The Secure Messaging for Medication Reconciliation Tool (SMMRT) Trial
NCT02482025

August 31, 2018

Research Protocol Narrative
Secure Messaging for Medication Reconciliation Tool (SMMRT) Trial
IRB #3156
Protocol Version 2.0, August 31, 2018

(1) RATIONALE

(a) Statement of the Problem. Briefly state the problem to be investigated.

- Medication discrepancies, which occur in all healthcare systems including VA, lead to adverse drug events (ADEs). ADEs contribute to readmissions and emergency department visits.
- Medication reconciliation, especially with pharmacist involvement, can reduce medication discrepancies and prevent readmissions, but little is known about interventions occurring post-discharge.
- Evaluation of the effectiveness of pharmacist-mediated medication reconciliation via Secure Messaging (SM) represents an opportunity to reduce Veterans' hospital utilization after discharge and may reveal potential future use of this technology to engage Veterans in their care.

(b) Hypotheses or Key Question. We hypothesize that a Secure Messaging for Medication Reconciliation Tool (SMMRT) will reduce medication discrepancies among Veterans discharged from the hospital and skilled nursing facility.

(c) Specific Objectives.

Aim 1. To conduct a RCT of usual care vs. usual care plus SMMRT to reduce medication discrepancies;
Aim 2. To evaluate how Veterans and staff perceived the impact of SMMRT on routine clinical practices and, specifically, on Veterans' interactions with their primary care providers.

(2)BACKGROUND AND SIGNIFICANCE

Summary Points

- Medication discrepancies, which occur in all healthcare systems including VA, lead to adverse drug events (ADEs). ADEs contribute to readmissions and emergency department visits.
- Medication reconciliation, especially with pharmacist involvement, can reduce medication discrepancies and prevent readmissions, but little is known about interventions occurring post-discharge.
- Evaluation of the effectiveness of pharmacist-mediated medication reconciliation via Secure Messaging (SM) represents an opportunity to reduce Veterans' hospital utilization after discharge and may reveal potential future use of this technology to engage Veterans in their care.
- Wagner's Chronic Care Model, emphasizing system transformation and prevention of complications, is a conceptual framework for the Secure Messaging for Medication Reconciliation Tool (SMMRT) Trial.

1. a. Medication Discrepancies, Adverse Drug Events and Hospital Utilization.

Medication discrepancies are defined as unintentional differences found in the patient's medical record compared with the patient's medication information.[7] Discrepancies may be commissions, omissions, duplications or alterations in dose or frequency. Medication discrepancies are associated with adverse drug events (ADEs), which are broadly defined as "injury resulting from the use of a drug."[8] In the US, ADEs result in 7,000 deaths annually and cost the health system $4.2 billion. One in four ambulatory patients in experience

ADEs,[9,10] while as many as 60% of patient records contain medication discrepancies.[11-13] Patients experiencing transitions in care, such as hospital discharge, are particularly vulnerable to medication discrepancies and ADEs, the latter occurring in as many as one in five patients within 30 days of discharge.[14-16] Medication discrepancies and ADEs are a major contributor to hospital utilization among patients recently discharged from the hospital,[17] a period frequently marked by multiple medication changes, alterations in health status, and extended period of time before return to primary care. Among patients discharged from the hospital, 14-20% will be readmitted within 30 days,[18,19] and more than 30% will seek emergency care during the same period.[20] *While numerous tools and approaches have been developed to improve care transitions,[21] medication safety after discharge remains a concern.[22]*

2. b. Medication Reconciliation: Policies and Approaches.

The Joint Commission introduced medication reconciliation as a National Patient Safety Goal in 2005 and continues to emphasize its importance in 2014,[23] including the imperative to "Make sure the patient knows which medicines to take when they are at home." VA has similarly mandated that medication reconciliation occur "at every episode or transition in level of care."[7] Considerable research has demonstrated benefits of medication reconciliation at care transitions. Two recent systematic reviews identified a relatively small number of rigorous studies of medication reconciliation at the time of hospital discharge.[24,25] Kwan et al included 3 RCTs and estimated that medication reconciliation at discharge reduces readmissions and emergency department visits by 23%; the authors noted that the effect may be larger when medication reconciliation is coupled with additional post-discharge follow-up, as it was in Project RED (Re-Engineered Discharge),[20] and as we propose in The SMMRT Trial. Additionally, Mueller et al noted that available evidence, albeit scarce, supports medication reconciliation interventions that rely on pharmacy staff,[25] as we propose herein.

Within VA, Boockvar et al found that a Computerized Patient Record System (CPRS)-based medication reconciliation tool used on hospital admission reduced both medication discrepancies and ADEs.[26] They are currently conducting a trial (IIR 10-146) of medication reconciliation on hospital admission with CPRS information enhanced by regional health information. A QUERI-funded pilot (RRP 11-242) identified medication reconciliation as a key element of successful interventions to improve hospital-to-home transition. Lesselroth et al have implemented an outpatient medication reconciliation: the Automated Patient History Intake Device [3,27] and are developing an interface for medication reconciliation on hospital admission.[28]

2. c. My HealtheVet (MHV) and Secure Messaging (SM).

MHV, VA's online patient portal, enables Veterans to access their health information and VA health care team on the Internet. MHV has over 2.5 million registered users, including 1.4 million Veterans who have completed in-person authentication (IPA). With IPA status, Veterans can use SM, akin to E-mail but behind the VA firewall and limited to Veterans, their designees, and VA providers; more than 789,000 Veterans have used SM.[29]

A growing body of literature indicates that Veterans are using the Internet in general and MHV in particular to access health information.[30,31] Early studies suggest the potential to employ MHV and SM for outreach to Veterans.[32] Aside from our pilot (described below, 4.a.1), no studies have examined the role of pharmacist-

(CONTINUED ON NEXT PAGE)

mediated medication reconciliation by SM. A recent study identified a pathway for SM to reduce hospital utilization.[33] In a recent HSR&D supported systematic review, Goldzweig et al found insufficient evidence linking patient portals to improved health outcomes,[34] but concluded that interventions using patient portals in conjunction with case management were most effective. Analogously, our study features pharmacists to review and reconcile medications. Moreover, Goldzweig et al called not only for rigorous RCTs in this area but also for studies that examine "organizational and provider context and implementation processes," as we propose herein (Aim 3). The SMMRT Trial will yield valuable information on the effects of MHV and SM-mediated medication reconciliation on health outcomes, guiding future efforts to employ these technologies.

2. d. Conceptual Framework.

Wagner's Chronic Care Model (CCM) provides the study's conceptual framework.[35-37] The CCM recognizes the importance of transforming systems to focus on preventing disease and its complications. Figure 1 shows how key innovative features of The SMMRT Trial are linked to elements of CCM interventions.

FIGURE 1. Chronic Care Model Elements and Key Innovative Features of The SMMRT Trial

Elements of the Chronic Care Model	Patient self-management support	Delivery system redesign	Use of clinical information systems	Provider decision support	Linkage to community resources	Health care organization support
Innovative Elements in the SMMRT Trial	▪MHV,SMMRT support self-management ▪Usability testing with Veterans to optimize SMMRT	▪Pharmacists play key role in SMMRT ▪Usability testing leads to redesign ▪Aim 3 heralds implement'n	▪SMMRT sent via MHV Secure Message ▪Includes med images from central data base	▪Pharmacists included in usability testing ▪Pharmacists update CPRS and notify PCP/PACT	▪Partnerships with all VISN-1 VAMCs ▪Pharmacists communicate with non-Boston PCPs via local CPRS	Operational Partnerships: ▪Layden, Co-I, MedRec,PBM ▪Nazi, Co-I, MHV, OIA ▪Calls + face-to-face mtgs

Summary Points

- This project is highly significant and concordant with HSR&D Research Priorities, VA's Transformational Initiatives and operational partners' objectives.
- The study design will distinguish between the effects of MHV and the effects of the Secure Messaging Medication Reconciliation Tool (SMMRT) on health outcomes and will include formative evaluation.
- Operational partners responsible for MHV, medication use and patient safety have invested in this research with active participation, which will ensure that study results will be useful in future operational planning.

3. a. HSR&D Priority C: Healthcare Informatics to Improve Veteran Care.

This priority integrates "biomedical knowledge systems with technology to improve decision-support systems, evidence-based practices, collaboration and continuity of care among providers, and Veteran and provider education." This project capitalizes on a widely used existing technology, SM within MHV, to facilitate Veteran-centered medication reconciliation. Aim 1 employs usability testing to optimize the tools. The trial design (Aim 2) will allow us to distinguish the independent effects of MHV engagement and pharmacist-mediated medication reconciliation by SM. Aim 3 features a formative evaluation for future implementation.

3. b. Transformational Initiative (T21): Employ state-of-the-art IT in Veterans' health care.

The SMMRT Trial directly addresses *VA's* vision of leveraging cutting-edge technology for improving Veterans' access to health care. MHV and, specifically, SM, enable Veterans to communicate directly with their health care providers from their own homes, at their own pace (i.e., asynchronous communication).

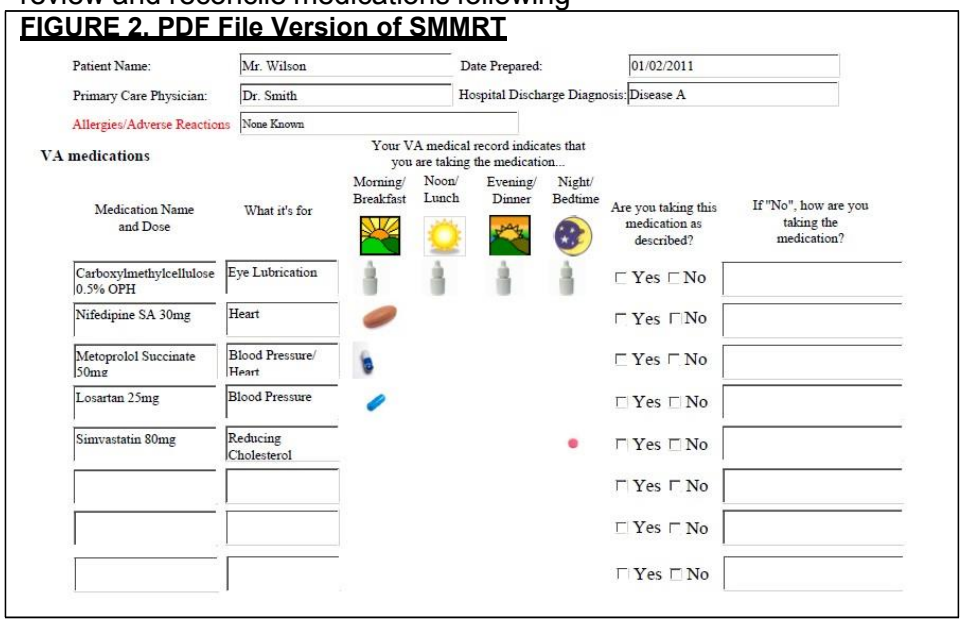
(3) WORK ACCOMPLISHED

The study team has experience in an array of scientific fields relevant to The SMMRT Trial. This section highlights studies laying the foundation for the proposed research.

#The SMMRT Pilot Study.

The study, published in *JAMIA*,[38] field tested the methods of the current proposal. We initially developed SMMRT as an interactive PDF file (Figure 2) for pharmacist and Veteran to interact asynchronously via SM to review and reconcile medications following discharge. Because the attachment feature of SM was not available at the time of the pilot, we instead used a text-based format, embedded in the body of the SM (figure 1 in Appendix 2), for the pharmacist and Veteran to reconcile medications. As we will do in the proposed SMMRT Trial, we recruited hospitalized Veterans, registered them for MHV, and trained them to use MHV and SMMRT. After discharge, our pharmacist reviewed the CPRS records of 51 eligible Veterans and identified 108 clinically important medication discrepancies (median 2 per Veteran), mostly medications that the Veteran was taking but were omitted from the discharge summary or discharge medication list. After correcting these discrepancies, the pharmacist sent SMMRT via SM to the Veteran. A total of 34 Veterans (67%) returned SMMRT. Of these 34 Veterans, 17 (50%) had additional discrepancies, most commonly duplicative medications prescribed for the Veteran at VA Boston and another VA facility. Nine of 10 Veterans completing post-intervention in-depth interviews (similar to those proposed in Aim 3) said they would use SMMRT again. Appendix 5 presents direct quotes about SMMRT from these Veteran participants. This study demonstrated the feasibility of recruiting hospitalized Veterans and training them in MHV and SM. Results highlighted the high prevalence of medication discrepancies immediately after discharge and the ability to detect and correct them by SMMRT.

FIGURE 2. PDF File Version of SMMRT



#Aligning Medication Reconciliation and SM: A Qualitative Study of Providers' Perspectives.

In this study, *published in JMIR*,[39] we conducted in-depth interviews with 15 primary care providers to characterize ambulatory medication reconciliation, the use of SM in primary care, and perceptions of a SMMRT-like medication reconciliation system. Providers recognized the value of medication reconciliation, especially after hospital discharge, and suggested numerous challenges to medication reconciliation. Providers emphasized the importance of collaborating with pharmacists in reviewing Veterans' medication regimens.

#Qualitative Study of Pharmacists' Role in Medication Review and Reconciliation.

Dr. Linsky recently completed a series of interviews with clinical pharmacists regarding their role in medication management. Preliminary analyses revealed considerable enthusiasm among pharmacists for developing relationships and monitoring patients to improve medication safety.

#Medication Discrepancies.

We evaluated the accuracy of VA's computer-generated medication listing to determine prevalence of

medication discrepancies*; 60% of ambulatory Veterans had at least one medication discrepancy*.[13]
#Usability Studies.
Colleagues Drs. Alissa Russ and Alan Zillich have conducted research at the VA HSR&D Human-Computer Interaction Laboratory in Indianapolis, IN that directly informs this investigation. These studies have included usability testing with VA patients or providers. For example, in a study published in *JAMIA*, Dr. Russ and colleagues evaluated usability of basic MHV features.[41] In this study, Dr. Russ designed scenarios to test the pharmacy refill function and improve its usability for Veterans; she will develop analogous scenarios for SMMRT in the proposed study. In the precursor project to the work proposed herein, Dr. Russ led usability studies to refine and enhance the SMMRT, leading to **two publications recently accepted for publication:**

- Russ AL, Jahn MA, Patel H, Simon SR. Usability Evaluation of a Medication Reconciliation Tool as a Precursor to a Clinical Trial: Blending Factual Scenarios with Artificial Safety Probes. J Biomed Inform. 2018 (In Press).
- Jahn MA, Porter BW, Patel H, Simon SR, Russ AL. Usability Assessment of Secure Messaging for Clinical Document Sharing between Healthcare Providers. Appl Clin Inform. 2018 (In Press).

(4) WORK PROPOSED

Timeline

	Month																		
Research Activity	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
IRB Approval		x																	
AIM 1 (SMMRT RCT)																			
Training of Research Assistant		x																	
Re-introduction of study to clinical stakeholders		x																	
Testing data flow processes (med list into SMMRT tool)		x	x																
Recruitment and enrollment (West Roxbury and Brockton)			x	x	x	x	x	x	x	x	x	x	x						
SMMRT Intervention Activities			x	x	x	x	x	x	x	x	x	x	x	x					
Data Collection (30-day follow-up interviews)				x	x	x	x	x	x	x	x	x	x	x	x				
Data Analyses														x	x	x	x		
Manuscript: Main outcomes of the SMMRT RCT																	x	x	x
AIM 2 (Implementation-oriented formative evaluation)																			
Recruitment and enrollment									x	x	x	x							
Telephone interviews										x	x	x							
Transcription and data analysis											x	x	x	x					
Manuscript: Veterans' and Staff experiences with SMMRT														x	x	x	x	x	x

(4) WORK PROPOSED (continued)

Methods for Aim 1 (SMMRT RCT):

1. Study setting and population

The setting of Aim 1 will include not only the acute inpatient hospital (located on the West Roxbury Division Campus) but also the CLC, located on the Brockton Division Campus.

2. Recruitment and enrollment

Approximately ten (10) patients per week are discharged to home from the CLC each week. Because of the strong relationships developed between the clinical teams and the Veterans and their families during the long (compared with acute inpatient) hospitalizations, typically 3-4 weeks, Veterans are likely to be amenable to enrolling in a clinical research trial that they see their clinical team members advocating. Conservatively, we estimate that at least 2 patients each week will enroll in SMMRT, such that over the course of 12 months (50 weeks), a minimum of 100 patients would be enrolled. In addition, we have ensured that resources are available to enroll 140 patients at the West Roxbury setting, resulting in a total sample size of 240 subjects. Recruitment and enrollment processes will follow these steps:

1. Research staff will communicate regularly with clinical staff (nurses and clinicians) on the inpatient service at VA Boston's West Roxbury and Brockton Divisions
2. Research staff will identify any Veterans hospitalized on the Inpatient Service meeting the following criteria by reviewing CPRS, patient lists, and consulting with clinical staff:
   a. age 18 years or older
   b. having a VA primary care provider (PCP) at any VA facility in VISN-1
   c. planned discharge home (as opposed to another facility)
   d. anticipated to be discharged with at least 5 medications
3. Research staff will confirm with clinical staff that the Veteran/patient may be approached and informed about the study.
4. Research staff will approach the hospitalized Veteran to describe the study and seek informed consent for participation.
5. The research staff will briefly describe the study and then administer the Callahan cognition screener (see separate document) and the eligibility screening questions below.
6. If the Veteran passes the Callahan cognition screener and eligibility screening questions, the research staff member will seek to obtain informed consent and HIPAA Authorization.

Script for Aim 2 Eligibility Screening Questions (after Callahan Screening and before Informed Consent):

- Thank you for allowing me the chance to tell you about our study. I would like to ask you a few questions first to see if you meet the requirements for eligibility. Would that be okay?

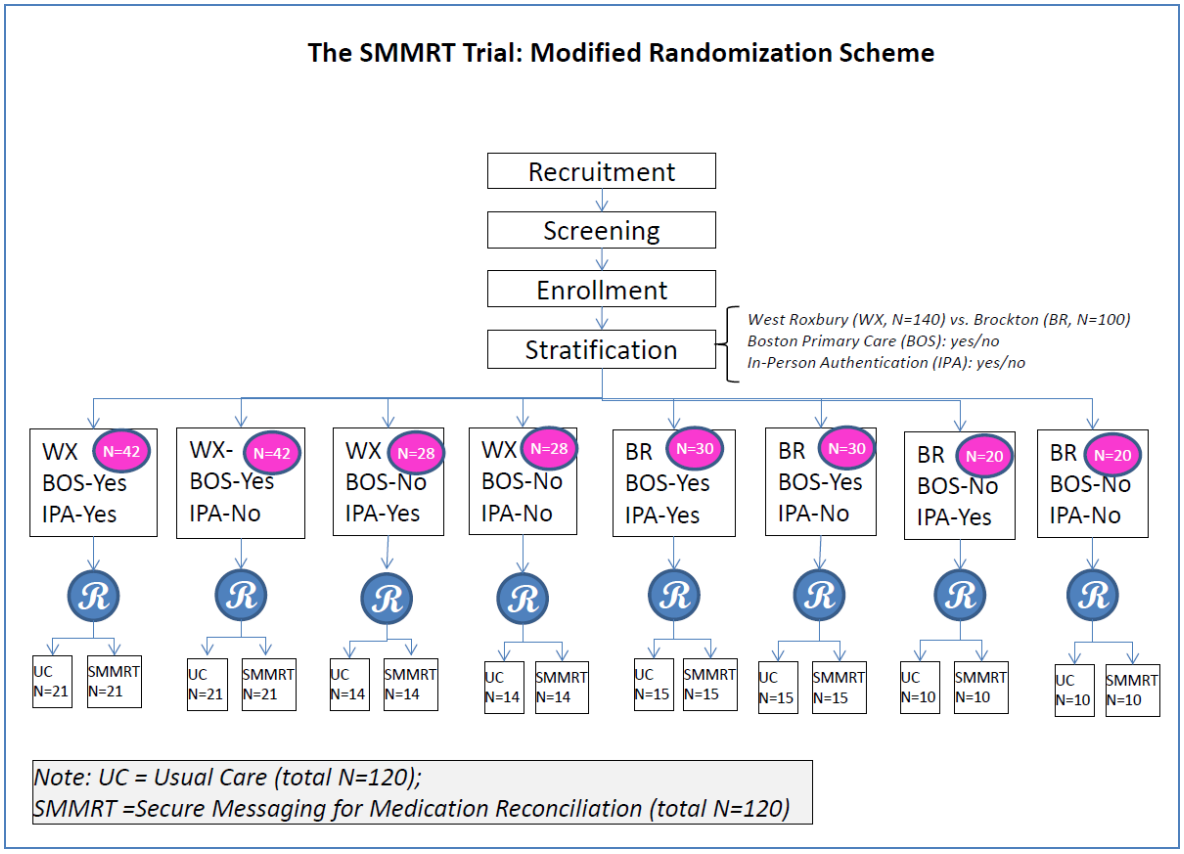
1. **Do you have access to a computer? Y/N** *(If yes, continue. If no skip to question 4)*
2. **Do you use a computer to connect to the internet, say to search websites or for email?**
3. *If yes, Do you use secure messaging? If no, would you be willing to use it if required for this study?*
4. **Does anyone help you manage your medicines? Y/ N** *(If yes, continue. If no, not eligible, go to Verbal consent)*
5. **Does that person use a computer/ internet/ email? Y/N** *(If yes, continue. If no, not eligible, Would you be willing to have your caregiver use secure messaging on your behalf if required for this study?*

If no to either 2 or 3: Unfortunately, you do not meet the criteria to participate in this study. Thank you for your time and interest.

→If Yes to 3 and 4, administer the Callahan screener. If patient passes the screener, then the patient is eligible. Continue on to ICF and HIPAA forms.

3. Randomization and intervention

Veterans successfully recruited and consented to participate will be randomly allocated to either UC or UC+SMMRT. Veterans randomized to UC+SMMRT will receive introduction to My HealtheVet and SMMRT. Within 3 business days of discharge, the SMMRT Research Pharmacist will engage with Veterans and/or their designated family members to conduct medication review and reconciliation via Secure Messaging. See randomization scheme below.



After baseline assessment is complete, participants will be randomly assigned via computer program to receive 1) usual care or 2) UC plus pharmacist-mediated medication reconciliation (SMMRT). After opening, the research assistant will inform the Veteran of the "treatment assignment."

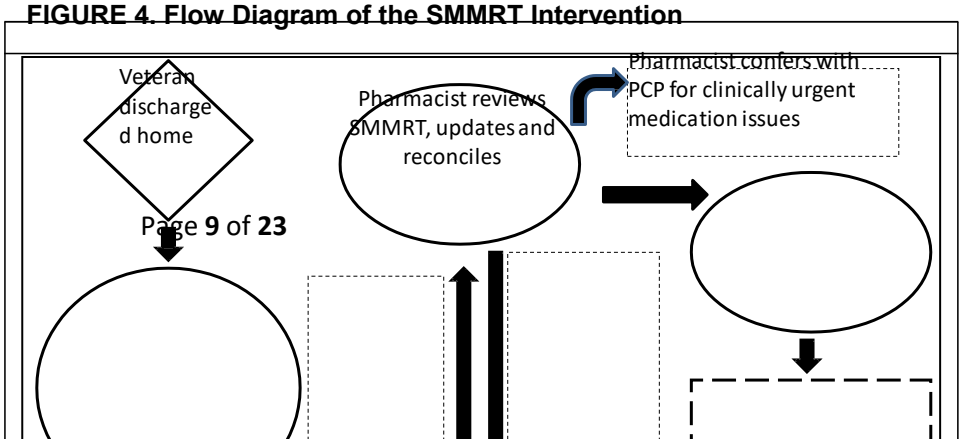
Overview of the Intervention

The intervention principally entails the creation of a personalized medication list for each Veteran/subject, incorporating most current data from Vista (the medical record) into a user-friendly PDF-file interface, i.e. the SMMRT. The research pharmacist will send the SMMRT via attachment to Secure Message to the Veteran and will then interact with the Veteran to ensure that the medical record accurately reflects what medications the Veteran is taking.

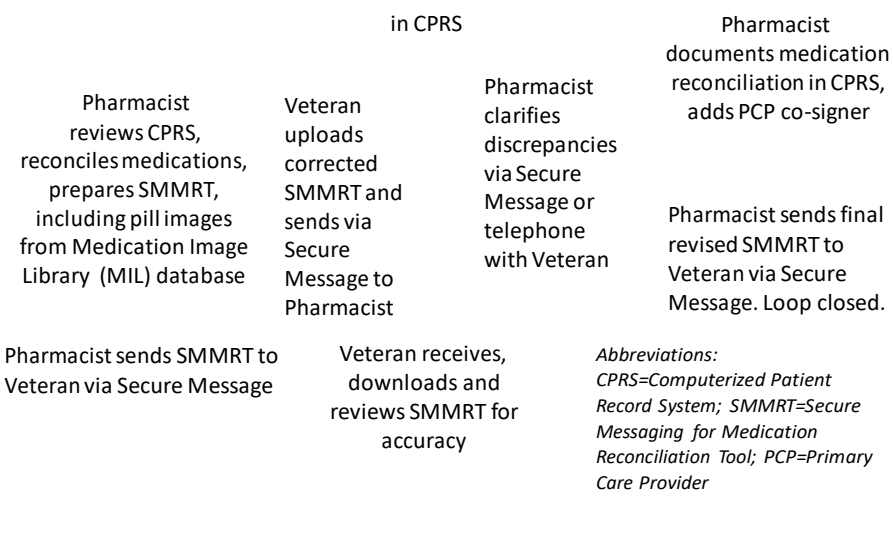
What Happens in the Intervention?

The SMMRT Intervention. Figure 4 shows the elements of the SMMRT intervention. In the figure, diamonds show Veteran activity; ovals show pharmacist activity; and dotted boxes show information exchanges. Not shown in the figure, Veterans will be trained to use MHV while still hospitalized. Starting at top left of the figure, within 3 business days after the Veteran is discharged

FIGURE 4. Flow Diagram of the SMMRT Intervention



home, the pharmacist reviews CPRS, reconciles medications, and prepares the SMMRT, including photographic images (JPEG files) of each medication from the Medication Image Library (MIL). The MIL is a database developed and maintained by VA Consolidated Mail Order Pharmacy *with* pharmacist-validated images for use in medication identification. The MIL has accurate image matches to 99.9% of VA-dispensed medications based on national drug index (NDI) numbers (personal communication, Richard Pham, CDW). *Following*



the approach developed by Lesselroth et al,[3] we will use automated processes to populate the SMMRT with the medication list and MIL images. After reviewing the SMMRT, the Pharmacist sends it via SM to the Veteran, who receives the SM, downloads the SMMRT, and reviews it for accuracy (in comparison with home medications). We learned from our pilot study that only about half of Veterans had their medications present when completing the SMMRT; our training for the proposed trial will include encouragement to have medications present while completing the SMMRT. Following review and correction, the Veteran returns the SMMRT to the Pharmacist within 3 business days, initiating a possible back-and-forth exchange of messages (or telephone calls) to confirm medication accuracy; this exchange is represented in the middle of the figure with bidirectional arrows. The pharmacist confers with PCP for clinically urgent or uncertain issues (occurred in only two cases during the pilot study) and documents medication reconciliation in CPRS. Finally, the pharmacist sends the final revised SMMRT to the Veteran. The research associate monitors the initiation of the exchange and will prompt either the pharmacist or the veteran to respond within 3 business days, via phone. The veteran will be informed at the beginning of the study and at the end if appropriate that access to the pharmacist ends in 30 days.

4. Ascertainment of Outcome

Outcomes will be ascertained via 30-day telephone interview (see Telephone Script for 30-Day Follow-up Call) and chart review. The research associate will send out a written reminder a few days before the 30 day follow-up call, and make a reminder call the day before the interview, to remind the veteran to have their medications ready. The research associate will ascertain the medications that the subject is currently taking, and the research associate will then compare that list with the medication list in the medical record to identify discrepancies. We will distinguish medication discrepancies as being of a) high significance, b) moderate significance, or c) low significance, based on how likely they would be to result in patient harm.

In the event the veteran was not reached for the interview, the research associate will send out a letter and call the veteran to reschedule the interview.

5. Sample size and power

We propose a two-arm RCT, with 120 participants in each arm. The main outcome measure will be combined number of medium- and high-significance medication discrepancies present at the 30-day follow-up. Conservative estimates suggest that we would expect a rate of 3.0 medium- or high-significance medication discrepancies per patient in the Usual Care group. Using a custom simulation, with two-tailed alpha error set at 5%, we calculated that this sample size (120 subjects per arm) would have 99.9% power to detect a lowering of the rate from 3.0 to 2.0 and 82% power to detect a lowering of the rate from 3.0 to 2.4.

6. <u>Measures.</u>

Study measures will be derived from baseline and 1-month follow-up interviews, as well as from CPRS.

Predictor Variable. The predictor variable will be the experimental condition (i.e., Usual Care SMMRT), assigned by random allocation (see above).

Main Outcome Variable. The primary outcome measure will be medication discrepancies detected 30 days after discharge. Secondary outcome measures will be 30-day hospital utilization (combined readmissions plus emergency department use) and Veterans' self-efficacy in medication use.

Secondary Outcome Variables. Secondary endpoints, ascertained *through a combination of CPRS review*

plus follow-up interview with participants, include community tenure (days spent outside of the hospital), medication discrepancies (overall and by subtype, i.e., omissions, commissions, duplications, and alterations in dose or frequency); health status (SF-12 health status scale; 12 items, 2-3 minutes), medication use self-efficacy (score of 0 to 8, based on validated 8-item yes/no MUSE scale;[62] 3 minutes); and the Care Transition Measure (score of 0 to 100, based on validated 15-item, 4-point [strongly agree, agree, disagree, strongly disagree] scale, linear transformed to 0 to 100 scale,[63] 5 minutes).

Other Variables. Prior to randomization, we will stratify participants on the basis of My Health**e**Vet in-person authentication status (yes/no) and VA Boston primary care (yes/no); see above Figure 2 and Section 4.e.5. Baseline data will include age, educational level, race/ethnicity. At baseline, we will administer the 7-item REALM-SF health literacy scale,[64] the SF-12, and the medication use self-efficacy scale (MUSE). During the 30-day follow-up we will re-administer the SF-12, the CARE Transition measure and the MUSE.

7. Statistical Analysis.

Preliminary Analyses. In preliminary analyses, descriptive statistics and bivariate associations will be computed. Then we will assess whether there are differences between the study arms for socio- demographic variables. We will assess imbalance formally using Analysis of Variance for continuous variables and Chi Square tests for dichotomous variables. In order to confound any observed effect of the treatment, a covariate must be imbalanced between the arms and also associated with the outcome. Thus, we will judge how plausible confounding is based on the formal tests, the degree of imbalance, and the plausibility of association with the outcome. Primary analysis will not include any potential confounders, but sensitivity analyses will adjust for plausible confounding variables with large imbalance between the arms.

Statistical Analyses. The primary hypothesis is that SMMRT will result in a reduction in 30-day medication discrepancies as compared with UC. The main outcome will be tested by a two-step analysis. First, we will conduct a logistic regression to compare SMMRT vs. UC. We will take an intent-to-treat approach to the analysis; Veterans will be included in our primary analyses regardless of their level of adherence with their assigned intervention. For participants who do not complete the telephone assessment, we will rely on CPRS/*CDW* data for outcome assessment.

Checks and treatment for "non-Response" Bias. The potential for differential drop-out rates among the three groups is itself an interesting and important empirical question, with clinical implications. Drop outs will be defined as active drop outs (Veterans who request discontinuation of participation) and passive drop outs (Veterans who cannot be reached for follow-up within 60 days of discharge). Factors that may contribute to drop-out rate will be tested by logistic regression. This logistic regression will be used to generate completion probabilities, which we will use as Inverse Probability Weights (IPWs). We will then use the IPWs in a weighted logistic regression for the outcome as predicted by study arm. Heuristically, Veterans with low probabilities of response who do respond are upweighted to represent Veterans who did not respond. Veterans who were quite likely to respond will not be upweighted as much. The result is a weighted sample that resembles the original population. In the weighted analysis, we will use the robust or "sandwich" variance estimator to account for the variability added by estimating the IPWs.

Methods for Aim 2: In-Depth Interviews

Aim 2 . To evaluate MHV training and SMMRT interventions for potential future implementation. For this formative evaluation, we will use qualitative research methods to examine in-depth how Veterans perceived their interactions with the MHV Training and SMMRT intervention components. *We will also interview PACT RNs and Pharmacists to solicit their perspective on the integration of SMMRT into the post-discharge PACT workflow and will analyze related information collected from chart abstraction.*

Rationale for formative evaluation.
Formative evaluation will inform future implementation efforts, specifically in the area of medication reconciliation and more generically for interventions using health IT to engage Veterans in their care. Formative evaluation is valuable in the context of an intervention that results in quantitative improvement of outcomes because it can yield information regarding characteristics of the intervention that seemed most useful and effective from the perspective of the study participants. Perhaps more importantly, formative evaluation is crucial in the context of an intervention that does not result in quantitative improvement in the target outcome (i.e., in the setting of a "negative study"), because it can identify the factors that may have prevented an otherwise-potent intervention from achieving the intended outcome.

Procedure for recruitment and consent of participants in Aim 2

Recruitment of Veterans
All Veterans recruited for Aim 1 and randomized to the SMMRT study arm will be eligible for Aim 2. At the time of initial recruitment, Veterans will be told that they may be selected to participate in this in-depth interview after completion of the 30-day outcome assessment interview for Aim 1. Because Veterans have already provided informed consent and signed the HIPAA authorization for participation in Aim 1, and because only the information obtained by virtue of that authorization will be used to determine eligibility for participation in Aim 2, no waiver of HIPAA authorization is needed for this Aim.

Recruitment of Staff (Nurses and Pharmacists)
We will send an email to PACT nurses and pharmacists who have had at least one Veteran participate in the SMMRT trial in the SMMRT study arm. Please see separate Staff Recruitment Email document. We will follow up the e-mail with a telephone call to recruit the staff member and to review elements of informed consent. Please see separate Telephone Script. Those staff members willing to participate will receive the informed consent form and will return it by whichever route/method they prefer (e.g., in-person, fax, e-mail).

Informed Consent of Veterans
A single Veteran informed consent form will be used for both Aim 1 and Aim 2. The ICF indicates that a subset of participants in Aim 1 (the RCT) will be invited to participate in Aim 2 (in-depth interviews). The ICF distinguishes the two study components and the compensation offered for participation in each study component. This informed consent form will be completed at the time of initial enrollment in the study, i.e., while the Veteran is hospitalized and prior to randomization for Aim 1.

Informed Consent of Nurses and Pharmacists
The Staff version of the informed consent form will be completed prior to the conduct of the in-depth interview.

In-depth Interviews.

Veteran Interviews

Note: The interviews with Veterans will be conducted by telephone or, if the Veteran requests, in person at VA Boston. We will carry out in-depth interviews with Veterans within 2 weeks after completion of the study to minimize perturbation of the experimental setting. In-depth interviews are characterized by extensive probing and the use of open-ended questions to elicit participants' thoughts in their own words. As we have done in prior studies,[66] we have prepared a semi-structured interview guide that includes a core list of questions to be supplemented by prepared and spontaneous follow-up questions and probes to seek clarification, expansion and examples, and to follow new relevant lines of inquiry. Interviews will focus on identifying and characterizing factors related to successful or unsuccessful implementation of the MHV Training and SMMRT interventions, beginning with study recruitment and enrollment, including MHV registration, training and encouragement, and continuing through actual engagement with SMMRT. To assess the fidelity of the intervention, the interview will encourage Veterans to provide feedback on specific details of the intervention that they found helpful and useful, as well as those features that were of little value or even counter-productive.

Broad topic areas will include the ease or difficulty associated MHV and SM in general, and SMMRT in particular; experiences with the medication reconciliation process at home; attitudes toward and reactions to SMMRT; and perceptions of how MHV and SMMRT influenced their health and health care. (See attached Interview Guide).

We will use purposive criterion-based extreme-case sampling[67,68] to identify potential Veteran participants (N=20) allocated to the SMMRT Arm. We will recruit approximately equal numbers of Veterans who were at the higher and lower extremes of number of medication discrepancies detected at the 1-month follow-up and will include both Veterans who experienced post-discharge hospital utilization as well and those who did not. As we have done previously, interviews will be conducted by telephone and, with the permission of the participants, will be audio-recorded for transcription and subsequent analysis. (See Human Subjects for details on protection of human subjects.)

Staff Interviews

Note: Interviews with staff members will be conducted by telephone or, if the staff member requests, in person at VA Boston. We will recruit 10-15 PACT nurses and 5-10 PACT pharmacists from multiple VISN-1 facilities for brief (~20-minute) focused interviews to explore how SMMRT influenced post-discharge calls and more generally their workflow and communication with Veterans. We will specifically inquire about potential duplication of effort and whether the SMMRT led to any unanticipated consequences. With permission, we will audio-record the interviews for transcription.

Analysis.

We will conduct content analysis of the transcribed in-depth interviews, incorporating the principles of the immersion-crystallization method.[69] This qualitative approach consists of repeated cycles of immersion into the collected data with subsequent emergence, after reflection, of an intuitive crystallization of the dominant themes.[69] Dr. Simon and research staff will independently listen to selected interview tapes, read all transcripts and write analytic notes for each interview. We will meet regularly to discuss each transcript and will compile detailed notes to document emerging themes and maintain a permanent record of the analysis.

We will then compare the data from the transcript under discussion with the data from other analyzed transcripts. Through this process, we will identify salient themes that crystallize from the interviews, and code categories for managing further interpretation of the data. Following the principles of the template organizing style of data interpretation,[70] Dr. Simon and the research staff will develop a code book based on the previous analysis activities, and then code the transcripts and observation guides using NVivo 10, a qualitative data

management software tool.[71] Team members will meet regularly to review the coding strategies and themes that emerge from further analysis of the thematic and categorical reports that will be generated following coding. We will continue analysis until no new major themes emerge. We will address recognized criteria for qualitative research: credibility, fittingness, auditability, and confirmability.[72]

(5) HUMAN SUBJECTS

The overall goal of this project is to evaluate the Secure Messaging for Medication Reconciliation Tool (SMMRT) for the purposes of post-discharge medication reconciliation. This project proposes two types of research: Aim 1 is quantitative: an RCT to compare the effect of an intervention on the medication reconciliation process following discharge from the hospital. Aim 2 is qualitative, gathering the preferences, attitudes, and behaviors of Veterans and VA pharmacists and nurses regarding the SMMRT tool and its implementation.

Aim 1: Risk to Subjects

Human Subjects Involvement and Characteristics

The goal of Aim 1 is to conduct a two-arm RCT to evaluate the effects of SMMRT. This trial will compare 1) Usual Care (UC) with 2) UC plus pharmacist-mediated medication reconciliation via SM using SMMRT among Veterans discharged from the hospital. A total of *240 V*eterans will be recruited for Aim 1 once deemed appropriate for the study. The study will be explained to Veterans who express interest, and informed consent will be obtained. Veterans will be informed that their care will not be affected if they choose not to participate in the study. Next, Veterans will be randomized to condition, and the baseline interview will be administered. If the Veteran is randomized to UC plus SMMRT, the research associate will instruct the Veteran on how the tool works. When the Veteran has completed the training with the SMMRT tool, the research associate will ensure no other questions remain. Veterans in the UC plus SMMRT Intervention condition will be monitored during the length of the study. A total of 20 Veterans from the experimental arm of Aim 1 will be contacted for a post- intervention in-depth interview (See Aim 2 below).

Sources of Materials

Data to assess the outcomes of the RCT will be derived from review of the medical record (CPRS and VistAWeb), *the Corporate Data Warehouse (CDW),* and telephone-based interviews with participants.

Potential Risks

The risks to subjects from our study are minimal. The primary risk to Veterans is disclosure of sensitive information. In general, as in virtually any human research study, there is a risk of data security breach and resulting loss of confidential study data. Our procedures are designed to prevent any unauthorized disclosure; see Adequacy of Protection from Risk, below. We do not anticipate any adverse effects of the research to require any medical or professional intervention.

Adequacy of Protection from Risk

Recruitment and Informed Consent

All research staff will be trained on protection of human subjects, and regularly supervised to ensure respect for potential participants, integrity of data collection, and appropriate interactions with staff. Veterans will be informed that their participation in the study is voluntary, and refusal to participate will not change the care they receive.

Protection against Risk

As described above, the potential risks to Veterans in Aim 1 are minimal. The main risk is loss of confidentiality of sensitive information. Recruitment will take place on inpatient units within VA Boston, as will the consent process, baseline interview and SMMRT tool training. If randomized to the SMMRT intervention,

all medication data will remain in My HealtheVet, never leaving the VA firewall. When conducting the follow-up telephone interviews, the *research associates* will confirm that they are speaking with the proper Veteran participant. The *research associate* will only leave telephone messages saying that the Veteran is participating in a health study.

We will only collect identifiable data when absolutely necessary and scientifically justified. The SMMRT will be sent through the secure messaging feature of My HealtheVet. Only the Veteran and study pharmacist will have access to the medication data. Data transmissions between study staff will be minimized, but when necessary, will meet or exceed all standards for encryption and security that are in place for the electronic transmission of Veterans' clinical information, with which the Principal Investigator is familiar.

Aims 2: Risk to Subjects

Human Subject Involvement and Characteristics

Aim 2 will involve telephone interviews with 20 Veterans who were allocated to the experimental arm of the RCT, with the use of semi-structured, in-depth interviewing techniques to assess Veterans' experience with the SMMRT tool. *In addition, Aim 2 will include brief, focused interviews with 10-15 PACT nurses and 5-10 PACT pharmacists from VISN 1 facilities regarding their perceptions of whether and how the SMMRT intervention may have affected their post-discharge follow-up calls. The interviews with nurses and pharmacists will also explore unanticipated consequences of the SMMRT intervention.*

Sources of Materials

During the course of conducting study Aim 2, we will collect data through interviews with Veterans, VA pharmacists, and nurses. Thus, all of the research material for this study will be data obtained specifically for research purposes.

Potential Risks

This study involves a low level of risk to all human subjects. There are no apparent physical risks for any of the subjects. In general, as in virtually any research study, there is a risk of data security breach and resulting loss of confidential study data. There is potential risk that the questions and conversations in the interviews could be psychologically upsetting to the Veterans. There is also the theoretical possibility that participating in the interviews could be physically taxing. Additionally, VA staff members are considered a vulnerable group, due protections exceeding their Veteran counterparts. The likelihood of any of these risks is low. None of these potential risks is serious.

Adequacy of Protection from Risk

Recruitment and Informed Consent

Veterans: For Aim 2, we will identify Veterans allocated to the experimental condition (Usual Care + SMMRT Intervention) at the time of the 30-day follow-up telephone call. These Veterans will already have provided informed consent at the time of their enrollment in Aim 1. However, they will be reminded of the key elements of informed consent at the time of invitation to participate in Aim 2. Veteran participants will be informed that the collection of data will be strictly confidential and that the participation of all human subjects will be completely voluntary. The "script" that research staff will use in approaching Veterans for recruitment in the interviews will explicitly indicate the voluntary nature of participation and the assurance of confidentiality of respondents.

VA Pharmacists *and Nurses*: A member of the study team will reach out to potential staff participants for Aim 2, as described in the Protocol. Those interested in participating will be educated on the study, made aware that participation will not impact employment status, and be provided a forum to address questions and

concerns. VA employee participants will be informed that their data collection from *interviews* will be strictly confidential and their participation will be strictly voluntary. Please refer to the e-mail and telephone script submitted separately, which explicitly indicate the voluntary nature of participation and the assurance of confidentiality of respondents, as well as special rights and protections afforded for VA staff participating as research subjects.

Protection against Risk

As described above, the potential risks to subjects in this study are of low likelihood and generally not serious. Nevertheless, we have given these risks careful consideration and have developed a plan to ensure that research subjects are protected against them. With respect to ensuring confidentiality and data security, we will take the following precautions. We will only collect identifiable data when absolutely necessary and scientifically justified. Data will only be stored on VA servers, never leaving the VA system. We note that our servers for data storage are located on a separate research-specific password-protected server, providing an additional layer of security. Data transmissions between study staff will be minimized, but when necessary, will meet or exceed all standards for encryption and security that are in place for the electronic transmission of Veterans' clinical information, with which the Principal Investigator is familiar. Recordings of participants during laboratory observations and in-depth interviews will be treated with similar care. The audio recordings will be made with a portable digital recording device that will always be maintained under lock-and-key of study staff (either in locked file cabinets within a locked office. or, when in transport between facilities, within a locked box). The digital recordings will be downloaded to password- protected computer files on the VA network server (behind the research firewall), and transcriptions from these recordings will be similarly stored and handled. Prior to processing the transcriptions for qualitative analysis, study staff will remove all names and other personal identifiers from the transcripts. *Transcripts will not be printed routinely. Rather, study team members will be instructed to review them as electronic files, to minimize the risk of PHI disclosure.*

We expect these processes, which our team members have employed in a variety of studies both within and outside the VA, will be highly effective in protecting subjects from the risks of data security and confidentiality breaches. With respect to protecting participants from the risk of psychological distress and physical taxation as a result of participating in the interviews, we will take the following precautions. First, we will ensure that VA facilities be accessible to all participants, with special attention to needs of those with physical disabilities. Second, we will train the research associate to be sensitive to any discomfort that the subject may be experiencing; Dr. Simon has extensive clinical and research experience related to interviewing and will ensure that the research associates have sufficient training in this regard. Third, we will ensure that sufficient research staff members are present to assist participants in locating restrooms and other necessary facilities.

We do not anticipate any adverse effects of the research to require any medical or professional intervention.

Aims 1 and 2: Potential benefits of research to subjects and others

This application proposes to develop a secure messaging medication reconciliation tool Intervention to improve the post-discharge medication reconciliation process, and compare its effectiveness with treatment as

usual. The potential benefits of this research to Veterans include greater accuracy in the post-discharge medication reconciliation process, resulting in improved health of Veterans. We also anticipate that this intervention, if proven effective and, ultimately, integrated successfully into the post-discharge medication reconciliation process, will lead to reduced medication errors, fewer hospitalizations and adverse drug events. Finally, this line of research can lead to the demonstration of the utility of an eHealth tool that Veterans with less comfort with technology can use, leading the way toward additional behavioral interventions that do not add to the clinic's workload. We believe that these benefits do outweigh the minimal risk of harm to research subjects, thus justifying the research.

Importance of knowledge to be gained

This project is unique in that it brings together three high priority areas for VA; improving medication reconciliation interventions, specifically, secure message based medication reconciliation tools; transforming care through the use of healthcare informatics, specifically, the SMMRT tool; and reducing racial and ethnic minority health care disparities, through the use of an eHealth tool that has few barriers to use by Veterans who may have poor health and computer literacy. If ultimately proven effective, the use of this eHealth tool for multiple behavioral issues can be integrated into the interface between primary care and behavioral health, and can fit well into the model of Patient Aligned Care Teams.

The knowledge to be gained from this study will be significant in addressing three high priority areas at once, and point to the pathway for using patient-facing technology to meet the 21st century requirements for all of our Veterans to be more involved in their own care. It will provide information on integrating eHealth tools into primary care as well as the effectiveness of this tool, at least for medication reconciliation. The potential knowledge to be gained from this project outweighs the minimal risks to participants.

Data and Safety Monitoring Plan

Dr. Simon, as principal investigator, and the VA Boston IRB will be responsible for monitoring the safety of participants. The Data and Safety Monitoring Plan will be carried out by Dr. Simon. Research staff will be trained to understand and document adverse and serious adverse events, and to immediately call Dr. Simon in the case of such an event. Dr. Simon will immediately notify the IRB of the adverse event and appropriate clinical action will be taken. A Case Report Form will be created that will be used to report all adverse events. This form will include the participant's study number and all relevant information about the adverse event. Case Report Forms will be filled out immediately by the staff person who is responding to the problem. Serious adverse events will be reported to the VA Boston IRB within 48 hours of its occurrence. All other adverse events will be reported annually to the IRB and HSR&D.

Inclusion of women, minorities and/or children

Both men and women Veterans will be included in this study. Minorities will be included to the greatest extent possible. All Veterans and staff, regardless of race, ethnicity, or sexual orientation will be included in this study. This research will not include any children.

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