eFramingham Heart Study Randomized Controlled Trial #2

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The objective is to test the effect of administering half of survey modules every 2 weeks versus all survey modules every 4 weeks on improving participants' response rates.

Methods

We prepared the protocol for this randomized factorial trial in compliance with the SPIRIT checklist and plan to register the trial on clinicaltrials.gov.

Study setting and Eligibility criteria

Our randomized controlled trial will include participants of the electronic Framingham Heart Study (eFHS). Participants in eFHS are invited to enroll from the FHS Offspring and Omni Group 1 Cohorts during the in-person examination 10/5 at the FHS Research Center in Framingham, MA, USA or remotely from home after the in-person examination. In order to be eligible in the eFHS, individuals have to meet the additional following criteria: English-speaking individual who owns an iPhone with compatible iOS (version 10.0 or higher) or Android (version 5.0 or higher); residence in the United States; provision of permissions for notifications and data sharing with the Research Center; provision of signed and dated informed consent (within the eFHS mobile app). Enrollment in the randomized controlled trial will start once approved by IRB.

Surveys and Interventions

All eFHS participants have the eFHS myDataHelps mobile app (developed by FHS investigators with CareEvolution our industry partner) installed on their smartphone. The eFHS app allows communication with participants through notifications and data collection. Participants are asked to answer health surveys administered through the app.

Survey assessments will include 6 modules: cognition, pain, mood, physical function and performance, physical activity, and events (table 1). The interventions are defined by the patterns of administration of survey modules to the experimental and control groups as described in Table 2. The administration of the cognition, pain, mood, and psychosocial

modules follow the same pattern for both groups. However, the administration of the physical function, physical activity, and events modules is shifted for the experimental group as compared to the control group.

The cognition and gait tasks are currently not available on android phones. Thus, we will not administer these modules to participants who have an android phone instead of an iphone and these participants will contribute data only to the other survey modules.

Table 1: survey modules

Cognition	
Trails	Task
Stroop	Task
Tapping	Task
Cognitive function	4-items
Cognitive abilities	4-items
Pain	
Pain Q (past 7 days)	5 items
Body Map (past 3 months)	
Mood	
Depression (past 7 days)	4 items
Anxiety (past 7 days)	4 items
Loneliness (no timeframe)	3 items
Psychosocial parameters (loneliness, social support, resilience)	3-items, 8-items, 11-items, 6-items
Physical function/performance	
Gait	Task
Mobility no timeframe	4 items
Sleep (past 7 days)	4 items
Fatigue (past 7 days)	4 items
Mobility outside home (past 4 weeks)	5 items (with more if yes)
Physical activity	
RAPA (no timeframe)	9 items
Events	
Falls/hospitalzn (past month)	2 items (with more if yes)

Table 2: pattern of administration of survey modules in the experimental and control groups

Week	0	2	4	6	8	10	12	14	16	18	20	22	24	26
Cognition	✓				✓				✓				✓	
Pain	✓		✓		✓		✓		✓		✓		✓	
Body map	✓						✓						✓	
Mood	✓				✓				✓				✓	
Psychosocial			✓				✓				✓			
Physical function	✓	✓			✓	✓			✓	✓			✓	✓
Physical activity	✓	✓					✓	✓					✓	✓
Events	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
# modules														
Exp. group	7		3		5		5		5		3		7	
Control group	4	3	2	1	3	2	3	2	3	2	2	1	4	3

Administration to both groups
Administration to control group
Administration to experimental group

Participants will be able to complete a survey module from its administration until the next wave. This time varies across survey modules given the frequency and timing of administration. For example, participants will be able to complete the first pain module between week 0 and week 4 post-randomization and they will be able to complete the last pain module between week 24 and week 28. For the physical function module, the first survey can be completed between week 0 and 8 in the control group and between week 2 and 10 for the experimental group; while the last survey can be completed between week 24 and 32 in the control group and between week 26 and 34 in the experimental group.

All participants will periodically receive notifications through the eFHS app to remind them to answer the surveys on the eFHS app. Based on our previous work, we will send personalized notifications, that include the name of participants and account for the number of surveys already completed, to improve response rate to surveys.[1] One week after randomization, we also will contact all participants by telephone to inquire about any technical issue with the app.

Duration of trial

We will conduct the trial over 32 weeks.

Outcomes

We define 4 survey periods. Period 1 encompasses all survey modules administered from baseline up to week 8 (19 surveys/tasks per participant); period 2 from week 8 up to week 16 (18 surveys/tasks per participant); period 3 from week 16 up to week 24; period 4 from week 24 (16 surveys/tasks per participant).

The primary outcome is the proportion of surveys/task returned per participant (partially or fully completed). The secondary outcome is the proportion of questions/task completed per participant. For both the primary and secondary outcomes, we will compare the mean proportions assessed longitudinally across the 4 periods between the experimental and control groups.

Random allocation

We will randomly allocate each participant to one of the 2 groups. A statistician will generate randomization lists with the use of randomly permuted blocks of varying sizes, with stratification according to participant's age (≤75 years vs. >75 years) and type of phone (android vs. iphone). Randomization will be implemented centrally through the app.

eFHS researchers and statistician will be masked to the group assignment. As part of eFHS, support staff help participants complete their remote monitoring and data transmission. The support staff uses standardized scripts to interact with participants over the phone to address technical questions.

Sample size

We calculated the sample size for the comparison of the mean proportion of surveys returned between the two groups across time. We assumed consistent difference over time and that the

distribution of the sample proportions are approximately normally distributed. We account for 4 time periods. We very conservatively assumed a correlation of the repeated measures of 0.6 and a standard deviation on the proportion of survey returned of 20%. A sample size of 300 participants per group guarantees 95% power to detect a mean difference of 5% between groups, for example between a mean of 50% of surveys returned per participants in the control group vs. a mean of 55% of surveys returned per participants in the experimental group.

Statistical methods

We will use a mixed-effects regression model to compare the mean proportions between groups across time. Analyses will be in intention-to-treat. We will fit random-intercept models as well random-intercept and random-trend models.

We will perform the following a priori subgroup analyses. We will assess and compare the primary and secondary outcomes in subgroups defined according to age (> vs. ≤75 years), sex (female vs. male), type of phone (iphone vs. android), cognitive status (impaired or not) and whether participants have an apple watch or not. The cognition and gait tasks are currently not available on android phones.

References

1. Trinquart L, McManus, D.D., Nowak, C., et al. Abstract 13084: Increasing Engagement in the Electronic Framingham Heart Study (eFHS): A Factorial Randomized Trial. *Circulation.* 2019;140(Suppl_1):A13084-A84. doi: doi:10.1161/circ.140.suppl_1.13084.