

# A Randomized Controlled Trial of Negative Co-Payments: The CHORD Trial

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Insurers are widely adopting value-based insurance design (V-BID), which is based on the premise that reducing costs will significantly increase the use of beneficial and cost-effective services. These approaches are seen as a way of trying to address widespread problems with adherence to medication for chronic diseases, as there is strong evidence that medication adherence for such chronic diseases as hypertension and hypercholesterolemia is low,<sup>1-5</sup> limiting the potential for medications with high efficacy in randomized controlled trials to improve the health of the population. V-BID designs are also being used more broadly to increase the use of high-value services and reduce the use of low-value services through differential co-payments tied to the value of services. However, although observational studies have consistently shown that increases in co-payments are associated with both decreases in utilization of medications and worse outcomes,<sup>6-14</sup> the impact of decreasing co-payments seen in observational studies has been more modest<sup>15-22</sup>; the underlying psychology of how people process changes in payments as losses compared with gains suggests that increases and decreases in co-payments may not be equivalent.<sup>23</sup>

Nearly two-thirds of Americans with hypertension have poor control,<sup>24</sup> which puts them at risk for substantial morbidity and mortality; poor adherence is an important factor in poorly controlled hypertension. Taking the logic behind V-BID initiatives that lower financial burden might improve adherence and patient outcomes one step further; we examined whether providing incentives of \$8 per medication per month (a type of “negative co-payment”) for all antihypertensive medications would significantly improve blood pressure control among patients with poorly controlled blood pressure at 3 medical centers in Pennsylvania.

## ABSTRACT

**Objectives:** Value-based insurance designs are being widely used. We undertook this study to examine whether a financial incentive that lowered co-payments for blood pressure medications below \$0 improved blood pressure control among patients with poorly controlled hypertension.

**Study Design:** Randomized controlled trial.

**Methods:** Participants from 3 Pennsylvania hospitals (n = 337) were randomly assigned to: a) be paid \$8 per medication per month for filling blood pressure prescriptions, b) a computerized behavioral intervention (CBI), c) both payment and CBI, or d) usual care. The primary outcome was change in blood pressure between baseline and 12 months post enrollment. We also measured adherence using the medication possession ratio in a subset of participants.

**Results:** There were no significant interactions between the incentive and the CBI interventions. There were no significant changes in medication possession ratio in the treatment group. Blood pressure decreased among all participants, but to a similar degree between the financial incentive and control groups. Systolic blood pressure (SBP) dropped 13.7 mm Hg for the incentive group versus 10.0 mm Hg for the control group (difference = -3.7; 95% CI, -9.0 to 1.6; *P* = .17). The proportion of patients with blood pressure under control 12 months post enrollment was 35.6% of the incentive group versus 27.7% of the control group (odds ratio, 1.4; 95% CI, 0.8-2.5; *P* = .19). Diabetics in the incentive group had an average drop in SBP of 12.7 mm Hg between baseline and 12 months compared with 4.0 mm Hg in the control group (*P* = .02). Patients in the incentive group without diabetes experienced average SBP reductions of 15.0 mm Hg, compared with 16.3 mm Hg for control group nondiabetics (*P* = .71).

**Conclusions:** Among patients with poorly controlled blood pressure, financial incentives—as implemented in this trial—did not improve blood pressure control or adherence except among patients with diabetes.

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### Take-Away Points

Improving medication adherence through small rewards that lower co-payments below \$0 may be effective in subgroups of the population, but may not improve outcomes overall. Consideration should be given to further testing of this approach in carefully selected high-risk populations in which increased adherence could have significant economic and health benefits.

## METHODS

### Study Population

Study participants were drawn from patients at 3 hospitals in Pennsylvania: the Philadelphia Veterans Affairs Medical Center (PVAMC), the Veterans Administration Pittsburgh Health Care System (VAPitt), and the PinnacleHealth clinic in Harrisburg, with recruitment occurring between March 2005 and July 2007. (Figure 1 shows the study flow.) Potential participation was elicited by sending letters to patients who met eligibility criteria based on electronic or manual screening of records. Eligible patients were aged  $\geq 21$  years, with 1 or more active prescriptions for an anti-hypertensive medication, and systolic blood pressure (SBP) of at least 140 mm Hg (130 mm Hg in patients with diabetes), and with eligibility to receive medications without co-payments (due to low income or disability). Exclusion criteria included participation in another experimental study, markedly shortened life expectancy (due to diagnosis of metastatic cancer, end-stage renal disease on dialysis, New York Heart Association class IV congestive heart failure, or dementia), or atrial fibrillation (because of concerns with accuracy of blood pressure measurement). We enrolled 337 of the 1253 potentially eligible participants in the study (see Figure 1); approximately 20% of screened potentially eligible patients were excluded due to ineligibility.

### Study Protocol

The protocol was approved by the Institutional Review Boards of the PVAMC, VAPitt, PinnacleHealth, and the University of Pennsylvania, and all participants provided written informed consent prior to randomization. The study was registered at [clinicaltrials.gov](http://clinicaltrials.gov) as Collaboration to Reduce Disparities in Hypertension, ID #NCT00133068. Participants were randomized to receive either: a) a financial incentive of \$8 per medication prescription filled per month, b) a computerized behavioral intervention (CBI) provided at enrollment and at the 6-month follow-up visit, c) both the financial incentives and the CBI, or d) usual care (with study follow-up visits every 3 months). After an initial visit, participants were requested to return for follow-up blood pressure readings and surveys at 3, 6, 9, and 12 months; financial rewards were paid at each fol-

low-up visit after confirmation that each prescription was filled using either the VA's computer records, a prescription bottle, or a receipt. The CBI was designed to help study participants learn the basics about blood pressure control and its impact. Participants watched a video testimonial from a patient

who had had multiple strokes due to medication nonadherence, and who felt he had learned the importance of medication adherence from that experience. This helped participants improve self-efficacy by reviewing techniques that could be used to enhance adherence.

### Randomization Procedures

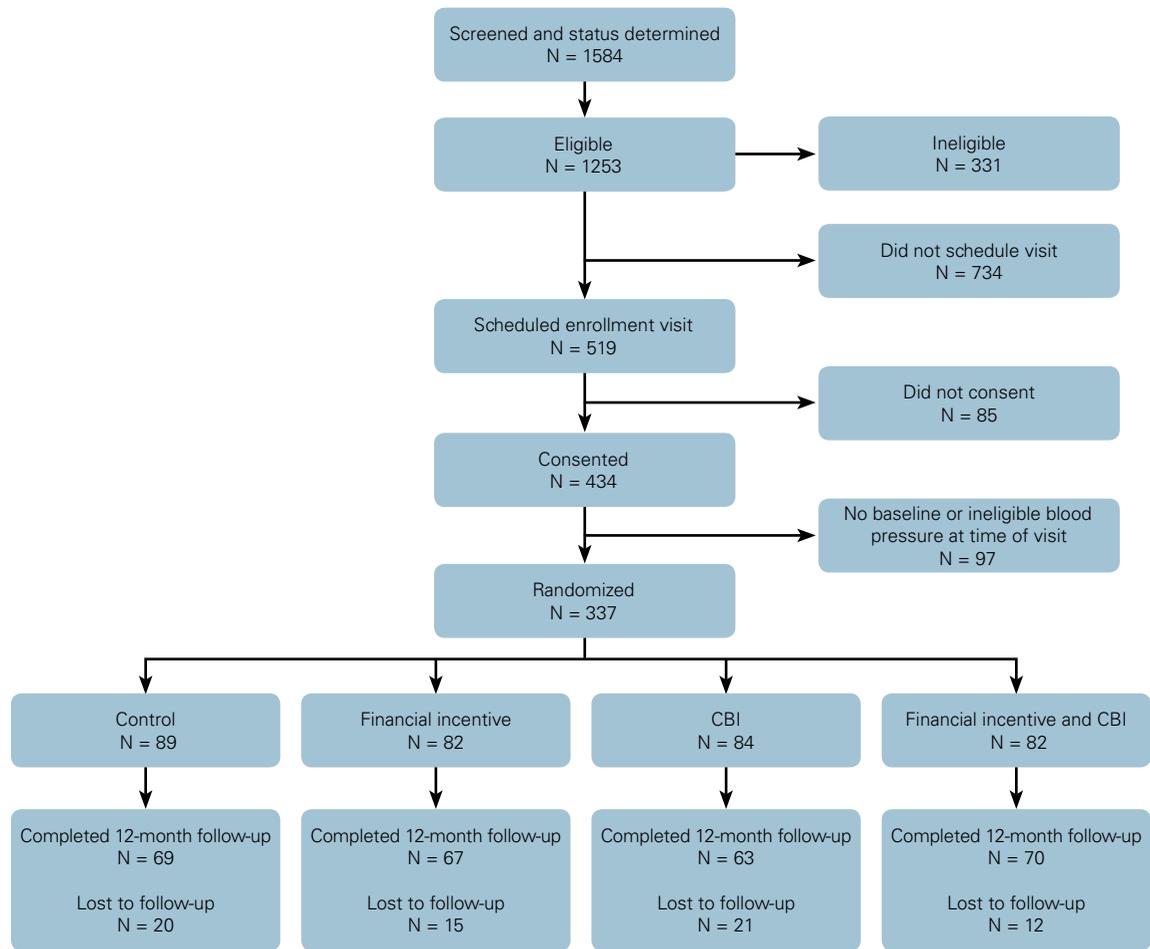
Randomization was carried out using a random number generator and via permuted block randomization with a block size of 4. Randomization was stratified by site, income (<100%, 100%-200%, 200%-300%, and >300% of the federal poverty level [FPL]), and baseline blood pressure (SBP <160 mmHg or SBP  $\geq 160$  mm Hg). Randomization was performed after signed written consent forms were received. Allocation assignments were concealed, with staff unable to access randomization assignment for each subject until all eligibility criteria were entered in an electronic tracking system and consent forms were completed. Neither staff nor study participants could be blinded due to the nature of the intervention; investigators and analysts, however, remained blinded to intervention assignments until unblinding occurred, in coordination with the Data Safety Monitoring Board, once follow-ups were nearly complete.

### Outcome Assessments

The primary outcome variable was change in blood pressure from enrollment to 12 months post enrollment. Secondary outcome variables included change in blood pressure 6 months post enrollment, the percentage of patients with blood pressure in control at 6 and 12 months post enrollment, self-reported medication adherence, and prescription refill data from the VA electronic medical record system. Blood pressure control was defined as SBP below 140 mm Hg and diastolic blood pressure (DBP) below 90 mm Hg for patients without diabetes; for participants with diabetes, blood pressure control was defined as SBP below 130 mm Hg and DBP below 85 mm Hg.

Measurement of blood pressure was done following a standardized protocol using an automated blood pressure cuff (Omron HEM-90R), ensuring that the correct cuff size was used.<sup>25</sup> Participants were instructed to relax for 5 minutes before their blood pressure was taken; then the pa-

■ **Figure 1.** Flow Diagram of Trial Participation



CBI indicates computer-based intervention.

tient’s arm (the dominant arm unless the patient expressed a preference to use the other arm) was supported on a chair or desk and the blood pressures were measured while the patient was sitting. Three measurements were taken, 2 minutes apart, and averaged. The blood pressure measurements were not revealed to the study participants. Although the study nurses could not be blinded to the randomization, the use of an automated blood pressure cuff and a standardized protocol protected against systematic differences among groups in the way blood pressure was measured.

Medication adherence was measured using self-reporting based on the Hill-Bone Scale,<sup>26</sup> with supplemental assessment using electronic prescription fill records where available. For these records, we calculated medication possession ratios (MPRs; number of days a patient had a filled prescription divided by 360 days) and gap ratios

of 30, 60, and 90 days (percentage of patients who had gaps in filled prescriptions of at least 30, 60, or 90 days).<sup>27</sup>

**Covariates**

Baseline blood pressure levels were assessed with other factors including height, weight, and creatinine level. We also collected information on income, baseline health status, health history, medication use, age, gender, and self-reported race or ethnicity. We used information on income and family size to calculate income as a percent of the FPL.

**Statistical Analysis**

To evaluate the similarity of the treatment groups with respect to baseline covariates, we compared groups using Student’s *t* test for continuous variables and  $\chi^2$  test for categorical variables, with Fisher’s Exact tests used for analy-

ses with 5 or fewer subjects per cell. The trial was designed to test the effects of the 2 interventions individually; we did not assume an interaction, but powered the study adequately for individual comparisons of the 3 active arms against control. The primary analysis of the financial incentive began with a formal statistical test of interaction between the incentive and CBI; there was no evidence of this, so we collapsed across the CBI arms to assess the effect of the financial incentive alone.

The primary unadjusted analyses tested the mean differences in the degree of change in SBP and DBP between the incentive and control groups from baseline to 12 months post enrollment using Student's *t* test. We similarly calculated differences in change in blood pressure from baseline to 6 months post enrollment. Some participants had missing blood pressure values at 6 and 12 months; we compared baseline data between participants with and without follow-up values. Missing values for 6-month and 12-month SBP and DBP readings were handled using the Markov Chain Monte Carlo multiple imputation method, utilizing 10 imputations after verification that this yielded relative efficiencies of 95% or higher; we also checked that imputed values were within the range of observed values.<sup>28</sup> Separate imputation regression models were implemented for SBP and DBP. The primary analyses were conducted on each of the 10 imputed data sets and the results combined using the standard approach to yield a single result. Unadjusted odds ratios (ORs) for achieving in-control blood pressure were estimated via logistic regression using the imputed data in the same manner. We compared the results using multiply imputed data with models using a baseline observation carried-forward approach and with a last observation carried-forward approach.

Regression coefficients and their 95% confidence intervals (CIs) were estimated from an unadjusted linear regression model that incorporated only a factor indicating receipt of incentives versus control; these were compared with regression coefficients estimated from a model adjusted for the stratification variables (site, high SBP, and income), in all cases using the imputed data. In addition to prespecified subgroup analyses on race and income, we examined changes in SBP and DBP in a priori subgroups defined by study site, initial SBP ( $\geq 160$  mm Hg vs  $< 160$  mm Hg), presence of diabetes, and education level (high school or lower, some college or college degree, beyond college). Homogeneity of the association between treatment groups and blood pressure change across subgroups was tested by assessing the significance of appropriate interaction terms included in the linear regression models described above.

The trial was powered to ensure that clinically meaningful differences in SBP of 10 mm Hg and in DBP of 5 mm Hg<sup>29,31</sup> could be detected in any of the contrasts discussed above, assuming an interaction between the CBI and incentive interventions. We used an alpha of 0.05 and standard deviations of change in SBP and DBP of 20 mm Hg and 10 mm Hg, respectively (based on the upper limit of standard deviation directly measured in clinical trials).<sup>32,33</sup> Based on these estimates, we projected we would need 63 subjects per arm to detect the clinically meaningful difference in BPs discussed above. To accommodate an estimated 20% loss to follow-up, recruitment goals for each arm were increased to 79 subjects, for a total of 316 subjects. The trial was not explicitly powered to detect effects on adherence; post hoc calculations indicate approximately 80% power to detect a difference of 8 percentage points in the MPR.

## RESULTS

Study characteristics were generally balanced across the arms of the study (Table 1); exceptions are noted below. The average age was 61 years, with approximately 81% males, 5% Hispanic, and 61% black; there were significantly more blacks in the control group ( $P = .01$ ). About 45% had incomes below 100% of the FPL, 26% at 100% to 200% FPL, 12% at 200% to 300% FPL, and the remainder above 300% FPL. Baseline SBP and DBP readings averaged 154 and 84 mm Hg, respectively.

Follow-up rates were slightly higher among incentive arm participants at 12 months, but the difference in follow-up rates was not significantly different (84% in incentive arms, 76% in nonincentive arms;  $P = .10$ ) (Figure 1). Baseline SBP, number of antihypertensive medications, or number of medications overall did not differ between those who were lost to follow-up and those participants for whom we had data at 12 months.

Mean changes in SBP were  $-9.8$  mm Hg (95% CI,  $-15.0$  to  $-4.5$ ) in the control group,  $-12.6$  (95% CI,  $-18.0$  to  $-7.1$ ) in the co-payment reduction group,  $-10.2$  (95% CI,  $-15.4$  to  $-5.1$ ) in the CBI group, and  $-14.8$  (95% CI,  $-19.9$  to  $-9.7$ ) in the combined co-payment/CBI group. There were no significant interactions between incentive payments and receipt of the computerized behavioral intervention with respect to 12-month outcomes ( $P = .76$ ). Therefore, the primary and all subsequent analyses are collapsed across CBI status to focus on the impact of \$8 incentives on blood pressure and outcomes (hereafter comparison of "incentive" vs "control").

### Primary and Secondary Outcomes

Baseline and follow-up MPR values were available for 79 control group participants and 69 incentive group par-

■ **Table 1.** Characteristics of Study Participants

Variable	Negative Co-Pay (n = 164)	Control (n = 173)	P
<b>Demographics</b>			
Average age: years (SD)	62.2 (11.5)	59.8 (11.4)	.05
Male: %	78.7	82.7	.35
White: %	37.4	30.6	
Black: %	54.6	67.1	.01
Other race: %	8.0	2.3	
Hispanic ethnicity: %	6.8	3.5	.22
<b>Site</b>			
Philadelphia VA: %	46.3	49.1	
Pinnacle: %	21.3	22.0	.79
Pittsburgh VA: %	32.3	28.9	
<b>Education</b>			
High school graduate or less: %	56.3	54.1	
Some college or college graduate: %	36.9	39.0	.92
Beyond college: %	6.9	7.0	
<b>Income</b>			
<100% FPL: %	43.9	45.7	
100%-200% FPL: %	25.0	27.2	.88
200%-300% FPL: %	13.4	11.6	
>300% FPL: %	17.7	15.6	
<b>Baseline blood pressure</b>			
Systolic blood pressure: mm Hg (SD)	155.3 (14.5)	153.3 (15.5)	.22
Diastolic blood pressure: mm Hg (SD)	83.8 (13.5)	83.9 (13.9)	.93
<b>Medication taking</b>			
No. of hypertensive medications (SD)	2.6 (1.3)	2.5 (1.4)	.62
No. of medications overall (SD)	6.2 (2.9)	5.8 (3.0)	.26
<b>Comorbidities (%)</b>			
Diabetes	56.7	51.5	.33
Congestive heart failure	14.1	13.9	.95
Heart attack or AMI	15.2	13.3	.61
Kidney failure	6.1	3.5	.31
Stroke	9.2	9.3	.99
TIA or mini-stroke	11.7	15.6	.29
High cholesterol	67.1	57.8	.08
AMI indicates acute myocardial infarction; FPL, federal poverty level; TIA, transient ischemic attack; VA, Veterans Administration.			

participants. There was no relative difference in the change in MPR between baseline and 12 months (−0.35% and 3.08% in the control and incentive groups, respectively;  $P = .36$ ). Changes, as measured by gaps in the MPR of 30

days (OR, 0.7; 95% CI, 0.3-1.4;  $P = .30$ ), 60 days (OR, 1.5; 95% CI, 0.6-3.6;  $P = .39$ ), or 90 days (OR, 1.7; 95% CI, 0.6-5.0;  $P = .32$ ) indicated no differences between the control and incentive groups.

■ **Table 2.** Change in Blood Pressure From Baseline to 12 Months

Outcome measures	Negative Co-Pay (n = 162)	Control (n = 173)	Difference Between Groups (95% CI)	P
Change in blood pressure				
Systolic blood pressure: mm Hg	-13.7	-10.0	-3.7 (-9.0 to 1.6)	.17
Diastolic blood pressure: mm Hg	-6.8	-4.1	-2.7 (-5.6 to 0.2)	.07
	Negative Co-Pay (n = 239)	Control (n = 240)	Odds Ratio (95% CI)	P
% who reached goal	35.6	27.7	1.4 (0.8-2.5)	.19

We found no significant difference in blood pressure reduction between the incentive and control groups (Table 2). The incentive group lowered their SBP by 13.7 mm Hg on average versus 10.0 mm Hg for the control group ( $P = .17$ ). The drop in DBP was 6.8 mm Hg for the incentive group compared with 4.1 mm Hg for the control group ( $P = .07$ ). At the end of 12 months, 35.6% of the incentive group had their blood pressure in control versus 27.7% for the control group (OR, 1.4; 95% CI, 0.8-2.5;  $P = .19$ ). Results of sensitivity analyses in which we assumed that the blood pressure in all patients lost to follow-up was equal to their last measured value or their baseline blood pressure (as opposed to the imputed blood pressure value) were qualitatively similar. Adjusted estimates of changes in SBP indicated no significant differences between incentive and control groups in the degree of change in blood pressure (Table 3).

### Subgroup Analyses

The degree of change in SBP between the incentive and control groups was compared among several a priori subgroups of the populations in the study, including those with and without diabetes, those with a baseline SBP above or below 160 mm Hg, and subgroups determined by race, income, and education. The subgroup of patients with diabetes showed a significant difference between the incentive and control groups ( $P$  for interaction = .04). Specifically, patients with diabetes in the incentive group had an average drop in SBP of 12.7 mm Hg between baseline and 12-month follow-up, while patients with diabetes in the control group had an average SBP reduction of only 4.0 mm Hg ( $P$  for the difference = .02). This difference was driven primarily by continued improvement in blood pressure between months 6 and 12 in the incentive group compared with a lack of such improvement in the control group (Figure 2). Patients without diabetes experienced an average SBP reduction of 15.0 mm Hg compared

with an average reduction of 16.3 mm Hg for individuals without diabetes in the control group ( $P$  value for the difference = .71.) None of the other subgroups experienced any significant differences.

## DISCUSSION

In the first randomized controlled trial to provide financial incentives for antihypertensive medication prescription filling among patients with poorly controlled hypertension, we found no overall improvement in blood pressure control. We did see a relative improvement in blood pressure among patients with diabetes, but not among other subgroups.

These findings are important to ongoing discussions about V-BID, and specifically efforts to improve patient outcomes through reducing financial burdens for high-value prescription medications.<sup>34,35</sup> Recent efforts to reduce the degree of patient cost sharing based on the value of prescriptions have garnered extensive interest among payers and employers.<sup>36,37</sup>

Whereas increases in prescription co-payments have been associated with decreases in medication adherence and worse outcomes in numerous studies,<sup>6,7,27</sup> only 2 clinical trials have examined the question of to what degree decreasing co-payments improves outcomes. The most definitive randomized trial on the impact of cost sharing on healthcare utilization—the RAND Health Insurance Experiment (HIE)—found sizable effects of patient cost sharing on use and expenditures, but more modest effects on health status. This was also performed more than 25 years ago when less effective medications were available; in addition, it excluded the elderly, more than 80% of the subjects were Caucasian, and it included a population with relatively few comorbidities<sup>38</sup>—a population for whom prescription drug coverage is most likely to be cost-effective. Of note, among low-income persons

■ **Table 3. Twelve-Month Systolic Blood Pressure Change—Regression Coefficient Estimates**

Group	Parameter	BP Change (95% CI)
Unadjusted model		
Intercept	No intervention	-10.0 (-13.5 to -6.5)
Study arm	Co-pay intervention	-3.7 (-9.0 to 1.6)
Adjusted for stratification variables only		
Intercept	No intervention Site = Philadelphia VA SBP at baseline <160 Income >300% FPL	-7.1 (-14.3 to 0.0)
Study arm	Copay intervention	-2.5 (-7.6 to 2.7)
Site	Pinnacle	1.3 (-6.0 to 8.5)
	Pittsburgh VA	-0.7 (-6.7 to 5.3)
SBP at baseline	SBP ≥160 mm Hg	-14.7 (-20.2 to -9.3)
	<100% FPL: %	3.2 (-4.1 to 10.4)
Income	100% to 200% FPL: %	-0.3 (-7.9 to 7.4)
	200% to 300% FPL: %	-0.3 (-9.6 to 9.1)

BP indicates blood pressure; FPL, federal poverty level; SBP, systolic blood pressure; VA, Veterans Administration.

with high blood pressure, free care resulted in significant improvements in blood pressure. However, the RAND HIE randomly assigned roughly 2000 families to 1 of 14 experimental health plans that varied in their cost-sharing arrangements for all medical goods and services. The Post-Myocardial Free Rx Event and Economic Evaluation Trial (MI-FREEE) demonstrated that making medications free post acute myocardial infarction increased MPRs by about 5 to 6 percentage points (control group average MPR, 38.9%), which was associated with reductions in the rate of total major vascular events or revascularization without any increase in total healthcare spending.<sup>36</sup>

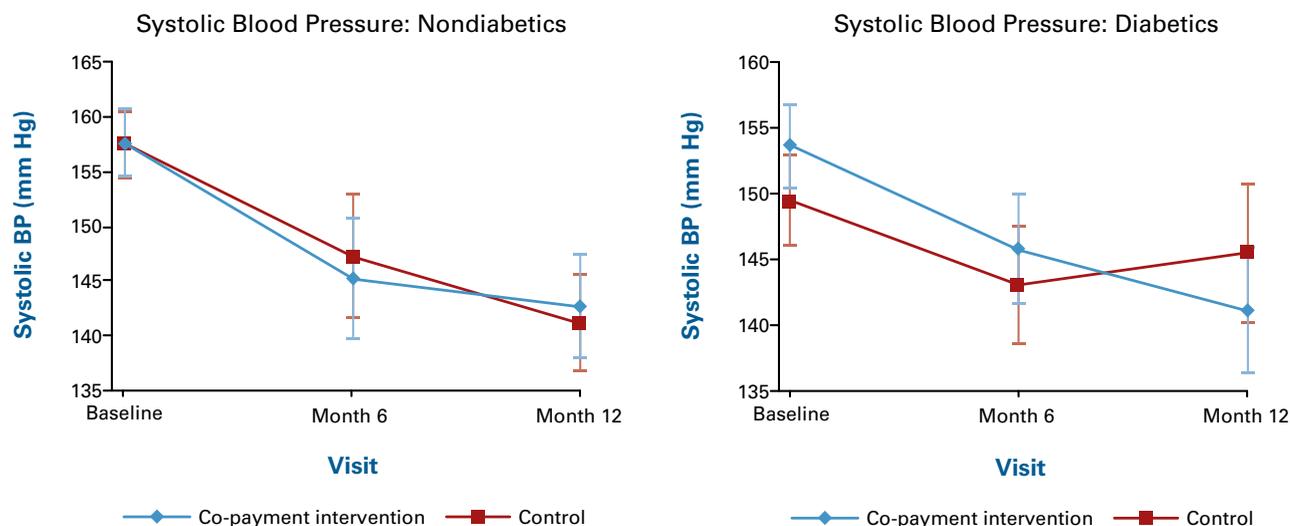
Several observational studies have now indicated that lowering co-payments in a V-BID framework is associated with increases in MPR of about 3 to 5 percentage points on a base of about 60% to 80%.<sup>15-19,22</sup> While such effects are statistically significant in large populations, these studies did not measure clinical outcomes and it seems unlikely that changes of this magnitude in MPR would have large clinical effects within a population. The findings of this study suggest that small reductions in co-payment below \$0 do not significantly improve blood pressure or MPRs.

### Limitations

There are a number of reasons why financial incentives may have less of an impact on health than increases in co-payments. First, increases in co-payments affect utilization primarily among adherent patients, whereas financial incentives are targeted at affecting utilization among nonadherent patients in whom a change in cost of a given magnitude (ie, from \$0 to -\$8) is likely to have less impact. Second, increases in co-payments are likely processed as a loss by patients and behavioral economists have demonstrated that losses are felt much more strongly than equivalent gains.<sup>23</sup> Third, incentives may be a bit like “the dog that didn’t bark.” For a nonadherent patient who doesn’t come to the pharmacy or fill prescriptions, communications about a financial incentive may be largely ignored. Fourth, we limited eligibility for the study to individuals who paid no co-payments at baseline; such individuals may have been less attuned to co-payments in relation to prescriptions since, at baseline, they would have had less reason to pay attention to co-payments.

Because studies have indicated that unbundling rewards from other payments make the rewards more

■ **Figure 2.** Change in Systolic Blood Pressure Over Time for Patients With and Without Diabetes



effective<sup>39</sup> and due to the fact that the PinnacleHealth system patients filled prescriptions at a large number of pharmacies in the Harrisburg area in which we could not control point-of-service pricing, we provided post hoc rebates rather than incentives at point of service. The lack of an overall effect on blood pressure or adherence could be due to this design feature of the trial. This had the disadvantage of introducing time delays in feedback after the incited behavior occurred. Other limitations include the incentive magnitude, as it may have been too small to induce changes in behavior, though previous work suggested that in low-income populations, co-payment increases as low as \$0.50 to \$1 per prescription (approximately \$2-\$3 adjusting for inflation) can reduce drug utilization.<sup>40</sup> The study was conducted primarily among veterans at 2 VA hospitals, and thus had primarily male participants, although there are no obvious reasons to believe that the interventions would be less effective in men than women.

## CONCLUSIONS

Financial incentives for blood pressure medications had little impact on blood pressure control except, perhaps, among patients with diabetes. Because this was an isolated finding in 1 subgroup, we conclude this intervention did not systematically improve patient outcomes. Further initiatives should examine the comparative effectiveness of different ways of delivering such incentives, the relationship between the magnitude of incentives and effectiveness, and the impact on different populations.

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