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Telemedicine cardiovascular risk reduction in veterans: The CITIES trial

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ABSTRACT

Background: Comprehensive programs addressing tailored patient self-management and pharmacotherapy may reduce barriers to cardiovascular disease (CVD) risk reduction.
Methods: This is a 2-arm (clinical pharmacist specialist–delivered, telehealth intervention and education control) randomized controlled trial including Veterans with poorly controlled hypertension and/or hypercholesterolemia. Primary outcome was Framingham CVD risk score at 6 and 12 months, with systolic blood pressure; diastolic blood pressure; total cholesterol; low-density lipoprotein; high-density lipoprotein; body mass index; and, for those with diabetes, HbA1c as secondary outcomes.
Results: Among 428 Veterans, 50% were African American, 85% were men, and 33% had limited health literacy. Relative to the education control group, the clinical pharmacist specialist–delivered intervention did not show a reduction in CVD risk score at 6 months (−1.8, 95% CI −3.9 to 0.3; $P = .10$) or 12 months (−0.3, 95% CI −2.4 to 1.7; $P = .74$). No differences were seen in systolic blood pressure, diastolic blood pressure, or low-density lipoprotein at 6 or 12 months. We did observe a significant decline in total cholesterol at 6 months (−7.0, 95% CI −13.4 to −0.6; $P = .03$) in the intervention relative to education control group. Among patients in the intervention group, 34% received at least 5 of the 12 planned intervention calls and were considered "compliers." A sensitivity analysis of the "complier average causal effect" of intervention compared to control showed a mean difference in CVD risk score reduction of 5.7 (95% CI −12.0 to 0.7) at 6 months and −1.7 (95% CI −7.6 to 4.8) at 12 months.
Conclusions: Despite increased access to pharmacist resources, we did not observe significant improvements in CVD risk for patients randomized to the intervention compared to education control over 12 months. However, the intervention may have positive impact among those who actively participate, particularly in the short term.

Cardiovascular disease (CVD) is the leading cause of death among adults worldwide.[1,2] Although adults can significantly decrease their CVD risk by adopting healthy behaviors, adherence to such behaviors is challenging and can be difficult to sustain.[3,4] There is growing consensus that the optimal management of CVD requires a comprehensive, multifactorial approach.[5,6]

The Veterans Affairs (VA) health care system continues to undergo significant changes, particularly regarding efforts to improve access to care as addressed in the VHA Blueprint for Excellence.[7] The VA, for example, has increasingly emphasized use of the Patient Aligned Care Team (PACT) to deliver multidisciplinary care. PACT is an application of the patient-centered medical home[8] that emphasizes team-based delivery of patient-centered care, coordination across specialties, open access, and value-driven care.[8] PACT stresses the utility of non–face-to-face patient care. These nontraditional encounters may reduce patients' travel cost, reduce clinic no-show appointments, and supplant some clinic visits. The VA health care system has been actively engaged in broadening the applications of telemedicine in part to increase access

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to services for its aging and often rural patient population.[9] Telephone-based care may be critical in supporting the PACT vision of coordination across different settings of care while improving both access and quality of care.

To achieve the goals of a high-functioning PACT, all members of the team must function at the highest level of their training by capitalizing on the skills and talents of all team members, which have created opportunities for evaluating the impact of different types of interventionists in the primary care setting.[10] The role of clinical pharmacist specialists (CPS) requires further evaluation in PACT settings. CPSs are pharmacists who have completed postgraduate residency training and are credentialed to prescribe, adjust, and monitor pharmacotherapy.[11] In the outpatient setting, CPS-delivered care has demonstrated improvement in the management of the individual major CVD risk factors,[11,12] but the role of CPSs supporting multifaceted CVD self-management programs is unclear.

The majority of CVD self-management care traditionally occurs in outpatient settings, where CPS-delivered care is well established. Because of time limitations and competing demands,[13,14] many aspects of CVD risk reduction may be transitioned outside of the traditional confines of an in-person clinic visit. In addition, the use of telehealth has potential for improving care delivery and health outcomes.[15] Telephone-based interventions provide an opportunity to reach more patients and may be more acceptable and convenient than in-person interventions.[16] Telephone-based strategies can facilitate individualized, personal interactions at minimal cost and without the patient time and transportation required for in-person programs. However, there is inadequate information regarding the role of CPSs in a telephonic role within the VA setting, the largest health care provider in the United States. Thus, we conducted a randomized trial to evaluate a CPS-delivered intervention administered by telephone to Veterans with hypertension and/or hypercholesterolemia.

Methods

Design, setting, and recruitment

We compared a 12-month CPS-delivered, telephone-based intervention with an educational control among Veterans receiving primary care at Durham Veterans Affairs Medical Center (VAMC) clinics. The Durham VAMC Institutional Review Board approved the study. Details of the study design have previously been reported.[17] The Clinical Trials number is NCT01142908.

Inclusion criteria

Patients were eligible if they (1) lived in North Carolina or Virginia, (2) were ≥40 years of age at baseline, (3) enrolled in 1 of 3 primary care clinics affiliated with the Durham VAMC (at least 1 visit with assigned primary care provider [PCP] in the past year), (4) had a diagnosis of hypertension or hypercholesterolemia, and (5) had poorly controlled hypertension defined by averaging all clinic-obtained blood pressure (BP) values recorded in the electronic medical record in the previous year of >150/100 mm Hg and/or *hypercholesterolemia* defined as low-density lipoprotein (LDL) value >130 mg/dL. LDL was also obtained by electronic medical record review for the same time period.

Sample identification

Participants meeting all inclusion criteria listed above were first identified from electronic medical records (Figure). Patients meeting initial screening criteria were mailed an introductory letter signed by their primary care physician offering participation in the study, as well as an opt-out phone number. The remaining eligible patients were contacted by study personnel for additional eligibility screening and to schedule an in-person meeting. At the in-person meeting, once informed consent to participate had been obtained from patients, the baseline outcome assessment was completed.

Patients were randomized 1:1 to the CPS-led intervention or education control within strata of gender, current smoking status, and current diabetes status (components of the CVD risk score) in blocks of size 2. The randomization scheme was generated via a uniform random number generator and loaded into the study's tracking database. Study team personnel informed participants of their assignment in-person at completion of the baseline outcome assessment.

Intervention

Medication management

During 12 monthly phone calls, medication adjustments were made at intervals based on patients' laboratory values, medication interactions, reported and observed medication adverse effects, clinical assessment, patients' report of medication adherence, and disease monitoring. The initial 2 encounters provided an intense review and complete medication history of the patients' cardiovascular medications.

For patients who required a prescription change, the CPS ordered the change through the VA pharmacy and coordinated any required follow-up testing through the VA laboratory. In cases where a medication change was made, a note was generated and included in the patient's medical record and co-signed by the patient's PCP acknowledging receipt of the treatment plan. When serious adverse events occurred, the CPS consulted with the patient's PCP and study clinicians to take appropriate action and/or make further recommendations.

Adverse effects of medication

At each phone call, the CPS queried the patient about any specific medication adverse effects. In the event of an adverse effect, the CPS examined how adverse effects may impact medication adherence and considered alternatives.

Cholesterol

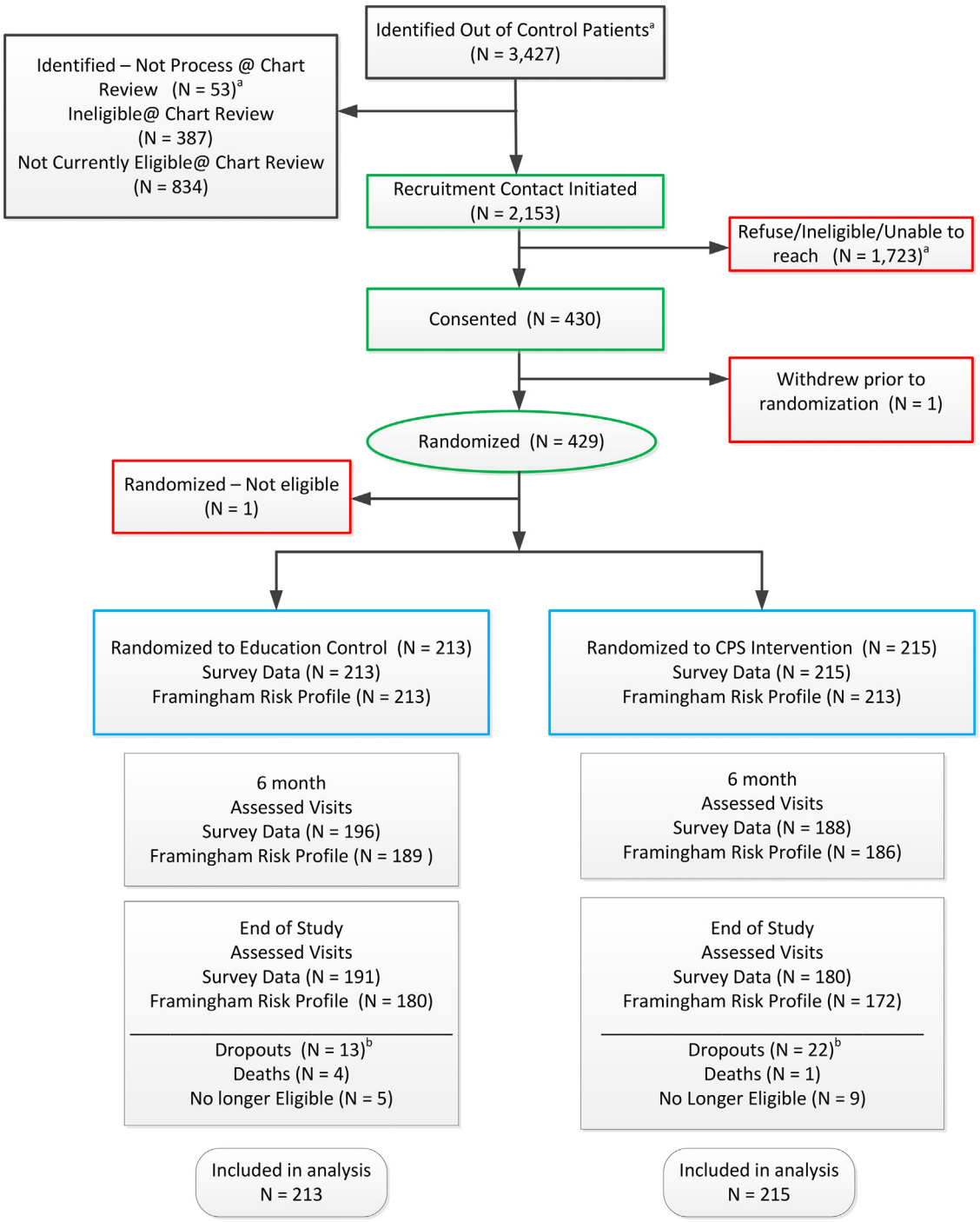
Cholesterol medication adjustments were made based on LDL concentrations obtained at the baseline and 6-month follow-up assessments. In accordance with VA guidelines at the time of the trial, cholesterol medication management was triggered for high–CVD risk patients at LDL levels >100 mg/dL.[18] The cholesterol algorithm focused on use of HMG-CoA reductase inhibitors (statins) as the primary means of bringing LDL to goal with a target LDL of <100 mg/dL.[19] Unless contraindicated, drug therapy was initiated to provide the reduction necessary to obtain LDL goals.

Home BP monitors

Patients randomized to the intervention received a VA-issued home BP monitor. Patients received training on BP monitor use and were instructed to measure and record their BP every other day.[20,21] Based upon prior work,[22] the CPS activated intensification of therapy in the intervention group based on a 2-week average home BP of >135/85 for nondiabetic and >130/80 for diabetic patients. We used these averages because BP measured at home averages 6-8 systolic BP (SBP)/5-6 diastolic BP (DBP) mm Hg lower than values obtained during a routine clinic visit.[23] The CPS reminded individuals at each encounter to record their BP values.

Blood glucose

Insulin-dependent patients performed daily self-monitored blood glucose testing equal to their number of daily insulin doses. Patients who were managed on oral hypoglycemic medications alone were encouraged to monitor blood glucose at least 1 time per week or if signs or symptoms of hypoglycemia occurred based on VA policy.[24] We evaluated each patient's monitoring technique at baseline and 6- and 12-month follow-up interviews. The medication management of diabetes followed contemporaneous American Diabetes Association standards



Foot Note: a- patients were unable to complete recruitment process due to phone outages, not showing for appointment, non-responders to phone calls. b – includes formal and informal withdrawal as well as exclusion after randomization.

Figure. Study consort. [a]Patients were unable to complete recruitment process due to phone outages, not showing for appointment, or being nonresponders to phone calls. [b]Includes formal and informal withdrawal as well as exclusion after randomization.

of care and focused on achieving target HbA1c <7.0% and preprandial fasting glucose between 90 and 130 mg/dL.[25]

Self-management component

During the monthly phone calls, the CPS delivered a tailored behavioral, concomitant telemedicine intervention to improve treatment adherence, exercise, diet, weight, and smoking cessation. The CPS also provided medication education based on patients' current understanding of their CVD medications. Behavior change theories were used for understanding treatment adherence.[26,27] Understanding the factors that hinder or promote health behaviors are central to the Transtheoretical Model[28] which is incorporated in the intervention. All information reviewed in the modules was supplemented with written materials in the study handbook provided to intervention patients at enrollment. In particular, the CPS focused on (1) expanding patients' understanding of each medication and its role in disease management, (2) education on preventive care, and (3) offering strategies to enhance adherence.

Medication adherence

Individuals lacking pill refills were queried about difficulties obtaining their prescriptions. Information on how to order and obtain medications was provided to all intervention patients. The full spectrum of medication adherence was addressed: initiation (eg, filling the first prescription) and persistence/discontinuation (eg, continuing the treatment for the prescribed duration).[29]

Knowledge/risk perception

Patients received tailored information about risk for CVD events based on their specific risk factors and laboratory values. To facilitate patient interpretation and understanding, this risk information was presented along with potential avenues for achievable risk reduction tailored to the patient's determinants of risk.

Diet

Patients may have received up to 4 diet modules. The diet modules focused on nutritional methods to improve cholesterol, BP, and HbA1c levels. The diet modules addressed salt intake, portion control, understanding food labels, heart-healthy diets, and healthy carbohydrate foods. The CPS emphasized increasing vegetable, fruit, fiber, and protein intake.

Weight loss

The CPS assessed patients' stage of readiness to change for weight loss. The CPS explored potential barriers to meeting recommended levels of weight loss using motivational interviewing techniques as well as set goals for weight loss. The CPS helped to ensure that patients set realistic goals.

Exercise

The CPS assessed patients' motivation regarding exercise and tailored information-based stage of change. The CPS explored potential barriers to meeting recommended levels of exercise using motivational interviewing techniques as well as setting goals for exercise.

Smoking cessation

A tailored behavioral intervention was initiated for smoking patients in encounters 2 and 8. Barriers to initiating and maintaining smoking cessation were explored and benefits emphasized. Among those in the process of quitting smoking or recently stopped, strategies to maintain this behavior were explored. The CPS explored potential barriers to smoking cessation using motivational interviewing techniques and setting goals for smoking cessation.

Education control group

Individuals in the education control group received primary care and management of CVD according to the discretion of their provider. At baseline and 6 months, individuals randomized to the education control group received generic printed educational material on CVD and how to reduce CVD risk.

Primary outcome

Because the intervention was designed to address multiple contributors to CVD risk, we chose the Framingham CVD risk score derived for use in primary care settings as the primary outcome.[30] The CVD risk risk[30] represents risk of a CVD event or mortality in the next 10 years and incorporates modifiable factors including SBP, total cholesterol, high density lipoprotein cholesterol (HDL-C), current smoking status, and diabetes status. Nonmodifiable characteristics include baseline age and gender. Data for CVD risk profile calculation were collected at baseline, 6 months, and 12 months; values were computed with the full formula as detailed in D'Agostino et al rather than risk score categories. The primary end point was improvement at both 6 and 12 months (omnibus test) for the intervention group as compared to education control.

Secondary outcomes

Secondary outcomes include improvements in systolic and diastolic blood pressure; LDL values; body mass index (BMI); and, for patients with diabetes, HbA1c.

Components of the CVD risk profile

Blood pressure

Blood pressure was measured as a continuous variable at baseline and every 6 months at follow-up. At each outcome assessment, 3 measures at 1-minute intervals were obtained after individuals rested for 5 minutes. BP values for each time point were the average of the 3 measures. All BP measurements were performed using electronic BP cuffs, which have been shown to be equivalent to the criterion standard of random zero sphygmomanometers.[31]

Total cholesterol and HDL-C

Total cholesterol and HDL-C were obtained from a lipid profile.

Smoking

Smoking was assessed as self-reported smoking abstinence over the last week at baseline and at 6 and 12 months of follow-up.

Diabetes status/hemoglobin HbA1c

For the CVD risk score, only diabetes status is required. This was obtained from patients' medical records over the last year or a patient self-reporting diabetes at each time point to detect incident cases. As a secondary outcome, HbA1c was measured at baseline and at 6 and 12 months of follow-up. HbA1c was measured by standard high-performance liquid chromatography methods on a machine calibrated to the national standard (mean = 5.0%, top of normal range = 6.0%). The reliability of high-performance liquid chromatography allowed us to take a single specimen from each patient at each follow-up visit.

Body mass index

BMI was calculated from height and weight measurements using standardized methods at baseline, 6 months, and 12 months. We used height at baseline. Weight was measured in light indoor clothes without shoes. Measurements were taken to the nearest 0.1 lb by a high-quality digital scale. Scales were calibrated annually by the Bureau of Weights and Standards and quarterly by trained study personnel using standard weights.

Analyses

The sample size estimate was based on the hypothesis that patients randomized to receive the intervention would have greater improvement in CVD risk over 12 months than those randomized to education control arm; calculations were based on a 2–degrees of freedom omnibus test contrasting the 2 treatment groups at the 2 follow-up time points.[32,33] From a previous study,[34] the baseline SD was estimated as 19.5, the correlation between baseline and 12 months as 0.7, and the 12-month dropout rate as 15%. To detect an intervention group versus education control difference of 6 by 12 months with 80% power and a type I error rate of 5%, 460 total (230 in each group) randomized patients were needed.

For the primary analysis of CVD risk, we used a general linear model with an unstructured covariance to account for the correlation of patients' repeated measurements over time using PROC MIXED in SAS v9.4 (Cary, NC). The outcome variable in this model was the calculated CVD risk at baseline and at months 6 and 12; model parameters included a common intercept (which constrains the baseline means to be equal), indicator variables for months 6 and 12, and indicators for the intervention interacted with each of the follow-up time point indicator variables. The primary hypothesis was tested by examining an omnibus test of differences at 6 and 12 months; the 6- and 12-month estimated

Table I
Baseline characteristics1*, †2

Baseline characteristics	Overall (N = 428)	CPS intervention (n = 215)	Education control (n = 213)
Age, y, mean (SD)	61.2 (8.7)	60.9 (8.4)	61.5 (8.9)
Male, n (%)	363 (84.8)	182 (84.7)	181 (85.0)
Hispanic/Latino(a) ethnicity,* n (%)	14 (3.3)	12 (5.6)	2 (0.9)
Race,* n (%)			
White	199 (46.7)	93 (43.5)	106 (50.0)
Black or African American	213 (50.0)	111 (51.9)	102 (48.1)
Other	14 (3.3)	10 (4.7)	4 (1.9)
Married or living together, n (%)	243 (56.8)	123 (57.2)	120 (56.3)
Education: High school graduate or less than high school, n (%)	128 (29.9)	71 (33.0)	57 (26.8)
Low literacy level (REALM score ≤60), n (%)	143 (33.4)	78 (36.3)	65 (30.5)
Current smoker, n (%)	124 (29.0)	63 (29.3)	61 (28.6)
	Medical history		
Hypertension, n (%)	386 (90.2)	201 (93.5)	185 (86.9)
Hyperlipidemia, n (%)	317 (74.1)	151 (70.2)	166 (77.9)
Diabetic, n (%)	171 (40.0)	85 (39.5)	86 (40.4)
	Outcome measures		
CVD risk profile,* mean (SD)	32.0 (18.7)	32.4 (18.8)	31.6 (18.6)
	Blood pressure in mm Hg		
Systolic,* mean (SD)	130.1 (18.7)	130.6 (18.5)	129.7 (18.8)
Diastolic,* mean (SD)	75.8 (12.0)	75.8 (11.5)	75.8 (12.4)
	Cholesterol in mg/dL		
Total,* mean (SD)	202.4 (44.9)	202.7 (45.8)	202.1 (44.0)
LDL,* mean (SD)	124.7 (36.7)	125.5 (37.3)	123.9 (36.2)
HDL,* mean (SD)	44.9 (14.8)	44.3 (14.6)	45.5 (15.1)
	Body mass		
BMI,* mean (SD)	31.8 (5.7)	31.9 (5.8)	31.6 (5.7)
	HbA1c		
HbA1c*,† in %, mean (SD)	7.8 (2.0)	8.0 (2.3)	7.6 (1.7)

REALM, Rapid Estimate of Adult Literacy in Medicine.
* Missing data: race (n = 2); Hispanic/Latino ethnicity (n = 3); CVD risk profile (n = 2); SBP (n = 1); DBP (n = 1); total cholesterol (n = 1); HDL (n = 1); LDL (n = 6); BMI (n = 6); HbA1c (n = 6).
† Restricted to those with diabetes.

difference in mean CVD risk improvement, 95% CI, and *P* value were also calculated. All available data, including data from participants who subsequently discontinued the study or did not fully comply with the intervention, were used for analyses. A *P* value < .05 was the threshold for statistical significance.

Between-group differences in the secondary outcomes (SBP, DBP, LDL, BMI, and HbA1c among the subgroup with diabetes) were also estimated and tested via a general linear model (PROC MIXED) with unstructured covariance. Model parameters were similar to the primary outcome model with the exception that randomization stratification variables (centered) were also included.

We had a lower-than-expected rate of compliance with the monthly intervention calls, primarily due to interventionist availability. Therefore, we conducted a post hoc sensitivity analysis to estimate the effect of receiving the intervention, known as the *complier average causal effect* (CACE).[35] *Compliance* was defined a priori as completing at least 5 phone calls. Because noncompliers were also more likely to drop out, we first multiplied imputed missing 6- and 12-month outcomes. Twenty multiple imputations for month 6 and 12 outcomes were generated via the MCMC option in PROC MI. The change between baseline and month 6 and baseline and month 12 was calculated for each outcome and imputed data set. The CACE was then calculated on these change scores following the formulas presented in Liang et al and averaged across the 20 imputed data sets.[35] CIs (95%) for the CACE estimates were computed via 1000 bootstrapped samples of the 20 multiply imputed data sets.[36]

Results

Of the 2,153 contacted patients, 429 were randomized (214 to educational control and 215 to CPS intervention); after randomization, 1 patient in the education control arm was found to be ineligible. The mean age was 61.2 years; 50% were African American; 85% were men; 33.4% had limited health literacy. The baseline CVD risk score for the full sample was 32.0% (SD = 18.7) (Table I). CVD risk factors in the sample were reasonably well controlled at baseline; for example, among the 90% of the sample with hypertension, mean systolic and diastolic BP was 131.0/ 75.9 mm Hg, respectively. Among the 40% (171) individuals with diabetes, the mean HbA1C was 7.8% at baseline. The proportion who reported smoking in the last week at baseline was approximately 29% across both intervention arms.

The mean number of calls completed for those in the CPS intervention was 3.6 (SD 2.6); 34.4% completed 5 or more calls. Among the 34.4% who completed 5 or more calls, the mean number of calls prior to 6 months was 3.6 (SD = 1.3) and between 6 and 12 months was 2.9 (SD = 1.7). The median time spent per encounter ranged from 16 to 45 minutes. CPSs spent the majority of their time explaining CVD medication management/knowledge on personal CVD risk (median time 24 minutes), followed by diet (10 minutes).

Individuals in both education control and the CPS intervention declined in CVD risk by 12 months (−3.3% in intervention; 95% CI −4.9 to −1.8 vs −3.0% for control; 95% CI −4.5 to −1.5). Relative to education control, the CPS-delivered intervention did not show a reduction

Table II
Model-estimated and CACE-estimated* differences in primary and secondary outcomes between CPS intervention and education control groups at 6 and 12a*, †b

Outcome time period	CPS intervention estimated mean	Education control estimated mean	Estimated difference and 95% CI between CPS intervention vs education control from baseline	Estimated difference and 95% CI between CPS intervention compliers vs education control compliers from baseline (CACE)
Primary outcome				
CVD risk				
Baseline	32.0	32.0		
6 m	29.2	31.0	−1.8 (−3.9 to 0.3)	−5.7 (−12.0 to 0.7)
12 m	28.7	29.0	−0.3 (−2.4 to 1.7)	−1.7 (−7.6 to 4.8)
Secondary outcomes				
Systolic BP				
Baseline	130.1	130.1		
6 m	128.1	128.0	0.1 (−2.8 to 3.1)	−0.6 (−11.3 to 10.4)
12 m	128.1	126.6	1.4 (−1.5 to 4.3)	3.5 (−6.4 to 14.7)
Diastolic BP				
Baseline	75.8	75.8		
6 m	74.1	74.2	−0.1 (−2.0 to 1.8)	0.3 (−6.1 to 6.5)
12 m	73.4	73.1	0.4 (−1.5 to 2.2)	1.8 (−4.3 to 8.6)
Total cholesterol				
Baseline	202.5	202.5		
6 m	188.8	195.8	−7.0 (−13.4 to −0.6)	−21.2 (−43.0 to −2.1)
12 m	189.3	190.4	−1.1 (−8.4 to 6.3)	−3.0 (−26.6 to 21.1)
LDL cholesterol				
Baseline	124.9	124.9		
6 m	114.1	119.0	−4.9 (−10.3 to 0.6)	−17.4 (−36.1 to −0.3)
12 m	115.2	116.0	−0.8 (−6.6 to 5.0)	−4.2 (−22.2 to 15.2)
HDL cholesterol				
Baseline	44.9	44.9		
6 m	45.2	44.7	0.5 (−1.3 to 2.3)	2.0 (−3.6 to 7.7)
12 m	47.1	44.9	2.2 (−0.2 to 4.7)	7.3 (0.4-14.9)
BMI				
Baseline	31.9	31.9		
6 m	31.7	31.8	−0.02 (−0.2 to 0.2)	−0.1 (−0.8 to 0.5)
12 m	31.8	31.8	−0.1 (−0.4 to 0.2)	−0.3 (−1.1 to 0.5)
HbA1c†				
Baseline	7.8	7.8		
6 m	7.6	7.8	−0.2 (−0.6 to 0.2)	−0.9 (−2.2 to 0.3)
12 m	7.6	7.7	−0.1 (−0.5 to 0.4)	−0.6 (−2.3 to 0.9)

CI, Confidence interval; *CACE*, complier average causal effect; *CVD*, Cardiovascular disease; *BP*, Blood pressure; *HDL*, High density lipoprotein; *LDL* Low density lipoprotein; *HbA1c*, Glycosylated hemoglobin.

* Estimates are based on a longitudinal data model with an unstructured covariance matrix.

† Restricted to those with diabetes at baseline.

in CVD risk at 6 months (−1.8%, 95% CI −3.9 to 0.3, $P = .10$) or 12 months (−0.3%, 95% CI −2.4 to 1.7, $P = .74$) (omnibus 2-degrees of freedom test P value = .22.).

Individuals decreased in SBP in both arms, and there was no statistical difference in change between the CPS intervention and education control arms across the 12 months (1.4, 95% CI −1.5 to 4.3, $P = .34$).

Similar patterns were observed for the secondary cholesterol outcomes. At 6 months, mean HDL was 0.5 mg/dl (95% CI −1.3 to 2.3, $P = .60$) higher in the intervention arm relative to the control and 2.2 mg/dl (95% CI −0.2 to 4.7, $P = .08$) higher at 12 months. For LDL, there was a decrease of 4.9 mg/dl in LDL relative to education control (95% CI −10.3 to 0.6, $P = .08$) at 6 months, but the difference was not sustained to 12 months. We observed a significant decline in total cholesterol at 6 months (−7.0, 95% CI −13.4 to −0.6, $P = .03$) in the intervention relative to education control group, but this difference was not sustained at 12 months. Among those with diabetes, HbA1c decreased over time in both groups; HbA1c decreased in the CPS intervention group (n = 85) by 0.2 (95% CI −0.6 to 0.2, $P = .29$) at 6 months and decreased by 0.1 at 12 months (95% CI −0.5 to 0.4, $P = .72$) relative to education control (n = 86).

CACE methods showed that *receipt of an effective dose of the intervention*, defined as at least 5 encounters, resulted in clinically important improvements in change in CVD risk from baseline to 6 months for intervention compared to control (difference in CACE estimated mean change = −5.7%, 95% CI −12.0 to 0.7), total cholesterol (difference in CACE estimated mean change = −21.2, 95% CI −43.0 to −2.1), and LDL cholesterol (difference in CACE estimated mean change = −17.4, 95% CI −36.1 to −0.3). However, these differences did not persist at 12 months (Table II). In contrast, CACE methods showed improvements for HDL cholesterol by 12 months for intervention group compliers compared to education control compliers (CACE estimated mean difference = 7.3, 95% CI 0.4-14.9). Finally, CACE methods did not show differences by group in mean change over time for the remaining secondary outcomes of SBP, DBP, BMI, and HbA1c.

Discussion

Among this sample of Veterans at high risk for CVD (32% risk of 10-year mortality) but with well-controlled individual factors, estimated mean CVD risk declined slightly over 12 months in both the intervention and education control groups. In post hoc sensitivity analyses accounting for the lower-than-expected rate of compliance among patients completing the intervention calls, we observed that individuals who received an effective dose of the intervention showed improvements in CVD risk at 6 months compared to compliers in the education control group, but these differences did not persist at 12 months.

Given that an estimated 1 in 3 American adults has CVD, examining alternative delivery methods that potentially improve access becomes increasingly important. The burden of CVD remains high; more than 80% of Veterans have at least 2 risk factors for CVD.[37] CPS-delivered care with physicians or nurses have demonstrated improvement in the management of the individual major CVD risk factors in outpatients.[11,12,38] Currently, within PACTs, face-to-face CPS and nurse management is the predominant mode of patient interactions. Although a face-to-face approach has proven to be successful, the process can be

time and labor intensive. The current intervention was directed at improving access by conducting a telehealth intervention.

Potential reasons for the overall lack of findings include the following: First, the overall time spent on the various patients' behaviors may have been inadequate to translate into significant biological outcomes. Second, the study was conducted in a "real-world" environment where the initial CPS became ill and it took approximately 5 months to replace and train the 2 CPS replacements. This delay in implementing the intervention resulted in a decrease in the overall dose (eg, number of calls) of the intervention that patients were able to receive. In fact, intervention patients who received at least 5 encounters had a mean of 5–percentage point reduction in their CVD risk score at 6 months. Third, the temporary loss of the pharmacist interventionist also led to a reduced sample size than originally planned (428 eligible out of the proposed 460 individuals were ultimately enrolled), as a hiatus in enrollment took place until the pharmacist was replaced. Fourth, despite our effort to identify a pool of individuals who had a greater than 20% CVD risk with potentially modifiable outcomes using the electronic health record, at baseline, a significant proportion of individuals had reasonably well-controlled CVD risk factors, meaning that the CPS had fewer opportunities to intervene. Fourth, there was the potential for co-intervention. Although individuals were excluded if they were enrolled in medication therapy management or care coordination home telehealth at baseline, during the trial, several patients were enrolled in both services ($n = 19$ medication therapy management; $n = 16$ care coordination home telehealth), particularly within the control arm.

Despite the overall lack of finding in reduction in CVD risk, we did observe meaningful differences in terms of reduction of CVD risk at 6 months among those with 5 or more completed calls. One explanation for why the impact on CVD risk reduction was not maintained beyond 6 months among those more engaged is that they were more likely to engage in the first 6 months—mean number of calls prior to 6 months was 3.6 ($SD = 1.3$) and between 6 and 12 months was 2.9 ($SD = 1.7$). The intervention was structured so that medication management was a significant portion of the initial calls. Future programs may want to continue the focus on medication management throughout among those identified as having challenges with meeting guidelines.

Other self-management interventions have targeted CVD risk factors with mixed results. Norris et al[39] reported results from 31 self-management trials that suggested early benefits in glycemic control decline over greater periods of follow-up. Relatedly, in a Cochrane review of 71 hypertension self-management trials, RCTs of educational interventions directed at patients or health professionals were heterogeneous but appeared unlikely to be associated with large net reductions in BP by themselves. Nurse- or pharmacist-led care may be a promising way forward, with the majority of RCTs being associated with improved BP control and mean SBP and DBP, but these interventions require further evaluation.[40] The intervention's dose of self-management education may not have been sufficient to affect CVD risk factor control in this low–health literacy (33%) population of Veterans; other investigators have cited this issue in similar studies.[41,42]

With respect to medication management, although the CPS made medication changes when necessary, there was limited contact between the remote CPS and PCP. Similar to a prior study, a centralized model for the intervention may limit the impact of the intervention.[42] We previously reported that PCPs may have been less willing to adjust therapy with research nurses; we saw that although PCPs replied to 76% of nurse contacts, only 18% of these replies resulted in medication change recommendations from providers. Inclusion of strategies to ensure appropriate treatment intensification is likely important for interventions targeting CVD risk reduction.

Despite these limitations, there continues to be a need to address access to care issues in the VA.[43,44] Also, clinic visits are primarily focused on symptom management, leaving little time for comprehensive risk factor and medication management. Thus, a telephone-based pharmacy intervention may be an efficacious intervention delivered remotely to patients for chronic disease health care (eg, for those engaging, a 5-point decrease in mean risk score of 10-year mortality at 6 months); however, we need to consider further how to match individuals' needs with available resources effectively.

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