Evaluating Individual and Patient-Selected Family/Friend/or Reciprocal Peer Notifications to Improve Statin Medication Adherence among Patients with Coronary Artery Disease

Dr. Judith Long, Investigator
PACT Demo Lab VISN4

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Note: this project is no longer collecting information or contacting Veterans as of 12/2014.

B. COLLECTIONS OF INFORMATION EMPLOYING STATISTICAL METHODS

1. Provide a numerical estimate of the potential respondent universe and describe any sampling or other respondent selection method to be used. Data on the number of entities (e.g., households or persons) in the universe and the corresponding sample are to be provided in tabular format for the universe as a whole and for each strata. Indicate expected response rates. If this has been conducted previously include actual response rates achieved.

With IRB approval, we extracted administrative, clinical and laboratory data through the VISN 4 Data Warehouse (VDW)to identify eligible patients for this intervention. The VDW contains CPRS data from VISN 4, which enabled us to filter for a sample of patients who met some preliminary eligibility criteria (diagnosis of coronary artery disease, age 30-75, prescribed a statin medication, 16-month medication possession ratio of less than or equal to 80%, etc). We identified 1173 patients using the VDW, 488 of whom did not meet inclusion criteria. Of the remaining 685 eligible patients, 397 declined to participate, and 162 were unresponsive to our recruitment efforts. Of the 224 targeted enrollment number we enrolled 126 participants in the study. To ensure 80% power to detect differences between each of the feedback arms and control arm, using a conservative adjustment for multiple comparisons, we calculated that we would need a sample of 50 participants in each of the 3 study arms to identify “moderate” intervention effects (Cohen’s d=0.6). Because the partner feedback group may have included mutual peer partners, we assumed a relatively large intra-cluster correlation (ICC) of ICC=.05 between the reciprocal pairs. Because the intervention was dependent on partner and our expectation of up to 15% attrition, this prompted us to recruit an additional 25 participants into the partner group. To account for reciprocal pairs in arm 3, we randomized at a 2:2:3 ratio so arm 3 was larger than the other arms. We randomized participants using a block structure.

To ensure we studied a population who are most likely to benefit from improving medication adherence in the future, we enrolled Veterans who were prescribed a statin by their provider and have a documented poor adherence as measured by a 16-month medication adherence rate (Medication Possession Ration) of less than or equal to 80%.

Because Veterans are typically older, sicker, and more socioeconomically vulnerable than patients outside VHA, this population is in need of better tools to monitor and improve patient adherence to medications.

Inclusion Criteria: Veterans between the ages of 30 and 75 were eligible for participation. Patients had a diagnosis of Coronary Artery Disease (CAD), were prescribed a statin, and had documented poor adherence as measured by a 16-month medication adherence rate (Medication Possession Ratio) of less than or equal to 80%. Patients spoke English, had a home address, telephone number, and were willing and able to identify a friend or family or willing to partner with a reciprocal peer.

Exclusion Criteria: We excluded patients with active substance abuse, significant hearing loss, homelessness, or reduced cognitive ability.

2. Describe the procedures for the collection of information, including:

- **Statistical methodology for stratification and sample selection**
- **Estimation procedure**
- **Degree of accuracy needed**
- **Unusual problems requiring specialized sampling procedures**
- **Any use of less frequent than annual data collection to reduce burden**

Data Collection: At baseline, we collected demographics (age, sex, race, ethnicity), the Morisky 4-Item self-report measure of medication-taking behavior (MMAS-4), self-report of the number prescribed medications the patient was currently taking, the self-administered comorbidity measure (SCQ) of their other medical diagnoses, the multidimensional scale of perceived social support (MSPSS), and the patient activation measure (PAM). We also collected a low-density lipoprotein (LDL) blood test to measure their baseline cholesterol level. Throughout the entire study (6 months), their GlowCap electronic pill bottle recorded information about their statin medication-taking behavior; this data was used to measure medication adherence.

The MSPSS and PAM surveys were repeated at the month 3 phone call and month 6 visit to measure whether the patients perceived any change in social support or patient activation. At the month 3 phone call, we repeated the MSPSS and PAM and collected a qualitative survey of their reactions to the different aspects of the intervention (the device, the feedback reports, and the study partner). At the month 6 in-person visit, again we repeated the MSPSS and PAM and collected a survey with both qualitative and quantitative items to get additional detail about their experience in the study. At the month 6 we also repeated the LDL blood test to measure their cholesterol level after the intervention.
All surveys were completed electronically, administered by a study coordinator.

Analysis: Our primary outcome was medication adherence (daily opening of pill bottle) during the intervention period (months 1-3). Adherence was calculated as the number of days the GlowCap bottle was opened during the period divided by 91 (number of days in each time period). Our secondary outcomes included adherence during the 3-month post-intervention period (months 4-6), change in the PAM and MSPSS (from baseline to 3 and from 4 to 6 months), and change in the LDL-direct level (from baseline to 6 months). We hypothesized that participants in both feedback groups would have greater adherence rates than participants in the control arm. We also hypothesized that the partner feedback group would have greater improvement in patient activation and social support.

To test the primary and secondary hypotheses we used an unadjusted intent-to-treat analysis. For those who died or withdrew during the first 3 months we assumed that unobserved days during this period and all days in the second 3 months were non-adherent. Adherence was compared among arms using one-way ANOVA for each time period separately. P-values were calculated using Tukey adjustment for multiple comparisons.[20] Additional methods of calculating adherence (adjustment of denominators to account for death, withdrawal and/or hospitalization, as well as multiple imputations for missing data) were also analyzed, and results were similar.

Changes in LDL level, PAM scores, and MSPSS levels were also compared among arms using one-way ANOVA. In a sensitivity analysis, we used a random effects regression model of random effects regression that accounted for correlation of measurements on the same person over time. The model, which included main effects for time and arm, used the interaction between time and arm to test for differences in change over time by arm. Results from both analyses were similar. Multiple imputations were performed in SAS using PROC MI and MIANALYZE to create and analyze the imputed data sets. Results were then combined using Rubin's formula.[21]

20. Tukey JW, Ciminera JL, Heyse JF. Testing the statistical certainty of a response to increasing doses of a drug. Biometrics. 1985;41(1):295-301.
21. Rubin DB. Multiple Imputation for Nonresponse in Surveys. Vol 81. John Wiley & Sons; 2004.

3. Describe methods to maximize response rate and to deal with issues of non-response. The accuracy and reliability of information collected must be shown to be adequate for intended uses. For collections based on sampling, a special justification must be provided for any collection that will not yield "reliable" data that can be generalized to the universe studied.

Recruitment: To try to reach our target enrollment, we made great efforts to reach patients at the recruitment time point. After screening for inclusion and exclusion criteria, eligible patients were mailed a letter letting them know that they may be eligible for a study. This letter included a brief description of the study and gave them a number of they would like to learn more or to request no further contact. After sending the letter, we attempted to reach the patients by phone. If the patient did not responded to either the letter or 3 separate recruitment phone calls, we discontinued efforts to recruit them into the study.

Enrollment: To try to reduce drop-out and loss-to-follow-up, we made great efforts to reach participants at the follow-up time points. The 3 month visit was conducted over the phone, and the 6 months visit was conducted in-person at the Corporal Michael J. Crescenz VA Medical Center (CMCVAMC). Once participants reached the 3 month time point, we contacted them to complete the month 3 survey. We continued to try to reach them by phone until they answered, declined to participate, or neared the 6 month visit. As participants approached the 6 month time point, we contacted them to schedule the month 6 visit. If participants did not show, we attempted to reschedule. We continued to try to reach them by phone or mail until they answered, declined to participate, or were unresponsive and months beyond their 6 month time point.

4. Describe any tests of procedures or methods to be undertaken. Testing is encouraged as an effective means of refining collections to minimize burden and improve utility. Tests must be approved if they call for answers to identical questions of 10 or more individuals.

We did not formally test our procedures or methods to try to reduce burden or improve utility. However, with IRB approval, we did add qualitative and quantitative survey questions at the 3 month and 6 month time points to get participant feedback on their experience and perceived effectiveness/utility of the intervention. Some participants also used these surveys as an opportunity to give more general feedback about the study procedures or methods.

5. Provide the name and telephone number of individuals consulted on statistical aspects of the design and the name of the agency unit, contractor(s), grantee(s), or other person(s) who will actually collect and/or analyze the information for the agency.

As delegated on the Research Staff Form, all statistical analyses were conducted by Anne Canamucio (Anne.Canamucio@va.gov, 215-823-5800 x3883) with assistance and input from the following staff:

Ashok Reddy (ashokr@upenn.edu, 215-823-5800 ext 6775),
Steven Marcus (marcuss@upenn.edu, 215-746-4695)
Judith Long (jalong@mail.med.upenn.edu, 215-823-5800 ext 5875)
Tiffany Huseman (Tiffany.Huseman@va.gov, 215-823-5800 ext 7108)

All staff were affiliated with the CMCVAMC in Philadelphia, PA.