Protocol

Implementation Strategies to Improve Tobacco Treatment for UF Health Cancer Center Patients

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1. Background

Smoking causes 30% of all cancers and 80% of mortality from head and neck and lung cancer.[1,2] Upward of 25% of the 12 million cancer survivors in the US are smokers.[3] Continued tobacco use among cancer survivors reduces the effectiveness of cancer treatments and is associated with increased overall and cancer-specific mortality, increased risk for recurrence and second primary cancers, and diminished quality of life after treatment.[4–10] The routine assessment of tobacco use and the provision of tobacco use treatment (TUT) are recommended by all major professional and advocacy groups in oncology.[11,12] Due to the competing demands of complex cancer care, however, cancer centers are challenged with implementing strategies that both assess tobacco use and link tobacco users with TUT services. Whereas assessment of tobacco use may be common in oncology settings, improved cessation outcomes will not be realized if patients are not offered counseling and TUT support.[13] TUT for cancer patients may be improved substantially with solutions to accurately identify tobacco use, provide patient-centered treatment support, and minimize the burden on clinical staff.

The purpose of this study is to investigate the feasibility of implementing multi-level strategies to improve the access and utilization of TUT for cancer patients. Our strategies includes 1) offering provider and clinical staff training on current best practices, 2) developing an audit and feedback process, and 3) offering patients the choice of a dedicated technology-based cognitive behavioral therapy (CBT) program in addition to existing evidence-based TUT programs (i.e., the Florida Quitline; and Area Health Education Center [AHEC][14]). The ultimate goal of this research is to provide new knowledge to facilitate the widespread adoption, implementation, and dissemination and sustained utilization of evidence-based tobacco use treatments in cancer care settings.

This protocol focuses on the patient-level trial only (Strategy 3).

A separate protocol was developed for the provider-level implementation strategies (Strategies 1 and 2; see IRB201800135).

The full protocol was approved by the UF Health Cancer Center Scientific Review and Monitoring Committee (Protocol # OCR1729; 01/26/2018).

2. Study Description

There is evidence that cancer patients benefit from dedicated services to help them quit smoking.[15] Our evidence-based mobile phone CBT (mCBT) intervention will capitalize on the convenience and growing ubiquity of smartphone technology to deliver CBT and verify abstinence.[16] We will offer patients at two UF Health Cancer Center (UFHCC) clinics 3 TUT options (i.e., AHEC, Quitline, or mCBT). Assignment to TUT options will be based on patient preferences. Patients who choose AHEC/Quitline will be referred by a nurse using Epic. Those choosing mCBT will participate in a 12-week tobacco treatment program via their smartphone. Only participants with a smartphone or data plan will be eligible to participate in mCTB; the research assistant will confirm verbally at enrollment. Participants in mCBT will use Vidyo, a HIPAA-compliant video-conferencing platform, on their smartphone to complete the treatment program. Participants will meet with a certified tobacco treatment specialist (CTTS) on Vidyo for 30 minutes, once a week, for 6 weeks. The counselor will cover topics that include addiction, withdrawal, dealing with triggers, overcoming cravings, and relapse prevention. To verify abstinence, we will collect breath carbon monoxide (CO) samples during weeks 1, 6 and 12 of the study and use Vidyo to confirm identity. To collect this sample, participants will blow into a CO monitor (iCOTM Smokelyzer®) that attaches to their smartphone.

In addition, participants in AHEC/Quitline/mCBTmay provide a saliva swab at the end of the study (week 12), using a saliva sample kit we provide by mail, to test for cotinine levels.

3. Research Plan

Study Design: This study uses a mixed methods approach and will inform the design of a pragmatic clinical trial to improve the delivery of tobacco use treatment services to cancer patients.

Study Setting: The pilot study will be conducted at the UF Health Medical Oncology, Ear, Nose & Throat (ENT), and Radiation Oncology clinics. Smoking is the leading cause of head and neck cancers, and almost one-third of patients continue to smoke after their head and neck cancer diagnosis, making this a priority population for intervention.

Population: UF Health cancer patients ≥18 yrs old who are current smokers and smartphone users; for mCBT, we will also ensure CO breath sample >5 parts per million (ppm). Patients with unstable medical or psychiatric illness or use disorder for illicit drugs will be excluded.

Procedures: Patients who are current smokers will be introduced to a research assistant (RA) by someone who has a clinical relationship with the patient. Following screening and brief counseling by the provider, the RA will offer eligible patients the 3 TUT options (i.e., AHEC, Quitline, or mCBT) and will use the "Choose to Quit" flyer to facilitate TUT choice. Three versions of the flyer exist to avoid order bias. Only smartphone users will be eligible to enroll in mCBT. If a patient is interested in TUT and the research study, the RA will describe the study in detail (based on their TUT selection) and obtain written informed consent. If patients are interested in the study but do not want to participate at the moment, the RA will use the back of the flyer to obtain the patient's consent to re-contact. If patients are interested in TUT but not interested in the research study, the RA will complete a referral request form to enroll the patient in AHEC/Quitline if desired. The RA will give this form to the patient's clinician or nurse to initiate the referral in EPIC. The RA will complete a referral request form for all patients interested in AHEC/Quitline.

Patients who are interested in the study will have the option to choose a paper-based or electronic informed consent (eIC) method. Prior to consenting, the RA will ask for the patient's preferred method. If the eIC method is selected, paper-based consent forms will be available if partially throughout the eIC process a patient changes his/her mind and prefers the paper-based method instead. Patients will be given the opportunity to consider whether or not to participate and to ask questions prior to signing the paper-based or eIC form. A copy of the written informed consent will be provided to patients; Patients who choose the eIC method can select to receive a copy via email.

After obtaining informed consent, the RA will administer the Patient Exit Interview (PEI) in REDCap and arrange a follow-up phone interview. Patients who choose AHEC/Quitline will be referred by a nurse using Epic. Those choosing mCBT will be trained on the use of Vidyo and the iCO™ Smokelyzer® by the RA and follow-up will be arranged with a CTTS counselor.

Consent to Re-Contact
The RA will follow-up with patients via telephone who gave consent to re-contact. The RA will briefly describe the study and the three TUT options, and ask patients if they are interested in participating. The RA will email interested patients a link to the eIC form (based on their TUT selection) and thoroughly review the form with the patient. Patients will give consent remotely by signing and submitting the eIC via REDCap. After receiving the signed eIC, the RA will administer the PEI over the telephone and arrange a follow-up phone interview. Participants who choose mCBT will receive the iCO™ Smokelyzer® via mail with instructions on how to use the CO Monitor and how to download and use the Vidyo app. A 2-week supply of nicotine replacement therapy (NRT) will also be provided to participants interested in NRT (see next section for NRT details).

mCBT
Participants in mCBT will meet with a trained certified tobacco treatment counselor on Vidyo for 30 minutes, once a week, for 6 weeks. The counselor will cover topics that include addiction, withdrawal, dealing with triggers, overcoming cravings, and relapse prevention. At enrollment, we will offer mCBT participants—if interested—a 2-week supply of nicotine replacement therapy (NRT). The 2-week supply of

NRT is consistent with what is offered to participants at AHEC and the Quitline. Participants who smoke less than 10 cigarettes per day will receive 14 mg of NRT, and those who smoke more than 10 cigarettes per day will receive 21 mg of NRT. Medical clearance from the provider will be obtained prior to NRT administration. At the end of the study (week 12), participants (all participants in mCBT and a random sample of patients referred to AHEC/Quitline) will complete the follow-up telephone interview. At the end of the study, participants (AHEC/Quitline & mCBT) may also provide a saliva sample by mail for us to test their cotinine level; this process will be remotely monitored via Vidyo for participants in mCBT and participants in AHEC/Quitline will be encouraged to contact study staff to answer any questions they may have.

Evaluation Procedures:

i. *Patient Exit Interviews (PEIs):* To assess provider adherence to TUT guidelines, the RAs will conduct PEIs after recruitment with all smokers at checkout (regardless of TUT choice). The RA will use an iPAD to administer the PEI in REDCap. The PEI is a brief patient-reported assessment of provider delivery of counseling.[17] A PEI index score (0-10) is the sum of intervention steps each patient reports that the provider implemented. All socio-demographics (e.g., age, gender, race/ethnicity, rural/urban residence) will be obtained at intake using questions from the PhenX toolkit;[18] We will also examine reasons for TUT selection and measure self-reported past-7-day point prevalence of cigarette smoking, number of cigarettes/day, cigarette type, age of onset[19] and cancer diagnosis experiences.

ii. *Telephone Survey:* Patients who participate in mCBT (n=50), and a random sample of patients referred to AHEC/Quitline (n=25/each), will complete a telephone survey at week 12 that includes: (1) *Treatment Acceptability Questionnaire* (TAQ), 16-items/7-point Likert scales assessing treatment acceptability (i.e., helpfulness in reducing smoking, and thoughts and feelings related to the treatment). Questions will relate to barriers/facilitators of TUT, and open-ended questions assessing suggestions for improvement. (2) *Quality of Life*: 26-item cross-culturally valid WHO Quality of Life-BREF,[20] and (3) prolonged abstinence (i.e., sustained abstinence after an initial period in which smoking is not counted as a failure) and past-7-day point prevalence of cigarette smoking.[19] A $20 incentive will be offered at completion.

iii. *CO Monitor (mCBT only):* Abstinence point prevalence will be defined as CO sample ≤4 ppm and reporting not smoking in the last 7 days. Abstinence will be assessed at weeks 1, 6 & 12. Missing data will be counted as positive for smoking.[16] We will also use CO to test for reduction in smoking over the 3 time points.

iv. *Cotinine level measurement (AHEC, Quitline, & mCBT participants):* At week 12, participants may be asked to provide a saliva swab using a saliva sample kit we provide . Participants will mail the swab in a prepaid envelope to the lab directly. The lab will send the test results to the study team at UF. We will use the test result to measure participants' cotinine levels.

Analysis Plan: All data collected will be entered in a REDCap database. The primary analysis will be the estimation of rates/means, with 95% CIs. To demonstrate the feasibility of the 3 implementation strategies, we will measure reach as the number of smokers visiting the 2 clinics who are referred to any TUT (i.e., AHEC/Quitline/mCBT) divided by the total number of smokers visiting the clinics. For each TUT, we will calculate enrollment as the total number of smokers who enroll in a given treatment divided by the total number of referred smokers; we will compare the rates of patients selecting into each of the 3 TUT programs. We will assess TUT completion as the number of enrolled smokers who complete the program. We will also evaluate acceptability using TAQ. As secondary outcomes, we will measure prolonged abstinence at week 12 and the change (baseline to week 12) in past-7-day point prevalence (all programs), as well as CO-verified abstinence at weeks 6 &12 (mCBT only). CO levels will also be modeled across time (weeks 1, 6, 12) to assess for reductions over time via linear mixed models.

Sample Size Justification: Sample sizes were chosen to obtain sufficiently precise estimates of outcomes to demonstrate feasibility and to provide estimates to power a future R01.[21] Assignment to TUT options will be based on patient preferences. Recruitment will end at week-30 post-trial initiation or sooner if 50 smokers enroll in mCBT. We estimate 14 smokers/week visit the 2 clinics (source: i2b2); thus, we are confident that, using the opt-out approach to TUT referral,[13] an average of 2 patients/week will choose

mCBT and ≥2 patients/week will choose AHEC/Quitline. For reach, 14 smokers/week x 25 weeks=350 leads to a 95%CI whose largest width=0.10 if the observed rate=0.50; any other rate would lead to more precision. If only ½ of 350 enroll in TUT, in obtaining rates of patient choices for the 3 TUT options, our maximum 95%CI width=0.15. Specific to the outcomes among the 50 in mCBT, our maximum 95%CI width for rates on completion/abstinence=0.28. We do not suspect abstinence rates to be as high as 0.50, in which case we will have more precision (95%CI =0.09, 0.31) when the rate=0.20. We expect 175 to enroll in any TUT by study end (when 50 enroll in mCBT). We will thus have 125 in the other 2 groups (AHEC/Quitline). We will randomly sample 25 from each of these 2 groups for follow-up. The corresponding 95%CI for a 0.20 abstinence rate for n=25 would be (0.04, 0.36). In assessing acceptability using TAQ, a similar study observed a SD=13.4.[22] Based on this estimate, n=40 (20% dropout) in mCBT would lead to a 95%CI width=8.6, and n=20 in the other 2 groups would lead to a 95%CI width=12.6.

4. Possible Discomforts and Risks

The risks or discomforts to participating in this study are minimal. The loss of confidentiality is the greatest potential risk to participants. We will take appropriate steps to protect participant confidentiality, and any information we collect from participants, including any identifying information, will be kept in REDCap, a secure, password-protected database. We will de-identify all data prior to moving it outside the REDCap environment. The de-identified data will be kept on a secure, password-protected server. These data will be associated with a unique identification number that we give participants at the beginning of the study. All identifying information in REDCap, including the link that matches participants with their unique identification number, will be destroyed at the end of the study.

5. Possible Benefits

Patients who participate in this program will have the benefits of improved access to tobacco treatment services. Some patients may individually experience no benefit. The information provided by this study will assist in the development of a larger study aimed at increasing tobacco treatment services for cancer patients across the UF Health system.

6. Conflict of Interest

None.

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