Protocol Title: Video Information Provider for HIV-Associated Non-AIDS (VIP-HANA)

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STUDY PURPOSE AND RATIONALE

The purpose of this study is to use technology to improve symptom status and ultimately improve patient centered outcomes in PLWHA. The primary purpose of the intervention (VIP- HANA) is to improve symptom status. We hypothesize that VIP-HANA will improve symptom frequency and intensity, our primary outcomes.

SPECIFIC AIMS

HIV has evolved from an acute to a chronic illness largely due to antiretroviral therapy (ART) (Chiasson, Shaw, Humberstone, Hirshfield, & Hartel, 2009). As a result, people living with HIV/AIDS (PLWHA) are living longer and by 2015 half of PLWHA in the US will be over 50 years old. As PLWHA age, they are developing chronic illnesses and co-morbid conditions that are often seen in older HIV negative patients (Parsons et al., 2005). Fifty to sixty percent of deaths in HIV-infected persons occur from HIV-associated non-AIDS (HANA) causes and people suffering from these conditions are more likely to be affected by adverse symptoms (Parsons et al., 2006). HANA conditions (e.g., cardiovascular disease, liver disease, diabetes, and asthma) are becoming more common as PLWHA age.

An individual's ability to identify and self-manage symptoms of HIV illness has been shown to improve patient outcomes and quality of life ("Endpoints and other measures in a multisite HIV prevention trial: rationale and psychometric properties. NIMH Multisite HIV Prevention Trial," 1997; Parsons, Missildine, et al., 2004; Parsons, VanOra, Missildine, Purcell, & Gomez, 2004). Holzemer (study consultant) developed a paper-based symptom management manual with self-care strategies for 21 common (non-HANA) HIV/AIDS symptoms. The efficacy of this manual for improving symptoms was established in a 775-person RCT over three months at 12 sites (Chiasson et al., 2005). To enhance uptake of these strategies by PLWHA, we developed and pilot tested the Video Information Provider (VIP), a web application (app) that delivered HIV-related symptom self-care strategies for PLWHA (P30NR010677- 03S1)(Parsons, Halkitis, Wolitski, & Gomez, 2003). Results from our 3-month pilot study (N=42) study overwhelmingly demonstrated the feasibility of the system. Participants reported a decrease in HIV-related symptom frequency and intensity after using the VIP system for 12 weeks.

However, Holzemer's symptom management manual and VIP were not developed for managing symptoms related to HANA conditions. Little is known about the symptom experience or self-care strategies used by PLWHA with HANA conditions. Based on the existing evidence and our previous work, we hypothesize that providing PLWHA with HANA conditions with tailored self-care strategies in their everyday settings has the potential to improve symptom status, reduce healthcare visits, decrease frailty, and improve ART adherence and quality of life. Therefore, there is a need to identify the symptom experience of PLWLHA with HANA conditions and the

self-care strategies they use to manage the symptoms. For this study, we propose to:

Specific Aim 1a: Identify the most prevalent symptoms and self-care strategies of PLWHA with HANA conditions in order to modify the VIP system into the VIP-HANA system.

To achieve this aim, we will conduct an online survey with 1,000 PLWHA with HANA conditions, recruited from national social networking websites, to learn about their symptom experience and self-care strategies that they use to mitigate their symptoms. Our study team will incorporate the most frequently reported symptoms and appropriate self-care strategies into our VIP system. The VIP-HANA system, which will provide tailored self-care strategies based on HANA conditions and gender.

Specific Aim 1b: Evaluate the VIP-HANA system for violations of usability principles.

Specific Aim 2: Compare the efficacy of VIP-HANA to a control arm for ameliorating symptom frequency and intensity and secondary health outcomes in 100 PLWHA with HANA conditions over 6 months.

Our hypotheses are that use of VIP-HANA as compared to a control arm will:

a) Decrease symptom frequency and intensity (primary outcome measures) in the treatment arm as compared to the control arm;
b) Decrease frailty as measured by Fried's frailty phenotype;
c) Improve functional and emotional status, quality of life, and morbidity; and
d) Improve adherence to antiretroviral therapy (ART).

Specific Aim 3: Understand PLWHA's perceptions of the predisposing, enabling, and reinforcing factors for VIP-HANA use with theoretically-guided focus group sessions.

We will conduct focus groups, using the PRECEDE-PROCEED model with Aim 2 intervention arm participants, to understand their perceptions related to VIP-HANA use.

DESIGN AND METHODS TABLE

Table 1 presents and overview of the design, participants and data analysis plan

Table 1. Overview of Design, Methods, Participants, and Data Analysis

Aim	Design/Methods	Participants	Data Analysis
1a	Online Survey	PLWHA with HANA conditions(N=1000) and PLWHA without HANA conditions (N=1000)	Descriptive and thematic analysis of most frequently reported symptoms, symptom attribution, self-care strategies and information source.

1b	Heuristic evaluation, Usability testing (including: cognitive walkthrough, user testing using think-aloud protocol)	Heuristic evaluation: human-computer interaction experts (N=5); User testing: PLWHA (N=20)	Quantitative and qualitative summary of heuristic violations; thematic analysis of think-aloud protocol, quantitative summary of mouse clicks, time, etc.
2	Randomized controlled design	PLWHA with HANA conditions (pilot: N=5; trial: N=100; intervention=50, control=50) for 26 weeks	Descriptive statistics; Linear regression model
3	Descriptive: focus groups	Focus groups: Participants in the intervention and control arms of the RCT (N=60)	Descriptive, thematic analysis to examine post-intervention perceptions related to VIP-HANA use, usefulness and impact on overall health

Population, Target Enrollment and Subject Compensation				
Aim	**Description**	**Participants**	**Target Enrollment**	**Compensation**
1a	Online Survey	PLWHA with HANA conditions(N=1000) and PLWHA without HANA conditions (N=1000)	2,500	$10 incentive offered female participants through paid campaign and on site female survey takers to reduce gender disparity in data collection; we have also offered $10 for participants who have taken the follow-up survey online.
1b	Heuristic evaluation, Cognitive walkthrough and user testing using think-aloud protocol	Evaluators: Human-computer interaction experts (N=5); Cognitive Walkthrough Expert (member of study team) (N=1); End User testing ((N=20)	26	Heuristic Evaluators: $150 PLWHA: $35

2	Randomized controlled design	PLWHA with HANA conditions (pilot: N=5; trial: N=100; intervention=50, control=50) for 26 weeks	105	$250
3	Descriptive: focus groups	Participants in the intervention and control arms of the RCT (N=60)	60	$30

Study Design, Subject Population, Setting and Sample, Procedures, are all detailed by Aim below:

Specific aim 1a: Identify the most prevalent symptoms and self-care strategies of PLWHA with HANA conditions in order to modify the VIP system into the VIP-HANA system. We will also include PLWHA without HANA conditions for a comparison analysis. In response to the reviewers' feedback, we have completely revised Aim 1 so that we can collect the best patient-reported evidence that is available. The goal of our work in Aim 1a is to identify the most frequently reported symptoms and self-care strategies of PLWHA with HANA conditions and integrate them into our existing VIP system. We will expand and refine the existing symptom list (21 symptoms) to include symptoms and self-care strategies by adding new symptoms that are the most frequently reported by survey participants with HANA conditions in Aim 1. The additional information that is collected will be synthesized and incorporated into the VIP system which will result in the VIP-HANA system. **The VIP-HANA system will deliver self-care strategies to PLWHA with HANA conditions tailored to symptom reporting, HANA condition(s) and gender**. VIP-HANA will be a web-application (app) and can be used on a computer or a mobile device.

Online Survey with 2,000 PLWHA:
This web-based survey will enroll approximately 1,000 PLWHA with HANA conditions and approximately 1,000 PLWHA without HANA conditions into an anonymous online survey that inquires about symptoms and self-care strategies of PLWHA with HANA conditions. Study participants will be recruited online from various social media sites such as Facebook.com (the largest online social networking site) and POZ (poz.com). Dr. Hirshfield (Co-I) has had great success using this recruitment strategy (Chiasson et al., 2005; Hirshfield, Remien, Humberstone, Walavalkar, & Chiasson, 2004; Hirshfield, Remien, Walavalkar, & Chiasson, 2004).

Eligibility criteria: 1. HIV+; 2. Age 18 or over; 3. Able to read and respond in English; 4. Reside within the US; 5. .Willing to participate in an online survey. We have chosen the following HANA conditions because they are the most frequently occurring conditions that result in mortality and/or morbidity (Crothers et al., 2006; A. Justice & Falutz, 2014; A. C. Justice, 2010; A. C. Justice, 2014; A. C. Justice et al., 2004; Kendall et al., 2014; Messeri, Lee, & Berk, 2009; So-Armah & Freiberg, 2014).

HANA Conditions: Cardiovascular Disease, Liver Disease, Asthma, Bronchitis, COPD, Osteoporosis, Diabetes, arthritis and/or Renal Failure

Exclusion: 1. HIV-negative; 2. under age 18; and 3. Unwilling to provide key data (i.e., age, information about symptoms) on the online survey.

Recruitment: We are using two online venues to recruit the survey sample. Online recruitment will enable us to reach more PLWHA and will ensure a more diverse sample by age, geography, and engagement in their healthcare services. We have had success in recruiting racially/ethnically diverse PLWHA from social networking sites, like Facebook and POZ, in previous studies (Chiasson et al., 2005; Hirshfield, Remien, Humberstone, et al., 2004; Hirshfield, Remien, Walavalkar, et al., 2004). POZ is a U.S.-based website serving the community of people living with, and those affected by, HIV/AIDS since 1994. POZ.com provides health information

about HIV, sexually transmitted infections, and other chronic health conditions. POZ.com also has a national health services directory, covers HIV-related local and international news, as well as blogs, forums, and a personals section for HIV-positive individuals, which currently has over 150,000 U.S. male and female members. Dr. Hirshfield has an ongoing collaboration with POZ.com, which includes an online pilot study of 463 HIV+ men, a publication based on this collaboration, and an NIH-funded online national intervention for HIV+ virally unsuppressed MSM recruited through POZ Personals. The Research and Evaluation Unit at Public Health Solutions has developed a registry of research participants, including a large number of HIV+ men who do not meet criteria for other ongoing studies. For the proposed study, Dr. Hirshfield will work with POZ to recruit the sample. We will use psychographic targeting (in-depth publicly available consumer data such as interests, occupation, and city) to recruit PLWHA with HANA conditions from around the US.

See Attachment: Qualtrics Survey VIP. HANA.pdf (stamped 04/25/2016)

Study banners will be created by Public Health Solutions for recruitment of PLWHA with HANA conditions for the aforementioned survey. The study banners will route people to our study landing page. We conservatively estimate that at least 50% of all PLWHA in the US suffer from at least 1 HANA condition based on our review of the literature (Crothers et al., 2006; A. Justice & Falutz, 2014; A. C. Justice, 2010; A. C. Justice, 2014; A. C. Justice et al., 2004; Kendall et al., 2014; Messeri et al., 2009; So-Armah & Freiberg, 2014). Given this estimate, of the 150,000 PLWHA who use POZ.com as well as additional PLWHA with HANA conditions who use Facebook, we should easily be able to collect our study data within our study timeframe. Dr. Hirshfield collaborated with POZ on a brief online pilot in NY, CA and GA, sending emails to a defined subset of HIV+ male members identifying as gay or bisexual (n=5,262). POZ's email system can target members by location, sexual orientation, race/ethnicity, age, and most recent log-on. Of the 5,262 emailed, 1,696 (32%) clicked through; 479 of those who clicked through consented (28%); and 464/479 completed the survey (97%). In 7 days, through direct email with POZ Personals members, we were able to collect 463 completed cases. For the proposed study, we will be using banner ads on POZ and may not have the same response rate; however, 4 months is a sufficient amount of time to recruit 1,000 participants, given our inclusion criteria.

During the initial stages of survey collection for Aim 1a we detected a significant gender disparity in our population being mostly males completing the survey. Due to this difficulty recruiting women, in an effort to increase the number of female participants we will close the enrollment for males at this time. We have modified our survey to include female reproductive system questions and created a recruitment flyer offering $10 as an incentive for female survey takers. A new survey has been created for this purpose.

See Attachment: VIP HANA Women Qualtrics Survey.pdf

For this purpose, we will launch a paid online campaign through POZ.com as well as flyers posted around the Columbia hospital and surrounding areas as well as other social media sites to include more women and reduce gender disparity. Online female survey takers will receive a $10 amazon gift code while on site female survey takers, recruited through posted flyers, will receive $10 in cash.

Procedures: PLWHA who click our banner advertisements posted online will be automatically

directed to a study landing page that will screen to see if they qualify for participation. If they do qualify then they will be directed to complete the consent form. Those who consent, by clicking a consent button, will then complete a one-time only anonymous online survey. Employing the methods used by Holzemer (consultant) and Bakken (Co-I) when they originally developed the HIV Symptom Self-Management Manual (Bakken et al., 2000; Corless et al., 2002), participants will be asked to identify the 3 most disruptive symptoms they experienced in the past month.
Survey questions related to Symptoms and Self-care strategies are in Table 4.The web-based survey will be hosted by Qualtrics software. Columbia University Medical Center has a license with Qualtrics and all data collected through this software is HIPAA compliant. Qualtrics is also CUMC-certified and PHI secured which is a requirement of the Columbia University IRB for data collection via the Internet. Qualtrics will automatically assign random subject ID#s to each participant. We will collect information on symptom reporting and self-care strategies. Data will also be collected regarding additional secondary measures such demographics, psychosocial measures, ART adherence and scheduled/missed healthcare visits. As we mentioned before we will include PLWHA without HANA conditions for a comparison analysis. At this time we have decided to close the enrollment for males and direct more efforts into including female participants.

Data Analysis: Frequency of symptom reporting will be calculated. Our analysis will look for differences in symptom reporting and self-care strategies based on HANA condition, age and/or gender. We anticipate that there will be differences in gender but not in age (See Section C.2.1 below). Symptoms must be attributed to a HANA condition to be included as part of the final list of symptoms in our intervention. We anticipate that some self-care strategies will be the same for different conditions. In other cases, strategies will be different and the VIP-HANA system will deliver a self-care strategy tailored to symptom reporting, HANA condition(s) and gender, if applicable. Content analysis will be used to analyze the self-care strategies and attribution data for inductive development of the category schemes. Initial codes or categories of self-care strategies will be identified inductively from the data. To reduce the number of categories, initial codes will be consolidated on the basis of theoretical similarities and clinical significance after consultation with our study team. Drs. Schnall, Siegel, Bakken and the research assistant will collaborate on this analysis. We will also categorize the self-care strategies by information source reported by the survey respondent. Strategies which are potentially harmful or illegal (e.g., substance use) will not be included in VIP-HANA. We will have precautions in place to advise patients who appear to be at-risk for negative outcomes (e.g., report of severe depression) to contact their healthcare provider, call 911 or go directly to the emergency room.

Study Team and Experts will finalize the symptom list and self-care strategies: In year 2, we will conduct a meeting with the study team and the EAB to finalize the symptom list and the self-care strategies to be included in the VIP-HANA system. Once this has been finalized, technical refinement of our existing web app will take place at CBITs (see facilities and resources). We have partnered with CBITs since they use Purple, an extensible, modular, and re-purposable system created for the development of Web-based and mobile-based applications for health behavior change (Schueller, Begale, Penedo, & Mohr, 2014). Dr. David Mohr (PI: CBITs) is the Site PI for this project. Figure 4 illustrates a sample screen created by CBITS of self-care strategies for depressive symptoms. In response to the reviewer's request, a letter of support

from the technical team is included.

Specific Aim 1b: Evaluate the VIP-HANA system for violations of usability principles. The goal of usability testing is to improve system design, identify potential problems with usability, and increase the likelihood of technology acceptance. To achieve this goal we will evaluate the user interface and system functions of the VIP-HANA system developed at CBITs. We will conduct three types of usability evaluations: A) Heuristic Evaluation B) Cognitive Walkthrough, and C) PLWHA Usability Testing. Using this combination of methods, which includes both experts and end-users, can be used to more comprehensively identify potential usability concerns (Jaspers, 2009; Tan, Lui, & Bishu, 2009) One set of user scenarios will be used across all three evaluation methods to facilitate comparisons between findings (Tan et al., 2009).

Heuristic Evaluation:

Sample: Five informaticians will be recruited as usability experts (J. Nielsen & Molich, 1990). Nielsen recommends using three to five evaluators since one gains little additional information by adding additional evaluators (J. Nielsen & Molich, 1990). Experts must have training in human-computer interaction and have published in the field of informatics. We will recruit faculty and doctoral students from the Columbia University Department of Biomedical Informatics via personal correspondence (see attachment Letter for Heuristic Evaluators dated 5/5/2017).

Procedures: Usability experts will be provided with an Alpha version of the VIP-HANA system. Similar to procedures used in our prior work (Gordon et al., 2012; Lee et al., 2011; Schnall, Kaufman, Hyun, & Bakken, 2009; Sheehan, Lee, Rodriguez, Tiase, & Schnall, 2012) each usability expert will be asked to evaluate the system using the Heuristic Evaluation Checklist and to think-aloud while doing so (Bertini, Gabrielli, & Kimani, 2006). Morae software™ (Techsmith Corporation, Okemos, MI) (TechSmith, 1995) will be used to record sound and screens during the heuristic evaluation for subsequent analysis. The participants will be asked to describe what they are thinking, seeing and trying to do as they perform the tasks required in the scenarios developed for usability testing in this study (see attachment "VIP HANA user scenarios with embedded symptom reports 05.05.17"). If a participant is silent for a long time, the researcher will remind the participants to think out loud. When a user finds errors or the researchers finds critical incidents that are characterized by comments, silence or looks of puzzlement, the researcher will record the users' activities. Recording the users' interactions and vocalizations provides additional feedback that can highlight problems not identified with static screen shots (Gibson, Gaffey, & Spendlove, 2003). In addition to the user scenarios, a symptom report will be provided to both end-users and their health care providers. Examples of how these symptom reports will appear are included in the user scenarios and will be presented to the heuristic evaluators, expert study member performing cognitive walkthrough, and the end users.

Instrument: Nielsen (2005) proposed a list of ten recommended heuristics for a usable interface design. Bright, Bakken, and Johnson (2006) developed a Heuristic Evaluation Checklist based on Nielsen's ten heuristics (Bertini et al., 2006) (Appendix). Each heuristic will be evaluated with one or more items and the overall severity of identified heuristic violations will be rated. Heuristic evaluators will complete an online questionnaire while working though their assessment of the system (see attachment Heuristic evaluation survey 05.01.17). Heuristic evaluators will be asked

the following four questions regarding the symptom report: 1) What are your initial thoughts when you look at the symptom report? 2) How can we modify the report to more appropriately meet the needs of end-users? 3) How can we modify these reports to effectively share information with health-providers? 4) Do you have any additional feedback or comments that may help us to improve these reports? Please feel free to create any additional sketches that you think would help communicate your ideas.

Data Analysis: The frequencies of usability issues will be calculated according to the heuristic principles adapted from Nielsen's checklist. Mean severity scores will be calculated for each heuristic principle. Evaluators' comments about usability problems on the evaluation form and the Morae recording will be grouped and content analyzed according to the usability factors of Nielsen's heuristics (1994). Responses to questions regarding the symptoms report will be compared for similarities and possibility for improvements will be determined.

Cognitive Walkthrough:

Sample: An expert study team member will identify usability concerns within the system.

Procedures: The study team member who is a usability expert will be provided with the same set of user scenarios symptom reports and will be asked to simulate a novice user and the process that user would go through to achieve the goals set forth in each of the scenarios (Jaspers, 2009). By doing this, the evaluator creates a cognitive model that simulates the cognitive processes a user might go through to effectively accomplish tasks within the system. There are four tasks that the expert will need to complete for each scenario: 1) The user must set an end goal to accomplish, 2) The user inspects available actions on the user screen (menu items, buttons, etc.), 3) The user must select one of those actions as the next step that leads to the end goal, and 4) The user would perform that action and evaluate system feedback for evidence that progress is being made.

For each action needed to accomplish a task, the evaluator will need to answer 4 questions: 1) Will the user try and achieve the desired effect, 2) Will the user notice that the correct action is available, 3) Will the user associate the correct action with the desired effect, and 4) Will the user notice that progress is being made toward the final goal. If there are positive answers to all of the questions, then it can be determined that there are not any usability concerns at this stage.

Instrument: The evaluator will be asked to use the scenarios included in the attached document (see attachment "VIP HANA user scenarios with embedded symptom reports 05.05.17") as a guide to the goals and sub-goals that users of the system will have to successfully complete. The expert will be asked to document each step that they deem necessary to successfully complete the tasks in the user scenarios and then answer the four questions above for each of the tasks identified in the user scenarios.

Data Analysis: Answers to questions from the cognitive walkthrough will be evaluated to determine if any potential usability concerns have been identified. Specific comments and recommendations will be compared to those identified in the heuristic testing and any concerns will then be aggregated and summarized for presentation to system developers for improvements. For any negative responses to the questions, specific concerns and

recommendations will be recorded.

Usability Testing with PLWHA: After the initial two usability tests, we will perform usability testing with PLWHA to identify violations of usability principles and any potential obstacle to their effective use of the VIP-HANA system. This is an iterative process that involves testing the system and then using the findings to change it to better meet users' needs.

Sample: We will recruit 20 PLWHA with HANA conditions to participate in the evaluation of the VIP-HANA system.

Procedures: Initially, participants will be provided a brief explanation of the app and what it is capable of doing and then will be provided with the same set of scenarios detailing ways in which they might use the VIP-HANA app as well as the example versions of the symptom reports that are associated with the user scenarios (see attachment "VIP HANA user scenarios with embedded symptom reports 05.05.17"). Each participant will be asked to perform tasks which closely mirror the intended end use of the application. The process will be recorded using Morae software™ (Techsmith Corporation, Okemos, MI) (TechSmith, 1995) which allows the researcher to record and analyze the audio recording and screen shots that are captured. After the usability evaluation, participants will be asked to rate the prototype's perceived ease of use and perceived potential usefulness using standardized questionnaires. The instruments are described below and are included in the Appendix.

Instruments: We will measure self-reported ease of use and usability with the Health Information Technology (IT) Usability Evaluation Scale (Health-ITUES) (Davis, 1989; Yen, Wantland, & Bakken, 2010). This tool varies from most traditional measurement scales in that it is designed to support customization at the item level to match the specific task/expectation and health IT system while retaining standardization at the construct level. The Health-ITUES supports evaluation of three levels of task/expectation: user-system, user-system-task, and user-system-task-environment. Schnall has published on the usefulness of the Health-ITUES for evaluating the usability of mobile health technology (Brown, Yen, Rojas, & Schnall, 2013). End users will be asked the following four questions regarding the symptom report: 1) What are your initial thoughts when you look at the symptom report? 2) How can we modify the report to more appropriately meet your needs? 3) How can we modify these reports to effectively share information? 4) Do you have any additional feedback or comments that may help us to improve these reports? Please feel free to create any additional sketches that you think would help communicate your ideas.

Data Analysis: The analysis will be based on the Morae recordings of user sessions, transcriptions, notes, and the user surveys. The mean task performance time will be calculated. The research assistant under the guidance of Dr. Schnall will search for critical incidents (Andersson & Nilsson, 1964), an event that indicates something (positive or negative) about usability and review these in detail using Morae. These incidents and users' written comments will be summarized. Content analysis, a technique for making replicative and valid inferences from data, will be performed. The comments will be categorized according to the positive characteristics, negative characteristics, and recommendations made by the usability testers. Survey data will be analyzed using SPSS version 20.0 (IBM, Armonk, NY). Descriptive statistics will be calculated to complement the findings from the usability assessment. The result of these analyses will inform refinements to the VIP-HANA system for subsequent use in the RCT (Aim 2). The research team is experienced with these methods (Lee et al., 2011; Schnall, Kaufman, et

al., 2009; Sheehan et al., 2012).

Specific aim 2: Compare the efficacy of VIP-HANA to a control arm for ameliorating symptom frequency and intensity and secondary health outcomes in 100 PLWHA with HANA conditions over 6 months.

Setting and Sample

Eligibility Criteria:

In order to participate in the RCT participants must

1) Be diagnosed with HIV/AIDS
2) Self-report of at least one of the following co-morbid/HANA conditions: cardiovascular disease, liver disease, asthma, bronchitis, COPD, osteoporosis, diabetes, arthritis and/or renal failure
3) Age of 18 years or older
4) Able to provide written informed consent
5) Able to communicate in English
6) Report at least 8 symptoms. Possible symptoms include: fatigue or loss of energy, sadness/depression, muscle aches/pains, difficulty falling asleep, difficulty staying asleep, nervousness/anxiety, difficulty remembering, pain/numbness/tingling in hands or feet, trouble concentrating, decreased sex drive, diarrhea/loose bowel movement, difficulty achieving or maintaining an erection (males only), shortness of breath, constipation/bloating/gas, thirst/dry mouth, difficulty with balance/clumsiness/dropping things frequently, unplanned weight changes, dizziness/lightheadedness, heartburn/acid reflux, dry eyes, changes in appetite, ringing in ears or intolerance to noise, cough, nausea/vomiting, fevers/chills, sweats, difficulty with urination, speech difficulties, pain or discomfort during sex
7) Taking antiretroviral therapy (ART).

While we anticipate that HANA conditions will be more prevalent in persons over age 50, we have not limited our inclusion criteria to this age range. We are collecting participants' age and will include that as a covariate in our final analysis. If our results in Aim 1 demonstrate a gross difference in symptom reporting and self-care strategies related to age of participants then the study team and external advisory board will meet and consider revising the inclusion criterion of age for the RCT.

Exclusion criteria include: pregnancy, unable to understand the consent procedure, and self-reporting no symptoms within the previous week or concurrent participation in a mobile app study for PLWHA including text messaging studies and any clinical problems that would not allow someone to use a cell phone or fulfill study procedures including meeting the criteria for dementia. Prior to participating in any study procedure, all potential participants must voluntarily provide informed consent.

Sample: We will recruit 5 PLWHA with HANA conditions to participate in a pilot and 100 PLWHA with HANA conditions to participate in a 6-month trial (see recruitment plan). They will be told the purpose of the study is to improve the quality of life of PLWHA. Sample size and statistical power calculations are based on the hypothesis test of improvement of symptom status after the use of VIP-HANA and on the comparison of the effect of VIP-HANA to the control group.
The intervention group will have access to VIP-HANA, a web app that provides self-care strategies tailored to symptom reporting, HANA condition(s) and gender. Both the control and

intervention groups will receive reminders to complete their symptom assessments every week. Details of the difference between the study arms can be found in Table 2.

Table 2. Detailed Comparison of Intervention vs. Control Group		
	Intervention	**Control**
VIP-HANA: Self-care strategies tailored to symptom reporting, HANA condition(s) and gender	✓	
Symptom assessment every week	✓	✓
Secure messaging reminders to complete symptom assessment	✓	✓

The criterion for significance (alpha) has been set at 0.05 for the two-sided test. We will recruit 100 PLWHA with at least 1 HANA condition for the trial with a proposed sample size of 50 in each of the two groups. To account for a potential attrition rate of 20% by the end of study (week 26 or month 6 after the intervention), we propose to achieve a final sample of 80 patients (40 per group). Additionally, each patient will have a 20% chance to miss at least one of the symptom reporting points between week 2 and week 24 after the start of the intervention. We believe the 20% attrition assumption is conservative since our feasibility study had a 20% attrition rate we did not provide study participants with smartphones and data plans (Schnall, Wantland, Velez, Cato, & Jia, 2014).

The power calculation for this study is not based on the feasibility study effect size as this was a pre-post study design and does not present equivalency to this study design. The purpose of the feasibility study was to show that participants are willing to use the system and that there was some meaningful change in symptom reporting after use of the VIP system (Bowen et al., 2009). The power analysis for this study is calculated to detect a clinically meaningful change in symptom frequency. For symptom frequency outcomes, 100 subjects gives more than 80.7% power to detect 13% decrease in symptom frequency (for example, from an average 8 symptoms to an average 7 symptoms) from the baseline to the end of study (i.e., 26th week). For the comparison between the control group and the VIP-HANA group, 100 subjects gives 82.4% power to yield a statistically significant result (assuming an intention-to- treat principle for the analysis) to test 10% difference in VIP-HANA over the control group (i.e., a decrease in symptom frequency). For the symptom intensity outcomes, the proposed sample yields at least 92.3% power to detect decrease in symptom intensity score of a small effect size of 0.1 from the baseline to the end of study. For the comparison of the two groups, this study will have about 87.4% power to yield a statistically significant result to test a small effect size of 0.24 difference in symptom intensity score for the VIP-HANA group over the control group.

Procedures

Recruitment Plan: We will post flyers at local clinics and community based organizations throughout New York City. Potential participants will be pre-screened for eligibility over the phone by study staff. In order to ensure that an eligible participant arrives at their visit, they will receive a confirmation email for their baseline visit which will be generated by REDCap.

Pilot: We will conduct a recruitment pilot that enrolls 5 PLWHA with at least 1 HANA condition

before the 6-month trial. This pilot will allow us to determine ease and feasibility of recruiting PLHWA that have HANA conditions, as well as examining any issues there may be in retention and adherence with regard to usage of the VIP-HANA app. Those enrolled in the pilot will follow the same procedure (randomization, data collection) as those enrolled in the 6-month trial.

Trial: We will enroll 100 PLWHA with HANA conditions in a 6 month trial with a baseline, 3 month and 6 month measurement.

Randomization: This will be a single-blinded study, with subjects blinded to study group assignment. Patients will be randomized (1:1) to VIP-HANA or an attention control group. Both groups will receive secure messaging reminders via their smartphone and will also be asked to report their symptoms on their smartphone via a web app every week. Participants in the VIP-HANA (intervention) group will also receive symptom strategies tailored to symptom reporting, HANA condition(s) and gender. Details of the differences between the intervention and control group can be found above in Table 5 (see Section D.1.b).

Data collection: We will have two levels of data collection.

1) Participants will report on their symptom frequency and intensity every week on the VIP-HANA app. Participants in both groups will receive reminder messages to report symptoms every week via the revised Sign and Symptom Check-List for HIV delivered via email. If a participant has not completed the checklist in more than 3 weeks, he/she will receive a reminder email or phone call. Intervention arm participants will complete the revised Sign and Symptom Check-List for HIV every week and receive tailored self-care strategies based on their symptom reporting, HANA condition, and gender. Control arm participants will complete the revised Sign and Symptom Check-List for HIV, but will NOT receive strategies.
2) Participants will complete all secondary study-related questionnaires (see outcome measures below) via an electronic survey at baseline, at a 3-month follow-up visit (after 12 weeks), and at the end of the study at a 6-month follow-up visit (week 26). Participants will complete the study questionnaires at our study site. The survey will be housed on Qualtrics software which is a web-based survey program freely available to Columbia University Medical Center employees. Qualtrics provides a secure HIPAA protected environment. Participants will also complete physical measures at all 3 time points. Participants' height, weight, grip strength, and time taken to walk 15 feet will be measured. We will also abstract information from their medical records, such as CD4 counts and viral load, as indicated in the grant submission. In addition all participants will complete demographic information and other related measures including PHQ-2 (Hirshfield et al., 2008; Kroenke, Spitzer, & Williams, 2003), GAD-2 (Kroenke, Spitzer, Williams, Monahan, & Lowe, 2007), HIV stigma (Berger, Ferrans, & Lashley, 2001; Bunn, Solomon, Miller, & Forehand, 2007), health literacy (Weiss et al., 2005), eHealth literacy (Norman & Skinner, 2006), and perceived social support (Brock, Sarason, Sarason, & Pierce, 1996; Kalichman et al., 2006). In response to the reviewers' concern, all participants will complete the social desirability scale (Reynolds, 1982) which will be included in our final analytic model.

Participants will receive $25 for completion of study questionnaires at baseline, $35 at the 3-month follow-up visit, and $40 at the 6-month follow-up visit for completing the assessment tools. Each week that a participant completes a session of the VIP HANA app, they will be given $5 (26 weeks x $5/week = $130). If a participant does not miss more than 5 sessions, they will earn a bonus of $20. Participants are eligible for up to $250.

Outcome Measures. Our primary outcome measures, symptom frequency and symptom intensity, will be measured at baseline and every week for 26 weeks. We used the same study-

related questionnaires in our feasibility trial. Based on our feasibility trial, symptom reporting takes about 10 minutes to complete. The remainder of the assessment tools will either be collected only at the 3-month follow-up and the 6-month follow-up or baseline, 3-month follow-up, and 6-month follow-up. Completion of all surveys takes about 30 minutes (see Table 6 and the Appendix for details on the surveys). The UCSF School of Nursing Symptom Management Model (The University of California, 1994) is based on the premise that effective management of symptoms demands that three dimensions are considered: Symptom Experience, Self-Care Symptom Strategies, and the Outcomes (Dodd et al., 2001). The interrelatedness of these three dimensions of symptom management is not consistently taken into account in research (Figure 5) (Lenz, Pugh, Milligan, Gift, & Suppe, 1997).

Outcome Measures for Aim 2 RCT is listed in Table 3 below:
Primary outcome: The primary purpose of the intervention is to improve symptom status. We hypothesize that VIP-HANA will improve symptom frequency and intensity, our primary outcomes.

Secondary outcomes: The potential benefits of the intervention are quite broad, so multiple secondary outcomes are of interest (see Table 3). As a result of improving symptom status and frequency among PLWH, several other factors that contribute to a subject's overall well-being may be affected. Changes in symptom status should have an effect on secondary health outcomes including quality of life, frailty, adherence to ART, and system use. Importantly, symptom burden has been identified as a predictor of ART adherence (Gay et al., 2011). Unlike treatments for other illnesses, ART medications are more likely to contribute to greater discomfort and treatment discontinuation (Chesney, Morin, & Sherr, 2000). As a result it is not surprising that only 25% of PLWHA in the US are virally suppressed. Therefore symptom management is of critical importance for improving clinical outcomes in PLWHA and of public health importance (Services, 2014).

Table 3. Outcome Measures

Outcomes	**Tool**	**Collection Time**
Primary: *Symptom Status*	The revised Sign and Symptom Check-List for HIV (SSC-HIVrev)(Holzemer, Hudson, Kirksey, Hamilton, & Bakken, 2001)	Every 1 week
Secondary Outcomes		
Quality of Life	Medical Outcomes Study Standard Form (SF 12) (Ware, Kosinski, & Keller, 1996)	Week 0, 3-month follow-up, 6-month follow-up
Engagement with Health care Provider	Engagement with Health care Provider Scale (Bakken et al., 2000)	
	Number of healthcare visits	Medical Record

CD4, Viral Load	Clinical outcomes	Abstraction
ART Adherence	Visual Analogue Scale Self-report (VAS) (Arnsten et al., 2001; Chesney, Ickovics, et al., 2000; De Costa et al., 2010; Walsh, Mandalia, & Gazzard, 2002)	Week 0, 3-month follow-up, 6-month follow--up
Frailty	Fried's Frailty Phenotype (Brothers et al., 2014; Fried et al., 2001); Used in numerous HIV-related studies (Desquilbet et al., 2007; Desquilbet et al., 2009; Piggott et al., 2013)	
System Use	Log Files	Automated

We are paying particular attention to the symptom experience of the study participants over time, the components of the symptom management strategies (e.g. content and frequency of use) through log files, and symptom status as our primary outcome but multiple secondary outcomes are also of interest. Of particular relevance, one of the assumptions of the model is that once symptoms have been successfully addressed then the secondary outcomes should show improvement. Findings from our RCT will inform this hypothesis.

Data Management and Analysis: All survey data will be stored on a secure server. All multivariate analyses will be preceded by standard descriptive statistics to profile participants in each study group and to examine distributions of all outcome variables and to identify outliers. Descriptive statistics (i.e., means, standard deviations, frequencies, and percentages) will be used to examine demographic characteristics of the sample and the frequency and intensity of the symptoms. We will use intention-to-treat principles for the primary outcome analysis.

Intention to treat implies all subjects are considered in analyses. Linear mixed model and generalized linear mixed model (negative binomial model) will be used for the analysis of symptom intensity outcomes and symptom frequency outcomes, respectively. Linear and generalized linear mixed models are statistical models that are particularly well suited to analyze repeated measured symptom data. This method does not require equal waves of data and allows missing outcome measures during the course of the study. This is an attractive method for longitudinal analyses, where participant attrition can be a problem, because participants often drop out and return for later follow-up or drop out entirely. Therefore, it is useful in retaining power in statistical analyses. The mixed models incorporate correlation between the reports of symptoms as these reports are measured from the same subject repeatedly over time and can account for this correlation for the model inference (Ugrinowitsch, Fellingham, & Ricard, 2004). An assumption for using linear and generalized linear mixed model methods is that the cases missing to subsequent follow-up assessments are missing at random. If missing data is related to intervention assignment or symptom outcome, we will estimate the probability of not missing a data point (i.e., the probability of reporting symptom) and include the inverse of this probability in the model as a selection weighting factor to correct for bias due to missing data.

For analysis of secondary outcomes, if the outcomes are measured more than once, we will use

linear and generalized linear (logistic or negative binomial model) mixed model. If the outcomes are measured only once, we will use linear or generalized linear model. We will also asses any net benefits in the patients' report of their healthcare provider's engagement with their treatment and care, quality of life, frailty, ART adherence and biological outcomes (CD4 and viral load). Analysis of additional hypotheses includes assessment of differences in the self- care strategy used to help alleviate a symptom and the recorded level of intensity following the strategy use will also be assessed. Based on the Symptom Management Model, we anticipate that VIP-HANA will be effective at improving symptom status and then we will see a positive change in our secondary outcome measures: quality of life, frailty, ART adherence, and CD4/ viral load.

Specific Aim 3: Understand PLWHA's perceptions of the predisposing, enabling, and reinforcing factors for VIP-HANA use with theoretically-guided focus group sessions.

The goal of these focus group sessions is to understand the experience of PLWHA using the VIP-HANA system. The adaption of this model for HIT was originally developed by Kukafka et al. (2003). Dr. Schnall has used this model in previous studies to understand the barriers and facilitators to implementation of health information technology systems (Schnall, Clark, Olender, & Sperling, 2013; Schnall, Gordon, Camhi, & Bakken, 2011). If VIP-HANA is found to be efficacious in our trial, then our follow-up focus groups will inform dissemination and implementation of the VIP-HANA intervention. If the intervention is not efficacious then we will learn why participants did not find the intervention to be useful or improve their outcomes.

Sample: Post-intervention, we will conduct five focus group sessions with approximately 6-12 participants per group. Focus group participants will be drawn from the VIP-HANA group (intervention arm) and the attention control group. We anticipate that 60 participants will agree to participate in the follow-up focus groups.

Procedures: The focus groups will be 60-90 minutes in length. We will include $30 reimbursement for participants' time. Following completion of the informed consent process, all focus group sessions will be audio-recorded. The PI, who has conducted focus groups for a number of studies in the past, will convene the groups with the study participants and will act as a facilitator (Lee et al., 2011; Okoniewski, Lee, Rodriguez, Schnall, & Low, 2013; Schnall et al., 2013; Schnall, Kaufman, et al., 2009; Schnall, Odlum, Gordon, & Bakken, 2009). The focus group guide will be informed by the Predisposing, Reinforcing, and Enabling Constructs in Evaluation (PRECEDE) portion of the PRECEDE- PROCEED Model of health program planning and evaluation (Green, Kreuter, Deeds, & Partridge, 1980). The integration of these frameworks for application in HIT implementation evaluation has been proposed by a number of authors as a strategy for assessing predisposing, enabling, and reinforcing factors for use and acceptance of HIT (Kukafka et al., 2003; Schnall et al., 2011). Sample focus group questions are: 1) Describe your use of the VIP-HANA system 2) What are some of the ways that your overall health benefited through the use of the VIP-HANA system (reinforcing factors)? 3) What were the barriers to your use of VIP-HANA in your everyday life? (predisposing factors) 4) What are your ideas about strategies for overcoming these barriers? (enabling factors) 5) What did you perceive as useful about the VIP-HANA system? (predisposing factors) 6) How would you envision VIP-HANA being used in your everyday life? (implementation) 7) How do you imagine that VIP-HANA would be shared with others PLWHA? (dissemination) 8) Any there any other thoughts about your experience using the VIP-HANA system that you would like to share?

The team will adhere to qualitative research processes to ensure the credibility, confirmability, dependability and transferability of the qualitative data from these analyses. To support

the credibility of the data, we will conduct peer debriefing and triangulate findings across multiple data sources (surveys, focus group data). In addition, we will use “member checks,” i.e., sharing of initial data interpretations with participants, to ensure accurate interpretations. Triangulation of findings, along with reflexivity, will enhance the confirmability of the interpretations. The investigators will carefully record an audit trail and keep extensive field notes to facilitate transferability of study findings into other contexts (Guba, 1981). Each focus group recording will be transcribed; transcripts will be analyzed independently for content by research team members.

Data Analysis: Field notes and transcripts will be analyzed by the researchers using NVivo™ (QSR International, Victoria, Australia) software. Participants’ statements will be captured using memoing and then sorted into the following categories of interest: predisposing, enabling, and reinforcing. These activities will result in a greater understanding of the use, usefulness, dissemination and implementation of VIP-HANA.

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