Study Protocol

“Using artificially intelligent text messaging technology to improve American Heart Association's Life's Essential 8 Health Behaviors: LE8 Bot + Backup”

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Project Title: Using artificially intelligent text messaging technology to improve American Heart Association's Life's Essential 8 Health Behaviors: LE8 Bot + Backup
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I. Hypotheses and Specific Aims

Our goal is to improve control of cardiovascular (CV) disease risk factors using a multilevel intervention leveraging cellphone-based text messages integrated within health systems to improve control of American Heart Association's Life's Essential 8 (LE8) lifestyle factors. We will test the comparative effectiveness of 3 text messaging delivery strategies (*vide infra*). The findings will provide evidence regarding the best population-based strategy for universal delivery to engage all patients with health disparities in self-management to improve the AHA's LE8. We hypothesize that the LE8 text message curriculum will improve patient self-management of the LE8 risk factors and there will be a significant change in the LE8 composite score between baseline and 12-months following study enrollment. We also hypothesize that the optimized AI chatbot text messages with proactive pharmacist management arm will show the greatest improvement in the LE8 risk factors compared to the optimized AI chatbot text messages alone and generic text messages.

- *Aim 1 (UG3; Year 1):* Iteratively update the infrastructure and expand content for the AI text message chatbot with attention to social determinants of health and sociocultural contextual relevant to the target population through stakeholder engaged N-of-1 and focus group interviews and nominal group sessions.
- *Aim 2 (UG3; Year 1):* Conduct a randomized pilot to demonstrate feasibility of intervention delivery and outcomes data collection to assess preliminary effects and to refine the intervention prior to widespread implementation.
- *Aim 3 (UH3; Years 2-5):* Conduct a pragmatic patient-level randomized intervention of 3 text messaging delivery strategies for self-management support of CV risk factors. Primary outcome will be change in LE8 health score. Secondary effectiveness outcomes will include individual components of the LE8 lifestyle factors, Framingham risk score, self-efficacy, medication adherence, clinical outcomes (e.g., CV related hospitalizations), and healthcare utilization.
- *Aim 4 (UH3; Years 2-5):* Evaluate the intervention using PRISM and a mixed methods approach to evaluate pragmatic clinical and implementation outcomes (reach, effectiveness, adoption, implementation, and maintenance) with an emphasis on equity and representativeness, and systematically assess contextual influences to inform sustainment and future tailoring, adaptations, and dissemination.

II. Background and Significance

At least 50% of the US population will develop two or more chronic medical conditions by age 45, with the prevalence increasing to >80% for those age 65 years and older. These chronic medical conditions include many CV diseases and CV disease risk factors (e.g., hypertension, hyperlipidemia, and diabetes). CV disease leads to significant disability, health care costs and death. To successfully manage these conditions, patients need ongoing care facilitated by health care providers who can help them monitor and manage their CV conditions themselves in between episodic health care visits.

Patients experiencing health disparities, those who are racial and ethnic minorities[1]; people with low income or low socioeconomic status (SES)[2]; rural residents[3] and people with limited English proficiency[4] are disproportionately affected by these CV conditions and suffer greater consequences from these conditions. The risk of diabetes is 77% higher for Black and 66% higher among Hispanic/Latino, than for White patients.[5] Hypertension control rates are lower among Non-Hispanic Black and Hispanic/Latino compared to Non-Hispanic White patients.[6] These differences contribute to disproportionate rates of mortality as the attributable risk for hypertension and 30-year all-cause mortality is nearly double for Non-Hispanic Black than Non-Hispanic White patients.[6] Data show similar disparities for people with low SES,[7] rural residents and people with limited English proficiency.[8,9] These statistics highlight an urgent need to address and control these CV risk factors, particularly among patients experiencing health disparities. Furthermore, most of the prior interventions addressing CV risk factor reduction have generally targeted individual risk factors rather than overall CV health as encompassed in the LS7 risk factors.

Self-management (SM) involves focusing on an individual's role in managing chronic disease and has strong evidence of benefit for patients with chronic medical conditions.[10] SM interventions have demonstrated improved self-efficacy, quality of life, health status, chronic disease measures, health behavior change and reduced healthcare utilization.[9,11–13] The American Heart Association has identified 8 key self-management behaviors that when optimized will collectively lead to better CV health, i.e., stopping smoking, eating better, being active, sustaining a healthy weight, manage blood pressure, control cholesterol and reduce blood sugar.[14,15] The LE8 score documents how well patients adhere to SM behaviors, with a score that quickly and effectively measures overall CV health ranging from 0-14, where 0-4 is considered "inadequate" 5-9 "average" and 10-14 "optimum" CV health.[16]

As healthcare becomes increasingly complex, alternative team-based approaches to chronic care that include clinical pharmacists, are becoming common.[17] Clinical pharmacists have advanced training in chronic disease management that includes both non-medication behavioral interventions (e.g., motivational interviewing) and all aspects of medication management (e.g., selection, monitoring, adjusting). There is clear evidence of their positive impact on patient outcomes, spanning from smoking cessation to glycemic control and blood pressure control across various care settings (e.g., Federally Qualified Health Centers (FQHC), academic health centers).[18–22] These benefits have led to widespread integration and reliance on clinical pharmacists, but with added health system costs associated with paying another doctoral-level health care provider.[23–30]

Mobile telephones are common with 96% of US adults owning a cellphone.[31] Use of text messaging to communicate is also common with 81% of cellphone owners using their phones to text messages.[32] Text messaging is used by people across the age spectrum, among racial and ethnic minority populations, rural populations[3], people with low (SES) as well as people with limited English proficiency.[4,33,34] Meta-analyses of text messaging interventions have demonstrated improved health behaviors including physical activity[35], weight loss, chronic disease control (i.e., glycemic control and BP)[36–38] and medication adherence. However, evidence such as optimal message content, conversational

approaches that facilitate bidirectional messaging, timing and dose of messages is limited, and it is unknown if patients experiencing health disparities benefit similarly.[39]

The use of text-message based artificially intelligent (AI) conversational chat bots is emerging as the next generation for technology-based health behavior interventions.[40,41] An AI conversational chatbot utilizes natural language processing (NLP) to classify the intent of a user-initiated question on specific topics and machine learning (ML) to continually update and refine the precision in offering a response that correctly addresses the intent of the question. This allows patients to initiate and direct organic text message communications to a specific phone number in support of self-management. Using *a priori* libraries focused on specific health behaviors that anticipate the intent of patient text-message queries, an AI chatbot can continuously use NLP to process questions and ML to update and refine messages to train the system to increase the precision in matching the correct response to user queries. A well-functioning AI chatbot using NLP and ML will return answers that are appropriately matched to user queries 80% of the time or more.[42] As of now, we have little understanding of the incremental benefits of this nascent tailored and user-centric approach compared to standard text message systems.

Tailoring SM interventions meets patient identified needs and increases the level of intervention effectiveness. A prior study[43] found that White patients had the lowest physical activity and highest adherence to insulin therapy whereas Hispanic patients were more interested in improving self-management behaviors, suggesting that targeted support to meet patient needs may be important. As another example, a tailored self-management intervention for Black patients with diabetes improved diabetes related clinical measures.[44,45] A systematic review of SM support interventions in low income and low health literacy patients showed that they were generally resource intensive and had inconsistent benefits.

Behavioral "nudges" from the fields of behavioral economics and cognitive psychology have the potential to augment the impact of text messaging interventions to support patient behavior change**.** The Dual-Process Theory of decision-making (one of two foundational theories supporting Dan Kahneman's 2002 Nobel prize in economics) states that people make decisions either 'intuitively,' quickly drawing on emotion and past experiences or 'reasonably' using a thoughtful, analytic approach. Nudges take advantage of the intuitive aspects of decision-making. [46,47] A nudge is defined as a small change in choice framing or choice architecture that "alters people's behavior in a predictable way without forbidding any options or significantly changing their economic incentives."[48] Behavioral nudges are more personalized and resonate better with patients, and have demonstrated impact on healthy eating[49], smoking[50], and physical activity[51,52]. A systematic review demonstrated the benefit of nudges to improve SM activities for patients with chronic conditions.[53] Use of persuasive message strategies can further impact message engagement. Theories in Health Communication emphasize the need to provide a message frame (e.g., with a positive or negative tone) to provide opportunities for bidirectional engagement that allow for senders to demonstrate pro-social characteristics, evoke an emotional response or include a narrative in order for audiences to resonate with and internalize message content.[54]

Interventions for SM are more likely to have a greater impact when addressing multilevel contributors to health inequities.[55] Per the social-ecological model, to effectively reduce CV risk, patients must have the knowledge and skills to adopt healthy behaviors; communities must have resources that align with cultural norms of the patients at risk; and health systems must have resources to identify and treat risk in an integrated, patient-centered manner.[56] SM interventions are primed for multi-level components that facilitate greater engagement with and support from interpersonal connections, health organizations,

communities and environments to facilitate health. The "Social Ecological Model, Inside Out" proposed by Golden et al.,[57] explicitly emphasizes an approach to health equity through conceptualizing how individuals, their personal social networks and group affiliations co-create the context that drives policy development and supportive physical and structural environments to support health. A key factor in this model is understanding how social determinants such as access to safe places to exercise, reliable transportation and food insecurity are considered in the intervention development and implementation. We attend to multiple levels of the model by making our intervention fairly and equitably distributed, by fostering interpersonal connections between patients and pharmacists, by automating identification of eligible patients through the EHR; by linking patients to community resources that support improvements in social determinants of health and through identification of infrastructural supports needed to replicate, sustain and scale the LE8 Bot + Backup intervention. As an example, an intervention that encourages participants to eat fresh vegetables and fruits but does not access whether this is feasible for participants or provide resources to find these foods at free or reduced costs will not equitably benefit all people.

IV. Research Methods

A. Outcome Measure(s)

Improvement in LE8 risk factor (Primary Outcome): The objective of this study is to determine the impact of the different text message delivery strategies on self-management support and subsequent change in the LE8 risk factors. We hypothesize that the LE8 text message curriculum will improve patient self-management of the LE8 risk factors and there will be a significant change in the LE8 composite score between baseline and 12-months following study enrollment. The LE8 score assesses how well patients' CV risk factors are controlled with a score that quickly and effectively measures overall CV health ranging from 0-14, where 0-4 is considered "inadequate" 5-9 "average" and 10-14 "optimum" CV health.[29] We also hypothesize that the optimized AI chatbot text messages with proactive pharmacist management arm will show the greatest improvement in the LE8 risk factors compared to the optimized AI chatbot text messages alone and generic text messages. The primary outcome will be improvement in initial qualifying LE8 components (those categorized as intermediate or poor at baseline and observable in the EHR, including blood pressure, total cholesterol, blood sugar and weight) between baseline and 12-months. We will obtain these measures from the EHR and take the measurement closest to baseline of those between 3-month prior to enrollment date and 1-month post enrollment date. Study inclusion criteria requires identification of at least one LE8 EHR component as poor or intermediate, thus all patients will have at least one qualifying LE8 component obtained from the EHR. We will encourage patients to talk to their physician about obtaining a measure (i.e., blood draw or BP measurement) close to 12 months consistent with LE8 recommendations. For the 12-month measurement, we will take the value closest to the 12-month post enrollment date with a 3-month window prior to and after the 12-month enrollment date. As a sensitivity analysis, we will also identify the lowest score within this window and the highest score then repeat the analysis.

Individual LE8 components (Secondary Outcome): Secondary outcomes will include change in the individual risk factors of the LE8, including change in blood pressure, total

cholesterol, blood sugar, weight, physical activity, health diet pattern and smoking between baseline and 12-months following enrollment. For patients without a baseline measure for an LE8 component derived from the EHR, we will encourage patients to talk to their physician about obtaining a measure (i.e., blood draw or BP measurement) consistent with LE8 recommendations. For the 12-month measurement, we will take the value closest to the 12-month post enrollment date with a 3-month window prior to and after the 12-month enrollment date. Since physical activity, health diet pattern and smoking are not observable in the EHR, we will ask patients via text to self-report their status at baseline and 12-months following enrollment via Qualtrics Survey. Qualtrics will send a push message three times, if patients not respond research staff will contact them by phone up to three times. We will use evidence-based practices[143] for text message survey completion, including pre-survey reminder notification and 2 follow-up reminders. We will review the patient response data weekly to ensure data validity. We will call patients if they do not complete the surveys and for any data discrepancies.

Self-Efficacy for Managing Chronic Diseases (Secondary Outcome): The Self-Efficacy for Managing Chronic Disease Scale is a valid and reliable instrument available in English and Spanish. The English version is made up of 6-items on a visual analog scale, ranging from 1 (not at all confident) to 10 (totally confident). The psychometric properties of the scale include Cronbach's alpha of .88 across all studies, minimal floor and ceiling effects, sensitive to change, and moderate and significant correlations provide convergent validity evidence when measured against selected health indicators. Baseline higher self-efficacy was associated with lower health distress, illness intrusiveness, activity limitation, depression and fatigue; improvements over 4 to 6-months in self-efficacy scores was associated with lower levels of the same health indicators.

Medication adherence (Secondary Outcome): We hypothesize the intervention will improve medication adherence by reducing the number of gap days between medication refills given that patients will be provided educational messages about the importance of medication adherence to help treat uncontrolled CV risk factors. We will measure medication adherence by identifying the number of gaps (frequency) and the length of each gap (severity) for every patient and medication. The gap days will be determined using pharmacy refill data based on the date of refill, the number of days supplied, and the subsequent refill date during the 12-month intervention period. Worse medication adherence will be identified as an increase in either the frequency of gaps or the length (severity) of the gaps. We are currently using this same methodology in the Nudge study.

Framingham CV disease risk score (Secondary Outcome): We will use the Coronary Heart Disease (2-year risk) – First Event or the Recurrent Coronary Heart Disease, for those with established coronary heart disease or ischemic stroke risk calculator. Both risk scores use similar risk factors to calculate risk including systolic blood pressure, Cigarette smoking status, Fasting lipid level (totals and HDL Cholesterol), diagnosis of diabetes, and use of antihypertensive medication. We will have already obtained these measures as part of our assessment of the LE8. We hypothesize that the self-management support intervention will lower the calculated Framingham risk score between baseline and 12-months of follow-up.

Clinic events (Secondary Outcome): We will also assess for clinical events defined by emergency department (ED) visits or hospitalizations. Our hypothesis is that improved LE8 risk factor control will lead to decreased ED visits and/or hospitalizations. We will assess specific clinical events we would expect improved LE8 risk factors could have an impact

upon and conversely where poor adherence can lead to clinical deterioration necessitating additional care. For example, poor adherence to antihypertensive medications can lead to uncontrolled blood pressure leading to hospitalization for heart failure or stroke. We will assess clinical events via the EHR within each health system.

Healthcare utilization (Secondary Outcome): In addition to the clinical events and adverse clinical events, we will also measure healthcare utilization defined by routine clinical visits and/or other procedures associated with the clinical condition. We hypothesize patients with more uncontrolled CV risk factors may be more likely to have clinic visits due to uncontrolled clinical conditions. For example, a patient with hypertension may not take their medications and therefore have uncontrolled blood pressure. They may have more clinic visits and have their medication uptitrated for better blood pressure control. It is also possible that non-adherent patients may be less likely to follow-up with clinic visits and they will have less healthcare utilization. Accordingly, it will be important to measure healthcare utilization to assess the impact of improved LE8 risk factor control as part of the study.

Assessment of patient perspectives: In Year 5, after the intervention and follow-up period has ended, we will survey all patients via text messaging using a previously developed text messaging survey[58] (**Figure 1**). In a random sample of 80 patients who respond to the survey, we will also contact them via telephone to get more in-depth feedback through qualitative interviews on the intervention. The sample will be stratified evenly across patients in the 3 intervention arms and prioritize representativeness of diverse patients. We have conducted similar interviews with patients following adherence interventions. These interviews will evaluate issues such as ease of use and acceptability and help inform future adaptation of the interventions[59] as we plan for broader dissemination of the intervention (if demonstrated to be effective) to more clinics and patients with other chronic conditions.

Figure 1. Patient Feedback Survey

Satisfaction—'How satisfied have you been with the text messages?'

Usefulness—'How useful the text messages?

Easiness—'How easy were the text messages to use?'

Harm—'Was there any harm you experienced from the text messages and if so how much?

Future use—'How likely would you be to use this kind of text message system in the future?

Responses to questions will be scaled from 1 to 5 where 1='not at all' or 'none' and 5='completely' or 'a lot'. with a 'do not know/uncertain' option.

Follow-up assessment of clinician and health system organization/setting perspectives**:** We will conduct key-informant interviews with up to 2-3 providers (6-9 across the 3 health systems) from each setting whose patients have received the intervention to get their feedback about the intervention and the intervention effects on their patient's self-management behaviors related to CV risk factors. For some providers, they may have received a note from the study pharmacist informing them of changes in clinical status with their patients and we will also interview the providers on their perceptions of that process.

B. Description of Population to be Enrolled:

N-of-1 interviews, nominal groups, and focus groups

10 patients from each healthcare system (30 total) will be recruited to take part in N-of-1 interviews. We will also convene one nominal group with 6-8 participants in each health system (18-24 total). Each group will be held via synchronous Zoom video conference and

last up to 90 minutes. Patients for N-of-1s and nominal group sessions will be recruited from designated clinics and will be a balance of older/younger patients, men/women, those with one versus multiple chronic CV conditions and native Spanish/English speakers.

We also will conduct at least 3 focus groups with multilevel stakeholders (patients, providers/pharmacists, community advocates, health system leaders) using purposive sampling to increase representation from diverse perspectives including those across the spectrum of health disparities.

Inclusion criteria for qualitative interviews: 1) diagnosis of >=1 of the following CV risk factors: hypertension, diabetes or hyperlipidemia, 2) poor medication adherence defined as a refill gap of >=7 days within 6 months, to 1 at least one of the CV medications outlined in **Table 1**; and 3) 1 or more of the risk factors in categorized as poor or intermediate health as defined by LE8 as outlined in **Table 2**. Exclusion criteria: 1) patients who do not have cellphone; 2) enrolled in hospice or palliative care; 3) Non-English/Spanish speaking; 4) enrolled in another clinical trial if denoted in the EHR.

Table 1: CV Medication eligibility

Condition	Classes of medications
Hypertension	Beta-blockers (B-blockers), Calcium Channel Blocker (CCB), Angiotensin converting enzyme inhibitors (ACEi), Angiotensin Receptor Blockers (ARB), Thiazide diuretic
Hyperlipidemia	HMG CoA reductase inhibitor (Statins)
Diabetes	Alpha-glucosidase inhibitors, Biguanides, DPP-4 inhibitors, Sodium glucose transport inhibitor, Meglitinides, Sulfonylureas, Thiazolidinediones, metformin

Table 2: Life's Essential 8 Health Categories for Study Inclusion

	Definition	Level of health for each metric		
		Poor	Intermediate	Ideal
Blood lipids	Metric: Non–HDL cholesterol (mg/dL)	≥220 mg/dl	130-189 mg/dl or treated to goal	<130 mg/dl
Blood pressure	Measurement: Appropriately measured systolic and diastolic BPs	SBP>140 mm Hg or DBP >=90 mm Hg Subtract 20 points if treated level	SBP 120-139 or DBP 80-89 mm Hg or treated to goal	<120 mm HG/<80 mm Hg
Blood glucose	Measurement: FBG or casual HbA1c Example tools for measurement: Fasting (FBG, HbA1c) or non-fasting (HbA1c) blood sample	Diabetes with HbA1c ≥8.0	No diabetes and FBG 100–125 or HbA1c 5.7–7.9	No history of diabetes and FBG <100 (or HbA1c <5.7)

For all qualitative interviews, participants will be consented via postcard consent due to the minimal risk presented.

Intervention

We will identify eligible patients using EHR data with the same inclusion and exclusion criteria as N-of-1 interviews and nominal groups. There will be minimal exclusions criteria: 1) patients who do not have cellphone; or 2) enrolled in hospice or palliative care; or 3) Non-English or Spanish speaking; or 4) enrolled in another clinical trial if denoted in the EHR.

The intervention will include patients based on the following: 1) diagnosis of one or more of the following CV risk factors (i.e., hypertension, diabetes or hyperlipidemia), 2) poor medication adherence defined as a refill gap of >=7 days within 6 months, to 1 at least one of the CV medications outlined in **Table 1**; and 3) 1 or more of the risk factors in categorized as poor or intermediate health as defined by LE8 as outlined in **Table 2**. While not part of the eligibility criteria, we are partnering with 3 safety-net health systems (Denver Health and Hospital Authority, Salud Family Health Centers, and STRIDE Community Health Centers) to further focus enrollment on Black, Hispanic/Latino, rural, low income and Spanish-only speaking patients.

Stakeholder Panel

The Stakeholder Panel will have 1 patient, 1 pharmacist or physician, and 1 administrative leader from each healthcare system. The panel will also include 3 representatives from local organizations, such as a food bank or other services. Members will be recruited through relationships of the investigators at the 3 sites. Stakeholder members will be consented via postcard consent due to the minimal risk presented.

Stakeholders will meet monthly during the UG3 (Y1) year and then quarterly during the UH3 (Y2-5) years. Meetings will be held virtually via Zoom or in person, as decided by the Panel. Participants will be reimbursed $50 per meeting in the form of a gift card.

C. Study Design and Research Methods

Aim 1 (UG3; Year 1): **Iteratively update the infrastructure and expand content for the AI text message chatbot with attention to social determinants of health and sociocultural contextual relevant to the target population through stakeholder engaged N-of-1 and focus group interviews and nominal group sessions.**

Data infrastructure development

The first step for Aim 1 will be to develop the technology platform to facilitate error free delivery of messages via text to user cell phones and to program our AI chatbot to use NLP and maximize the chatbot precision so that users are more often sent a response from our system that matches the intent of their query. We previously built a technologically current AI NLP chatbot system that operates via short message service (the textbot).[113] We will first develop and categorize anticipated "intents"—i.e., the specific anticipated topics patients will want to learn or ask about LE8. To generate a comprehensive list of intents, we will review topics of frequently asked questions about the topics in LE8 from reputable clinical websites. We will also build intents that anticipate questions about addressing, managing or overcoming social factors demonstrated as common moderators of healthy behavior for patients[114]. Once we have an initial set of intents, we will generate multiple variations on questions that users could ask related to that intent so the system could be "trained" to infer the intent of a query based on many possible ways of asking a query. For example, one user may ask "When do I call my doctor if my blood pressure is high?", while another might ask, "what do numbers on my blood pressure mean?", and both queries would be matched to an "understanding blood pressure" intent. Our AI chatbot system can facilitate branch logic conditioning by branching to provide responses based on patient specific queries. This infrastructure provides flexibility to facilitate tailoring of content to be responsive to individually specific preferences for information.

Generating message library intents. To generate an initial library of question variations for each intent, we will rely on the Amazon Mechanical Turk (MTurk), a crowdsourcing platform where one can offer a small incentive for users to complete tasks. We will ask 50 MTurk participants to generate 3 to 5 variations of questions with the same intent for each of the LE8 topics and social factor intents, randomly assigning topics and factors until we have 25 variations on queries for each intent. This allows the system to have enough initial data to learn how to interpret user questions, tolerate misspellings, and recognize the underlying intent of each question. Although the crowdsourcing activity allows us to develop a robust set of question variations, there is still the likelihood that we will not anticipate every possible variation on questions. When the system does not match a response to the question intent, it reverts to the fixed choice (also called a "pick list") set of responses, e.g., "I think you are asking about one of these 4 topics: (a) healthy eating, (b) cost of healthy food, (c) how to access a food pantry, (d) how much you can eat in a day. Please type the letter corresponding to the topic you wish to explore or try your question again." Our goal is to correctly match the response to the intent of the question ≥85% of the time. As more users engage with the system, we can review logs and re-classify content that resulted in a pick list to match an intent daily, which will increase the precision of the system.

Technology. The platform that will send text and chatbot messages will be built by Clinic Chat, LLC. Clinic Chat is hosted in a scalable cloud environment using Amazon Web Services. The NLP pipelines for textbot are built using Python 3.8 with NumPy, Pandas, and scikit-Learn, flask, npm, pm2 Python modules.

N-of-1 interviews

We will ask participants during synchronous sessions to react to content presented during a live demonstration of the message content using an interactive AI chatbot text messaging platform through multiple N-of-1 (i.e. within subject) assessments that conform to evidence-based strategies for persuasive message design. *A priori* messages presented to N-of-1 participants will represent theoretical constructs intended to (1) increase norms, commitment, and salience, key components of behavioral nudge messages; and (2) facilitate a sense of autonomy, competence and relatedness, key components of the Theory of Self-Determination. The messages and system combine to create the mechanism through which patients will develop greater SM autonomy, competence and relatedness. All content will be translated into Spanish and reviewed by our Health Equity and Engagement core to ensure relevance of content and that it is appropriate for Spanish speakers. Because messages will include assessments of social factors that can modify behavior, we will explicitly ask participants to comment on how best to assess these topics through the AI chatbot text messages to minimize concerns about confidentiality, privacy and relevance. We will deploy a content analysis of N-of-1 data and update our *a priori* library for initial text and chatbot messaging to identify the range of popular approaches for communication of the LE8 intervention content.

Nominal Groups

After completing N-of-1 interviews, we will convene up to three virtual nominal group sessions in each health system to further refine content and develop a final library of messages. The nominal group technique has been used in health promotion and in the design of mobile and digital health interventions[119,120] to facilitate the free exchange of ideas in a structured but non-hierarchical manner.[121] The nominal group is structured like a focused group discussion, where 6-8 participants are invited to react to and offer opinions on a series of topics. In a focused group discussion, the emphasis is on exploring a full

range of ideas, including outliers. In contrast, the nominal group is focused on generating consensus. In a nominal group session, there are multiple rounds of engagement, beginning with an initial round explaining a goal and answering clarifying questions. In subsequent rounds participants identify their preference for message content and discuss their preferences with the moderator with a goal to gain consensus across diverse participants. In this round, we will pay particular attention to message content that resonates for specific racial/ethnic groups and is relevant for low-income and rural communities; we will also review modifiable social determinants of health to consider if message content appropriately recognizes variable experiences with housing, income, employment, etc. that will influence self-management behaviors. It is beneficial if participants in a nominal group have different demographic characteristics so all can hear and contemplate diverse perspectives in working towards consensus on messages. This effort will also allow us a deeper understanding of how we can use message tailoring to maximum effect by asking patients both during the N-of-1 and Nominal group sessions to react to message tailoring examples.

Each group will be held via synchronous Zoom video conference and last up to 90 minutes. We will review findings to determine if a second group in each setting would be needed to gain a higher degree of consensus on the message content. Aim 1 will yield a library of contextually relevant messages to be deployed for the pilot and pragmatic trial. The library will be designed to be delivered over an 8 week period (consistent with one week for each of the LE8 topics; for people who are non-smokers, we will offer a week on a self-management topic of their choice; in the eighth week, the topic will focus on medication adherence and its importance given that all patients randomized to the study will have already demonstrated poor medication adherence). Each week for 8 weeks patients will be sent four messages that are specific to the topic for that week and with each message, they will be invited to engage with the chatbot to ask more questions about that topic.

Focus groups

We will conduct at least 3 focus groups with multilevel stakeholders (patients, providers/pharmacists, community advocates, health system leaders) using purposive sampling to increase representation from diverse perspectives including those across the spectrum of health disparities. A semi-structured moderator guide will be informed by PRISM and the Health Equity in Implementation Framework and will be reviewed by the Health Equity and Engagement and Implementation Science cores to guide a systematic evaluation of contextual determinants that positively and negatively influence the success of text messages (content, dose, access to community resources). We will also ask these stakeholders to help identify resources available locally to address social determinants of health which we will be able to incorporate into our educational material for patients.

We will capture audio recordings of focus groups and interviews and will transcribe these recordings. We will analyze these data using a thematic content analysis facilitated by use of Atlas Ti, enabling the investigators to code, index and retrieve participant responses containing key themes, concepts or events, and group them into larger categories. Coding and analysis of data will be facilitated by the use of a codebook that will be created prior to data collection, containing codes and categories (groups of codes) of themes, concepts, events, people, actions and things that may be encountered in the data (e.g., oral history “vignette” or “soap-opera” styles to convey preferences for structure of messages). These a priori codes will be based on what the investigators may expect to find based on the literature and what the investigators hope to find based on the research questions. Coding strategies will be based on the grounded theory techniques of open and axial coding, as

described by Strauss and Corbin.[60] Open coding is used to categorize key concepts, categories and patterns of experience. Axial coding is used to specify the relationship of categories to the phenomenon under study. Summary coding will synthesize the relationships across themes to generate actionable responses, such as ensuring all messages are branded with a clinic name, or all communication with the chatbot about a risk event has to happen within one hour.

Pharmacist training

We will develop a training and capacity building effort to support pharmacists from each health system who will be integral to arm 3 of our pragmatic trial that links users of our AI chatbot text messaging to pharmacists for additional self-management support. Dr. Katy Trinkley will lead this effort and will use an optimized instructional design method to create a brief online training program and a series of resources (e.g. Frequently asked questions; community resources with links and contacts to provide patients; templates for reporting patient concerns in the EHR) for pharmacists. The training program will include access to three 1.5-hour training modules on Motivational Interviewing via telemedicine offered by the University of Colorado School of Nursing Continuing Education program.[125] Motivational Interviewing (MI) is an evidence-based approach for eliciting intrinsic motivation to change using open ended questions, reflective listening and decisional balancing that has been shown in systematic reviews to be superior to more traditional methods of supporting patient health behavior change.[126] We will also include an orientation to LE8 and resources from the American Heart Association that offer specific details on each of the 8 self-management components of LE8,[127] strategies to improve any of them, and articles providing further information. The training will also include explicit skills building in soliciting detail about patient contextual factors that impact self-management, including social determinants of health. Pharmacists will be oriented to resources such as the American Association of Family Practitioners website[128] that offers local resources such as food banks, housing, transportation vouchers, access to good such as medical supplies, access to information on financial assistance programs, educational programs, jobs training programs and legal assistance as well as information of resources from our health systems and stakeholder groups. The training will offer Pharmacists guidelines and templates for engaging with patients and to document and log each engagement. The training will be designed as a self-paced, fully asynchronous online module and will be housed on the Canvas Learning Management System.[61] We will ask each health system partner to identify the pharmacist(s) they will dedicate to the patient support tasks for arm 3 of our pragmatic trial and will ask them to complete the training during the first year of the award.

Aim 2 (UG3; Year 1): **Conduct a randomized pilot to demonstrate feasibility of intervention delivery and outcomes data collection to assess preliminary effects and to refine the intervention prior to widespread implementation.**

We will conduct the trial at 3 health systems that care for large patient populations affected by health disparities, including Black, Latino/Hispanic, Spanish speaking, low-income and rural patients. In Year 1, we will conduct stakeholder engagement (patients, providers, community advocates, and health system leaders) guided by PRISM and the Health Equity Framework[12] to further understand the context of the optimized patient communication, and to generate input on the sustainable design of automated communications that include

attention to social determinants of health and ensure linguistic and community relevance. We will also engage these implementation partners to obtain feedback on intervention design, and outcomes as well as throughout the study to help address potential barriers to implementation, make necessary adaptations, help ensure sustainability of the program and plan for dissemination. Following refinement of the automated patient communication content, we will pilot the intervention at each health system to ensure that all aspects of the protocol have been operationalized and refine any potential barriers.

We will update the infrastructure for our text messages for the Nudge study, expanding the content beyond medication refill adherence to incorporate LE8 topics and providing structure to facilitate pharmacist support. Health Equity and Engagement scientists will work to ensure robust participation of patients, providers, community advocates, and health system leaders to provide feedback on the messages, intervention and implementation strategy design, and outcomes. We will also solicit routine feedback from these groups during the study to help address potential barriers to adoption and implementation and help ensure program sustainability. These activities will be guided by PRISM and the Health Equity in Implementation Framework to systematically assess the dynamic interactions of contextual factors (including SDoH and indices of health disparities) that influence success and sustainability of the implementation and its generalizability across populations experiencing inequities. To achieve the contextual assessment with a health equity lens, we will prioritize diverse representation across patients, providers (including pharmacists), community advocates and health systems.

Aim 3 (UH3; Years 2-5): **Conduct a pragmatic patient-level randomized intervention of 3 text messaging delivery strategies for self-management support of CV risk factors. Primary outcome will be change in LE8 health score. Secondary effectiveness outcomes will include individual components of the LE8 lifestyle factors, Framingham risk score, self-efficacy, medication adherence, clinical outcomes (e.g., CV related hospitalizations), and healthcare utilization.**

The objective of this study is to conduct a pragmatic patient level randomized trial to evaluate the implementation and effectiveness of 3 different automated patient communication approaches for self-management support to improve control of CV disease risk factors defined by AHA's Life Essential 8 risk factors.

In Years 2-5, we will conduct a patient level randomized pragmatic trial comparing the following strategies (study arms): 1) generic text messages; 2) interactive AI chatbot text messaging incorporating tailoring to increase message relevance and address social context; behavioral nudges to facilitate intuitive decision-making; and persuasive messaging to increase motivation to change over time; or 3) interactive AI chatbot text messaging plus proactive pharmacist management. We have not included an usual care group because prior studies have generally found that control of the LE8 factors are not ideal and generic text messages have generally been more effective than usual care for behavior change. The study will randomize at the patient level rather than a cluster level because: 1) our intervention uses automated and interactive text messages that are delivered directly to patients greatly reducing the risk of intervention contamination; and 2) we will include all patients who meet eligibility criteria into the study with an opt-out option for patients who do not wish to participate due to the low risk nature of the study intervention, consistent with the Nudge study.

Opt out process
Among patients who fulfil the eligibility criteria, we will send them an opt out packet. The packet will include an introductory letter signed by the Site PI, information about the study, the opt out consent form, and a self-addressed, stamped envelope. A member of the study team will remove the participant from the potential list if an opt out form is received; forms will be saved in a secure, locked cabinet, as noted in the IRB application. Should an opt-out package be returned as undeliverable, the study team will remove the patient from the study. All materials will be available and sent to patients in both English and Spanish. If they have previously specified in their contact preferences that they prefer English or Spanish, we will send materials in their preferred language. Upon the deadline for response to the opt-out consent has expired, patients that have not opted-out will be randomized accordingly.

Upon the start of the intervention, there will be a secondary opt out option, which patients can opt out at any time by the patient responding to a message with “STOP”. The first message sent to patients will inform patients they can opt out this way.

Message arm descriptions
Once randomized, we will send patients an introductory text message about the study. In the message, we will briefly share LE8 risk factors and elicit baseline information via text messaging on lifestyle factors that are not available in the EHR, including current physical activity, healthy diet as defined by the LE8 categories and smoking status (if not available within the EHR). For those with missing baseline values for blood pressure, weight, total cholesterol or blood glucose, we will recommend that they get the appropriate testing or measurement as recommended in LE8. Finally, we will also assess via a text message survey the 6-item patient self-efficacy for managing chronic conditions. Self-efficacy for Managing Chronic Conditions is defined as an individual's confidence in his/her ability to successfully perform specific tasks or behaviors related to one's health in a variety of situations.

1) Generic text messages: The information content for these messages will be derived from trusted sources of medical information and contain links to websites such as American Heart Association. An example of such a message would be: *Remember to take your blood pressure today! You can find more information from the American Heart Association by clicking here.* Patients will be able to return texts with questions which will be addressed by the study team, including a clinical pharmacist if needed.

2) AI chatbot text messages: This AI system will utilize NLP and ML to facilitate bi-directional system-patient dialogue with messages that incorporate content utilizing tailoring, behavioral nudges and persuasive messaging as described above. An example message would be: *Make a promise to yourself to check your blood pressure today! Your goal is to have the top number at 120 or lower and the bottom number at 80 or lower.* Each message will end with a question for the participant that will encourage engagement with the AI conversational chatbot that allows greater opportunity to use theoretical content to engage patient autonomy, competence and relatedness, the mechanisms through which we will impact behaviors.

3) AI chatbot text messages plus proactive pharmacist management: The AI chatbot will be the same as arm 2. In arms 1 and 2, pharmacist will respond to clinical questions from

patients in a reactive manner. In arm 3, pharmacists will review patient's baseline LS7 risk factors and proactively contact patients via telephone and/or the EHR patient portal to address any risk factor that is in poor/intermediate health categories. We are proposing proactive pharmacist involvement as a population-based approach to address patients with uncontrolled CV risk factors. Prior studies[131] including meta-analyses and systematic reviews have demonstrated the effectiveness of pharmacist management to reduce CV risk factors (i.e., blood pressure, cholesterol and smoking). The proactive pharmacist involvement is increasingly common but our proposal is to actively link them to our AI chatbot to better facilitate tailored SM support. Pharmacists will proactively manage these patients and will be able to identify their specific SM needs through a review of the AI chatbot logs prior to engagement with patients using telephone or EHR portal.

Plan for responding to text messages from patients
In arms 1 and 2, a PRA or pharmacist will respond to clinical questions from patients in a reactive manner. A PRA will check the patient responses in regular intervals throughout the day and either 1) respond to questions regarding the study or 2) triage clinical questions to the pharmacist.

Aim 4 (UH3; Years 2-5): **Evaluate the intervention using PRISM and a mixed methods approach to evaluate pragmatic clinical and implementation outcomes (reach, effectiveness, adoption, implementation, and maintenance) with an emphasis on equity and representativeness, and systematically assess contextual influences to inform sustainment and future tailoring, adaptations, and dissemination.**

We will use PRISM for evaluation with RE-AIM outcome measures and consideration of health equity. PRISM pragmatically focuses on four categories of contextual factors that influence implementation success: 1) organizational and participant characteristics; 2) organizational (health system and providers) and participants' perspectives (i.e., patients) on the intervention; 3) implementation and sustainability infrastructure (e.g., resources and support processes); and 4) external environment. These four elements will be assessed both qualitatively and quantitatively and will be critical to understanding how to sustain and further disseminate the intervention if demonstrated to be effective. The component RE-AIM (i.e., Reach and Effectiveness, Adoption, Implementation, and Maintenance) outcomes informs the development of pragmatic outcomes important to different stakeholder perspectives (e.g., executive-level decisionmakers, clinicians, patients). PRISM focuses on health equity by emphasizing both representation in terms of the persons involved in planning and evaluation for each outcome dimension, and especially the representativeness (equity) of outcomes across different groups or types of settings. Below we highlight the measures that we will assess a part of the RE-AIM outcomes evaluation.

D. Description, Risks and Justification of Procedures and Data Collection Tools

The study team believes this project poses minimal risk to all subjects involved, based on the study team's previous work (COMIRB Protocol #18-2779). There is no clinical intervention being proposed, and no deeply personal matters will be discussed. The goal of this study is to ensure that patients increase healthy behaviors.

Study information including risks of data, confidentiality, breach of confidentiality, and other risks will be addressed in the opt out packet. Consent will be assumed unless the postcard

opting the study subject out of the study is returned. Study subjects can also opt out of the study if they wish at any point by replying with a text message with the word “STOP.” Alternative treatment in this study is the standard care with no texting communication.

We do not anticipate substantial risks to be associated with participation in this study. As with any study involving participants with chronic disease, however, there is some risk of psychological discomfort related to discussing disease management. Participants will be informed that if they choose to discontinue the study at any time, this will not interfere with their usual medical care.

Trained and certified professional staff will obtain all data according to detailed study protocols. Phone numbers and patient information including eligibility criteria will be obtained through EHR. Only IRB-approved individuals on the study team will have access to individually identifiable information about human subjects. This will include the PIs, co-investigators, project coordinator, statisticians, database/programming team, and research assistants. Some of the data above will be accessed from information already collected as part of usual care. Depending on the study arm they are randomly assigned, study subjects will receive, generic messages or interactive AI chatbot messages that incorporate English or Spanish-language versions depending on patient choice.

Minimal risks to human subjects are anticipated for this study. Nevertheless, remaining risk is expected to include:

- *Behavioral incentives* (nudges) will be administered to the participants as a method to reinforce lifestyle factors related to their risk factors of cardiovascular disease. The nudges themselves will reinforce healthy behaviors and therefore will not introduce any new instructions/treatments. However, there is some risk that patients will misinterpret the text message information that is sent to them in text messages.
- *Data Confidentiality.* As with all research, there is also a slight risk of loss of confidentiality and/or anonymity, especially for participants being interviewed. We have standard operating procedures for data acquisition and data management designed to protect against data loss and maintain patient confidentiality. These procedures have been developed and used in many studies and we will adhere to these procedures for the proposed study. Paper files related to the study (i.e., consent forms) will be stored in a secure location in a locked file cabinet accessible only to study personnel who must access these files. Computer files will be password protected. Files containing names, addresses, or other personal identifiers will have a separate password and will be accessible only to personnel who need to contact subjects.
- *Breach of confidentiality.* All participant information collected in the context of this research study, and even the fact that an individual is participating in the study, will be considered confidential. This confidentiality will be assured through several mechanisms. First, each participant will be assigned an anonymous study ID. Second, all study forms and paper records that contain participant information will be kept in secured, locked areas when not in use. In addition, such materials, when in use, will be kept away from public scrutiny. Third, access to all participant data will be restricted to authorized personnel. In the case of computerized study data, access to data will be password protected, and staff members will be assigned individualized passwords that allow them access to only those elements of the data management system to which they are authorized. In addition, all study personnel

will maintain certification with training in research ethics, which includes training on confidentiality. Finally, participants will not be identified by name in any reports or publications, nor will data be presented in such a way that the identity of individual participants can be inferred. All information obtained in the course of the study that identifies an individual will be treated as confidential in accordance with section 903C of the Public Health Service Act (42 U.S.C.299a-1). We will strip all identifiers from analytic data sets after data merging and keep all personal identifiers in a separate location from the analytic data. Database files needed to generate mailing labels will contain no research data. All research data files are organized by study ID number and have no names or other identification attached. This ID number links all computerized research records.

- *Financial, Legal, or Other Risks*. There are no financial or legal risks associated with this study. Since personal data will be collected as part of this study, there is a risk of loss of confidentiality. However, we will take several measures to minimize this risk. First, we will only collect the data necessary for the study. Second, all electronic data will be stored on a secure server, rather than on individual desktop or laptop computers. Third, electronic study data will be kept in folders and databases that are only accessible to key personnel who are IRB-certified and whose job functions require access to these data. Fourth, all paper copies of data (i.e., consent forms) will be stored in locked cabinets and offices. Any paper documents that must be transported to/from clinic enrollment sites will be carried in a locked briefcase.

Adequacy of Protection of Risk
To mitigate the above risks, the text message nudges will contain a secondary opportunity for opt-out, and will contain pharmacy contact information, should the patient decide to discontinue their participation or want to contact the pharmacist with questions or need more information about the intervention or their prescribed medications. Contact information for those opting out of the study will be maintained in a separate file and deleted as soon as recruitment is complete. The opt out consent will also state that the text messages are not from their doctor.

As is the standard, all staff participating in the project will complete compliance and human subject research training and all recruitment materials and consent forms will be approved by the Colorado Multiple Institutional Review Board (COMIRB).

Potential Benefits to Subjects
No claim is made that subjects will benefit from participation in this project. However, the results of the study may improve care to the extent that our study improves medication adherence.

E. Potential Scientific Problems:

What if the text messages are not delivered as planned? For Aims 2 and 3, we anticipate there may exist system failures, e.g., messages sent multiple times or incorrect branching. To ensure minimal disruption in message delivery, we will conduct system alpha testing at each health system to ensure correct message distribution and branching prior to conducting the trial. It is possible that even once we implement a pilot trial there could be a system failure, such as sending three versions of a single message or sending a message in the middle of the night. We will minimize the impact of such an occurrence by having

designated staff at each participating health system that can shut down the system and reboot as needed. We will continuously monitor for potential systems failures and deviations and implement standardized processes to correct them immediately.

Is there potential for contamination in the proactive pharmacist arm? It is possible that if we train pharmacists in motivational interviewing and proactive case management to support SM for patients they will engage with all patients in this manner, regardless of study arm. We are reducing the likelihood of this happening by sharing with them the specific list of patients randomized to the "proactive pharmacist" arm and will share with them the logs documenting chatbot engagement by each patient in that arm so the pharmacist will have a priori information on each patient's questions and SM experiences that can offer context for why they are struggling with SM outcomes. None of the settings where we are deploying the intervention are currently using a proactive population-based approach so we think it unlikely they will begin doing this for everyone. However, we will monitor the patient portals for all patients enrolled to determine if pharmacists are proactively engaging with patients outside the "proactive pharmacist" arm and document this for our analysis.

What is the likelihood of successfully changing health behaviors or addressing social determinants? We are proposing a population-level intervention that uses ubiquitous technology (e.g., cellphones). We hypothesize that arm 3 (interactive AI text messages with proactive pharmacist management) will have the greatest effect and that the combination of the AI chatbot and pharmacist management will be able to successfully address medication adherence, SDoH and change health behaviors. We acknowledge that this intervention is not appropriate for more challenging cases or situations and these patients will need more intensive support from providers and the health system than can be provided by the various intervention arms. This intervention is not meant to supplant those resources but provide health systems with a low-cost, generalizable population-based intervention that can address a majority of patients who need reminders and support that is light touch while they focus their resources on the most difficult cases.

F. Data Analysis Plan:

Sample size calculations using the Life's Essential 8 (LE8):
We conducted a simulation-based power analysis for the LE8 outcome to address feasibility. Using LE8 as the outcome and conservative assumptions about effect size, we will have adequate power (>90%) if we analyze 5,059 subjects at the conclusion of the study. If we enroll 6,070 patients and assume a ~20% loss to follow-up, we will still have > 90% power to detect a small change in the proportion of patients with an improvement in one of the LE8 risk factors. We define improvement if a patient moves from one category to another as defined by each of the individual LE8 risk factors. For example, the following clinical scenario would be defined as an improvement in a LE8 risk factor: patient starts with non-HDL cholesterol of 200 mg/dL (equivalent to 20 points) and improves to a non-HDL cholesterol of 160 mg/dL (equivalent to 40 points) at the 1-year follow-up.

The above is based on the following assumptions: 1) 25% of the patients in the generic text arm will have an improvement in a LE8 risk factor (lipids, glucose or BP); 2) 28% of patients in the AI chatbot text message group will have an improvement in a LE8 risk factor (3% more than the generic text group; and 3) 31% of patients in the AI chatbot plus proactive pharmacist support will have an improvement in a LE8 risk factor (6% more than the generic text group). We will have adequate patient populations across the 3 proposed health

systems (Denver Health, Salud, and STRIDE) in which to enroll 6000 patients with 1 or more uncontrolled LE8 risk factor.

Further details of this power analysis are summarized below:
We will target for enrollment patients with the following abnormal values of LE8 measures observable in the medical record:

- Lipids: >= 190
- Glucose: HbA1c >= 8.0
- BP: systolic >= 140 or diastolic >= 90

Using the qualifying measures from above, we will calculate a baseline LE8 measure (single value of 0-100; mean of qualifying measures at baseline) and at follow-up LE8 measure (single value of 0-100; mean of qualifying measures at follow-up). The difference between baseline and follow-up will be the primary outcome (for LE8).

Primary hypothesis comparison: There will be three comparisons for the primary hypotheses, thus we adjust for multiple comparisons with alpha = (0.5/3) in these power estimates.

- Group 1 (generic text) versus Group 2 (AI chatbot text messages)
- Group 2 versus Group 3 (AI chatbot text messages plus proactive pharmacist support)
- Group 1 versus 3

Small (conservative) effect size assumptions:

- All groups: patients have a 5% chance of decreasing one LE8 category on a qualifying health state category.
- Group 1: patients have a 25% chance of increasing one LE8 category on a qualifying health state category.
- Group 2: patients have a 28% chance of increasing one LE8 category on a qualifying health state category.
- Group 3: patients have a 31% chance of increasing one LE8 category on a qualifying health state category.

Moderate effect size assumptions:

- All groups: patients have a 5% chance of decreasing one LE8 category on a qualifying health state category.
- Group 1: patients have a 25% chance of increasing one LE8 category on a qualifying health state category.
- Group 2: patients have a 30% chance of increasing one LE8 category on a qualifying health state category.
- Group 3: patients have a 35% chance of increasing one LE8 category on a qualifying health state category.

Effect Size	Power	Total Sample size across 3 arms	Sample in each arm
Moderate	80%	1,605	535
Moderate	85%	1,824	608
Moderate	90%	2,085	695
Small (conservative)	80%	4,032	1,344

Small (conservative)	85%	4,461	1,487
Small (conservative)	90%	5,508	1,836

G. Summarize Knowledge to be Gained:

Summary of evidence and gaps in knowledge: (1) We lack interventions that successfully address multiple CV conditions, particularly for racial/ethnic minorities, poor, rural, and non-English speaking patients, all of whom face disparities in chronic CV health outcomes. (2) SM can be successful but often fails to consider the complex social determinants of health on behaviors that can be amplified for persons experiencing disparities in chronic CV conditions. (3) One way to improve SM programs is to design interventions that acknowledge and support patients in addressing influences on their SM behaviors at the interpersonal, organizational and community level. (4) Interventions that are successful in facilitating SM for persons experiencing disparities can likely suffer from being too resource intensive or too complex for delivery. Therefore we must consider approaches that are easy for health systems to adopt, implement and maintain. (5) Using technology that relies on cellphone based text messaging is one such approach. Although we know text messaging can be effective to facilitate healthy behavior, we have not fully integrated emergent systems that utilize artificial intelligence in combination with strategic, evidence-based messaging to increase the impact of low intensity interventions, or evaluated the incremental benefits of adding health system-level, proactive pharmacist engagement..

How our intervention addresses these gaps: Our goal is to improve control of CV disease risk factors by engaging patients experiencing CV disparities with “LE8 Bot + Backup,” an innovative technology-based SM intervention with linkages to health system providers focusing on control of the American Heart Association’s Life’s Essential 8 (LE8) lifestyle factors (blood glucose, cholesterol, blood pressure, physical activity, weight, sleep, diet, and smoking). Using a patient level randomized pragmatic trial design, we will test the comparative effectiveness of 1) generic unidirectional text messages; 2) theory-based, tailored and socially contextualized communications using an artificially intelligent (AI) text messaging chatbot for self-management support; or 3) Optimized AI chatbot messages with proactive pharmacist management for self-management support. We plan to enroll 6000 patients with sub-optimal control of their CV risk factors and poor adherence with medications to treat the CV risk factors since they are more likely to benefit from a SM support intervention. Further, given that Black patients, Hispanic/Latino patients , Spanish-speaking only patients, rural residents, and low-income patients experience disparities in CV outcomes, we will target enrollment to include these groups from clinics within 3 health systems that care for large populations of patients experiencing health disparities: 1) Salud Family Health Centers, an FQHC with 13 clinics including clinics serving rural Colorado residents, 2) Denver Health and Hospital Authority, a safety net health system for Denver county with 9 FQHCs, and 3) STRIDE Community Health Centers, a FQHC with 18 locations surrounding Denver County.

If the proposed intervention proves successful, it may lead to improved cardiovascular health as measured by the Life’s Essential 8 score for each study subject as well as

decreases in other cardiovascular risk factors and increased engagement with their health care system. If the intervention does not improve patients' LE8 score, investigators will know to direct the attention to the evaluation of other, potentially more fruitful interventions. The results of the work may lead to new knowledge and guidance for medical institutions to utilize the accessible and inexpensive service of text messaging.

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