

# A Multicomponent Intervention to Improve Blood Pressure Management in Chronic Kidney Disease: A Protocol for a Pragmatic Clinical Trial

John L. Kilgallon (✉ [jkilgallon@bwh.harvard.edu](mailto:jkilgallon@bwh.harvard.edu))

Brigham and Women's Hospital <https://orcid.org/0000-0002-4948-1226>

**Michael Gannon**

Brigham and Women's Hospital

**Zoe Burns**

Brigham and Women's Hospital

**Gearoid McMahon**

Brigham and Women's Hospital

**Patricia Dykes**

Brigham and Women's Hospital

**Jeffrey A. Linder**

Northwestern University Feinberg School of Medicine

**David W. Bates**

Brigham and Women's Hospital

**Sushrut Waikar**

Boston University Medical Center: Boston Medical Center

**Stuart Lipsitz**

Brigham and Women's Hospital

**Heather J. Baer**

Brigham and Women's Hospital

**Lipika Samal**

Brigham and Women's Hospital

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## Study protocol

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# Abstract

## Background

Chronic kidney disease is common, leads to end stage renal disease, and is a major risk factor for cardiovascular disease. Although both chronic kidney disease and hypertension, the main risk factor for disease progression, are not difficult to diagnose, both often go unrecognized by primary care providers. It has yet to be determined whether a multicomponent intervention that leverages electronic health records and behavioral economic principles can improve diagnosis, treatment, and control of hypertension in chronic kidney disease.

## Methods

The aim of this pragmatic, cluster-randomized controlled trial is to evaluate a clinical decision support system based in behavioral economic and user-centered design principles that will: 1) synthesize existing laboratory tests, medication orders, and vital sign data; 2) increase recognition of chronic kidney disease, 3) increase recognition of uncontrolled hypertension in chronic kidney disease patients, and 4) deliver evidence-based chronic kidney disease and hypertension management recommendations. The intervention has been designed and piloted. The primary endpoint is the change in mean systolic blood pressure between baseline and 6 months compared across arms. We will use an effectiveness-implementation hybrid trial type 2 design and the RE-AIM framework to guide evaluation of process and outcome measures. Patients with two prior eGFR 16-59 mL/min/1.73m<sup>2</sup> separated by 90 days or two prior UACR >30mg/g, one SBP >140 mmHg within the 2 years preceding the enrollment visit, and SBP >140 mmHg at enrollment will be included; patients with a most recent eGFR  $\leq$  20 or 2 previous eGFRs within 2 years separated by at least 90 days  $\leq$  15 will be excluded. Rao-Scott chi-square tests and GEE z-tests will be used. We calculated that 497 evaluable patients per arm and an average of 6 patients per provider would provide over 80% power to detect an average 3 mmHg SBP decrease in the intervention arm.

## Discussion

The proposed study, if successful, would be the first to improve hypertension in chronic kidney disease patients through a multicomponent intervention that incorporates clinical decision support and behavioral methods.

## Trial Registration

ClinicalTrials.gov identifier: NCT03679247. Registered September 20, 2018,  
<https://clinicaltrials.gov/ct2/show/NCT03679247?term=Samal&draw=2&rank=1>.

## Contributions To The Literature

- This pragmatic clinical trial of a multicomponent intervention will be the first to incorporate clinical decision support, computable phenotypes, user-centered design principles, and behavioral economic theories for the purpose of improving hypertension in chronic kidney disease patients.
- This study's success will be measured not only by its clinical potential (i.e., improvement of hypertension in chronic kidney disease patients), but by the feasibility and potential utility of its application, offering a real-world evaluation of implementation science frameworks.
- The use of implementation science frameworks in this pragmatic trial will provide valuable lessons for researchers hoping to leverage multiple components, from electronic health records to usability principles, into a single application.

## Background

Chronic kidney disease (CKD) is prevalent, afflicting 26 million Americans, and is associated with high morbidity and mortality. Medicare costs for CKD and end-stage renal disease (ESRD) total \$84 billion and \$36 billion, respectively.<sup>1</sup> CKD diagnosis, monitoring, and treatment must be improved in primary care. Hypertension (HTN) is a leading risk factor for long-term outcomes such as kidney failure, cardiovascular events, and death. There are effective approaches to monitoring and treatment that must be disseminated broadly to cut costs and save lives. Dissemination efforts must focus on primary care clinics because 95% of patients with CKD have early disease and are cared for by primary care providers (PCPs). Only 15% of patients whose estimated glomerular filtration rate (eGFR) is less than 60 mL/min/1.73m<sup>2</sup> are aware that they have CKD, so it is especially important that PCPs become aware of the diagnosis early.<sup>2-6</sup> Furthermore, there is evidence that CKD is under-diagnosed by PCPs. Data from our 15 primary care clinics showed that only 15% of patients with CKD had a documented diagnosis of CKD and only 40% had a urine albumin test.<sup>7</sup> Many effective approaches for recognition of CKD and treatment of uncontrolled HTN in CKD are appropriate for the primary care setting.

Behavioral science studies have shown that decision-making is complex and involves conscious and unconscious drivers. One simple strategy is to display clinical decision support (CDS) with pre-checked, no-action defaults. These defaults greatly impact user behavior, as shown in studies on organ donation, end-of-life planning, and generic drug prescribing.<sup>8-11</sup> One study tested an accountable justification intervention within the CDS that asked PCPs, who were in the act of prescribing an antibiotic, to explicitly justify this decision in a free text response.<sup>12</sup> Accountability improves decision making accuracy and requiring a justification frames the antibiotic prescribing behavior as non-normative.<sup>13 14</sup>

Additionally, providers tend to respond to emotional cues (e.g., fear) and social circumstances (what they think their peers think) rather than reason, known as being "predictably irrational."<sup>15</sup> Therefore, another simple external intervention is to ask PCPs to publicly commit to a new behavior. In one study, PCPs were asked to sign and post a letter that stated a commitment to following appropriate antibiotic use guidelines.<sup>16</sup> The intervention led to a decrease in inappropriate antibiotic use. The effect was attributed to three factors: 1) PCP's aim for consistency and fear that inconsistency will lead to disapproval by

peers, 2) publicly committing to a behavior connects that behavior with the PCP's self-image, and 3) the visible poster affects patients' behavior. Our objective in this pragmatic clinical trial is to incorporate behavioral economic principles and user-centered design principles into a multicomponent intervention for the management of uncontrolled HTN in CKD in primary care.

## Methods

# Implementation Science and Randomized Clinical Trial Conceptual Frameworks

This study will incorporate the effectiveness-implementation hybrid trial type 2 design.<sup>17</sup> Under this framework, our study will have the coprimary aims of determining the effectiveness of the clinical intervention and establishing the intervention's feasibility and potential utility.<sup>17</sup>

This study will also use the RE-AIM framework to conduct the evaluation. The RE-AIM Framework is well suited for technology innovation projects because it focuses on external validity in study design and guides the planning, conduct, evaluation, and maintenance of the intervention.<sup>18</sup> In this project, the RE-AIM framework will be used to derive practical measures of how well the intervention works in real-world clinical settings and to produce a 360-degree assessment of its efficacy.

## Overall Study Design

We will evaluate the effectiveness of the intervention in a pragmatic, cluster-randomized controlled trial, randomized at the provider level. The rationale for this is that the behavioral economic and usability components of intervention apply at the provider level; additionally, PCPs are expected to learn from the CDS, and thus there would be potential for contamination if randomization occurred at the patient level. The primary endpoint of the study is the change in mean SBP between baseline and 6 months compared across arms. Secondary endpoints include hypertension-specific process measures, process measures for CKD quality of care, adverse drug events, and hypotension. We also hope to assess whether the intervention improves process measures for quality of CKD care such as annual urine albumin tests. The overarching structure supporting the evaluation is the RE-AIM framework, and this protocol was reported in accordance with SPIRIT guidelines (Fig. 1).

## Study Setting

The Brigham and Women's Primary Care Practice-Based Research Network (BWPC PBRN) is one of 155 PBRNs nationally certified by the Agency for Healthcare Research and Quality (AHRQ). The BWPC PBRN is a network of 15 practices which includes hospital-based practices, community-based practices, and community health centers affiliated with Brigham and Women's Hospital.

## Eligibility Criteria

Patients: All patients over the age of 18 who have a visit with a PCP at one of the intervention practices during the 2 years preceding the visit date will be eligible for enrollment. The first inclusion criteria will be CKD, defined as two prior eGFRs 16–59 mL/min/1.73m<sup>2</sup> separated by 90 days, as calculated by CKD-EPI, or two prior UACR > 30mg/g. The second inclusion criteria will be uncontrolled hypertension, defined as at least one SBP > 140 mmHg within the 2 years preceding the enrollment visit, as well as SBP > 140 mmHg at the enrollment visit. Patients with a most recent eGFR ≤ 20 or two previous eGFRs within 2 years separated by at least 90 days ≤ 15 will be excluded.

Providers: Our objective is to include PCPs who have a consistent panel of primary care patients and represent primary care providers broadly outside of the academic medical center setting, and thus our criteria excludes providers who only see urgent care and walk-in patients. We also excluded residents in training. We compiled a list of currently employed physicians, physician assistants and nurse practitioners in our primary care network. The network includes 220 PCPs who care for approximately 150,000 patients. Of the 220 PCPs, 184 were eligible to be enrolled, and the remainder were excluded; no PCPs opted out of the trial.

## Study Intervention

One component of the intervention is a series of Epic Best Practices Advisories (BPAs). These CDS are designed to utilize computable phenotypes (CPs), defined as disease definitions or algorithms that allow curation of disease populations using data from electronic health records (EHRs).<sup>19</sup> We developed five CPs, each with its own CDS recommendation. The first CP includes patients with CKD and uncontrolled SBP for whom it is advised that an angiotensin converting enzyme inhibitor (ACEi) be prescribed. The second includes patients with CKD and uncontrolled SBP for whom an angiotensin receptor blocker (ARB) should be prescribed. The third CP includes patients who are currently on an ACEi but not at an optimal dose, while the fourth CP includes those who are on a suboptimal dose of an ARB. The fifth CP includes patients who are maximized on an ACEi or ARB, but are not on a diuretic. The CDS prompts PCPs to make clinical decisions specific to these phenotypes. For example, the PCP of a patient exhibiting the first CP would be prompted to prescribe a starting dose of an ACEi (e.g., lisinopril), while the PCP of a fourth CP patient would be prompted to increase the dose of the patient's currently prescribed ARB (e.g., losartan).

Another aspect of the multicomponent intervention, developed utilizing user-centered design principles, is the display of patient specific data explaining why the CDS fired. Our team performed contextual inquiry sessions and two rounds of usability testing (group design and individual think aloud sessions) on the CDS prototype. The main focus of the contextual inquiry sessions was to assess the different activities, steps, and thinking processes involved in managing uncontrolled blood pressure using EHRs and any other resources used by PCPs during a patient encounter. The goal of the group design sessions was to validate the requirements gathered during the contextual inquiry sessions and gain a greater understanding of user preferences and mental models. The goal of the individual think aloud sessions

was to uncover usability issues and validate design decisions. Additionally, hyperlinks to clinical guidelines supporting the CDS recommendation are included in the final CDS.<sup>20 21</sup>

Finally, a pre-commitment email was sent to all participating PCPs asking them to pledge to follow recommendations about blood pressure management. We will evaluate whether the pledge makes people more likely to either follow the recommendation or to add an accountable justification (stated rationale for why one disagrees with the recommendation) when interacting with the BPA, incorporating the behavioral economic principle of accountability into the intervention.

## Implementation of CDS in Epic

Each of the rules were added to the Epic database. The BPAs appear at the time of chart opening by the PCP if criteria are met (see example in Fig. 2). The CDS was moved to the Production environment in “silent mode” for approximately six weeks before the scheduled start date of the trial, where a report recorded when it would fire but it was not displayed to the user. When the trial begins, we will identify control patients in real time according to the same inclusion criteria as intervention patients. This will allow us to validate that the rules are accurately identifying patients and producing the correct recommendations through a chart review. The CDS was also activated in the Production environment for a pilot study.

In practice, the CDS will fire only on the initial enrollment visit, except if the PCP chooses the “remind me next visit” option in the “acknowledge reason” section. However, if the patient’s SBP has dropped below 140/90 mmHg, the patient is already on the recommended medication or a new allergy to an ACE/ARB has been entered, this follow-up firing will be suppressed.

## Outcomes and Measures

Within an implementation-effectiveness framework, a hybrid trial type 2, defined as the *simultaneous testing of a clinical intervention and an implementation intervention/strategy*, will be conducted.<sup>17</sup> This decision is motivated by the intervention’s multiple components, ranging from aspects of clinical effectiveness (management of HTN in CKD patients) to usability principles and strategies (PCP adherence to CDS guidelines). Additionally, outcomes and measures will be guided by the RE-AIM framework.

Reach will refer to the overall use of the CKD CDS, including the number of PCPs and patients for whom it fires. To assess the reach of the CDS, statistics on the quantity and types of firings will be collected through enterprise data warehouse (EDW) and Epic queries. Concurrent manual review of Epic reports and chart review on CDS firing statistics will be conducted by team members to verify the automated monthly summaries. Analytic variables will include the percentage and types of clinicians in primary care who use the software, descriptions of excluded clinicians, PCP review and/or response to pledge email, PCP interaction with the CDS, signing of orders or accountable justification documentation within the CDS, and whether the BPA fired appropriately during encounter.

Effectiveness will refer to the clinical efficacy (process and outcome measures), usability of the software in the primary care environment, process measures, and both positive and negative unanticipated consequences. In evaluating effectiveness, the primary endpoint is the change in mean SBP between baseline and 6 months compared across arms. This outcome was chosen as the primary outcome because of the growing need in primary care to monitor patients' HTN in order to help mitigate negative long-term outcomes of CKD such as kidney failure, cardiovascular events, and death. A meta-analysis of three large cohorts of CKD patients without diabetes concluded that maintaining blood pressure below 140/90 mmHg decreases risk of these outcomes significantly.<sup>22</sup> Several guidelines have been issued to emphasize the importance of HTN control in CKD.<sup>23-25</sup> Additional secondary outcomes are listed in Table 1 and Table 2.

Table 1  
Outcome Variables and Measures for Both Arms

<b>Measurement Variable</b>	<b>Form of Variable</b>	<b>Analysis Metric</b>	<b>Time Point from First Visit</b>
Primary			
Mean SBP	Continuous	Change from baseline	6 months
Secondary			
Mean SBP	Continuous	Change from baseline	12 months, 18 months
Controlled SBP Rate	Dichotomous	Proportion of patients with controlled SBP rate	6 months, 12 months, 18 months
Urine Albumin to Creatinine Ratio	Continuous	Urine Albumin to Creatinine Ratio	6 months, 12 months, 18 months
Serum Creatinine > 2.0	Dichotomous	Proportion of patients with Creatinine > 2.0	6 months
Smoking Status	Dichotomous	Proportion of patients who smoke	6 months
eGFR	Continuous	eGFR	6 months, 12 months, 18 months
Medication ordered	Dichotomous	Proportion of patients with recommended medication ordered	6 months
Basic metabolic panel ordered	Dichotomous	Proportion of patients with basic metabolic panel ordered	6 months
Referral to e-consults	Dichotomous	Proportion of patients with referral to e-consults	6 months
BPA acceptance	Dichotomous	Proportion of patients for whom BPA interaction was not an acknowledge reason	6 months
Mean SBP of less than 110	Dichotomous	Proportion of patients with mean SBP of less than 110	6 months
Newly documented allergy	Dichotomous	Proportion of patients with newly documented allergy due to adverse drug events	6 months

<b>Measurement Variable</b>	<b>Form of Variable</b>	<b>Analysis Metric</b>	<b>Time Point from First Visit</b>
K + > 5.2	Dichotomous	Proportion of patients with K + > 5.2	6 months
K + < 3.6	Dichotomous	Proportion of patients with K + < 3.6	6 months
Mean SBP analysis with imputation of missing 6-month BP measurement	Continuous	Change from baseline	6 months
Controlled SBP Rate analysis with imputation of missing 6-month BP measurement	Dichotomous	Proportion of patients with missing 6-month BP measurement	6 months
Mean SBP as-treated analysis (patient level)	Continuous	Change from baseline in patients whose provider ordered the recommended medication	6 months
Mean SBP as-treated analysis (provider level)	Continuous	Change from baseline in patients whose provider ordered the recommended medication	6 months

Table 2  
Outcome Variables and Measures for Intervention Arm Only

<b>Measurement Variable</b>	<b>Form of Variable</b>	<b>Analysis Metric</b>	<b>Time Point from First Visit</b>
Acknowledge reason entered	Dichotomous	Proportion of patients with acknowledge reason entered	6 months
Feedback button clicked	Dichotomous	Proportion of patients with feedback button clicked	6 months
PCP participation on pledge email survey	Dichotomous	Proportion of patients whose PCPs participated in pledge email survey	6 months
Guideline accessed	Dichotomous	Proportion of patients with guideline accessed	6 months

Adoption will refer to the percentage and types of settings and staff that embrace the innovation. We will analyze the various ways in which the intervention PCPs accept, reject, and generally interact with the BPA. Using a BPA report extracted through Epic, we will collect which CDS fired, the date and time of the firing, the MRN and demographic information of the patient on whom it fired, and the user (PCP). We will also extract the user follow-up action (whether the PCP indicated they would order a medication or basic metabolic panel through the BPA) or which acknowledge reason the PCP chose. If “other” is indicated as an acknowledge reason, the PCP will be asked to elaborate with a comment. Finally, in conducting our

manual chart review, we will record whether the BPA firing for the patient was appropriate and whether the course of action that the PCP indicated they would take through the BPA differed from the course that they actually took.

Implementation will refer to the consistency of CDS use, any support resources used, any barriers and/or enabling factors that are identified, any workarounds to barriers that develop, any changes from pre-intervention to intervention period, and any unintended consequences to patient safety or workflows. Prior to the clinical trial, a pilot study was conducted in live clinical settings. The BPAs were turned on for approximately two weeks for all intervention providers, and the patients for whom the BPAs fire during this period were classified as “Pilot Patients.” Interaction with the BPAs was monitored. The first time a BPA fired for a PCP, the research team contacted the PCP by email to gather feedback through a survey or an interview. The experiences of these PCPs were noted, but no changes were made to the BPA. However, some early workarounds that were discovered included selecting the accountable justification “Other” without a valid reason (e.g., “x”) in order to circumvent the BPA, as well as ordering a medication or panel without completing the order by signing off on it.

Maintenance will refer to how well the innovation components and their effects are sustained, as well as any strategies that are used to uphold the intervention over time. This will be recorded by qualitative descriptions of system performance longitudinally, emerging workflow changes, and long-term unintended consequences, and how the BPA fit into the existing PCP workflow. The methods used will include contextual inquiry sessions, interviews, and surveys.

## **Sample Size and Power Calculation**

According to our analysis of patients who saw a PCP at one of the 15 BWPC practices in 2009,

there were 3,118 patients with two prior eGFR 16–59 ml/min/1.73m<sup>2</sup> measured at least 90 days apart between 2007-2008.<sup>70</sup> We determined that 42% (n = 1309) of these patients had at least two BP > 140/90 mmHg. Those patients with elevated SBP had a mean SBP of 153.9 mmHg and standard deviation of 14.0 mmHg. We will assume that 71% of the enrolled patients will have at least one follow-up visit during the 6 month follow-up period.<sup>26</sup> According to an analysis of 2013 data, 56,461 patients visited a PCP at one of the 15 BWPC practices in 2013.<sup>27</sup> We identified 5,593 patients with CKD who visited a PCP during 2013, when CKD was defined as two prior eGFR < 60 ml/min/1.73m<sup>2</sup> or UACR ≥ 30 mg/g measured at least 90 days apart between 2007–2012. Combining our findings from the two studies, we expect 42% of these 5,593 patients to fit both of our inclusion criteria, so N = 2,349 patients. We based our power calculation on an expected decrease in the mean of the final SBPs for patients in the intervention arm of at least 3 mmHg as compared to the mean of the final SBPs in the control arm, which is a clinically important decrease. The two arms will be compared using a robust generalized estimating equations z-test for continuous data; this approach does not assume normality of the outcome, and accounts for a possible cluster effect of patients within PCP.<sup>28</sup> Using the GEE z-test with a 2- sided type I error rate of 2.5%, we calculated that 497 evaluable patients per arm and an average of 6 patients per PCP would provide over 80% power to detect an average 3 mmHg SBP decrease in the intervention arm. We assumed

an intra-cluster (clinician) correlation coefficient of 0.1, as is commonly assumed in this type of cluster randomization study.<sup>29</sup> Therefore, we have power to detect a 3 mmHg decrease in mean of final SBPs in the intervention arm.

## Recruitment

This is a pragmatic clinical trial. Once the study period begins, each patient who has an office visit with a PCP and fulfill criteria for CKD and uncontrolled HTN will be automatically enrolled in the study. Both inclusion criteria will be assessed, in real time, for every adult patient who visits a PCP. The patients will be designated as belonging to the intervention or control arm based upon the PCP that the patient sees. The subgroup of PCPs included in the pilot study will remain enrolled in the clinical trial; the patients they saw during this period will be excluded from the final analysis.

## Allocation

This study will utilize a matched-pair cluster randomized design with the intervention on the cluster level, and the main outcome (6-month minus baseline change in SBP) measured at the patient level. We will have 174 clusters (made up of 184 clinicians) in the study (Fig. 3). Clusters were made up of either one PCP with their own panel of patients, or two PCPs who share a panel, also known as a “co-management dyad.” We will match pairs of clusters with similar number of patients and prior year mean blood pressure of patients in the cluster. One cluster in each pair will be randomized to the intervention and unit one to usual care.

## Data Collection and Follow-Up

Patients will be electronically identified and included in the study over the course of 12 months. Patients seen by PCPs during the pilot study will be excluded. Retrospective data indicates that 70% of patients have a follow-up around 6 months. Outcomes assessment will occur at 180 days (+/- 60 days). After the 12-month enrollment period ends, data collection will continue for 6 months so that those enrolled toward the end of the enrollment period will have a full 6 months to complete any interventions ordered by the PCP. Clinical outcomes will be recorded and reviewed every month over the course of the trial.

## Statistical Methods

Using the Haybittle–Peto approach, the conventional p-value of 0.05 can be used in the primary analysis (difference in final SBP between intervention and control arm PCP panels). In other words, the p-value for the GEE z-test must be  $\leq 0.05$  for the intervention and control groups to be declared significantly different. Descriptive statistics (e.g., means and standard deviations, medians and interquartile ranges, frequencies) will be used to examine the distributions of demographic (e.g., age, sex, race/ethnicity) and clinical characteristics (e.g., comorbidities, baseline eGFR, smoking status). We will compare intervention and control groups on baseline characteristics with Rao-Scott chi-square tests for categorical variables (accounting for clustering) and GEE z-tests for continuous variables (accounting for clustering).<sup>30</sup> The primary endpoint is the change in mean SBP between baseline and 6 months compared across arms and the primary analysis will be an intent-to-intervene analysis. SBP at intermediate visits will not be used in

this analysis. We expect the baseline SBP mean and standard deviation to be the same in both arms. If there is a difference at baseline, we will use a difference in differences approach.

## **Secondary Analyses**

We will perform a secondary analysis for patients who did not have a subsequent visit after the enrollment visit. We will use multiple imputation to estimate the final SBP for patients who have missing data. We will perform another secondary analysis, as "as-treated" analysis, on patients where the provider chose to order the recommended medication. We will also perform a secondary analysis at the provider level. This "as-treated" analysis will include only providers who did not choose to opt out after randomization.

## **Ethical Considerations**

The Human Subjects Institutional Review Board at Brigham and Women's Hospital approved this study protocol, and a Data Safety Monitoring Board will ensure the ongoing safety of the trial. Potential harm outcomes will be monitored and addressed as needed. Any relevant protocol modifications will be to relevant parties.

## **Discussion**

During this study, we expect to demonstrate a decrease in mean SBP in CKD patients following the implementation of CDS in the form of an Epic BPA. We also expect to demonstrate that PCPs receiving the live BPA will show higher levels of action in the management of their CKD patients' HTN than those receiving the silent BPA. Through this pragmatic, cluster-randomized controlled trial, we hope to build a greater base of information in how PCPs interact with CDS in real-world settings, as well as determine some of the most successful strategies for CDS implementation. Taking PCP feedback into consideration will be a vital aspect of this process. By using the RE-AIM framework, we can inform future implementations of this system in similar settings. The framework will provide insight on the ideal approach for the application of CDS to assist in the management of chronic diseases in primary care. Potential areas of focus include other multidisciplinary chronic diseases with high HTN comorbidity such as diabetes mellitus, hyperlipidemia, or cardiovascular disease.

At the conclusion of this study, we will have: 1) validated an intervention that combines lab tests, medication records, and clinical information collected by EHR to recognize uncontrolled HTN in CKD patients and recommend a course of care, 2) tested the effectiveness of said intervention, and 3) collected information about the implementation of the intervention that will aid in dissemination of the intervention to other practice settings. There are various factors that contribute to successfully addressing these issues, from the participation of the care team to the specific medications that are prescribed. We believe that results of this trial will provide valuable information regarding the implementation of CDS to help detect and treat CKD and HTN in primary care settings. The lessons learned in conducting this trial will also serve as references for future endeavors in implementation of CDS for primary care.

# Abbreviations

ACEi: Angiotensin converting enzyme inhibitor; AHRQ: Agency for Healthcare Research and Quality; ARB: Angiotensin receptor blocker; BPA: Best practice advisory; BWPC PBRN: The Brigham and Women's Primary Care Practice-Based Research Network; CDS: Clinical decision support; CKD: Chronic kidney disease; CP: Computable phenotype; EDW: Enterprise data warehouse; eGFR: Estimated glomerular filtration rate; EHR: Electronic health records; ESRD: End-stage renal disease; HTN: Hypertension; PCP: Primary care provider; SBP: Systolic blood pressure.

# Declarations

## Ethics approval and consent to participate

The Human Subjects Institutional Review Board at Brigham and Women's Hospital approved this study protocol, and a Data Safety Monitoring Board will ensure the ongoing safety of the trial.

## Consent for publication

Not applicable.

## Availability of data and materials

Not applicable.

## Competing interests

The authors have no competing interests to declare.

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## Authors' Contributions

JLK was a major contributor in writing the manuscript, executively advised by LS. MG worked extensively on the usability portion of the study. ZB managed the project. GM and SW provided nephrology expertise throughout the design of the trial. PD, JAL, and DWB provided primary care expertise throughout the design of the trial. SL conducted all statistical methods, sample size, and power calculations. HJB provided epidemiological expertise throughout the design of the trial. LS is the principal investigator of this trial. All authors have read, revised, and approved the final manuscript.

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## Figures

	<b>Trial Design and Usability Sessions</b>	<b>Enrollment</b>	<b>Allocation</b>	<b>Post-allocation</b>	<b>Close-out</b>
<b>TIMEPOINT*</b>	Y1 Q1 – Y2 Q3	Y2 Q4 – Y2 Q3	Y3 Q2	Y3 Q3 – Y4 Q4	Y5 Q1 – Y5 Q4
Define BPA rule logic	X				
Validate BPA rule logic	X				
Iterative refinement	X	X			
Silent run-in period		X			
Pledge email to obtain commitment from PCPs		X			
Retrospective data review to identify PCPs with eligible patients		X			
Stratify and randomize PCPs			X		
Implement intervention				X	
Pilot study				X	
Data collection				X	
Data analysis					X

**Figure 1**

Schedule of enrollment, interventions, and assessments. \*Y = Year, Q = Quarter

**Important (1)**

⚠ Patient has CKD, 2 SBP's  $\geq 140$  mmHg, and is on an ACE, which could be increased

provide feedback: 😊 😐 😞

Why did this alert fire?

- Pt has CKD: 2 eGFR  $< 60$  within the past 2 years, at least 90 days apart - Most recent eGFR: **40** (7/28/2020)
- Pt has had 2 elevated SBP's  $\geq 140$  mmHg - Today's SBP: **160 mmHg**
- Pt is on Lisinopril - Current Dose: **5 mg**
- Most recent K: 3.5 (7/28/2020)

Consider increasing Lisinopril dose. Consider ordering a BMP to monitor creatinine.

Order	Do Not Order	🏠 Lisinopril 10 MG Tablet
Order	Do Not Order	🏠 Basic Metabolic Panel in 1 week
Order	Do Not Order	🏠 Ambulatory BWH Renal E-Consult

Acknowledge Reason \_\_\_\_\_

Figure 2

Example CDS with explanation, clinical information, recommended actions, and accountable justification ("Acknowledge Reason").

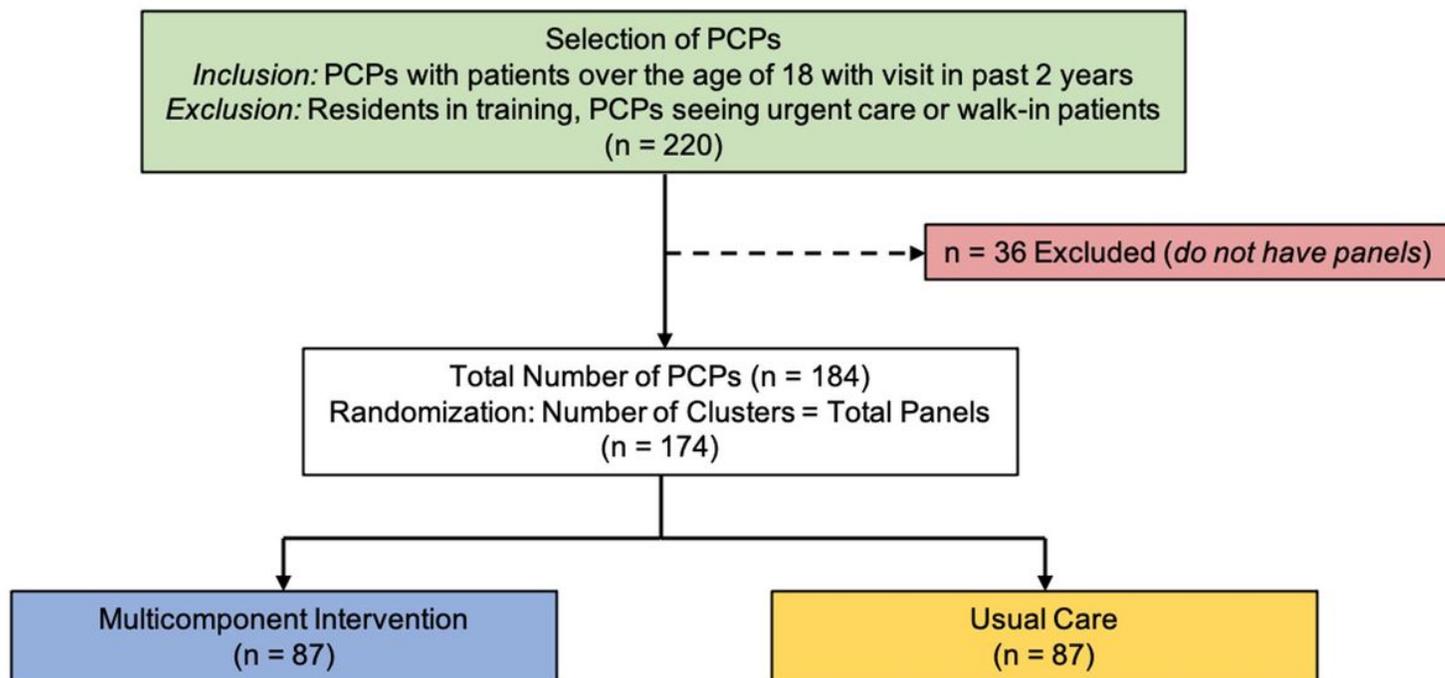


Figure 3

Participant Timeline.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [BCKDR01CONSORTChecklist.doc](#)
- [BCKDR01SPIRITChecklist.doc](#)
- [NIHNOA1R01DK11689801A1.pdf](#)
- [ReviewLetter.pdf](#)