MEMORANDUM OF UNDERSTANDING

BP-MAP: Improving Clinic-Level Blood Pressure Control

Monterey County Health Department
Laurel Family Practice
Elsa Jimenez, Director of Health

Principal Investigator: Mark Pletcher, MD, MPH
University of California-San Francisco (UCSF)

OCHIN Site Principal Investigator: Jonathan Todd, PhD, MSPH

This Memorandum of Understanding ("MOU") is made between OCHIN and Monterey County Health Department ("Provider"), each wishing to establish a cooperative research relationship. OCHIN and Provider are collectively referred to as the "Parties" or individually as a "Party". This MOU shall be effective upon the signature of both parties' authorized officials.

WHEREAS, OCHIN has been engaged by Patient-Centered Outcomes Research Institute (PCORI) on behalf of UCSF ("Researcher") to provide certain assistance with respect to BP-MAP: Improving Clinic-Level Blood Pressure Control ("Project"), as is further described below; and

WHEREAS, Provider is a member of the OCHIN community and wishes to contribute to and participate in the Project as specified in this MOU;

NOW THEREFORE, OCHIN and Provider, as Parties to this MOU, agree as follows:

1. Project Scope

1.1 *Purpose.*

BP-MAP is a quality improvement (QI) initiative to support implementation of the **M.A.P.** (**M**easuring Accurately, **A**cting Rapidly, and **P**artnering with Patients) program in OCHIN member clinics. The M.A.P. program is an evidence-based protocol developed by the American Medical Association (**AMA**) to guide the way care teams assess and treat people with high blood pressure. This study aims to compare the effectiveness of the M.A.P. program with Full Support (dedicated practice facilitation) vs. a Self-Guided version of the program. By participating in this study, care teams can access the latest research, tools, and resources to reach and sustain clinic targets for blood pressure rates. This study aims to build on the AMA's pilot study, which demonstrated a clinically and statistically significant improvement in blood pressure (**BP**) control in clinics that implemented the M.A.P. program[1].

The primary outcome for this study will be change in clinic-level BP control after 6 months. Secondary outcomes will include other blood pressure control metrics, other time points (12 and

[1] Hanlin RB, Asif IM, Wozniak G, et al. Measure Accurately, Act Rapidly and Partner with Patients (MAP) Improves Hypertension Control in Medically Underserved Patients: Care Coordination Institute and American Medical Association Hypertension Control Project Pilot-Study Results. Journal of Clinical Hypertension. 2017;IN PRESS.

18 months), and process measures such as blood pressure measurement accuracy, medication intensification, and average systolic BP reduction after a medication intensification.

1.2 *Project Activities and Goals.* Researcher and the Parties intend to collaboratively pursue the following research activities and goals:

A. WHAT PARTICIPATING CLINICS WILL RECEIVE:

1. All participating clinic will receive 6+ months of support and resources to implement the M.A.P. program, a quality improvement program that has demonstrated successful improvement of BP control rates in a variety of practice settings. Each clinic will be placed in one of two implementation strategies – Self-Guided or Full Support.

   Self-Guided Clinics will receive:

   - Access to AMA/AHA website and digital guide with M.A.P. implementation tools and resources
   - Improvement plans
   - Monthly clinic-level BP metric QI reports
   - Limited access to AMA staff
   - Access to a *NEW* Epic EHR-integrated hypertension dashboard

   Full Support Clinics will receive all of the above, plus:

   - Hands-on implementation support from an OCHIN Practice Coach

2. Clinics will also receive access to a quality improvement framework that can be adapted for use in several chronic conditions.

B. WHAT PARTICIPATING CLINICS AGREE TO DO:

1. Identify a clinic staff member who will serve as a **Site Champion**. This person will be the primary study contact and will lead the M.A.P. program implementation efforts (approx. 2-3 hrs/wk). For Full-Support clinics, the site champion will also receive implementation support from an OCHIN Practice Coach.

   The identified *Site Champion* should have:

   - clinical experience
   - familiarity with clinical workflows in the practice
   - an understanding of the roles and responsibilities of clinical care team members and the principles of team-based care
   - experience participating in a quality improvement initiative
   - an understanding of how change happens and decisions are made in the clinical practice

2. Identify a **Provider Champion**. This person will be a project advocate and will support implementation, as needed (approx. 3 hrs/month).

   The identified *Provider Champion* should have:

   - clinical experience
   - a regular role providing care in the clinic
   - familiarity with clinical workflows in the practice

- an understanding of the roles and responsibilities of clinical care team members and the principles of team-based care
- experience obtaining buy-in and influencing change in the practice
- authority to make decisions within the practice

3. Your health center has confirmed that your participating clinic(s) has not participated in the *Target:BP* initiative and is not currently involved in any ongoing clinical trials or other QI projects that conflict with this study.

1.3 *Leadership.* The Project will be directed by the University of California-San Francisco (UCSF) Principal Investigator, Mark Pletcher, MD, MPH and OCHIN Site Principal Investigator, Jonathan Todd, PhD, MSPH.

1.4 *Oversight.* The Project has been reviewed by the UCSF Institutional Review Board ("IRB") and OCHIN review process, and was determined to be Exempt.

1.5 *Duration.* The Project will be conducted until 7/31/2021, with clinic implementation activities lasting six (6) months, subject to continued availability of funds.

2. Activities & Responsibilities

2.1 *Point of Contact.* Each Party will designate an individual to serve as a primary point of contact with respect to Provider's participation in the Project. An IRB contact is also identified below.

2.1.1 Provider's Primary Contact: _Caroline Kennedy_

2.1.2 OCHIN's Primary Contact: April Lee leean@ochin.org

2.1.3 Researcher Primary Contact: Madelaine Faulkner Madelaine.Faulkner@ucsf.edu and Mark Pletcher Mark.Pletcher@ucsf.edu

2.1.4 IRB Contact: Shiffen Getabecha Shiffen.Getabecha@ucsf.edu

2.2 *Subject Engagement.*

BP-MAP is a quality improvement (QI) initiative to implement the M.A.P. program in clinical settings. This study will not require UCSF or OCHIN-led patient engagement. Sites randomized into the Full Support arm will engage with an OCHIN Practice Coach while receiving implementation support.

3. Data Sharing

3.1 The Parties agree that protected health information, as defined at 45 CFR 160.103 ("PHI"), of Provider's patients will be shared in connection with the Project, as follows:

3.1.1 Provider hereby authorizes OCHIN, Researcher, and the PCORnet Coordinating Center to view aggregated, clinic-level blood pressure-related study data. Such use shall consist only of (a) activities preparatory to research, consistent with the Health Insurance Portability and Accountability Act of 1996, its implementing regulations, and guidance issued by the Department of Health and Human Services; or (b) activities approved via a waiver issued by the IRB.

4. Compensation & Benefits

4.1 By participating, Provider is providing its clinical staff an opportunity to contribute to scientific knowledge about BP control rates.

In recognition of Provider's contribution to the Project, OCHIN will pay Provider either a $3,000 (Self-Guided) or $7,000 (Full Support) clinic impact payment for each participating clinic, which will be distributed in two payments, as described below:

The Provider will receive $1,000 upon completion of pre-implementation activities (signing MOU, identifying site and provider champion, any other prep activities).

The Provider will receive the remaining amount of either $2,000 (Self-Guided) or $6,000 (Full Support), at the conclusion of the 6-month implementation period.

4.2 OCHIN will inform Provider of Project results and any publications of such results.

5. Timeline

The Parties anticipate the following activities to take place as described below:

Initiate Project Activities: between April and July 2019

The exact timing of the project kick-off is flexible, based on the needs and preferences of each clinic and the study team.

Pre-Implementation activities will begin approximately one month before implementation, sometime between April and July 2019. This will include:

- General Onboarding: This consists of discussions between your health center and the OCHIN study team, as needed, to onboard clinic staff to the project, make sure clinics have the necessary resources, identify a site champion and provider champion, and notify clinics of randomization. For Full Support clinics, this will include an in-person or by-phone meeting with an OCHIN Practice Coach.

Initiate M.A.P. program implementation: between May and August 2019 + 6 months

Implementation activities (kickoff and improvement work) will begin between May and August, 2019. The implementation period will continue for 6 months.

For example, if your site decides to conduct pre-implementation activities in June, the implementation period may start in July and end in December 2019.

Implementation activities will include:

- Implementation Kickoff: During the kickoff, AMA staff will introduce the team to the M.A.P. BP improvement program by phone or in person.

- Implementation Improvement Work: This consists of various tasks required to make improvements in BP diagnosis and management, such as review of improvement program

content, training, workflows and environments, auditing charts and BP measurement technique, development of a QI plan to execute process changes and evaluate effectiveness/progress. All participating clinics will receive resources and support to facilitate this work. However, Full Support and Self-Guided clinics will receive different levels of support, as noted above.

6. General Terms

6.1 *Term.* This MOU shall remain in effect until 7/31/2021. Either Party may terminate this MOU by providing at least thirty (30) days prior written notice to the other Party.

6.2 *Amendments.* This MOU may be amended only in writing, signed by each Party's authorized signatory.

6.3 *Confidentiality.* In the course of the activities contemplated by this MOU, a Party may disclose Confidential Information to the other Party. Unless otherwise agreed in writing, "Confidential Information" includes any and all information, correspondence, financial statements, records, data, or information that is or would reasonably be understood to be competitively sensitive and generally not known to the public, including formulations, analysis, inventions, improvements, patient records, and activities of the disclosing Party and other documents that are marked as confidential or proprietary and are transmitted or communicated by the disclosing Party to the receiving Party. Except for PHI, which is always deemed Confidential Information, Confidential Information does not include information that (a) is publicly known at the time of the disclosure, (b) is lawfully received by the receiving Party from a third party which does not have confidentiality obligations to the disclosing Party, or (c) the receiving Party can demonstrate was in its possession or known prior to receipt from the disclosing Party. Confidential Information shall be received and treated in confidence, and shall not be used except as necessary to perform the activities contemplated in this MOU and shall not be further disclosed except as permitted by Article 3 or Section 6.8 herein without prior written consent of the disclosing Party; provided that, if a receiving Party is required by law to disclose Confidential Information, the receiving Party shall notify the disclosing Party and reasonably cooperate with the disclosing Party's efforts to prevent disclosure.

6.4 *Compliance.* The Parties will each abide by applicable laws, including, without limitation, the disclosing and handling of intellectual property, developed technologies, and Confidential Information, including PHI.

6.5 *Indemnification.* Each Party agrees to hold harmless and indemnify the other Party and its officers, agents and employees from and against any and all liability, loss, expense, attorneys' fees, or claims for injury or damages arising out of the activities under this MOU, but only to the extent such liability, loss, expense, attorneys' fees, or claims for injury or damages are caused by or result from the negligent or intentional acts or omissions of the indemnifying Party.

6.6 *Notice.* All notices permitted or required by this MOU shall be in writing; given by registered or certified mail, postage prepaid, or delivered by nationally recognized courier service; addressed to the addresses set forth below the signature lines, or such other address for which a Party may provide notice in accordance with this Section from time to time; and deemed effective upon receipt by the receiving Party.

6.7 *Relationship.* The relationship of the Parties is that of independent contractors. Neither Party is the partner, joint venturer, or agent of the other, and neither Party has authority to make any statement, representation, commitment, or action which would bind the other without prior written

authorization. Each Party shall be solely responsible for any wages, employment taxes, fringe benefits and work schedules of its own employees or agents.

6.8 *Publication.* Subject to Section 6.3 above, OCHIN and/or Researcher may, at their respective discretion, release information or publish any data, writings, or material resulting from the Project, or use such information or publications in any way for their educational and research purposes.

6.9 *Independent Inquiry.* Nothing in this MOU is intended or shall be construed as limiting any Party's right to engage in similar research, whether independently or pursuant to grants, contracts, or other agreements with third parties.

6.10 *Governing Law.* This MOU is made in accordance with and shall be governed and construed under the laws of the State of Oregon, without regard to conflicts of laws principles.

6.11 *Other Agreements.* This MOU is not intended to conflict or supersede any term of the Master Service Agreement ("MSA") between OCHIN and Provider ("Agreement"). In the event of a conflict between this MOU and the Agreement with respect to matters specifically pertaining to the Project, this MOU shall control.

6.12 *Other Agreements.* OCHIN is permitted to share service area, clinic and/or department-level identified information with the Researcher and additional external partners involved in this initiative, including PCORI's Clinical Data Research Networks and the PCORI Coordinating Center, as part of this research project, provided they are bound by the same confidentiality provisions that OCHIN has with you and/or as stated in the IRB review and approval.

Monterey County Health Department	**OCHIN**
_____	_____
By: _____ Elsa Jimenez_____	By: _____Vance Bauer_____
Title: _____ Director of Health _____	Title: __Vice President of Research_____
Address: _____	Address: __1881 SW Naito Parkway_____
_____	____Portland, OR 97201_____
Attn: _____	Attn: _____

Attachment A
IRB Determination

Attachment B
Study Application

Attachment C
Study Protocol

UCSF
University of California
San Francisco

Human Research Protection Program
Institutional Review Board (IRB)

IRB Determination

Date: December 13, 2018

Principal Investigator
Dr. Mark Pletcher, MD, MPH

Co-Principal Investigator
Dr. Valy Fontil MD, MAS, MD, MAS, MPH

Study Title: Improving Blood Pressure Control in Diverse Populations by Measuring Accurately, Acting Rapidly, and Partnering with Patients: the BP MAP Study
Study #: 18-25890
Reference #: 237826

We have reviewed your project and have made the following determination:

Based on the information you have provided to us, this is a project that includes program evaluations and quality improvement activities that do not require further IRB oversight according to the federal regulations summarized in 45 CFR 46.102(d).

You are not required to submit anything further to the IRB. Should you have any questions, or should key project activities change, you may contact me directly, or you can contact the IRB office at 476-1814.

Study Application (Version 1.0)

1.0 General Information

***Enter the full title of your study:**

Improving Blood Pressure Control in Diverse Populations by Measuring Accurately, Acting Rapidly, and Partnering with Patients: the BP MAP Study

***Enter the study number or study alias**

BP MAP
* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

2.0 Add Department(s)

2.1 List departments and/or research programs associated with this study:

Primary Dept?	Department Name
◉	**UCSF** - *112100* - M_Epidemiology & Biostatistics
○	**UCSF** - *707019* - DIVISION OF GENERAL MEDICINE

3.0 Assign key study personnel(KSP) access to the study

3.1 *Please add a Principal Investigator for the study:

Pletcher, Mark, MD, MPH

Select if applicable

☐ Department Chair ☐ Resident

☐ Fellow

If the Principal Investigator is a Fellow, the name of the Faculty Advisor must be supplied below.

3.2 If applicable, please select the Research Staff personnel:

A) Additional Investigators

Fontil, Valy MD, MAS, MD, MAS, MPH
Co-Principal Investigator

B) Research Support Staff

Faulkner, Madelaine E
Study Coordinator
Getabecha, Shiffen
Study Coordinator

3.3 *Please add a Study Contact:

Faulkner, Madelaine E

Fontil, Valy MD, MAS, MD, MAS, MPH

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The project contact(s) are typically either the Study Coordinator or the Principal Investigator themselves).

3.4 If applicable, please add a Faculty Advisor/Mentor:

3.5 If applicable, please select the Designated Department Approval(s):

Add the name of the individual authorized to approve and sign off on this protocol from your Department (e.g. the Department Chair or Dean).

4.0 Initial Screening Questions

Updated June 2017

4.1 * PROJECT SUMMARY: (REQUIRED) Give a brief overview of this project (250 words or less). Tell us what this study is about, who is being studied, and what it aims to achieve. If you have an NIH Abstract, paste it here: Click on the orange question mark to the right for more detailed instructions.

BP-MAP is a cluster randomized controlled trial (RCT) designed to compare the effectiveness of BP lowering from a clinic-based quality improvement program with Full Support (dedicated practice facilitation) vs. a Self-Guided version of the program. The American Medical Association (AMA) developed the framework for the interventions. The trial will be conducted within the National Patient-Centered Clinical Research Network (PCORnet) that enables distributed querying of electronic health record data in a common data model. The primary outcome will be change in clinic-level blood pressure (BP) control at 6 months. Secondary outcomes will include other blood pressure (BP) control metrics, other time points (12 and 18 months), and process measures such as BP measurement accuracy, medication intensification, and average systolic blood pressure (SBP) reduction after a medication intensification, and repeat visit within 4 weeks after a visit with elevated BP. We will also conduct non-randomized comparisons of BP control in the Full Support and Self-Guided intervention arms to BP control in non-participating "Usual Care" institutions in PCORnet.

4.2 * HUD DEVICE: (REQUIRED) Does this application involve a Humanitarian Use Device (HUD):

- (●) No
- ( ) Yes, and it includes a research component
- ( ) Yes, and it involves clinical care ONLY

4.3 * TYPE OF RESEARCH: (Click the Help link for definitions and guidance): (REQUIRED)

- (●) Biomedical research
- ( ) Social, behavioral, educational, and/or public policy research
- ( ) Hybrid - includes aspects of BOTH types of research (check this option if your research is mainly social /behavioral but also involves specimen collection or blood draws to look at biological measures)

4.4 * SUBJECT CONTACT: (REQUIRED) Does this study involve ANY contact or interactions with participants:

- ○ Yes (including phone, email or web contact)
- ◉ No (limited to medical records review, biological specimen analysis, and/or data analysis)

NOTE: The 'No' option is for studies like chart reviews and specimen analysis where the participants won't even know they are in a research study.
Checking the wrong option here will give you the wrong form and your study will be sent back to you to redo it. Call our office at 415-476-1814 if you are not sure if your study involves subject contact.

4.7 * REVIEW LEVEL: (REQUIRED) Requested review level (Click on the orange question mark to the right for definitions and guidance):

- ○ Full Committee
- ○ Expedited
- ◉ Exempt

4.9 * EXEMPT REVIEW CATEGORY: (REQUIRED)

- ☐ Category 1: Evaluation of educational strategies, curricula and/or classroom management methods
- ☐ Category 2: Use of educational tests, surveys, interviews, or observations of public behavior
- ☐ Category 3: Use of educational tests, surveys, interviews, or observations of public behavior when the subjects are elected or appointed officials or candidates for public office, or if federal statute(s) require without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and therafter
- ☑ Category 4: Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects

4.10 * DATA/SPECIMEN ANALYSIS ONLY (REQUIRED) Does this study ONLY involve records review and /or biospecimen analysis:

○ Yes ◉ No

4.13 * INVESTIGATOR-INITIATED: (REQUIRED) Is this an investigator-initiated study:

◉ Yes ○ No

4.14 * CANCER: (REQUIRED) Does this study involve cancer (e.g., the study involves patients with cancer or at risk for cancer, including behavioral research, epidemiological research, public policy research, specimen analysis, and chart reviews):

○ Yes ◉ No

If you don't know if you should answer 'Yes' or 'No,' please **email** the Cancer Center's Protocol Review Committee for help.

4.16 * STEM CELLS: (REQUIRED) Does this study involve human stem cells (including iPS cells and adult stem cells), gametes or embryos:

- (●) No
- ( ) Yes, and requires IRB and GESCR review
- ( ) Yes, and requires GESCR review, but NOT IRB review

4.17 * FINANCIAL INTERESTS: (REQUIRED) Do you or any other responsible personnel (or the spouse, registered domestic partner and/or dependent children thereof) have financial interests related to this study:

( ) Yes (●) No

5.0 Funding

5.1 * FEDERAL FUNDING: (REQUIRED) Is this study currently supported in whole or in part by Federal funding, *even by a subcontract*, OR has it received ANY Federal funding in the past:

( ) Yes (●) No

5.2 * DoD INVOLVEMENT: Is this project linked in any way to the Department of Defense (DoD): (REQUIRED)

( ) Yes (●) No

5.3 SPONSORS: Identify all sponsors and provide the funding details. If funding comes from a Subcontract, please list only the Prime Sponsor:

External Sponsors:

View Details	Sponsor Name	Sponsor Type	Awardee Institution	Contract Type:	UCSF RAS "P number" or eProposal number	UCSF RAS System Award Number ("A" + 6 digits)
⊟	Patient-Centered Outcomes Research Inst	05	UCSF	Contract		

Sponsor Name:	Patient-Centered Outcomes Research Inst
Sponsor Type:	05
Sponsor Role:	Funding
Grant/Contract Number:	
Awardee Institution:	UCSF
Is Institution the Primary Grant Holder:	Yes
Contract Type:	Contract
UCSF RAS "P number" or eProposal number:	
UCSF RAS System Award Number ("A" + 6 digits):	
Grant Number for Studies Not	

Funded thru UCSF:	
Grant Title:	PCORnet BP Control Laboratory
PI Name: (If PI is not the same as identified on the study.)	
Significant Discrepancy:	

If the funding is coming through UCSF and you don't know the A or P number, you can search the eProposal side for the contract or grant (this does NOT replace adding the sponsor by name above AND entering the A or P number):

Project Status	Proposal Number	Project Title	Principal Investigator
No Projects are Linked to this IRB Study			

Other Funding Sources and Unfunded Research - Gift, Program, or Internal Funding (check all that apply):

- ☐ Funded by gift (specify source below)
- ☐ Funded by UCSF or UC-wide program (specify source below)
- ☐ Specific departmental funding (specify source below)
- ☐ Unfunded (miscellaneous departmental funding)
- ☐ Unfunded student project

6.0 Sites, Programs, Resources, and External IRB Review

6.1 UCSF AND AFFILIATED SITES (check all that apply):

- ☐ UCSF (including Laurel Heights and all the other sites outside the main hospitals)
- ☐ Parnassus
- ☑ Mission Bay
- ☐ China Basin
- ☐ Mount Zion
- ☐ Helen Diller Family Comprehensive Cancer Center
- ☐ Langley Porter Psychiatric Institute
- ☐ San Francisco General Hospital (SFGH)
- ☐ SF VA Medical Center (SF VAMC)
- ☐ Blood Centers of the Pacific (BCP)
- ☐ Blood Systems Research Institute (BSRI)
- ☐ Fresno Community Medical Center
- ☐ Gallo
- ☐ Gladstone
- ☐ Jewish Home
- ☐ Institute on Aging (IOA)
- ☐ SF Dept of Public Health (DPH)

6.4 RESEARCH PROGRAMS: Check any UCSF research programs this study is associated with:

- ☐ Cancer Center
- ☐ Center for AIDS Prevention Sciences (CAPS)

- [ ] Global Health Sciences
- [ ] Immune Tolerance Network (ITN)
- [ ] Neurosciences Clinical Research Unit (NCRU)
- [ ] Osher Center
- [ ] Positive Health Program

6.6 * MULTI-CENTER TRIAL: (REQUIRED) Is this a multicenter research trial? By multi-center trial, we mean a study where the protocol is developed by an industry sponsor, consortium, a disease-group, etc., who then selects sites across the nation or in different countries to participate in the trial. The local sites do not have any control over the design of the protocol.

(•) Yes ( ) No

Is UCSF the coordinating center:

(•) Yes ( ) No

6.7 OTHER SITE TYPES: Check all the other types of sites not affiliated with UCSF with which you are cooperating or collaborating on this project: Do NOT check any boxes below if this is a multi-center clinical trial, UCSF is just one of the sites, and neither UCSF nor its affiliates are the coordinating center.

- [ ] Other UC Campus
- [x] Other institution
- [ ] Other community-based site
- [ ] Foreign Country
- [ ] Sovereign Native American nation (e.g. Navajo Nation, Oglala Sioux Tribe, Havasupai, etc.)

6.10 * RELYING ON AN EXTERNAL IRB: Does this application include a request to rely on an external IRB other than the NCI IRB (e.g. UC reliance, private/commercial IRB, or institutional IRB): (REQUIRED) Check out the orange question mark to the right to find out if your study is eligible for external IRB review.

( ) Yes (•) No

7.0 Outside Site Information

7.1 Outside Site Information

Click "Add a new row" to enter information for a site. Click it again to add a second site again to add a third site, a fourth site, etc.

8.0 Records Review, Biospecimen Analysis Projects and Research Database / Registry / Repository Details

(Exempt 4 and Expedited Review Category 5)

8.1 * AIMS/OBJECTIVES: What do you hope to accomplish with this study: (REQUIRED)

Aim
To compare effectiveness of the M.A.P. program with "Full Support" (dedicated practice facilitation) versus a "Self-Guided" version (online access to M.A.P. materials and orientation webinar only). A secondary aim is to compare these active interventions to usual care.

Hypothesis
We hypothesize clinics randomized to the Full Support version will achieve a larger increase from baseline in the proportion of their hypertensive patients with controlled BP at 6 months as compared to clinics randomized to the Self-Guided version, and also as compared with usual care.

8.2 * INCLUSION CRITERIA: Describe the population being studied (e.g. condition, age, etc.): (REQUIRED)

Active Clinics
For inclusion as an Active Clinic in this study, clinics may participate must be able to identify:

- A Site Champion who works at the clinic and who is willing to take primary responsibility for implementing the M.A.P. intervention
- A Physician Champion who works at the clinic and who is willing to advocate actively for the M.A.P. intervention
- A Practice Change Facilitator willing to attend a 1-day training and help guide implementation of the M.A.P intervention for Full Support sites, with the support of AMA staff (may be the Site Champion or Physician Champion, or a person with regional responsibilities who can support multiple sites)

Sites will be excluded if they:

- Have implemented any high blood pressure quality improvement component from the M.A.P. BP improvement program as part of Target: BP or from the AMA or Target: BP websites
- Are currently involved in an ongoing clinical trial or grant funded project related to high blood pressure or hypertension

Usual Care Clinics
We will include PCORnet Datamarts participating in BP TRACK, a concurrently-running BP Control Registry within PCORnet that will provide quarterly datamart-level estimates of BP control and other aggregate metrics relevant to BP control. All participating datamarts will be included, with the following exceptions:

- We will exclude datamarts with any Active Clinics participating in BP MAP
- We will exclude datamarts that obscure dates via date-shifting, as this will not allow for control of concurrent secular trends

8.3 * SPECIAL POPULATIONS: Indicate if the primary study population includes (do not check if the records may be incidentally reviewed but are not a primary target population of your study): (REQUIRED)

- ☐ Children or minors (<18 years old)
- ☐ Pregnant women
- ☐ Neonates
- ☐ Fetuses
- ☐ Prisoners
- ☑ None of the above

8.4 SAMPLE SIZE: Approximate number of individuals whose records or biospecimens you will review /analyze: (This question may not be relevant if your research is based on a date period rather than a sample size.)

Not available

If you cannot estimate the number of records you will need, explain why:

Queries will be limited only by inclusion criteria above, as well as dates (statistics generally look back for 1 year, but will use information such as past diagnoses that may look at much older data as well), and it is not yet clear how many datamarts will participate, so sample sizes cannot be anticipated ahead of time. Aggregate results with cell sizes < 10 will be omitted from reports.

8.5 * TYPES OF ACTIVITIES: (REQUIRED)

- (•) Record review
- ( ) Biospecimen analysis
- ( ) Both record review and biospecimen analysis
- ( ) Repository administration (specimens are collected and sent under a separate approval - no specimen collection or analysis occurring under this protocol)

8.6 DATA/SPECIMEN COLLECTION: Will the data and/or specimens be collected specifically for this proposed research project or are they all already pre-existing or collected for other purposes:

- ( ) Some or all of the data and/or specimens will be collected specifically for this project
- (•) This project only involves secondary analysis of records and/or specimens that were collected for another research project

8.7 * RETROSPECTIVE VS. PROSPECTIVE: (REQUIRED)

- ( ) Retrospective record or biospecimen review only – all of the information or specimens you want to use have already been collected as of the date of this application
- ( ) Prospective record or biospecimen review only – the information or specimens you want have not yet been created or collected
- (•) Both retrospective and prospective review – some of the data and/or specimens already exist and some have yet to be created

List the study period (e.g. the date range during which the records or specimens included in this study were or will be created):

From:

01/01/2010

To:

08/01/2021

8.8 * PATIENT RECORDS: Are any of the people whose records will be looked at patients at UCSF: (REQUIRED)

( ) Yes (•) No

8.10 * CONSENT: Do you plan to obtain consent from any of the people whose records/specimens will be studied: (REQUIRED)

( ) Yes (•) No

8.11 * SOURCE OF RECORDS/SPECIMENS: (REQUIRED)

- [x] Medical record or other health record (identify source below)
- [ ] Data Repository (IDR) or The Health Record Data Service (THREDS)
- [ ] Existing research records (including OnCore) or identifiable biospecimens (identify source below)
- [ ] Records or specimens sent from an outside source

☐ Records open to the public (identify source below)

Source of the records or specimens:

EHR data in the PCORnet Common Data Model, which is maintained by healthcare institutions involved in the PCORnet research network.

8.13 * IDENTIFIERS: Check all identifiers that you will collect and include in your research records, even temporarily: (REQUIRED) For banks receiving and storing biospecimens, check the identifiers that will be associated with specimens.

☐ Names
☐ Dates
☐ Postal Addresses
☐ Phone numbers
☐ Fax numbers
☐ Email addresses
☐ Social Security Numbers
☐ Medical record numbers and/or pathology or radiology accession numbers
☐ Account numbers
☐ License or certificate numbers
☐ Vehicle ID numbers
☐ Device identifiers or serial numbers
☐ Web URLs
☐ IP address numbers
☐ Biometric identifiers
☐ Facial photos or other identifiable images
☐ Any other unique identifier
☑ None of the above

The UCSF IRB can approve the use of PHI as part of a 'Limited Data Set.' A limited data set is described as health information that excludes direct identifiers but that may include:

- City
- State
- ZIP Code
- Elements of date (including dates such as admission, discharge, service, month and year but not day of birth)
- Other numbers, characteristics, or codes not listed as direct identifiers, including ages in years, months or days or hours

For more information about HIPAA, identifiers in research sets and limited data sets, check out our **HIPAA FAQs**.

Are you requesting use of PHI as part of a Limited Data Set:

○ Yes ◉ No

8.14 * DATA POINTS: List the variables you are collecting from the records or that will be received with the data or specimens: (REQUIRED)

We will collect the following aggregate-level statistics from participating clinics:
1) Change in % BP Control at 6 months (primary outcome). Our primary outcome will be clinic-level change in the proportion of patients with controlled BP from baseline to 6 months after the start of the intervention. We define BP control according to NQF 0018 as the percent of eligible patients (defined above) with SBP <140 mmHg and DBP < 90 mmHg, based on measurements obtained at the most recent

ambulatory clinical encounter at baseline (using the lowest measures of SBP and DBP at that encounter) and similarly at the 6-month time point after initiation of the intervention.
2) BP Control to 2017 Guideline Goal, %. This alternative overall measure of BP control is identical to Metric 1, except that attainment of BP Control is defined by lower thresholds for blood pressure (SBP < 130 mmHg and DBP < 80 mmHg), as per the goal stated in the 2017 ACC/AHA Hypertension Guideline4.
3) Improvement in blood Pressure, %. This overall measure of BP improvement defines BP improvement as either a reduction of 10 mmHg in SBP or achievement of SBP that is "adequately controlled" (SBP < 140 mmHg) over a period of 3 months, among hypertensive patients not previously controlled.19
4) Confirmatory repeated blood pressure measurement, %. This process measure is designed to capture the practice of repeating a blood pressure measurement in the same visit when the first measurement done in clinic is high (SBP>140 mmHg or DBP>90 mmHg).
5) Medication intensification, %. This process measure captures the proportion of visits where BP is uncontrolled where a medication is ordered that is of a different class of medications than had previously been used. Note that this explicitly does not give credit for ordering a simple refill or medication dose increase, or use of a different medication in the same class.
6) Repeat visit in 4 weeks after uncontrolled HTN, %. This process measure captures the proportion of persons who had uncontrolled HTN who made a subsequent outpatient visit within the following 4 weeks.
7) Average SBP reduction after medication intensification, mmHg defined as the change in SBP observed between a visit with a medication intensification to the subsequent visit.
8) Terminal digit = zero, %. Inappropriate rounding of blood pressure measurements (usually to zero) leads to measurement error and worse treatment decisions. This metric is designed to catch this behavior, which would lead to a terminal digit of zero of greater than 10% (if using an automated BP monitor is used) or greater than 20% (if a manual BP monitor is used with recommended rounding to even digits).
9) Use of fixed dose combination medications among patients taking 2 or more classes of medications, %. Use of fixed dose combination medications helps with adherence, promotes rational combinations of medications, and increases likelihood of achieving BP control.
10) Use of a CCB or thiazide-type diuretic among African-American patients on one medication %. Calcium channel blockers (CCB) and thiazide-type diuretics are medication classes recommended to treat black or African American patients as first line monotherapy due to increased efficacy.

9.0 Waiver of Consent/Authorization

(August, 2013)

9.1 * IMPACT OF WAIVER ON RIGHTS AND WELFARE: I affirm that subjects' rights and welfare will not be adversely affected by waiving informed consent:

- (•) Yes

9.2 * PRACTICABILITY: It is not practicable to conduct the research without the waiver of consent / authorization because (check all that apply):

- [x] Many subjects are no longer being followed at the institution or are deceased
- [x] The attempt to contact subjects poses a greater risk than this study
- [x] The large number of records required makes it impracticable to contact all potential subjects
- [x] The researchers do not know the identity of the study subjects and therefore cannot contact them
- [ ] The data being used was collected under a different IRB-approved study and subjects gave their consent for data to be used in research of this type

9.3 * INFORMING SUBJECTS POST-PARTICIPATION: Will subjects be provided with pertinent information after their participation:

- ( ) Yes (•) No

9.4 * IDENTIFIERS: Are you recording identifiers in the research records: (REQUIRED)

- ( ) Yes (•) No

10.0 Confidentiality - Records Review / Specimen Analysis Research and Registry / Repository Administration

10.1 * **CONFIDENTIALITY ASSURANCE: firm below that you will keep data confidential: (REQUIRED) I will keep any data sets that include identifiers secure and protected from improper use and disclosure by using methods such as:**

- **Physical Security – Keeping data in locked file cabinets, locked offices, locked suites, and physically securing computers and servers.**
- **Electronic Security – Following UCSF minimum security standards for electronic information resources, which includes (but is not limited to): not storing identifiers on portable devices like laptops or flash drives if they are unencrypted, encrypting portable devices, and storing data in password-protected files and on secure networks.**

(•) Yes

10.2 ADDITIONAL CONFIDENTIALITY MEASURES: Describe any additional measures to assure confidentiality and protect identifiers from improper use and disclosure, if any:

We will not receive any patient-level data, just reports of aggregate statistics. Statistics will be aggregated at the level of the datamart, and also (for participating institutions) at the level of the clinical unit. Please see above (Aims and Objectives) for the aggregate statistics we will collect.

10.3 * **DATA SHARING: Might identifiable information be shared with outside groups (people outside the research team): (REQUIRED)**

( ) Yes (•) No

11.0 Qualifications of Key Study Personnel

11.1 **NOTE: This information is required and your application will be considered incomplete without it. If this study involves invasive or risky procedures, or procedures requiring special training or certification, please identify who will be conducting these procedures and provide details about their qualifications and training. Also identify each person who will be involved in the consent process. Click the orange question mark for more information and examples.** **Under qualifications, please include:**

- **Academic Title**
- **Institutional Affiliation (UCSF, SFGH, VAMC, etc.)**
- **Department**
- **Certifications**

November, 2015 - NEW Definition of Key Study Personnel and CITI Training Requirements:

UCSF Key Study Personnel include the Principal Investigator, other investigators and research personnel who are directly involved in conducting research with study participants or who are directly involved in using study participants' identifiable private information during the course of the research. Key Personnel also include faculty mentors/advisors who provide direct oversight to Postdoctoral Fellows, Residents and Clinical Fellows serving as PI on the IRB application. **The IRB requires that all Key Study Personnel**

complete Human Subjects Protection Training through CITI prior to approval of a new study, or a modification in which KSP are being added. More information on the CITI training requirement can be found on our website.

KSP Name	Description of Study Responsibilities - Briefly describe what will each person be doing on the study. If there are procedures requiring special expertise or certification, identify who will be carrying these out. Also identify who will be obtaining informed consent.	Qualifications, Licensure, and Training
Dr. Fontil, Valy MD, MAS, MD, MAS, MPH	Dr. Fontil will lead the implementation of BP MAP of the grant, working closely with Dr. Pletcher, the American Medical Association and American Heart Association.	Dr. Fontil is a general internist physician, health services researcher, and implementation scientist focused on studying healthcare interventions and innovations in real-world settings targeted to reduce cardiovascular risk in high-risk populations vulnerable to health disparities-- is at UCSF in the department of Medicine. He was the lead PI on a practice-based hypertension intervention that led to improved blood pressure control in a network of 12 urban safety-net clinics in San Francisco county funded by the National Institute of Neurological Diseases and Stroke. Given his experience with hypertension interventions
Dr. Pletcher, Mark, MD, MPH	Dr. Pletcher is the Principal Investigator (PI) for the Blood Pressure Control Laboratory project; this study is Aim 2 of that project.	Mark Pletcher is a cardiovascular epidemiologist and general internal medicine physician at UCSF in the department epidemiology and biostatistics. He is the lead PI for the Health eHeart Alliance PPRN, lead PI for the Cardiovascular Health Collaborative Research Group and leads the Hypertension Research Interest Group.

12.0 End of Study Application

12.1 End of Study Application Form

To continue working on the Study Application: Click on the section you need to edit in the left-hand menu. Remember to save through the entire Study Application after making changes. If you are done working on the Study Application: Important: Before proceeding, please go back to Section 4.0 Initial Screening Questions and Save and Continue through the form to make sure all the relevant sections and questions have been included. If you've changed any answers since you started, the branching may have changed. Your application will be incomplete and it will

have to be returned for corrections. Once you are sure the form is complete, click Save and Continue. If this is a new study, you will automatically enter the Initial Review Submission Packet form, where you can attach consent forms or other study documents. Review the Initial Review Submission Checklist for a list of required attachments. Answer all questions and attach all required documents to speed up your approval.

The UCSF IRB wants your feedback about this new form. Please click the link to take a brief survey about the new application form.

Improving Blood Pressure Control in Diverse Populations by Measuring Accurately, Acting Rapidly, and Partnering with Patients: the BP MAP Study

Protocol

I. EXECUTIVE SUMMARY

BP-MAP is a cluster randomized controlled trial (RCT) designed to compare the effectiveness of BP lowering from a clinic-based quality improvement program with Full Support (dedicated practice facilitation) vs. a Self-Guided version of the program. The American Medical Association (AMA) developed the framework for the interventions. The trial will be conducted within the National Patient-Centered Clinical Research Network (PCORnet) that enables distributed querying of electronic health record data in a common data model. The primary outcome will be change in clinic-level blood pressure (BP) control at 6 months. Secondary outcomes will include other blood pressure (BP) control metrics, other time points (12 and 18 months), and process measures such as BP measurement accuracy, medication intensification, and average systolic blood pressure (SBP) reduction after a medication intensification, and repeat visit within 4 weeks after a visit with elevated BP. We will also conduct non-randomized comparisons of BP control in the Full Support and Self-Guided intervention arms to BP control in non-participating "Usual Care" institutions in PCORnet. We are requesting certification of exemption from IRB oversight given that both arms will implement accepted guideline-based minimal risk quality improvement interventions.

II. BACKGROUND

Uncontrolled BP is the leading preventable cause of death in the US after smoking, causing nearly 400,000 deaths per year [1]. While effective medications are available to control BP, multiple rounds of medication adjustment and intensification are typically required, and BP control is often not achieved[2,3].

The usual configuration of healthcare delivery – periodic and relatively infrequent office visits with a physician – is not ideal for achieving BP control quickly and efficiently[4,5]. In-office measurement of BP is often performed using poor technique, while the patient is getting settled after arrival at the office[6]. Due to these reasons and the "white coat effect", it is often artificially elevated and may not be a reliable indicator of actual BP. Inaccurate BP measurement may result in missed opportunities for BP treatment intensification, which is common in the US, and a major cause of delay in attainment of BP control[4,7]. Patients' lack of adherence to BP medications is also a common cause of delay in control. While discontinuation of medications is sometimes due to medication side effects[8,9], it may also result from a lack of adequate time and attention paid to shared decision-making about the need for treatment intensification[10].

Some institutions have successfully reconfigured the way they deliver care for hypertension and manage their hypertensive patient population. Kaiser Permanente Northern California, for example, achieved BP control rates of 80% by using population management, frequent non-physician visits and evidence-based treatment protocols for optimal treatment intensification ([11]. Other programs utilize pharmacists and nurses as case managers to provide medication management between visits. Reconfiguring services with additional staff dedicated to medication and disease management programs[11-16], however, may not be feasible or sustainable in all settings, particularly in resource-poor settings such as safety net clinics[17-19]. Deployment of sustainable programs may enhance clinic-based BP management.

The AMA developed a framework for clinic-based quality improvement that works within traditional office-based configuration of healthcare delivery (the "Measure Accurately, Act Rapidly, and Partner with Patients" (M.A.P.) Program, described below). The AMA is collaborating with AHA in the initiative,

"Target:BP" to 1) recognize health care organizations achieving ≥ 70% BP control and 2) improve BP control by scaling the M.A.P. program to build a healthier nation. The initiative includes a set of tools, resources and detailed plans to support clinics interested in implementing the M.A.P framework as a structured intervention program.

Pilot implementation of this program led to dramatic improvements in BP control (from 63% to 90% in a single clinic and 64% to 74% in a group of 16 clinics). Although these results are promising, questions remain regarding how to optimize and efficiently scale the program in order to maximize sustained clinic-level involvement remain[20,21].

In this study, we will randomize 20-28 clinics to receive one of two types of support interventions: 1) a set of self-evaluation tools, improvement plans, and other resources that can be accessed by clinics and used independently ("Self-Guided"), and 2) a practice facilitation support program that helps clinics understand those tools/plans/resources and actually train people to implement the tools and plans ("Full Support"). We will then compare BP control between those arms, and against Usual Care control institutions.

III. METHODS

Aim

To compare effectiveness of the M.A.P. program with "Full Support" (dedicated practice facilitation) versus a "Self-Guided" version (online access to M.A.P. materials and orientation webinar only). A secondary aim is to compare these active interventions to usual care.

Hypothesis

We hypothesize clinics randomized to the Full Support version will achieve a larger increase from baseline in the proportion of their hypertensive patients with controlled BP at 6 months as compared to clinics randomized to the Self-Guided version, and also as compared with usual care.

Study design

This is a pragmatic, cluster-randomized, comparative effectiveness trial designed to compare the effectiveness of the M.A.P. program with Full Support versus a Self-Guided version of the program, and versus usual care.

Study Population and Setting

We will recruit Active Clinics from REACHNet and ADVANCE, two of the 10 Clinical Data Research Networks (CDRNs) that comprise PCORnet. We chose these two CDRNs to focus clinic recruitment in safety net clinics and to boost numbers of underserved populations and enhance power to detect heterogeneity of treatment effects. We are targeting clinics that have varied racial/ethnic composition with substantial proportions of Hispanic and Black patients, and patients with lower socioeconomic status. Usual Care Clinics will come from other CDRNs within PCORnet.

<u>Active Clinics</u>

For inclusion as an Active Clinic in this study, clinics may participate must be able to identify:

- A Site Champion who works at the clinic and who is willing to take primary responsibility for implementing the M.A.P. intervention
- A Physician Champion who works at the clinic and who is willing to advocate actively for the M.A.P. intervention
- A Practice Change Facilitator willing to attend a 1-day training and help guide implementation of the M.A.P intervention for Full Support sites, with the support of AMA staff (may be the Site

Champion or Physician Champion, or a person with regional responsibilities who can support multiple sites)

Sites will be excluded if they:

- Have implemented any high blood pressure quality improvement component from the M.A.P. BP improvement program as part of Target: BP or from the AMA or Target: BP websites
- Are currently involved in an ongoing clinical trial or grant funded project related to high blood pressure or hypertension

Usual Care Clinics

We will include PCORnet Datamarts participating in BP TRACK, a concurrently-running BP Control Registry within PCORnet that will provide quarterly datamart-level estimates of BP control and other aggregate metrics relevant to BP control. All participating datamarts will be included, with the following exceptions:

- We will exclude datamarts with any Active Clinics participating in BP MAP
- We will exclude datamarts that obscure dates via date-shifting, as this will not allow for control of concurrent secular trends

Patients

Within clinics (Active or Usual Care), patients will be eligible (and identified from the electronic health record) if they meet National Quality Forum BP Control Metric (NQF 0018) criteria[22]:

- Age 18-85 on the date of analysis
- At least one outpatient encounter with a diagnosis of hypertension during the first six months of the measurement year (ending on the date of analysis)
- No diagnosis or evidence of end-stage renal disease on or prior to the end of the measurement year
- No pregnancy during the measurement year
- No admission to an inpatient setting during the measurement year

Interventions

This trial will compare two strategies for improving BP control at the clinic level and compare these two strategies to a group of non-randomized usual-care clinics. Both strategies rely on an extensive set of materials developed by the AMA to support clinic implementation of the M.A.P. Program. These materials have been tested, validated and include clinician and patient targeted resources. We will compare two different ways of helping clinics use these materials to implement the M.A.P. Program:

Arm 1: Self-Guided: Active Clinics randomized to the Self-Guided Arm will receive access to an AHA/AMA web platform that includes the posted M.A.P. materials as described in the appendix and limited access to AMA Staff who are available to answer questions. We will facilitate access to staff by hosting a kick-off webinar for program participants that will include an orientation to the materials on the website, general advice and practical tips about what works for implementation, and time for answering questions and discussion with the group.

Arm 2: Full Support: Active Clinics randomized to the Full Support Arm will receive online access to M.A.P. materials and orientation webinar, as described above, but also a Practice Facilitator (personnel trained to implement the M.A.P. BP Improvement Program) who will be supported by AMA staff, and will lead the health center clinical staff, site champions and physician leads at

each clinic over the course of 6 months to support the implementation of the MAP Program. With support from an AMA "Improvement Advisor", the Practice Change Facilitators will perform a baseline assessment of current workflows and assess each domain of M.A.P. They will 1) identify gaps and plan for specific incremental modifications tailored to address specific clinic needs; 2) perform periodic evaluations with the AMA Improvement Advisor to monitor use of M.A.P assessment tools and checklists; and 3) support use of EHR-based reporting that displays clinic-level BP control and secondary outcome measures. The goal of the Full Support program is to help care teams develop skills and sustainable workflows that are effective at attaining and maintaining high levels of BP control.

Usual Care: Usual Care Clinics will receive no intervention.

Randomization

We will use a random number generator to randomize 10-14 Active Clinics to the Full Support Arm and 10-14 Active Clinics to the Self-Guided Arm. Randomization will be stratified (and balanced within strata) by CDRN and by participation (or not) in BP HOME, a concurrently running individual-level RCT that will provide home blood pressure monitoring devices to participating patients with a high blood pressure reading in clinic. As this is a real-world intervention that clinics will have to implement, they will not be blinded to the randomization.

Outcomes and measurements

We will measure all outcomes by running a series of queries against EHR data maintained in the PCORnet Common Data Model. The outcomes will use individual patient-level data, reported in aggregate, for each participating clinic. Individual patients will not be followed over time across different repeat queries. While all measurements will be obtained on approximately a monthly basis for the purpose of guiding implementation of the intervention, the primary outcome will compare the metrics obtained at baseline (initiation of the intervention) and at 6 months (and at 12 and 18 months in secondary analyses) for each clinic. We list the outcome measures of interest below. Additional details on data query and description for each measure is provided in the supplemental material.

1) Change in % BP Control at 6 months (primary outcome). Our primary outcome will be clinic-level change in the proportion of patients with controlled BP from baseline to 6 months after the start of the intervention. We define BP control according to NQF 0018 as the percent of eligible patients (defined above) with SBP <140 mmHg and DBP < 90 mmHg, based on measurements obtained at the most recent ambulatory clinical encounter at baseline (using the lowest measures of SBP and DBP at that encounter) and similarly at the 6-month time point after initiation of the intervention.

Secondary outcomes will include nine additional EHR-derived clinic-level metrics relevant to BP control. These metrics include alternate measures and BP control and improvement, as well as process and proxy measures aligned to the domains of the M.A.P. program including: indicators of BP measurement accuracy, medication intensification, average SBP reduction after medication intensification, and repeat visit within 4 weeks after a visit with uncontrolled HTN. Each metric below (and the primary outcome) will be measured as a change from baseline to 6 months (our primary time point), and change from baseline to 12 and 18 months. We will assess each metric overall (in all eligible patients) and within subgroups defined in Table 3.

2) BP Control to 2017 Guideline Goal, %. This alternative overall measure of BP control is identical to Metric 1, except that attainment of BP Control is defined by lower thresholds for blood pressure (SBP < 130 mmHg and DBP < 80 mmHg), as per the goal stated in the 2017 ACC/AHA Hypertension Guideline[4].
3) Improvement in blood Pressure, %. This overall measure of BP improvement defines BP improvement as either a reduction of 10 mmHg in SBP or achievement of SBP that is "adequately controlled" (SBP < 140 mmHg) over a period of 3 months, among hypertensive patients not previously controlled.[19]
4) Confirmatory repeated blood pressure measurement, %. This process measure is designed to capture the practice of repeating a blood pressure measurement in the same visit when the first measurement done in clinic is high (SBP>140 mmHg or DBP>90 mmHg).
5) Medication intensification, %. This process measure captures the proportion of visits where BP is uncontrolled where a medication is ordered that is of a different class of medications than had previously been used. Note that this explicitly does not give credit for ordering a simple refill or medication dose increase, or use of a different medication in the same class.
6) Repeat visit in 4 weeks after uncontrolled HTN, %. This process measure captures the proportion of persons who had uncontrolled HTN who made a subsequent outpatient visit within the following 4 weeks.
7) Average SBP reduction after medication intensification, mmHg defined as the change in SBP observed between a visit with a medication intensification to the subsequent visit.
8) Terminal digit = zero, %. Inappropriate rounding of blood pressure measurements (usually to zero) leads to measurement error and worse treatment decisions. This metric is designed to catch this behavior, which would lead to a terminal digit of zero of greater than 10% (if using an automated BP monitor is used) or greater than 20% (if a manual BP monitor is used with recommended rounding to even digits).
9) Use of fixed dose combination medications among patients taking 2 or more classes of medications, %. Use of fixed dose combination medications helps with adherence, promotes rational combinations of medications, and increases likelihood of achieving BP control.
10) Use of a CCB or thiazide-type diuretic among African-American patients on one medication %. Calcium channel blockers (CCB) and thiazide-type diuretics are medication classes recommended to treat black or African American patients as first line monotherapy due to increased efficacy.

Analysis Plan

Overview: We will use an unadjusted difference-in-differences analytic approach to testing comparative effectiveness hypotheses, weighting for differences in cluster size. Despite expected between-clinic differences in baseline characteristics and BP control (especially in the non-randomized comparison with Usual Care control institutions), the difference-in-differences approach provides some protection against confounding because the outcome being compared is a within-clinic change score, as described below. We will first conduct 3 pairwise primary hypothesis tests (adjusting for multiple comparisons), as described below. We will then conduct a series of exploratory analyses of secondary outcomes, sensitivity analyses adjusting for baseline clinic-level characteristics, subgroup analyses to examine heterogeneity of effect, and exploratory mediation analyses to understand the mechanisms by which the full-support intervention might provide greater effectiveness.

Differences-in-differences analytic approach: We will calculate difference-in-differences through the following steps:

1. Use clinic-level metrics (e.g., % BP control) at baseline for each clinic before intervention starts (t_0) and at 6 months (t_6)
2. Calculate the clinic-level pre-post difference in the metric ($t_6 - t_0$)
3. Calculate the mean pre-post difference in each treatment group, the between-group difference of differences, both with 95% confidence intervals, and compare the 20-28 pre-post differences by arm using weighted linear regression; observations will be weighted by the inverse of the site-specific variances of the change scores, which will be approximated using the site-specific sample size and level of the time-specific metrics, and the average correlation of the pre- and post-metrics across clinics. Weights will be normalized to sum to the total number of clinics in the Arm 1 vs. Arm 2 comparisons (and to the number of included clinics plus the number of participating PCORnet datamarts for the comparisons of each Arm with Usual Care).

Primary hypothesis tests, with adjustment for multiple comparisons

Our primary hypothesis tests will be 3 pairwise comparisons:

- Test 1: Arm 1 vs Arm 2
- Test 2: Arm 1 vs. Usual Care
- Test 3: Arm 2 vs. Usual Care

In order to maintain an overall type 1 error rate of 5%, we will set our critical p-value threshold for Test 1 at p=0.04, and then at p=0.005 for Test 2 and Test 3 since they will benefit from the very large sample size expected in the Usual Care groups. No other adjustments for multiple comparisons are planned for secondary outcomes or other exploratory analyses described below.

Descriptive analyses comparing clinic-level baseline characteristics: *Descriptive statistics* will be used to compare clinic-level characteristics between the two intervention arms at baseline. We will include descriptions of clinic-level patient population characteristics (age groups, gender, race/ethnicity, type of insurance, mean number of current antihypertensive medication classes prescribed, and prevalence of comorbid conditions such as diabetes, chronic kidney disease, or heart failure), workforce composition (i.e. proportion of nurse practitioners, physician assistants, physicians, and physician specialty - internal vs family medicine), clinic size and staffing level (total number of patients, nurses, and medical assistants), level of access (availability of same-day appointments, mean time to third next available appointment), and possibly other characteristics depending on availability.

Sensitivity analyses: In a sensitivity analysis, we will perform multivariable linear regression analyses to compare clinic-level pre-post differences in our primary and secondary outcomes. The regression models will adjust for health system as well as for whether the clinic was engaged in BP HOME, a concurrently running individual-level randomized trial that will provide home blood pressure monitoring devices to participating patients with a high blood pressure reading in clinic. We will also consider models including baseline clinic-level baseline characteristics that are imbalanced between arms based on our descriptive baseline analysis and/or clinic-level distributions of age, sex and race-ethnicity.

Subgroup analysis to test for heterogeneity of treatment effects (HTE): We will produce clinic-level subgroup-specific analyses limited to subgroups defined by the characteristics listed in Table 3, and test for interactions by intervention group (as well as with Usual Care) and subgroup categories. We

hypothesize that the BP Control effect from the Full-Support intervention relative to Self-Guided and Usual Care groups will be smaller in patients who are younger, male, and Black given published BP control difficulties in these patients. We will also specifically test for an interaction between treatment group and enrolling CDRN, given health IT infrastructures may differ by CDRN in ways that can interact with the effectiveness of the interventions. All subgroup analyses will be reported.

Table 3. Subgroups for HTE analysis
Age: 18-44 vs. 45-64 vs. 65+
Race/ethnicity: NH White vs. NH Black vs. NH Asian vs. Hispanic (any race) vs. Other
Sex: Male vs. Female
Enrolling CDRN
HTE – Heterogenelty of treatment effects NH – Non-Hispanic

Exploratory Mediation analysis: As many of our secondary outcomes are presumably process measures in the causal pathway to achieving BP control, we will perform a mediation analysis to understand the degree to which the potential added benefit of the Full Support intervention on BP control is explained by changes in the process measures. We will perform a mediation analysis using nested linear regression models for the effect of randomization assignment (i.e. Full Support vs. Self-Guided) on clinic level pre-post differences in percent control, first omitting, then adding each of our proposed mediators to the base model. The hypothesized process mediators will include pre-post changes in BP measurement accuracy, medication intensification, and average SBP reduction after medication intensification, and repeat visit in 4 weeks after uncontrolled HTN. These analyses will be implemented using the Paramed module in Stata statistical software [26] to calculate natural direct effect (NDE) of full-support on BP control and the natural indirect effect (NIE) through each mediator. The total causal effect (TCE) is the sum of the NDE and NIE. Dividing each NIE by the TCE will calculate the proportion of the causal effect explained by each mediator. [27]

Additional exploratory analyses: We will explore temporal patterns in the effect of randomization assignment using linear mixed models for repeated clinic-level changes since baseline in primary and secondary outcomes assessed at 6, 12, and 18 months. These models will include random effects for clinic, as well as fixed effects for treatment assignment (as a categorical variable), and their interaction. Heterogeneity of treatment effects across time will be tested using a 2 degree-of-freedom chi-square test; in addition, a chi-square test for linear trend will be obtained by comparing the fitted treatment assignment effects at 6 and 18 months.

Data source, collection, management, and safety: Consistent with principles of pragmatic clinical trials, we will use EHR data for patient identification and assessment of intervention implementation and outcomes. Both interventions (and usual care) are consistent with standard of care. Therefore, both the interventions and data collection in this study carry minimal risk to patients. We will leverage the data infrastructure and resources in the PCORnet Common Data Model to collect de-identified, clinic-level aggregate data needed for analysis. Additional details on the PCORnet Common Data Model procedures for data collection and linkage, and data management and safety are described elsewhere.

Sample Size and Power: Preliminary data from "Wave 2" implementation of the M.A.P. Program by AMA in 16 clinics shows average pre-post improvements (without a control group) in BP control of 6.8% (65.6%-->72.4% overall) +/- 4.4% (standard deviation of change in control rate). Assuming negligible change in the Self-Guided arm, standard sample size calculations show that we will have 83% power to detect a difference in differences of 6% in the BP control rate (or 92% power for 7% difference) between Self-Guided and Full-Support arms with 10 clinics randomized to each arm of the study; these results were confirmed using simulations. Power will be higher for comparisons of the Self-Guided and Full-Support groups with the large Usual Care comparison group in PCORnet under similar effect-size assumptions. For the HTE analysis comparing the difference in differences between the 10 clinics in CDRN 1 (5:5 in each arm) and the 10 clinics in CDRN 2 (5:5 in each arm), we expect to have 80% power to detect an interaction effect (i.e., the difference in the difference in differences) of 12% in the BP control rate. Corresponding minimum detectable interaction effects would be 15%, 13%, and 12% for demographic subgroups comprising 20%, 30%, and 40% of the overall population.

References

1. Danaei G, Ding EL, Mozaffarian D, et al. The preventable causes of death in the United States: comparative risk assessment of dietary, lifestyle, and metabolic risk factors. PLoS Med 2009;6:e1000058.
2. Nwankwo T, Yoon SS, Burt V, Gu Q. Hypertension among adults in the United States: National Health and Nutrition Examination Survey, 2011-2012. NCHS Data Brief 2013:1-8.
3. Wald DS, Law M, Morris JK, Bestwick JP, Wald NJ. Combination therapy versus monotherapy in reducing blood pressure: meta-analysis on 11,000 participants from 42 trials. Am J Med 2009;122:290-300.
4. Fontil V, Bibbins-Domingo K, Kazi DS, et al. Simulating Strategies for Improving Control of Hypertension Among Patients with Usual Source of Care in the United States: The Blood Pressure Control Model. J Gen Intern Med 2015;30:1147-55.
5. Wozniak G, Khan T, Gillespie C, et al. Hypertension Control Cascade: A Framework to Improve Hypertension Awareness, Treatment, and Control. J Clin Hypertens (Greenwich) 2016;18:232-9.
6. Kallioinen N, Hill A, Horswill MS, Ward HE, Watson MO. Sources of inaccuracy in the measurement of adult patients' resting blood pressure in clinical settings: a systematic review. J Hypertens 2017;35:421-41.
7. Basile J, Neutel J. Overcoming clinical inertia to achieve blood pressure goals: the role of fixed-dose combination therapy. Ther Adv Cardiovasc Dis 2010;4:119-27.
8. Elliott WJ. Improving outcomes in hypertensive patients: focus on adherence and persistence with antihypertensive therapy. J Clin Hypertens (Greenwich) 2009;11:376-82.
9. Bautista LE. Predictors of persistence with antihypertensive therapy: results from the NHANES. Am J Hypertens 2008;21:183-8.
10. Kambhampati S, Ashvetiya T, Stone NJ, Blumenthal RS, Martin SS. Shared Decision-Making and Patient Empowerment in Preventive Cardiology. Curr Cardiol Rep 2016;18:49.
11. Jaffe MG, Lee GA, Young JD, Sidney S, Go AS. Improved blood pressure control associated with a large-scale hypertension program. Jama 2013;310:699-705.
12. Glynn LG, Murphy AW, Smith SM, Schroeder K, Fahey T. Interventions used to improve control of blood pressure in patients with hypertension. Cochrane Database Syst Rev 2010:CD005182.
13. Guthmann R, Davis N, Brown M, Elizondo J. Visit frequency and hypertension. J Clin Hypertens (Greenwich) 2005;7:327-32.
14. Clark CE, Smith LF, Taylor RS, Campbell JL. Nurse led interventions to improve control of blood pressure in people with hypertension: systematic review and meta-analysis. BMJ 2010;341:c3995.
15. Morgado MP, Morgado SR, Mendes LC, Pereira LJ, Castelo-Branco M. Pharmacist interventions to enhance blood pressure control and adherence to antihypertensive therapy: Review and meta-analysis. Am J Health Syst Pharm 2011;68:241-53.
16. Rader F, Elashoff RM, Niknezhad S, Victor RG. Differential treatment of hypertension by primary care providers and hypertension specialists in a barber-based intervention trial to control hypertension in Black men. Am J Cardiol 2013;112:1421-6.
17. Mueller M, Purnell TS, Mensah GA, Cooper LA. Reducing racial and ethnic disparities in hypertension prevention and control: what will it take to translate research into practice and policy? Am J Hypertens 2015;28:699-716.
18. Ogedegbe G, Tobin JN, Fernandez S, et al. Counseling African Americans to Control Hypertension: cluster-randomized clinical trial main effects. Circulation 2014;129:2044-51.
19. Landon BE, Hicks LS, O'Malley AJ, et al. Improving the management of chronic disease at community health centers. N Engl J Med 2007;356:921-34.
20. The 2015 M.A.P. checklists for improving BP control. 2015. (Accessed Oct 26, 2017, at https://targetbp.org/wp-content/uploads/2017/03/MAP-Checklist.pdf.)
21. Hanlin RB, Asif IM, Wozniak G, et al. Measure Accurately, Act Rapidly and Partner with Patients (MAP) Improves Hypertension Control in Medically Underserved Patients: Care Coordination Institute

and American Medical Association Hypertension Control Project Pilot-Study Results. Journal of Clinical Hypertension 2017;IN PRESS.
22. 0018: Controlling High Blood Pressure. 2017. (Accessed October 29, 2017, at http://www.qualityforum.org.)
23. Groenwold RHH, van Smeden M. Efficient Sampling in Unmatched Case-Control Studies When the Total Number of Cases and Controls Is Fixed. Epidemiology 2017;28:834-7.
24. Zhu H, Zhang S, Ahn C. Sample size considerations for historical control studies with survival outcomes. J Biopharm Stat 2016;26:657-71.
25. Makuch RW, Simon RM. Sample size considerations for non-randomized comparative studies. J Chronic Dis 1980;33:175-81.
26. StataCorp. Stata Statistical Software: Release 15, College Station, TX: StataCorp LLC. 2017.
27. Valeri L, Vanderweele TJ. Mediation analysis allowing for exposure-mediator interactions and causal interpretation: theoretical assumptions and implementation with SAS and SPSS macros. Psychol Methods 2013;18:137-50.