### **ORIGINAL ARTICLE**

# Clinic-Based Strategies to Reach United States Million Hearts 2022 Blood Pressure Control Goals

## **A Simulation Study**

**BACKGROUND:** The Centers for Disease Control and Prevention's Million Hearts initiative includes an ambitious ≥80% blood pressure control goal in US adults with hypertension by 2022. We used the validated Blood Pressure Control Model to quantify changes in clinic-based hypertension management processes needed to attain ≥80% blood pressure control.

**METHODS AND RESULTS:** The Blood Pressure Control Model simulates patient blood pressures weekly using 3 key modifiable hypertension management processes: office visit frequency, clinician treatment intensification given uncontrolled blood pressure, and continued antihypertensive medication use (medication adherence rate). We compared blood pressure control rates (using the Seventh Joint National Committee on hypertension targets) achieved over 4 years between usual care and the best-observed values for management processes identified from the literature (1-week return visit interval, 20%–44% intensification rate, and 76% adherence rate). We determined the management process values needed to achieve ≥80% blood pressure control in US adults. In adults with uncontrolled blood pressure, usual care achieved 45.6% control (95% uncertainty interval, 39.6%-52.5%) and literature-based best-observed values achieved 79.7% control (95% uncertainty interval, 79.3%–80.1%) over 4 years. Increasing treatment intensification rates to 62% of office visits with an uncontrolled blood pressure resulted in ≥80% blood pressure control, even when the return visit interval and adherence remained at usual care values. Improving to best-observed values for all 3 management processes would achieve 78.1% blood pressure control in the overall US population with hypertension, approaching the ≥80% Million Hearts 2022 goal.

**CONCLUSIONS:** Achieving the Million Hearts blood pressure control goal by 2022 will require simultaneously increasing visit frequency, overcoming therapeutic inertia, and improving patient medication adherence. As the relative importance of each of these 3 processes will depend on local characteristics, simulation models like the Blood Pressure Control Model can help local healthcare systems tailor strategies to reach local and national benchmarks.

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**Key Words:** adults ■ blood pressure ■ cardiovascular disease ■ hypertension

medication adherence

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#### WHAT IS KNOWN

- The US Centers for Disease Control and Prevention Million Hearts initiative aims for a blood pressure control rate of 80%, but only about half of US adults with hypertension have controlled blood pressure.
- Comprehensive clinic-based hypertension programs have demonstrated that 80% blood pressure control is attainable, but it is unclear which program components improved blood pressure control the most.

#### WHAT THE STUDY ADDS

- The Blood Pressure Control Model accurately predicts hypertension treatment outcomes using 3 clinic-based processes of hypertension care: office visit frequency, clinician treatment intensification given an uncontrolled blood pressure, and continued antihypertensive medication use.
- When providers intensify treatment at 62% of office visits with an uncontrolled blood pressure, 80% blood pressure control can be attained.
- Simultaneously improving all 3 hypertension management processes to the best-observed values in the literature would nearly achieve 80% control rates in US adults with hypertension.

he US Centers for Disease Control and Prevention estimates that over 16 million preventable cardiovascular disease events will occur from 2017 to 2021.1 The Centers for Disease Control and Prevention's Million Hearts initiative aims to prevent 1 million of these events by the year 2022. A key component of the initiative is attaining a blood pressure control rate ≥80% in US adults with hypertension. Blood pressure control is critical because hypertension is the leading modifiable risk factor for cardiovascular disease, it affects nearly 86 million US adults, and only about half of all US adults with hypertension and 72% of those treated with antihypertensive medications have blood pressure controlled to recommended treatment goals.<sup>2,3</sup> Although the Million Hearts blood pressure control goal is ambitious, it aligns with blood pressure control quality benchmarks, and comprehensive hypertension control programs demonstrate attaining it is feasible.4-7 However, it remains unclear which components of these comprehensive programs had the largest impact on improved blood pressure control rates. The Blood Pressure Control Model (BPCM) is a validated computer simulation model that predicts blood pressure according to the week-to-week processes of clinic-based hypertension management (ie, return visit interval, clinician treatment intensification after an uncontrolled blood pressure, and patient antihypertensive medication adherence).8 Prior BPCM analyses found substantial improvements in clinic-based management processes are needed to improve blood pressure control rates within 1 year but did not predict blood pressure control over longer time horizons.<sup>8</sup>

In this study, we adapted the BPCM to examine the impact of individual and joint changes in key components of hypertension management processes on long-term blood pressure control. Our objective was to quantify the extent to which feasible changes in the processes of clinic-based hypertension management of patients with uncontrolled hypertension and a usual source of medical care could contribute to attaining the Million Hearts goal of 80% blood pressure control before the goal year 2022.

#### **METHODS**

The authors declare that the data supporting the BPCM development and this analysis are either available within the article, its Data Supplement files, or are publicly available.

#### **Blood Pressure Control Model**

The BPCM is a microsimulation (ie, individual patient simulation) model that uses the processes of clinic-based hypertension treatment and control to predict the weekly blood pressure of patients receiving usual care (Figure 1).8 Specifically, the BPCM incorporates (1) time interval to next clinic visit that includes blood pressure measurement and hypertension management (in weeks), (2) office blood pressure measurement accuracy and variability, (3) probability the health care provider will intensify antihypertensive medications given an uncontrolled office blood pressure, (4) patient adherence to antihypertensive medications (ie, patients continuing to take antihypertensive medication), and (5) expected blood pressure reduction in patients adherent to antihypertensive medications. In the current study, we extended the BPCM blood pressure predictions out to 10 years by incorporating age-related changes in blood pressure, adding diastolic blood pressure, and simulating the process of antihypertensive medication dose titration (Supplemental Methods in the Data Supplement).

#### **Simulated Population**

The BPCM simulated patients aged ≥20 years with diagnosed but uncontrolled hypertension and access to a usual source of primary medical care. The simulation cohort was derived from pooled US National Health and Nutrition Examination Survey (NHANES) exams data (1999–2014; Supplemental Methods Data Supplement). Using the NHANES survey weights, we probabilistically sampled (with replacement) individuals meeting the inclusion criteria to create nationally representative cohorts of 10000 patients. The mean of  $\geq$ 2 systolic and  $\geq$ 2 diastolic research-quality NHANES office blood pressures served to represent each patient's true blood pressure at baseline. If a selected NHANES participant reported being on antihypertensive medications at baseline, his or her untreated blood pressure (ie, blood pressure without any antihypertensive medications) was estimated based on the expected blood pressure reduction with standard dose antihypertensive medications from a large meta-analysis.9

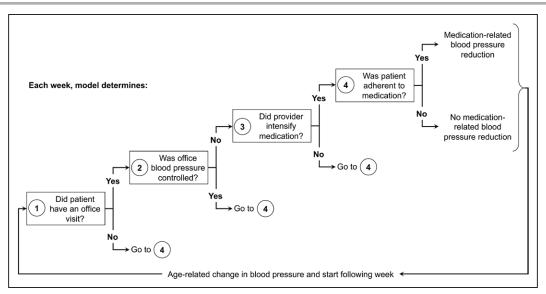


Figure 1. Structure of the blood pressure control model.

The figure shows the structure of the Blood Pressure Control Model and how blood pressures are estimated. Each week, the model determines if (1) the patient had an office visit with a provider, (2) the patient's measured office blood pressure was controlled, (3) he provider intensified antihypertensive medication, and (4) the patient was adherent to antihypertensive medication. The model assumed that blood pressure was taken at all office visits and adherence was defined as patients continuing to take the last added antihypertensive medication (ie, did not permanently discontinue use).

#### **Simulation Overview**

The BPCM hypertension treatment simulation starts with patients carrying a diagnosis of hypertension presenting for an office visit with their primary care provider and having their blood pressure measured as part of usual care (Figure 1). At this and each subsequent office visit, the model generates a measured office blood pressure by incorporating intraindividual blood pressure variability and measurement error (Supplemental Methods in the Data Supplement).8,10 Due to variability in measured blood pressure, at a proportion of office visits, the measured blood pressure will be above goal in controlled patients (false positive measurement) and below goal in uncontrolled patients (false negative measurement). If the measured blood pressure is uncontrolled, providers may act to intensify a patient's antihypertensive medication regimen. If the measured blood pressure is controlled, the model assumes that no changes are made to antihypertensive medications at that visit.

Regardless of other events, each week patients may remain adherent to or discontinue their antihypertensive medication. If the patient is adherent, an antihypertensive medication-related reduction in the true blood pressure occurs. If the patient discontinues the antihypertensive medication, the true blood pressure returns to the value before adding that antihypertensive medication. Then, the return interval (in weeks) until the next office visit is determined (conditioned on perceived control status and patient characteristics) and age-related blood pressure changes are applied. The BPCM repeats this process weekly to estimate patients' blood pressure over time.

# **Model Inputs for Process of Hypertension Management**

The model simulates 3 key processes of hypertension management: (1) the probability of intensifying antihypertensive

medications when blood pressure is uncontrolled, (2) the probability of remaining adherent to the last antihypertensive medication added, and (3) the return visit interval (in weeks) after an uncontrolled blood pressure. The model inputs are reported in Table I in the Data Supplement. We derived the probability of intensifying and adhering to antihypertensive medications from reviews of published literature (Supplemental Methods and Tables II and III in the Data Supplement). Under usual care, the probability of antihypertensive medication intensification for the first antihypertensive medication added and titrated during the simulation was stratified by the severity of the uncontrolled blood pressure, with higher values more likely to result in medication intensification; all subsequent antihypertensive intensifications were not stratified by blood pressure value (Table I in the Data Supplement). 11-16 Our usual care 1-year antihypertensive medication adherence rates included patients switching medications while finding an acceptable regimen, were pooled by antihypertensive medication class, and were weighted by 2013 to 2014 NHANES utilization (Supplemental Methods and Tables I and IV in the Data Supplement). 17-22 For usual care, the number of weeks until a return visit after an uncontrolled blood pressure was derived from a multivariable analysis of hypertensive patients with diabetes mellitus (Supplemental Methods and Table I in the Data Supplement).12

#### **Simulated Interventions**

To evaluate the impact of clinic-based hypertension care improvements on attainment of the 2022 Million Hearts blood pressure control goal, we first simulated usual care management over 4 years (from January 1, 2018 to December 31, 2021) and tracked cohort mean achieved systolic and diastolic blood pressures. We then simulated the best-observed values identified from published literature, which were defined as the highest probabilities of antihypertensive medication

intensification (19.5%–44.0%), highest antihypertensive medication adherence rate (75.6%), and 1 week until a return visit after an uncontrolled blood pressure (Table 1). Finally, we simulated perfect care, defined as 100% probability of antihypertensive medication intensification after an uncontrolled blood pressure, 100% antihypertensive medication adherence rate, and 1 week until a return visit after an uncontrolled blood pressure.

#### **Outcomes**

Our primary outcome was the blood pressure control rates according to the Seventh Report of the Joint National Committee (JNC 7) on hypertension (ie, percentage of the population with blood pressure <140/<90 mmHg or <130/<80 mmHg if diagnosed with diabetes mellitus or chronic kidney disease).<sup>23</sup> Secondarily, we examined the blood pressure control rates according to the 2017 American Heart Association/American College of Cardiology blood pressure guidelines (ie, <130/<80 mmHg).<sup>24</sup>

#### **Model Validation**

The model updates were programmed by one author (B.K. Bellows) and independently verified by a second (N. Ruiz-Negrón). To verify that the BPCM calculations were internally consistent, the model outputs for key hypertension management process parameters were compared with and found to reproduce the model inputs (Figure I and Table V in the Data Supplement). To ensure that the BPCM accurately predicted blood pressure outcomes of both usual care and interventional strategies over time, we simulated cohorts and trial-based hypertension management processes, as appropriate, to match 3 sources (Supplemental Methods and Table VI in the Data Supplement). Usual care was simulated using a cohort matching MESA (Multi-Ethnic Study of Atherosclerosis), an observational cohort of >6000 individuals across the US with ≈10 years of follow-up.<sup>25</sup> Interventional strategies were simulated using cohorts and management processes matching ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) and VALUE (Valsartan Antihypertensive Long-term Use Evaluation Trial), 2 large randomized controlled trials of antihypertensive medications with 5 to 6 years of follow-up.<sup>26,27</sup> We visually and quantitatively compared the estimated blood pressure outcomes to prespecified validation ranges and determined the number of model iterations within those bounds.<sup>28</sup>

#### **Analysis**

We simulated 1000 probabilistic iterations of 10000 patients in the simulation cohorts and compared projected blood pressure outcomes for the usual care, best-observed values, and perfect care interventions. To determine independent thresholds and combinations of hypertension management process parameters needed to achieve the Million Hearts 2022 blood pressure control goal of 80%, we used one- and multiway sensitivity analyses that varied these parameters from usual care up to perfect care values.

Finally, we evaluated the potential impact of improved clinic-based hypertension care on population-wide blood pressure control rates. We first plotted the current state of blood pressure control based on 2014 NHANES data.<sup>2</sup> Then, we reestimated the overall blood pressure control rate after simulating both best-observed values and perfect care among patients who were aware of their diagnosis but not treated and patients who were treated but uncontrolled (ie, those included in our simulation).

A summary of the key model assumptions and input parameters for the validations and Million Hearts analyses can be found in Table VI in the Data Supplement. This analysis was reviewed and approved by the Columbia University Medical Center Institutional Review Board. All analyses were performed using TreeAge Pro 2018 (TreeAge Software, Inc, Williamstown, MA) and R (R version 3.3.2, Vienna, Austria).

#### **RESULTS**

#### **Model Validation**

The BPCM accurately recreated the validation study cohorts and predicted the blood pressure outcomes in both the usual care and interventional validations, with all simulated means being within the validation bounds at the end of follow-up (Figures II through IV and Tables VII and VIII in the Data Supplement). In the usual

Table 1. Comparison of Key Hypertension Process Inputs Across Simulated Interventions.

Variable	Usual Care	Best-Observed Values	Perfect Care
Probability of adhering to last antihypertensive medication at 1 year	57.0% <sup>17–22</sup>	75.6%22	100.0%
Probability of intensifying antihypertensive medication when:			
Adding/titrating first antihypertensive medication during simulation			
Systolic blood pressure ≥160 mmHg or blood pressure ≥140/90 mmHg with diabetes mellitus or chronic kidney disease	33.3%13-15	44.0%14	100%
Systolic blood pressure is uncontrolled but <160 mm Hg or blood pressure is uncontrolled but <140/90 mm Hg with diabetes mellitus or chronic kidney disease	20.8%11,12	31.0%11	100%
Adding/titrating additional antihypertensive medications	13.0% <sup>16</sup>	19.5% <sup>16</sup>	100%
Return visit interval when blood pressure uncontrolled	≈13.8 wk¹²	1 wk <sup>12</sup>	1 wk

The table shows the model inputs for the key hypertension management processes; best-observed values were preferentially derived from the highest reported mean or calculated using sample size or variance estimates as available. Perfect care values were based on the best input possible for each parameter.

care validation, the observed blood pressure control rate in MESA at 9.5 years, 57.0% (validation bounds, 52.0%–62.0%), was similar to the 57.6% (95% uncertainty interval [UI], 45.4%–69.5%) predicted by the BPCM (Figure II and Table VIII in the Data Supplement). In the interventional validations, the blood pressure control rates predicted by the BPCM were similar to those observed in ALLHAT (observed 65.9% [validation bounds, 60.9%–70.9%] versus BPCM 70.3% [95% UI, 68.6%–72.4%]) and VALUE (observed 59.0% [validation bounds, 54.0%–64.0%] versus BPCM 59.6% [95% UI, 55.5%–64.9%]; Figures III and IV and Table VIII in the Data Supplement).

#### **Usual Care Blood Pressure Outcomes**

When using JNC 7 blood pressure control targets, a 4-year simulation of usual care led to a mean systolic blood pressure decrease from 147.3 to 136.7 (95% UI, 135.4–138.0) mmHg and mean diastolic blood pressure decrease from 77.3 to 72.2 (95% UI, 71.8–72.7) mmHg (Table 2 and Figure V in the Data Supplement). The resulting percent of patients with controlled blood pressure was estimated to be 45.6% (95% UI, 39.6%–52.5%; Figure 2 and Table 2). When using the 2017 American Heart Association/American College of Cardiology guideline blood pressure control targets, systolic blood pressure decreased from 147.1 to 134.5 (95% UI, 132.8–136.2) mmHg, diastolic from 76.5 to 70.7 (95% UI, 70.1–71.3) mmHg, and percent with controlled blood pressure was 32.8% (95% UI, 26.7%–39.7%).

## **Key Hypertension Management Process Improvements**

When using the best-observed values obtained from the literature for all 3 parameters simultaneously, 79.7% (95% UI, 79.3%–80.1%) of patients achieved blood pressure control over 4 years using JNC 7 targets and 66.9% (95% UI, 66.6%–67.2%) using the 2017 American Heart Association/American College of Cardiology blood pressure targets (Figure 2 and Table 2). With perfect care, the model predicted that 88.6% (95% UI, 88.4%–88.9%) and 76.1% (95% UI, 75.9%–76.3%) of individuals would achieve blood pressure control using JNC 7 and 2017 American Heart Association/American College of Cardiology blood pressure targets, respectively.

When individually varying the hypertension process management parameters, we found that increasing the probability a provider intensified antihypertensive medication after an uncontrolled blood pressure to ≥62% (from 13.0%–33.3% under usual care), regardless of prior antihypertensive intensification or baseline blood pressure, would achieve ≥80% blood pressure control rates under the JNC 7 blood pressure targets (Figure VI in the Data Supplement). If intensification rates were independently increased to 100% (perfect care), 87.2% of patients would achieve blood pressure control. However, individually varying either the return visit interval or medication adherence across the values obtained from the literature was not sufficient to reach the Million Hearts 80% blood pressure control goal (Figure VI in the Data Supplement). Independently improving patient adherence to 100% (from 57.0%) under usual care) would increase blood pressure control rates to 57.0% and independently reducing the return visit interval to 1 week (from mean 13.8 weeks under usual care) would increase control rates to 67.6%.

We performed multiway analyses using the JNC 7 guideline targets to determine combinations of parameters that would achieve 80% blood pressure control rates (Figure 3). Designers of clinic-based blood pressure control programs can use these results to select a

Table 2. Blood Pressure Outcomes Over 4 y (2018–2021) for Usual Care, Best-Observed Values, and Perfect Care.

Analysis	Baseline	Usual Care	Best-Observed Values	Perfect Care			
JNC 7							
Systolic blood pressure, mean (95% UI)	147.3	136.7 (135.4–138.0)	130.7 (130.6–130.8)	125.3 (125.2–125.3)			
Diastolic blood pressure, mean (95% UI)	77.3	72.2 (71.8–72.7)	70.0 (69.8–70.1)	67.9 (67.7–68.0)			
Blood pressure control rate, % (95% UI)	0	45.6 (39.6–52.5)	79.7 (79.3–80.1)	88.6 (88.4–88.9)			
% Iterations with 80% controlled blood pressure		0%	6.6%	100.0%			
2017 AHA/ACC							
Systolic blood pressure, mean (95% UI)	147.1	134.5 (132.8–136.2)	127.1 (127.0–127.2)	123.0 (122.9–123.1)			
Diastolic blood pressure, mean (95% UI)	76.5	70.7 (70.1–71.3)	67.8 (67.7–68.0)	66.3 (66.1–66.4)			
Blood pressure control rate, % (95% UI)	0	32.8 (26.7–39.7)	66.9 (66.6–67.2)	76.1 (75.9–76.3)			
% Iterations with 80% controlled blood pressure		0%	0%	0%			

The table shows the predicted 4-year blood pressure outcomes when simulating the week-to-week hypertension management processes using usual care, the best-observed estimates obtained from the literature, and perfect care. Controlled blood pressure defined for JNC 7 analysis as <140/90 mm Hg or <130/80 mm Hg for diabetes mellitus or chronic kidney disease and for 2017 AHA/ACC analysis as <130/80 mm Hg. 2017 AHA/ACC denotes 2017 AHA and ACC hypertension guideline; and 95% UI, 95% UI derived using 2.5th and 97.5th percentile of simulation results. ACC indicates American College of Cardiology; AHA, American Heart Association; JNC 7, Seventh Report of the Joint National Committee; and UI, uncertainty interval.

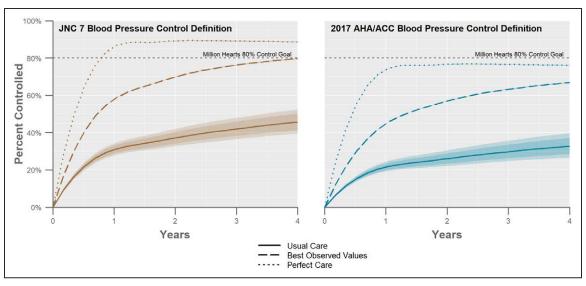


Figure 2. Predicted percent achieving controlled blood pressure according to national guidelines.

The figure shows the predicted percent of the population with controlled blood pressure under usual care, best-observed values for hypertension process management variables obtained from the literature, and perfect care. Blood pressure control was defined according to the Seventh Report of the Joint National Committee (JNC 7) guidelines as <130/80 mm Hg for patients with diabetes mellitus or chronic kidney disease and <140/90 mm Hg for all others. Blood pressure control was defined according to the 2017 AHA/ACC (American Heart Association/American College of Cardiology) guidelines as <130/80 mm Hg for everyone. The shaded regions show the 80% and 95% uncertainty intervals from 1000 probabilistic iterations of the model.

combination of interventions most likely to accelerate attainment of 2022 Million Hearts blood pressure control goals based on current performance in their populations. For example, a  $\geq$ 70% adherence rate,  $\geq$ 30% intensification rate, and  $\leq$ 4-week return visit interval, achieved 80% blood pressure control in our simulation.

## US Population-Wide Blood Pressure Control

Optimizing clinic-based hypertension care in patients with uncontrolled blood pressure and a usual source of medical care has the potential to move the US population close to the 2022 Million Hearts goal of 80% overall control in people living with hypertension (Figure 4). Starting with the overall blood pressure control rate of 54.4% under current usual care, attaining the best-observed values for return visit interval, probability of provider treatment intensification, and patient medication adherence could lead to a 78.1% blood pressure control rate; attaining perfect care would lead to >80% control. However, clinic-based care improvements would do nothing to improve blood pressure control in 15.9% of patients with hypertension who are currently unaware of their diagnosis.

#### DISCUSSION

We used computer simulations to determine practical clinic-based strategies for the management of patients with uncontrolled blood pressure that would achieve 80% blood pressure control by the year 2022, as targeted by the Centers for Disease Control and Preven-

tion's Million Hearts initiative. Based on our simulations. only 46% of patients who present with uncontrolled blood pressure at the beginning of 2018 would achieve blood pressure control by the end of 2021 under usual care. However, practical changes to key hypertension management processes (eg, ≥70% medication adherence, ≥30% probability of treatment intensification, and having follow-up visits within 4 weeks after an uncontrolled office blood pressure) would achieve a blood pressure control rate of 80% within 4 years. Increasing the likelihood that a provider intensifies antihypertensive medication in response to an uncontrolled office blood pressure had the most significant impact on achieving 80% blood pressure control in our analysis. When the probability of treatment intensification was ≥62% (increased from 13.0%-33.3% under usual care), at least 80% of patients achieved blood pressure control, even when patient medication adherence and the return visit interval were kept at usual care values. By improving key hypertension management processes in patients with known but uncontrolled hypertension to the best-observed values obtained from the literature, we could nearly achieve the Million Hearts 80% blood pressure control goal for all US adults with hypertension.

Our model assumes that changes to key clinic-based hypertension management processes, both individually and in combination, can be used to improve blood pressure control. Although prior studies show increased treatment intensification and visit frequency improve blood pressure control rates, an inconsistent association between adherence and blood pressure control has been identified. 12,29–34 Both Kaiser Permanente of Northern California and the Veterans Health Admin-

		Ave	Average Antihypertensive Adherence Rate					Average Return Visit Interval After			
		100%	90%	80%	70%	60%	50%	40%		Uncontrolled Blood Pressure	
sification Pressure	70%	16.0	16.0	16.0	16.0	16.0	16.0	12.0	Maxi Achi	≤16 weeks	
Intensification lood Pressure	60%	16.0	16.0	16.0	16.0	15.2	11.9	8.0	Maximum Achieving	≤12 weeks	
	50%	16.0	16.0	14.7	12.2	10.5	8.2	4.0	Average 80% Blo	≤8 weeks	
rtensi	40%	13.1	11.7	9.3	8.1	5.8	4.0	2.0	요~~	≤4 weeks	
Antihypertensive er Uncontrolled B	30%	7.6	6.3	5.0	3.3	1.4	-	-		Will not reach 80% control	
	20%	2.0	1.1	-	-	Usual Care*	-	-			
Average Rate Aft	10%	-	-	-	-	-	-	-	Interval Control		

Figure 3. Return visit interval needed to achieve Million Hearts 2022 goal of 80% blood pressure control at different antihypertensive intensification and adherence rates.

The figure shows the 4-year results when varying key hypertension management process parameters and the combination needed to achieve ≥80% blood pressure control. The columns are the average antihypertensive adherence rate (ie, proportion of patients continuing antihypertensive medication for at least 1 year). The rows are the average antihypertensive intensification rate (ie, proportion of clinic visits with an uncontrolled blood pressure where antihypertensive medication was intensified). The boxes are the maximum average return visit interval (in weeks) after an uncontrolled blood pressure. \*Usual care input for adherence was 57.0%, return visit interval was ≈13.8 wk, and mean simulated usual care intensification rate over 4 y was 18.7%.

istration showed improved blood pressure control through comprehensive blood pressure management programs, but the impact of the components of these programs is not described.<sup>4,5</sup> However, none of these studies considered the potential blood pressure control

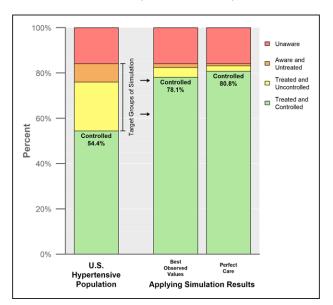


Figure 4. Hypertension awareness, treatment, and control status among US adults with hypertension in 2022 after simulating bestobserved values and perfect care.

The figure shows the percentage of US adults with hypertension in 2014<sup>2</sup> and the estimated impact on blood pressure control rates when improving clinic-based hypertension management to the best-observed values obtained from the literature and perfect care.

rates achieved through individual and combined variation in the key processes involved in medication management of hypertension as we have done in this study.

Computer simulation models have been used to inform clinical and policy decision making on strategies to improve blood pressure control and subsequent cardiovascular disease in the US (eg, intensive systolic blood pressure targets, team-based care, benefit-based treatment).<sup>8,35-40</sup> To our knowledge, however, the BPCM is the only model that uses the clinic-based processes of hypertension management to predict blood pressure outcomes. This analysis can be used by decision makers to estimate the potential impact of multifaceted hypertension interventions and guide development of tailored management strategies.

Our analysis identifies combinations of clinic-based hypertension management interventions that are predicted to achieve the Million Hearts blood pressure control goals in patients with uncontrolled blood pressure and a usual source of medical care. Although achieving 80% blood pressure control in these individuals will help the overall US population with hypertension approach the Million Hearts blood pressure control goal, there is significant variation across clinics and healthcare systems. Systems with less engagement and enthusiasm for hypertension management may require more resources and incur higher costs to implement the interventions described in our analysis, which may decrease the ability to achieve the Million Hearts blood

pressure control goal. Additionally, coaching patients to improve medication adherence and training providers may have only a small impact on blood pressure.<sup>41</sup> Systems will need to determine what facilitators and barriers to changing hypertension management processes exist in their clinics to effectively implement new practices. Furthermore, not all interventions are wellsuited for every healthcare system, and strategies need to be tailored to each setting. For example, in rural areas where frequent, in-person return visits may not be feasible, other management strategies may need to be considered. Additionally, as nearly 16% of adults with hypertension are unaware of their diagnosis, adding population-wide programs (eg, limiting dietary salt) may increase the likelihood of achieving the Million Hearts 2022 blood pressure control goal across the entire US population.

Our study has several limitations that should be taken into consideration when interpreting the results. First, the model incorporated several assumptions related to antihypertensive medication adherence that may not fully reflect clinical practice. For example, the model assumed that patients continuing use of antihypertensive medications for at least 1 year would not later discontinue use. Although some evidence suggests that discontinuation in subsequent years is small, this may not be true for all patients.<sup>42</sup> Also, while the studies we used to determine 1-year adherence rates included discontinuations for any reason, we did not explicitly model the risk of medication-related adverse events, which may have lasting effects on patient adherence. We also assumed that management processes were independent. However, clinical care of patients is complex, and correlations between management processes may exist (eg, providers may be more willing to intensify therapy when patients are adherent or less likely to intensify therapy in nonadherent patients regardless of the number of clinic visits).

Another limitation is that we made simplifying assumptions about antihypertensive medication treatment regimens. For example, the model uses the average effects of antihypertensive medication classes at half- and full-standard doses from a large meta-analysis.9 However, there are class- and dose-specific effects on blood pressure and adverse events that could be considered.<sup>43</sup> Similarly, although our analysis modeled usual care with a start low and go slow approach to treatment and titration, using one medication class at a time, there are many approaches to hypertension management, including early use of low-dose combination antihypertensive medications.<sup>23,24,44</sup> Also, the BPCM does not simulate the impact of nonmedicationrelated changes in blood pressure, such as regression to the mean and lifestyle modifications. 45,46 Incorporating these would allow the model to account for decreases in blood pressure even among patients wishing to avoid

antihypertensive medications. Nevertheless, our validations approximated the blood pressure outcomes of a large observational cohort of patients in whom regression to mean and lifestyle modifications are presumed to have occurred and the observed results from seminal hypertension drug trials. Finally, our interventional strategy model validation assumed that if hypertension management processes in clinical practice were similar to those used in the clinical trials, the blood pressure control rates achieved would be similar. Future research may consider validating the model against implemented clinic-based blood pressure control interventions.

In conclusion, our analysis showed the blood pressure control rates achieved by changing 3 clinic-based management processes (ie, time interval between clinic visits, probability of medication intensification, and patient medication adherence) to optimal levels observed in published literature did not quite achieve the Million Hearts 2022 goal of ≥80% blood pressure control. However, under our model assumptions, changes to these processes, both individually and in combination, could have a large impact on blood pressure control and progress towards meeting the Million Hearts 2022 goal. In our model, increasing the likelihood a provider intensifies antihypertensive medication in response to an uncontrolled blood pressure had the greatest impact on the overall blood pressure control rate. The relative importance of each process may differ, however, according to local patient and healthcare system characteristics. Tools such as the BPCM can be used by local healthcare systems to guide development of tailored hypertension management strategies to achieve quality benchmarks and improve population health.

#### **ARTICLE INFORMATION**

Received March 4, 2019; accepted April 12, 2019.

The Data Supplement is available at https://www.ahajournals.org/doi/suppl/10.1161/CIRCOUTCOMES.118.005624.

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#### **Sources of Funding**

B.K. Bellows is supported by K01 HL140170 from the National Heart, Lung, and Blood Institute, Bethesda, MD. Dr Bibbins-Domingo is supported by K24 DK103992. Dr Moran is supported by R01 HL130500-01A1 and R01 HL139837

from the National Heart, Lung, and Blood Institute, Bethesda, MD. Dr Fontil is supported by K23 HL136899 from the National Heart, Lung, and Blood Institute, Bethesda, MD. This research was supported by contracts HHSN268201500003I, N01-HC-95159, N01-HC-95160, N01-HC-95161, N01-HC-95162, N01-HC-95163, N01-HC-95164, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168, and N01-HC-95169 from the National Heart, Lung, and Blood Institute, and by grants UL1-TR-000040, UL1-TR-001079, and UL1-TR-001420 from National Center for Advancing Translational Sciences. We thank the other investigators, the staff, and the participants of the MESA (Multi-Ethnic Study of Atherosclerosis) for their valuable contributions. A full list of participating MESA investigators and institutions can be found at http://www.mesa-nhlbi.org. The views expressed in this article are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute; the National Institutes of Health; or the US Department of Health and Human Services.

#### **Disclosures**

None.

#### REFERENCES

- Ritchey MD, Wall HK, Owens PL, Wright JS. Vital signs: state-level variation in nonfatal and fatal cardiovascular events targeted for prevention by million hearts 2022. MMWR Morb Mortal Wkly Rep. 2018;67:974–982. doi: 10.15585/mmwr.mm6735a3
- Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, Chiuve SE, Cushman M, Delling FN, Deo R, de Ferranti SD, Ferguson JF, Fornage M, Gillespie C, Isasi CR, Jiménez MC, Jordan LC, Judd SE, Lackland D, Lichtman JH, Lisabeth L, Liu S, Longenecker CT, Lutsey PL, Mackey JS, Matchar DB, Matsushita K, Mussolino ME, Nasir K, O'Flaherty M, Palaniappan LP, Pandey A, Pandey DK, Reeves MJ, Ritchey MD, Rodriguez CJ, Roth GA, Rosamond WD, Sampson UKA, Satou GM, Shah SH, Spartano NL, Tirschwell DL, Tsao CW, Voeks JH, Willey JZ, Wilkins JT, Wu JH, Alger HM, Wong SS, Muntner P; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. *Circulation*. 2018;137:e67–e492. doi: 10.1161/CIR.00000000000000558
- Fryar CD, Ostchega Y, Hales CM, Zhang G, Kruszon-Moran D. Hypertension prevalence and control among adults: United States, 2015–2016. NCHS Data Brief. 2017:1–8.
- Jaffe MG, Lee GA, Young JD, Sidney S, Go AS. Improved blood pressure control associated with a large-scale hypertension program. *JAMA*. 2013;310:699–705. doi: 10.1001/jama.2013.108769
- Fletcher RD, Amdur RL, Kolodner R, McManus C, Jones R, Faselis C, Kokkinos P, Singh S, Papademetriou V. Blood pressure control among US veterans: a large multiyear analysis of blood pressure data from the Veterans Administration health data repository. *Circulation*. 2012;125:2462–2468. doi: 10.1161/CIRCULATIONAHA.111.029983
- Fontil V, Gupta R, Moise N, Chen E, Guzman D, McCulloch CE, Bibbins-Domingo K. Adapting and evaluating a health system intervention from kaiser permanente to improve hypertension management and control in a large network of safety-net clinics. *Circ Cardiovasc Qual Outcomes*. 2018;11:e004386. doi: 10.1161/CIRCOUTCOMES.117.004386
- 7. Hanlin RB, Asif IM, Wozniak G, Sutherland SE, Shah B, Yang J, Davis RA, Bryan ST, Rakotz M, Egan BM. Measure accurately, act rapidly, and partner with patients (MAP) improves hypertension control in medically underserved patients: Care Coordination Institute and American Medical Association Hypertension Control Project Pilot Study Results. *J Clin Hypertens (Greenwich)*. 2018;20:79–87. doi: 10.1111/jch.13141
- Fontil V, Bibbins-Domingo K, Kazi DS, Sidney S, Coxson PG, Khanna R, Victor RG, Pletcher MJ. Simulating strategies for improving control of hypertension among patients with usual source of care in the united states: the blood pressure control model. *J Gen Intern Med.* 2015;30:1147– 1155. doi: 10.1007/s11606-015-3231-8
- Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ. 2009;338:b1665. doi: 10.1136/bmj.b1665
- 10. Kronish IM, Lynch AI, Oparil S, Whittle J, Davis BR, Simpson LM, Krousel-Wood M, Cushman WC, Chang TI, Muntner P. The association between antihypertensive medication nonadherence and visit-to-visit variability of blood pressure: findings from the antihypertensive and lipid-low-

- ering treatment to prevent heart attack trial. *Hypertension*. 2016;68:39–45. doi: 10.1161/HYPERTENSIONAHA.115.06960
- Desai N, Madhavankutty Saraswathy V, Hunter K, McFadden C. Prevalence of true therapeutic inertia in blood pressure control in an academic chronic kidney disease clinic. *J Clin Hypertens (Greenwich)*. 2013;15:375–379. doi: 10.1111/jch.12095
- Turchin A, Goldberg SI, Shubina M, Einbinder JS, Conlin PR. Encounter frequency and blood pressure in hypertensive patients with diabetes mellitus. *Hypertension*. 2010;56:68–74. doi: 10.1161/HYPERTENSIONAHA.109.148791
- Kerr EA, Zikmund-Fisher BJ, Klamerus ML, Subramanian U, Hogan MM, Hofer TP. The role of clinical uncertainty in treatment decisions for diabetic patients with uncontrolled blood pressure. *Ann Intern Med.* 2008;148:717–727.
- Krein SL, Hofer TP, Holleman R, Piette JD, Klamerus ML, Kerr EA. More than a pain in the neck: how discussing chronic pain affects hypertension medication intensification. *J Gen Intern Med.* 2009;24:911–916. doi: 10.1007/s11606-009-1020-y
- Selby JV, Uratsu CS, Fireman B, Schmittdiel JA, Peng T, Rodondi N, Karter AJ, Kerr EA. Treatment intensification and risk factor control: toward more clinically relevant quality measures. *Med Care*. 2009;47:395– 402.
- Bolen SD, Samuels TA, Yeh HC, Marinopoulos SS, McGuire M, Abuid M, Brancati FL. Failure to intensify antihypertensive treatment by primary care providers: a cohort study in adults with diabetes mellitus and hypertension. J Gen Intern Med. 2008;23:543–550. doi: 10.1007/s11606-008-0507-2
- 17. Bloom BS. Continuation of initial antihypertensive medication after 1 year of therapy. *Clin Ther.* 1998;20:671–681.
- Wogen J, Kreilick CA, Livornese RC, Yokoyama K, Frech F. Patient adherence with amlodipine, lisinopril, or valsartan therapy in a usual-care setting. J Manag Care Pharm. 2003;9:424–429. doi: 10.18553/jmcp.2003.9.5.424
- Elliott WJ, Plauschinat CA, Skrepnek GH, Gause D. Persistence, adherence, and risk of discontinuation associated with commonly prescribed antihypertensive drug monotherapies. J Am Board Fam Med. 2007;20:72–80. doi: 10.3122/jabfm.2007.01.060094
- Chen S, Macaulay D, Swallow E, Diener M, Farooqui S, Xie J, Wu EQ. Real-world adherence and persistence associated with nebivolol or hydrochlorothiazide as add-on treatment for hypertension. *Curr Med Res Opin*. 2014;30:637–643. doi: 10.1185/03007995.2013.864267
- Chen S, Swallow E, Li N, Faust E, Kelley C, Xie J, Wu E. Economic benefits associated with beta blocker persistence in the treatment of hypertension: a retrospective database analysis. *Curr Med Res Opin*. 2015;31:615–622. doi: 10.1185/03007995.2015.1013624
- Tajeu GS, Kent ST, Kronish IM, Huang L, Krousel-Wood M, Bress AP, Shimbo D, Muntner P. Trends in antihypertensive medication discontinuation and low adherence among Medicare beneficiaries initiating treatment from 2007 to 2012. *Hypertension*. 2016;68:565–575. doi: 10.1161/HYPERTENSIONAHA.116.07720
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ; Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension*. 2003;42:1206– 1252. doi: 10.1161/01.HYP.0000107251.49515.c2
- 24. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbiagele B, Smith SC Jr, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA Sr, Williamson JD, Wright JT Jr. 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. Hypertension. 2018;71:e13–e115. doi: 10.1161/HYP.000000000000000000065
- Bild DE, Bluemke DA, Burke GL, Detrano R, Diez Roux AV, Folsom AR, Greenland P, Jacob DR Jr, Kronmal R, Liu K, Nelson JC, O'Leary D, Saad MF, Shea S, Szklo M, Tracy RP. Multi-ethnic study of atherosclerosis: objectives and design. Am J Epidemiol. 2002;156:871–881.
- Julius S, Kjeldsen SE, Weber M, Brunner HR, Ekman S, Hansson L, Hua T, Laragh J, McInnes GT, Mitchell L, Plat F, Schork A, Smith B, Zanchetti A; VALUE trial group. Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the VALUE randomised trial. *Lancet*. 2004;363:2022–2031. doi: 10.1016/S0140-6736(04)16451-9

- 27. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. The antihypertensive and lipid-lowering treatment to prevent heart attack trial. major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA. 2002;288:2981–2997.
- Corro Ramos I, van Voorn GAK, Vemer P, Feenstra TL, Al MJ. A new statistical method to determine the degree of validity of health economic model outcomes against empirical data. *Value Health*. 2017;20:1041–1047. doi: 10.1016/j.jval.2017.04.016
- Margolis KL, Asche SE, Bergdall AR, Dehmer SP, Maciosek MV, Nyboer RA, O'Connor PJ, Pawloski PA, Sperl-Hillen JM, Trower NK, Tucker AD, Green BB. A Successful multifaceted trial to improve hypertension control in primary care: why did it work? *J Gen Intern Med.* 2015;30:1665–1672. doi: 10.1007/s11606-015-3355-x
- Glynn LG, Murphy AW, Smith SM, Schroeder K, Fahey T. Interventions used to improve control of blood pressure in patients with hypertension. Cochrane Database Syst Rev. 2010;3:CD005182.
- Daugherty SL, Powers JD, Magid DJ, Masoudi FA, Margolis KL, O'Connor PJ, Schmittdiel JA, Ho PM. The association between medication adherence and treatment intensification with blood pressure control in resistant hypertension. *Hypertension*. 2012;60:303–309. doi: 10.1161/HYPERTENSIONAHA.112.192096
- 32. Rose AJ, Berlowitz DR, Manze M, Orner MB, Kressin NR. Intensifying therapy for hypertension despite suboptimal adherence. *Hypertension*. 2009;54:524–529. doi: 10.1161/HYPERTENSIONAHA.109.133389
- Vigen R, Shetterly S, Magid DJ, O'Connor PJ, Margolis KL, Schmittdiel J, Ho PM. A comparison between antihypertensive medication adherence and treatment intensification as potential clinical performance measures. Circ Cardiovasc Qual Outcomes. 2012;5:276–282. doi: 10.1161/CIRCOUTCOMES.112.965665
- 34. Guthmann R, Davis N, Brown M, Elizondo J. Visit frequency and hypertension. *J Clin Hypertens (Greenwich)*. 2005;7:327–332.
- Bress AP, Bellows BK, King JB, Hess R, Beddhu S, Zhang Z, Berlowitz DR, Conroy MB, Fine L, Oparil S, Morisky DE, Kazis LE, Ruiz-Negrón N, Powell J, Tamariz L, Whittle J, Wright JT Jr, Supiano MA, Cheung AK, Weintraub WS, Moran AE; SPRINT Research Group. Cost-effectiveness of intensive versus standard blood-pressure control. N Engl J Med. 2017;377:745–755. doi: 10.1056/NEJMsa1616035
- Dehmer SP, Baker-Goering MM, Maciosek MV, Hong Y, Kottke TE, Margolis KL, Will JC, Flottemesch TJ, LaFrance AB, Martinson BC, Thomas

- AJ, Roy K. Modeled health and economic impact of team-based care for hypertension. *Am J Prev Med.* 2016;50(5 suppl 1):S34–S44. doi: 10.1016/j.amepre.2016.01.027
- Eddy DM, Adler J, Patterson B, Lucas D, Smith KA, Morris M. Individualized guidelines: the potential for increasing quality and reducing costs. *Ann Intern Med.* 2011;154:627–634. doi: 10.7326/0003-4819-154-9-201105030-00008
- Moise N, Huang C, Rodgers A, Kohli-Lynch CN, Tzong KY, Coxson PG, Bibbins-Domingo K, Goldman L, Moran AE. Comparative cost-effectiveness of conservative or intensive blood pressure treatment guidelines in adults aged 35-74 years: the cardiovascular disease policy model. *Hypertension*. 2016;68:88–96. doi: 10.1161/HYPERTENSIONAHA.115.06814
- Moran AE, Odden MC, Thanataveerat A, Tzong KY, Rasmussen PW, Guzman D, Williams L, Bibbins-Domingo K, Coxson PG, Goldman L. Costeffectiveness of hypertension therapy according to 2014 guidelines. N Engl J Med. 2015;372:447–455. doi: 10.1056/NEJMsa1406751
- Sussman J, Vijan S, Hayward R. Using benefit-based tailored treatment to improve the use of antihypertensive medications. *Circulation*. 2013;128:2309–2317. doi: 10.1161/CIRCULATIONAHA.113.002290
- Mills KT, Obst KM, Shen W, Molina S, Zhang HJ, He H, Cooper LA, He J. Comparative effectiveness of implementation strategies for blood pressure control in hypertensive patients: a systematic review and meta-analysis. *Ann Intern Med.* 2018;168:110–120. doi: 10.7326/M17-1805
- 42. van Wijk BL, Shrank WH, Klungel OH, Schneeweiss S, Brookhart MA, Avorn J. A cross-national study of the persistence of antihypertensive medication use in the elderly. *J Hypertens*. 2008;26:145–153. doi: 10.1097/HJH.0b013e32826308b4
- Law MR, Wald NJ, Morris JK, Jordan RE. Value of low dose combination treatment with blood pressure lowering drugs: analysis of 354 randomised trials. BMJ. 2003;326:1427. doi: 10.1136/bmj.326.7404.1427
- 44. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, Lackland DT, LeFevre ML, MacKenzie TD, Ogedegbe O, Smith SC Jr, Svetkey LP, Taler SJ, Townsend RR, Wright JT Jr, Narva AS, Ortiz E. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014;311:507–520. doi: 10.1001/jama.2013.284427
- 45. Shepard DS, Finison LJ. Blood pressure reductions: correcting for regression to the mean. *Prev Med.* 1983;12:304–317.
- Kronish IM, Edmondson D, Shimbo D, Shaffer JA, Krakoff LR, Schwartz JE.
  A comparison of the diagnostic accuracy of common office blood pressure monitoring protocols. Am J Hypertens. 2018;31:827–834.