NIH Collaboratory Rethinking Clinical Trials®

Health Care Systems Research Collaboratory

Regulatory/Ethics Consultation Call:

Personalized Patient Data and Behavioral Nudges To Improve Adherence to Chronic Cardiovascular Medications (Nudge)

Wednesday, August 15, 2018
Meeting Participants

Sheana Bull (Co-Principal Investigator, University of Colorado), Judith Carrithers (Advarra), John Heldens (University of Colorado), Adrian Hernandez (Duke), Michael Ho (Co-Principal Investigator, University of Colorado), MariJo Mencini (Duke), Cathy Meyers (NIH), Tammy Reece (Duke), Lisa Sandy (University of Colorado), Jeremy Sugarman (Johns Hopkins), Wendy Weber (NIH), Barbara Wells (NIH), Liz Wing (Duke)

AGENDA ITEMS	DISCUSSION August 15, 2008	PROPOSED ACTIONS August 15, 2018	CURRENT STATUS As of August 30, 2019
Review of Demonstration Project	• Co-Principal Investigator Sheana Bull (University of Colorado) gave an overview of the Nudge demonstration project. The trial plans to use pharmacy system data across 3 healthcare systems to identify patients who have delayed refilling their prescriptions for managing chronic cardiovascular conditions. Data are downloaded nightly and stored behind a University of Colorado firewall. Participants are randomized to one of four study arms: (1) usual care (2) a generic text reminder to refill the prescription, (3) an optimized text reminder that includes additional prompts based on age, gender, and geographic location, and (4) the optimized reminder plus the ability to interact with a real-time chatbot to help identify and overcome barriers to refilling		

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	the prescription. After a refill delay of ≥7 days is identified, participants in the intervention arms will begin receiving these automated text messages ("nudges") on their phone depending on their randomized arm.
	• **Collaborative network partners:**
	  ○ University of Colorado Health
	  ○ VA Eastern Colorado Health Care System
	  ○ Denver Health
	• **NIH Institute:** National Heart, Lung, and Blood Institute (NHLBI)
	• **Study design:** Nudge is designed as a mobile technology-delivered intervention embedded in 3 integrated healthcare systems. The trial will evaluate the effectiveness of theory-informed text messages intended to improve medication adherence and health outcomes in patients treated for chronic cardiovascular conditions such as hypertension, atrial fibrillation, coronary artery disease, diabetes, or hyperlipidemia. In the UG3 phase, the study team will develop and program a technology-based text message library and an artificial intelligence (AI) interactive chatbot content library to optimize content for a range of diverse patients.		

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	○ **Primary outcomes:** Demonstrate feasibility of delivering the intervention and evaluate preliminary effects of text messaging within the 3 healthcare systems (UG3). Evaluate the effectiveness of the intervention through a mixed methods approach and apply the RE-AIM framework to inform the tailoring, adaptation, and expansion of the intervention (UH3). • During the UG3 phase, the study team will develop, test, and refine the text message intervention by enrolling patients as key informants in a series of N of 1 trials (20 participants) and convening a Stakeholder Panel (4 participants). This phase also will ensure the ability to retrieve and download pharmacy data, assign participants to study arms, send out correct automated messages, and follow up on the prescription refill behavior subsequent to receiving the message. • The technology platform has the capacity to detect whether the patient's phone is a landline and can send a voice message as an alternative. The study team plans to assess whether the text message is actually being sent to a text-enabled phone. • While the program can verify that the message is sent to the patient's device (via phone number recorded in the EHR), there		

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	is no ability to ensure that the patient is the person reading the message.		
Status of IRB approval	• The central IRB for all 3 trial sites is the Colorado Multiple Institutional Review Board (COMIRB), which has approved the initial application (UG3). The study team plans to submit an amendment to the protocol before the UH3 phase is implemented.		The central IRB approved the UH3 application on 4/9/19.
Risk classification	• The study team believes this project poses minimal risk to all subjects involved. There is no clinical intervention being proposed, and no personal matters will be discussed. • Those on the call discussed the risks to participants in both the UG3 and UH3 phases and agrees with the study team that both phases seem to be minimal risk.		The IRB believes this project poses minimal risk.
Consent	• In the UG3 phase, participants in the N of 1 trials will be identified using electronic data. Participants in the Stakeholder Panel will be recruited through relationships with the study team. The study team requested a waiver of written consent for both groups of participants as the study is low risk, the contact with participants will primarily take place remotely, and the IRB granted the waiver. • In the UH3 phase, hard-copy letters will be mailed to patients at designated study clinics. The letters will be generated and		• Our approach is unchanged. We have an opt-out strategy. Patients will be sent a letter informing them of the study. They can opt out at that time by returning a postcard. During the intervention period, they can also opt out with each text message they receive by replying "STOP." • The team plans to disseminate study findings via a website. Access to the site will be

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	sent by the study team. Clinic directors have agreed to sign the letter on behalf of the study to inform patients about the study. Included in the letter is a return postcard for patients who wish to opt out. When patients have a 7-day gap in refilling the identified prescriptions, they will be randomized to the study arm, and those receiving a text message will have a second opportunity to opt out of the text messages. From the patients' perspective, the letters come from the clinic. • Those on the call discussed that while opt out makes sense for this study, it will be helpful to learn how patients respond to text messaging from clinics, whether they feel overloaded, and how institutions manage the amount of messaging sent to patients. • The study team will obtain feedback from patient engagement groups in each study setting about their perspectives on best methods of disseminating study findings to participants (e.g., link to a website, letter, or final text message).		available through multiple means, including through links sent via text message.
Privacy/HIPAA	• The COMIRB has granted a full waiver of HIPAA authorization for the UG3 phase of the study.		COMIRB has granted a full waiver of HIPAA authorization for the UH3 phase of the study.
Monitoring and oversight	• The sponsoring institute, NHLBI, will assist in convening a protocol review committee as a	Completed: The coordinating center sent the study team the	• We will continuously monitor the response to the text

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	preliminary step before establishing an independent data and safety monitoring board (DSMB) for the UH3 phase of the study. NHLBI wants to ensure that DSMB members have the expertise to be mindful of embedded pragmatic clinical trials (ePCTs) as distinct from traditional RCTs with respect to, for example, pharmacy issues or information technology issues of data integrity. • Data monitoring plans are in place in each healthcare system to ensure accurate retrieval and storage behind the university firewall. Staff will also test accuracy of outgoing text messages. A person is designated at each system to ensure data security. • If clinical guidelines for cardiovascular medications were to change during the course of the trial, the study team would modify the protocol to include, for example, a new medication to treat a cardiovascular condition. New guidelines could be reviewed by the DSMB or from an *ad hoc* NIH group.	related ethics paper "Data monitoring committees for pragmatic clinical trials" (Ellenberg et al., Clin Trials 2015) and a template document to customize for DMC charters for PCTs.	messages. We have a weekly call with our pharmacist team to discuss patient responses to the text messages to ensure that any clinical messages from patients are responded appropriately. • The protocol review committee/DSMB in Year 1 provided strategic input on the statistical and dissemination methods to be used for the study. A DSMB meeting is scheduled for 9/11/19.
Issues beyond the study	• A certificate of confidentiality will be automatically provided per new NIH policy. This certificate adds provisions for future research uses and confidentiality obligations for future data sharing. It was suggested that the study team review the new		We have included an opt-out questionnaire developed by the Collaboratory Ethics & Regulatory Core that we will include in our packets sent to patients.

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	certificate requirements in advance so that the team is prepared for data sharing later on. • It is hoped that the study team can design the opt-out mechanism to be able to capture rates of opting out and reasons for opting out, which could be informative to other embedded PCTs in the future. The study team will consider doing this.		