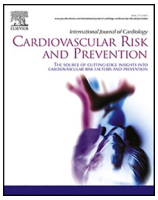
International Journal of Cardiology Cardiovascular Risk and Prevention 15 (2022) 200156

Contents lists available at ScienceDirect

International Journal of Cardiology Cardiovascular Risk and Prevention

journal homepage: www.journals.elsevier.com/international-journal-of-cardiology-cardiovascular-risk-and-prevention



Study design of BETTER-BP: Behavioral economics trial to enhance regulation of blood pressure

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ARTICLE INFO

Keywords:
Hypertension
Behavioral economics
Nonadherence

ABSTRACT

Background: Nonadherence to antihypertensive medications remains a persistent problem that leads to preventable morbidity and mortality. Behavioral economic strategies represent a novel way to improve antihypertensive medication adherence, but remain largely untested especially in vulnerable populations which stand to benefit the most. The Behavioral Economics Trial To Enhance Regulation of Blood Pressure (BETTER-BP) was designed in this context, to test whether a digitally-enabled incentive lottery improves antihypertensive adherence and reduces systolic blood pressure (SBP).

Design: BETTER-BP is a pragmatic randomized trial conducted within 3 safety-net clinics in New York City: Bellevue Hospital Center, Gouveneur Hospital Center, and NYU Family Health Centers – Park Slope. The trial will randomize 435 patients with poorly controlled hypertension and poor adherence (<80% days adherent) in a 2:1 ratio (intervention:control) to receive either an incentive lottery versus passive monitoring. The incentive lottery is delivered via short messaging service (SMS) text messages that are delivered based on (1) antihypertensive adherence tracked via a wireless electronic monitoring device, paired with (2) a probability of lottery winning with variable incentives and a regret component for nonadherence. The study intervention lasts for 6 months, and ambulatory systolic blood pressure (SBP) will be measured at both 6 and 12 months to evaluate immediate and durable lottery effects.

Conclusions: BETTER-BP will generate knowledge about whether an incentive lottery is effective in vulnerable populations to improve antihypertensive medication adherence. If successful, this could lead to the implementation of this novel strategy on a larger scale to improve outcomes.

1. Background and rationale

Adherence to antihypertensive medications remains unacceptably low despite decades of research [1, 2]. This is especially true in vulnerable populations including socioeconomically disadvantaged and/or minority patients who simultaneously experience the highest rates of adverse hypertension-related sequelae (such as myocardial infarction and stroke), and have the lowest levels of medication adherence [1, 2]. Nonadherence to antihypertensive medications is associated with more hospitalizations for cardiovascular disease events [3, 4], increased healthcare costs [5], and increased mortality [3, 4]. A program that successfully improves antihypertensive adherence would therefore represent a means of implementing a low-cost and readily available prevention strategy with known benefits.

Historically, patient education and counseling interventions have shown some benefit in improving adherence [5, 6] but they are resource-intensive and may not translate across health systems. Although initial reports showed that direct financial incentives for patients improved adherence, subsequent studies yielded mixed results [7, 8], and questions have been raised concerning their long-term sustainability. Recently, several behavioral economic approaches have been developed to enhance purely financial incentives; these strategies aim to leverage innately human tendencies (such as overweighing of immediate benefits) to improve health behaviors [9, 10]. Results of several studies using a lottery incentive program ("regret lottery") approach, whereby participants are encouraged to undertake healthy behaviors

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https://doi.org/10.1016/j.ijcrp.2022.200156
Received 18 March 2022; Received in revised form 19 July 2022; Accepted 27 October 2022
Available online 31 October 2022

through the desire to avoid regret over losing financial incentives, have been promising [10,11]. However, other interventions tested have been negative [12–14] or effective only in limited subgroups [15]. Further, with few exceptions [16], whether these incentives translate to sustainable behavior change in vulnerable populations is unclear.

In this context, we designed the Behavioral Economics Trial To Enhance Regulation of Blood Pressure (BETTER-BP). This pragmatic randomized trial, which is conducted at three safety-net clinics in New York City, builds on foundational work in behavioral economics [17,18] to test whether a lottery incentive program promotes adherence to antihypertensive medication and blood pressure control at 6 and 12 months. This manuscript describes the study design for BETTER-BP.

2. Methods

2.1. Overview

BETTER-BP (NCT04114669) is recruiting 435 participants with hypertension at three safety-net clinics in New York City: Bellevue Hospital Center, Gouveneur Hospital Center, and NYU Family Health Centers – Park Slope. All three clinics, which serve as teaching affiliates of NYU Grossman School of Medicine, treat a racially and ethnically diverse population that is predominately Medicaid-insured or uninsured. Participants are randomized in a 2:1 manner (intervention:control). The study intervention lasts for 6 months, and all participants are followed for a total of 12 months to examine durable effects. BETTER-BP employs several principles of a pragmatic trial, including broad eligibility, use of existing medications, pairing of study visits with regular ambulatory follow-up care, and capture of data elements obtained as part of routine care (e.g. laboratory testing) [19]. The first BETTER-BP participant was enrolled 7/14/20.

2.2. Conceptual model

BETTER-BP is designed based on self-determination theory (SDT) (Fig. 1), a theory of human motivation that postulates that individuals are more likely to pursue health behaviors when actions are autonomously (intrinsically) motivated [20]. Although it may seem counter-intuitive to pair a short-term lottery incentive, based on principles of behavioral economics (an extrinsic motivator) with the concept of building autonomous motivation and competence for behavior change, several studies in health-related behaviors have found that behavioral economic interventions do not "crowd out" intrinsic motivation [21,22]. Instead, previous research has shown that when incentives are small they serve as a "nudge" that can strengthen autonomous motivation to increase engagement and adoption of healthy behaviors (i.e., antihypertensive adherence) [23,24]. Importantly, the resultant increase in autonomous motivation reinforces an individual's feelings of competence, which can in turn sustain the behavior change, even when the incentive is extinguished [25].

2.3. Eligibility criteria

Patients are eligible for BETTER-BP if the following criteria are met: age ≥18 years, clinical diagnosis of hypertension, on ≥1 antihypertensive medication, suboptimal blood pressure control (defined as ≥1 outpatient systolic blood pressure [SBP] ≥140 within the past year), and poor self-reported adherence (defined as <80% adherent with prescribed antihypertensive medication over the prior week). Exclusion criteria (Table 1) include an inability to use study software in English or Spanish, or a clear barrier to technology use (e.g. vision or hearing impairment).

2.4. Screening and randomization

We are screening consecutive patients with a scheduled ambulatory clinic visit (primary care or cardiology) at Bellevue Hospital Center, Gouveneur Hospital Center, and NYU Family Health Centers – Park Slope. Potentially eligible individuals are identified by review of the electronic health record (EHR) on the day prior to their clinic visit by a research coordinator, using a simple algorithm to identify adult ambulatory patients who meet inclusion criteria. Patients deemed eligible by this initial screen are then contacted by phone and, if they agree, complete a brief screening questionnaire developed by Voils et al. [26] that ascertains antihypertensive adherence over the past 7 days. If they

Table 1
Eligibility criteria for BETTER-BP.

Inclusion:
•Age ≥18 years
•Diagnosis of hypertension
•Active prescription for ≥1 antihypertensive medication
•≥1 outpatient SBP ≥140 mmHg (on therapy)
•Suboptimal adherence (self-report)
Exclusion:
•Incarcerated
•Pregnant
•Unable to use study software (Way To Health) in English or Spanish
•Unable/unwilling to consent
•Clear barrier to technology use (e.g. visual or hearing impairment)
•Projected life expectancy <12 months

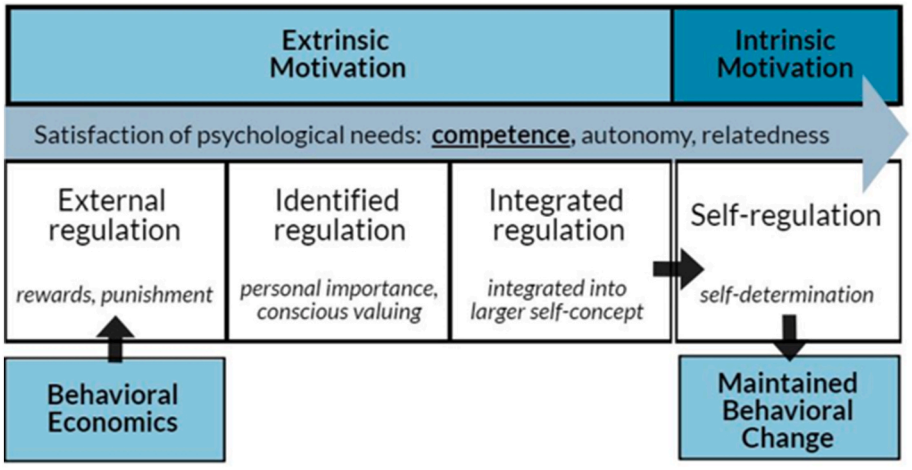

Fig. 1. Conceptual Model. Self-determination theory includes both extrinsic and intrinsic motivators. The BETTER-BP intervention aims to sustain behavioral change through promoting self-regulation.

report missing at least 2 doses of medication, they are then offered informed consent on the day of their clinic visit. The baseline assessment is performed on the same day as this visit in order to minimize travel burden.

3. Study outcomes

Primary Endpoint – Efficacy: There are two primary efficacy endpoints: (1) change in SBP from baseline to 6 months, and (2) maintenance of SBP change from 6 to 12 months. SBP is assessed in-person (baseline, 6 months, and 12 months) [27]. Briefly, 3 seated BPs using an appropriately sized upper arm BP cuff are measured after a rest period (5 min) in the seated position with the back supported, feet flat on the floor, and legs uncrossed using a validated automated oscillometric device (Omron HEM 907-XL, Lake Forest, IL). The non-dominant arm is used for measurement. The device is programmed to take the 3 BP measurements, 1 min apart between readings, and after a programmed waiting period of 5 min. All measurements are obtained using the attended approach with an observer (research coordinator) present. There is no talking between the participant and observer during BP measurements. Initial training on BP measurement for coordinators was provided at baseline by a study consultant with expertise in BP measurement (Dr. Shimbo), who also reassessed coordinators after the first 4 months of study launch in order to ensure protocol adherence. The full BP assessment protocol is supplied by the manufacturer (Omron) and available at https://omronhealthcare.com/wp-content/uploads/HEM-907XL-2013-IM.pdf.

Primary Endpoint – Process: The process endpoint is antihypertensive medication adherence, which is assessed by an electronic monitoring device (EMD) developed by AdhereTech (New York, NY) and fully described below. Adherence is calculated by the scheduling adherence metric, which is the proportion of days on which a patient takes his/her medication as prescribed divided by the total number of days that s/he is expected to take them in that period [28]. Good adherence is defined as ≥80% of days adherent, from baseline to 6 months (intervention period) and 6–12 months (passive monitoring period).

4. Study intervention

The intervention consists of a lottery incentive program ("regret lottery") that is delivered for 6 months via lottery software that is paired with an adherence EMD. The specific components of the study intervention are as follows:

Lottery Software: The software has been developed by Way to Health (Philadelphia, PA) which is a technology platform broadly focused on patient engagement and clinical trial administration, including delivery of lottery incentive programs on portable electronic devices. These lotteries are customizable including the amount, frequency of administration, and probability of winning. The platform is capable of surveillance, patient communication (via text message, email, or automated phone call), and data capture. The platform automates connections among other devices as well as feedback to patients, self-administered surveys, and payments. For purposes of our study Way to Health delivers text messages via Short Message Service (SMS) that can be delivered on any text-capable cellular phone, obviating the need for participants to own a smartphone.

Electronic Adherence Monitoring: Adherence is assessed via a wireless EMD pill bottle provided at no cost to each study participant (AdhereTech, New York, NY). Bottles are connected to a cellular network; when opened, the bottle sends a wireless signal to Way to Health. Although all participants in the intervention arm are entered in the lottery each day, they are eligible to win only if the bottle is opened the day before. Although the AdhereTech EMD is capable of medication reminders (chime or blinking light), these are not activated, in order to isolate the effect of the lottery incentive on adherence.

Only one EMD is given to the participant to track a single antihypertensive medication, similar to previous trials [29,30]. Preference is given to once-daily medications in this selection process. If there are multiple once-daily medications prescribed, we select a single medication based on the following hierarchy that was developed by several study physicians (JAD, NKL, DS): 1. ACE inhibitor or angiotensin receptor blocker; 2. Calcium channel blocker; 3. Beta blocker; 4. Diuretic (thiazide or aldosterone antagonist); 5. Other (e.g. clonidine). Although many patients take ≥2 antihypertensive medications, the single medication strategy simplifies the study intervention which is especially important in participants with low health literacy. In addition, there is evidence that the pattern of adherence to a single medication reflects adherence to others [31]. When possible, medications are placed in the EMD on the day of the initial study visit. In the event that participants do not bring their medications, the research coordinator teaches the participant how to use the EMD at the study visit and then calls the participant later that day to ensure proper transfer of the correct antihypertensive medication to the EMD. The participant needs to refill the EMD as medication runs out, and therefore also receives training on this process by the research coordinator at the baseline visit.

Lottery Incentive: The lottery is administered through the Way to Health application in a similar manner to prior studies using the same approach and software [32,33]. Briefly, the lottery is designed as a "combined lottery" with a low frequency chance of winning a large reward and a higher frequency chance of winning a small reward [33] (Fig. 2). Each participant is assigned a 2-digit number for the trial, and each day the Way to Health platform randomly generates a 2-digit number. Participants receive $50 if both digits match (1 in 100 chance) and will receive $5 if one digit matches (18 in 100 chance). The expected daily value (EDV) for this lottery, which is calculated by multiplying the incentive amounts by the probabilities of winning, is $1.40. This EDV is consistent with other financial incentives described in a meta-analysis by Haff et al. [10] The lottery also includes the powerfully motivating "regret" feature: patients whose number matches (for either a small or a large prize) are informed of the result *whether or not* they were adherent the previous day. Those who did not take their antihypertensive medication receive a message indicating that *had they been adherent*, they *would have won* either a small or large prize. When participants accrue winnings, payments are calculated monthly and deposits are made on a rechargeable debit card (ClinCard) provided to study participants by the research coordinator at their baseline visit. On a monthly basis, the research coordinators review the lottery text messages delivered to the participant via individual portals created on the Way to Health dashboard. The research coordinators calculate the sum of winnings and the total amount is then deposited to their account using the ClinCard portal. The lottery (with text messages) runs for 6 months; adherence is then monitored for an additional 6 months, without delivery of text messages, to examine durable effects. If a participant does not own a cellular phone capable of text messaging, we provide a device for the duration of the study. We created variable wording for each condition (adherent/wins, adherent/loses, nonadherent/would have won, nonadherent/would have lost), with the rationale that different text messages (5 within each condition) would help to avoid alert fatigue. These messages are selected randomly within the condition a participant meets on a given day. A full list of potential messages is shown in the Appendix.

4.1. Control group

Participants in the control group receive an AdhereTech EMD in order to passively monitor adherence with a single antihypertensive agent over the course of the study (12 months). We chose not to activate any EMD features (e.g. electronic reminders) for control participants, so that we can compare the incentive lottery to the closest approximation of usual care. Similar to the intervention arm, the primary endpoint (SBP) is measured at baseline, 6 months, and 12 months. There is no lottery (and no text messages) for participants assigned to the control

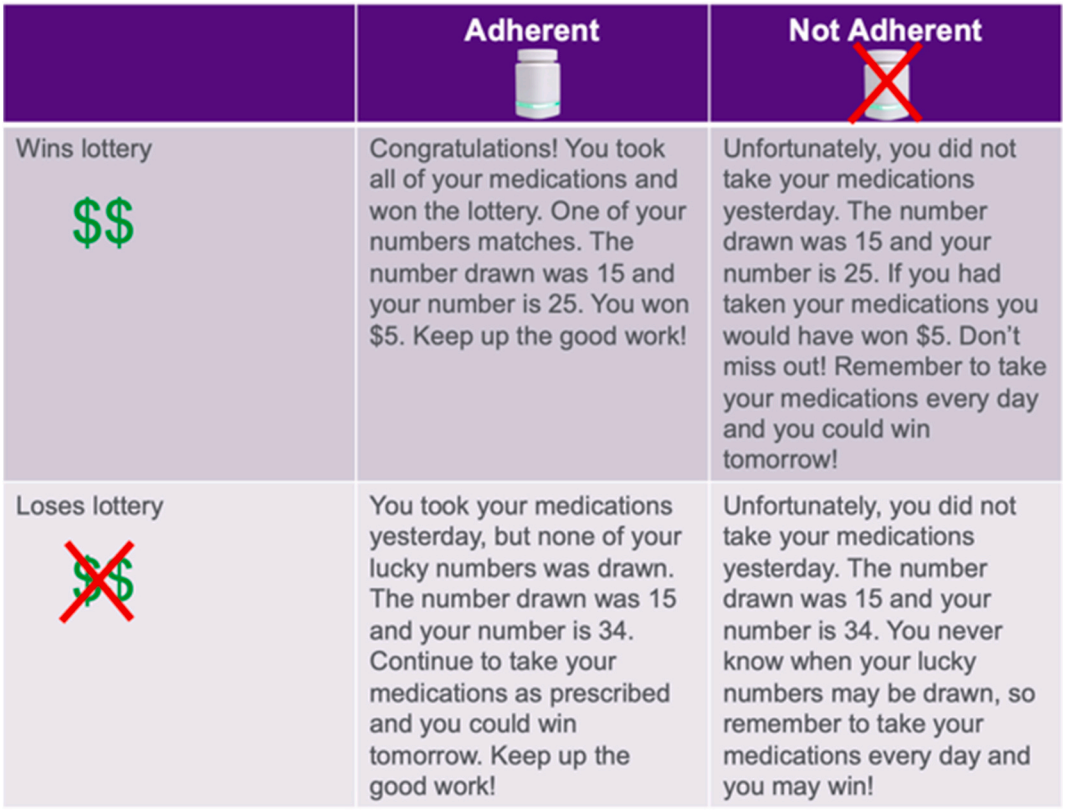

Fig. 2. Potential conditions in incentive lottery. There are four potential conditions as shown. The chance of winning the lottery (1 in 100 for a large reward ($50) and 18 in 100 for a small reward ($5).

group, and therefore no potential for financial winnings.

4.2. Study visits

All participants undergo visits at baseline, 6 months, and 12 months. All 3 visits are led by a research coordinator who measures elements in Table 2. The baseline and follow-up visits take approximately 60 min and 30 min, respectively. Between visits, research coordinators maintain regular contact with study participants for purposes of troubleshooting and to promote retention. On the day baseline visits are conducted, participants are provided with a telephone number to contact a study team member with questions or concerns. Additionally, the research

Table 2
Timeline for study participants.

	Baseline	Home activities	6 months	12 months
Intervention and control arms	In-person assessment •Demographics •Height, weight •Blood pressure, pulse •Treatment Self-Regulation Questionnaire (TSRQ) •Charlson Comorbidity Index •Medication Adherence Self Efficacy Scale (MASES) •Patient Health Questionnaire 9 (PHQ-9) •Short Form 12 (SF-12) •AdhereTech EMD setup (one antihypertensive medication) Chart abstraction •Medications, laboratory values	•AdhereTech electronic monitoring device (EMD) use and monitoring (baseline to 12 months) •Hypertension management as directed by clinician (independent of study)	In-person assessment •Blood pressure, pulse •TSRQ •MASES •Safety events* Chart abstraction** •BP values recorded at ambulatory visits (baseline to 6 months) •Laboratory values (baseline to 6 months) •Hospitalizations (baseline to 6 months)	In-person assessment •Blood pressure, pulse •TSRQ •MASES •Return AdhereTech EMD •Safety events* Chart abstraction** •BP values recorded at ambulatory visits (6–12 months) •Laboratory values (6–12 months) •Hospitalizations (6–12 months)
Intervention arm only	In-person assessment •Introduction to lottery incentive app (via Way to Health)	•Daily lottery incentive via Way to Health (baseline to 6 months)	Return study-provided smartphone, if applicable	

*Safety events include adverse events plausibly related to better antihypertensive adherence (fall-related injury, syncope, hypotension, bradycardia, renal or electrolyte abnormality), and will be assessed by interview to capture both in-system and out-of-system utilization. Electronic health records will also be reviewed on a monthly basis to evaluate for in-system events that may occur sooner than follow-up assessment (especially those unlikely to be reported by the participant, e.g. laboratory abnormality).
**6- and 12-month chart abstraction will formally capture serial BP, laboratory, and hospitalization data, for both adjudication of safety events and for potential exploratory analyses.

coordinators are responsible for surveillance of the Way to Health and Adheretech dashboards. If participants are labeled as "halted" on the AdhereTech dashboard (medication missed for 7 consecutive days), they contact the participant to confirm there are no technical issues. Finally, participants in the intervention arm receive monthly calls to inform them of their lottery winnings and updated ClinCard balance.

4.3. Study management

The Steering Committee consists of the Principal Investigator (JAD), Biostatistician (SA), and Co-Investigator (AS). Four Data Safety Monitoring Board (DSMB) members (three cardiologists and one biostatistician) have been appointed by the study sponsor (National Heart, Lung, and Blood Institute). The DSMB meets on a biannual basis to review recruitment and monitor for participant safety.

4.4. Participant safety

The intervention involves promoting antihypertensive medication adherence, which may have the unanticipated consequence of medication-related adverse effects. We are capturing any injury/adverse event that is, or might be, a result of the intervention, including any of the following: (1) fall-related injury; (2) syncope; (3) hypotension; (4) bradycardia; (5) renal or electrolyte abnormality. Safety events are ascertained both by questionnaire at the 6- and 12-month follow-up visits and by periodic (monthly) EHR review of ambulatory visits and hospitalizations. All potential safety endpoints are reported directly to the Principal Investigator and subsequently the DSMB.

5. Statistical analysis

General: Statistical comparisons will be performed after enrollment of the full study sample, using two-sided significance tests at alpha = 0.05 and two-sided confidence intervals; no interim comparative analyses are planned. We will begin all analyses with descriptive summary statistics and graphical displays of all variables, with attention to assessing balance in these characteristics by intervention group, and with assessment of the distribution of variables relevant to the choice of statistical tests. Statistical software R will be used for analysis.

Primary Endpoint Analysis – Efficacy: We will compare the change in SBP between groups from baseline to 6 months by calculating difference scores for each participant and comparing the intervention and control groups with an independent groups *t*-test allowing for unequal variances. We will also regress 6-month BP on a binary indicator of treatment group, with adjustment for baseline BP and the stratification factor (enrollment site). Although randomization should obviate the need for additional adjustment, we will explore whether adjustment for participant-level characteristics (e.g., race, ethnicity, sex) is necessary, using the change-in-estimate criterion [34].

To test the durable effect of the lottery program after cessation (6–12 months) on SBP, we will proceed in a similar manner. We will fit longitudinal mixed effects models (MEM) of the 3 repeated SBP measures (baseline, 6 months, 12 months), with indicator for treatment arm as a binary covariate, site-level fixed effects, patient-specific random effects, and modeling time using indicator variables or using piecewise linear splines, to allow differential rates of change from baseline to 6 months and from 6 months to 12 months. Adjustment for participant-level covariates will be made, if necessary, as discussed above.

Primary Endpoint Analysis – Process: To test the effect of a lottery incentive program on antihypertensive adherence (defined as ≥80% of days covered as assessed by EMD) at 6 months, we will first classify participants in the intervention and control arms as adherent versus nonadherent based on the 80% threshold (i.e., total number of days adherent divided by 183 days). We will then use the chi-squared test to evaluate differences in rates of adherence between groups. We will also explore different thresholds for "adherent" (e.g., ≥60%) in sensitivity analyses. To evaluate the durable effect of the incentive lottery on adherence (after cessation of the study intervention), we will perform similar analyses between 6 and 12 months. Further, we will perform a secondary analysis using adherence as a continuous variable that ranges from 0% (completely non-adherent) to 100% (perfect adherence). We will use longitudinal generalized linear mixed effects models to assess the effect of treatment on repeated measures of adherence over 12 months, with random effects for participants and fixed time effects accounting for trend.

Exploratory Mediators and Moderators of Intervention Effect: We will capture mediators of adherence based on our theoretical model including intrinsic versus extrinsic motivation (TSRQ) [35] and self-efficacy (MASES) [36] and estimate a just-identified path model [37]. We will also capture moderators to explain effects in different subgroups based on prior studies of adherence. These include comorbidity burden (Charlson Comorbidity Index) [38], depression (PHQ-9) [39], patient reported health status (SF-12) [40], number of chronic medications prescribed, and demographic characteristics (age, sex, race, ethnicity). Moderation will be assessed by including a moderator × treatment interaction term in outcome regression models.

Analysis of Adherence Trajectories: We will explore responsiveness to the incentive lottery among intervention group participants. We hypothesize that, among intervention group participants: (1) there will be distinct trajectories of adherence (e.g., improving adherence, deteriorating adherence, sustained non-adherence); and (2) there will be significant engagement differences among groups. We will test whether the following characteristics are significant: motivation, self-efficacy, age (≥65 years), sex, race/ethnicity, comorbidities, patient-reported health status, depressive symptoms, and medication burden, based on prior literature [41,42]. We will conduct latent class analysis to identify profiles of adherence and explore whether these factors indicate membership in a class; these models use maximum likelihood estimation and are implemented with the iterative EM algorithm to identify an optimal number of latent classes for the set of indicators.

6. Power calculations

We are aiming to randomize 435 participants using a 2:1 allocation, which will result in 290 participants in the intervention group and 145 participants in the control group. We are using unbalanced (2:1) randomization in order to have greater statistical power to understand adherence trajectories among participants receiving the study intervention. While we aim to minimize participant dropout, we include adjustment for up to 20% dropout in each arm, resulting in about 348 with evaluable endpoints (232 intervention, 116 control). Endpoints for efficacy (≥10 mmHg reduction in SBP) and process (≥80% days adherent) were selected based on clinically meaningful thresholds derived from prior literature. For SBP, we wish to be able to detect a between-group difference in change in SBP from baseline to 6 months of 10 mmHg. Assuming 232 intervention and 116 control participants with an evaluable endpoint, and a conservative standard error estimate of 28 mmHg [43], we have approximately 88% power to detect a difference between groups of 10 mmHg, using a two-sided, 0.05-level test; there is 80% power to detect a difference between groups as small as 8.9 mmHg. For the outcome of adherence (dichotomized at ≥80% adherent vs. <80% adherent), we will have 93% power to detect a 20% difference in adherence between groups, and 80% power to detect a 15% difference, assuming a baseline adherence rate in the control group of about 25%.

7. Discussion

Although a growing number of studies have investigated behavioral economic approaches in a range of conditions including obesity, physical inactivity, smoking cessation, and medication adherence, many have focused on populations from privately insured health plans and/or those employed by large companies [18,44,45]. This is despite

vulnerable patients standing to gain the most from these approaches: in hypertension, low income and Black race are both associated with considerable early cardiovascular morbidity including premature myocardial infarction [46] and stroke [47], both of which can plausibly be reduced by adequate BP control. BETTER-BP was therefore designed in the context of promising behavioral economics approaches to cardiovascular risk factor management that have largely been untested in these individuals.

New approaches to medication adherence are critical to reduce hypertension-related morbidity and mortality. Consistent control of blood pressure requires that patients take their prescribed medication on a daily basis, but poor adherence to daily regimens is a pervasive problem that represents a lost opportunity to improve health [48]. Observational studies have shown that estimates of poor adherence to antihypertensive medications, using the common definition of <80% days adherent, range from 25% to 77% after 1 year [48–50]. Adherence is even lower among vulnerable populations as seen in studies of patients insured by Medicaid, with adherence rates routinely below 40% [50–52]. For example, Bailey et al. reported that over 60% of Medicaid-insured patients with hypertension in Tennessee were nonadherent with antihypertensive medications (using a threshold of days adherent <80%) [1].

The BETTER-BP study intervention takes place for 6 months, and our design aims to evaluate whether there are both immediate (6 months) and durable (12 months) effects of the incentive lottery. We hypothesize that the lottery incentive will increase participants' perceived autonomous motivation for adhering to their antihypertensive medications, which will be sustained due to increased feelings of competence (i.e., self-efficacy) once the incentive is withdrawn [17]. Examining durable effects is critical as it speaks to the long term financial viability of behavioral incentives, which can be costly. While data on the efficacy and durability of behavioral economic incentives in vulnerable populations are generally lacking, we acknowledge the work of Shapiro and colleagues who enrolled 207 participants with uncontrolled hypertension from two federally qualified health centers (FHQCs) in California [16]. Participants were randomized to receive behavioral economic incentives for 6 months (versus usual care) and both groups were followed for 12 months. People randomized to behavioral economic incentives (a combination of incentive-based payments for achieving BP targets, attending study visits, and a lottery based on other healthy behaviors) had improved control of hypertension at 6 months but not 12 months (after these incentives were removed). Their findings speak to the challenge of long-term behavior change for blood pressure control. Our study differs in several important ways: first, in explicitly requiring nonadherence for study enrollment; second, in leveraging mHealth capabilities including wireless adherence monitoring and daily text messaging; and third, in delivering a simpler intervention that is predicated on adherence alone. Our projected study sample is also double the size of this prior study, which will allow us to better understand within-group variation (including medication adherence). In this context, BETTER-BP will generate evidence that is complementary to the foundational work of Shapiro and colleagues.

There are several potential limitations to our approach. For example, by design we choose only a single medication to be placed in the EMD, even though in practice some patients are prescribed multiple antihypertensive medications. We made this decision because a more complex behavioral economic intervention can potentially overwhelm participants and lead to negative findings, as documented by others [53]. Initiating combination antihypertensive therapies to reduce pill burden may also improve adherence but is beyond the scope of our pragmatic trial. Second, we are using an EMD as a proxy for antihypertensive adherence (rather than measuring it directly). The only true measures of adherence are either directly observed therapy or biomarker measurement, both of which are not feasible in the setting of a pragmatic trial. However, prior adherence studies have generally considered EMD closer to gold standard than most other measures (e.g. self-report) [54,55]. Third, our study is focused solely on improving antihypertensive medication adherence. Other trials have examined whether antihypertensive medication intensification to overcome clinical inertia can improve BP control. Fourth, we acknowledge that intervening on medication adherence over time may be different from one-time interventions that may be more practical to implement over the short term – for example, smoking cessation. In addition, while we are evaluating at 12 months for durable effects, we are unable to collect data on longer-term durability (e.g. 2 years) due to budgetary and timeline constraints. Fifth, enrollment is based on a single ambulatory SBP value > 140 mmHg within the past year, coupled with self-reported nonadherence. While more stringent criteria have been used (e.g. multiple high ambulatory readings, or serial research-grade measurements), our aim was to conduct a pragmatic clinical trial that was broadly inclusive. Further, treatment decisions in practice (e.g. medication escalation or adding new therapies) are often made on a single high ambulatory SBP value. Finally, while BETTER-BP was not explicitly designed to address cost effectiveness, it should be noted that incentive lotteries have a cost associated with them. BETTER-BP participants are estimated to receive, on average, $1.40 per day for adherence ($252 per participant over 6 months). Lunze and colleagues highlight several ethical concerns with paying people for healthy behaviors, including undermining personal responsibility, interfering with therapeutic relationships, and being unfair to those already engaged in healthy behaviors [56]. However, there are also potential benefits: on a population level, adequate BP control should in theory lead to reduced health system costs. Further, we would argue that the benefits of achieving target BP on an individual level – namely, reducing morbidity and mortality from cardiovascular events – outweigh these theoretical concerns.

In conclusion, BETTER-BP will test whether behavioral economics incentives for antihypertensive medication adherence are effective in vulnerable populations. This trial will generate important knowledge about whether these incentives can be deployed in everyday practice to help solve the vexing challenge of inadequately controlled hypertension and its sequelae.

Sources of funding

This BETTER-BP trial is supported by the National Heart, Lung, And Blood Institute (NHLBI) of the National Institutes of Health (R01HL148275). REDCap is supported by the National Center for Advancing Translational Sciences (NCATS, National Institutes of Health (NIH), through grant UL1 TR00000. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Dr. Shimbo is supported by K24HL125704 from the NHLBI.

Credit author statement

John A. Dodson MD, MPH: Conceptualization, Writing - Original Draft, Supervision, Funding acquisition, Antoinette Schoenthaler EdD: Conceptualization, Writing - Original Draft, Funding acquisition, Ana Fonceva MS: Project administration, Writing - Review & Editing, Yasmin Gutierrez BS: Project administration, Daichi Shimbo MD: Writing - Original Draft, Darcy Banco MD: Writing - Review & Editing, Samuel Maidman MD: Writing - Review & Editing, Ekaterina Olkhina MD: Project administration, Writing - Review & Editing, Kathleen Hanley MD: Project administration, Writing - Review & Editing, Carson Lee NP: Project administration, Writing - Review & Editing, Natalie K. Levy MD: Project administration, Writing - Review & Editing, Samarchana Adhikari PhD: Conceptualization, Writing - Original Draft, Funding acquisition, Data Curation, Formal analysis.

Declaration of competing interest

No authors report relevant disclosures.

Appendix. text messages generated for study intervention (English and Spanish versions)*

English Text	Character count	Spanish Text	Character count
***Outcome 1: Participant is eligible for the lottery (took medication) and won.**			
Congratulations! You took your medication and won the lottery. The number drawn was WN and your number is YN. You won $$. Keep up the good work!	144	¡Felicidades! Tomaste tu medicación y ganaste la lotería. El número extraído fue WN y su número es YN. Ganaste $$. Siga con el buen trabajo!	140
Great news! You took your medication and won the lottery. The number drawn was WN and your number is YN. You won $$. Keep up the good work!	139	Buena noticia! Tomaste tu medicación y ganaste la lotería. El número extraído fue WN y su número es YN. Ganaste $$. Siga con el buen trabajo!	141
Great news! You took all your medication and won the lottery. The number drawn was WN and your number is YN. You won $$. Go for it again tomorrow!	146	Buena noticia! Tomaste tu medicación y ganaste la lotería. El número extraído fue WN y su número es YN. Ganaste $$. Vuelve mañana!	132
Well done! You took your medication and won the lottery. The number drawn was WN and your number is YN. You won $$. Keep up the good work!	138	¡Bien hecho! Tomaste tu medicación y ganaste la lotería. El número extraído fue WN y su número es YN. Ganaste $$. Siga con el buen trabajo.	140
Good job! You took your medication and won the lottery. The number drawn was WN and your number is YN. You won $$. Nice going!	126	Buen Trabajo! Tomaste tu medicación y ganaste la lotería. El numero extraído fue WN y su número es YN. Ganaste $$. Que bien!	125
***Outcome 2: Participant is eligible for the lottery (took medication) and lost.**			
You took your medication yesterday, but your numbers weren't picked. The number drawn was WN and your number is YN. Keep it up! Tomorrow is a new chance to win!	160	Ayer tomo sus medicamentos, pero tus números no fueron elegido. El número extraído fue WN y su número es YN. Siga así, Mañana es una nueva oportunidad de ganar!	160
You took your medication yesterday, but none of your numbers were chosen. The number drawn was WN and your number is YN. Keep going, you could win tomorrow!	156	Ayer tomaste tu medicamento, pero ninguno de tus números fue extraído. El número extraído fue WN y su número es YN. Quedarse con eso. ¡Podrías ganar mañana!	156
You took your medication yesterday, but your numbers weren't drawn. The number drawn was WN and your number is YN. Keep at it! Everyday is a new chance to win.	159	Ayer tomaste tu medicamento, pero tus números no fueron extraídos. El número extraído fue WN y su número es YN. Síga! Cada día hay nuevas oportunidades de ganar	160
You took your medication yesterday, but none of your numbers was drawn. The number drawn was WN and your number is YN. Stay committed. You could win tomorrow!	159	Ayer tomaste tu medicamento, pero ninguno de tus números fue extraído. El número extraído fue WN y su número es YN. Mantente comprometido ¡Podrías ganar mañana!	160
You took your medication yesterday, but your numbers weren't drawn. The number drawn was WN and your number is YN. Stay on track! You may win tomorrow.	151	Ayer tomaste tu medicamento, pero tus números no fueron extraídos. El número extraído fue WN y su número es YN. ¡Quedarse en el camino! Puedes ganar mañana.	156
Outcome 3:*Participant isn't eligible for the lottery (didn't take medication) but would have won			
You missed your medication yesterday. The number drawn was WN and your number is YN. If you took your medication you would have won $ $. Don't miss out!	152	Usted no se tomó su medicación ayer. El número extraído fue WN y su número es YN. Si se hubiera tomado su medicamento, hubieras ganado $ $. ¡No te lo pierdas!	158
The lottery number drawn was WN and your number is YN. If you took your medication you would have won $$. Be consistent. Everyday is a new chance to win!	153	El número de lotería ganador es WN y su número es YN. Si tomara su medicamento, hubieras ganado $$. Sea consistente. Cada día hay nuevas oportunidad de ganar!	159
You missed your medication yesterday. The number drawn was WN and your number is YN. Take your medication for a chance to win. Don't give up!	141	Usted no se tomó su medicación ayer. El número extraído fue WN y su número es YN. Si hubiera tomado su medicamento, habría ganado $$. ¡No te rindas!	149
You missed your medication yesterday. The number picked was WN and your number is YN. If you took your medication you would have won $ $. Try a reminder!	153	Usted no se tomó su medicación ayer. El número extraído fue WN y su número es YN. Si hubiera tomado tu medicamento, hubieras ganado $$. ¡Ponga un recordatorio!	159
The lottery number picked was WN and your number is YN. If you took your medication you would have won $$. Always take your medications for a chance to win!	156	El número de lotería ganador fue WN y su número es YN. Si tomara su medicamento, hubieras ganado $$. Siempre tome su medicamentos para la oportunidad de ganar!	160
Outcome 4: *Participant isn't eligible for the lottery (didn't take medication) and would have lost.			
The number picked was WN and your number is YN. You never know when your numbers may be chosen. Remember to take your medication every day and you may win!	155	El número extraído fue WN y su número es YN. Nunca se sabe cuándo pueden sacarse sus números. ¡Recuerde tomar su medicamento todos los días y puede ganar!	155
The number drawn was WN and your number is YN. You never know when your numbers may be drawn. Take your medications every day for a chance to win!	146	El número extraído fue WN y su número es YN. Nunca se sabe cuándo pueden salir sus números. Tome sus medicamentos todos los días para la oportunidad de ganar!	158
You missed your medication yesterday. The number picked was WN and your number is YN. If you take your medication every day, you could win tomorrow!	148	No se tomó su medicación ayer. El número extraído fue WN y su número es YN. Si toma su medicamento todos los días, podría ganar mañana!	136
You missed your medication yesterday. The number drawn was WN and your number is YN. Always take your medications and you could win tomorrow!	141	No se tomó su medicación ayer. El número extraído fue WN y su número es YN. Siempre toma tus medicamentos y podrías ganar mañana!	130
The number drawn was WN and your number is YN. You can do better! Take your medications every day and you could still win tomorrow!	131	El número extraído fue WN y su número es YN. ¡Puedes hacer mejor! Tome sus medicamentos todos los días y aún podría ganar mañana!	130

*Each message is randomly selected within outcome category that participants meets on a given day.

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