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Smoker-to-Smoker (S2S) Peer Marketing and Messaging to Disseminate Tobacco Interventions

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RESEARCH STRATEGY

A. BACKGROUND

Acronyms Used	
S2S	Smoker-to-Smoker
Decide2Quit	www.decide2quit.org
DISC	Digital Intervention for Smoking Cessation
CTHC	Computer-tailored health communication

A.1. Overview

Building on our PCORI pilot (1IP2P1000582)[1,2] and National Cancer Institute (NCI) funded studies (R21CA158968, 1R01CA129091),[2-8] we propose "**Smoker-to-Smoker (S2S) Peer Marketing and Messaging to Disseminate Tobacco Interventions.**" S2S will test two smoker-driven, social marketing innovations to recruit and engage smokers in Decide2Quit, an evidence-based, effective "Digital Intervention for Smoking Cessation" (DISC).[5,9] These S2S innovations, designed to utilize the power of peers and social networks for dissemination are:

1. **Recommender computer tailored health communication (recommender CTHC):** Complex machine learning algorithms (recommender systems) that uses smokers' feedback (explicit and implicit) in the current and prior studies to adapt its selection of messages to smokers (PCORI IP2P1000582).
2. **Access to peer recruitment toolset:** Access to peer recruitment tools to facilitate dissemination of the trial (recruitment) – with smokers' recruiting their peers to increase Decide2Quit access (NCI R21CA158968).

Thus, this study is a hybrid effectiveness-dissemination study. First, to test the *effectiveness* of the recommender CTHC, smokers will be recruited online to a randomized trial hosted on Decide2Quit.[10] Smokers will be consented and randomized to receive either the recommender CTHC (the enhanced intervention) or a standard tailored messaging system (the comparison). Second, to test *dissemination* (after randomization to the enhanced or comparison messaging system), some randomized and enrolled smokers will be further allocated to receive access to peer recruitment tools; and these smokers will be encouraged to recruit other smokers in their social network. Allocation to receive the peer recruitment tools occurs in two phases or waves (Wave 1: Half of the enrolled smokers are randomized to receive peer recruitment tools, while the others do not receive the tools; and Wave 2: all subsequent smokers who are randomized to the effectiveness trial and also report they were peer-recruited are given access to the peer-recruitment tools. This two-wave allocation follows principles of respondent driven sampling, as is designed to increase both 1) the **Speed** of dissemination, and 2) the **Diversity** of smokers recruited. Note that in a prior NIH-funded pilot study, we found peer recruitment was particularly effective for engaging African American smokers. Thus, we will also test the potential of peer recruitment to target African American smokers, a disproportionally affected group due to tobacco use, compared with online recruitment without peer recruitment, in this dissemination study.[11-17]

A.2. Condition impact (smoking) on health of individuals and populations (Criterion 1)

Smoking is the number one preventable cause of death in the United States (USA).[18-22] Yearly, over six million deaths in the world are attributable to smoking, including 480,000 in the USA.[23] The CDC estimates that for every person who dies because of smoking, at least 30 people live with a serious smoking-related illness, including cancer, heart disease, stroke, lung diseases, diabetes, and chronic obstructive pulmonary disease (COPD).[23] One estimate suggested that the proportion of USA health care expenditure attributable to smoking ranges between 6-18% of the budget across different states.[24] The cost per life year saved from use of pharmacological treatment interventions ranged between US$128 and US$1,450 and up to US$4,400 per quality-adjusted life years saved.[24] As noted in Section B.3., African Americans are disproportionately affected by tobacco and many of their health issues are directly related to their tobacco use.[11-17] Thus, reducing tobacco use will have considerable health impact, and play an important role in reducing health disparities.

A.3. Evidence gap (RQ-1)

Our proposal addresses a key question — *What are the effective strategies for increasing consumer demand for and use of proven, individually oriented cessation treatments, including among diverse populations?* — raised in the State-of-the-Science Conference Statement on Tobacco Use.[25] We are focused on identifying effective strategies to disseminate and improve effectiveness of a DISC — www.decide2quit.org (Decide2Quit). DISCs are health communication programs accessible via Internet connections and smart phones. DISCs can include a number of functions designed to support a smoker's cessation attempt. As detailed in Table 5, Decide2Quit includes self-management functions, pushed and tailored motivational messages (email or text-messages), online community, and peer support. Several studies, including systematic reviews,[26-28] have shown that DISCs can be effective. A Cochrane review found a statistically significant effect comparing tailored DISCs to usual care or written self-help (RR 1.48, 95% CI 1.11, 2.78).[28] Although this evidence is mixed, two factors are typically associated with the effectiveness of DISCs.[20,26-36] These include the use of CTHC to personalize messaging to smokers, and the engagement of smokers (recruitment and repeated system use). In our previous randomized trial [1R01CA129091] testing Decide2Quit (n=900), at 6-months, 30% of smokers who received the CTHC

messages reported quitting at 6 months compared to 20% of smokers who received an interactive DISC but no messages [odds ratio 1.70 (95% CI 1.03-2.81)].[10] We have also demonstrated that the repeated use of Decide2Quit functions was significantly associated with six-month, 30-day point prevalence cessation. Using a repeated use measure — an ordinal scale of the number of functions used after the first visit to the website (0: use of no functions, 1: use of 1-2 functions, 2: > 2-4 functions) — we found a linear association with six-month cessation. For every increase by one in this scale, odds of smoking cessation increased (OR= 2.10, 95% CI = 1.03, 4.30).[37] In conclusion, DISCs can be an effective resource for smokers, but the success depends on the implementation of CTHC, and the longitudinal engagement of smokers.

Outside healthcare, companies have innovated to use bottom-up, "user-driven" approaches to increase their websites' access and engagement. Peer marketing — engaging one customer to recruit others — has become the preferred approach to increase access to their websites. To motivate users to repeatedly use their system, companies like Amazon and Netflix Use recommender systems to deliver enhanced personalization (Section B.5). **However, these tools have not been rigorously tested for disseminating health interventions in comparative effectiveness studies.** In our prior studies [PCORI IP2P1000582, NCI R21CA158968], we have developed and demonstrated the efficacy of peer recruitment and recommender CTHC to disseminate Decide2Quit — recruit and motivate smokers to repeatedly use the system — and improve its effectiveness. We will rigorously test these tools in a comparative effectiveness study, compared with the standard Decide2Quit (online recruitment and standard CTHC). In the RFA, PCORI defines dissemination as the active and targeted approach of spreading evidence-based interventions to potential adopters and the target audience through determined channels using planned strategies, and its goals as to increase the reach of information, motivation, and patients' ability to use and apply evidence.[38-40] Thus, both recruitment and use measures are needed to appropriately evaluate our DISC dissemination strategy. If recruitment is unsuccessful, then the intervention's reach is low. If recruitment is successful, but the intervention does not motivate repeated use, then there is low intervention fidelity, reducing the patient's motivation and ability to apply evidence. Beyond measuring dissemination, the primary goal of this RFA, we will evaluate our interventions' effectiveness by measuring six-month cessation (as recommended by prior reviews), and measuring reduction in cigarettes, as advised by our patient panel.

B. SIGNIFICANCE

Because prior literature and our own preliminary data suggest multiple barriers in the reach of smoking cessation interventions, including those online, new approaches to increasing dissemination are needed.[41] The majority of smokers are not interested in quitting at any given time.[42] Even those highly motivated to quit often fail in their attempts.[43] Peer recruitment and recommender CTHC are unique in that they harness the power of smokers to disseminate a cessation intervention (recruit and motivate to repeatedly use), and encourage cessation. In this section, we describe the potential impact and reach of DISCs, potential to target those most in need, and the two patient-centric and patient-driven S2S innovations (peer recruitment and recommender CTHC), including their theoretical foundations.

B.1. Impact of DISC (Impact = Reach × Effectiveness)

Per the RE-Aim framework,[44] an intervention's impact is a product of its reach and effectiveness. Although in-person and telephone counseling are effective, they are costly and **underused** (reducing their reach). DISCs can serve as important augmentation for those receiving in-person and telephone counseling (to use in between sessions and for longitudinal support). For those who do not have access to these options, DISCs may serve as the only source of tobacco cessation support. As noted, Decide2Quit achieved a cessation rate of 30% at six months, much higher than the rate (7%) at which smokers quit without support.[45] Thus, it is important to innovate and increase dissemination and effectiveness of DISCs.

B.2. DISCs: Internet, Social Media Use, and Digital divide

DISCs are health communication programs readily accessible via the Internet and smart phones. Thus, it has considerable potential to reach a large and diverse group of smokers. In 2014, an estimated 87% of Americans had Internet access.[46,47] Digital divide in Internet access has decreased considerably, especially with increasing smart phone use. In 2015, an estimated 61% of Whites, 70% of African Americans, and 71% of Hispanics had smart phones. Most of these smart phone users had accessed a wide range of functions, including getting information about a health condition (62%) and online banking (57%). The use of online functions on smart phones is higher in lower income than higher income users.[48] Use of social media has also considerably increased.[49] Over 74% of USA Internet users use online social networks including 71% that use Facebook. Again, smart phones have decreased the digital divide in use of social networks. A higher proportion of African Americans (48%) and Hispanics (49%) access social networks on their phones than Whites (36%).[48]

However, because of this lingering perception that vulnerable populations have little technology access, these populations are underrepresented in technology research. It may not be the lack of technology access, but that the dissemination strategies have not sufficiently evolved to engage these groups.

B.3. Increasing Reach of DISCs to African American Smokers

We focus on African American smokers for several reasons: **1)** These smokers suffer disproportionately due to smoking-related diseases including several cancers, cardiovascular disease, and cerebrovascular disease.[11-17] Although they smoke fewer cigarettes and start smoking at an older age, these smokers are more likely to die from smoking-related diseases than Whites.[11] They are less likely to be successful at quitting than White or Hispanic smokers because they are less likely to seek cessation support, including DISCs.[11-14] **2)** The standard CTHC in Decide2Quit successfully motivated African Americans smokers to quit (Section C.4.1.2). **3)** Our NCI funded pilot demonstrated that peer recruitment significantly enriched the sample with African American smokers (11-23%) (Figure 4). This increase happened without our tools prompting the peer recruitment of African American smokers. In S2S, with our patient advisory panel (See Section F), we will further refine our instructions to encourage African American smokers' recruitment. Thus, we anticipate an even higher increase in proportion of African American smokers in S2S.

B.4. Smoker-to-Smoker (S2S) peer recruitment: Peer-referrals as an online marketing Strategy

Health information and healthy behaviors can be "infectious" — spreading between social contacts, creating cascading effects throughout the network.[50,51] For example, over time, smokers in the Framingham cohort were less likely to smoke if someone in their network (spouse, sibling) had quit smoking.[51] Public health interventions can use these infectious effects by using engaged smokers to recruit their peers who smoke.[52,53] Peer recruitment leverages current online marketing trends. Outside of public health, several marketing groups are using peer recruitment to enhance spread of products for a number of reasons. Customers are more likely to trust a peer referral than traditional advertisements.[54] Peer recruited customers are also more profitable than traditional customers.[54] There are several examples of successful peer-marketing (e.g., Zynga, the online social gaming company) on social media.[2,3] To enhance the effectiveness and efficiency of these campaigns, companies have developed a more proactive approach, providing customers referral tools that allow them to easily refer others to the product (e.g. email referral form).[55] As detailed in Section C.4.2.1, the use of Facebook referral plugin in our peer recruitment system[4] was an example of this approach. Our peer recruitment experiment (NCI R21CA158968) to test whether smokers would recruit other smokers was successful. In a one-year period, peer recruitment quadrupled our sample —from 190 smokers to 759 smokers.[3,56] Peer recruitment also increased proportions of not ready-to-quit and African American smokers (11-24%), groups that other recruitment techniques have had difficulty encouraging participation. .

B.5. Computer-tailored health communication (CTHC): Standard and S2S recommender

Standard "if-then-else" theory-based CTHC systems: Theory-based CTHC is a tool that is frequently used to support behavior change. [57] It builds on the concepts of personal relevance, relatedness, and cultural similarity, constructs of multiple behavioral theories including the transtheoretical model, the theory of reasoned action, social cognitive theory, and self-determination theory.[58-60] Standard CTHC systems use selected variables from patients' baseline profile and if-then rules to send tailored messages to specific subsets of patients. [57,61-65] These rules are developed by experts based on their knowledge of the targeted population, literature, and health behavior theories. These rules specify how the messages should be selected (what messages need to be sent to that patient subset). Table 1 illustrates how a standard CTHC system might tailor a message as part of a smoking cessation intervention.[66]

Table 1: **An Example: Tailored messages addressing weight gain on DISC.***

John Smith, a 38 year old smoker, has been smoking for 15 years. He has made multiple quit attempts in the past, but during each attempt he gained between 10 and 20 pounds. Currently, fear of weight gain is a significant barrier to another quit attempt.

John is trying to quit again and registers on Decide2Quit. For eight weeks, the system sends two tailored emails per week to John Smith to help him quit.

Standard CTHC

In this approach, tailoring is based on information that John provides when he registers. For this example, we focus on one characteristic only: gender. Since women are typically more concerned about weight gain after quitting,[67-71] experts have specified that half of the emails sent to women should contain information related to weight gain, but only one quarter of the emails sent to men should be focused on weight gain. After registering on Decide2Quit, John receives the first email that targets weight gain support in the second week (3rd message) of the intervention. John likes the message and finds the tips it offers useful. He looks forward to receiving similar messages. However, the next 5 messages he receives focuses on other topics. The next weight gain message arrives only on week 5.

John does not think the system helped and fails in his attempt to quit.

Recommender CTHC

In this approach, the selection of the message is based upon the collective-intelligence data, not on preset rules. After registering on Decide2Quit, John visits the weight gain support page on the website (implicit data). The system uses this data and selects one of the messages targeting weight gain and sends it to John on Week 2 (3rd message). John likes the messages and rates the message highly (explicit data). The system then notes both of these items of implicit and explicit feedback and regularly sends messages targeting weight gain to John. The system also repeats the message that John rates highly. Because the intervention targeted his needs more specifically, John finds these messages useful and succeeds in his attempt to quit.

**This example was kept simple to be easily understandable. We have not included how the group's feedback can help John.*

Recommender CTHC systems: New approaches to tailoring based on collective-intelligence may be able to augment standard CTHC systems. Many people already encounter collective-intelligence tailoring as they interact with companies like Netflix and Amazon. These companies use a special class of machine learning algorithms (**recommender systems**) to tailor content. These systems tailor content based on collective-intelligence data (i.e., data derived from the behavior of users as they interact with the system) in addition to user profiles.[72-74] Collective-intelligence data include implicit and explicit user feedback. Implicit data are derived from user actions (e.g., website pages and products purchased data). Explicit data consist of self-reported item ratings (e.g., ratings provided by users for items like books or movies, often on a five-star scale). However, in the health promotion arena, patients could be asked to rate relevance, influence, or other properties of a message or product. Using these data, along with user demographic characteristics, the algorithms underlying the recommender system generate personalized item recommendations for each user. As these recommender systems learn more about the user, they can continually adapt to improve the recommendations.

Table 2: Standard CTHC vs. Recommender CTHC[66]

Feature	Standard CTHC	Recommender CTHC
Message Selection **(Primary Difference)**	**Rules-driven:** Experts develop rules based on the literature and theory. These rules link user profiles to the messages, selecting messages for a patient subset.	**Data-driven:** Recommender systems derive the tailoring rules from the collective-intelligence data of the individual, as well as the group.
Complexity (Number of variables)	The number of variables incorporated can become quickly unmanageable dependent on the programming team's skills, project's timeline and budget.	Recommender systems can potentially consider all the variables collected in the intervention.
Use of theory	Tailoring limited to theoretical constructs	Augments theory by deriving recommendations from user data
Adaptation	Limited to predicted changes in behavior.	System can continuously adapt, potentially improving with each message delivered. Responds to the user's behavior and to the group's behavior over time.

The lower portion of Table 1 provides an example of how a recommender system could be implemented to provide tailoring as part of smoking cessation intervention. It shows how applying a recommender approach to health promotion could potentially improve upon the tailoring provided by current rule-based CTHC approaches. The primary difference between current and recommender CTHC systems is how the messages are selected. In standard CTHC, message selection is based on preset expert-written if-then-rules. In recommender CTHC, messages selection is based on data, i.e., recommender systems learn from the data (patient profiles and implicit and explicit feedback ratings) to select the variables and generate the rules that specify how the message will be selected. As new data about the users are collected, these recommender systems have the ability to refine the message selection algorithm. As summarized in Table 2 and detailed in our paper,[66] there are a number of other potential advantages of using recommender CTHC over standard CTHC systems. Our pilot experiment (Section 4.2.2) demonstrated that the recommender CTHC performed better than Decide2Quit's standard CTHC, a demonstrated to be effective system, even over a short duration of 30 days.

B.6. S2S Theoretical Foundations — Relatedness and personal relevance to increase engagement and motivation:
Peer recruitment: By providing peer recruitment tools to smokers, S2S facilitates smokers to reach out to their peer smokers to participate in a cessation intervention, thereby extending the intervention's reach. Peer recruitment draw strength from the constructs of relatedness, as proposed in self-determination theory (SDT).[75] Relatedness between individuals — the desire to feel connected to others — can support behavior change. [75,76] When individuals engage in activities that are social in nature, such as providing social support, perceptions of relatedness play an important role in predicting motivation and increasing engagement.[77] Thus, both the peer recruitment act, and being peer recruited, might motivate the smoker to use the DISC, and quit smoking.

Recommender CTHC: Recommender CTHC draws strength from personal relevance, relatedness, and cultural similarity, constructs of multiple behavioral theories (Table 3). Increasing the personalization of a message, increases the relevance and relatedness of the message to the user.[57] Personally relevant messages are more carefully processed, tend to be retained longer, and more predictive of behavior change.[78] By incorporating smoker's feedback, the recommender CTHC is able to adapt and continuously improve the personalization of its messages, which can increase the DISC's use, as well as cessation outcomes**.**

Table 3: The importance of personalization across multiple theories[59]

Methods	Description	Theories
Persuasive Communication	Messages relevant to individual's beliefs	Persuasion-Communication Matrix, Elaboration Likelihood Model, Social Cognitive Theory
Tailoring/ Individualization	Targeting messages based on behavior change and/or relevance variables	Transtheoretical Model, Precaution Adoption Model, Protection Motivation Theory, Persuasion-Communication Matrix

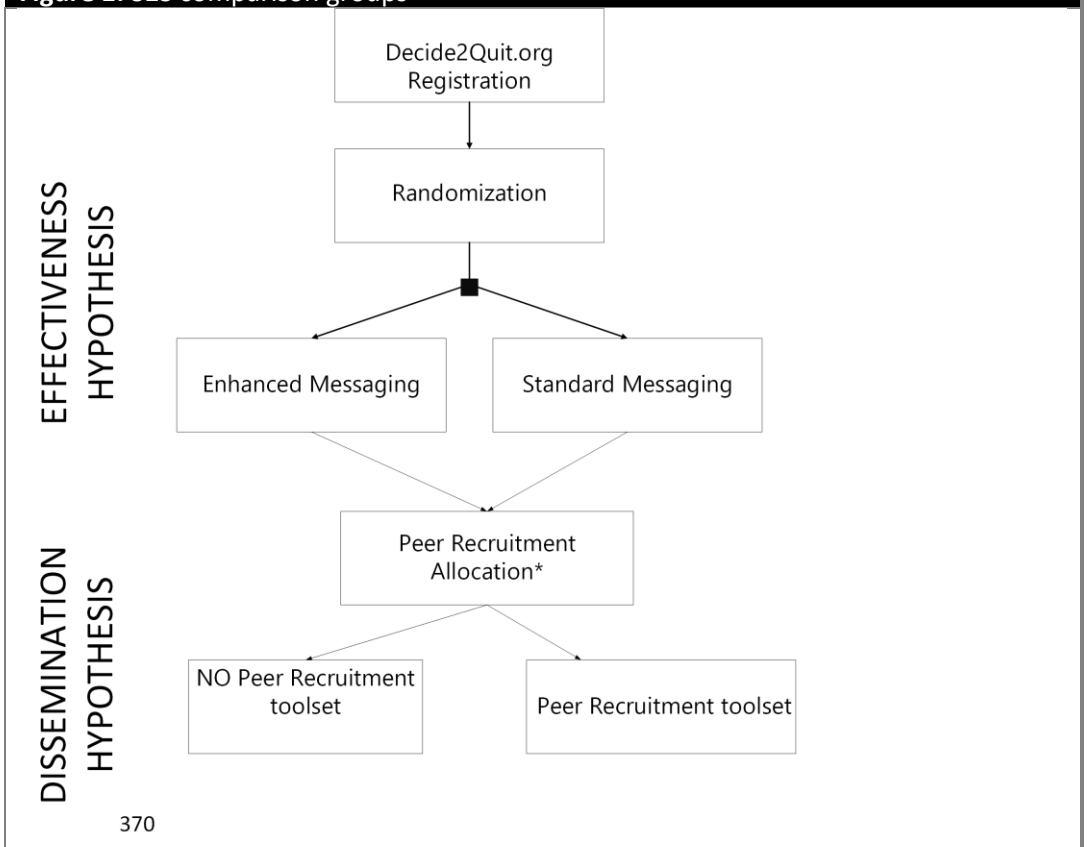
In conclusion, our prior work has demonstrated the benefit of each S2S function, and in S2S, we will test the dissemination potential of these functions in a hybrid effectiveness-dissemination trial.

C. STUDY DESIGN
Using a study design that includes both randomized and non-randomized elements, we will evaluate S2S. Our specific Aims:

C.1. Specific Aims: (Criterion 3)

AIM 1: Implement the hybrid effectiveness-dissemination trial of S2S enhanced functions to increase dissemination (recruitment and repeated use) and effectiveness of Decide2Quit with 1200 smokers (See **Figures 1a and 1b**).

Figure 1: S2S comparison groups



*Allocation to receive the peer recruitment tools occurs in two phases or waves (Wave 1: Half of the enrolled smokers are randomized to receive peer recruitment tools, while the others do not receive the tools; and Wave 2: all subsequent smokers who are randomized to the effectiveness trial and also report they were peer-recruited are given access to the peer-recruitment tools.

Effectiveness Trial Components (Figure 1a):

1. **Recommender computer tailored health communication (recommender CTHC):** Complex machine learning algorithms (recommender systems) that uses smokers' feedback (explicit and implicit) in the current and prior studies to adapt its selection of messages to smokers.
2. **Standard computer tailored health communication (CTHC)** using expert-written rules to tailor messages to smokers based on a single factor readiness to quit.

Dissemination Study (peer recruitment, Figure 1b):

1. **Access to a peer recruitment toolset:** to facilitate smokers' recruiting their peers to increase Decide2Quit access.
2. **No peer recruitment:** standard online recruitment using search engine and social media advertisements to recruit smokers to Decide2Quit.

As noted above, as the study is enrolling, we will evaluate the potential of peer recruitment to 1) increase the speed of dissemination, and 2) enhance the diversity of smokers recruited. Related to the Dissemination Study, we have the following hypotheses:

H1: Recruitment

H1A: Enhancing Diversity: Peer recruitment will recruit a greater proportion of African American smokers, compared to standard online recruitment.

H1B: Increasing the speed of recruitment: Peer recruitment will reduce recruitment time (time to recruit each participant), compared to standard online recruitment.

Further, as the study progresses, we will monitor the use of the Decide2Quit.org online system.

Note that both the recommender CTHC and the peer recruitment tools are designed to increase engagement with Decide2Quit.org. Thus, we propose that the recommender CTHC and peer recruitment tools will be synergistic. To test the potential for increased engagement, we propose the following hypothesis:

H2:* Increased Engagement (use of Decide2Quit functions over time).

H2A: Repeated use among those exposed to the fully enhanced group (access to peer recruitment toolset and recommender CTHC) will be greater than repeated use among those exposed to: a) peer recruitment toolset only b) recommender CTHC with no peer recruitment toolset and c) standard group (no peer recruitment toolset and standard CTHC).

H2B: Repeated use among those exposed to peer recruitment toolset will be greater than repeated use among those exposed to the standard group.

H2C: Repeated use among those exposed to recommender CTHC will be greater than repeated use among those exposed to the standard group.

Thus, we have preliminary hypotheses for dissemination (H1) and engagement (H2). The main effectiveness outcome is described below in Aim 2.

AIM 2: For the Effectiveness randomized trial, we will recontact participants after six months of enrollment. Compared to the standard messaging group, the recommender CTHC is designed to increase smoking cessation rates at follow-up. Thus, we hypothesize the following hypotheses:

H3: * Quit — six month, 7-day point prevalence biochemically verified — and **risk reduction** in number of cigarettes smoked (patient panel recommended outcome).

H3A: Quit rates among those exposed to the fully enhanced group (peer recruitment toolset and recommender CTHC) will be greater than quit rates among those exposed to a) peer recruitment toolset only b) recommender CTHC only and c) standard group (no peer recruitment toolset and standard CTHC).

H3B: Quit rates among those exposed to peer recruitment toolset will be greater than quit rates among those exposed to the standard group.

H3C: Quit rates among those exposed to recommender CTHC will be greater than quit rates among those exposed to the standard group.

H3A, H3B, and H3C will be tested for the risk reduction outcome also.

**For H3, we will compare all smokers across the groups, and African American smokers across groups, and African American and White smokers for assessing heterogeneity of treatment effects.*

TABLE 4: S2S standard and enhanced groups (Criterion 3)

		Standard		Enhanced	
		Recruitment	**Tailoring (CTHC)**	**Recruitment**	**Tailoring (CTHC)**
A	**Fully Enhanced S2S**			Access to peer Recruitment toolset###	recommender CTHC*** (pushed motivational messages via email and text)
B	**Half Enhanced** Recommender CTHC only	Standard Online recruitment via search engine and social media advertisements (no access to Peer Recruitment Toolset)			recommender CTHC*** (pushed motivational messages via email and text)
C	**Half Enhanced** Peer Recruitment toolset only		Standard CTHC*** (pushed motivational messages via email and text)	Access to peer Recruitment toolset###	
D	**Standard Comparator**	Standard Online recruitment via search engine and social media advertisements (no access to Peer Recruitment Toolset)	Standard CTHC*** (pushed motivational messages via email and text)		

Peer recruitment starts with the online recruitment of seeds. Peer recruited smokers will be in the same group as their recruiters to minimize contamination.
****The recommender CTHC adapts to influence ratings provided by current participants in the study (See Section C.4.2.2). Each message will include a link to rate the message. Although our standard CTHC does not adapt to this feedback, we will include the ratings question in the standard CTHC groups to minimize differences between the two systems.*

C.2. Study Design: This hybrid effectiveness-dissemination trial uses a combination of study designs. The effectiveness study is a two-group randomized trial comparing the recommender CTHC (enhanced intervention) with standard messaging (comparison). For the dissemination trial, allocation occurs in two waves (as described in Figure 1b). Allocation to receive the peer recruitment tools occurs in two phases or waves (Wave 1: Half of the enrolled smokers are randomized to receive peer recruitment tools, while the others do not receive the tools; and Wave 2: all subsequent smokers who are randomized to the effectiveness trial and also report they were peer-recruited are given access to the peer-recruitment tools.

Also as noted above, all Decide2Quit functions (Table 5) will be available to all groups. Our goal is to test the enhancements offered by peer recruitment and recommender CTHC (individually and collectively). **(RQ-2)**

Table 5: Major Components of Decide2Quit

Component	Description
Online Community	Interact with peer smokers through a resource website
Health Risks	Information about specific health risks of smoking
Thinking About Quitting	Helpful ideas and motivational recommendations (e.g: interactive calculators assessing triggers, decisional balance)
Family Tools	Tips to get help family support, and deal with nagging,
Provider Tools	Tips to include healthcare provider in the quit plan
The Library	Library about smoking risks and treatments
Web Resources	We've identified valuable additional websites

Online Randomization: In our prior technology-assisted randomized trials, we have embedded randomization within the technology, and we will use a similar approach in S2S for the effectiveness trial. As smokers register on the website, they will be allocated to the four comparators based on a block-randomization allocation table integrated into the website. Our statistician will generate a randomization table; the randomization sequence will be conducted in random blocks of different sizes (8, 12) to ensure balance among the groups and reduce predictability of allocation process. Thus, randomization will occur automatically at the time of initial registration. For the dissemination study, the initial randomization (see description of Wave 1 allocation above) will occur after randomization to recommender CTHC or comparison, and will also use the online randomization technology.

C.3. Identify, select, recruit, and retain study participants: In Aim 1, we will recruit 1200 smokers online. In S2S, recruitment is part of the experiment. Smokers will either be recruited through online advertisements or by peer recruitment as further detailed below. **(PC-2)**.

C.4. Comparators: (RQ-5)
Smokers in all groups will be given access to all of the primary Decide2Quit functions (Table 5). We describe the comparators below.

C.4.1 Standard Functions

C.4.1.1. Standard Online recruitment via search engine and social media advertisements:

Smokers will be recruited online using search engine advertisements. These advertisements will be customized to appear to smokers searching for quit smoking related search terms online. When smokers click on these advertisements, they will be redirected to Decide2Quit, where they will be provided study information and registration instructions. We will use the functions provided in the ad managers of the search and social media websites to target ads for smokers. For example, the Facebook ad manager allows advertisers to target users based on their interests derived from their profile's keywords, pages they like, and groups they visit. Advertisements will be displayed on the Facebook page of the user. We will work with our patient advisory panel to identify relevant interests, as well as create advertisements with content that will be attractive to smokers. We will continuously monitor and refine these advertisements with our patient panel.

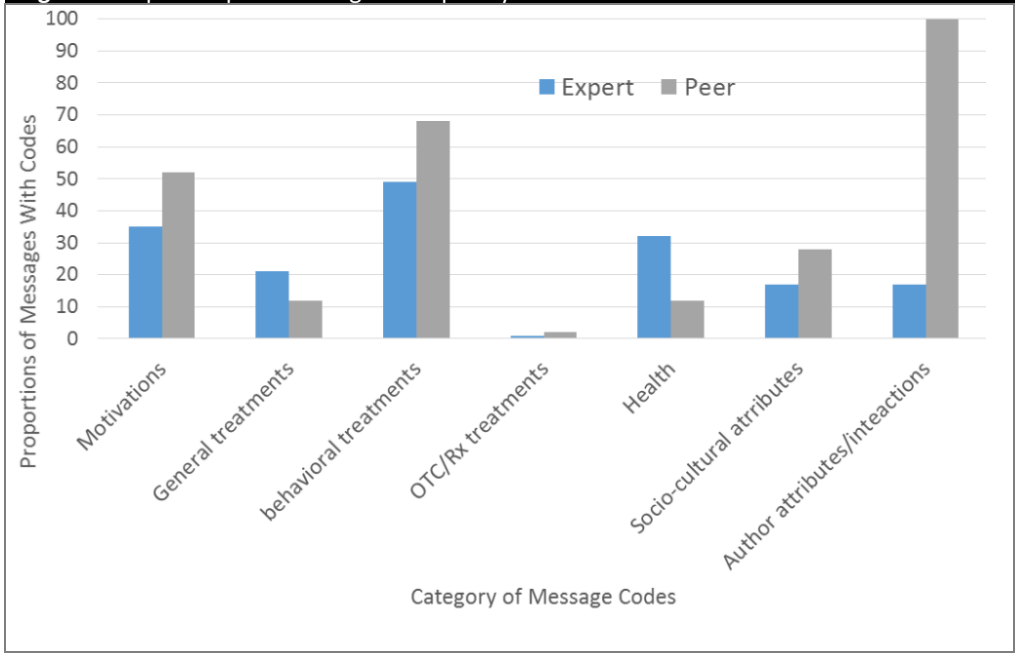
Supportive evidence for online recruitment:

We are using online advertisements as our recruitment comparison because it is the current "state-of-the-art" approach to recruit smokers, with demonstrated efficacy **(RQ-5)**. Several studies, including our own, have shown that these advertisements are successful in recruiting smokers.[79,80] Over a five-month period (1R01CA129091-01), we used this approach to recruit 300 smokers, as well as 100 smokers in 1.5 months in our PCORI pilot.[81]

C.4.1.2 Standard CTHC

As noted (Section B.4), the difference between the standard and recommender CTHC is how messages are selected. Our study goal is to test the ability of the two systems to select influential messages for individual subjects. **Thus, both messaging systems will use the same message database.** We plan to send 2 messages weekly in the first four weeks of the intervention. We will then send 1 message per week until the smoker completes six months in the intervention (from registration date of a smoker). Below, we first describe the messaging database and then the standard CTHC system.

Figure 2: Expert vs peer messages: Frequency of codes



The Motivational Messaging database: The messaging database includes 500 messages that were developed in our prior RCT and includes both expert-written messages and peer-written messages.[82] Expert-written messages (behaviorists, physicians, nurses) were developed through an iterative expert group review process. These messages was informed by current guidelines[83] and Social Cognitive Theory.[84] The current guidelines provided evidence-based content on successful cessation strategies. The Social Cognitive Theory, which incorporates vicarious learning and verbal persuasion, guided the writing of the expert messages. Messages reflect theoretical determinants of quitting, such as positive outcome

expectations and self-efficacy enhancing small goals.[84] Peer-written messages were written by current and former smokers responding to an online survey that presented four scenarios tailored by gender, age and readiness-to-quit. These messages were then reviewed for use in our system. More details of our methodology to generate peer written messages has been previously published.[82] Our messaging database includes a comprehensive coding of the messages. We developed these codes to facilitate further understanding of what worked and what did not in these messages. These codes include constructs from multiple behavioral theories such as the Social Cognitive Theory, the Transtheoretical Model, and Theory of Reasoned Action.[85] We also coded the messages for content that may be pertinent to a specific user, including health and lifestyle status, health issues, and treatment options. Overall, we developed 48 codes divided into 8 categories (General Treatments, Behavioral Treatments, Over the Counter and Prescription Treatments, Motivations, Health, Socio-Cultural Attributes, Author Attributes, and Author Interaction). A higher proportion of expert-written messages include codes related to behavioral treatments (49%) and motivations (35%). Peer-written messages have more codes related to author attributes and interaction (100%), behavioral treatments (68%), and motivations (52%). (Figure 2) Our messages are also categorized by readiness to quit.

Standard Decide2Quit CTHC System:

As noted, our comparison standard CTHC is a rule-based (if-then-else) system that tailors messages based on a smoker's readiness to quit. For example, when a smoker logs on to Decide2Quit and indicates his readiness as "not ready to quit", then a message from those categorized for "not ready to quit" smokers will be picked at random and sent to the smoker. Similarly, if the smoker indicates his readiness as "set a quit date", then a message categorized for "set a quit date" smokers will be sent to the smoker. The messages can either be sent via emails or text messages.

Supportive evidence for Standard CTHC system

We had previously demonstrated this system to be effective in a large nationwide RCT (N=900), compared to a robust website control. This website control included such functions as risk, decisional balance, and cessation barrier calculators; games linking the chemicals in smoking with their other uses (e.g., formaldehyde is used in both cigarettes and in embalming); and a library of informational resources about smoking.[10] In the RCT, the messages were sent at the same rate as our current plan for the S2S intervention. **The messages increased six-month smoking cessation outcomes.** Using a 6-month, 7-day point prevalence cessation outcome, smokers who received the motivational messages were assessed to be more likely to quit than those smokers who received the control website (30% Intervention and 20% comparison, Odds Ratio 1.69, 95% CI 1.03-2.8).[10] The difference between those who received the CTHC messages and those who did not was more pronounced with African Americans (19% versus 3% control). **The messages also increased DISC use.** Compared to non-message days, Decide2Quit use was most likely to occur within 3 days after the motivational message (OR=5.4, 95% CI=4.02-7.31). As we also published, the peer messages were most effective in increasing use. Peer messages were twice as likely to generate new activity (OR=2.03, 95% CI=1.74-2.35), compared with the expert-written messages,[82] after adjusting for time from registration and smoker characteristics. Hearing from others "just like me" and "in their own words" adds value and credibility to smokers regarding how to quit smoking, and successful attempts.

C.4.2. S2S Functions

C.4.2.1. Access to peer recruitment toolset:

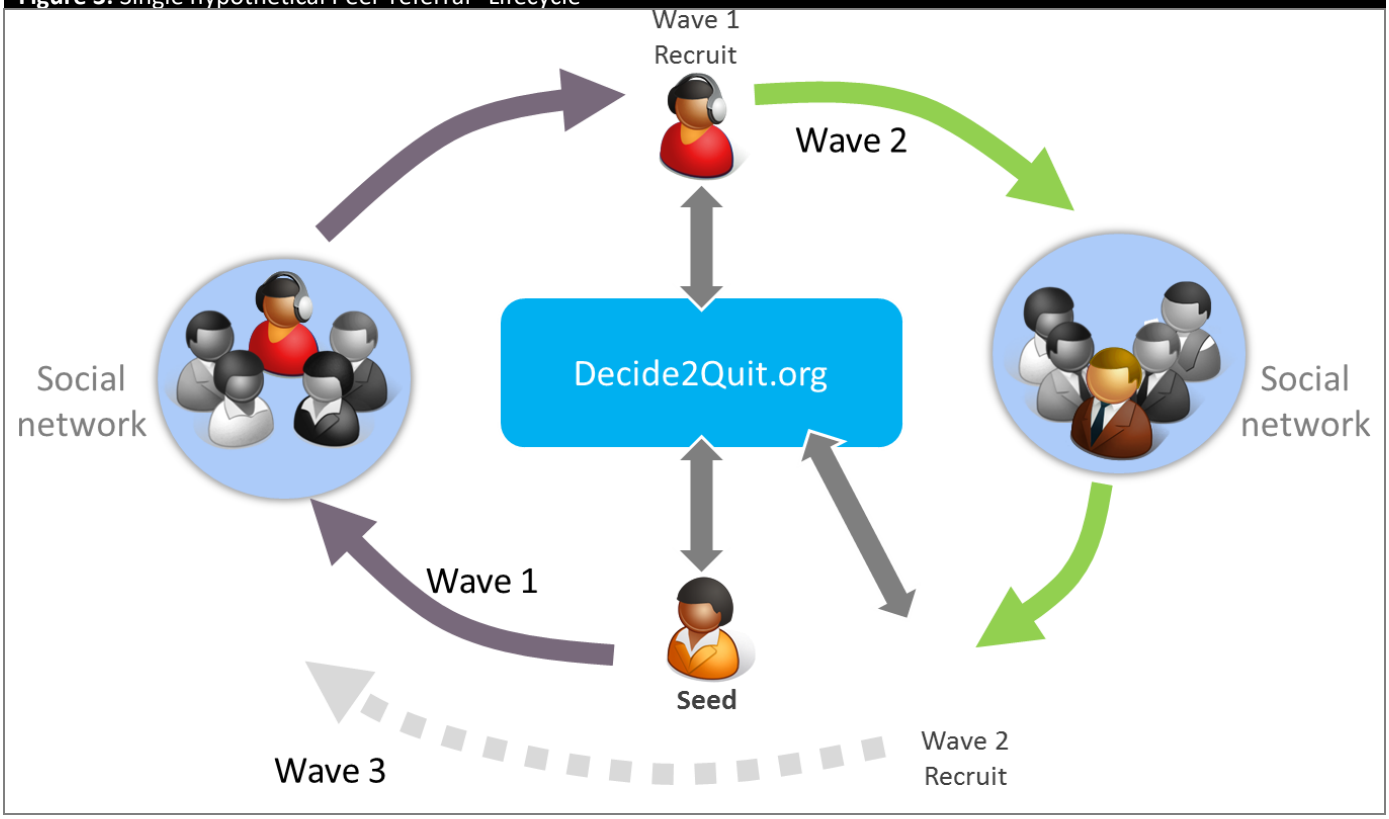
We will provide smokers access to a peer recruitment toolset to facilitate recruitment of their peer smokers to the study. The first wave of smokers who will be given access to the toolset will be referred to as seeds. The peer recruitment toolset includes a Facebook website plugin, an online training video, and a recruitment tracker (Appendix A). Our Facebook website plugin was developed in our NCI-funded pilot (R21CA15896).[3,4] The Facebook plugin will allow smokers to browse through their Facebook friends and recruit them by sending private recruitment messages. The online training video will teach the recruiter how to use available tools to recruit other smokers from their social network. The recruitment tracker will allow smokers to track successful peer recruitment. To encourage recruitment, the system also will email or text a weekly recruitment report to the potential recruiter. The basic flow of a single hypothetical smoker through the peer-referral, registration, and subsequent initiation of new peer-recruitment is described in Figure 3. Once a seed registers on Decide2Quit and receives the peer recruitment toolset, we expect the following steps:

1. The seed consents to be in the study and recruit smokers from his/her network using the peer-recruitment tools (by sending a Facebook private message).
2. The successfully peer-recruited smoker (Wave 1 recruit) registers on the system and consents to then recruit other smokers in their social network.

3. The Wave 1 recruit then continues the peer-recruitment chain, recruiting smokers from their social network.
4. The successfully peer-recruited smoker then registers (Wave 2 recruit).
5. The waves progress until the target sample size is reached.

In addition to supporting the smokers' ability to recruit via Facebook by sending a message, we will also support recruitment messaging via emails and text-messaging to further expand reach in this study.

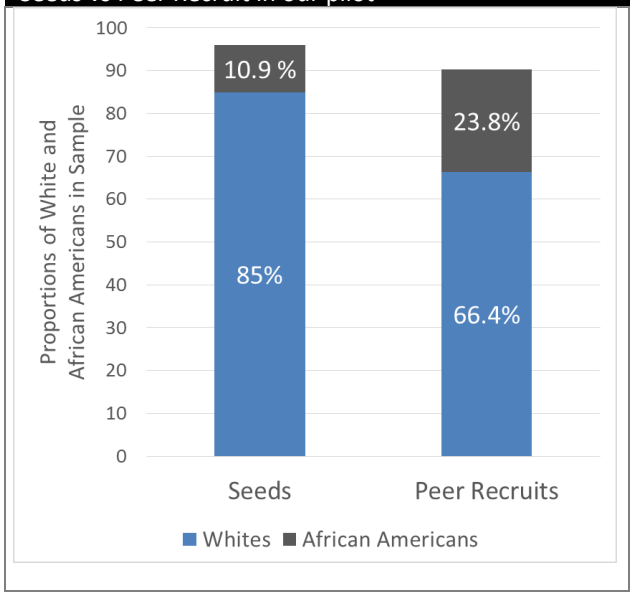
Figure 3: Single hypothetical Peer-referral "Lifecycle"



Supportive evidence for peer recruitment:

In our NCI-funded pilot study, we recruited smokers on Facebook to Decide2Quit using online advertisements. These seeds (first wave smoker) and peer recruits (subsequent wave smokers) were provided the peer recruitment toolset described above to recruit other smokers. Smokers were incentivized for up to seven successful recruitments and had 30 days to recruit from date of registration. Successful peer recruitment was defined as a peer-recruited smoker completing Decide2Quit registration following a referral. Our primary questions were 1) whether smokers will recruit other smokers and 2) if this peer recruitment process increases the reach of the intervention to harder-to-reach groups, including those not ready to quit and minority smokers. In just over a year (July 2013 to Sept 2014), peer recruitment quadrupled our sample (seeds: 190; peer recruit: 569 smokers) resulting in a total sample of 759 smokers. Participants reported being connected to 6914 smokers [mean 9.1, (SD 5.51), median 8, intra quartile range 4]. Overall, 15% (n=117) of participants successfully peer recruited (54% recruited 7 smokers, 21% recruited 4 to 6 smokers, 18 recruited 2 to 3, and 24% recruited one smoker). Peer recruitment resulted in four waves of participants after the initial wave of seeds (wave 0 to wave 4).

Figure 4: Increase in proportion of African Americans: Seeds vs Peer Recruit in our pilot



Compared to direct recruits, peer recruits were less likely to be ready to quit (74.2% vs. 95.1%). They were also more likely to be African American (23.8% vs. 10.8%) ($P < 0.01$ for all comparisons). (Figure 4) This increase happened without our tools prompting the peer recruitment of African American smokers. As noted (Section B.3), we will work with our patient advisory panel (See Section F) to further refine our instructions to encourage African American smokers' recruitment. Thus, we anticipate an even higher increase in proportion of African American smokers in S2S.

Most participants strongly agreed or agreed that peer recruitment was beneficial to their own quit smoking efforts (75.4%), motivated them to get support from those around them to quit smoking (64.4%), did not increase their cravings (83.1%), and made them feel like they were being helpful to their family and friends who are smokers (71.2%). We will test benefit of peer recruitment to cessation in this study.

C.4.2.2. Recommender CTHC system:

As detailed above (Section C.4.1.2), the difference between the standard and the recommender CTHC is the approach to message selection and not the messages. We will use the same motivational messages as the standard CTHC system. Our recommender CTHC system is a hybrid recommender system. Recommender systems can be implemented using either a content-based,[91] collaborative filtering,[92] or hybrid approach.[93] Given a sample of rating data, content–based recommender systems learn a function to match users to items based on the provided user profile information (e.g, age, gender) and the messages' metadata description. Metadata is defined as data about data; it describes the structure or content of particular resource, object, or entity.[94] In computer engineering, this assignment of messages to categories is referred to as metadata. Our messages coding by the readiness to quit categories in the comparison standard CTHC is an example of the type of metadata that can be used by content-based recommender systems. Content-based recommender systems work similarly to standard CTHC systems, but the matching function can be optimized based on rating data instead of specified by experts. In contrast to content-based recommender systems, collaborative filtering recommender systems match users to items based on past rating history. The simplest examples of this approach are nearest neighbor methods.[92] These methods match a target user with other users that have given similar ratings to the items the users have rated in common. The set of users matched to the target user are referred to as the target user's nearest neighbors. The method then recommends items to the target user that their neighboring users have rated highly.

The assumption behind these methods is that if two users are observed to have close agreement on the ratings of a sufficiently large number of items, they will likely agree closely on the ratings for the remainder of the items.

For the recommender CTHC, we chose a hybrid approach because they merge the strengths of content-based and collaborative filtering recommender systems.[93] Thus, they can potentially benefit from expert-driven rules (content-based), and the recommender algorithms. Our hybrid recommender system uses three input data sources to generate the recommendations, including the **1)** metadata description of the messages, **2)** implicit, and **3)** explicit feedback data (smokers in prior and current study). As explained above, our metadata includes a comprehensive coding of the messages (section 4.1.2 and Figure 2). Implicit feedback data are derived from user actions. As our implicit feedback data, we used the website return data of 900 smokers that participated in our prior RCT.[10] When an email was sent to these smokers, we tracked their website usage in the days following the email. Thus, we had data on the frequency at which each message promoted use of Decide2Quit, and the characteristics of the smokers that received these messages.

Table 6: Influence Question used in recommender CTHC pilot:

This message influences me to QUIT smoking?
1. Strongly agree
2. Agree
3. Neutral
4. Disagree
5. Strongly disagree

Explicit feedback data consists of self-reported item ratings. Two pilot studies were used to generate the explicit feedback data for recommender CTHC.[95] We first recruited 100 current or former smokers to refine the explicit ratings question. Each subject was asked to provide ratings using a 5 point Likert scale of four different aspects of messages: influence, emotional response, relevance and preference. Each subject provided ratings for five different randomly selected messages. Per-message analysis showed a positive correlation between the means and variances of the ratings for each question. Thus, balancing the need to obtain multiple ratings per message and the resulting cognitive load, we decided to choose only one question for developing the recommender CTHC system. We chose the influence question (Table 6) because it had demonstrated strong predictive validity in a prior RCT.[96] A second pilot test was performed to collect a larger rating dataset to bootstrap the learning and evaluation of collaborative filtering models for the recommender CTHC. [95] We recruited 846 current or former smokers from online and local sources to rate the messages on the influence scale. Each smoker was asked to rate 20 messages, resulting in 16,920 ratings. Several classic and state-of-the art collaborative filtering methods were evaluated for accurate prediction methods. The Bayesian Probabilistic Matrix Factorization (BPMF) was identified as the best single model in our evaluation and was used to develop the recommender CTHC. The BPMF model estimates a probability distribution over a joint embedding of users and items into complementary latent spaces. The rating a given user supplies for a given item is approximated by the expected value of the product of the latent user and item factor vectors representing the user-item pair, with the expectation taken over the uncertainty in embeddings.[1] In addition to explicit feedback ratings from smokers in prior studies, the recommender CTHC is programmed to also use the explicit ratings of smokers receiving the messages. Thus, when a smoker is sent an email, we will include a link to rate the message on the influence scale (Table 6). Although our standard CTHC does not adapt to this feedback, we will include the ratings question in the standard CTHC messages to minimize group differences.

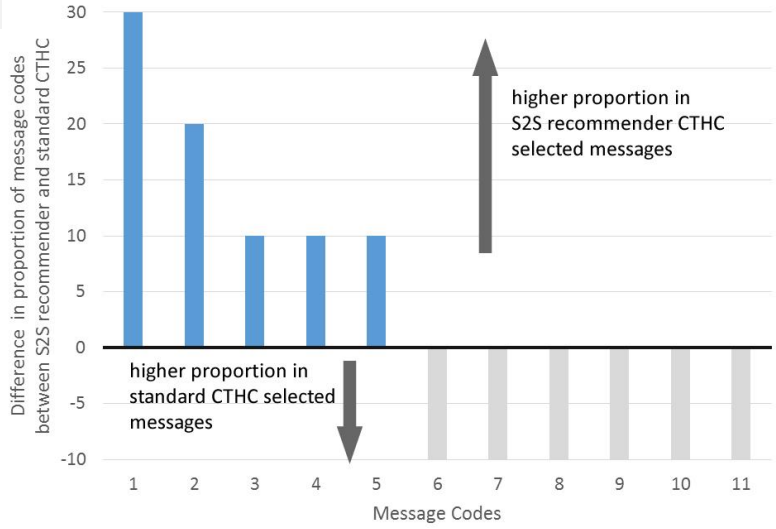
Supportive evidence for recommender CTHC system

Using PCORI pilot funding (1IP2P1000582),[1,2] we tested the efficacy of the recommender CTHC system in a small randomized experiment. Our comparison system was the standard Decide2Quit CTHC system. Smokers in both arms were emailed daily motivational messages (30 messages) and incentivized to rate messages on the influence scale. We tested this in a number of ways: 1) daily ratings of messages using the influence question (Table 6), 2) perceived influence of the intervention, and 3) cessation behavior. In all these analyses, the recommender CTHC system performed better. Comparing the daily ratings of the two systems, the proportion of days when smokers agreed/strongly agreed (daily rating >= 4) that the messages influenced them to quit was significantly (*P=.02)* higher in the Intervention (74%) than comparison (45%). In our assessment of the perceived influence of the intervention, compared with the standard CTHC system, smokers strongly agreed or agreed that the recommender CTHC system significantly influenced them to quit smoking and use Nicotine Replacement Therapy. Even in the short time span of our study (30-days) and compared with an effective rule-based CTHC, the recommender CTHC system demonstrated a higher influence on cessation behavior. Although not significant, more intervention smokers reported that they had already quit or set a quit date (39.7% versus 29.7%). At 30-days, more intervention smokers (36%) stopped smoking for one day or longer than comparison (32%) (P=.70).

What messages were selected by the recommender CTHC system in the pilot: We conducted a coding-level analysis (see codes description in Section 4.1.2) to understand how the message selection differed from the standard CTHC system. As noted above, in our pilot experiment, the standard CTHC system tailored based on readiness to quit, and messages in

each readiness category were picked at random. We identified the top 10 most frequently selected messages by each system. We then calculated the proportion of messages with each code, and then calculated the difference in the proportions of each code. Compared to the standard CTHC messages (Figure 5), the recommender CTHC had a higher proportion of messages with the codes "Health: Physical Functioning: Smoking Risk" and "Motivations: Aesthetics". As noted above, messages selected by the recommender CTHC were rated as more influential than the standard CTHC messages (see Appendix B for example messages).

Fig 5: Differences in Message Codes Between top 10 most frequently selected messages (recommender vs. Standard CTHC)



	Message Codes
1	Health: Physical Functioning: Smoking Risk
2	Health: Medical Problems
3	Motivations: Aesthetics
4	Family/Friend Problems
5	Socio-Cultural Attributes: Money
6	Behavioral Treatments: Distraction
7	Motivations: Safety
8	Health: Cognitive Functioning: Smoking Risk
9	Health: Emotional Functioning: Quit Benefit
10	Socio-Cultural Attributes: Family/Friend Benefits
11	Health: Physical Functioning: Quit Benefit

C.5. Aim 1: Conduct the S2S RCT testing (A) peer recruitment and (B) recommender CTHC

In preparation of the study, we will work with our patient advisory panel to refine our recruitment materials (advertisements content, study description, peer recruitment instructions, etc.), especially focusing on encouraging the peer recruiters to recruit African American smokers. We will work with our biostatistician to help integrate the new randomization table in Decide2Quit. As noted (Section C.2.), our program will automatically assign smokers to the groups as they register on our site. Our patient-centered measures and analytic plan are described below.

C.5.1. Patient-centered outcome measures. (RQ-6)

S2S will include multiple data collection stages (Table 7). We developed our outcome measures based on over 15 years of DISC research with smokers **(RQ-6)**.[4-6,56,97,98] As noted (Section A.3), to appropriately measure dissemination, we need both recruitment and use measures. We also will test effectiveness in this study. Our primary measures are described below:

Dissemination Measures (Hypothesis 1):

H1a: African-American recruitment: Related to H1a, we will use the number of African-Americans recruited.

H1b: Recruitment time: When smokers register on Decide2Quit, they will be assigned a unique identifier and their registration date and time will be recorded. We will compute recruitment time from this data as the time taken to recruit each participant from the time that the first participant in the group was recruited. (see equation below).

$$\textbf{Recruitment time } T_i = \mathrm{X_i} - \mathrm{X_1}$$

where $\mathrm{X_i}$ is date of registration of $\mathrm{i^{th}}$ participant; $\mathrm{X_1}$ is the date of registration of 1^{th} participant.

We also considered number of recruits as a measure. In a "real-world" dissemination project, number of recruits would be an ideal measure. However, in a trial with a stated goal of recruiting 600 smokers each in the peer and standard recruitment groups and with a time limit, number of recruits would not be a good comparative measure. Recruitment time would allow us to assess differences between the two groups, and we chose this measure.

H2: Repeated Use: We use repeated use over other use measures (number of logins) because of the demonstrated association with smoking cessation.[37] This is an ordinal scale of number of Decide2Quit functions used after the first DISC visit (0: no functions used; 1: use of 1-2 functions, 2: > 2 functions used).

H3: Effectiveness Measures:

7 day point prevalence cessation biochemically verified using saliva NicAlert®: 7 day point prevalence will be assessed at six months using: Do you currently smoke cigarettes (smoked even 1 puff in the last 7 days)?[100] The Society of Nicotine and Tobacco Research have recommended this measure for multiple reasons.[101] Point prevalence can capture delayed effects of an intervention. Continuous or prolonged abstinence measures assume that once someone fails they are unlikely to return to long-term abstinence during the remainder of study. A psychometric analysis comparing continuous, prolonged, and point prevalence outcomes found that point prevalence was the measure that had highest concurrent validity.[101] The 7-day window provides an appropriate stringent measure to account for a cross-sectional snapshot. As recommended by reviewers, we will verify quitting using the **biochemical measure — saliva NicAlert® test** .[102-104] The NicAlert® test (Nymox Corporation) is a semi-quantitative method that uses a dipstick to measure the level of cotinine in a sample of saliva. The test strip displays the result in seven zones. Each zone represents a range of levels of cotinine/smoking [e.g. zone 0 (0–10 ng/mL, a nonsmoker) to zone 6 (>1000 ng/mL, a heavy smoker)]. The results will be read as 0-6, and as recommended, any value ≥ 1 will be considered as tobacco use.[105-107] The feasibility of mailed NicAlert testing has been demonstrated.[107-109] We will mail the strips with self-addressed return envelope with clear instructions and a link to a training video. Our staff will also be available by phone to help the smokers complete testing.

Table 7: Key Data Elements	Search Ad Manager	Baseline during registration	Every Decide2Quit visit	Every email message	6th month Follow-up (Online or phone)	6th month Follow-up Mailed)
Online advertisement stats (no of users who saw ads, etc.)	X					
Demographics[99]		X				
Participant smoking characteristics (level of addiction, allowing smoking at home, quit in last 12 months)[99]		X				
Number of cigarettes/day		X			X	
Readiness to quit		X	X			
Use of website			X			
Explicit influence ratings				X		
7-day point prevalence smoking cessation[99]					X	
Biochemical verification saliva NicAlert®						X

Risk reduction or the reduction in the number of cigarettes smoked (PC-3): For the smokers participating in our prior studies, reduction in number of cigarettes smoked was an important outcome. In preparing this revision, we further confirmed with our patient panel that this was an important outcome. We asked each of them an open-ended question – besides quitting what would the most meaningful outcome as a result of participating in a smoking cessation intervention? All of them chose risk reduction as their first choice. If needed, we gave them prompts that included: reduction in number of cigarettes smoked, ability to be active without feeling short of breath, increased sense of taste and smell, improved dental health, and increased energy level in random orders. These prompts were selected from a recent study that assessed the top patient-centered outcomes of primary care smokers using focus groups.[110] In this study, risk reduction or decreased use of tobacco (cutting back, not necessarily quitting) was assessed as the top measure in the patient behavior change category. We will calculate risk reduction using the below formula:

Risk reduction = Number of cigarettes smoked at follow-up – Number of cigarettes smoked at baseline

C.6. Aim 2: Follow participants in the randomized trial for six months testing S2S

C.6.1. Analytical Plan (IR-4)

As noted above, our study is powered for our primary effectiveness study. As the outcome for H3 is the most challenging to change, and has a meaningful but modest effect size, H3 requires the most power. As a results, we will be *over-powered* to detect meaningful differences for H1 and H2. As the analytic plan for H3 is the most complex, we spend the majority of our focus on the analytic plan for this hypothesis. For H1 and H2, we demonstrate that we will be able to detect small differences with the large sample size required for H3.

For the effectiveness trial (H3), to preserve randomization, all primary analyses will be on an intent-to-treat basis **(IR-3)**. Secondary analyses will explore dose-response effects among those with variable levels of adherence to the intervention. All analyses will be two-sided and alpha error will be set at 0.05. We will begin our analysis by examining univariate statistics (means, medians, standard deviations and 95% confidence intervals) and distributions. We will examine the balance of participant characteristics by study groups and account for any imbalances in our multivariable analysis. As

appropriate, differences in measured characteristics (i.e., demographics and pre-baseline smoking behaviors) by group will be tested using chi-square tests of independence (categorical variables), ANOVA (continuous variables) or the equivalent non-parametric tests depending on the distribution of the variables. Per best practice, differences in baseline characteristics of the intervention and comparison groups will be assessed.[111,112]

For the dissemination study (H1), we will compare the speed of recruitment and percent of African-Americans recruited in the peer-recruitment and no peer-recruitment groups. Note that our goal in the dissemination study is to increase speed of dissemination and the diversity of recruitment (and dissemination study includes and randomized and non-randomized wave of recruitment. Thus, we anticipate that, and hypothesize that, African-Americans will be imbalanced (with greater recruitment in the peer recruitment group). We will use a chi-square test to compare the difference in proportions (H1A).

We note below that H2 has a has a limitation, in that it relies both on the randomization of the main effectiveness study, and the allocation to peer-recruitment tools (which is, not randomized as required by hypothesis 1). We also describe below our approach to address this limitation.

H1: Analytic plan, sample size, and power calculation

H1A Analytic Plan: To monitor dissemination (H1) through social networks requires a non-randomized allocation for those smokers peer-referred. For H2, we need to consider the Randomized and non-randomized (i.e.: peer referred) components of this study.

Based on our pilot (Section C.4.2.1), we anticipate that peer recruitment will be more effective in recruiting African Americans. To test this, we will categorize the smokers as either African Americans or not, and then use the Chi-Square statistic to test for differences.

As a secondary, exploratory analysis, Within the peer recruitment tools group, we will conduct a secondary analysis examining differences in demographic characteristic between peer recruited and directly recruited smokers. As noted in Section C.4.2.1, peer recruitment resulted in increasing reach of the intervention to harder to reach smokers (not ready to quit and African American smokers). Using data provided by search engine advertisement managers, we will evaluate the performance of our online advertisements (number of users registered on Decide2Quit following an advertisement on the search engine).

Sample Size and Power Calculations: In our NCI-funded pilot (R21CA15896),[3,4](Section C.4.2.1), peer recruitment increased the proportion of African Americans to 23%, compared to 11% in the initial seeds (those recruited by advertisements). Using 10% as the base rate in the non-peer recruitment group (recruitment by online advertisements), we estimated sample size requirements varying the proportion in the peer recruitment from 16 to 20%. With these assumptions, we will need 219 smokers in each group to detect difference of 10% (power = 80%, alpha=.05). If we reduce the difference to 8% and 6%, we will need 319 and 525 in each group respectively. Given that we will work with our panel to encourage recruitment of African American smokers in the peer recruitment group and may see bigger differences than our pilot, we will have adequate power particularly with the proposed sample size of 600 in each recruitment method.

H1B Analytic Plan: For H1B, we will compare mean recruitment time between the two types of recruitment method using a t-test. .

Sample Size and Power Calculations: In the NCI pilot (R21CA15896),[3,4] we estimated that the mean number of days to recruit a sample of 700 smokers was 244 days with a standard deviation of 81. Assuming that peer recruitment proceeds with the same rate and with the same standard deviation, we can detect a difference in recruitment time as low as 14 days. Since we expect the comparison rate to be much slower, we are adequately powered to detect differences with a sample of 600 (power=0.8). See other sample size requirements varying the mean and standard deviation of the number of days to recruit in the intervention and comparison (Table 8). Calculations were made in STATA.[113]

Table 8: Power Calculations to estimate the minimum difference in the mean number of days to recruit

Intervention (Mean)	Comparison Mean	Standard Deviation (Both groups)	Sample Size Required
244	257	81	610
244	258	81	526
244	260	100	614
244	261	100	544
244	263	120	627
244	264	120	566

H2: Analytic plan, sample size, and power calculation

H2 Analytic Plan:

We will analyze across the four groups: (A: Fully enhanced; B: Recommender CTHC only; C: Peer recruitment only; D: Standard), as we hypothesize there may be an additive effect on engagement of peer recruitment and the recommender CTHC system (See section X above). We will use the following generalized linear model, which includes indicators of peer recruitment and recommender CTHC and the interaction between the two indicators as independent variables, to test H2A:

$$E(\boldsymbol{f}(\boldsymbol{u})) = b_0 + b_1 \times P + b_2 \times R + b3 \times P \times R + potential\ confounders\ (demographics, readiness\ to\ quit)$$

where u is the outcome measure (repeated use measure), the function $f(u)$depends on the distribution of u,

P=1 for peer recruitment, =0 for standard recruitment, *R*=1 for recommender CTHC, =0 for standard CTHC.

The adjusted $f(u)$ (i.e., adjusting for the potential confounders) for each of the 4 groups can be expressed in terms of the regression coefficients defined in the box below.

A	B	C	D
$b_0 + b_1 + b_2 + b_3$	$b_0 + b_2$	$b_0 + b_1$	b_0

In the model, $b_2 + b_3$ is the estimated difference between group A (peer recruitment and recommender CTHC) and group C (peer recruitment only); $b_1 + b_3$ is the estimated difference between group A and group B (recommender CTHC only); and $b_1 + b_2 + b_3$ is the estimated difference between group A and group D (standard). Significant positive values of the estimated differences will support H2A. In the event that there is an interaction effect between the two S2S enhancements (peer recruitment and recommender CTHC), i.e., b3 is significantly different from zero, H2B and H2C will be tested by comparing groups C vs. D (peer recruitment alone vs. standard Decide2Quit; estimated by b1) and groups B vs. D (recommender alone vs. standard Decide2Quit; estimated by b2). If there is no interaction effect, i.e. b3 is not significantly different from zero the following model will be used to test H2B and H2C:

$$\boldsymbol{E}(\boldsymbol{f}(\boldsymbol{u})) = a_0 + a_1 \times P + a_2 \times R + potential\ confounders\ (demographics, readiness\ to\ quit).$$

In the model, a_1 is the estimated effect of peer recruitment [(A+C) – (B + D)]; a_2 is the estimated effect of recommender CTHC [(A+B) – (C+D)]. A significant positive value of a_1 or $a_2$will support the hypotheses of positive effects of these two individual components respectively (H2B and H2C).

We will examine the distribution of the dependent variable u to determine the link function to be used in the generalized linear model. In our previous study, we used an ordinal variable for the dependent variable Repeated Use with log link function to fit an ordinal logistic regression.[37]

We will also conduct a secondary analysis using the influence ratings. As noted above, both standard and recommender CTHC will include a link to rate the messages on the influence scale (Table 6). For this analysis, the dependent variable for each smoker is the mean of all influence ratings (an influence score) and the independent variable is study arm [recommender (A+B) or standard CTHC (C+D)]. We predict that the mean influence score will be higher in recommender CTHC than the standard CTHC arm. For this analysis, we will start with a t-test for differences in mean, but acknowledge that the influence scores may not be normally distributed and only approximate a continuous variable. Thus, we will use a Wilcoxon rank-sum. As an exploratory evaluation for H2, we will also compare African American smokers across the groups, and African American and White smokers to test for heterogeneity of effect. This will provide us important data for design future interventions. **(HTE)**

As noted above, H2 will rely both on the randomization of the main effectiveness study, and the allocation to peer-recruitment tools (which is, not randomized as required by hypothesis 1). Thus, we need to consider the Randomized and non-randomized (i.e.: peer referred) components of this study. To do this, we will adjust the analyses for measured covariates that differ between the non-randomized and non-randomized groups from the dissemination study."

Sample Size and Power Calculations: We used the method published by Whitehead to calculate power for this hypothesis.[114] As noted above, in our prior RCT (1R01CA129091), we found a linear association with six-month cessation using the repeated use scale. For every increase by one in this scale, odds of smoking cessation increased (OR= 2.10, 95%

CI = 1.03, 4.30),[37] with the current sample size of 300 per group for H2A, we can detect a difference a cumulative odds ratio of 1.7. Thus, our study is adequately powered to measure a reasonable difference in the repeated use measure. Power for these hypotheses is driven by H2A, as this analysis is looking at the smaller sample (fully enhanced). For H2B and H2C, power is even greater, as the sample size is 600 per group for each.

H3: Analytic plan, sample size, and power calculation

Quitting: We will compare those randomized to enhanced CTHC, against those randomized to standard CTHC. We will test the 6-month, 7-day point prevalence cessation as the dependent variable for these analyses. As described in the missing data section (C.6.2), we will use a number of approaches to account for missing data, including using a selection modeling approach as recommended by experts.[115] Using mediation analysis, we will examine the potential mechanisms through which we anticipate the intervention may produce a beneficial effect.[116] We will categorize the NicAlert® test into smokers and not categories, and use the Chi-Square statistic to test for differences.

Sample Size and Power Calculations:

We assumed a control cessation rate of 15%,[117] a two-sided significance level of 0.05. A sample size of 300 in each group (H3c) will achieve 80% power to detect a difference of 9% (quit rate in intervention=24%) in quit rates between the two groups, based on a Z-test with pooled variance.

Table 9: Power Calculations to estimate risk reduction using a measure of the mean difference in the number of cigarettes smoked (baseline to follow-up)

Power	Intervention (Mean)	Comparison (Mean)	Both arms (Standard Deviation)	Detectable difference
80%	3.76	3.3	2	0.46
	3.99	3.3	3	0.69
90%	3.83	3.3	2	0.53
	4.10	3.3	3	0.80

Risk reduction: As noted above, risk reduction is measured by change in cigarettes smoked from baseline to follow-up. If risk reduction is normally distributed, we will use identity link function in the generalized linear model. We will also model risk reduction using count regression, using a Poisson or negative binomial regression modeling if the variance of the distribution of risk reduction is over dispersed.

Sample Size and Power Calculations:

We calculated the detectable difference in risk reduction with 300 smokers in each group and the mean in the comparison group of 3.3 using standard deviations of 2 and 3 with 80% and 90% power (**Table 9**). We will have 90% power to detect a difference of 0.80 (or smaller) number of cigarette smoked reduction between two groups. This difference is likely to be achieved based on the results of our PCORI pilot in which we achieved a reduction of 0.85 (4.15 to 3.3) in 30 days; compared to smokers receiving the standard CTHC messages, smokers receiving the recommender CTHC had a higher reduction in number of cigarettes at 30 days (Standard CTHC: mean 3.3; *S2S adaptive CTHC*: 4.15).

Resources needed to replicate the intervention: As requested by reviewer, we have now added Dr. Bridget Smith to our team to help us quantify the resources needed to successfully replicate our intervention. From the perspective of an implementing organization, we will compare the costs of the four groups. The research team will track staff time associated with each intervention arm, including time for training, recruiting, and administering the different aspects of the intervention. In addition, we will estimate development costs of each intervention in our prior NIH and PCORI-funded studies and any equipment or supply costs. We will compare the costs of the different intervention arms in multiple scenarios in which we examine how costs change based on changes in the components of the intervention and the types and amount of staffing provided for implementation. The economic analyses for this will primarily consist of descriptive statistics. Using the estimates of costs of supplies, equipment, and staff time and the potential savings that result from decreased healthcare costs related to smoking cessation, we will conduct a budget impact analysis to calculate the resources needed to implement any particular treatment strategy from the perspective of an implementing and/or disseminating organization. We will follow the guidelines outlined for best practices in budget impact analysis.[121] We will create tables to describe the assumptions of our inputs and outputs of our budget impact analysis, and perform sensitivity analyses to examine how changing the assumptions of the model impact the potential costs for an organization implementing the intervention.

C.6.2. Missing data analysis and handling dropouts

For our effectiveness study, missing data due to dropouts is only an issue for Hypothesis 3 (H3). For hypothesis 1 and 2, missing data is part of the outcome of interest, and will be considered as indicative of no recruitment and lack of use. For hypothesis 3, our primary approach to dealing with missing data is to minimize its occurrence. Drawing upon our prior experience, our staff will make multiple attempts to contact the patient and obtain their follow-up **(MD-1)**. We will also provide smokers multiple modes (telephone and web) to complete the follow-up **(MD-1)**. However, we recognize that there will be missing data. This is especially true in light-touch technology-assisted interventions.[115,122,123] As recommended in literature, we will take multiple approaches to analyzing the data. Our primary analysis will be **an intent-to-treat analysis** where all participants with missing data **(MD-4)** will be considered smokers **(MD-2)**. We will also conduct a **complete case analysis**. If missing cessation data is greater than 10-20%, experts recommend using **selection modeling** to examine the robustness of findings **(MD-3).**[115] Thus, we will implement selection modeling using inverse probability weighting to determine the potential effect of missing data. As a sensitivity analysis, we will compare these results with results of complete cases, and last baseline or observation carried over and the multiple imputation method of Hedeker et al **(MD-5)**.[124] We anticipate missing data in the biochemical verification, and we will use rates of refusal in sensitivity analyses.

Addressing multiple outcomes and multiple comparisons: The statistical literature has reviewed methods for accounting for multiple comparisons, and noted that adjustment is controversial and may be over-conservative in some contexts.[118-120] Adjusting for multiple comparisons is highly appropriate in exploratory analyses that are not testing specified hypotheses (as example: genome-wide association studies). However, studies that conduct analyses focused on a set of specific, pre-analysis-specified hypothesis are conceptually not the same. In these hypothesis-driven studies, the articles cited above, would argue that the concept of adjustment for multiple comparisons would be over-conservative. In this project, we are pre-specifying primary and secondary hypotheses, we will present each p-value "as-is" allowing consumer of the results to consider the strength of the complete set of findings using his or her preferred way of placing the separate findings in context, without imposing a specific, controversial "multiple comparisons" interpretation.

C.6.3. Strengths, Limitations, and Future Opportunities.

Our proposal has several strengths. S2S is the first study to evaluate smoker-driven innovations to disseminate DISCs. S2S is an example of a transdisciplinary innovation. We have combined concepts and theories from behavior change, health communication, computer recommender systems, and social marketing together to develop the S2S tools. Patients developed several of the S2S tools as content experts (see Section F). The S2S functions have the potential to significantly transform the way we disseminate our interventions. By facilitating the spread of the tools from patient to patient, peer recruitment provides a naturalistic approach for spreading the intervention reaching hard-to-reach populations that have a great need for such tools, leveraging current trends in social networking. One of the challenges with current DISCs is that attrition rates are high. [125-128] By continuously adapting to the behavior and needs of the patient, the recommender CTHC may continuously engage the patients and reduce attrition rates.

In this study, we focus on testing peer recruitment for recruiting African American smokers. While Hispanics or Latinos are also disproportionately affected by smoking, we do not have current evidence demonstrating the strategies described in this proposal can successfully recruit them. Other strategies such as adaptive peer recruitment may be needed for engaging Hispanics in DISCs and we will explore these in future projects. While we will make significant advance, future methodological and dissemination opportunities remain. The S2S tools have applications in other health and wellness interventions including motivation for weight-loss and compliance. In collaboration with our colleagues at the Center for Intelligent Information Retrieval (CIIR) at UMass Amherst, we will develop more complex, machine learning algorithms for adaptive recruitment. These algorithms can learn from the recruitment data and adapt to the changes in real-time. We will learn several lessons from the S2S study, which can all be used to train the machine learning algorithms. We can also develop the recommender CTHC to incorporate contextual and physiological information from smart phones and sensors, as a form of patient feedback. On the dissemination front, we envision a large, pragmatic study to fully evaluate the integration of S2S into health care systems. Our team has extensively worked with multiple clinical systems integrating behavioral change research with clinical-system tethered Personal Health Records (PHRs).[5,129-143] We will support a warm-handoff between providers and patients using an integrated EHR/PHR that will automatically flag patients that are eligible to be champion recruiters and support automated motivational messaging to them. This should enable us to gain the benefits of having providers recruit while not burdening them with additional work. We have conducted

several large pragmatic studies integrated with healthcare systems.[5,7,8,129,144-146] In our CTSA efforts, we are working to create a multi-institutional consortium of Healthcare systems using the same EHR/PHR platform. In conclusion, in planning S2S, we have built on our strong efficacy data from current NIH and PCORI -funded research, integrated several methodological innovations, and have a clear plan for further dissemination of S2S tools.

D. Patient Population

We will recruit 1200 smokers (400 smokers per group) for this study (Table 10). All current smokers over 19 years of age, can read or speak English, and have Internet access at home will be eligible (RQ-3). Our target is any smokers who view our advertisements on Google and Facebook and register on the website. Thus, screening is not applicable for this study. This is a recruitment experiment. Thus, we can only estimate the characteristics of smokers participating in our study. As noted, we will continuously monitor recruitment with our patient panel and revise advertisements as needed.

Table 10. Estimated Final Racial/Ethnic and Gender Enrollment Table

Race	**Male (N)**	**Female (N)**	**Total (N)**
American Indian/Alaska Native	5	5	10
Asian	60	58	118
Black/African American	130	110	240
Hawaiian/Pacific Islander	5	5	10
White	385	395	780
Multirace	15	27	42
Ethnicity	**Male (N)**	**Female (N)**	**Total (N)**
Hispanic (Latino/Latina)	50	50	100
Non-Hispanic	550	550	1200

E. Research Team and Environment

Research Team: We have a multidisciplinary research team (computer engineers, behavior change, tobacco cessation, clinicians, and patient participants), with an established collaboration record.[5-9,147] Drs. Sadasivam, Houston, and Allison have collaborated together for over 10 years to develop Decide2Quit,[5,7,8,10,37,56] and the S2S innovations[1,2].[3,4] Dr. Allison has over 20 years of research expertise in health disparities and has successfully collaborated with Dr. Houston to develop interventions targeting African Americans.[96,148]. In response to reviewer's critiques, we have recruited Dr. Bridget Smith, a health economist, to help us conduct a budget impact analysis of our intervention. Drs. Sadasivam, Houston, and Smith have conducted a similar budget impact analysis of our prior intervention.[8] Dr. Marlin, our consultant, collaborated with us to develop the recommender CTHC.[1,2] Mr Seward is a tobacco treatment counselor at the UMass Memorial Health Care system, and has collaborated with us over the last 3 years providing input on various projects, as well as supporting the recruitment and participation of smokers.[149] Dr. Sadasivam shadowed Mr. Seward as part of his clinical tobacco treatment specialist training for his career development award. Patients will be an integral part of our team, as decision leaders and content developers (see Section F).

Environment: We will make use of the considerable resources available at the University of Massachusetts Medical School (UMMS, see letter of support). UMMS ranks near the top among public medical schools in the Northeast in the amount of funding awarded by the NIH. Since 2010 (renewed again in 2015), UMMS is home to the prestigious NIH-funded Clinical and Translational Science Award (CTSA) and have established the UMass Center for Clinical and Translational Science (UMCCTS). UMCCTS serves as the academic home for clinical and translational scientists across all UMass campuses and has considerably enhanced the UMMS research infrastructure by developing innovative core facilities. The mission of the UMCCTS is closely tied with the mission of the Quantitative Health Sciences department, academic home of Drs. Sadasivam, Houston, and Allison. All three investigators hold leadership position in the UMCCTS. Dr. Allison is a co-leader of the Special Resource Population Center (the SPRC) of the UMCCTS. The SPRC was formed to increase engagement of special populations in translational research through tailored, culturally responsive strategies. Dr. Houston leads the UMCCTS Biomedical Informatics (BMI) Component. Under his leadership, BMI has fostered collaborations between the UMMS Division of Health Informatics and Implementation Science, Academic and Research Computing, and the UMass Memorial Healthcare Information Systems. This collaboration has resulted in the continued development of multiple core infrastructure resources, including the clinical Data Warehouse, the Biomedical Research Informatics Development Group (BRIDG), and the Technology Usability lab. Dr. Sadasivam is the director of BRIDG and the Technology Usability lab. Under his leadership, the BRIDG has developed a state-of-the-art infrastructure to support eHealth and mHealth research projects, and Decide2Quit and the S2S functions were developed, and is currently housed in this infrastructure. We have also developed close collaboration with the UMass Amherst Center for Intelligent Information Retrieval (CIIR), a world-class group of researchers conducting cutting edge information retrieval research. The recommender CTHC development was a direct result of this relationship. Dr. Person is a member of Quantitative Methods Core (QMC), the statistical core of the UMMCCTS (see details in People and Places resources). **In summary**, UMass academic units and the UMCCTS provide an environment uniquely suited to the innovative work proposed in S2S.

F. Engagement Plan

Engagement: We strongly believe that interventions will fail if they do not fully address patient perspectives and cultural or ethnic experiences as part of the full continuum of patient perspectives **(PC-1)**. Incorporating patient perspectives is critical to the development of patient-centered interventions that most closely reflect patients' goals. As noted on the Resubmission Letter, reviewers praised our proposal as exemplary in patient-centeredness and patient-engagement. In particular, they noted that the S2S functions were driven by patients (peer recruitment, explicit and implicit feedback), and that several messages of our motivational messaging system were written by patients. However, reviewers were unsure about how we selected members of the patient panel, and their role in the dissemination plan. Reviewers also suggested to diversify the panel to include minorities. In response, we have significantly expanded the panel, clarified our selection process, and the role of the patients. In our prior research, patients have participated not just as subjects**, but as decision leaders and content experts**. We will pay them to be a part of the team as research consultants (see budget justification). We have found that this model works best as the patients have a bigger ownership, greater motivation and assurance to participate in decision-making. We anticipate that our panel will be involved for 10-15 hours per year distributed over 8-12 meetings. We detail our approach below.

Patient selection process: As noted, we will have 5 patients in our panel (3, including one African American, are named in the proposal and we will recruit 2 others). These patients were all participants in our current R01 trial (1R01CA190866-01A1) and demonstrated an interest and commitment to research. In addition, our staff identified these as star participants, i.e., they were able to understand our research needs in a complex study that involves gaming and mHealth tools and articulate their critiques. Because of their critiques, we have made several changes to our current R01 trial, including modifying our recruitment strategy, our approach to teaching the patients about the study's mHealth tools, and changes to the text messages that will be sent to smokers. We will continue identifying star participants in our current study to recruit the two additional patients to our panel, including one more African American smoker. Mr. Seward, a tobacco treatment specialist at the UMass Medical Center, will also serve in the panel. He will bring over 30 years of experience counseling smokers in both in-patient and out-patient settings to our panel. Mr. Seward has collaborated with us in research, including helping identifying patients for our studies, planning the intervention, as well as evaluating and writing manuscripts.[149]

1. PLANNING THE STUDY: Stakeholders and patient participants were directly involved in the development of the S2S tools and the research question. As noted in Section C.4.1.2 , our motivational CTHC system included messages written by smokers.[82] In our prior evaluation, we have found that these messages increased longitudinal engagement with the system (OR=2.03, 95% CI=1.74, 2.35), compared to expert messages.[82] As noted, our S2S recommender systems also uses explicit and implicit patient feedback to adapt the personalization of the system. Our research focus of testing new tools to increase engagement with the system was also a result of several years of usability evaluations.[81] In preparation of this study, Dr. Sadasivam also shadowed the tobacco treatment counselors at the UMass Memorial Health Care and interacted with smokers. When we assessed barriers to the access of tools such as Decide2Quit, we found that while smokers were interested in online tools, they did not use them for several reasons, including lack of awareness of the system, forgetting about the system, and lack of motivation. We have over the years designed several approaches to overcome these barriers, including provider referral tools in our prior RCT, and the tools being tested in S2S - the peer recruitment and recommender CTHC system. As noted in the proposal, our outcome measure (risk reduction) was recommended by patients in our prior studies, and confirmed by the panel.

2. CONDUCTING THE STUDY: Our patient panel will serve as **decision leaders** and help us in all phases of the study, including helping with **1)** Refining our online recruitment strategy (in terms of content or where to place the ads); **2)** Monitoring our implementation progress and helping refine our approach in case of issues such as slow recruitment; **3)** Evaluating the data and helping present results to smokers and community-based organizations; and **4)** Helping us prepare for approaches (EHR integration, community integration) to disseminate the intervention beyond the scope of the project. We will use a semi-structured approach. Our first meeting will establish the roles, duties, and expectations of all involved in this partnership. We will focus on building team cohesiveness and highlighting the important contribution the panel will make in our study. We will continually stress that the panel's role is to serve as decision leaders, and not as subjects. In our later meetings, we will have open-ended discussions followed by a structured nominal group technique (NGT) process to make decisions. NGT is a highly structured, multi-step, consensus building procedure often used in formative research to elicit and prioritize group responses to a specific question. [150,151] We have found that NGT's worked well to prioritize and establish decisions. [7] Our panel will continuously be kept updated using a dashboard available over Web and smart phones that we will collaboratively develop with them.

Patients as content experts: As noted above, patients were directly involved in the development of the tools of the intervention. With our panel, we will continually monitor and refine our recruitment strategy (content and placement of advertisements) to increase the likelihood of success.

3. DISSEMINATING THE STUDY RESULTS:

Patients as disseminators: We have a detailed plan for dissemination of the tools, including peer recruitment, integration with healthcare organizations, and community organizations (see Dissemination section). Our patient panel will help develop lay summaries of our tools and results and help lead these efforts. Peer recruitment is a naturalistic way of disseminating tools, and our panel will help us identify places in various communities where we can initiate the peer recruitment. Moreover, Dr. Allison is the lead of the Special Population Resource Center, of the UMass Clinical and Translational Science Center, as well as the Vice Provost for Health Disparities research. Under his leadership, UMass is developing relationships with several local and national community organizations. Dr. Allison (key investigator) will continue to support our efforts to identify different groups with whom we can collaborate. We will work with our patient panel to help us market our intervention to these groups. We also have several prior and ongoing research in which we have established relationship with healthcare organizations and developed tools for provider to refer patients to online resources.[5,7,8,10] In his role as TTS, Mr. Seward refers smokers to several online tools and he will continue to include Decide2Quit in his referrals, as well as identify new avenues for dissemination. In addition, all panel members will be invited to serve as authors in the development of manuscripts for peer-reviewed publications.

4. PRINCIPLES FOR ENGAGEMENT

- **Reciprocal Relationships:** Our panel will be involved in all aspects of study development. As noted, we will continually stress that the panel's role is to serve as decision leaders, and not as subjects. Through the dashboard and other communication channels (e.g., listserv), we will ensure that the panel is constantly updated of new information. Major decisions will be undertaken through the NGT process. The panel will serve as authors in any manuscripts we develop to reflect their contributions to the study.
- **Co-learning:** Patients and stakeholders will participate as decision leaders and content experts. Patient perspectives are essential in the development, implementation, and dissemination of an intervention. Patient input teaches researchers about what outcomes are important and methods that are feasible for the intervention's target population. We will ensure that the patient investigators understand the research process by keeping an open line of communication and to thoroughly explain all research processes and protocols.
- **Partnership:** The time and contributions of patient partners are valued due to the patients' perspectives. Patient investigators can provide researchers with feedback and direction that is more pertinent to the patients' needs than what researchers believe to be beneficial for the population. Patient investigators will receive $50 per meeting.
- **Trust, Transparency, Honesty:** The patients in our panel have all participated in our research projects. Thus, we already have an ongoing relationship to build on. In our first meeting, our goal is to establish early the value of the patient investigators and the significant contribution they are making to the overall intervention. We will emphasize the importance of the patients' viewpoints and personal experiences on helping to design and implement the intervention. We will demonstrate how patient input has led to several of our research success. Each patient investigator will receive a "reference handbook" summarizing the research process (e.g., the intervention process, contact information for the researchers, the time commitment for this partnership, the intervention phases, and tasks associated with each research step). Throughout the research process, the researchers will share information about the intervention aims. As noted above, we will collaboratively develop a dashboard to continuously update the panel on the research progress.

DISSEMINATION AND IMPLEMENTATION POTENTIAL

A. Describe the potential for disseminating and implementing the results of this research in other settings.

The Decide2Quit.org digital intervention for smoking cessation and the smoker-to-smoker (S2S) peer recruitment and recommender computer-tailored health communication (recommender CTHC) system are all products of over a decade of research. **They are integrally tied to the overarching scientific mission of our department of Quantitative Health Sciences at UMass Medical School, and we are committed to their ongoing support and dissemination (see support letter).** Consistent with the Communication and Dissemination RFA, our tools have considerable dissemination potential. As noted in the proposal (Section B2), DISCs are health communication programs that can be accessed via the Internet and smart phones. As the majority of people in the United States, including vulnerable populations, now have Internet connectivity through broadband and smartphones, DISCs have the potential to reach a large and diverse group of smokers. The S2S tools also have the potential to be self-sustaining. Peer recruitment promotes a naturalistic approach of spreading the intervention from one smoker to another. By adapting to the needs of the user, the recommender CTHC has the potential to continuously engage the user. We will pursue a **multipronged dissemination plan** extending beyond the traditional venues of presentation at scientific conferences and publication in the peer-reviewed literature. Our patient panel will be central to this effort — in helping shape the strategy as well as the implementation of the strategy. Our plan is detailed below:

- Presentation and Publications: We have an exemplary track record in publishing and presenting results from our funded studies. We will diligently apply this experience and skill to disseminate S2S results. In addition to presenting our findings at scientific meetings and in peer-reviewed literature, we will also present key findings at community-based meetings, on our webpage, and social media sites. Our patient panel will be an integral part of this effort.
- Community-based outreach: With our patient panel, we will develop lay summaries and marketing materials and start identifying opportunities for continued dissemination of Decide2Quit and S2S tools in community-based settings. As noted in Section F, Dr. Allison (key investigator) is the lead of the Special Population Resource Center, of the UMass Clinical and Translational Science Center, as well as the Vice Provost for Health Disparities research. Under his leadership, UMass is developing relationships with several local and national community organizations). Dr. Allison will continue to support our efforts to identify different groups with whom we can collaborate to disseminate Decide2Quit.
- Integration with EHR/PHR and other healthcare settings: We will also take a proactive approach to dissemination of the tools leveraging our past research. In our prior RCT, [5,8,10,152] we tested an electronic referral system to market Decide2Quit. As smokers were seen by their primary care providers, providers were trained to refer them into Decide2Quit website by entering their email address into a secure form. Once e-referred, Decide2Quit website sent them up to 10 emails encouraging their participation into the study. This project was highly successful. We had 2166 referrals from 74 practices, out of which, 672 smokers registered. The next step in this approach is to link the e-referral to EHRs around the country. We have several national connections with the Veterans Health Administration (VHA) and healthcare systems through our Clinical and Translational Sciences Award. Through these connections, we will explore adapting the e-referral system to their environment. In our PCORI pilot (1IP2P1000582), we also experimented with identifying smokers in the EHR and mailing them for participation in the study. As the majority of smokers see a healthcare provider, this is potentially a powerful approach for disseminating Decide2Quit tools. We will again make use of our national connections to assess interest in this approach in various healthcare systems.
- Other social media opportunities: During initial conversations, our patient panel members were excited about the use of social media outlets (e.g., Twitter, Facebook) for dissemination and outreach with study participants (see below). Dr. Sadasivam is the social media chair of the Society of Behavioral Medicine and has expertise in developing social media campaigns. For example, we will create a twitter group and work with our patient panel to develop tweets. In previous work,[153] we found that Twitter tobacco cessation groups whose tweets had a higher frequency of socioemotional support and encouraging/engaging tweets had higher followership. We will use these findings to increase the followership of our group. Our study participants will also be invited to subscribe to social media channels

after they complete the study (see below), and we will use these mediums to disseminate study results. We will also feature the intervention as part of the social media outreach program of our National Institute on Minority Heath and Health Disparities funded Center for Health Equity Intervention (CHEIR). Dr. Allison is the lead of CHEIR, and Drs. Sadasivam and Houston play a lead role in shaping the social media outreach of CHEIR.

- Other media opportunities: Dr. Houston's previous interventions have been incorporated into the Innovations Exchange. Our work have been featured in the in the New York Times,[154] the Boston Globe,[155] Time Magazine,[156] and Wall Street Journal.[157] We will continue to explore opportunities to have our results featured in these outlets.
- Technological advancements to support dissemination: As noted (Section C.6.3), we will pursue technological advancements of the S2S tools to further their dissemination potential. With our colleagues at the Center for Intelligent Information Retrieval (CIIR) at UMass Amherst (Dr. Marlin), we will develop targeted peer recruitment strategies using algorithms to identify potential "best" recruiters. Instead of pursuing everyone, this will allow dedicating resources to further the potential of these recruiters. This will also support targeting those that can best reach a vulnerable population. We will continually work to enhance the recommender CTHC algorithm, including tailoring the timing of the message delivery, and incorporating additional real-time information from sensors.

B. Describe possible barriers to disseminating and implementing the results of this research in other settings.

A primary barrier to dissemination of research results are funding issues. As noted above, Decide2Quit and S2S tools are integrally tied to our department's research mission. Thus, we have a strong commitment towards the dissemination and implementation of these tools in other settings. There are also technical barriers to linking the tools to EHRs. Our team has several years of experience developing plug-ins for EHRs and we have worked with all the major products, including AllScripts and Epic. In addition, we have also developed our tools using a "third-party" Web-service model, similar to how credit-card companies develop their products. Thus, any EHR tool can use our Web services to request motivational messages for their smokers in a secure manner. Third, there could be buy-in issues. As noted, our goal is to start preparing for dissemination throughout the study years for continued dissemination of our tools. Through the UMass Clinical and Translational Sciences Award (Dr. Houston is the leader of the Biomedical Informatics core), we are also continually interacting with various healthcare systems and exploring potential opportunities for integrating evidence-based tools in their organizations. As we pursue these opportunities, we will also explore the potential of integrating Decide2Quit within these organizations.

C. Describe how you will make study results available to study participants after you complete your analyses.

We will work with our patient panel to tailor the results in a manner that is understandable to study participants. We will prepare these for dissemination via multiple formats, including on our website, brochures, social media channels, as well as video formats. We will use an iterative approach to developing these results. We will first prepare for dissemination of study results using mock data, since the final dataset is only available at the end of year 3. We will prepare different versions of the report and continue to refine them with the panel until a suitable format is developed. As noted in the proposal, we will use nominal group technique (NGT) process to make panel decisions. After the study data is analyzed, we will then prepare the final formats of the reports and use the above channels for dissemination. As participants complete the study, they will be invited to subscribe to our web and social media channels for continued updates about the study.

In conclusion, our team will pursue multiple opportunities to disseminate the tools tested in this study, and our patient panel will lead our marketing efforts, including helping develop the marketing materials and shaping our strategy. Our team is committed to the ongoing support and dissemination of these tools.

REPLICATION AND REPRODUCIBILITY OF RESEARCH AND DATA SHARING

1. Describe the ability to reproduce potentially important findings from this research in other data sets and populations.

Transparency of study methods and results is essential for replication of research. The Quantitative Methods Core (QMC) and the UMass Clinical and Translation Sciences Center (UMCCTS) have developed a rigorous protocol for ensuring reproducibility of UMass studies. Under the guidance of Dr. Sharina Person (our statistician and QMC investigator), we will follow this protocol in S2S.

A.1. Documentation of study protocol

We will develop an overall study protocol that includes an operations manual, information about the study population, hypotheses to be tested, data source, and information on primary and derived variables. The analysis plan will expand upon the aims and models included within this proposal. Rationale for analytic decision (e.g., exclusion of items, selection of a scoring approach) will be documented in detail. The development of the study protocol will be completed and available in Year 1 of the study. This protocol will be made available to PCORI staff to circulate as they deem appropriate. We will also make the protocol available on demand to individuals with an interest in replicating our findings in a research setting or in using the protocol for dissemination of our findings to other healthcare settings and or/validation of our approach and resulting measures. All newly developed study documentation materials will be submitted to PCORI with the six month progress reports.

A.2. Documentation of study datasets

Documentation of study data sets will be provided within six months of the end of the final funding year. We will conduct ongoing documentation including codebooks, meta-data for the datasets, and programming code used to conduct outcomes analyses. Our code will be documented and annotated, so that it can be adapted for use in similar projects.

2. Describe your data management and sharing plan, including how you will make study data sets available in a manner that is consistent with applicable privacy, confidentiality and other legal requirements, if requested.

All datasets will be cleaned and provided upon request in SAS, Stata, and CSV format, accompanied by detailed documentation describing all procedures used in dataset creation. We will follow similar procedures established by the QMC for sharing datasets, including creating a website that designates the contact person and a request form for the dataset. Anyone requesting a dataset will be able to access this form online.

3. Propose a budget to cover costs of your data-sharing plan, if requested.

The Department of Quantitative Health Science and the Health Informatics and Implementation Science Division at the University of Massachusetts Medical School are committed to this research and will provide support for funding the website for data sharing and staff effort. No additional funds for data-sharing are requested.

PROTECTION OF HUMAN SUBJECTS

Describe the protection of human subjects involved in your research.

1. Risks to the Subjects

A. Human Subjects Involvement and Characteristics

In Smoker-to-Smoker (S2S) Peer Marketing and Messaging to Disseminate Tobacco Interventions (S2S), we will test the dissemination and effectiveness effects of two smoker-driven interventions:

2. **Access to peer recruitment tools:** Tools to facilitate smokers' recruiting their peers to increase Decide2Quit access (NCI R21CA158968).
3. **Recommender computer tailored health communication (recommender CTHC):** Complex machine learning algorithms (recommender systems) that uses smokers' feedback (explicit and implicit) in the current and prior studies to adapt its selection of messages to smokers (PCORI IP2P1000582).

Our goal is to test the enhancements offered by the peer recruitment and recommender CTHC (individually and collectively) over an active comparison group (recruitment using online advertisements and the motivational messages tailoring of the standard CTHC system of Decide2Quit). Human subjects will be involved in the study. In this study, we will recruit we will recruit 1200 smokers online (Aim 1 and 2).

Table 1: Compensation Type.	
One month online or telephone follow-up	$25
Six month online or telephone follow-up	$25
Mailed saliva NicAlert® test	$50

B. Data Collection

There are several data sources in this project (see plans for collecting and storing this data in UMass regulated environment). The regulated environment is located in the data center and maintained by the UMass Information Services department. It provides a secure environment for hosting the applications, as well as the databases of the applications. The setup of regulated environment provides the needed security protocols for the regulatory and Federal standards required. Access for programmers is restricted through a Virtual Private Network and a secure RSA token and only restricted personnel are allowed access to the regulated environment The Regulated environment is secured using hardware and software firewalls, along with access restrictions to enforce governmental policies requiring to enforcement. Applications and the database are hosted on different servers to provide additional security for the data. Web and mobile applications can connect to the application server via HTTPS. HTTPS or secure socket layer (HTTPS) is the current standard for secure connectivity to servers on an encrypted channel. The application sever connects to the database server on a secure, password protected port. We have programs continually monitoring these ports to detect any unauthorized access.

Table 1: Data Collection			
Data Source	**Data Elements**	**Private identifiers**	**Data Stored In**
Search Ad Manager	Online advertisement stats (no of users who saw ads, etc.)	NO	Search ad managers (Aggregate data)
Baseline during registration	Demographics, Participant smoking characteristics (allowing smoking at	Yes	UMass Regulated Environment

	home, quit in last 12 months), Number of cigarettes/day		
Every Decide2Quit visit	Readiness to quit, Use Of Decide2Quit	Yes	UMass Regulated Environment
Every message (email or text-messaging)	Explicit influence ratings, message sent date	Yes	UMass Regulated Environment
6th month Follow-up (Online or phone)	7-day point prevalence smoking cessation, number of cigarettes	Yes	UMass Regulated Environment; Survey will be entered by research staff directly into our server.
6thmonth Follow-up (mailed)	Biochemical verification saliva NicAlert®	Yes	Our research staff will receive the mailed sample, verify the results and, upload them to the database in the UMass Regulated Environment. We will then dispose of the saliva sample.

B.1 UMass Regulated Environment:

C. Potential Risks

The risks of the study are not high, and thus the safety monitoring plan has been matched to the risk to subjects in this study. Risks to participants relate mostly to misinterpretation of what is research and what is loss of confidentiality. The major risk is the accidental disclosure of information; however, every precaution will be taken to prevent this and the study team has an excellent track record of protection of confidential data. As noted, all data will be stored in the regulated environment. All data collected will be stored in a HIPAA compliant regulated environment and access will be only through a secure VPN network. All smokers' related identifiers are encrypted in the database. Our biostatistician will organize data security and archiving. In no way will individual participant data be released to the public or cited in a publication. We have substantial experience with implementing these methods successfully. All our research staffs are trained in HIPAA compliance and will complete all human subjects training.

There may be some stress involved in completing the follow-up survey, but we will emphasize that this participation is voluntary. Note that all participants will receive saliva NicAlert® test available over the counter. The NicAlert detects cotinine, the major metabolite of nicotine. Cotinine is the preferred marker for tobacco use because cotinine stays in the body much longer than does nicotine. The presence of cotinine in saliva is a reliable indicator for tobacco use within the past several days. Every saliva NicAlert® test kit comes with saliva collection containers, which will make it easy for participants to mail it to us. We will have a research staff available by phone or email to help the participants complete the saliva NicAlert® test.

II. Adequacy of Protection Against Risks

A. Recruitment and Informed Consent

As described above, individuals who are smokers will be recruited for the study. Our investigators (including patient investigators) and staff will be trained in HIPAA compliance and complete all human subjects training. Smokers will be recruited through online advertisements (Facebook and Google) or by peer recruitment. These smokers will be asked to

provide online consent. We have conducted multiple online studies and will format our online consent to be easily understandable to the participants.

B. Protection against Risk

We have minimized data collection to only data needed to answer study hypotheses. We have stringent protection against breach of confidentiality using secured servers and locked office spaces for data entry at UMMS. The study statistician will do periodic checks to ensure that participant confidentiality is protected at all stages of data management and analysis. At the start of the study, all study staff will be trained in practices that ensure participants' confidentiality and privacy. We will only share aggregate data with our patient panel.

Specifically, there may be two situations that could accidently reveal the participation in an online study. Our Facebook website plugin will facilitate peer recruitment of smokers to the study. Through the website plugin, smokers will be able to post private messages. These private messages are only viewable by the person that the message is sent to. We will emphasize with the recruiter the importance of using private messages, and the potential risks of posting messages on Facebook through other means. We will make all effort to minimize risks during biochemical verification. The cover for the mailing of the sample will only contain a random number and not the participants' identifier. This random number will be stored in another database in the regulated server (not our study database) and be linked via another identifier to the participants' data. Only our research staff and the PI will have access to this random number database. This way, we reduce the potential of linking the random number to the participants' data by others.

Risks for participation in the intervention are not high, and we anticipate that participation may increase cessation. The alternative to participation for smokers is not to participate. Although we do not anticipate any adverse health events intervention, the participants will be asked to call the project manager and/or IRB at UMMS to report any adverse events (AEs) or serious adverse events (SAEs). Again, participants will be informed not to report urgent symptoms (chest pain) to the study personnel, specifically not to be reported through the website, but to call their physician or an emergency number. Any hospitalizations or deaths discovered by the research team will be promptly reported to the IRB with an assessment of whether any study procedures may have contributed to these outcomes. Should any SAEs occur they will be reported immediately to the UMMS IRB and to NIH. Actions taken by the IRB in response to SAEs will also be reported to NIH, as will reports of changes or amendments to the protocol as a result of an SAE.

As noted, in order to ensure patient-centeredness, we will hire 5 patient Investigators to serve on a patient-expert panel. These patients will be considered part of the research team and will give input on research design, implementation and dissemination. These patients will paid for their time; they will receive $50/meeting and will be invited to 15 meetings/year. However, even though these patients will have completed human subjects training, we will only share with them de-identified and aggregate data. Our study staff will create these reports for them before every meeting. Our interaction with participants is minimal, and all data will remain confidential and only reported in aggregate. There may be some stress involved in referrals for the direct and peer recruits, but we will emphasize that this participation is voluntary. *The study does have the potential to increase smoking cessation, which may likely provide direct health benefits to the participant.*

III. Potential Benefits of the Proposed Research to the Subjects and Others

The major benefit to smokers is the additional resources to encourage smoking cessation and the potential for supporting cessation attempts resulting in quitting smoking and the resulting health benefits.

IV. Importance of the Knowledge to be Gained

This project will help to identify effective strategies for increasing use of cessation treatments. This project is focused on the effective dissemination of Decide2Quit, a Digital intervention for Smoking Cessation (DISC). Engaging smokers to DISCs has been challenging due to limited reach and limited longitudinal engagement. Even if DISCs succeed in getting smokers to access, they do not longitudinally engage with them limiting their effectiveness. The aim of this study is to test two methods for increasing dissemination and effectiveness of DISCs.

V. Data and Safety Monitoring Plan

A. OVERVIEW

The risks associated with the data collection and participation in this study are low. The primary risk to subjects is the accidental disclosure of information; however, every precaution will be taken to prevent this and the study team has an excellent track record of protection of confidential data. There are no health or safety risks for participation in the S2S study. To that end the purpose of this Data and Safety Monitoring Plan (DSMP) is to specify the procedures and rationales of the current study to ensure the safety of participants' data and the validity and integrity of the data.
For smokers, the major benefit of participation in the S2S study, is the additional resources to encourage smoking cessation and the potential for supporting cessation attempts resulting in quitting smoking and the resulting health benefits.

B. OVERSIGHT RESPONSIBILITIES

Oversight of the trial is provided by the Principal Investigator (PI), Dr. Sadasivam, Dr. Person, the faculty statistician and co-investigators, Dr. Thomas Houston and Dr. Jeroan Allison ("co-investigators" throughout).

C. MONITORING PROCEDURES

Dr. Sadasivam assures that informed consent is obtained prior to performing any research procedures, that all subjects meet eligibility criteria, and that the study is conducted according to the IRB-approved research plan.

Study data are accessible at all times for the PI and co-investigators to review. The PI, Dr. Sadasivam, the biostatistician, the project manager and the analyst will regularly review database admin reports to inspect for data collection completeness. Furthermore study recruitment and retention will be monitored using the aggregated summary reports available on the admin site. Project team monitoring includes regular review (monthly) reports which present statistics regarding recruitment, retention and general tracking of study participants in a CONSORT type diagram in order to monitor study progression. In addition study data will be assessed every three months (once a quarter) to examine completeness of survey responses. In addition to these reports, the Decide2Quit website has an Admin Portal which provides real-time reports with the following metrics:

- user lists provides data such as the user's contact information, consent date, randomization arm, their follow-up survey status, referral source, registration date, basic demographic characteristics coded into categories, email message counts (to track the number of messages sent to them from the system)
- exports of follow-up data which includes all the data collected on the follow-up surveys
- summary reports which provide us an aggregated count of the total number of registered users overall and within each randomization arm. In addition, we have summary reports to provide us aggregated counts of users within racial/ethnic and gender categories.

All of these reports require login authentication and are only accessible behind the UMMS firewall. The PI ensures all protocol deviations and unanticipated events are reported to the IRB according to the applicable regulatory requirements.

D. COLLECTION AND REPORTING OF SAEs AND AEs

For this study, the following standard AE definitions are used:

Adverse event: Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure.

Serious Adverse Event: Any AE that results in any of the following outcomes:

- Death
- Life-threatening
- Event requiring inpatient hospitalization or prolongation of existing hospitalization
- Persistent or significant disability/incapacity

AEs are graded according to the following scale:

Mild: An experience that is transient, & requires no special treatment or intervention. The experience does not generally interfere with usual daily activities. This includes transient laboratory test alterations.

Moderate: An experience that is alleviated with simple therapeutic treatments. The experience impacts usual daily activities. Includes laboratory test alterations indicating injury, but without long-term risk.

Severe: An experience that requires therapeutic intervention. The experience interrupts usual daily activities. If hospitalization (or prolongation of hospitalization) is required for treatment it becomes an SAE.

The study uses the following AE attribution scale:

Not related: The AE is clearly not related to the study procedures (i.e., another cause of the event is most plausible and/or a clinically plausible temporal sequence is inconsistent with the onset of the event).

Possibly related: An event that follows a reasonable temporal sequence from the initiation of study procedures, but that could readily have been produced by a number of other factors.

Related: The AE is clearly related to the study procedures.

Identification of AEs

As previously stated, given that this is not a medical or therapeutic intervention there are no health or physical safety risks associated with participation in the S2S study. Furthermore, contact between the study participants and study research staff is extremely limited and occurs primarily via email with some limited contact over the phone.

Should an AE involving a single participant occur it could potentially be identified is through notification from the participant directly to the study staff, PI or UMMS IRB. The only other occasion might be if a participant chose to complete a follow-up survey over the phone and the participant informed the study staff of an issue at that time.

Reporting of Unanticipated Events

With regard to unanticipated events, our study adheres to the University of Massachusetts Medical School IRB's SOPs. In particular we follow the "SOP HRP-112: Reportable New Information" which states that should our project team become aware of any information that represents an unanticipated problem involving risk to subjects or others, we will notify the IRB chair or vice-chair within 24 hours of becoming aware of the information for consideration of whether any immediate actions are necessary to protect the rights and welfare of subjects in advance of the meeting and then we will submit the report to the IRB Committee for review.

Should participants have any questions or concerns they are provided with the contact information for our study team as well as the UMass IRB.

E. MANAGEMENT OF RISKS TO SUBJECTS

Expected AEs

As previously stated, there are no health or physical safety risks associated with participation in the S2S study. The primary risk to subjects is the accidental disclosure of information or a data security breach of the decide2quit website. Our site is located on servers setup as part of the regulated environment maintained by the University of Massachusetts Medical School Information Services (UMMS IS). Please reference the Data Management section for a detailed description of the UMMS IS servers. These servers are continuously monitored for any suspicious activity.

Management of AEs

Should a data breach occur UMMS IS will immediately inform the PI and take necessary steps to fix the breach. The PI will work collaboratively with UMMS IS to ascertain the scope of the breach to determine which participants may have been affected and what data were leaked. The UMMS IRB would also be notified within 24 hours of the PI becoming aware of the breach and a decision would be made as to how to proceed with regards to the study protocol.

Dose Escalation and Dose-Limiting Toxicities

Not applicable.

F. DATA ANALYSIS PLANS

This study does not involve an intervention which requires safety or efficacy monitoring nor does it have any study stopping rules. Ongoing data monitoring as described above in the Monitoring Procedures Section is focused on recruitment and retention. In addition we will perform limited checks on overall data quality to ensure that our data capture system is operating correctly and that the survey data is written to the database.

G. PLAN FOR DATA MANAGEMENT

Compliance of regulatory documents and study data accuracy and completeness will be maintained throughout the study duration.

Our approach to maintaining confidentiality is as follows:

1) Only collect the necessary Information and ensure that it is as anonymous or de-identified as possible

    a. We have minimized data collection to that which is needed to answer our hypotheses. Or to operationally execute our study's protocol. The only identifiable information collected are email (necessary for logging into the system) and phone number also critical for the follow-up data collection. Data that is collected solely for the purposes of the protocols operations include first name and last name and mailing address. However, we only request the mailing address if a participant indicates that they are willing to complete a NicAlert test at their six month follow-up.

    b. To ensure that the study data is held confidential, consented participants will be assigned a study ID (identifier). We will not be collecting Social Security numbers, Date of Birth, or other unique identifiers other than those previously mentioned.

c. In no way will individual participant data be released to the public or cited in a publication. Our group has substantial experience with implementing these methods successfully. Our interaction with participants is minimal, and all data will remain confidential and only reported in aggregate.

2) Training Staff

a. All project team members will be trained in practices that ensure participants' confidentiality and privacy. In order to obtain access to any identifiable participant data, staff must be added to our IRB and complete CITI training on HIPAA protections and Good Clinical Practices.

b. Furthermore, research staff are instructed to only access identifiable information when it's necessary to conduct their work on the protocol. For example, if they are conducting follow-up phone calls to participants who have not completed the online survey or if they are mailing out gift cards to those who have completed the survey. At no time will they download the identifiable data from the secure UMMS servers.

3) Security of our Decide2Quit Website

a. The data will be encrypted and stored in a HIPAA compliant UMMS regulated environment and access will be only through a secure VPN network. The UMMS Regulated Environment provides applications a secure network for confidential data. The Regulated Environment has been securely configured to allow application access via the secure socket layer (HTTPS) protocol — a protocol that delivers server authentication, data encryption, and message integrity. The setup of Regulated environment provides the needed security protocols for the regulatory and Federal standards required. The Regulated Environment is secured using hardware and software firewalls, along with access restrictions to enforce governmental policies requiring to enforcement.

CONSORTIUM CONTRACTUAL ARRANGEMENTS

Describe the proposed research projects that subcontracted organizations will perform. Explain the strengths that these partners bring to the overall project.

This study will primarily be conducted at the University of Massachusetts Medical School. We have two aims.

- **AIM 1:** Implement the hybrid effectiveness-dissemination trial of S2S enhanced functions to increase dissemination (recruitment and repeated use) and effectiveness of Decide2Quit with 1200 smokers
- **AIM 2:** For the Effectiveness randomized trial, we will recontact participants after six months of enrollment. Compared to the standard messaging group, the recommender CTHC is designed to increase smoking cessation rates at follow-up.

As recommended by reviewers, we have added Dr. Bridget Smith (Feinberg School of Medicine at Northwestern University in Chicago, IL) to our team to help us quantify the resources needed to successfully replicate our intervention. From the perspective of an implementing organization, we will compare the costs of standard Decide2Quit, the peer recruitment enhanced Decide2Quit, and the recommender CTHC enhanced Decide2Quit, and the fully enhanced Decide2Quit. As a research associate professor at Northwestern and a research health scientist at the Center of Innovation for Complex Chronic Healthcare and formerly the co-director of the Spinal Cord Injury Quality Enhancement Research Initiative (SCI QUERI), Dr. Smith has over 15 years of experience in the areas of health economics and outcomes. She has experience designing methods and performing economic and statistical analyses. She has extensive experience with cost, primary data collection using surveys and medical record reviews, and with studies integrating qualitative and quantitative methods and has previously collaborated with Dr. Sadasivam to examine costs associated with a tobacco cessation intervention. Dr. Smith will help the team track staff time associated with each intervention arm, including time for training, recruiting, and administering the different aspects of the intervention. In addition, she will help us will estimate development costs of each intervention in our prior NIH and PCORI-funded studies and any equipment or supply costs. Using best practices outlined budget impact analysis, she will use these information to will create tables to describe the assumptions of our inputs and outputs of our budget impact analysis, and perform sensitivity analyses to examine how changing the assumptions of the model impact the potential costs for an organization implementing the intervention.

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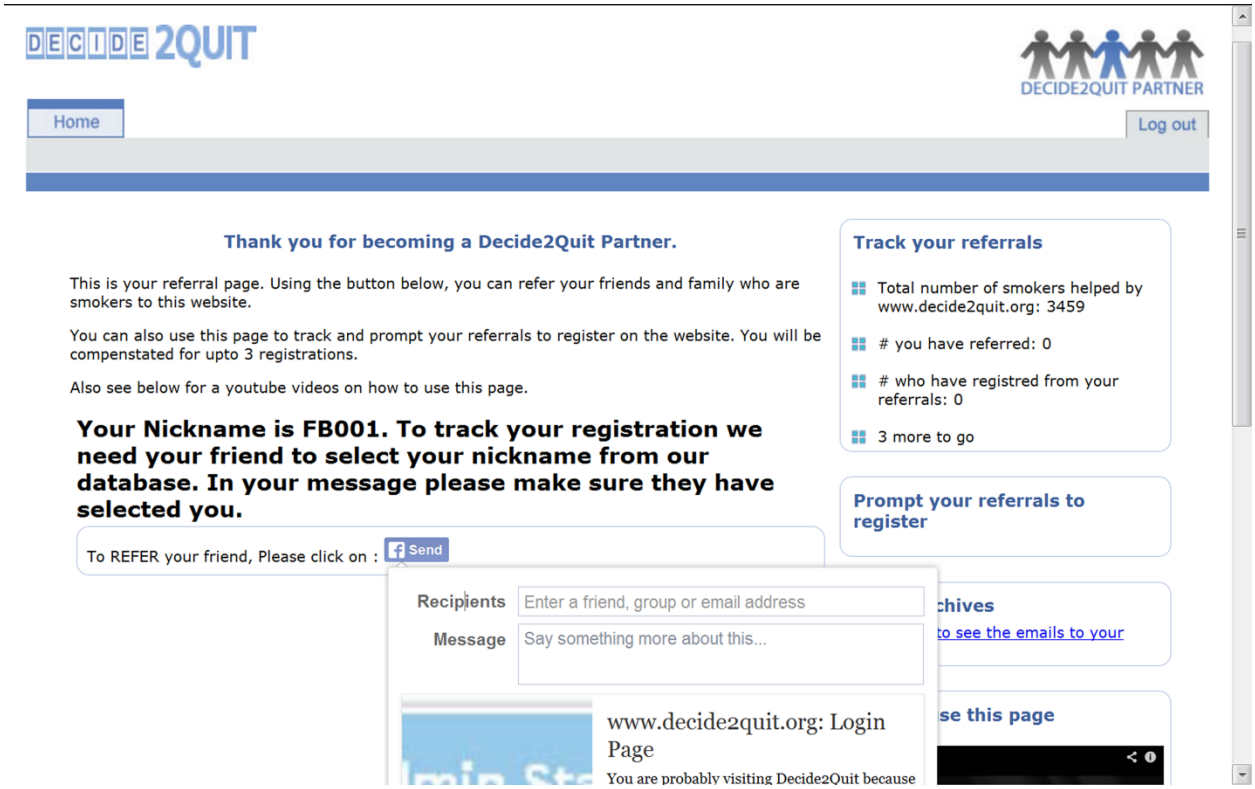
APPENDIX

APPENDIX A



APPENDIX B

What's in your wallet? A Message from Your Online Community Darcy, a 39-year-old, has thought about the financial savings of quitting smoking and say. Plan to save all the money you spent on cigarettes just like you were still buying them and put it away to see how much you can save and use it for something great :). Saving to reward yourself for quitting can be really motivating. Remember to use the money you save for something you really want and not for something you need! To learn more, please visit www.decide2quit.org	***Socio-Cultural Attributes-Money*** ***Behavioral treatment general*** ***General Treatment-Decide2Quit.org***
Smoking hurts more than just your lungs: A Message from Your Online Community. Tina, a 21-year-old, realizes that when quitting, it's important for women to think about longevity of life. Many women have children and want to see them grow, but you can't if you die of cancer. Smoking harms nearly every organ in the body. Not only do smokers potentially shorten their life but they also are sick more often, take more days off work, and have longer hospital stays. To learn more, please visit www.decide2quit.org.	***Socio-Cultural Family/Friend Problem*** ***Health: Physical Functioning - Smoking Risk*** ***General Treatment-Decide2Quit.org***
It's not too late Even though smoking really harms your body, it's not too late you can undo much of the damage by quitting smoking now. To learn more, please visit www.decide2quit.org.	***Health: Physical Functioning - Smoking Risk*** ***Health: Physical Functioning-Quit Benefit*** ***General Treatment-Decide2Quit.org***
How do I love thee? Are you concerned about how your smoking affects your family and friends? Until you are ready to quit, try to avoid smoking around your loved ones by going outside or not smoking in the car. Taking small steps may help you prepare to quit. To learn more, please visit www.decide2quit.org.	***Socio-Cultural Family/Friend Problem*** ***Behavioral treatments- general*** ***General Treatment-Decide2Quit.org***
And the list goes on… Long term risks of smoking include heart attacks and stroke, cancer of all types, osteoporosis, long-term disability, and the need for extended care. Think about what your life will be like if you keep smoking. To learn more, please visit www.decide2quit.org.	***Health-Medical problems*** ***Health: Physical Functioning - Smoking Risk*** ***General Treatment-Decide2Quit.org***