**UNIVERISTY OF WASHINGTON**
**Clinical Research Protocol**

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| Protocol Number: | STUDY00011578 |
| Version Date: | 3/29/2023 |
| Sponsor-Investigator: | Kathleen Ramos-Alexander, MD MSc<br>1959 NE Pacific Street<br>Seattle, WA 98195-6522 |
| Funding Organization: | National Institutes of Health (NIH) - The National Heart, Lung, and Blood Institute (NHLBI) |
| Site Investigator: | Kathleen Ramos-Alexander, MD MSc<br>Ramoskj@uw.edu |

**Approval:**

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*PI or Sponsor Signature (Name and Title)* *Date*

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## LIST OF ABBREVIATIONS

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| **AE** | Adverse Event |
| **CF** | Cystic Fibrosis |
| **CFFPR** | Cystic Fibrosis Foundation Patient Registry |
| **CFTR** | Cystic fibrosis transmembrane conductance regulator |
| **DSMB** | Data Safety Monitoring Board |
| **FDA** | Food and Drug Administration |
| **$FEV_1$** | Forced expiratory volume in 1 second |
| **GCP** | Good Clinical Practice |
| **HIPAA** | Health Insurance Portability and Accountability Act of 1996 |
| **ICF** | Informed Consent Form |
| **IEC** | Independent Ethics Committee |
| **IPDAS** | International Patient Decision Aid Standards |
| **IRB** | Institutional Review Board |
| **LTx** | Lung Transplant |
| **PI** | Principal Investigator |
| **PrepDM** | Preparation for Decision Making Scale |
| **SAE** | Serious Adverse Event |
| **ToT** | Take on Transplant |
| **UNOS** | United Network for Organ Sharing |

## PROTOCOL SYNOPSIS

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| **TITLE** | Lung Transplant READY (Resources for Education and Decision-making for Your CF) Pilot Study |
| **SPONSOR** | University of Washington |
| **FUNDING ORGANIZATION** | National Institutes of Health (NIH) - The National Heart, Lung, and Blood Institute (NHLBI) |
| **NUMBER OF SITES** | 1 |
| **SPECIFIC AIMS** | 1. Determine whether Take on Transplant (online educational tool) improves patient preparedness for lung transplant (LTx) discussions using a pilot study that employs randomized, controlled, rollover trial design.<br>2. Longitudinally assess time spent using Take on Transplant through patient-level analysis of tool usage and identify predictors of increased usage. |
| **RATIONALE** | 1. Despite therapeutic advances in CF care, many CF patients will go on to require LTx, including individuals already affected by advanced lung disease, those for whom highly effective CFTR modulators are not available or not tolerated, and for some despite CFTR modulators. Individuals with CF seek information about LTx and feel underprepared for the LTx decision. Use of a decision support tool or online educational materials about LTx may improve the quality, efficiency and effectiveness of LTx education in CF clinic and empower patients to engage in discussions about this complex medical treatment by increasing their sense of preparedness for the discussion. Feasibility must be established. The Preparation for Decision Making (PrepDM) Scale[1] is a validated measure of preparedness for decision making with known variance and high internal consistency (a 0.92-0.96), but it has not been studied in the CF population. Individual questions within the PrepDM Scale are informative and reflect IPDAS process measures[2, 3]. It is unclear whether there are ceiling or floor effects for particular questions within the PrepDM scale when evaluating a LTx decision support tool in the CF population, and the proposed pilot study utilizing a test-retest approach will establish preliminary means standard deviations, and reliability in this population. A prior decision aid for LTx in CF was shown to decrease decisional conflict in a randomized clinical trial and we will assess change in the Decisional Conflict Scale as a secondary endpoint.[4]<br>2. Engagement with Take on Transplant over time allows users to explore the content, potentially viewing more 'CF Stories', 'Resource Library', and 'Frequently Asked Questions' content and more interactions with 'My CF Stage'. Shared decision-making may naturally appeal to and benefit individuals who seek out health-related information, feel empowered to advocate for their own needs, and have more advanced educational attainment, while potentially increasing disparities for patients who are already disadvantaged. Shared decision making interventions |

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| | tailored to disadvantaged groups can increase knowledge, informed choices and participation in decision-making, and reduce decisional conflict for patients in disadvantaged groups. We will obtain an individualized, longitudinal view of the participants' usage data as they interact with Take on Transplant, including page views and time spent per page, to characterize usage patterns over the 1 month. Characterization of different use patterns among individuals with disadvantaged backgrounds (oversampled in Aim 1) could inform enhancements to t Take on Transplant to improve usage and acceptability by patients with limited access to LTx. Carefully assessing health literacy with the TOFHLA[5], an instrument that measures health-related reading comprehension and numeracy, could lead to understanding of mechanisms underlying differential use of Take on Transplant and change in PrepDM Scale. |
| **STUDY DESIGN** | This is a prospective, multi-center, randomized, controlled single-blind rollover pilot study |
| **PRIMARY OBJECTIVE** | To test feasibility and efficacy of Take on Transplant to improve patient preparedness for decision making about LTx. |
| **SECONDARY OBJECTIVES** | • Understand LTx knowledge gained.<br>• Assess changes in decisional conflict.<br>• Measure changes in preparedness for LTx discussions.<br>• Assess changes in depression and anxiety symptoms.<br>• Longitudinally characterize time spent using Take on Transplant through analysis of patient-level usage data and determine whether ongoing use of the tool is associated with maintaining or increasing ratings of preparedness at 1-month.<br>• Identify baseline demographic and health literacy predictors of increased Take on Transplant usage<br>• Analyze interview transcripts to inform revision of Take on Transplant prior to a large randomized controlled trial |
| **NUMBER OF SUBJECTS** | ~50 |
| **SUBJECT SELECTION CRITERIA** | Inclusion Criteria:<br>• Diagnosis of CF<br>• Adult, greater than or equal to 18 years of age<br>• Able to read and understand English, but English can be a second language<br>• Forced expiratory volume in one second ($FEV_1$) less than 50% predicted<br>Exclusion Criteria:<br>• Previously underwent LTx |
| **INTERVENTION ARM** | Take on Transplant – Educational website that couples real-life CF patient experiences of LTx in the form of personal narratives with up-to-date, CF-specific, and guideline-based medical information about LTx. |
| **CONTROL ARM** | UNOS.org – Educational website that contains general information about transplantation (all organs). |

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| **DURATION OF SUBJECT PARTICIPATION AND DURATION OF STUDY** | Subjects will be on study for up to 4 weeks with a total of three study sessions: Introduction Session, 2-Week Follow-up Session, and 4-Week Follow-up Session. |
| **PRIMARY ENDPOINT** | The co-primary endpoint is feasibility, which will be defined as successful by 90% of enrolled participants completing the 2-week study visit.<br><br>The co-primary endpoint is an intention-to-treat assessment of the difference in mean PrepDM Scale in the intervention versus control arms of the study at the 2-week study visit. |
| **SECONDARY ENDPOINTS** | • Difference in mean confidence-weighted true false (CTF) knowledge score will be measured in the intervention versus control arms of the study. CTF scoring adds points for certainty in correct responses and deducts points for certainty in incorrect responses. Participants receive +2 points when "sure" about a correct response, +1 if unsure about a correct response, -1 if unsure about an incorrect response and -2 if sure about an incorrect response. For a 14-item knowledge test, the maximum score is +28 and the minimum score is -28, with higher scores indicating more knowledge about lung transplant.<br>• Decisional Conflict Scale change will be measured from the baseline study visit to the 2-week study visit. The intention-to-treat analysis will compare mean change in the Decisional Conflict Scale between the intervention and control arms of the study. Scores range from 0 [no decisional conflict] to 100 [extremely high decisional conflict].<br>• Likert rating of preparedness will be measured at the 2-week study visit (0=Don't know, 1= Not at all prepared, 2 = A little prepared, 3 = Moderately prepared, 4 = Very prepared). The intention-to-treat analysis will compare mean Likert-scale rating between the intervention and control arms of the study.<br>• PHQ-9 is a scale that measures symptoms of depression in the prior 2 weeks on a 0-27 scale, with higher scores indicating worsening depression and a score of 10 or higher consistent with a diagnosis of depression. Investigators will assess the difference in mean PHQ-9 score in the intervention versus control arms of the study at the 2-week study visit. Investigators will also determine the proportion with new PHQ-9 score greater than or equal to 10 in each arm.<br>• GAD-7 is a scale that measures symptoms of anxiety in the prior 2 weeks on a 0-21 scale, with higher scores indicating worsening anxiety and a score of 10 or higher consistent with a diagnosis of generalized anxiety disorder. Investigators will assess the difference in mean GAD-7 score in the intervention versus control arms of the study at the 2-week study visit. Investigators will also determine the proportion with new GAD-7 score greater than or equal to 10 in each arm.<br>• Longitudinally characterize time spent using Take on Transplant through analysis of patient-level usage data. Average |

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| | time spent using the research website from baseline to 2 weeks will be compared across study arms. Further, time spent using the investigator-designed website will be assessed as a predictor of: 1. change in CTF knowledge about LTx (14-question investigator-designed survey) from baseline to 2-week study visit, 2. change in Likert preparedness from baseline to 2-week study visit, 3. change in Decisional Conflict Scale from baseline to 2-week study visit, and 4. mean PrepDM Scale at 2-weeks.<br>• The PrepDM Scale will be measured for all participants with respect to Take on Transplant and mean score will be compared for participants in the intervention (4 weeks of exposure) versus control arms (2 weeks of exposure). PrepDM scores range on a scale from 0 to 100 with higher scores indicating a higher perceived level of preparation for decision making.<br>• Identify baseline demographic and health literacy predictors of increased tool usage. |

# 1.0 PURPOSE OF THE INVESTIGATION

## 1.1. Name of intervention

Take on Transplant (ToT): an educational website that couples real-life CF patient experiences of LTx in the form of personal narratives with up-to-date, CF-specific, and guideline-based medical information about LTx.

## 1.2. Intended use of the intervention

ToT addresses patient-identified knowledge gaps and provides personalized educational content to help CF patients prepare for LTx discussions and decisions.

## 1.3. Objectives of the clinical investigation

### 1.3.1. Primary objective

The primary research objectives are to pilot test feasibility and efficacy of ToT to improve patient preparedness for decision making about LTx. The co-primary endpoint is feasibility, which will be defined successful by 90% of enrolled participants completing the 2-week study visit. A co-primary endpoint is an intention-to-treat assessment of the difference in mean PrepDM Scale in the intervention versus control arms of the study at the 2-week study visit.

### 1.3.2 Secondary objective(s).

The secondary objectives are to:

- Understand LTx knowledge gained.
- Assess changes in decisional conflict.
- Measure changes in preparedness for LTx discussions.
- Assess changes in depression and anxiety symptoms.
- Longitudinally characterize time spent using ToT through analysis of patient-level usage data and determine whether ongoing use of the tool is associated with maintaining or increasing ratings of preparedness at 1-month.
- Identify baseline demographic and health literacy predictors of increased ToT usage
- Analyze interview transcripts to inform revision of ToT prior to a large randomized controlled trial

## 1.4 Anticipated duration of the clinical investigation

The total duration of the clinical investigation is expected to be approximately 4 weeks: 2 weeks randomized to one arm of the study and 2 additional weeks with access to both websites.

# 2.0 CLINICAL PROTOCOL

## 2.1 Protocol number and title

STUDY00011578: Lung Transplant READY (Resources for Education and Decision-making for Your CF) Pilot Study

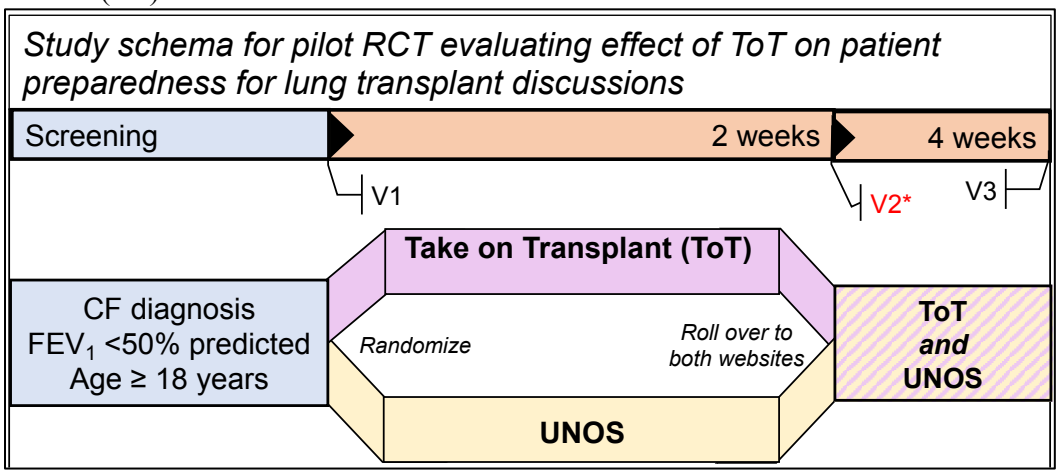
## 2.3 Study design

### 2.3.1 General study design

This is a prospective, multi-center, randomized, controlled single-blind rollover pilot study

### 2.3.2 Study design schematic

Figure 1: The study will last four weeks with a total of three study sessions including the following: Baseline Session (V1), 2-Week Follow-up Session (V2), and 4-Week Follow-up Session (V3).




## 2.4 Subject selection

### 2.4.1 General characteristics of the proposed subject population(s)

Study subjects will be volunteer CF patients, age 18 years or above with $FEV_1$ of less than 50% predicted and have not yet undergone LTx. Approximately 50 subjects who give informed consent, meet all of the inclusion criteria and none of the exclusion criteria will be enrolled in the study.

LTx is an option for treating end-stage lung disease in CF. The population of CF patients with $FEV_1$ less than 50% represents a subset of individuals living with CF who are closer to the stage where LTx might become a viable option. These patients are the ones most likely to benefit from access to ToT, making them a relevant and representative group for this investigation. Additionally, individuals with low socioeconomic status have historically limited access to lung transplant and worsened outcomes. We aim to include individuals considered to be from "communities of concern" as a minimum of 30% of our study population. The "communities of concern" will be individuals who are racially

minoritized, Hispanic ethnicity, Medicaid insurance status (primary or secondary), and/or a high school education or less.

### 2.4.2 Anticipated number of research subjects

The study will enroll approximately 50 adults with CF and an $FEV_1$<50% predicted, without prior LTx. Individuals will be recruited from the University of Washington and collaborating adult CF centers across the United States.

We anticipate 90% (45 participants) of enrolled participants will complete the 2-week study visit.

### 2.4.3 Inclusion criteria

1. Diagnosis of CF
2. Adult, greater than or equal to 18 years of age
3. Able to read and understand English, but English can be a second language
4. $FEV_1$ <50% predicted

### 2.4.4 Exclusion criteria

1. Previously underwent LTx

## 2.5 Study procedures

### 2.5.1 Screening procedures

Research coordinators and lead researchers at the University of Washington (UW) Adult Cystic Fibrosis Clinic will conduct eligibility screening by utilizing the Cystic Fibrosis Patient Registry database (PortCF), medical records, and clinic schedules. Eligible individuals will be contacted before their clinic appointments, with study information provided via phone, and consent forms offered through mail or email.

Additionally, in STUDY0007475 approved by the UW HSD IRB, participants will be distributed a screening survey which provides the ability to voluntarily opt-in to being contacted by the UW research team for additional opportunities to participate in related studies. Collaborators at external sites will screen their local PortCF registry for participants meeting eligibility criteria and advertise the availability of the screening survey. CF patients consent separately to participate in the CFF registry which allows for screening for research study eligibility. The screening survey will be advertized to eligible participants at collaborating CF centers which allows for the recruitment of participants from within and outside of the UW to enable generalizable results. Per HHS guidelines, collaborating sites were considered not engaged in the research and did not require site-IRB approval to advertise the availability of this screening survey.

Individuals recruited from STUDY0007475 who opt-in to being contacted by the UW research team will be contacted to participate in this study. Study staff at the UW will call the patient and provide detailed information about the study. UW study staff will provide informed consent over the phone and the patient will provide verbal consent to participate. The UW research coordinator will mail or email copies of the consent form for participants to keep for their records.

### 2.5.2 Study procedures

The study will last four weeks with a total of three study sessions including the following: Baseline Session (V1), 2-Week Follow-up Session (V2), and 4-Week Follow-up Session (V3). All study visits will occur remotely via Zoom videoconferencing.

Study procedures will include the following:

Surveys – Participants will be asked to complete surveys at each study session. Surveys may consist of the following instruments: PrepDM Scale[1], Decisional Conflict Scale[6], Shortened Test of Functional Health Literacy in Adults (S-TOFHLA)[5], questions from the Health Information National Trends Survey (HINTS)[7], assessment of health numeracy[8], GAD-7[9], an investigator-designed lung transplant knowledge assessment, System Usability Scale (SUS)[10], general satisfaction scale, Hospital anxiety and depression scale (HADS)[11], PHQ-9[12], Cystic Fibrosis Questionnaire – Revised (CFQ-R)[13], Acceptability of Intervention Measure (AIM)[14], Intervention Appropriateness Measure (IAM)[14], and Feasibility of Intervention Measure (FIM)[14]. Each set of surveys will take approximately 15-20 minutes to complete.

Interview – Interviews will take place at each study session, via Zoom teleconferencing. Interviews will take approximately 30-60 minutes. All interviews will be recorded and transcribed for qualitative analyses. The research team will use an interview guide with directed questions discussing topics including shared decision making and general feedback on ToT and the attention control website (unos.org) including perceptions of and experience with using the resources, and any barriers to ongoing use of the research website. Structured interviews on the day of the baseline session may also address preparedness to discuss LTx, ask participants to describe the most impactful aspect of the research websites, and summarize the 'CF Story' that was most meaningful.

Research website – Participants will be introduced to the research website during the baseline session (V1). The research website is a portal that will contain links to two interventions including ToT and an attention control (unos.org). Before accessing the research website during the baseline session, participants will be randomized to first receive access to only one of the two websites through the portal. The research website will track website usage (i.e. time spent, content accessed, etc.) for all study participants for both ToT and unos.org. Once the participant completes the 2-week study visit (V2), the portal will contain access to both ToT and unos.org for the remainder of the study (2 more weeks).

### 2.5.3 Allocation to treatment arms

Participants will be randomized 1:1 to either the intervention ("Take on Transplant") or the attention control (unos.org), stratified by $FEV_1$ <30% versus 30-50%. Participants will be given access to their assigned website via the research website portal for two weeks. After the 2-week session interview, access to the opposite arm assignment will be unlocked and participants will have unlimited access to both the intervention (ToT) and the attention control (Unos.org).

### 2.5.6 Withdrawal of subjects

Subjects can withdraw at any point in time. They will be given contact information of the study staff if they decide they would like to withdraw or if they have any questions pertaining to their involvement in the study.

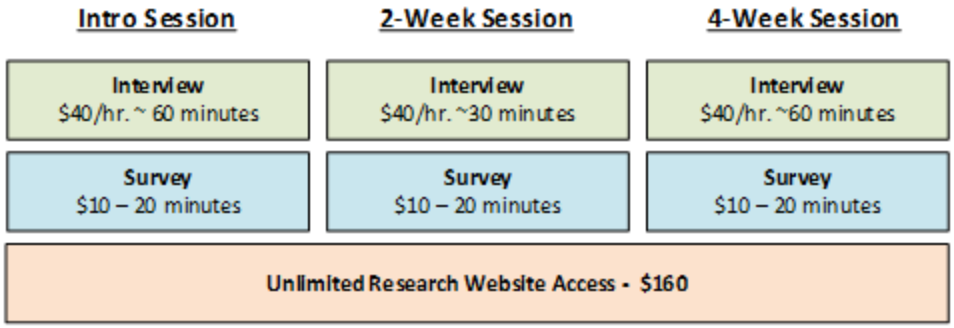
### 2.5.8 Procedures to assess safety

We will assess safety using the PHQ-9[12] and GAD-7[9] survey assessments.

The topic of LTx can be distressing to some with CF. There could be a risk of increasing depression symptoms and/or suicidality through the introduction of LTx education in this patient population. The PHQ-9 and GAD-7 surveys will be administered at the baseline visit (V1) and at both study visits (V2, V3) after patients gain access to ToT or unos.org to assess whether introduction of transplant education has a negative psychological impact on patients including an increase in anxiety, depression, and/or distress. Patients with an abnormal PHQ-9 or GAD-7 will be allowed to enroll in the study because depression and anxiety are prevalent in advanced CF lung disease. We hypothesize use of ToT may actually lessen patients' depression and/or anxiety with time.

The interviewer (UW research staff) will review PHQ-9 responses immediately after responses are submitted. The interviewer will also probe, via discussion with the participant, for any indicators of negative psychological impacts of use of the decision support tool. If possible suicidality is endorsed on the PHQ-9 (positive response to question #9), the interviewer will provide a subject who endorses possible suicidality with the National Suicide Hotline phone number and will inform them to call the National Suicide Hotline if they need help prior to receiving the call from Dr. Ramos or another study physician about the PHQ-9 results. Additionally, the PI, or another study physician, will be notified immediately after the abnormal PHQ-9 result is entered. The patient's CF clinician will be contacted directly immediately via secure communication, by the PI, in the setting of possible suicidality. The PI or another study physician will call the patient within 8 hours of a PHQ-9 response that indicates suicidality and the Columbia-Suicide Severity Rating Scale (C-SSRS) screen with triage points for primary care will be completed. The C-SSRS response protocol will be followed and a safety contract will be established with the patient by the physician by phone. Dr. Ramos, and the other study physicians, are trained physicians, practicing medicine in populations with advanced diseases, end of life concerns, and high rates of mental illness. Dr. Ramos has clinical experience with patients who report suicidality and has the resource of a trained CF mental health specialist for complex cases.

### 2.5.9 Schedule of study visits and compensation




## 2.6 Study outcome evaluations

### 2.6.1 Study endpoints

Primary endpoints

- The co-primary endpoint is feasibility, which will be defined as successful by 90% of enrolled participants completing the 2-week study visit.

- The co-primary endpoint is an intention-to-treat assessment of the difference in mean PrepDM Scale in the intervention versus control arms of the study at the 2-week study visit.

Secondary endpoints

- Difference in mean confidence-weighted true false (CTF) knowledge score will be measured in the intervention versus control arms of the study. CTF scoring adds points for certainty in correct responses and deducts points for certainty in incorrect responses. Participants receive +2 points when "sure" about a correct response, +1 if unsure about a correct response, -1 if unsure about an incorrect response and -2 if sure about an incorrect response. For a 14-item knowledge test, the maximum score is +28 and the minimum score is -28, with higher scores indicating more knowledge about lung transplant.
- Decisional Conflict Scale change will be measured from the baseline study visit to the 2-week study visit. The intention-to-treat analysis will compare mean change in the Decisional Conflict Scale between the intervention and control arms of the study. Scores range from 0 [no decisional conflict] to 100 [extremely high decisional conflict].
- Likert rating of preparedness will be measured at the 2-week study visit (0=Don't know, 1= Not at all prepared, 2 = A little prepared, 3 = Moderately prepared, 4 = Very prepared). The intention-to-treat analysis will compare mean Likert-scale rating between the intervention and control arms of the study.
- PHQ-9 is a scale that measures symptoms of depression in the prior 2 weeks on a 0-27 scale, with higher scores indicating worsening depression and a score of 10 or higher consistent with a diagnosis of depression. Investigators will assess the difference in mean PHQ-9 score in the intervention versus control arms of the

study at the 2-week study visit. Investigators will also determine the proportion with new PHQ-9 score greater than or equal to 10 in each arm.

- GAD-7 is a scale that measures symptoms of anxiety in the prior 2 weeks on a 0-21 scale, with higher scores indicating worsening anxiety and a score of 10 or higher consistent with a diagnosis of generalized anxiety disorder. Investigators will assess the difference in mean GAD-7 score in the intervention versus control arms of the study at the 2-week study visit. Investigators will also determine the proportion with new GAD-7 score greater than or equal to 10 in each arm.
- Longitudinally characterize time spent using Take on Transplant through analysis of patient-level usage data. Average time spent using the research website from baseline to 2 weeks will be compared across study arms. Further, time spent using the investigator-designed website will be assessed as a predictor of: 1. change in CTF knowledge about LTx (14-question investigator-designed survey) from baseline to 2-week study visit, 2. change in Likert preparedness from baseline to 2-week study visit, 3. change in Decisional Conflict Scale from baseline to 2-week study visit, and 4. mean PrepDM Scale at 2-weeks.
- The PrepDM Scale will be measured for all participants with respect to Take on Transplant and mean score will be compared for participants in the intervention (4 weeks of exposure) versus control arms (2 weeks of exposure). PrepDM scores range on a scale from 0 to 100 with higher scores indicating a higher perceived level of preparation for decision making.
- Identify baseline demographic and health literacy predictors of increased tool usage.

### 2.6.2 Sample size determination

This will be a pilot and feasibility study, and we anticipate 90% of 50 enrolled participants (95% CI 79-96%) will complete the 2-week study visit (V2).

### 2.6.3 Statistical analysis plan

Primary endpoints

The co-primary endpoint is feasibility, which will be defined successful by 90% of enrolled participants completing the 2-week study visit (V2). Descriptive statistics will be used to determine whether this threshold was met.

The co-primary endpoint of difference in PrepDM scale score (Difference = intervention – control) at 2-weeks will be assessed using linear regression, with statistical significance level set at 2-sided alpha $<0.05$.

Secondary endpoints

Continuous secondary endpoints will be assessed using linear regression, with statistical significance level set at 2-sided alpha $<0.05$.

Categorical secondary endpoints will be assessed using Pearson's chi-squared test of independence, with statistical significance level set at 2-sided alpha $<0.05$.

Graphical methods and descriptive statistics will be used to evaluate differences in usage during the 4 weeks of access across subsets of the cohort with different socioeconomic

status (based on insurance status, income, education level) and health literacy (based on S-TOFHLA). Exploratory models will test for a dose-response relationship by 1) time spent using the tool (uses/week) and 2) number of 'CF Stories' viewed and PrepDM Scale at 2-week and 4-week study visits. Linear regression may be used to determine whether predictors of increased time spent using the tool can be identified from baseline demographics and questionnaire results. Subgroup analyses will compare changes across instruments among participants with adequate health literacy to those with inadequate or marginal health literacy. We will also perform subgroup analysis for patients with $FEV_1$ <30% predicted.

These data will inform the feasibility of completing a larger, multicenter, randomized controlled trial of ToT and will inform duration of the larger trial.

#### 2.6.4 Data and Safety Monitoring Committee

A data safety monitoring board (DSMB) will not be necessary for this research protocol. Research in this pilot study poses no more than minimal risk to participants. There will be no statistical monitoring to determine whether the clinical trial should be terminated for reasons of safety. There will be no interim evaluations for efficacy. There are no planned stopping rules for futility since this is a pilot study. Safety monitoring will focus on ensuring participants are not experiencing any significant or unexpected psychological distress and that they are satisfied with the study intervention and interviews. The Principal Investigator will provide ongoing observation for psychological distress as reported in satisfaction surveys or during interviews. The PI will monitor for Adverse Events related to the study, but there is a very low risk for adverse events with the proposed intervention. Dr. Ramos has three years of experience as a medical monitor for the Cystic Fibrosis Foundation Therapeutics Development Network Coordinating Center, and is well-qualified to review and make a determination of relatedness of a serious adverse event (SAE) to the study intervention.

## 3.0 RISK ANALYSIS

### 3.1 Anticipated risks

Subjects may be exposed to minimal risks associated with the conduct of this study.

Psychological risks: Given the sensitive nature of LTx as a treatment option for CF, it is possible that patients may experience psychological distress from reading about transplant, especially in cases where CF patients have died after LTx. We have worked to mitigate this risk by allowing participants to moderate the amount of information they read about particular patient stories or 'Resource Library' content. Specifically, we have applied labels to 'CF Stories' with a "bad outcome" or "death," which are visible prior to entering the story. Additionally, over the course of a participant's involvement in this research study we will monitor mental health by administering mental health assessments, including the PHQ-9 survey. It is possible that a participant may experience psychological discomfort by completing these assessments. To protect a participant's wellbeing, if abnormal results are reported in the PHQ-9 the UW research team will notify their CF doctor for follow-up care.

There is no proven benefit of ToT at this time, but a prior (now outdated) decision aid for LTx in CF showed a reduction in decisional conflict and we hypothesize that the proposed intervention will increase preparedness for decision making and decrease decisional conflict related to LTx. Further, this pilot study will provide important feedback to optimize ToT for future users.

## 3.2 Adverse event reporting

### 3.2.1 Adverse event definitions

An adverse event (AE) is any untoward medical occurrence in a clinical investigation of a patient administered a pharmaceutical product or undergoing an investigational procedure that does not necessarily have a causal relationship with the treatment or procedure. An AE is therefore any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the administration of an investigational product or procedure, whether or not related to that investigational product. An unexpected AE is one of a type not identified in nature, severity, or frequency in the currently accepted risk profile for the treatment or procedure.

An unanticipated problem (UP) is defined as any incident, experience, or outcome that meets all of the following criteria:

1. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
2. related or possibly related to participation in the research (in this guidance document, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
3. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

An SAE is defined as any untoward medical occurrence that at any level of procedural intensity:

1. Results in death
2. Is considered life threatening (i.e., in the view of the Investigator the adverse experience places the patient or participant at immediate risk of death from the response, as it occurred; it does not include a reaction that, had it occurred in a more severe form, might have caused death)
3. Requires hospital admission or prolongation of an existing hospitalization
4. Results in persistent or significant disability/incapacity (i.e., a substantial disruption of a person's ability to conduct normal life functions)
5. Is an important medical event (i.e., when based upon appropriate medical judgment, the adverse experience may jeopardize the patient or participant and

may require medical or surgical intervention to prevent one of the above listed outcomes)

For the purposes of the proposed study, participant report of possible suicidality on the PHQ-9 is an immediately reportable AE, even if it is not an SAE. An alternative approach would be to utilize the PHQ-8 (which excludes the question about suicide), but it is important to understand whether there is a risk of increasing suicidality through the introduction of LTx education in this patient population. Avoiding the question in our study will not prevent the thoughts/feelings from occurring and we determined that it is in the interest of patient safety to include the question about suicidality and have a plan in place for responding in the case of this AE of special interest.

### 3.2.3 Recording and assessment of adverse effects

The Principal Investigator and/or research team staff will probe, via discussion with the participant, for the occurrence of AEs/UPs during each participant visit/call and record the information in the study's records. AEs will be described by duration (start and stop dates and times), severity, outcome, treatment and relation to study procedure, or if unrelated, the cause.

All observed or volunteered adverse events (serious or non-serious) and abnormal test findings, regardless of treatment group, if applicable, or suspected causal relationship to the investigational device or, if applicable, other study treatment or diagnostic product(s) will be recorded in the subjects' case histories. For all adverse effects, sufficient information will be pursued and/or obtained so as to permit 1) an adequate determination of the outcome of the event (i.e., whether the effect should be classified as a *serious adverse event*) and; 2) an assessment of the casual relationship between the adverse effect and the investigational device or, if applicable, the other study treatment or diagnostic product(s).

### 3.2.5 Causality and severity assessment

The National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) Version 4.03, as modified for CF, will be used to assess and grade AE severity, including laboratory abnormalities judged to be clinically significant. If the experience is not covered in the modified criteria, the guidelines shown in Table 1 below will be used to grade severity. It should be pointed out that the term "severe" is a measure of intensity and that a severe AE is not necessarily serious.

**Table 1. Adverse Event Severity Grading**

| Severity (Toxicity Grade) | Description |
|---|---|
| Mild (1) | Transient or mild discomfort; no limitation in activity; no medical intervention or therapy required. The participant may be aware of the sign or symptom but tolerates it reasonably well. (e.g. fatigue during study visit) |
| Moderate (2) | Mild to moderate limitation in activity, no or minimal medical intervention/therapy required. (e.g. psychological discomfort during study visit that may lead to crying or other emotional displays) |
| Severe (3) | Marked limitation in activity, medical intervention/therapy required, hospitalizations possible. (e.g. profound symptoms of anxiety or depression prompting hospitalization) |
| Life-threatening (4) | The participant is at risk of death due to the adverse experience as it occurred. This does not refer to an experience that hypothetically might have caused death if it were more severe. (e.g. suicidality that leads to a suicide attempt) |

The relationship of an AE to the study procedure should be assessed using the following the guidelines in Table 2.

**Table 2. Adverse Event Relationship to Study Procedure**

| Relationship to study procedure | Comment |
|---|---|
| Definitely | Previously known risk of procedure; or an event that follows a reasonable temporal sequence from performance of the procedure/testing; that follows a known or expected physiologic response to the procedure; that is confirmed by stopping or reducing the intensity of the procedure; and that is not explained by any other reasonable hypothesis. |
| Probably | An event that follows a reasonable temporal sequence from performance of the procedure; that follows a known or expected physiologic response to the procedure; that is confirmed by stopping or reducing the intensity of the procedure; and that is unlikely to be explained by the known characteristics of the participant's clinical state or by other interventions. |
| Possibly | An event that follows a reasonable temporal sequence from performance of the procedure; that follows a known or expected physiologic response to the procedure; but that could readily have been produced by a number of other factors. |
| Unrelated | An event that can be determined with certainty to have no relationship to the study procedure. |

### 3.2.6 Reporting adverse effects to the responsible IRB

All unanticipated problems that are SAEs (whether procedure related or not) that occur within 48 hours of a study visit will be documented and reviewed by the Investigator within 24 hours. SAEs that occur not within 48 hours of a study visit will be captured through patient's self-report at the next study visit, but will not be reported. All SAEs within 48 hours of a study visit will be sent the UW IRB within 24 hours. Reporting of unanticipated problems that are SAEs to the IRB will be performed by the Investigator in accordance with the standard operating procedures and policies. Adequate documentation will be provided showing that the IRB was properly notified. All episodes of reported suicidality documented on PHQ-9 administered during study visits, or patient report of suicidality between study visits, will be reported to the UW IRB within 24 hours. Additionally, the patient's CF clinician will be contacted directly immediately via secure communication, by the PI (Dr. Ramos), and a study physician will establish a safety contract with the patient by phone in the interim within 8 hours of becoming aware of an abnormal result.

## 5.0 MONITORING PROCEDURES

Study staff at the University of Washington will be responsible for monitoring for data accuracy and completeness.

## 7.0 INFORMED CONSENT

Once an eligible participant is identified from UW or at external sites via REDCap screening survey, a UW research coordinator will call the patient and verbal consent will be obtained. Before obtaining verbal consent, UW study staff will review the consent form with participants, allow time to answer any questions, and ensure participants demonstrate an understanding of study requirements and agree to participate.

Study staff will ask the subject if they fully understand everything that was explained in the consent documents and if they have any questions. Consent documents will be emailed or mailed to subjects if additional information is requested before verbal consent is obtained. Subjects will also be provided with a copy of the consent document for their records which includes study staff contact information if they have additional questions.

Before obtaining verbal consent, all subjects will be told that this research study is voluntary and they are able to withdraw at any time. They will be given contact information of the study staff if they decide they would like to withdraw or if they have any questions pertaining to their involvement in the study.

## 8.0 IRB INFORMATION

This pilot RCT was reviewed and approved by the University of Washington Human Subject's Division IRB. Collaborating institution who distributed screening surveys for recruitment purposes were considered not engaged per HHS guidelines and did not require additional IRB approval from their local IRBs.

Any documents that the IRB may need to fulfill its responsibilities (such as protocol, protocol amendments, consent forms, information concerning patient recruitment, payment or compensation procedures, or other pertinent information) will be submitted to the IRB. The IRB's written unconditional approval of the study protocol and the informed consent form will be in the possession of the Investigator before the study is initiated.

Protocol and/or informed consent modifications or changes may not be initiated without prior written IRB approval except when necessary to eliminate immediate hazards to the patients or when the change(s) involves only logistical or administrative aspects of the study. Such modifications will be submitted to the IRB and written verification that the modification was submitted and subsequently approved should be obtained.

The IRB must be informed of revisions to other documents originally submitted for review; new information that may affect adversely the safety of the patients of the conduct of the study; an annual update and/or request for re-approval; and when the study has been completed.

# 10.0 ADDITIONAL RECORDS AND REPORTS

## 10.1 Data handling and record-keeping

All study data will be maintained using REDCap. Only authorized individuals will be permitted to access study data.

All investigators and staff involved will have completed human subjects' protection training, have HIPAA training, and be bound by the agreement of confidentiality. A copy of the protocol will be given to all study team members and regular meetings will be held to discuss matters including questions and responsibilities relating to the study. All study databases will be maintained at the UW on password protected computers and backed up to an encoded password protected file. All procedures for the handling and analysis of data will be conducted using good clinical practices meeting FDA guidelines for the handling and analysis of data for clinical trials.

## 10.2 Record maintenance and retention

This study will comply with records retention periods set by Washington State.

## APPENDIX 1: Interview Guides

Overall Research Questions:

1. In what ways did the website(s) affect perceptions of preparedness to discuss transplant?
2. How well does ToT (stories/Resource Library/FAQ) or UNOS address the information needs of people living with CF? What information/information sources were meaningful, impactful, and salient (ToT or UNOS)?
3. What could be potential barriers and facilitators to using ToT or UNOS? What is the acceptability and feasibility of ToT (or UNOS)? How could ToT be improved?

Intro Session (prior to randomization) – 60-minute session

Goals of interview:

- Understand prior discussions and current understanding of LTx before exposure to the website(s) - what went well/not well during prior LTx discussions; has the participant thought about transplant; how could understanding be improved (information needs)?
- Questions to complement survey responses - explore baseline preparedness for discussions; could the participant decide about LTx already?
- Introduction to research website - 10 minute maximum plus demo video

1. Can you tell me about a time when you discussed lung transplant with your CF doctor?

    If transplant has been discussed:
    - Who initiated the conversation? If the patient initiated, why? If the doctor initiated, how did you react?
    - What were some of the emotions you felt during the conversation?
    - Did you feel prepared to have the conversation? Why/why not?
    - Was anyone else present during the conversation? If yes, was it useful to have someone with you? If not, would you have preferred someone to be there?
    - What could have made the conversation better?

    If transplant has not been discussed:
    - Has there ever been a time you wanted to discuss lung transplant with your doctor, but didn't? If yes, what stopped you from initiating the conversation?
    - When do you think would be the right time to talk to your doctor about lung transplant?
    - CF Foundation guidelines are now recommending people have annual conversations about transplant with their doctor once someone's $FEV_1$ is <50% predicted? In what ways might it be beneficial to talk about transplant early on? Could there be any harms or problems from discussing it too early?

2. Can you tell me about a time when you discussed lung transplant with a loved one (e.g friend or family member, etc.)?
    If transplant has been discussed:
        - How was this conversation similar or different from a conversation you might have with your doctor?
        - How might you benefit from having these conversations with your loved one?
    If transplant has not been discussed:
        - If your loved one talked with you about lung transplant, how might you react?
        - What might prompt you to talk about transplant with a loved one?
3. Do you know anyone who has received a lung transplant?
        - If yes, how has knowing about transplant from recipients affected how you think of it?
        - If no, how might hearing stories from people with CF who have undergone transplant affect how you think of it?
4. Can you tell me about any research you have done on lung transplant (for example, reading online or talking to others about it)?
    If prior research:
        - What prompted you to look into lung transplant?
        - How was your experience looking for information about lung transplant?
        - Did your doctor recommend or provide any resources to you?
        - How did you discover other information sources?
        - Did you trust the information you found? Why or why not?
        - How informed do you think you are about lung transplant?
        - Do you still have questions or concerns about transplant? If so, what are they?
    If no prior research:
        - How informed do you think you are about lung transplant?
        - Where do you think you would start to look for information about lung transplant?
        - What information would you look for?
        - How might you benefit from learning about lung transplant?
5. What is your understanding of the timing of lung transplant for advanced CF?
        - How did you come to understand the timing of transplant?
        - What do you understand about how CFTR modulators (for example, Trikafta) play a role in the timing of transplant?
6. How ready do you feel to talk to your CF doctor about transplant? Why?
        - What types of questions or concerns do you have about lung transplant?
7. Based on your conversations and/or research, how ready do you feel to make a decision about lung transplant?
    If decision has been made:
        - How did you come to make this decision?
        - What might influence your decision, making you more or less certain?
    If decision has not been made:
        - What could help you make a decision?

- When do you think you need to make this decision?
- What might influence your decision?

Week 2 - 30-minute session

1. Can you tell me about how often you looked at the website over the past two weeks?
2. Did the reminders impact your interest in visiting the website? What did you think about the frequency of the reminders?
3. Was there anything that prevented you from using the website? If yes, can you walk me through them in more detail and discuss ways they could be addressed?
4. Can you tell me about any technical issues you may have experienced with the website or devices?
5. How satisfied are you with the amount of time you spent visiting the site over the past two weeks? Do you think there could be any value in returning at another time? What would you spend more time looking at? What might prompt you to return to the website again?
6. Now can you tell me some of your general opinions about the website? Why was or wasn't it engaging?
7. Can you give me an example of some topics you enjoyed reading about or topics you might have preferred to avoid?
8. Can you give me an example of information you might have found surprising? Why was it surprising to you?
9. How did the content in the website make you feel?
10. Do you think this website would be a good place to start your search for information about lung transplant for CF? Why or why not? Describe the questions about lung transplant that still remain after your use of this website.
11. Why might you recommend this website to others or not?
12. Do you think this would be a good website for your doctor to recommend?
13. Imagine you have an appointment tomorrow with your CF doctor, how prepared do you feel to discuss lung transplant after using this website? Why? (consider asking: why not [lower on Likert scale]? why not [higher on Likert scale]?)
14. How might you benefit from using the website with others (e.g. your doctor, friend, family)? Did you share any of the information on the website with others? If yes, what did you discuss?

Week 4 - 60 minute session

Goals of interview:

- Feasibility of use
- Preparedness for CF clinic visit
- Psychological impact
- Duration of RCT (4 weeks vs 3 months)

1. Can you tell me about how often you looked at the website over the past two weeks? Was there anything that prevented you from using the website, technical issues or something else? If yes, can you walk me through them in more detail and discuss ways they could be addressed?

2. How satisfied are you with the amount of time you spent visiting the sites over the past four weeks? Do you think there could be any value in returning to either site at another time? What would you spend more time looking at? What might prompt you to return to the websites again?

3. Can you compare your experience using the UNOS website to the Take on Transplant website?

    - Were you able to find information more easily in one website compared to the other? Can you give an example? What made it difficult to find the information you were looking for?
    - Did you find the information in the websites trustworthy? Why? Was there one website that was more or less reliable than the other?
    - Did one website help you feel more informed about lung transplant over the other?
    - Do you still have questions or concerns about transplant? If so, what are they and to which website would you choose to return to find answers? Why would you choose to return to one website over the other?
    - How often could you see yourself returning to the UNOS website? What about the Take on Transplant website?
    - Can you give me an example of something one website did better or worse than the other?

4. How did the content in the websites make you feel? Did one website evoke more or less of an emotional reaction than the other? If so, can you elaborate or provide an example?
    - Did you find any of the content distressing or disturbing?
    - Did you find yourself thinking about the content when you were not looking at the website? For example, were you thinking about information from the website when you were trying to work, read, or fall asleep?
    - Did the website impact your mental health? If yes, how?
5. Imagine you have an appointment tomorrow with your CF doctor, how prepared do you feel to discuss lung transplant after using the websites? How have they helped you feel more or less prepared to have a discussion with your CF doctor about lung transplant? As a reminder, two weeks ago you said you felt "XX" to have a discussion about lung transplant with your CF doctor? What are some things that changed or influenced this feeling? Was there one website that helped you to feel more prepared? Why/why not?

Shifting focus to the ToT website:

6. Can you tell me some of your general opinions on the three content areas (resource library, CF stories, and FAQs)?
    a. How would you improve your experience with [each content area]?
    b. Did you have any concerns with any of the content?
7. What did you think about the lung transplant discussion urgency meter?
8. Was the recommended content you received relevant to you? Why/why not?

9. Did the website suit your learning style? If not, why? What changes or additions could help? Would you prefer having the content in a different format (e.g. audio or video)?
10. Can you tell me about the CF stories you read? Why did you choose to read those stories? How did you relate or not relate to them? How do you think the CF stories might be similar or different to conversations you would have with transplant recipients?
11. How much of the content in ToT were you already familiar with (estimate a percentage)? Were you surprised by how much or how little you knew? Why/why not?
12. Do you think ToT could be used by individuals with CF at various stages of their health?
    a. Why might you choose to use ToT when you are healthier?
        i. What information would you look for?
        ii. How could you benefit from using ToT?
        iii. What would be the ideal amount of time for you to spend with the website?
    b. What about when you are closer to needing a transplant?
        i. What information would you look for?
        ii. How could you benefit from using ToT?
        iii. What would be the ideal amount of time for you to spend with the website?
13. In what ways could ToT help someone who is getting ready to talk to their doctor about lung transplant? How has it helped you feel more ready for these conversations?
14. Can you give some examples of topics you want to discuss with your CF doctor?
15. Would you have benefitted from using ToT with someone else like your doctor, a friend, or loved one? Did you get a chance to share anything from the site with anyone else?
    a. What would be the ideal amount of time for you to have with ToT prior to an appointment with your CF doctor? Would you want to access ToT again after you visit with your CF doctor?
16. Why might you recommend this website to others or not?
17. Do you think this would be a good website for your doctor to recommend?
18. In what ways did ToT change what you know about lung transplant? Did it change any of your beliefs?
19. What are some advantages of using ToT over to other resources about lung transplant? In what ways could ToT supplement other resources about lung transplant?
20. Do you have any additional comments that you would like to share about your experience using ToT?

<u>[If research website not used] Barriers to using the tool:</u>

Please share the reasons you found it difficult to utilize the website.

1. Time: what prevented you from taking time to use the website? What competing priorities were you dealing with over these two weeks?
2. Access: did you experience issues with technology at all or with devices (laptop, tablet, phone)?
3. Interest: can you share your opinions about the website? Why wasn't it engaging? Do you have criticisms? Did the email and/or text message reminders increase/change your interest in accessing the website? Were reminders too frequent, not frequent enough?
4. Pertinence: why was the website not relevant for you? Do you think lung transplant is a treatment option you will ever need to consider? If not, why?
5. Emotions: did you find the content upsetting or disturbing? In what ways? What particular parts of the content did you not want to read about or see?
6. Considerations: can we talk about the reasons that prevented you from using the website? I'd like to walk through them in more detail and discuss ways they might be addressed.
7. Would you have benefitted from using this website with someone else like your doctor, a friend, or a loved one?

# APPENDIX 2: Consent Form

Approved
11/9/2021
UW IRB

**UNIVERSITY OF WASHINGTON - CONSENT FORM**

Lung Transplant READY (Resources for Education and Decision-making for Your CF) Pilot Study

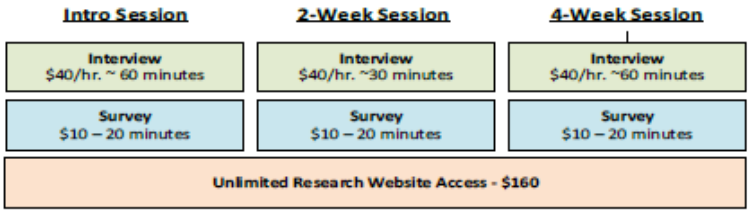
| Lead Researcher | | |
|---|---|---|
| Kathleen Ramos, MD MSc | Assistant Professor,<br>Pulmonary, Critical Care & Sleep Medicine | 206-543-0393 |
| **Contacts for Participants** | | |
| Lauren Bartlett, BS | Research Coordinator,<br>Pulmonary, Critical Care & Sleep Medicine | lrejman@uw.edu<br>503-583-2869 |

We are asking you to be in a research study. This form gives you information to help you decide whether or not to be in the study. Being in the study is voluntary. Please read this carefully. You may ask any questions about the study. Then you can decide whether or not you want to be in the study.

**PURPOSE OF THE STUDY**

Lung transplant is an option for treating end-stage lung disease in people living with cystic fibrosis (CF). In the United States, more CF patients with advanced lung disease (very low lung function or $FEV_1$) die each year than undergo lung transplant. Additionally, more than half of the patients who die without lung transplant are never referred for consideration. The CF Foundation (CFF) established lung transplant referral guidelines that recommend individuals with CF have annual conversations about lung transplant with their CF doctor once their $FEV_1$ is less than 50% of predicted. Considering lung transplant as a treatment option ahead of when it is medically needed will allow more time to learn about lung transplant and address any barriers to lung transplant that may exist. Our research team is interested in understanding how people with CF use lung transplant educational resources and how one prepares for having discussions and/or making decisions about lung transplant as a treatment option for advanced CF. The purpose of this study is to test whether a research website can improve patient preparedness for shared decision making about lung transplant.

**STUDY PROCEDURES**




Involvement in this study will last four weeks with a total of three study sessions including the following: Introduction Session, 2-Week Follow-up Session, and 4-Week Follow-up Session.

Survey – You will be asked to complete a survey at each session. Surveys will assess your preparedness for decision making about lung transplant, knowledge about lung transplant, mental health, and evaluation of the research website. Surveys will take approximately 15-20 minutes to complete and you may refuse to answer any questions you do not feel comfortable answering.

Interview – You will be asked to take part in an interview via Zoom at each study session. Interviews will last approximately 30-60 minutes and will be recorded and transcribed. During the interviews we will explore your experiences with talking about lung transplant with your doctors, introduce a research website that will provide educational content about lung transplant, and discuss your experiences using the research website.

Research Website – During the Introduction Session interview, you will gain access to a research website and will be given login credentials for continued use for the remainder of the study. For two weeks you will be randomized and will have access to one educational resource, then after two weeks you will be able to unlock access to an additional educational resource. Access to the research website and educational resource(s) will be unlimited during your four weeks of study involvement. Your use of the tool will be captured using website analytics (e.g. time spent using the tool, number of page views, and number of clicks).

Medical Record Access (University of Washington Patients Only) - During this study, we will access your medical records from the UW electronic health record. The information we access will be clinically relevant to this study. This information could include your past medical history, demographic information, etc.

## RISKS, STRESS, OR DISCOMFORT

Psychological risks: Discussing and considering lung transplant as a treatment option for CF can be a sensitive topic. It is possible that you may experience distress from reading about lung transplant on the research website. If you have questions about your clinical care, you should talk to your CF doctor for medical advice. Additionally, over the course of your involvement in this research study we will monitor your mental health by administering mental health assessments, including the PHQ-9 (depression) and GAD-7 (anxiety) surveys. It is possible that you may experience psychological discomfort by completing these assessments. To protect your wellbeing, if abnormal results are reported on the PHQ-9 or the GAD-7 surveys, the UW research team will notify your CF doctor for follow-up care.

Risks to Confidentiality: As with any research study, there is a potential risk of loss of confidentiality. We will take all precautions to ensure the confidentiality of your data if identifiable information is obtained. Your name will not be used in any publications about this study or the research website.

Interview audio and video will be recorded and stored indefinitely in a password protected file on the UW server. You will not be given the opportunity to listen to these recordings, but you may request access to the transcribed version of the interview to confirm accuracy. All recordings will be transcribed and de-identified. These de-identified transcripts will potentially be shared with other researchers.

## ALTERNATIVES TO TAKING PART IN THIS STUDY

Your alternative choice is to not participate in this study. If you are a patient at the University of Washington Adult CF Clinic, choosing not to participate in this study will not affect your care at the University of Washington Medical Center or its affiliated hospitals or clinics.

## BENEFITS OF THE STUDY

There is no proven benefit of the research website at this time, but we think that the research website will increase preparedness for shared decision making and decrease discomfort related to lung transplant discussions.

## SOURCE OF FUNDING

The study team and/or the University of Washington is receiving financial support from the National Institutes of Health (NIH) and the Cystic Fibrosis Foundation (CFF).

## CONFIDENTIALITY OF RESEARCH INFORMATION

We will keep your identity as a research subject confidential. All study documents will be kept in a secured locked office or on a password-protected computer. Your information will not be identified by name in the study database, but will be identified by a subject identification number unique to this study. Only authorized individuals will be able to link the study ID to your name. The link between your identifiers and the research data will be destroyed after the records retention period required by state and/or federal law.

Government or university staff sometimes review studies such as this one to make sure they are being done safely and legally. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy. The study records will not be used to put you at legal risk of harm.

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

We have a Certificate of Confidentiality from the federal National Institutes of Health (NIH). This helps us protect your privacy. The Certificate means that we do not have to give out information, documents, or samples that could identify you even if we are asked to by a court of law. We will use the Certificate to resist any demands for identifying information.

We can't use the Certificate to withhold your research information if you give your written consent to give it to an insurer, employer, or other person. Also, you or a member of your family can share information about yourself or your part in this research if you wish.

There are some limits to this protection. We will voluntarily provide the information to:

- a member of the federal government who needs it in order to audit or evaluate the research;
- individuals at the institution(s) conducting the research, the funding agency, and other groups involved in the research, if they need the information to make sure the research is being done correctly;
- the federal Food and Drug Administration (FDA), if required by the FDA;
- individuals who want to conduct secondary research if allowed by federal regulations and according to your consent for future research use as described in this form;

The Certificate expires when the NIH funding for this study ends. Currently this is March 31, 2023. Any data collected after expiration is not protected as described above. Data collected prior to expiration will continue to be protected.

## USE OF INFORMATION AND SPECIMENS

The information that we obtain from you for this study might be used for future studies. We may remove anything that might identify you from the information and specimens. If we do so, that information and specimens may then be used for future research studies or given to another investigator without getting additional permission from you. It is also possible that in the future we may want to use or share study information that might identify you. If we do, a review board will decide whether or not we need to get additional permission from you.

## RETURNING RESULTS TO YOU

During your involvement in this study, we will monitor your mental health through the use of various survey assessments, including the PHQ-9. In the event of an abnormal result (for example, endorsement of suicidal ideation) that requires clinical intervention, you will be contacted by Dr. Kathleen Ramos (the study PI) or another study physician within 8 hours, and your survey results will be communicated to your CF doctor for follow-up care.

## OTHER INFORMATION

You may refuse to participate and you are free to withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled. If you wish to withdraw, please contact the researcher listed on

page 1 of this consent form. If you choose to withdraw from this study, data will not be discarded and instead will be de-identified.

You will receive compensation in the form of a Tango gift card at the rate of $40/hour for each session involving an interview and surveys and $10 for the completion of surveys at each session. You will also be compensated for 4 hours at $40/hour for time spent using the research website outside of scheduled interviews with study staff, although you are encouraged to use the tool as much as you wish in the four week period. Total compensation will be approximately $290 and will be pro-rated for those who are unable to complete the research. Compensation will be distributed via email within 1-3 business days after each study session.

**RESEARCH-RELATED INJURY**

If you think you have been harmed from being in this research, contact Dr. Kathleen Ramos at 206-543-0393.

**SUBJECT'S STATEMENT**

This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions later about the research, or if I have been harmed by participating in this study, I can contact one of the researchers listed on the first page of this consent form. If I have questions about my rights as a research subject, I can call the Human Subjects Division at (206) 543-0098 or call collect at (206) 221-5940. I give permission to the researchers to use my medical records as described in this consent form. I will receive a copy of this consent form.

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