

**Capstone for Impact Submission | GY2021**

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Project Title: Reach Out: a multi-arm randomized trial of behavioral interventions for hypertension initiated in the Emergency Department

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If this project can be continued by another UMMS student, please include your contact information or any other details you would like to share here: This could be continued. Please either contact me at [detrimbl@med.umich.edu](mailto:detrimbl@med.umich.edu) or reach out to Dr. Will Meurer.

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**SUMMARY** (~250-500 words):

This project uses a health system focused, multicomponent, health theory based, mobile health behavioral intervention to reduce blood pressure among ED patients. Hypertension is the most important modifiable risk factor for cardiovascular disease, the leading cause of mortality in the United States. The Emergency Department represents an underutilized opportunity to impact difficult-to-reach populations. There are 136 million visits to the Emergency Department each year and nearly all have at least one blood pressure measured and recorded. Additionally, an increasing number of African Americans and socioeconomically disadvantaged patients are overrepresented in the Emergency Department patient population. In the age of electronic health records and mobile health, the Emergency Department has the potential to become an integral partner in chronic disease management if it can be leveraged to identify hypertensive patients and, in partnership with mobile health behavioral interventions, impact otherwise unreachable populations.

Hypertension experts have called for the evaluation of multilevel interventions addressing barriers to hypertension care.<sup>1</sup> In line with this request and informed in part by the Social Ecological Model, Reach Out is designed to intervene at the individual patient, the health system, and the community levels.<sup>2</sup> At the individual level, Reach Out will advance the identification of hypertension through ED screening, providing BP self-monitors, and encouraging healthy behaviors, which are considered barriers to

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<sup>1</sup> 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? *American journal of hypertension* 2015, 28(6):699-716.

<sup>2</sup> Woods VD: African American Health Initiative Planning Project: A Social Ecological Approach Utilizing Community-Based Participatory Research Methods. *Journal of Black Psychology* 2009, 35(2):247-270.

hypertension management in urban, under-resourced populations.<sup>3,4,5,6,7</sup> At the health system level, Reach Out will work to reduce barriers by scheduling primary care provider appointments and will also assist with reducing the barrier of medication cost. For participants who establish care with the Federally Qualified Health Center (FQHC), medications are typically provided on a sliding fee scale, but additional guidance may be useful for some participants; therefore, healthy behavior text messages will be used to provide information about pharmacies with generic drug programs in the area. Additionally, Reach Out will work to reduce community barriers by providing free transportation to and from outpatient provider appointments. If we are ultimately successful, this trial could herald a significant shift in the capability of providers to care for the under-resourced and underserved, ultimately improving patient outcomes for these populations.

The Reach out study is designed to determine which behavioral intervention components or 'dose' of components contributes to a reduction in systolic blood pressure after one year (Aim 1). The study will also assess the effect of primary care provider appointment assistance on total primary care follow-up visits of hypertensive patients treated in an urban, safety net Emergency Department (Aim 2). Ideally, the Reach Out system will contribute to hypertension management, serving as a model for safety net hospitals and Federally Qualified Health Centers to improve chronic disease management in underserved communities.

#### **METHODOLOGY:**

Reach Out is a randomized, controlled, 2x2x2 factorial design clinical trial allocating subjects to one of eight available combinations of mobile health components. An initial three-week eligibility phase is used to assess for persistent hypertension and responsiveness to text messages. Participants are randomized into the main study if they have persistent hypertension (any self-reported systolic BP  $\geq 140$  or diastolic BP  $\geq 90$ ) and have submitted at least one BP by text during the screening period. If participants do not meet both criteria, they receive no further communication from the study team following the eligibility phase. A baseline assessment will occur at enrollment with outcome assessments at six and twelve-months. The Reach Out program is designed to identify which mobile health components or 'dose' of components (healthy behavior text messaging, prompted BP self-monitoring and facilitated PCP appointments with transportation) contributes to a reduction in BP among hypertensive participants recruited from an urban, safety net ED.

The formal statistical analysis plan was codified prior to enrollment and is available upon request. The primary analysis (aim 1) will fit a linear regression model with the outcome of systolic BP change (baseline minus 12 months) and main effect encoded as binary products of healthy behavior texts (yes vs. no), prompted BP self-monitoring frequency (high vs. low), and primary care provider visit scheduling and transportation (active vs. passive). Initial analyses will focus on the main effects. Additional analyses will include all the two-way interactions of the three intervention components, focusing on interactions where

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<sup>3</sup> Bosworth HB, Dudley T, Olsen MK, Voils CI, Powers B, Goldstein MK, Oddone EZ: Racial differences in blood pressure control: potential explanatory factors. *The American journal of medicine* 2006, 119(1):70 e79-15.

<sup>4</sup> Hill MN, Bone LR, Kim MT, Miller DJ, Dennison CR, Levine DM: Barriers to hypertension care and control in young urban black men. *American journal of hypertension* 1999, 12(10 Pt 1):951-958.

<sup>5</sup> Kressin NR, Orner MB, Manze M, Glickman ME, Berlowitz D: Understanding contributors to racial disparities in blood pressure control. *Circulation Cardiovascular quality and outcomes* 2010, 3(2):173-180.

<sup>6</sup> Ostchega Y, Berman L, Hughes JP, Chen TC, Chiappa MM: Home blood pressure monitoring and hypertension status among US adults: the National Health and Nutrition Examination Survey (NHANES), 2009-2010. *American journal of hypertension* 2013, 26(9):1086-1092.

<sup>7</sup> Redmond N, Baer HJ, Hicks LS: Health behaviors and racial disparity in blood pressure control in the national health and nutrition examination survey. *Hypertension* 2011, 57(3):383-389.

at least one of the factors in the interaction demonstrates a sufficiently large main effect. As the goal of this exploratory trial is to find interventions or combinations that improve BP control, we will use an alpha level of 0.10 for all main effects and 0.20 for interactions. We plan to include elements meeting this threshold for statistical significance in a subsequent multicenter trial. If significant interactions exist (i.e. the combination of facilitated transportation and high frequency home BP monitoring), the future study will assess the combination of elements that has the highest expected reduction in SBP – assuming we achieve significance at the  $p=0.1$  (main effects) or 0.2 (interaction) level for at least one component. In the event of an overall “null” trial, we would re-examine the expected change in systolic BP for arm 1, represented by the intercept. If this was significantly greater than 0 at the  $p=0.1$  level, we will propose a subsequent multi-center trial using only weekly prompted BP self-monitoring.

The main secondary analyses (aim 2) will use logistic regression to describe the time-to-event (Cox Proportional Hazards). For the endpoint of interest, either time to first PCP visit or a binary variable indicating attendance at two or more PCP visits within one-year of randomization, we will fit an adjusted regression model. The main predictor of interest for these models is assignment to the active PCP scheduling and transportation arm (50% of all participants randomized in the trial), while adjusting for the change associated with assignment into other groups, such as healthy behavior text messages and prompted BP self-monitoring, as in aim 1.

We will conduct additional exploratory analyses using the stratification factors of age, sex, and anti-hypertensive use as covariates. As uncertainty exists on the distribution of enrolled participants within these strata (e.g. young men taking antihypertensive medication), we cannot estimate a preliminary statistical power for these exploratory aims. Thus, we will estimate the power based on the strata sizes prior to conducting the exploratory analyses. Interaction terms (e.g. age or sex with behavioral interventions, etc.) will be utilized to determine if specific groups respond better than others to specific intervention elements. Baseline BP may also play an important role, which will be examined by dividing the cohort into terciles. We will repeat the above primary and exploratory modeling within each of the three initial BP strata to determine if there is heterogeneity of effect, such as whether patients with the highest baseline BPs get the most benefit from the intervention components. We will similarly assess the impact of the intervention components on the exploratory and process outcomes using linear, Poisson, logistic, or ordinal regression depending on the distributions. In addition, we will conduct longitudinal analyses that include all BP measurements over time (including those by text and at the in-person visits) to assess the temporal profiles of response in the intervention components. The detailed system application and product in data processing outlines procedures for handling missing outcome data.

This study is funded by the NIH - National Institutes of Minority Health and Disparities R01.

## **RESULTS:**

Recruitment began March 25, 2019 and primary enrollment was completed in March 2021 with 833 participants. The study will continue to follow participants for one year. At the six-month analysis, patients presenting to the ED, who were found to have persistent hypertension, were more than 50% African American, 60% of approached patients and 62% of randomized participants were African American. Approximately 95% of participants were under the age of 65. The most common reason for non-enrollment was absence of mobile phone.

Final results are not available for this study as it is ongoing in the 1-year data capture phase.

**CONCLUSION** (~250-500 words):

Traditionally, multicomponent interventions are determined a priori and then the entire intervention is tested in a randomized controlled trial (RCT). Due to component data limitations or non-existence, RCTs are limited when evaluating multicomponent behavioral interventions and as a result it is a slow, costly process of intervention refinement that is susceptible to multiplicity from subgroups. Prior text-messaging based interventions have had mixed results, although meta-analyses generally favor positive effects suggesting underpowered or potentially mis-specified interventions.

An alternative to traditional two-arm trials comparing multicomponent interventions to a control is the Multiphase Optimization Strategy (MOST), a three-phase strategy adapted from an engineering framework. Preparation is the first step and includes development and pilot testing of the intervention components based on a theoretical model. The Reach Out study has completed this stage and is currently in optimization, the second phase. In optimization data is gathered, often using factorial design, to determine which components and 'dose' of the components of the behavioral intervention are most effective. Factorial designs allow for an estimate of the individual effects of the components, the component interactions between groups and whether they are an efficient use of time, money or resources. The third and final stage is evaluation in which the effectiveness of the optimized intervention is determined.

While not a traditionally defined vulnerable population, the people of the city of Flint have faced unique challenges recently with the water crisis. The University of Michigan Department of Emergency Medicine has a long-standing relationship with Hurley Medical Center and the city of Flint with faculty staffing the emergency department for 20 years. Additionally, an active research infrastructure is available on location and to mitigate the anticipated community distrustful of government-funded research and we have partnered with community leaders in the development of the study and employed research staff sensitive to diverse populations. This research study involves limited risks to the community and is designed to improve access to hypertension treatment, so it is unlikely to provoke significant controversy.

### **Potential Challenges**

We may observe few differences between higher and lower levels of intervention components or no effect with the intervention components. In this scenario, given the established benefits of BP self-monitoring in the general ambulatory population, we plan to pursue a large, simple trial of prompted BP self-monitoring in a population of ED patients.<sup>[6, 7, 9, 10, 32]</sup> Costs of purchasing BP cuffs present a potential barrier to widespread implementation; however, a recent cost-benefit analysis found that BP self-monitoring saved money long-term and coverage is supported by major medical societies.<sup>[33]</sup>

### **Generalizability**

In the US, about a quarter of all hospitals (~1000) are safety net hospitals, which, in addition to the additional non-hospital FQHC locations per state, are often co-located in underserved areas where outpatient post-ED follow-up is rarely prioritized.<sup>[34]</sup> Given the ubiquity of Reach Out components, EPIC and text messaging, it could be implemented nationwide.

### **Impact**

Reach Out has the potential to serve as a model for safety net health systems to optimize hypertension care among their patient populations. The pragmatic design of Reach Out including broad enrollment criteria, use of the EHR to identify potential participants, and use of technology for health intervention. These key features will allow for future implementation of the trial components in real-world health systems.

### **REFLECTION / IMPACT Statement:**

I would like to offer advice to other students in finding projects, especially if unsure of what to do, consider just looking for interesting people to work with. I am passionate about and have worked on disaster response and mitigation as well as with veterans' organizations throughout medical school so initially thought I should do something in that arena, but I had met Dr. Meurer as an M1 and thought it might be a great experience to learn from him on a research project. When the opportunity was presented to work on a project in Flint, MI, I had only been to the city once for a volunteer day with Habitat for Humanity several years ago. I had, of course, read about the water crisis but had no idea what the community was about. I jumped on it anyway, partly out of curiosity and partly because of a yearning for opportunities with underserved populations, which had been my entire reason for joining the Global Health and Disparities Path of Excellence

As a safety net hospital, the Hurley ED is, for many, their primary source of healthcare and though this is far from ideal, it did add a familiarity and community-centric vibe that I truly cherished. This project gave me a great third-party view of both the ED and the variety of patients and conditions, as well as, the interaction between the community and the hospital. I could not have predicted just how deeply I would connect with the rawness and vulnerability. Though research has never been a particular interest of mine, the poignancy of the patient interactions made this experience exceptional. You never know what will catch your attention and change your future trajectory. The experience ultimately solidified my desire to work in underserved communities and my interest in Emergency Medicine.