Dr. Patricia Weitzman
Environment and Health Group
Cambridge, Massachusetts

Digital health for medication adherence among African Americans with hypertension

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Protocol

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Table of Contents:

1.0 Background

Hypertension (HTN) is more common and more harmful for African Americans than for any other ethnic group (AHA, 2020a). More than half of African American adults, about 15 million people, have HTN (AHA, 2017; Annie E. Casey Fdn, 2019). Furthermore, African Americans are 4 times less likely to adhere to HTN meds compared to their white counterparts (Schoenthaler et al. 2016). Tailored approaches to reduce the racial gap in HTN morbidity and mortality, particularly those supporting med adherence, are needed in primary care (NHLBI, 2020). Importantly, HTN is one of most common co-morbidities in Covid19 hospitalizations, particularly for African Americans (CDC 2020). Moreover, media coverage of a possible link between certain HTN meds, called RAAS inhibitors, and severe Covid19 outcomes may have alarmed HTN patients about the safety of their meds. As a result, the ACC (March, 2020) issued guidelines recommending all patients adhere to HTN meds during the pandemic unless advised by their physicians, as there is no evidence of a link between HTN drugs and Covid19 severity. In fact, severe heart complications have been reported among Covid19 patients that stopped HTN meds, including RAAS inhibitors, could worsen outcomes (ACC, July 2020). Thus, in the time of Covid19, supporting med adherence of African Americans with HTN is extremely urgent.

2.0 Goals

We propose a digital adherence solution to help reduce HTN-related disparities among African Americans, called Memento.HTN, which is innovative in three key ways: 1) it is the first-ever linked digital provider platform and patient SMS text system for HTN medication adherence; 2) it is culturally-tailored for African Americans with HTN; and 3) it has unique monitoring functionality allowing providers to monitor individual patient adherence, support 'new start' patients, who are at increased risk for non-adherence, and to track group adherence rates by drug class, pill format, and patient demographics in order to inform clinical therapeutics. Requiring only minutes of staff or prescriber monitoring per day, the Memento system simplifies and facilitates provider delivery of adherence support. The provider platform sends patients interactive SMS pill reminders plus culturally-sensitive motivational, educational, spiritual/stress-supportive, and customizable texts, along with texts that target intentional non-adherence. Importantly, Memento allows 2-way communication between providers and patients, and automatically alerts providers when a patient is having clinically-significant pill lapses.

Specific Aim 1: Develop an individually-tailored, culturally-sensitive digital health intervention comprised of a provider platform and linked patient SMS system to promote medication adherence in African Americans with HTN.

Specific Aim 2: Implement a 6-wk pilot to evaluate feasibility and short-term effectiveness for improving adherence.

3.0 Inclusion/Exclusion Criteria

A detailed description of how subjects will be consented, study procedures, materials and potential risks for the study is provided below:

Inclusion/Exclusion Criteria for Patient usability and formative testing focus groups or individual interviews:
Inclusion: African American adults, age 18 and older, diagnosed with hypertension/high blood pressure, prescribed HTN meds, own a cellphone (basic or smart). Exclusion: Undergoing cancer treatment; pregnancy; end stage renal disease.

Inclusion/Exclusion Criteria for Patient 6 week pre-post evaluation: Inclusion: African American adults, age 18 and older, diagnosed with hypertension/high blood pressure, prescribed HTN meds, own a cellphone (basic or smart). Exclusion: Participation in other clinical research; undergoing cancer treatment; pregnancy; end stage renal disease.

Inclusion/Exclusion Criteria for Clinician usability and formative testing focus groups: Inclusion: Licensed clinicians (MD, PA, NP, RN, PharmD et al.) who work in primary care settings and prescribe anti-hypertensive medication treatment to adult patients with primary hypertension. Exclusion: Participation in other health services research.

4.0 Enrollment

Recruitment:

Patient recruitment usability and formative usability testing: Primary care recruitment resources include: UChicago Primary Care Group, Prisma Baptist Hospital, and Brigham & Women's Hospital, including affiliated clinics, and UserInterviews, an online recruitment source. Clinic ads and flyers will be posted on bulletin boards and other clinic-based outlets, and we will ask clinic staff to share flyers and study information with potential participants. Flyers & ads will state what the study is about, who is funding it, who might be eligible, what the length of time & compensation would be, and will provide contact number for more information about the study. Individuals who contact us will be screened (via zoom, phone or face-to-face) further for inclusion/exclusion criteria. Individuals who meet study criteria and agree to participate in the study will complete an online consent form in Qualtrics.

Patient Recruitment 6 week pre-post evaluation. Primary care recruitment resources include: UChicago Primary Care Group, Prisma Baptist Hospital, and Brigham & Women's Hospital, including affiliated clinics, and UserInterviews. Clinic ads and flyers will be posted on clinic bulletin boards and other clinic-based outlets, and we will ask clinic staff to share flyers and study information with potential participants. Individuals who contact us will be screened further via zoom or phone for inclusion/exclusion criteria. Individual who meet study criteria and agree to participate in the study will complete an online consent form in Qualtrics. Individuals who meet study criteria and sign the informed consent will complete online baseline assessments, including obtaining a BP reading using a BP cuff which we will donate to each person as a part of the study.

Healthcare provider usability and formative focus group participants. Healthcare providers will be recruited through signs and word of mouth in the University of Chicago Medicine, Prisma Hospital and Brigham & Women's Hospital, as well as through Boston-area community health centers where Dr. Weitzman has numerous contacts and/or through UserInterviews.

Consent Process:

The study will be conducted according to ethical principles stated in the Declaration of Helsinki (2013), ethics approval will be obtained before initiating study, consent forms will take into consideration the well-being, free-will and respect of the participants, including respect of privacy, etc. A detialed

Focus groups (or interviews) with Patients *and* Focus Groups (or interviews) with Healthcare Providers: All participants in focus groups will complete the consent process via Qualtrics online platform. The consent statement will emphasize that participation will not in any way affect the services he/she receives from any provider or agency. The potential participant will read that participation is voluntary and that the potential participant may

terminate participation at any time and may skip any questions that he or she does not wish to answer. Individuals, who are comfortable proceeding, will provide a signature online in the Qualtrics form.

Patient 6 week Pre-post evaluation: All potential participants will review inclusion criteria and online consent form via Qualtrics. The consent form for patient participants in the 6-week evaluation of Memento will describe procedures and potential risks. It will emphasize that participation is voluntary and will not in any way affect employment or access to any services received from any provider or agency or clinic, and that participants can discontinue involvement at any time. Furthermore, as done in our other adherence studies, the consent will state the possibility that SMS texts or the linked provider platform may malfunction during the evaluation, and that participants should continue to use whatever other methods they normally use to remember their pills for the duration of the study. It will also state that any information offered as a part of the study should not replace a participant's own physician's advice. It will also state that the study involves potential privacy loss and breach of confidentiality. After the informed consent is electronically signed, the study will proceed. At the completion of the 6-week period, participants will participate in a focus groups with up to 10 others or individual interviews (via zoom/phone) to gain their feedback on their experience with of the Memento program.

5.0 Study Procedures

Patient Focus Groups: For the formative & usability patient group (or individual interviews), after providing online consent, individuals will meet for a 1.5 hour conversation via Zoom, during which they will either provide formative feedback on the Memento approach and on new text messages & the usability of the prototype Memento system. Focus groups/interviews will be audiotaped. Participants will receive $50 in an Amazon gift card at the end of each group/interview.

Healthcare Provider Focus Groups: For usability groups with healthcare providers (or individual interviews), after providing online consent, individuals will meet for a 1.5 hour conversation via Zoom, during which they will either provide formative feedback on the prototype Memento system, including how it might fit into clinical workflows, or usability feedback on its functioning. Focus groups will be audiotaped. Participants will receive $75 Amazon gift card at the end of the group.

Patient 6-week pre-post evaluation: After signing the online consent, participants will complete baseline assessments, pill regimen (including medication name, dosing, retail or mail-order pharmacy, the preferred time for pill reminders, refill due date, and how long they have been on HTN meds), and demographic data in the online Qualtrics platform. Participants will receive $20 Amazon gift card for completion of baseline assessments. We will describe how to measure their arm with a tape measure (which we will have sent to them in advance) so that we can send them a correct size BP cuff. After taking the measurement, a new BP cuff (clinically- validated, blue-tooth enabled, Omron 5) will be delivered to each participant**.** Staff will meet again with participant (face-to-face or via zoom or phone) to guide them in getting baseline BP. The participant will be asked to sit quietly in a chair with their feet on the floor for several minutes, then measure their BP and pulse. Staff will record numbers. After another 5 minutes, the process will be repeated, yielding 2 BP readings, which will be averaged. Afterward, the participant will begin receiving SMS texts from the provider platform.

During the 6-week study period, patient participants will receive several types of text messages: daily interactive pill reminders, educational, motivational, spiritual/stress-supportive. Individuals that are 'new starts,' i.e. have been prescribed HTN meds within the last 8 weeks, will receive additional texts to support their implementation and persistence with their HTN med regimen. Study staff will monitor backend data to

determine if any patient participants are not opening their text messages or if a patient has missed pills 2 out of 7 days, which Dr.Perez has advised us is a clinically-significant pill lapse. In such instances, study staff will reach out to patients to see if they need support to help them with engagement.

At 6 weeks, patient participants will receive a phone call and text informing them it is time to re-take baseline assessments as well as to participate in end-of-study focus group (or individual interview). At the end of the study, participants will be invited to participate in a zoom focus group with up to 10 other participants or an individual interview (zoom or phone) to provide feedback on the Memento system.

After re-taking baselines and participating in the end-of-study focus group/interview, pre-post participants will be emailed a link for $130 Amazon gift card.

6.0 Reporting of Adverse Events or Unanticipated Problems involving Risk to Participants or Others

We consider the risks to participants in both the patient and the healthcare provider focus groups to be minimal, i.e. there is a minor risk that other members of the patient focus group will know that a given participant is taking HTN medications. We will be clear in consenting patients that such a risk exists. There is a small risk of the time demand of the focus group will feel burdensome. We will make clear in informed consents for patients and for providers that they may end their participation at any time if the time demand becomes a problem.

Additionally, there is a risk to pre-post evaluation participants that someone will see their text messages and realize that the participant is taking HTN meds. In the pre-post informed consent, we will advise participants to delete any texts that they do not wish others to see. We will inform participants that state-of-the-art and HIPAA-compliant security protections are in place for any data in transit from the platform to their phone, but that there is still a risk to data in transit or privacy loss due to someone reading their text messages or breach of confidentiality due to data in transit or data storage. We will advise participants uncomfortable with those risks not to participate in the study. We will also outline in the informed consent measures that the team will take to protect their data.

7.0 Compensation and Costs

Focus Groups: For their participation in the focus groups, hypertension patient participants will receive a $50 Amazon gift card. Healthcare providers will receive $75 Amazon gift card.

Patient 6-week pre-post evaluation. Participants will receive $20 in an Amazon gift card for completion of baseline assessments (e.g. blood pressure (BP) measures). At the completion of the pre-post study, patient participants will be offered $130 Amazon gift card for their time. In total, pre-post participants will receive $150 in Amazon gift card.

There will be no costs to participants.

8.0 Study Withdrawal/Discontinuation

Any participant may choose to withdraw from the focus group study or the pre-post study at any time and for any reason. Participants will need simply to contact the investigator.

9.0. Outcome Measures

HTN med adherence will be assessed by the Adherence to Refills and Medication Scale (ARMS), a well-validated self-report measure used widely in studies with minority patients and/or those with low literacy (Buis et al., 2019; Kripalani et al., 2009; McNaugton et al., 2014). We will also use Segeral et al. (2010) 3-item adherence measure, as in our prior research (Pagan-Ortiz et al., 2019). Validated self-report measures correlate with clinical outcomes and are desirable to use in research with African American patients, who may resist providing bio-specimens due to historical mistrust (Ewing et al., 2019, Stirratt et al., 2015). Lastly, electronic pill bottles are cumbersome, expensive, and often ineffective for promoting and tracking adherence (Choudhry et al., 2017; Volpp et al., 2017). **Secondary:** Adherence self-efficacy will be assessed with the HTN med adherence self-efficacy scale (MASES) (Ogedegbe et al. 2003). HTN knowledge will be assessed using the NHLBI HTN Knowledge Scale (Carter-Edwards et al., 2002). Stress burden will be assessed using Perceived Stress Scale (Cohen et al., 1983). **Exploratory:** BP will be measured at baseline and 6 weeks. **Primary Hypothesis**: Participants will show greater HTN med adherence at 6 wks compared to baseline. **Secondary Hypothesis:** Participants will show greater HTN adherence self-efficacy, greater HTN knowledge, and lower stress burden at 6 wks compared to baseline. **Exploratory Hypothesis**: Participants will show a decrease in systolic BP at 6 wks compared to baseline. **Data analyses:** We will conduct one-tailed paired t-tests at the .05 level for primary and exploratory hypotheses and McNemar's chi square for secondary hypotheses. Data from our Phase 1 evaluation of short-term effectiveness will be used to determine the sample size necessary for an adequately-powered Phase 2 RCT.

10.0 Statistical Considerations

Because this is a feasibility study, the pre-post evaluation sample size is not based on power calculations. In Phase 2, a sample size will be created with a power of at least 90% with a two-sided alpha level of .05.

11.0 Privacy/Confidentiality Issues

For the pre-post evaluation, privacy breach due to electronic exchange of information will be protected against via technical safeguards including secure transmission modes for communication, including virtual private networks (VPN) or secure sockets layer (SSL), and encryption techniques, developed and utilized in other projects by 52Inc.

The entire Memento.HTN system will use industry standard practices for access control, data security in transit, and data security at rest. The system will meet or exceed OWASP standards. All data in encrypted at rest using AES 256. All data is encrypted in transit using TLS 1.2 or 1.3 with pinned certificates where appropriate. Only users on the technical team with a direct need to view user data have access to said data and all access by the technical and/or study team will be fully logged.

Following the study, the pre-post data will be moved to a long-term storage database with Amazon Web Services and will only be accessible by EHG staff.

In the patient pre-post informed consent, we will also state that online data collected for this study will be removed from the Qualtrics platform, which is HIPAA compliant, stored in our HIPPA compliant EHG Google Drive, and backed up on encrypted folders on an EHG MacBook Pro. Passwords to access the folders will be stored in LastPass, which uses strong encryption algorithms and provides extra

security. LastPass is considered highly secure by industry standards.

12.0 Follow-up and Record Retention

Any audio recordings made will be kept in a password protected computer, separate from participant names. Access will be limited to the PI and study staff.