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Physician-Pharmacist Collaboration versus Usual Care for Treatment-Resistant Hypertension

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Abstract

Team-based care has been recommended for patients with treatment-resistant hypertension (TRH), but its efficacy in this setting is unknown. We compared a physician-pharmacist collaborative model (PPCM) to usual care in patients with TRH participating in the Collaboration Among Pharmacists and physicians To Improve Outcomes Now (CAPTION) study. At baseline, 169 patients (27% of CAPTION patients) had TRH: 111 received the PPCM intervention and 58 received usual care. Baseline characteristics were similar between treatment arms. After 9 months, adjusted mean systolic BP was reduced by 7 mmHg more with PPCM intervention than usual care (p=0.036). BP control was 34.2% with PPCM versus 25.9% with usual care (adjusted OR, 1.92; 95% CI, 0.33–11.2). These findings suggest that team-based care in the primary care setting may be effective for TRH. Additional research is needed regarding the long-term impact of these models and to identify patients most likely to benefit from team-based interventions.

Keywords

collaborative care; hypertension; treatment resistant hypertension; pharmacist

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INTRODUCTION

Treatment resistant hypertension (TRH), defined simply as requiring ≥4 antihypertensive agents to achieve blood pressure (BP) control,[1] is a clinically challenging hypertension phenotype that has been consistently linked with substantially decreased quality of life, increased cardiovascular risk, and increased mortality.[2-10] According to data from the National Health and Nutrition Examination Survey (NHANES), the prevalence of TRH appears to have more than doubled over the past quarter-century from 8.8% in 1988-1994 to 20.7% in 2005-2008.[11,12] Although the mechanisms underlying TRH development have not been elucidated, likely contributors include poor medication adherence, suboptimal antihypertensive regimens, obesity, alcohol consumption, high sodium intake, and concomitant use of medications that promote sodium retention or otherwise decrease antihypertensive efficacy.[12] Importantly, many of these contributing factors are modifiable, offering the potential for intervention.

Evidence-based treatment modalities for reducing BP in patients with TRH are limited at present. Many patients with TRH could benefit from optimization of antihypertensive regimens, yet studies on the most appropriate three- and four-drug antihypertensive combinations are virtually nonexistent. Aldosterone receptor antagonists have the most compelling evidence for lowering BP in TRH,[13,14] but their use remains quite limited in this population.[15] Additionally, recent phase 3 studies suggest a limited benefit to non-drug interventions, such as renal denervation therapy and carotid baroreceptor activation in patients with TRH.[16,17] Thus, novel approaches are needed to address the modifiable factors contributing to TRH.

One approach that has demonstrated success in the general hypertension population is physician-pharmacist collaborative care.[18-22] A recent meta-analysis of 37 studies of team-based interventions found significantly decreased BP with patient education or pharmacist treatment recommendations.[18] Likewise, in the Collaboration Among Pharmacists and physicians To Improve Outcomes Now (CAPTION) study, physician-pharmacist collaboration was associated with a 6/3 mm Hg greater decrease in BP relative to usual care.[22] However, to our knowledge, collaborative care models have not been tested in patients with TRH. Accordingly, we aimed to compare a physician-pharmacist collaborative care model (PPCM) to usual hypertension care (from a primary care provider) among a geographically- and racially-diverse primary care patient population with TRH who were participating in the CAPTION study. We hypothesized that patients assigned to PPCM would achieve greater reductions in BP than those assigned to usual care from their primary care provider.

METHODS

Full details of the design and principal results for CAPTION have been reported previously.[22,23] Briefly, CAPTION was a prospective, cluster-randomized multi-center clinical trial in 32 medical offices across the United States. All participating clinics had an imbedded clinical pharmacist prior to enrollment in the trial. Offices were stratified by the percent of minority patients and level of clinical pharmacy services at each clinic and then

randomly assigned to 1 of 3 groups in approximately equal proportion: a 9-month PPCM intervention, a 24-month PPCM intervention, or usual care (control). English- or Spanish-speaking patients were included if they met the following criteria: age >18 years, current diagnosis of hypertension, uncontrolled BP (>140 mm Hg systolic or >90 mm Hg diastolic for uncomplicated hypertension or >130 mm Hg systolic or >80 mm Hg diastolic for patients with diabetes mellitus or chronic kidney disease [CKD]) at study entry, and receiving care from the participating primary care office. Key patient exclusion criteria included left ventricular ejection fraction <35%, glomerular filtration rate <20 mL/min or documented proteinuria >1 gram/day. The study was approved by the respective Institutional Review Boards for each medical office.

Treatment Strategies

The recommended PPCM intervention included medical record review by the pharmacist and a structured interview, assessing medical history, knowledge of BP medication regimens, adherence, and other barriers to BP control at each visit. Pharmacist treatment recommendations were documented in care plans that were provided to the collaborating physician. The collaborating physician was then free to accept or modify the treatment plan, followed by implementation of the final plan by the pharmacist. The recommended visit schedule included a structured baseline visit, a call at 2 weeks and additional structured face-to-face visits at months 1, 2, 4, 6, and 8, with additional visits as needed. Because CAPTION was an implementation trial, pharmacist-physician teams could modify the proposed PPCM intervention schedule. Pharmacist and physician providers in offices randomized to the PPCM intervention arms also received additional training that focused on three areas: (1) strategies to overcome clinical inertia and patient barriers to achieve blood pressure control; (2) education on JNC 7 and major antihypertensive trials (i.e., ALLHAT), as well as use of treatment aids (e.g., medication use cards, adherence aids); and, (3) methods for effective communication and collaboration between physicians and pharmacists. Providers were not educated specifically on TRH.

Primary care providers at clinics assigned to usual care received no additional training or instructions other than to continue usual hypertension care for enrolled patients. Pharmacists in usual care offices were instructed to avoid interventions for study participants with hypertension, but they could provide usual consultations if physicians specifically asked questions.

Cohort Development

For the present analysis, we restricted the CAPTION dataset to patients taking ≥3 antihypertensive medications at study entry (i.e., those who met the definition of TRH[1]), because all patients had uncontrolled BP as assessed by a structured research measurement (described below). We used this definition to encompass those with “true” and “apparent” TRH to increase generalizability of the study results. Furthermore, we did not require patients to be taking a diuretic as part of their baseline antihypertensive regimen because previous studies have demonstrated no difference in outcomes comparing a TRH definition requiring a diuretic and the more simple definition used here (i.e., based on the number of antihypertensive drugs without regard to the presence of a diuretic).[2,4,5] Consistent with the

overall CAPTION protocol approved by the study sponsor (NHLBI) and data & safety monitoring board, we combined data from patients in both the 9-month and 24-month PPCM intervention groups to create one pooled PPCM intervention group since the PPCM interventions were identical for the first 9 months of the study. Consequently, the final dataset for the present study contained approximately a 2:1 ratio of PPCM intervention-to-control patients.

Data Collection

Baseline and 9-month BP was measured by a trained study coordinator at each clinic using a Omron HEM 907-XL device. Measurements were taken in triplicate in the sitting position at each visit; the second and third readings (taken 1 minute apart) were averaged for the visit BP. If the second and third readings were >4 mm Hg apart, another reading was taken and the 2 closest values were averaged to determine the visit BP. Additional baseline measures included height, weight, heart rate, duration of hypertension, presence of other cardiovascular risk factors, symptoms and adverse drug reactions, sociodemographic indices, comorbidities, and current antihypertensive medication regimens. Patient-reported medication adherence was assessed using a validated 4-item questionnaire at the baseline and 9-month visits.[24,25]

Outcomes

The primary outcome was change in BP at 9 months based on intention-to-treat. Secondary outcomes included BP control at 9 months based on intention-to-treat. Blood pressure control was defined according to the then-current JNC7 guidelines as BP <140/90 mm Hg for uncomplicated hypertension or <130/80 mm Hg for patients with CKD or diabetes mellitus.[26] We hypothesized that BP would be reduced and BP control per guideline criteria would be increased in patients receiving the PPCM intervention compared to those receiving usual care at 9 months.

Statistical Analyses

Baseline characteristics were reported using descriptive statistics. For categorical variables, a generalized estimating equation model (GEE) was used to compare proportions across groups while accounting for the correlation within a clinic. For continuous variables a generalized linear regression model was used to compare means across groups while accounting for correlation within a clinic. For the primary outcome, BP data were analyzed using a linear mixed model with random effects for office and subject within office to determine the difference in mean BP for patients in the PPCM intervention compared to the control group. The clinic random effects were assumed to be normally distributed and have compound symmetric covariance structure and the within subject random errors were assumed to have an AR(1) covariance structure. The model was adjusted for baseline BP, age, study arm, presence of CKD or diabetes, and medication adherence at the 9-month study visit. A non-linear mixed effect model with a logit link was used to estimate the log-odds of BP control in the PPCM intervention compared to usual care at 9 months. These models assumed the same covariance structure and adjusted for the same variables as the linear mixed models described above. Secondary outcomes included comparing antihypertensive use across groups using the model described previously for the baseline

characteristics, and comparing mean BP and BP control across adherence levels, using the same methods described previously for the primary outcome and BP control outcome, respectively. Statistical significance was established *a priori* as $p<0.05$.

RESULTS

Study cohort development is summarized in the Figure. A total of 169 patients were included in the present analysis. Of these, 111 were assigned to the PPCM intervention (27.7% of all CAPTION patients assigned to the PPCM intervention) and 58 were assigned to usual care (25.9% of all CAPTION patients assigned to usual care). Baseline characteristics were generally similar between treatment groups (Table 1). Overall, the mean age of patients with TRH was 63.7 years, 68% were women, 64% identified as a minority, and 28% had established diabetes or CKD, with no significant differences between groups at study entry. Patients assigned to PPCM intervention clinics had a mean ± SD of 8.9 ± 5.3 clinically-related visits or phone calls with the pharmacist or physician provider over the 9-month study period, compared with 4.2 ± 4.3 in the usual care group ($p=0.0007$). For hypertension-related clinic visits only (i.e., excluding phone calls or other non-hypertension-related visits), the respective means ± SDs were 6.2 ± 3.7 for the PPCM intervention group and 1.0 ± 1.5 for the usual care group ($p<0.0001$).

Antihypertensive Use

At baseline, patients in the PPCM intervention were prescribed a mean ± SD of 3.5 ± 0.8 antihypertensive drugs, compared with 3.5 ± 0.8 in the usual care group. Most patients (~64%) were taking 3 antihypertensive agents at baseline and none were prescribed greater than 6 antihypertensive medications (Table 1). Baseline antihypertensive use, by class, is summarized in Table 2. In general, the proportion of patients taking each class of antihypertensive agents was similar comparing treatment groups, although angiotensin converting enzyme inhibitor (ACE-I) and α_2-agonist use was modestly higher in the usual care group, whereas diuretic use was marginally higher in the PPCM intervention group. A greater proportion of patients in the usual care group were taking a fixed-dose combination pill (19%) compared with the PPCM intervention group (8%; $p=0.05$).

At 9 months, the mean number of medications per person was 3.6 in the PPCM intervention arms compared with 3.3 in the usual care arm ($p=0.31$). Significantly more dose increases or medication additions were observed in the PPCM intervention arms (mean ± SD, 3.6 ± 3.0), compared with the usual care arm (0.7 ± 1.1; $p=0.0004$). Nevertheless, overall use of most antihypertensive classes remained similar between groups (Table 3). In particular, diuretic remained similar between the PPCM intervention group (89%) and the usual care group (80%; $p=0.14$). The use of fixed-dose combination pills increased modestly in the usual care group (26%) compared to a modest reduction in the PPCM intervention group (6%; $p<0.01$ for the difference at 9 months). In contrast, use of aldosterone antagonists increased substantially in the PPCM intervention group (18%) compared with only a modest increase in the usual care group (6%; $p=0.07$ for the comparison between treatment arms at 9 months). Spironolactone was also titrated to a higher dose at 9-months in 74% of patients receiving the drug at baseline in the PPCM intervention arm, whereas none of the patients

receiving spironolactone at baseline in the usual care arm had their dose titrated. Likewise, a greater proportion of patients in the PPCM intervention arm, compared with the usual care arm, had an upward dose titration of their β-blocker (32% vs. 14%; p=0.02) or non-dihydropyridine calcium channel blocker (47% vs. 0%; p=0.02). Finally, use of duplicate drugs from a single class decreased in the PPCM intervention arm from baseline (12%) to 9 months (2%), whereas it remained basically unchanged (9% vs. 8%) in the usual care group.

Adherence

Self-reported medication adherence at baseline was high, with ~88% of patients in the overall study population reporting high adherence, and no appreciable difference was observed between groups at study entry. At the 9-month visit, the proportion of patients reporting high adherence was also similar in the PPCM intervention (81%) and usual care (77.6%) groups (p=0.44), although data were missing for 15% of patients. An improvement from low to high medication adherence was observed in 6.3% of patients in the PPCM intervention arm versus 1.7% of patients in the usual care arm (p=0.36). Among minorities only, the corresponding proportions were 8.1% vs. 0% (p=0.016).

Blood Pressure

Mean systolic and diastolic BP were similar at baseline comparing patients in the PPCM intervention (149/84 mm Hg) and usual care (150/79 mm Hg) groups. At 9 months, patients in the PPCM intervention group had achieved a mean BP of 132/75 mm Hg, whereas those in the usual care group, with hypertension managed by their primary care provider, had achieved a mean BP of 141/73 mm Hg. Thus, unadjusted mean reductions in BP were 17/9 mm Hg in patients assigned to PPCM intervention clinics and 9/6 mm Hg in those assigned to the usual care clinics. After adjustment, mean systolic BP remained significantly lower in the PPCM intervention group compared to the usual care group (Table 4). Adjusted mean diastolic BP change was similar between groups. Blood pressure control at 9 months was 34.2% in the PPCM intervention and 25.9% in the control group (adjusted OR, 1.92; 95% CI, 0.33–11.2; p=0.47). Similar results were observed adjusting for medication adherence level and minority status, as well as using last-observation carried forward for BP (data not shown).

DISCUSSION

Treatment-resistant hypertension represents an increasingly common and clinically challenging phenotype associated with lower health-related quality of life and substantial risk for major adverse cardiovascular events and death. Unfortunately, few strategies have been shown to effectively reduce BP in patients with TRH. Team-based care has been recommended as a potential strategy in patients with TRH,[27] but to date has not been studied rigorously in this patient population. We demonstrated, for the first time, that physician-pharmacist collaborative management of TRH effectively reduces BP compared with usual care in a racially-diverse group of patients treated in the primary care setting. Importantly, the magnitude of difference seen in systolic BP between the two groups is on par with similar team-based interventions in the general hypertensive population. Moreover, we found

that greater than one-third of patients with previously uncontrolled TRH were able to achieve BP control using this team-based approach.

Our finding that the PPCM intervention resulted in an adjusted net reduction of nearly 7 mm Hg systolic BP in the present study is significant for several reasons. First, although data are lacking in the TRH population, per se, a sustained reduction of this magnitude in the general hypertensive population may be expected to substantially reduce cardiovascular mortality by 10% to 20% and all-cause mortality by 8% to 10%.[26] Secondly, this reduction is remarkably similar to that observed in the overall CAPTION trial, despite the fact that this analysis was restricted to a more difficult-to-treat subset of patients with uncontrolled hypertension. This finding suggests that patients with TRH may be particularly ideal candidates for PPCM intervention or team-based care more broadly. Thirdly, this reduction was observed in a predominantly minority population, most of whom were African American, who are known to have disproportionately greater difficulty in achieving BP control, and a corresponding increased risk for developing TRH.[2,8,28] Consistent with these previous studies, minorities (mainly African Americans) accounted for nearly two-thirds of CAPTION participants with TRH, compared with only about one-half of overall CAPTION participants.[22] African Americans, in particular, also have some of the highest rates of adverse outcomes associated with TRH.[3,5] Finally, although BP control at 9 months was not significantly different between groups (a finding similar to that in the overall CAPTION population), it is noteworthy that just over one-third of patients in the PPCM intervention arm, most of whom had hypertension for >10 years prior to study enrollment, achieved BP control.

The observed reduction in BP in the PPCM intervention is likely a result of the multifaceted approach inherent to the PPCM intervention, rather than any single factor. For example, recent data demonstrate that spironolactone is an effective add-on agent in patients with TRH, leading to a placebo-adjusted home systolic BP reduction of ~9 mm Hg.[14] In the present study, greater spironolactone use in the PPCM intervention arms may have accounted for some of the observed difference in BP reduction, but only 18% of patients in the PPCM intervention arm (vs. 6% in the usual care arm) were prescribed an aldosterone antagonist at the 9-month visit. Another likely contributor to the overall reduction in mean BP was reduced clinical inertia as evidenced by more frequent follow-up, which has been linked with greater BP control,[29,30] and a greater number of antihypertensive regimen modifications in the PPCM intervention arms.[31] Finally, greater reinforcement of lifestyle modifications and dietary salt restriction in the PPCM intervention groups may also have played a role, although the extent to which these recommendations were made in usual care clinics is not known.

Although we observed no difference in adherence rate improvement between treatment arms overall, adherence was improved significantly more among minority patients in the PPCM intervention arm compared with minorities in the usual care arm. This finding also may help explain the greater reduction in BP with the PPCM intervention since greater treatment adherence is known to facilitate BP control in patients with TRH.[32] Of note, baseline self-reported adherence was remarkably high among this study population and generally similar to previous reports in patients with TRH using self-reported adherence[33] and medication fill data.[34] However, recent data suggest that self-reported adherence may not adequately predict

true adherence (i.e., as assessed by therapeutic drug monitoring) in patients with TRH.[35] It seems plausible that the self-report adherence tool used in CAPTION may have overestimated true adherence at baseline and thus underestimated any improvement in adherence resulting from the PPCM intervention. Nevertheless, better strategies clearly are needed to identify nonadherence among persons with TRH; such strategies could help inform pharmacist and physician providers to further enhance the potency of the PPCM intervention.

Physician-pharmacist collaboration is becoming a more common strategy in the treatment of hypertension.[27,36] Importantly, previous work has demonstrated that patients, pharmacists and physicians express positive attitudes towards future implementations of PPCM interventions, regardless of whether they have had previous experience with such models.[37,38] Primary care providers also appear to be accepting of these models once in place, with ~95% of providers considering at least 1 of their patients appropriate for such interventions.[39] Moreover, once engaged in these models, physicians tend to have a very high (95%) level of agreement with pharmacist recommendations, especially when the clinical pharmacist is housed within the same clinic.[19] Thus, the approach described herein appears to be both feasible (where clinical pharmacy services exist) and effective for patients with TRH. A similar collaborative approach, using pharmacists in the community setting may also be effective,[40] although this approach has not been studied explicitly in those with TRH. Where clinical pharmacy services are unavailable, other collaborative care models may also be effective, for example, by using team-based care with physicians and nurses.[18]

This study has several noteworthy limitations. First, we performed a post-hoc subgroup analysis of the CAPTION trial. As such, enrollment criteria were not developed to explicitly study patients with TRH; thus, we cannot exclude the possibility that the benefits of randomization were lost in the present analysis. Nevertheless, measured baseline characteristics were generally well-balanced between treatment arms and a number of factors were controlled for in the primary outcome models. Second, although the prevalence of CKD or diabetes was similar between treatment arms, it was quite low overall in this study population (28%) compared with the overall CAPTION population (50%) and many previous studies of patients with TRH. The reason for this discrepancy is unclear, but it is possible that patients with TRH and more advanced CKD had their hypertension managed by someone other than their primary care provider (e.g., a nephrologist), which may have led to lower inclusion of these patients in the CAPTION trial. Lastly, clinic assignment was unmasked and these results are generalizable only to similar primary care settings. Importantly, all clinics had existing clinical pharmacy services prior to enrollment in the trial; whether our results would be duplicated in clinics without prior clinical pharmacy services is not known.

Conclusion

We observed, for the first time, a significantly greater reduction in systolic BP with physician-pharmacist collaboration, compared with usual care in the primary care setting, among a geographically- and racially-diverse group of patients with TRH. The benefits of the PPCM model are likely multifactorial in this population, and may include more frequent

follow-up, optimization of antihypertensive regimens, and greater medication adherence. Strategies to further improve the efficacy of this model need to be explored. Additional research also is needed to determine the impact of this intervention, and others, on hard outcomes beyond BP-lowering in persons with TRH.[41] Nevertheless, our results add further empirical evidence to the use of such models in hypertension treatment generally, and extend these previous findings to those with TRH.

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Highlights

- Treatment-resistant hypertension is common among patients with hypertension treated in the primary care setting
- Pharmacist/physician team-based care is more effective than usual primary care at reducing blood pressure in treatment-resistant hypertension
- The benefits of team-based care may derive from more frequent follow-up, drug optimization, and improved adherence

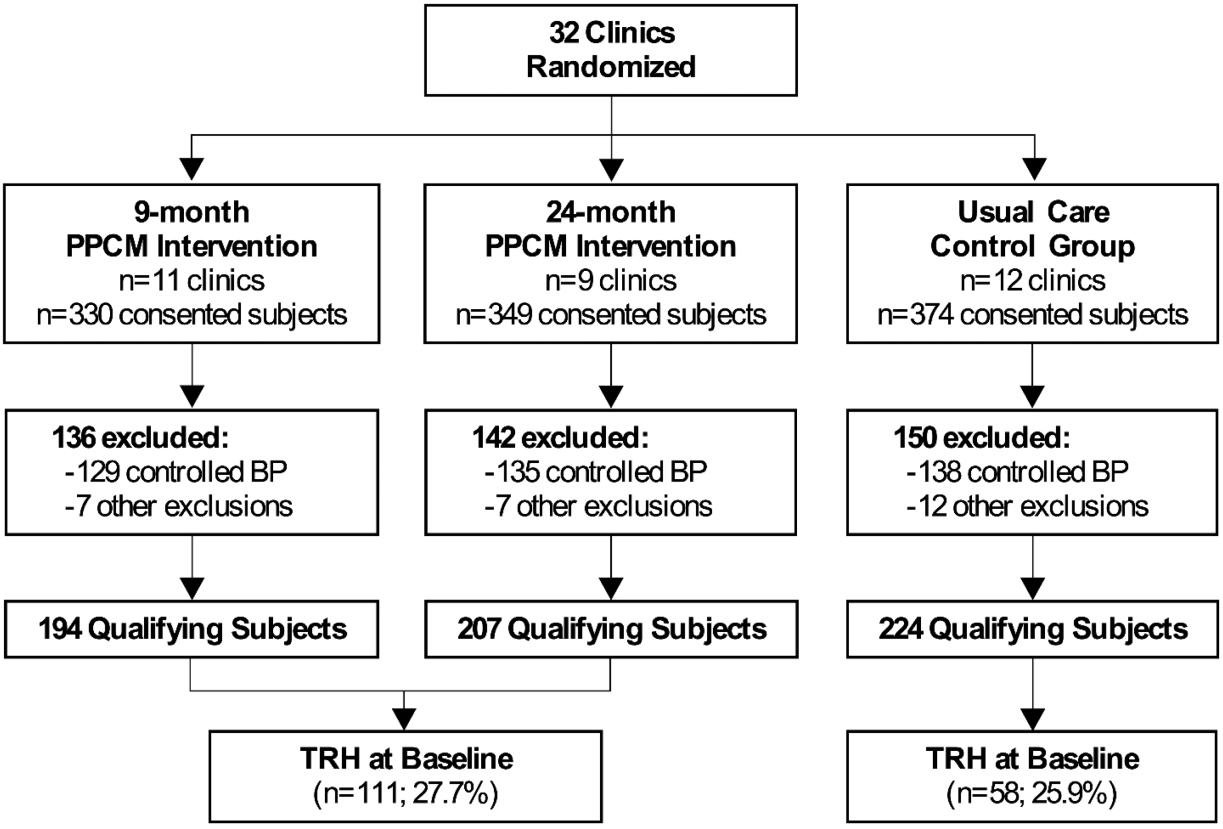

Figure.
Flow diagram for study cohort development.

Table 1

Baseline characteristics of patients by treatment arm.

Variable	PPCM Intervention (n=111)	Usual Care (n=58)	p-value
Age, years	62.9 (11.7)	65.2 (11.2)	0.17
Female Sex	81 (73%)	34 (58.6%)	0.12
Race/Ethnicity			
Non-Hispanic White	35 (31.5%)	23 (39.7%)	0.34
Minority	74 (66.7%)	35 (60.3%)	
Non-Hispanic Black	52 (46.8%)	23 (39.7%)	
Hispanic	18 (16.2%)	11 (18.9%)	
Other	4 (3.6%)	1 (1.7%)	
Declined to answer/missing	2 (1.8%)	0 (0.0%)	
Education Level			
≤12 Years	63 (56.8%)	32 (55.2%)	0.81
>12 Years	48 (43.2%)	26 (44.8%)	
Marital Status			
Married	51 (45.9%)	27 (46.6%)	0.25
Not married	60 (54.1%)	31 (53.4%)	
Insurance coverage			
Medicare	44 (39.6%)	30 (51.7%)	<0.0001
Private and Other	35 (31.5%)	16 (27.6%)	
Medicaid	18 (16.2%)	7 (12.1%)	
Free and None/Self-Pay	14 (12.6%)	5 (8.6%)	
Annual income			
<$25,000	67 (60.4%)	33 (56.9%)	0.11
≥$25,000	44 (39.6%)	25 (43.1%)	
Smoking status			
Current smoker	17 (15.3%)	6 (10.3%)	0.28
Former smoker	35 (31.5%)	14 (24.1%)	
Never smoker	57 (51.4%)	38 (65.5%)	
Missing	2 (1.8%)	0 (0.0%)	
Alcohol intake			
No alcohol intake	73 (65.8%)	42 (72.4%)	0.46
Any alcohol intake	37 (33.3%)	15 (25.9%)	
Missing	1 (0.9%)	1 (1.7%)	
Diabetes or Kidney Disease	34 (30.6%)	14 (24.1%)	0.22
Duration of Hypertension			
≤3 years	5 (4.5%)	4 (6.9%)	0.27
>3 to ≤10 years	39 (35.1%)	17 (29.3%)	
>10 years	67 (60.4%)	37 (63.8%)	

Variable	PPCM Intervention (n=111)	Usual Care (n=58)	p-value
Systolic Blood Pressure, mm Hg	149.0 (15)	150.2 (16)	0.038
Diastolic Blood Pressure, mm Hg	83.5 (13)	78.9 (12)	0.21
No. of Antihypertensive Medications			
3	70 (63.1%)	38 (65.5%)	0.99
4	26 (23.4%)	12 (20.7%)	
5	11 (9.9%)	6 (10.3%)	
6	4 (3.6%)	2 (3.4%)	
Antihypertensive Medication Adherence			
High (score ≤1)	97 (87.4%)	51 (87.9%)	0.75
Low (score >1)	14 (12.6%)	6 (10.3%)	
Missing	0 (0.0%)	1 (1.7%)	

Data are presented as n (%) or mean (SD).

Table 2

Baseline antihypertensive medication use, by treatment arm.

Antihypertensive Use	PPCM Intervention (n=111)	Usual Care (n=58)	p-value
By Antihypertensive Class			
Diuretic	96 (86.5%)	44 (75.9%)	0.09
ACE-I	71 (64.0%)	45 (77.6%)	0.08
ARB	33 (29.7%)	12 (20.7%)	0.27
DHP-CCB	66 (59.5%)	34 (58.6%)	1.00
Non DHP-CCB	12 (10.8%)	9 (15.5%)	0.46
β-blocker	82 (73.9%)	45 (77.6%)	0.71
Aldosterone Antagonist	5 (4.5%)	3 (5.2%)	1.00
DRI	1 (0.9%)	0 (0.0%)	1.00
α_1-antagonist	3 (2.7%)	6 (10.3%)	0.06
α_2-agonist	9 (8.1%)	10 (17.2%)	0.12
Vasodilator	6 (5.4%)	2 (3.4%)	0.72
By Specific Regimen			
ACE-I + diuretic + DHP-CCB	32 (28.8%)	17 (29.3%)	1.0
ACE-I + diuretic + non-DHP-CCB	7 (6.3%)	5 (8.6%)	0.55
ARB + diuretic + DHP-CCB	17 (15.3%)	6 (10.3%)	0.48
ARB + diuretic + non-DHP-CCB	4 (3.6%)	1 (1.7%)	0.66
ACE-I + ARB	5 (4.5%)	1 (1.7%)	0.67
ARB + DRI	1 (0.9%)	0 (0%)	1.0
β-blocker + diuretic + DHP-CCB	40 (36%)	14 (24.1%)	0.12
DHP-CCB + non-DHP-CCB	1 (0.9%)	3 (5.2%)	0.12
β-blocker + non-DHP-CCB	7 (6.3%)	5 (8.6%)	0.55
Any fixed-dose combination pill	9 (8.1%)	11 (19%)	0.05
Any duplication of single class	13 (11.7%)	5 (8.6%)	0.61

ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; DHP, dihydropyridine; DRI, direct renin inhibitor.

Table 3

Nine-month antihypertensive medication use, by treatment arm.

Antihypertensive Use	PPCM Intervention (n=94)	Usual Care (n=50)	p-value
By Antihypertensive Class			
Diuretic	84 (89.4%)	40 (80.0%)	0.14
ACE-I	53 (56.4%)	33 (66.0%)	0.29
ARB	30 (31.9%)	14 (28.0%)	0.71
DHP-CCB	60 (63.8%)	30 (60.0%)	0.72
Non DHP-CCB	12 (12.8%)	7 (14.0%)	0.80
β-blocker	71 (75.5%)	35 (70.0%)	0.55
Aldosterone Antagonist	17 (18.1%)	3 (6.0%)	0.07
DRI	1 (1.1%)	0 (0.0%)	1.00
α_1-antagonist	2 (2.1%)	6 (12.0%)	0.02
α_2-agonist	7 (7.4%)	4 (8.0%)	1.00
Vasodilator	3 (3.2%)	2 (4.0%)	1.00
By Specific Regimen			
ACE-I + diuretic + DHP-CCB	33 (35.1%)	17 (34%)	1.0
ACE-I + diuretic + non-DHP-CCB	8 (8.5%)	4 (8%)	1.0
ARB + diuretic + DHP-CCB	11 (11.7%)	7 (14%)	0.79
ARB + diuretic + non-DHP-CCB	4 (4.3%)	0 (0%)	0.30
ACE-I + ARB	2 (2.1%)	3 (6%)	0.34
ARB + DRI	1 (1.1%)	0 (0%)	1.0
β-blocker + diuretic + DHP-CCB	39 (41.5%)	16 (32%)	0.29
DHP-CCB + non-DHP-CCB	6 (6.4%)	6 (12%)	0.34
β-blocker + non-DHP-CCB	0 (0%)	0 (0%)	-
Any fixed-dose combination pill	6 (6.4%)	13 (26%)	<0.01
Any duplication of single class	2 (2.1%)	4 (8%)	0.18

ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; DHP, dihydropyridine; DRI, direct renin inhibitor.

Table 4

Adjusted mean systolic and diastolic blood pressure at 9 months.

Blood Pressure	PPCM Intervention (n=94)	Usual Care (n=50)	Adjusted Difference (95% CI)	p-value
Systolic BP				
Mean ± SD	132 ± 16	141 ± 20	−6.62 (−12.8, −0.44)	0.036
(Min, Max)	(96, 167)	(83, 185)		
Diastolic BP				
Mean ± SD	75 ± 12	73 ± 13	−0.37 (−4.07, 3.33)	0.84
(Min, Max)	(52, 103)	(38, 101)		