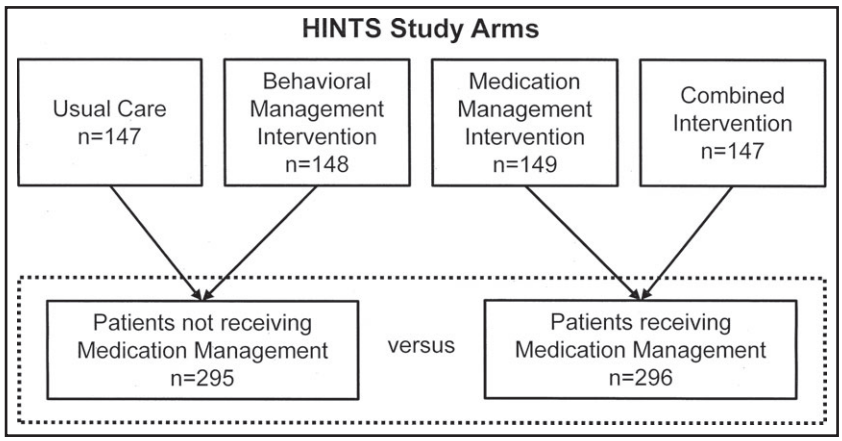

FIGURE 1. Schematic for defining analysis populations. HINTS indicates Hypertension Intervention Nurse Telemedicine Study.

prescribed antihypertensive medications at study baseline. Relevant medications included thiazide and loop diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, β-blockers, α-blockers, and other miscellaneous antihypertensive agents (eg, clonidine, hydralazine, minoxidil). For fixed-combination antihypertensive pills, we counted each component separately (n=59 patients used a combination pill at baseline).

We wished to examine baseline antihypertensive drug count in a manner that would: (1) allow us to evaluate the identified evidence gap, namely, the impact of telemedicine-based medication management among patients taking three or more antihypertensive medication counts, and (2) allow us to examine treatment intensification as a possible mediator of the effect of medication management. We therefore chose to dichotomize baseline antihypertensive drug count as prescription of two or fewer antihypertensive agents (low-count group) or three or more antihypertensive agents (high-count group). This dichotomization threshold was also informed by the American Heart Association (AHA) definition of resistant hypertension (BP that remains above goal despite concurrent use of three or more agents from different classes, including a diuretic).[12]

Outcomes

The main analysis outcome was mean change in SBP from baseline. BP was measured at 6, 12, and 18 months post-randomization for all patients; a blinded research assistant asked patients to rest for 5 minutes before using a digital sphygmomanometer (BpTRU, model BPM-100; Coquitlam, British Columbia, Canada) to obtain two measures, which were averaged. As additional outcomes, we assessed mean change in diastolic BP (DBP) and evaluated the impact of medication management on treatment intensification in antihypertensive drug count subgroups. We used EHR medication data from baseline and 6, 12, and 18 months to identify episodes of treatment intensification (medication dose increase or addition of new medication class) during the study.

Analyses

General linear models (PROC MIXED in SAS, version 9.2, Cary, NC) were used to estimate mean SBP and DBP at 6, 12, and 18 months for each antihypertensive count subgroup (two or fewer and three or more baseline antihypertensive agents). First, we individually examined the impact of medication management on BP within each antihypertensive drug count subgroup, and subsequently determined the differential impact of medication management between the low- and high-count subgroups. The final model parameters included a common intercept for patients taking two or fewer antihypertensive agents, a common intercept for patients taking three or more antihypertensive agents, dummy-coded time, a medication management intervention arm indicator variable interacted with each follow-up time point, and each of these terms interacted with antihypertensive drug count subgroup. Estimates and confidence intervals (CIs) from this model were used to test for BP differences at 6, 12, and 18 months. An unstructured covariance was included to account for patients' repeated measurements over time.

Likewise, we examined the impact of medication management on treatment intensification within each antihypertensive drug count subgroup, and then determined the differential effect of medication management on treatment intensification between the low- and high-count subgroups. We used EHR data to determine the mean number of intensification events during three periods: baseline to 6 months, baseline to 12 months, and baseline to 18 months. Separate linear models were fit to this continuous outcome for each of these periods; model predictors included medication management intervention arm, baseline antihypertensive subgroup, and their interaction.

RESULTS

Population Baseline Characteristics

Table I summarizes population demographics and baseline clinical data. The HINTS population comprised mainly male veterans with a mean age of 63 years. Despite inclusion criteria specifying poorly controlled hypertension based on the prior year's EHR values, nearly 60% of patients had well-controlled BP as determined at their post-enrollment baseline study assessment; 22% of the cohort met AHA criteria for resistant hypertension. Rates of baseline BP control were similar for patients with low and high antihypertensive medication counts. Compared with the 286 patients taking two or fewer antihypertensive mediations at study baseline, the 305 patients taking three or more antihypertensive medications were: (1) slightly older and more likely to be African American, (2) more likely to have diabetes and low health literacy, and (3) less likely to be employed and to have graduated high school. Patients taking three or more medications were more likely to report medication nonadherence at study baseline.

Antihypertensive Count and Response to Medication Management

Within the low-count subgroup (two or fewer baseline antihypertensive agents), patients receiving medication management achieved a clinically significant reduction in SBP relative to patient not receiving medication management (Table II, Figure 2a). This relative SBP reduction reached statistical significance at 6 months (−4.6 mm Hg, 95% CI, −8.2 to −0.9) and 18 months (−6.5 mm Hg, 95% CI, −10.5 to −2.6). By contrast, within the high-count subgroup (≥3 antihypertensive agents), medication management did not impact SBP at any time point (Table II, Figure 2b). In comparing the differential impact of medication management between

TABLE I. Baseline Demographic and Clinical Data for the HINTS Trial Population, Stratified by Baseline Antihypertensive Medication Count

Characteristic	Overall (N=591)	Two or Fewer Baseline BP Medications (n=286)	Three or More Baseline BP Medications (n=305)
Demographics			
Mean age, y (SD)	63.5 (10.3)	62.4 (10.2)	64.6 (10.3)
Male, %	542 (92)	255 (89)	287 (94)
African American, %	284 (48)	125 (44)	159 (52)
Married, %	387 (66)	188 (66)	199 (65)
Employed full- or part-time, %	204 (35)	116 (41)	88 (29)
Graduated from high school, %	509 (86)	257 (90)	252 (83)
Low health literacy (REALM ≤60)	227 (38)	95 (33)	132 (43)
Cannot pay bills without cutting other costs, %	107 (18)	51 (18)	56 (18)
Clinical data			
Mean systolic BP, mm Hg (SD)	129.0 (19.6)	128.6 (18.0)	129.4 (21.0)
Mean diastolic BP, mm Hg (SD)	77.4 (13.1)	78.8 (12.6)	76.1 (13.5)
BP medications at baseline, No. (SD)	2.5 (1.3)	1.4 (0.7)	3.5 (0.7)
Hypertension controlled by JNC 7 criteria, No. (%)	348 (59)	170 (59)	178 (58)
Resistant hypertension, No. (%)[a]	131 (22)	0 (0)	131 (43)
Self-reported medication nonadherence, No. (%)	323 (55)	149 (52)	174 (57)
Diabetes, No. (%)	252 (43)	85 (30)	167 (55)
Current tobacco user, No. (%)	122 (21)	63 (22)	59 (19)

Abbreviations: BP, blood pressure; HINTS, Hypertension Intervention Nurse Telemedicine Study; JNC 7, Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; REALM, rapid estimate of adult literacy in medicine; SD, standard deviation. [a]Resistant hypertension as defined by the American Heart Association, or BP remaining above goal despite concurrent use of three or more agents from different classes (including a diuretic).

TABLE II. Differences in Estimated Mean SBP and Treatment Intensification Over Time for Patients Receiving Medication Management vs Those Not Receiving Medication Management, by Antihypertensive Count Subgroup

Variable/Time Period	Medication Management vs No Medication Management (≤2 Baseline Antihypertensives Subgroup)	Medication Management vs No Medication Management (≥3 Baseline Antihypertensives Subgroup)	Differential Effect of Medication Management (≤2 vs ≥3 Baseline Antihypertensives)
Difference from baseline in mean systolic BP (95% CI)[a]			
6 months	−4.6 (−8.2 to −0.9)	1.8 (−2.7 to 6.4)	−6.4 (−12.2 to −0.6)
12 months	−3.5 (−7.2 to 0.2)	−1.2 (−5.7 to 3.3)	−2.3 (−8.1 to 3.5)
18 months	−6.5 (−10.5 to −2.6)	−0.6 (−5.4 to 4.2)	−6.0 (−12.2 to 0.2)
Difference from baseline in mean diastolic BP (95% CI)[a]			
6 months	−1.7 (−4.0 to 0.5)	−0.1 (−2.7 to 2.4)	−1.6 (−5.0 to 1.8)
12 months	0.2 (−2.4 to 2.7)	−0.4 (−3.0 to 2.3)	0.6 (−3.1 to 4.2)
18 months	−2.3 (−4.8 to 0.2)	−0.3 (−3.1 to 2.6)	−2.0 (−5.7 to 1.8)
Difference in mean treatment intensification episodes (95% CI)[b]			
0–6 months	0.1 (0.01–0.3)	0.3 (0.2–0.4)	−0.2 (−0.4 to 0.02)
0–12 months	0.2 (0.02–0.4)	0.4 (0.2–0.6)	−0.2 (−0.5 to 0.1)
Overall (0–18 months)	0.3 (0.04–0.5)	0.3 (0.1–0.6)	−0.1 (−0.4 to 0.3)

Abbreviations: BP, blood pressure; CI, confidence interval; SBP, systolic blood pressure. [a]Results based on general linear longitudinal model estimates; medication management and nonmedication management groups share a common model-estimated baseline. Negative values indicate greater improvement. [b]Results based on separate linear regression models for each interval, cumulative over the study period. Positive values indicate a greater mean number of treatment intensification episodes.

the two antihypertensive drug count subgroups, there was a clinically meaningful difference in SBP favoring the low-count subgroup throughout the study period, which reached statistical significance at 6 months (−6.4 mm Hg, 95% CI, −12.2 to −0.6) and approached statistical significance at 18 months (−6.0 mm Hg, 95% CI, −12.2 to 0.2) (Table II). Relative to the high-count subgroup, there was a nonstatistically significant trend toward improved DBP with medication management among low-count patients.

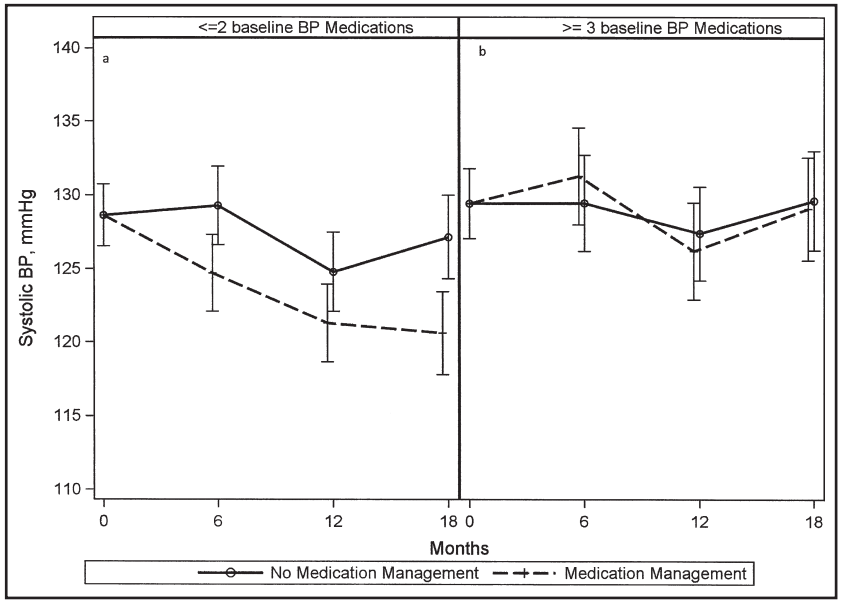

FIGURE 2. (a, b) Estimated changes in mean systolic blood pressure (BP) over time (with 95% confidence intervals) for patients receiving medication management vs patients not receiving medication management, by antihypertensive medication count subgroup.

With regard to treatment intensification, medication management led to significantly more intensification events within both antihypertensive drug count subgroups (Table II). However, rates of treatment intensification with medication management did not differ between the low- and high-count subgroups.

DISCUSSION

This secondary analysis of randomized trial data showed that patients taking two or fewer antihypertensive agents at study baseline achieved clinically meaningful improvements in SBP with telemedicine-based medication management, while patients taking three or more antihypertensive agents did not. Comparing the low- and high-count subgroups, the differential improvement in SBP with medication management was clinically and statistically significant at 6 months and remained clinically meaningful (although not statistically significant) at later time points. We saw a trend toward an analogous differential improvement in DBP among patients taking two or fewer antihypertensive medications, which did not reach statistical significance.

These findings are generally consistent with our hypothesis, and support the idea that patients with high medication counts may respond differently to telemedicine-based medication management than patients taking fewer medications. While we have demonstrated that treatment regimen complexity impacts response to care delivery innovations for diabetes,[18] no prior study to our knowledge has examined how baseline antihypertensive drug count affects patient response to hypertension medication management.

Findings in the Context of Existing Literature

Our findings provide valuable context for prior seminal medication management studies. Green and colleagues[4] saw a statistically significant, 9-mm Hg reduction in SBP at 12 months with an intervention combining medication management, web-based self-management training, and home BP telemonitoring vs usual care. Over 84% of this study's population took two or fewer antihypertensive agents at baseline. Similarly, in a study of telemedicine-based medication management, Margolis and colleagues[8] found statistically significant SBP reductions of 11 mm Hg, 10 mm Hg, and 7 mm Hg at 6, 12, and 18 months, respectively. At baseline, this study population took an average of 1.5 antihypertensive agents. Finally, in a recent study of a novel medication self-management intervention, McManus and colleagues[19] saw statistically significant SBP reductions of 6 mm Hg and 9 mm Hg at 6 and 12 months, respectively. This population took 1.6 antihypertensive medications at baseline. These studies' populations differ from that in HINTS, where the overall mean medication count at baseline was 2.5 and over half of the study population took three or more antihypertensive agents at study start.

While the cited medication management interventions may well be equally effective for patients taking three or more antihypertensive agents at baseline, our findings highlight the need to evaluate how these approaches generalize to this population. Because (1) the proportion of patients requiring three or more antihypertensive agents is rising,[12] and (2) requiring three or more antihypertensive medications may portend a higher risk for negative cardiovascular outcomes,[13–15] patients with

suboptimal BP control despite high antihypertensive drug counts represent an important target for care delivery redesign. Maximizing the impact of telemedicine-based medication management thus calls for additional research assessing available intervention approaches in high-count populations.

Additional Implications of Findings

Although we found that telemedicine-based medication management appears more effective for patients taking two or fewer antihypertensive agents than for patients taking three or more antihypertensive medications, the basis for this differential effect remains unclear. In this analysis, medication management did enhance treatment intensification vs no medication management, but rates of treatment intensification were similar between the low- and high-count subgroups. Intensification frequency alone therefore did not mediate the greater relative impact of medication management for patients taking two or fewer antihypertensive agents.

Our findings may instead suggest that equivalent rates of treatment intensification have a greater impact on SBP for underintensified individuals vs patients already prescribed multiple medications. Higher rates of medication nonadherence (Table I) could likewise have attenuated the impact of the observed medication changes in the high-count group. It is also possible that maintenance of poor control despite three or more antihypertensive agents is simply a marker for harder-to-control hypertension, making treatment intensification less effective. In addition, demographic differences (eg, older age, higher rates of diabetes, lower employment, and lower health literacy among patients taking three or more antihypertensive medications) may help explain why medication management appeared less effective for the high-count group. Additional research is needed to both confirm our findings and further explore underlying reasons for why patients with low antihypertensive drug counts seem to respond better to medication management than high-count patients.

Of note, patients with suboptimal BP control despite three or more antihypertensive agents (including a diuretic) are deemed to have resistant hypertension,[12] a designation used to identify individuals who could benefit from special diagnostic and therapeutic measures. Because of the relatively low rate of resistant hypertension in the HINTS population (Table I), it is unclear how well our findings might generalize to the wider resistant hypertension population. However, our findings do raise questions about the effectiveness of medication management in resistant hypertension and emphasize the need to uncover effective strategies for lowering BP in this group.

LIMITATIONS

In addition to the limitations discussed above, HINTS was conducted at a single center in a primarily male, veteran population, which may affect the generalizability of our results. Our findings should be interpreted in light of the population demographics.

Although our population had out-of-control hypertension based on EHR data during the year prior to enrollment, patients had better-than-expected BP at study baseline. Previous work has documented that clinic- and research-based BP measurements often differ, with patients more commonly defined as "in control" based on research measurements.[20] This phenomenon may be related to white-coat hypertension or less rigorous BP measurement technique in the clinic setting.[21,22] The HINTS population's relatively good baseline control may affect the generalizability of our findings to more poorly controlled populations, including patients with resistant hypertension, as above.

In addition, our population's better-than-expected baseline BP introduces the possibility of type 2 error in our analysis, which may be relevant for the high antihypertensive drug count subgroup. However, because the HINTS population's better-than-anticipated baseline BP would be expected to reduce the rate of medication management intervention activation, type 1 error is less likely in this analysis; in other words, there is a low probability that the present analysis overestimates the impact of medication management for the low-count subgroup.

CONCLUSIONS

This analysis provides evidence that baseline antihypertensive medication count may impact the effectiveness of hypertension medication management. These novel findings lend valuable context for prior studies and highlight the need to evaluate effective care redesign strategies among patients with higher antihypertensive drug counts. Future research should confirm our findings in other populations and clarify the underlying basis for the apparent lack of effect of medication management in high-count patients.

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Author contributions: Dr Crowley designed the project, researched data, and wrote the manuscript. Dr Olsen contributed to project design, analyzed data, and reviewed/edited the manuscript. Ms Woolson analyzed data and reviewed the manuscript. Dr King contributed to project design and reviewed/edited the manuscript. Dr Oddone contributed to project design and reviewed/edited the manuscript. Dr Bosworth contributed to project design and reviewed/edited the manuscript.

References

1. Navar-Boggan AM, Pencina MJ, Williams K, et al. Proportion of US adults potentially affected by the 2014 hypertension guideline. *JAMA*. 2014;311:1424–1429.

2. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42:1206–1252.
3. Yoon PW, Gillespie CD, George MG, Wall HK; Centers for Disease Control and Prevention (CDC). Control of hypertension among adults–National Health and Nutrition Examination Survey, United States, 2005-2008. *MMWR Morb Mortal Wkly Rep*. 2012;61 (suppl):19–25.
4. Green BB, Cook AJ, Ralston JD, et al. Effectiveness of home blood pressure monitoring, Web communication, and pharmacist care on hypertension control: a randomized controlled trial. *JAMA*. 2008;299:2857–2867.
5. Bosworth HB, Powers BJ, Olsen MK, et al. Home blood pressure management and improved blood pressure control: results from a randomized controlled trial. *Arch Intern Med*. 2011;171:1173–1180.
6. McKinstry B, Hanley J, Wild S, et al. Telemonitoring based service redesign for the management of uncontrolled hypertension: multicentre randomised controlled trial. *BMJ*. 2013;346:f3030.
7. Bove AA, Homko CJ, Santamore WP, et al. Managing hypertension in urban underserved subjects using telemedicine – a clinical trial. *Am Heart J*. 2013;165:615–621.
8. Margolis KL, Asche SE, Bergdall AR, et al. Effect of home blood pressure telemonitoring and pharmacist management on blood pressure control: a cluster randomized clinical trial. *JAMA*. 2013;310:46–56.
9. Omboni S, Gazzola T, Carabelli G, Parati G. Clinical usefulness and cost effectiveness of home blood pressure telemonitoring: meta-analysis of randomized controlled studies. *J Hypertens*. 2013;31:455–467.
10. Kuznik A, Mardekian J. Trends in utilization of lipid- and blood pressure-lowering agents and goal attainment among the U.S. diabetic population, 1999-2008. *Cardiovasc Diabetol*. 2011;10:31.
11. Wong HK, Ong KL, Cheung CL, Cheung BM. Utilization of glucose, blood pressure, and lipid lowering medications among people with type II diabetes in the United States, 1999-2010. *Ann Epidemiol*. 2014;24:516–521.e1.
12. Calhoun DA, Jones D, Textor S, et al; American Heart Association Professional Education Committee. Resistant hypertension: diagnosis, evaluation, and treatment: a scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. *Circulation*. 2008;117:e510–e526.
13. Kumbhani DJ, Steg PG, Cannon CP, et al; REACH Registry Investigators. Resistant hypertension: a frequent and ominous finding among hypertensive patients with atherothrombosis. *Eur Heart J*. 2013;34:1204–1214.
14. Daugherty SL, Powers JD, Magid DJ, et al. Incidence and prognosis of resistant hypertension in hypertensive patients. *Circulation*. 2012;125:1635–1642.
15. De Nicola L, Gabbai FB, Agarwal R, et al. Prevalence and prognostic role of resistant hypertension in chronic kidney disease patients. *J Am Coll Cardiol*. 2013;61:2461–2467.
16. Bosworth HB, Olsen MK, McCant F, et al. Hypertension Intervention Nurse Telemedicine Study (HINTS): testing a multifactorial tailored behavioral/educational and a medication management intervention for blood pressure control. *Am Heart J*. 2007;153:918–924.
17. Weisser B, Mengden T, Dusing R, et al. Normal values of blood pressure self-measurement in view of the 1999 World Health Organization-International Society of Hypertension guidelines. *Am J Hypertens*. 2000;13:940–943.
18. Crowley MJ, Melnyk SD, Coffman CJ, et al. The impact of baseline insulin regimen on glycemic response to a group medical clinic intervention. *Diabetes Care*. 2013;36:1954–1960.
19. McManus RJ, Mant J, Haque MS, et al. Effect of self-monitoring and medication self-titration on systolic blood pressure in hypertensive patients at high risk of cardiovascular disease: the TASMIN-SR randomized clinical trial. *JAMA*. 2014;312:799–808.
20. Powers BJ, Olsen MK, Smith VA, et al. Measuring blood pressure for decision making and quality reporting: where and how many measures? *Ann Intern Med*. 2011;154:781–788.
21. Kim JW, Bosworth HB, Voils CI, et al. How well do clinic-based blood pressure measurements agree with the mercury standard? *J Gen Intern Med*. 2005;20:647–649.
22. Jones DW, Appel LJ, Sheps SG, et al. Measuring blood pressure accurately: new and persistent challenges. *JAMA*. 2003;289:1027–1030.