PROTOCOL TITLE:

Multimodal Mobile Intervention Application (app) to Address Sexual Dysfunction in Hematopoietic Stem Cell Transplant Survivors

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1.0 Objectives

The goal of this study is to develop, refine, and test the feasibility and preliminary efficacy of a self-administered, mobile sexual dysfunction intervention application (app) in improving outcomes of hematopoietic stem cell transplant (HCT) survivors. Sexual dysfunction is the most common complication post-HCT with over 40% of male and 60% of female survivors reporting long-term sexual dysfunction post-transplant. Importantly, sexual dysfunction is associated with worse quality of life (QOL), relationship dissatisfaction, and psychological distress, which further contributes to the morbidity in this population. HCT survivors experience a unique and wide range of biologic, interpersonal, psychological, and social factors that impact their sexual function. Given the multifactorial nature of sexual dysfunction, a multimodal approach is necessary to address patients' specific issues and concerns. Despite the increasing use of HCT and the burden of sexual dysfunction in this often young patient population, there are currently no interventions to address their sexual dysfunction. We completed a pilot study in which we recruited HCT survivors with sexual dysfunction causing distress to participate in a multimodal intervention that entailed monthly visits with trained study nurse practitioners. We demonstrated that the intervention was feasible and led to statistically and clinically significant improvements in patients' satisfaction and interest in sex, sexual health and function, QOL, and symptoms of depression and anxiety. Despite the success of our prior work, the majority of HCT survivors will not have access to clinicians with expertise to address their sexual dysfunction.

Therefore, we are currently adapting our sexual health intervention to a mobile app, which patients can self-administer via tablet computer to ensure the accessibility and scalability of the intervention. The sexual health intervention manual and the content of the app has been outlined and will be submitted as an appendix to this protocol. The app development is currently under way with our industry partner. We now seek IRB approval for this project to evaluate the feasibility and preliminary efficacy of the intervention versus enhanced standard care in 60 HCT survivors. If the IRB would like to view wireframes of the mobile app, or the app itself after the final development phase (in addition to the manual and content as outlined in the appendix), we will submit it as an amendment for review to the IRB prior to initiating study recruitment procedures.

1.1 Specific Aims

Specific Aim 1: To examine the feasibility of the intervention to address sexual dysfunction in HCT survivors.

Specific Aim 2: To determine the preliminary efficacy of the intervention in improving patient-reported sexual function, quality of life (QOL), and psychological outcomes.

1.2 Hypotheses

Hypothesis 1: The intervention will be will be deemed feasible if at least 60% of eligible patients enroll in the study, and of those enrolled, at least 60% engage in at least 70% of the intervention modules.

Hypothesis 2: Patients randomized to the intervention will report better sexual function, QOL, and depression and anxiety symptoms compared to those randomized to the control arm.

Exploratory Aim: to qualitatively explore patients' general perceptions of the sexual health mobile app and their overall satisfaction with the intervention.

2.0 Background

2.1 Background

Hematopoietic stem cell transplantation (HCT) is a commonly used and potentially curative treatment strategy for many hematologic conditions.[1-4] The use of HCT has increased over the last decade with more than 20,000 transplants performed in the United States each year, with over 40% of those in patients younger than 45 years of age.[4-7] HCT survivors experience a significant and drastic deterioration in their sexual function that persists for many years following their therapy. In fact, sexual dysfunction is the most common and persistent complication post-HCT with over 40% of male and 60% of female survivors reporting long-term sexual dysfunction post-transplant.[8-11] Studies demonstrate that sexual dysfunction is associated with worse quality of life (QOL), relationship dissatisfaction, and psychological distress.[12-18] Consequently, the National Institute of Health Late Effects Initiative identified sexual dysfunction as a major concern facing HCT survivors and highlighted the critical need to develop interventions to enhance sexual function in this population.[19]

Despite the prevalence of sexual dysfunction in HCT survivors, interventions to improve sexual function are lacking.[14,19,20] Addressing sexual health in this population is complicated by the multiple factors that contribute to dysfunction, including biologic, interpersonal, psychological, and social factors.[10,12,20-30] Common biologic factors include hormonal alterations, scarring from chronic graft-versus-host disease, and pain due to transplant related complications.[10,12,20-26] Patients often experience interpersonal issues such as relationship discord, fear of intimacy, and lack of communication with their partner.[14] Depression, anxiety, and body-image concerns further exacerbate dysfuntion.[27-30] Lastly, personal values and social norms play a substantial role in patients' comfort addressing their sexual health.[14] Thus, interventions that comprehensively address a wide range of factors contributing to sexual dysfunction in HCT survivors are needed to enhance sexual function.[14]

We completed a pilot study to assess the feasibility and preliminary efficacy of a multimodal intervention to address sexual dysfunction in HCT survivors.[31] Given the lack of available sexual health clinicians at most cancer care settings,[9,26] we trained nurse practitioners to deliver the intervention during monthly visits integrated with patients' routine outpatient oncology care. We demonstrated clinically significant improvement in patients' satisfaction and interest in sex, as well as sexual health and function including orgasm, erectile function, and vaginal discomfort post-intervention. Notably, patients also experienced improvement in their QOL and symptoms of depression and anxiety. This study established the feasibility and preliminary efficacy of this intervention to enhance sexual function, QOL, and mood in HCT survivors.

Although our pilot study had promising findings, a number of participants reported that attending monthly visits was burdensome, especially for those living far from their transplant center. The study nurse practitioners also cited the visit frequency as a barrier to broad dissemination of the intervention given their limited time and availability to address sexual health concerns during routine clinic visits. In addition to the time burdens for both the study patients and clinicians, the majority of HCT survivors will not have access to clinicians with expertise in sexual dysfunction, which limits the scalability of this effective intervention. We recently secured funds through the MGH Transformative Scholar Program to adapt our intervention to a mobile application (app), which patients can self-administer via tablet computer to ensure the accessibility and scalability of the intervention. An app also enables patients to access the intervention in the privacy of their homes, more easily engage their partners in the intervention, and avoid the need for monthly clinic visits. We are currently developing the mobile app with our industry partners. The sexual health intervention manual and the content of the app has been outlined and will be submitted as an appendix to this protocol. We now seek IRB approval to conduct a pilot randomized trial of the mobile app versus enhanced standard care in 60 HCT survivors to assess the feasibility and preliminary efficacy of the mobile app for improving patients' sexual function, QOL, and mood. If the IRB would like to view wireframes of the mobile app, or the app itself after the final development phase (in addition to the manual

and content as outlined in the appendix), we will submit it as an amendment for review to the IRB prior to initiating study recruitment procedures.

2.1.2 Gaps in Current Knowledge

Despite the high prevalence of sexual dysfunction in HCT survivors, there are currently no interventions to address the sexual problems affecting this population. Additionally, to our knowledge, no published studies exist regarding the efficacy of a mobile app specifically to address sexual dysfunction. This study will address the high prevalence of sexual dysfunction in this population to evaluate an innovative intervention to ameliorate sexual health and quality of life in HCT survivors.

2.2 Preliminary Data

A Multimodal Intervention to Address Sexual Dysfunction in HCT survivors

We conducted a pilot study to assess the feasibility and preliminary efficacy of a multimodal sexual dysfunction intervention to improve sexual function in HCT survivors. We screened all HCT survivors and found that 33.1% (50/151) reported significant sexual dysfunction causing distress. The intervention entailed monthly visits with a trained study nurse who assessed and treated sexual dysfunction as per a treatment guide that was developed based on a systematic review of the literature. Overall 94.0% (47/50) of patients who screened positive for sexual dysfunction causing distress agreed to participate in the study. Using a pre-post design, we demonstrated significant improvement in patients' satisfaction and interest in sex as well as sexual health and function, QOL, and depression and anxiety symptoms post-intervention [Table 1]. This study established the feasibility and preliminary efficacy of the multimodal sexual dysfunction intervention which serves as the basis for this randomized controlled trial.

Table 1: Intervention Effects on Patient-Reported Outcomes

Patient outcomes:	Pre-Intervention	Post-Intervention	Cohen's D	P- Value
Satisfaction with sex	16.07	29.70	1.34	**<0.0001**
Interest in sex	10.98	15.39	0.91	**<0.0001**
Climax/orgasm	2.19	4.22	1.35	**<0.0001**
Erectile function	19.58	32.74	1.61	**<0.0001**
Lubrication	19.44	34.31	1.27	**0.0001**
Vaginal discomfort	33.77	14.92	1.32	**0.0005**
QOL	107.98	123.88	0.81	**<0.0001**
Depression	4.28	2.33	0.60	**0.0002**
Anxiety	4.59	2.59	0.49	**0.0019**

2.3 Significance

Sexual dysfunction affects many hematopoietic stem cell transplant (HCT) survivors

HCT is a potentially curative treatment for many patients with hematologic conditions.[1-4] The number of HCT survivors is increasing with over half a million projected survivors in the United States by 2030.[4,5] Over 40% of these survivors will be younger than 45 years of age.[7] Sexual dysfunction is the most common long-term complication in HCT survivors.[8,9,12,20] Nearly half of HCT survivors are dissatisfied with the quality of their sexual life.[32] The incidence of sexual dysfunction is 40% in male and 60%-80% in female HCT survivors, which is significantly higher than other cancer survivors.[8-12,20] Consequently, the National Institute of Health Late Effect Initiative identified sexual dysfunction in HCT survivors as a highly unmet need that requires further research.[19]

Sexual dysfunction has negative consequences on patients' quality of life (QOL) and mood

Sexual health plays a central role in an individual's identity, QOL, and self-esteem.[20] Moreover, sexual dysfunction has been associated not only with worse QOL and mood in cancer survivors,[14-17] but also with worse fatigue, relationship discord, intimacy problems, and distress.[12-18] Notably, 70% of HCT survivors who have sexual dysfunction report substantial marital dissatisfaction post-HCT. [12-18] Therefore, improving patient's sexual function post-transplant may have a positive effect on their QOL, physical and psychological health, and intimate relationships, thereby decreasing the overall morbidity of HCT.

The etiology of sexual function in HCT survivors is multi-factorial

HCT survivors experience a wide range of conditions which impact their sexual function.[10,12,20-30] Biologic, interpersonal, psychological, and social factors all contribute to sexual dysfunction in this population. [10,12,20-30] Biologic factors secondary to HCT include decreased libido, vaginal alterations, erectile dysfunction, hormonal deficiency, dyspareunia, and infertility.[10,12,20-25] Chronic graft-versus-host disease (GVHD), the most common cause of morbidity in allogeneic HCT survivors, can cause vaginal stenosis, and injury to blood vessels, which can manifest as erectile dysfunction in men and anorgasmia in women.[10,26,33] Patients also struggle with interpersonal problems including relationship disruptions and intimacy concerns with their partner.[14,27-30] Psychological factors that affect sexual function include depression, anxiety, and body-image concerns. [14,27-30] Lastly, personal values affect patients' comfort addressing their sexual health.[14] Thus, sexual dysfunction in HCT survivors is multi-factorial, requiring a multimodal approach to address patients' sexual health concerns.

Clinicians lack sufficient training to address sexual dysfunction in cancer survivors

HCT survivors report having little communication with their clinicians about sexual health.[8,24,34-37] Clinicians infrequently engage in discussions with their patients about their sexual health,[8,24,34,35] citing inadequate time, insufficient training, and patient discomfort as barriers to addressing sexual dysfunction.[38,39] Notably, patients who reported participating in a discussion with their clinician about sexuality noted fewer sexual functioning problems compared to those who did not communicate with their clinicians.[8] HCT survivors would greatly benefit from interventions to empower them to communicate with their clinicians about their sexual health.

Interventions to comprehensively address sexual dysfunction post-HCT are lacking

Despite the well-documented burden of sexual dysfunction on HCT survivors, there have been no interventions to date to improve sexual health in this population.[14,19,20] Given the multi-factorial nature of sexual dysfunction in HCT survivors, interventions must address these diverse sexual health needs.[14,20] The management of sexual dysfunction in HCT survivors would therefore be ideally addressed by a multidisciplinary team of sexual health experts, psychologists, gynecologists, and urologists.[14,26] Although few cancer centers have a multidisciplinary sexual health clinic, the lack of professionals trained in addressing sexual dysfunction severely limits the dissemination of such a complex service model.[9,26] In addition, HCT survivors often find it difficult to attend multiple clinic appointments and coordinate their care among various specialists.[19] Novel models of care that address the medical and psychosocial aspects of sexual dysfunction in HCT survivors in a feasible, patient-centered, and scalable manner are critically needed.

Mobile applications (apps) can broadly disseminate innovative interventions

Mobile health apps offer an innovative strategy to enhance the accessibility and scalability of interventions addressing the needs of patients who cannot access health care clinicians with particular expertise. Once patients receive appropriate instructions on their use, mobile interventions are highly acceptable to patients regardless of their age, health literacy, or computer experience.[40,41] Mobile behavioral interventions have shown promising efficacy in addressing a variety of health problems including depression, anxiety, substance abuse, and insomnia.[40,42-47] While some behavioral web-based

and mobile interventions have suffered from low adherence, mobile apps that incorporate features to enhance patients' engagement including gamification, adaptive skill-building, and a record of personal progress through the app content have shown 85-100% usability and retention rates.[48] Using mobile app to deliver a sexual health intervention is an innovative strategy to overcome the shortage of trained sexual health clinicians to care for HCT survivors. A mobile app will enable patients to access the intervention in the privacy of their home, engage their partners with the content, and avoid additional clinic visits. To our knowledge, no published studies exist regarding the efficacy of a mobile app to address sexual dysfunction.

We propose to adapt our successful intervention for addressing sexual dysfunction to a mobile app
We completed a pilot study of a multimodal intervention to address sexual dysfunction in HCT survivors (see preliminary studies).[31] Participants attended monthly intervention visits with trained study nurse practitioners who 1) assessed the causes of their sexual dysfunction; 2) educated, normalized, and empowered them to address their sexual health; and 3) implemented therapies targeting their specific sexual health concerns. The intervention was feasible and led to statistically and clinically significant improvements in patients' satisfaction and interest in sex, QOL, and symptoms of depression and anxiety. While we were encouraged by these results, a number of participants reported that attending monthly visits was burdensome, especially for those living far from their transplant center. The study nurse practitioners also cited the visit frequency as a barrier to broad dissemination of the intervention given their limited time and availability to address sexual health concerns during routine clinic visits. In addition to the time burdens for both the study patients and clinicians, the majority of HCT survivors will not have access to clinicians with expertise in sexual dysfunction, which limits the scalability of this effective intervention. We recently secured funds through the MGH Transformative Scholar Grant to adapt our successful intervention to a mobile app, which patients can self-administer to ensure the accessibility and scalability of the intervention. These funds can only be used for app development. We are working currently with our industry partners to develop the mobile app. The sexual health intervention manual and the content of the app has been outlined and will be submitted as an appendix to this protocol [Appendix A]. We now seek IRB approval to conduct a pilot randomized trial of the mobile app versus enhanced standard care in 60 HCT survivors to assess the feasibility and preliminary efficacy of the mobile app for improving patients' sexual function, QOL, and mood. If the IRB would like to view wireframes of the mobile app, or the app itself after the final development phase (in addition to the manual and content as outlined in the appendix), we will submit it as an amendment for review to the IRB prior to initiating study recruitment procedures.

3.0 Inclusion and Exclusion Criteria

We will recruit a total of 60 HCT survivors who are at least 3 months post-HCT and without evidence of disease from Massachusetts General Hospital Cancer Center and Dana-Farber Cancer Institute to participate in this randomized trial.

3.1 Screening for Eligibility

We will use the same successful screening, recruitment, and enrollment procedures from our prior pilot study. An RA and Dr. El-Jawahri will screen the weekly transplant clinic schedule to identify potentially eligible patients. The RA will then send an email to the treating oncology clinician to notify him or her that the patient is potentially eligible for study participation and inquire about any concerns regarding his or her study participation. If the treating clinician has any objections regarding the patient's participation, the RA will document the reasons and not approach those individuals. If there is no concern regarding study participation, the RA or the oncology clinician will screen the patient for sexual dysfunction at their next scheduled visit using the two-question approach based on the NCCN Survivorship Guidelines: 1) "do you have

problems with sexual function?" and 2) "are these problems causing you distress?". The RA will then offer study participation for those who screen positive for sexual dysfunction causing stress.

3.2 Eligibility

3.2.1 Inclusion Criteria

1. Adult patients (≥18 years) who underwent an autologous or allogeneic HCT at least 3 months prior to study enrollment.
2. Ability to speak English or able to complete questionnaires with assistance required from an interpreter or family member.
3. Positive screen for sexual dysfunction that is causing distress based on the NCCN survivorship guidelines.

3.2.2 Exclusion Criteria

1) Recurrent disease requiring treatment

2) Significant uncontrolled psychiatric disorder (psychotic disorder, bipolar disorder, major depression) or other co-morbid disease (dementia, cognitive impairment), which the treating clinician believes prohibits the ability to participate in study procedures.

3.3 *Special Populations* We will not include adults unable to consent, individuals who are not yet adults, pregnant women, or prisoners.

4.0 Study-Wide Number of Subjects: 60 patients

5.0 Study-Wide Recruitment Methods:

We will use the same successful screening, recruitment, and enrollment procedures from our prior pilot study. An RA and Dr. El-Jawahri will screen the weekly transplant clinic schedule to identify potentially eligible patients. The RA will then send an email to the treating oncology clinician to notify him or her that the patient is potentially eligible for study participation and inquire about any concerns regarding his or her study participation. If the treating clinician has any objections regarding the patient's participation, the RA will document the reasons and not approach those individuals. If there is no concern regarding study participation, the RA or the oncology clinician will screen the patient for sexual dysfunction at their next scheduled visit using the two-question approach based on the NCCN Survivorship Guidelines: 1) "do you have problems with sexual function?" and 2) "are these problems causing you distress?". The RA will then offer study participation for those who screen positive for sexual dysfunction causing stress. The RA will then review the study procedures and informed consent document and obtain written informed consent.

Alternatively, if a patient is unable to be approached in-person to determine primary eligibility due to external factors, such as a lack of clinic space, or patient time constraints, the study team may reach out to potential participants over the phone. Prior to initiating phone contact, the study team will contact the treating oncology clinician to assess if the clinician has any reservations about study staff contacting the patient. Study staff will call the potentially eligible patient using the recruitment and screening phone script (see verbal consent) to gauge interest and screen the patient to determine eligibility. Study staff will not call more than three times total. If unable to reach the patient, study staff will leave a voicemail with staff contact information (see voicemail script). If the patient expresses interest and screens in, the RA will conduct informed consent over the telephone. Alternatively, study staff may approach the

patient at their next clinic visit to review the study procedures and the informed consent document and obtain written informed consent.

The study team will additionally have the option of providing study information to eligible patients via Patient Gateway, using a template with recommended language (Appendix L). Patients will be given a summary of the study and will be encouraged to contact the study team using provided contact information if interested in hearing more about the study.

***We are requesting a Waiver of Written Documentation of Consent**
This waiver is being requested to assist with patient recruitment, as a result of the COVID-19 pandemic. This study meets the waiver requirements given it is considered no more than Minimal Risk and all study procedures could be conveyed verbally. This waiver will reduce the risk to patients and is necessary for research procedures to continue.

6.0 Multi-Site Research: Not Applicable

7.0 Study Timelines

7.1 Timelines

We anticipate that we will need approximately 2 years to enroll the sample size for this study. Participants will remain on the study for up to 1 year.

8.0 Study Endpoints

8.1 *Primary endpoint:* The primary endpoint of this pilot RCT is to assess the feasibility of the intervention. The proposed intervention app will be deemed feasible if at least 60% (95% CI +/- 12%) of eligible patients are enrolled in the study, and of those enrolled, at least 60% engage with at least 70% of the intervention modules. Modules engagement will be captured by the app.

8.2 *Secondary endpoints:*

- Compare patient-reported global satisfaction with sex (PROMIS Sexual Function and Satisfaction Measure) scores at 8 weeks between the study groups
- Compare patient-reported interest in sexual activity (PROMIS Sexual Function and Satisfaction Measure – Interest in sexual activity domain) scores at 8 weeks between the study groups
- Compare patient-reported global satisfaction with sex (PROMIS Sexual Function and Satisfaction Measure – Global satisfaction with sex domain) at 12 weeks between the study groups
- Compare patient-reported interest in sexual activity (PROMIS Sexual Function and Satisfaction Measure – Interest in sexual activity domain) at 12 weeks between the study groups
- Compare patient-reported orgasm (PROMIS Sexual Function and Satisfaction Measure – Orgasm domain) at 8 weeks and 12 weeks between the study groups
- For males: compare patient-reported erectile function (PROMIS Sexual Function and Satisfaction Measure – Erectile function domain) at 8 and 12 weeks between the study groups

- For females: compare patient-reported lubrication and vaginal comfort (PROMIS Sexual Function and Satisfaction Measure – lubrication and vaginal comfort domains) at 8 and 12 weeks between the study groups
- Compare patient reported QOL (FACT-BMT) at 8 and 12 weeks between the study groups
- Compare patient reported anxiety and depression symptoms (HADS) at 8 and 12 weeks between the study groups

9.0 Procedures Involved

9.1 Study Design

We will conduct a single-site pilot randomized trial in 60 HCT survivors to assess the feasibility and preliminary efficacy of the intervention for improving patient-reported sexual function, QOL, and mood. Patients will be randomized in 1:1 fashion and stratified by transplant type (autologous vs. allogeneic) to either receive only a sexual health visit with a transplant clinician specializing in sexual health or a sexual health visit with a transplant clinician specializing in sexual health with access to the app. This visit may be in clinic or conducted via secure video-based conference. As transplant type is an important variable that affects sexual function and recovery post-HCT, we will stratify by HCT type to ensure balanced representation between the study groups. Both study groups will attend a visit with a transplant clinician specializing in sexual health who will conduct a brief examination and assess the need for any treatments or medications to address sexual health problems; this visit may be in clinic or conducted virtually via secure video-based conference.. The intervention group will have access to the mobile app. We will also conduct qualitative interviews with 10 patients that are randomized to the mobile app intervention, in order to understand and assess patient experience using the app. Qualitative interviews will be conducted in clinic, or over the telephone.

9.2 Procedures

We will recruit 60 patients 3 months after autologous or allogeneic HCT who report having sexual dysfunction causing distress for this study. The research assistant (RA) will review the consent form with potential participants and obtain verbal or written informed consent. Upon study enrollment, participants will complete baseline study measures and then they will be randomized to the mobile app versus enhanced standard care.

Intervention Arm: Patients randomized to the intervention will first meet with a transplant clinician, in clinic or via secure video-based conference, for a brief medical examination to assess the need for medications for erectile dysfunction, vaginal atrophy, or vulvovaginal GVHD given their prevalence in this population. We will then provide patients with a tablet computer that they will use to access the mobile app. We chose to use tablet computers for intervention delivery in this proof-of-concept study. However, the mobile app can be further adapted in the future to be delivered via mobile phones to enhance dissemination. Upon study enrollment, the RA will provide patients with a comprehensive tutorial and detailed instructions regarding how to use the app, in person or via secure video-based conference. The RA will encourage patients to engage their partners with the app content. The app will also prompt patients to engage their partners with specific exercises. Given the pilot nature of this study, we will not measure the effect of the intervention on partners. Patients will complete the intervention modules at their desired pace over 8 weeks. The app will prompt patients with reminders to complete their modules and utilize incentives to enhance patient engagement, as noted previously. The mobile app

will collect data on intervention fidelity (the number of completed modules, proportion of each module completed, time spent on each module, partner engagement with each module). Participants will complete additional surveys 8 and 12 weeks after clinician consult and examination.

Additionally, we will conduct qualitative interviews with 10 patients who are randomized to the intervention arm, to understand their experience of using the application and to assess patient opinions regarding the app. We will purposefully sample patients to ensure adequate representation based on age and sex. If we see different themes emerge based on age/sex, we will amend the protocol to increase our sample size for these qualitative interviews. We have developed a semi-structured qualitative interview guide to explore 1) patients' general experience using the SHIFT app and 2) patients' opinions regarding app content (Appendix M). Qualitative interviews will be conducted after patients complete all of their quantitative study assessments. Trained study staff will conduct and audio-record one-on-one interviews with patients via telephone or in-person. The estimated time to complete the patient qualitative interview is approximately 30 minutes. Audio recordings of the qualitative interviews will be stored for six months following interview completion.

Enhanced Standard Care: Patients assigned to the enhanced standard care group will not receive the mobile app. However, they will meet with a transplant clinician for a brief medical examination to assess the need for medications for erectile dysfunction, vaginal atrophy, or vulvovaginal GVHD; this visit will be conducted in clinic or virtually via secure video-based conference. The treating transplant clinician may refer patients to a psychologist, urologist, or gynecologist at the patients' request or at their discretion. At MGH, < 1% of transplant survivors are referred to a specialist to address sexual health concerns. Importantly, we did not see an increase in rate of referral to specialists during our pilot study. We will also collect data on referrals to specialists in both study groups. Although most transplant practices across the country do not systematically screen or treat sexual dysfunction, we chose a conservative control group to allow us to most accurately assess the effect of the mobile app.61 Participants will complete additional surveys 8 and 12 weeks after clinician consult and examination.

Institutions will register eligible participants in the Clinical Trials Management System (CTMS) OnCore as required by DF/HCC SOP REGIST-101.

Once the patient has been registered, a member from of the MGH Cancer Outcomes Research Program (CORe) team (independent from the study staff) will perform randomization procedures using a computer-generated randomization schema, stratified by study site and transplant type.

9.3 Procedure to Lessen Risk

9.3.1 Procedures to Lessen Risk

We do not anticipate that participation in this study will pose risk to patients other than the risk of breach in confidentiality. Prior studies of psychoeducational apps demonstrated that patients utilize the apps without any adverse emotional reactions. Should a participant express distress while using the app or completing study assessments or qualitative interview, the RA will reassure the participant that they can stop using the app and they need not answer any of the assessment questions which they find upsetting. The RA will also remind the participant that study participation is voluntary. If participants remain distressed, both the Principal Investigator and the oncology clinician will be notified. Additionally, we will offer participants who remain distressed an opportunity to meet with either the principal investigator (Dr. Areej El-Jawahri) or a clinical psychologist (Dr. Joseph Greer, a co-investigator) to help address their distress.

We will prevent breaches in confidentiality by keeping participant data on password protected Partners computers and in a locked office on MGH campus. Data logged online will be saved in password protected documents. Only study team will have access to the data.

The MGH research team will meet on weekly basis throughout the study period and will discuss any issues or concerns that may arise regarding the study procedures. Should the protocol require modifications or amendments based on these meetings, the PI will make the necessary changes and submit them to the DF/HCC IRB for approval.

9.3.2 Source Records

We will administer the following measures at baseline prior to randomization, 8 weeks, and 12 weeks from the time of clinician consult and examination:

• **Demographic Questionnaire (only at baseline):** Participants will self-report their age, sex, race/ethnicity, marital status, religion, and education. [Appendix B]

• **Sexual Function:** We will utilize the PROMIS-2 Sexual Function and Satisfaction Measure including the following domains: global satisfaction with sex life, interest in sexual activity, and orgasm.[49] For men, we will also include the erectile function domain. For women, we will also administer the lubrication and vaginal comfort domains. [Appendix C]

• **QOL:** We will use the Functional Assessment of Cancer Therapy-Bone Marrow Transplant (FACT-BMT) to assess QOL.[50] [Appendix D]

• **Mood:** We will use the Hospital Anxiety and Depression Scale (HADS) to assess symptoms of depression and anxiety during the past week in all study participants.[51] [Appendix E]

• **Usability of mobile app (only those randomized to intervention):** We will use the system usability scale at eight weeks post-intervention to assess the usability of the mobile app. [52][Appendix F]

• **Perceptions and satisfaction with mobile app (sample of those randomized to intervention):** We will qualitatively assess patient experience using the intervention using a semi-structured qualitative interview guide. [Appendix M]

Administration of self-report measures: We will collect and enter all patient-reported data electronically using Research Electronic Data Capture (REDCap). An RA will ask study participants to complete questionnaires in-person during clinic visits, via email, or over the telephone.

9.4 Long-Term Follow-Up Data Collection

We will collect demographic information, sexual function, QOL, mood, and usability of the mobile app (only in patients randomized to the intervention).

Table 2: Quantitative Data Collection Timeline

Participant	**Baseline**	**8 weeks (+/- 1 week)**	**12 weeks (+/- 1 week)**
Patient Measures:			
Demographics	X		
PROMIS Sexual Function and Satisfaction Measure	X	X	X
Functional Assessment of Cancer Therapy-Bone Marrow Transplant (FACT-BMT)	X	X	X
Hospital Anxiety and Depression Scale (HADS)	X	X	X

System Usability Scale (only intervention participants)		X	
Medical Record Review:			
Chart review from electronic health record	X		

10.0 Data and Specimen Banking: Not Applicable

11.0 Data Management and Confidentiality

11.1 Analysis **Data analysis Aim 1 (feasibility):** We will report baseline characteristics of all study participants. The primary endpoint of the proposed study is feasibility. The proposed intervention app will be deemed feasible if at least 60% (95% CI +/- 12%) of eligible patients are enrolled in the study, and of those enrolled, at least 60% engage with at least 70% of the intervention modules (modules engagement will be captured by the app). The 60% feasibility and intervention module completion cut-off is commonly used in behavioral intervention studies.[53-55] We will also use descriptive statistics to examine the usability of the mobile app based on the system usability scale.

Data analysis Aim 2 (preliminary efficacy): We will compare patients' sexual function (PROMISE Sexual Function and Satisfaction), QOL (FACT-BMT), and depression (HADS) at week-8 and week-12 using analysis of covariance adjusting for baseline values. Mixed linear models will be fitted to adjust for selected demographic and clinical factors when examining change in outcomes of interest across all time points. We will also test for potential moderators of the intervention effect using interaction terms for the mixed linear models to assess whether differences in patient-reported outcomes are moderated by patient factors (age, gender, computer experience), or transplant type. We will use conservative (alpha=0.05) and liberal (alpha=0.25) values to assess statistical significance in this pilot study. When handling missing data, if data appear to be missing at random, we will employ multiple imputation. If data are not missing at random, we will employ pattern mixture modeling.

Data analysis Exploratory aim: We will analyze the qualitative data using a multi-step process using coding and content analysis to explore 1) patients' perceptions and satisfaction with the mobile app; 2) patients' opinions regarding the app content. This will involve coding to structure data into categories and creating groups according to the broader issues or themes. We will identify major and minor themes within each content area and we will extract and highlight messages. Two independent coders will examine discrepant, unexpected, or unclear data until agreement is reached. To assure the trustworthiness of our findings, we will take steps to maximize reliability and credibility including: investigator triangulation (using a multidisciplinary team of investigators), and team debriefs of the interview content.

11.2 Power Analysis

The primary aim of the proposed pilot is feasibility. We chose the sample size of 60 patients based on the feasibility of completing the project during the proposed timeframe and the ability to assess the preliminary efficacy of the intervention. In a pilot study, at least 30 patients are needed in each group to estimate a parameter.[56,57] Thus, the proposed sample size will provide us with preliminary data that can be used to determine the effect size and adequately power future trials. Based on our prior pilot study, with a sample size of 60, we would have >80% power to detect a clinically significant 7-point difference in satisfaction with sex (SD=8) between the two groups.

11.3 Data Security

The research team is trained in protecting patient health information. All data will be saved in a password-protected document on Partners computers. Only the research team will have access to the document. Patient data and study identifiers will be kept in separate documents and information linking participants to the study will be kept in a different document that will also be password-protected. Paper consent forms and surveys will be stored in a locked office at Massachusetts General Hospital. All patient-reported data will be reported electronically using Research Electronic Data Capture, a tool for creating and managing online surveys (REDCap). Our research team has significant experience using REDCap and will design the surveys in a web browser, assisted by institutional information technology support. Based on preference and feasibility, participants will be offered either paper surveys or electronic reporting through REDCap on computer tablets provided by the RA at the time of consent. Participant information will be kept confidential throughout the study period.

11.4 Quality Control

An RA will enter hard-copy surveys into REDCap and review all surveys once. Another RA will perform a quality check on 10% of the surveys. If an error is found, an additional 5% will be checked until no errors are found.

11.5 Study-Wide Data Handling: please see description above regarding data security. We only have questionnaire data that will be stored electronically through REDCap. Paper questionnaires will be stored in a locked cabinet by the study team.

12.0 Provisions to Monitor the Data to Ensure the Safety of Subjects:

This project does not pose more than minimal risk to study participants. We do not anticipate any risks to study participation. We have utilized the study questionnaires and conducted interviews in prior studies without any adverse events. If a participant becomes distressed due to their involvement in the study, both the PI and their oncology clinician will be notified. We will offer participants who remained distressed the opportunity to meet with the PI (Dr. El-Jawahri) or a psychologist (Dr. Greer, a co-investigator).

13.0 Withdrawal of Subjects

Participants will be withdrawn without their consent if it is in their best interest, if the study procedures are demonstrated to be risky or ineffective, if any problem arises following study procedures, if issues arise with research funding, or any other unforeseen circumstance. Participants will be notified if they are removed from the study.

14.0 Risks to Subjects

Though the intervention involves topics of a sensitive nature, we do not anticipate risks to subjects other than the risk of breach of confidentiality. Participation in our pilot study was not associated with any negative outcomes. No adverse reactions are anticipated during the proposed study as a result of the study procedures.

While no adverse or unanticipated events are expected in this behavioral trial, any such events will be immediately reported to the IRB. There is a minimal chance of causing harm with this study. We have administered all the questionnaires to over 100 transplant recipients with no adverse events. While some

topics probed in the app and study assessments are sensitive in nature, no adverse or unanticipated events occurred in previous studies discussing these topics. Additionally, our research team has extensive experience conducting studies using psychoeducational apps on sensitive topics without any adverse events. Further, our research team has experience conducting qualitative patient interviews.

Should participants exhibit or express distress or anger, they will be reassured by the study staff that they need not answer any questions which they find upsetting. They will also be reminded that study participation is voluntary. If participants remain distressed, both the PI and the oncologist will be notified. Should several participants express distress over an individual item, the research team will review the questionnaire and contact the IRB to consider removing it from the study.

We will prevent breaches in confidentiality by keeping participant data on password protected Partners computers and in a locked office on MGH campus. Data logged online will be saved in password protected documents. Only study team will have access to the data.

15.0 Potential Benefits to Subjects

15.1 Potential benefits

Participants may or may not experience improved sexual function through taking part in this study. Participants (regardless of their study group assignment) will have the opportunity to meet with a transplant clinician to conduct a brief evaluation and that might be helpful in identifying problems related to their sexual dysfunction that can be addressed.

15.2 Participant compensation

Participants will not be compensated for their involvement.

16.0 Vulnerable Populations: Not Applicable

17.0 Community-Based Participatory Research: Not Applicable

18.0 Sharing of Results with Subjects

Given the nature of the population included in the study, it is not appropriate to proactively contact participants at the conclusion of this study. We anticipate that a proportion of our participants will relapse or die after completing the study. We do not wish to cause unnecessary distress to participants' family members by attempting to contact participants who have died. Therefore, we provide the research team contact information to each participant and encourage them to contact us if they would like to receive updates and information on the research findings.

19.0 Setting

The research team will recruit potential subjects in the MGH Cancer Center and Dana Farber Cancer Institute oncology clinics. Beth Israel Deaconess Medical Center patients will be recruited by clinician referral. Consent and a baseline demographics survey will take place in the clinic or over the phone, at the time of recruitment. Participants will attend their visit with a transplant clinician with expertise in sexual health in the MGH Transplant Oncology Clinic; this visit may occur in clinic or virtually via secure video-based conference. Participants randomly assigned to the mobile app will use the mobile app in the privacy of their homes. Research procedures will occur on an out-patient basis or will occur remotely.

20.0 Resources Available

Team Qualifications

Dr. El-Jawahri, Dr. Dias and Dr. Cutler (co-investigator) have the experience to ensure the success of the proposed project. Dr. El-Jawahri has led several trials studying interventions to improve the quality of life and care of patients with cancer. Our investigative team has substantial expertise in developing and testing supportive care interventions, adapting these interventions to mobile applications, and addressing sexual health concerns in cancer survivors. Our team additionally has extensive experience in conducting qualitative interviews with patients.

The study team will train the RA to identify potentially eligible patients, approach patients for study participation, obtain informed consent, and conduct qualitative interviews and provide patients randomized to the intervention with a comprehensive tutorial regarding how to use the app. Our research team has extensive experience training RA to work with medically ill cancer population, recognizing participants' burden and distress, conducting qualitative patient interviews, as well as educating participants on the use of mobile apps. We will utilize similar training procedures to our prior studies.

20.1 *Other Resources*

The MGH Transplant Program performs approximately 200 new transplants per year and cares for over 700 HCT survivors. Therefore, we are confident in our ability to meet accrual goals.

The research team will devote as much time as is needed to conducting and completing the research. Our facilities are located on the Massachusetts General Hospital main campus within walking distance of the transplant clinic. Our research team uses Partners computers and have access to Partners resources to undertake this endeavor.

Though we do not anticipate adverse reactions as a result of participation in this study, participants who express distress will have access to psychologist Dr. Joseph Greer.

The research team will have access to the protocol and documents regarding research procedures. Responsibilities will be communicated in a timely manner through weekly team meetings and email.

21.0 Prior Approvals: Not applicable

22.0 Recruitment Methods

22.1 Recruitment

Potential subjects will be recruited from the transplant clinics at Massachusetts General Hospital or Dana Farber Cancer Institute at their routine appointments with their oncology clinicians, or via telephone. Beth Israel Deaconess Medical Center patients will be recruited by clinician referral. A trained RA will recruit potential subjects whose transplant clinicians have no objections to their participation and who screen positive for sexual dysfunction causing distress according to NCCN guidelines.

22.2 Source of Subjects

Subjects will be recruited from the population of patients receiving follow up care at Massachusetts General Hospital Cancer Center, Beth Israel Deaconess Medical Center, or Dana Farber Cancer Institute.

22.3 Identifying Potential Subjects

Potential subjects will be identified by screening the transplant clinic schedule at Massachusetts General Hospital and Dana Farber Cancer Institute. Beth Israel Deaconess Medical Center patients will be recruited by clinician referral. A trained RA will further determine eligibility by evaluating potential subjects' medical records. The RA will then reach out to the patient's oncology clinician to determine if the clinician believes participation is appropriate. The last screening test will be the two questions in the NCCN guidelines used to determine the presence of sexual dysfunction causing distress.

22.4 Recruitment Materials

No materials will be used to recruit subjects.

22.5 Subject Payment

Subjects will not be paid for participation.

23.0 Local Number of Subjects:

We anticipate that 60 subjects will be recruited from MGH, BIDMC and DFCI. Based on our prior data, approximately one third of HCT recipients will screen positive for sexual dysfunction causing distress. Therefore, we anticipate that we will screen approximately 200 patients to identify 60 subjects eligible for study participation. 10 patients randomized to the intervention will undergo qualitative interview to assess perceptions and experience of using the mobile application.

24.0 Provisions to Protect the Privacy Interests of Subjects

24.1 Privacy Interests

Participant privacy interests will be protected by limiting individuals in the room during the time of consent and follow up survey or interview administration (if done in person). The RA will also answer any participant questions regarding who has access to participant information and reassure them of the steps taken to ensure confidentiality.

24.2 Subjects' Feeling of Ease

The research team has significant experience interacting with this patient population as well as experience training RAs with these patients. During the consent process and survey or interview administration, the RA will remind subjects that participation is voluntary and that they can decline to respond to any questions that they do not wish to answer. Subjects will also be reminded that they can skip any mobile app modules that they find distressing.

24.3 Research Team Information Access

The research team is permitted to access the medical records of subjects and any subject-reported data collected during this research.

25.0 Compensation for Research-Related Injury: Not Applicable

26.0 Economic Burden to Subjects: Not Applicable

27.0 Consent Process

The RA will obtain consent from potential subjects in the oncology clinic at MGH, BIDMC or DFCI, or will obtain verbal consent over the phone. A waiting period will be available between approaching the potential subject and obtaining the consent if the potential subject requests it. The RA will remind the potential subject that participation is voluntary, and that participation or

refusal to participate will not impact the quality of care received. To ensure ongoing consent, the RA will explain the participant's right to withdraw at any time and will explain the appropriate means of contacting the research team to initiate the withdrawal process. We will follow SOP: Informed Consent Process (CON-100).

Non-English Speaking Subjects: Not Applicable

Subjects who are not yet adults (infants, children, teenagers): Not Applicable

Cognitively Impaired Adults: Not Applicable

Adults Unable to Consent: Not Applicable

28.0 Process to Document Consent in Writing

We will obtain written consent using the submitted consent form, consistent with SOP: Informed Consent Process (CON-100). We will obtain verbal consent using the submitted verbal consent form.

29.0 Drugs or Devices: Not Applicable

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31.0 Appendix A

Due to the size of this document Appendix A has been included as a separate file.

32.0 Appendix B

Appendix B: Demographics

Patient Demographics

Please check the appropriate box or boxes.

1. Ethnicity

☐ Hispanic or Latino

- ☐ Not Hispanic or Latino

2. Race (please check all that apply)
   - ☐ American Indian or Alaskan native
   - ☐ Asian
   - ☐ African American or Black
   - ☐ Native Hawaiian or Other Pacific Islander
   - ☐ White
   - ☐ Other (please specify)_____

3. Religion
   - ☐ Catholic Christian
   - ☐ Other Christian (such as Protestant, Orthodox, etc.)
   - ☐ Jewish
   - ☐ Muslim
   - ☐ Atheist
   - ☐ None
   - ☐ Other (please specify)_____

4. Current relationship status:
   - ☐ Married or living with someone as if married
   - ☐ Non-cohabiting relationship
   - ☐ Single, never married
   - ☐ Divorced/Separated
   - ☐ Loss of long term partner/Widowed

5. Please indicate your highest or current education level:
   - ☐ Grade 1-8
   - ☐ Some high school
   - ☐ Completed high school
   - ☐ General education diploma (G.E.D)
   - ☐ Associate degree
   - ☐ Some college credit
   - ☐ Graduated college
   - ☐ Masters' degree (MA, MS, MEng, MEd, MSW, MBA)
   - ☐ Professional degree beyond a bachelors' degree (MD, DDS, DVM, LLB, JD)
   - ☐ Doctorate degree (PhD, EdD)

6. What is your annual combined household income?
   - ☐ Less than $25,000
   - ☐ $25,000 – $49,999
   - ☐ $50,000 – $99,999
   - ☐ $100,000 – $149,999
   - ☐ Greater than $150,000

7. What sex were you assigned at birth?
   - ☐ Male
   - ☐ Female
   - ☐ Other (please specify):_____

8. What is your current gender identity?

- ☐ Male
- ☐ Female
- ☐ Transgender Male/Trans Man/ Female-to-Male
- ☐ Transgender Female/Trans Woman/Male-to-Female
- ☐ Genderqueer, neither exclusively male or female
- ☐ Other (please specify):_____

9. Do you think of yourself as:
- ☐ Heterosexual/straight
- ☐ Gay/Lesbian
- ☐ Bisexual
- ☐ Something else, please specify _____
- ☐ Don't know

10. Please indicate who you live with (you may check more than one box):
- ☐ By myself
- ☐ Partner/Spouse
- ☐ Roommate/Friend
- ☐ Children under 18
- ☐ Children 18 & older
- ☐ Group home/assisted living/nursing home
- ☐ Parent
- ☐ Other (please specify) _____

11. Current employment status (check all that apply):
- ☐ Employed (full-time or part-time)
- ☐ Caring for home or family (not currently working and not looking for paid work)
- ☐ Unemployed and looking for work
- ☐ Unable to work due to illness or disability
- ☐ Retired
- ☐ Student
- ☐ Other (please specify)_____

Please enter your email (will only be used if necessary):

_____

What is the best phone number to use if we needed to reach you? _____

33.0 Appendix C

Appendix C: The PROMIS Sexual Function and Satisfaction Measures

Global Satisfaction with Sex Life	
IN THE PAST 30 DAYS	
How satisfied have you been with your sex life?	**1. Not at all** **2. A little bit** **3. Somewhat** **4. Quite a bit** **5. Very**
How much pleasure has your sex life given you?	**1. None** **2. A little bit** **3. Somewhat** **4. Quite a bit** **5. A lot**
How often have you thought that your sex life is wonderful?	**1. Never** **2. Rarely** **3. Somewhat** **4. Often** **5. Always**
How satisfied have you been with your sexual relationship(s)?	**0. have not had a sexual partner in the past 30 days** **1. Not at all** **2. A little bit** **3. Somewhat** **4. Quite a bit** **5. Very**
When you have had sexual activity, how much have you enjoyed it?	**1. Not at all** **2. A little bit** **3. Somewhat** **4. Quite a bit** **5. Very much**

Interest in Sexual Activity	
IN THE PAST 30 DAYS	
How interested have you been in sexual activity?	1. Not at all 2. A little bit 3. Somewhat 4. Quite a bit 5. Very
How often have you felt like you wanted to have sexual activity?	1. Never 2. Rarely 3. Sometimes 4. Often 5. Always
How often have you had sexual thoughts or fantasies while you were awake?	1. Never 2. Rarely 3. Somewhat 4. Often 5. Always
How often were you interested enough to start a sexual activity?	1. Never 2. Rarely 3. Sometimes 4. Often 5. Always
Orgasm	
IN THE PAST 30 DAYS	
How much pleasure have your orgasms or climaxes given you?	1. None 2. A little bit 3. Some 4. Quite a bit 5. Very much
How often have your orgasms or climaxes been satisfying?	0. Never 1. Rarely 2. Sometimes 3. Often 4. Always
How satisfying have your orgasms or climaxes been?	0. Not at all 1. A little bit 2. Somewhat 3. Quite a bit 4. Very

Erectile Function (males only)	
IN THE PAST 30 DAYS	
How often were you able to get an erection (get hard) during sexual activity?	**1. Almost never/never** **2. A few times (much less than half the time)** **3. Sometimes (about half the time)** **4. Most times (much more than half the time)** **5. Almost always/always**
When you had erections with sexual stimulation how often were your erections hard enough for penetration?	**1. Almost never/never** **2. A few times (much less than half the time)** **3. Sometimes (about half the time)** **4. Most times (much more than half the time)** **5. Almost always/always**
When you attempted sexual intercourse how often were you able to penetrate (enter) your partner?	**0. Did not attempt intercourse** **1. Almost never/never** **2. a few times (much less than half the time)** **3. Sometimes (about half the time)** **4. Most times (much more than half the time)** **5. Almost always/always**
During sexual intercourse <u>how often</u> were you able to maintain your erection (stay hard) after you had penetrated (entered) your partner?	**0. Did not attempt intercourse** **1. Almost never/never** **2. A few times (much less than half the time)** **3. Sometimes (about half the time)** **4. Most times (much more than half the time)** **5. Almost always/always**
During sexual intercourse <u>how difficult</u> was it to maintain your erection (stay hard) to completion of intercourse?	**0. Did not attempt intercourse** **1. Extremely difficulty** **2. Very difficult** **3. Difficult** **4. Slightly difficult** **5. Not difficult**
Please rate your ability to have an erection. If you use any aids to help you get an erection (e.g. pills, injections, or a penis pump) please answer this question thinking about the times you used these aids	**0. Very poor** **1. Poor** **2. Fair** **3. Good** **4. Very good**
How difficult has it been for you to get an erection (get hard) when you wanted to? If you use any aids to help you get an erection (e.g. pills, injections, or a penis pump) please answer this question thinking about the times you used these aids	**0. Have not tried to get an erection (get hard) in the past 30 days** **5. Not at all** **4. A little bit** **3. Somewhat** **2. Quite a bit** **1. Very**
How often have you been able to <u>keep</u> an erection (stay hard) as long as you wanted to?	**0. Have not had an erection (been hard) in the past 30 days** **1. Never** **2. Rarely** **3. Sometimes** **4. Often**

	5. **Always**
IN THE PAST 30 DAYS	
How hard have your erections been?	0. **Have not had an erection in the past 30 days** 1. **Penis was large but not hard** 2. **Penis was hard but not hard enough for penetration** 3. **Penis was hard enough for penetration but not completely hard** 4. **Penis was completely hard**
How would you describe the usual QUALITY of your erections?	1. **Not at all** 2. **Not firm enough for any sexual activity** 3. **Firm enough for masturbation and foreplay only** 4. **Firm enough for intercourse**
How would you describe the FREQUENCY of your erections	1. **I NEVER had an erection when I wanted one** 2. **I had an erection LESS THAN HALF the time I wanted one** 3. **I had an erection ABOUT HALF the time I wanted one** 4. **I had an erection MORE THAN HALF the time I wanted one** 5. **I had an erection WHENEVER I wanted one**

Vaginal Discomfort (females only)	
IN THE PAST 30 DAYS	
How would you describe the comfort of your vagina during sexual activity	1. Very comfortable 2. Comfortable 3. Uncomfortable 4. Very uncomfortable
How often have you had difficulty with sexual activity because of discomfort or pain in your vagina?	1. Never 2. Rarely 3. Sometimes 4. Often 5. Always
How often have you had discomfort inside your vagina during sexual activity?	1. Never 2. Rarely 3. Sometimes 4. Often 5. Always
How often have you had discomfort from feelings of rubbing or burning inside your vagina during sexual activity?	1. Never 2. Rarely 3. Sometimes 4. Often 5. Always
How often have you had discomfort from feelings of pulling or ripping inside your vagina during sexual activity?	1. Never 2. Rarely 3. Sometimes 4. Often 5. Always
How often have you had pain inside your vagina during sexual activity?	1. Never 2. Rarely 3. Sometimes 4. Often 5. Always
How often did you have discomfort or pain during vaginal penetration? (Vaginal penetration is when something is put inside your vagina)	1. Never 2. Rarely 3. Sometimes 4. Often 5. Always
How often did you have discomfort or pain after vaginal penetration? (vaginal penetration is when something is put inside your vagina)	5. Never 6. Rarely 7. Sometimes 8. Often 9. Always
When you have had sexual activity, how much discomfort have you felt inside your vagina?	1. None 2. A little bit 3. Some 4. Quite a bit 5. A lot

When you have had sexual activity, how much pain have you felt inside your vagina?	**1. None** **2. A little bit** **3. Some** **4. Quite a bit** **5. A lot**
IN THE PAST 30 DAYS	
How would you rate your level (degree) of discomfort or pain during or after vaginal penetration? **(vaginal penetration is when something is put inside your vagina.)**	**1. Very low or none at all** **2. Low** **3. Moderate** **4. High** **5. Very high**

Lubrication (women only)	
IN THE PAST 30 DAYS	
How often have you felt your vagina was lubricated ("wet") enough during sexual activity?	**1. Never** **2. Rarely** **3. Sometimes** **4. Often** **5. Always**
How difficult was it to become lubricated ("wet") during sexual activity or intercourse?	**1. Extremely difficult or impossible** **2. Very difficult** **3. Difficult** **4. Slightly difficult** **5. Not difficult**
How difficult was it to maintain your lubrication("wetness") until completion of sexual activity or intercourse?	**1. Extremely difficult or impossible** **2. Very difficult** **3. Difficult** **4. Slightly difficult** **5. Not difficult**
How difficult has it been for your vagina to get lubricated ("wet") when you wanted it to?	**0. Have not tried to get lubricated in the past 30 days** **1. Very** **2. Quite a bit** **3. Somewhat** **4. A little bit** **5. Not at all**
How often did you become lubricated ("wet") during sexual activity or intercourse?	**1. Almost never or never** **2. A few times (less than half the time)** **3. Sometimes (about half the time)** **4. Most times (more than half the time)** **5. Almost always or always**

34.0 Appendix D

Appendix D: Patient Quality of Life (FACT-BMT)

Below is a list of statements that other people with your illness have said are important**. Please circle or mark one number per line to indicate your response as it applies to the <u>past 7 days</u>.**

	PHYSICAL WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

	SOCIAL/FAMILY WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box* ☐ *and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

Please circle or mark one number per line to indicate your response as it applies to the <u>past 7 days</u>.

	EMOTIONAL WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope in the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

	FUNCTIONAL WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

Please circle or mark one number per line to indicate your response as it applies to the <u>past 7 days</u>.

	ADDITIONAL CONCERNS	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
BMT1	I am concerned about keeping my job (include work at home)	0	1	2	3	4
BMT2	I feel distant from other people	0	1	2	3	4
BMT3	I worry that the transplant will not work	0	1	2	3	4
BMT4	The effects of treatment are worse than I had imagined	0	1	2	3	4
C6	I have a good appetite	0	1	2	3	4
C7	I like the appearance of my body	0	1	2	3	4
BMT5	I am able to get around by myself	0	1	2	3	4
BMT6	I get tired easily	0	1	2	3	4
BL4	I am interested in sex	0	1	2	3	4
BMT7	I have concerns about my ability to have children	0	1	2	3	4
BMT8	I have confidence in my nurse(s)	0	1	2	3	4
BMT9	I regret having the bone marrow transplant	0	1	2	3	4
BMT10	I can remember things	0	1	2	3	4
Br1	I am able to concentrate	0	1	2	3	4
BMT11	I have frequent colds/infections	0	1	2	3	4
BMT12	My eyesight is blurry	0	1	2	3	4
BMT13	I am bothered by a change in the way food tastes	0	1	2	3	4
BMT14	I have tremors	0	1	2	3	4
B1	I have been short of breath	0	1	2	3	4
BMT15	I am bothered by skin problems (e.g., rash, itching)	0	1	2	3	4
BMT16	I have trouble with my bowels	0	1	2	3	4
BMT17	My illness is a personal hardship for my close family members	0	1	2	3	4
BMT18	The cost of my treatment is a burden on me or my family	0	1	2	3	4

35.0 Appendix E

Appendix E: Hospital Anxiety and Depression Scale (HADS):

1. I feel tense or "wound up." a. Most of the time b. A lot of the time c. From time to time, occasionally d. Not at all	2. I still enjoy the things I used to enjoy. a. Definitely as much b. Not quite as much c. Only a little d. Hardly at all
3. I get a sort of frightened feeling as if something awful is about to happen. a. Very definitely and quite badly b. Yes, but not too badly c. A little, but it doesn't worry me d. Not at all	4. I can laugh and see the funny side of things. a. As much as I always could b. Not quite so much now c. Definitely not so much now d. Not at all
5. Worrying thoughts go through my mind. a. A great deal of the time b. A lot of the time c. From time to time but not too often d. Only occasionally	6. I feel cheerful. a. Not at all b. Not often c. Sometimes d. Most of the time
7. I can sit at ease and feel relaxed. a. Definitely b. Usually c. Not often d. Not at all	8. I feel as if I am slowed down. a. Nearly all the time b. Very often c. Sometimes d. Not at all
9. I get a sort of frightened feeling like "butterflies" in the stomach. a. Not at all b. Occasionally c. Quite often d. Very often	10. I have lost interest in my appearance. a. Definitely b. I don't take so much care as I should c. I may not take quite as much care d. I take just as much care as ever
11. I feel restless as if I have to be on the move. a. Very much indeed b. Quite a lot c. Not very much d. Not at all	12. I look forward with enjoyment to things. a. As much as I ever did b. Rather less than I used to c. Definitely less than I used to d. Hardly at all
13. I get sudden feelings of panic. a. Very often indeed b. Quite often c. Not very often d. Not at all	14. I can enjoy a good book or radio or TV program. a. Often b. Sometimes c. Not often d. Very seldom

36.0 Appendix F

Appendix F: The System Usability Scale

Please check the box that best indicates how much you agree with the following statements about the SHIFT mobile app.

1. I think that I would like to use this system frequently.

Strongly Disagree 1	2	3	4	Strongly Agree 5

2. I found the system unnecessarily complex.

Strongly Disagree 1	2	3	4	Strongly Agree 5

3. I thought the system was easy to use.

Strongly Disagree 1	2	3	4	Strongly Agree 5

4. I think that I would need the support of a technical person to be able to use this system.

Strongly Disagree 1	2	3	4	Strongly Agree 5

5. I found the various functions in this system were well integrated.

Strongly Disagree	2	3	4	Strongly Agree 5

1				

6. I thought there was too much inconsistency in this system.

Strongly Disagree 1	2	3	4	Strongly Agree 5

7. I would imagine that most people would learn to use this system very quickly.

Strongly Disagree 1	2	3	4	Strongly Agree 5

8. I found the system very cumbersome to use.

Strongly Disagree 1	2	3	4	Strongly Agree 5

9. I felt very confident using the system.

Strongly Disagree 1	2	3	4	Strongly Agree 5

10. I needed to learn a lot of things before I could get going with this system.

Strongly Disagree 1	2	3	4	Strongly Agree 5

37.0 Appendix G

Appendix G: Email to transplant clinicians

Hi _____,

You have a patient eligible for the SHIFTstudy coming to clinic DAY OF WEEK, DATE.

PATIENT NAME (MRN)

As a reminder, SHIFTis a randomized clinical trial investigating the effect of a sexual health intervention hematopoietic stem cell transplantation survivors vs. standard transplant care. We would like to approach Ms. NAME during her appointment at TIME and offer them the study.

Would you have any objections or concerns with offering Ms. NAME the study? Please let us know at your earliest convenience so that we would have a chance to enroll them in the time window. If we do not hear from you in 24 hours, we will assume there are no objections to approaching.

Thank you and feel free to email back with any questions or concerns.

Best,

[Name of Study Coordinator]

38.0 Appendix H

Appendix H: Letter for participants completing questionnaires by mail

Date
Dear Mr. or Ms. _____,

I am pleased to be in touch with you regarding the mobile app research study in which you are enrolled at the Massachusetts General Hospital. As part of the study, we ask that you complete this questionnaire by [end of questionnaire window date] and mail it back using the included envelope. Thank you again for your continued participation and feel free to call with any questions.

Sincerely,
[Name of study coordinator]

39.0 Appendix I

Appendix I: Verbal telephone script for study questionnaire administration for patients

Hello—is [name of patient/or caregiver] there? Hi, my name is [research coordinator's name] I work at the MGH Cancer Center, and I am calling about the mobile app research study in which you are participating. Is now a good time to talk briefly?

If yes→ *Move on to next section.*
If no→ "Is there a better time at which I could call back?"

As part of the study procedures, we would like to ask you to complete a questionnaire over the phone. Do you have about 20 minutes to complete it with me now?

If yes→"Great, thank you." *Proceed to administering the questionnaire.*
If no→ "Is there a better time at which I we could complete the questionnaire?"

40.0 Appendix J

Appendix J: Email for participants completing questionnaires by email

Dear Mr. or Ms. _____,

I am pleased to be in touch with you regarding the mobile app research study in which you are enrolled at the Massachusetts General Hospital. As part of the study, we ask that you complete another questionnaire just like the one you completed in the clinic by following the link in this email.

If possible, we ask that you please complete the survey by [end of questionnaire window date]. Again, feel free to email or call with any questions, and we greatly appreciate your participation in the study.

Sincerely,
[Name of study coordinator]

41.0 Appendix K

Protocol Title: Multimodal Mobile Intervention Application (App) To Address Sexual Dysfunction in Hematopoietic Stem Cell Transplant Survivors

DF/HCC Principal Research Doctor / Institution: Areej El-Jawahri MD/MGH

Main Consent

INTRODUCTION AND KEY INFORMATION

All research is voluntary. It is your choice whether you take part in this research or not.

The following is a short summary of this research study to help you decide whether you would like to be a part of this study. More detailed information is provided later in this form.

For purposes of this research, you will be referred to as a "participant."

1. Why am I being invited to take part in a research study?

You are invited to take part in in this research study, because you have undergone stem cell transplantation.

2. Why is this research being done?

Frequently survivors of stem cell transplantation report significant problems with their sexual function that impacts their quality of life, mood, and their intimacy and relationship with their partners. These issues can be very distressing to patients and their loved ones. The study doctors want to know if the use of a mobile app intervention focused on improving sexual function may improve your overall care.

3. What does this research study involve and how long will it last?

This research study involves screening for eligibility and a series of questionnaires to measure your quality of life and sexual function. Study questionnaires can be completed in the hospital, clinic, over email, through the mail, or telephone with assistance as provided.

You will be in this research study for up to twelve weeks after you consent. Each questionnaire should take you about 20 minutes to complete. We will keep track of your medical information only by reviewing your medical record and we will not be contacting you again in the future. Once you finish your last questionnaire at twelve weeks after enrollment, you will not be contacted by us again. However, we will keep track of your medical information only by reviewing your medical record for the next 2 years.

It is expected that about 60 people will take part in this research study.

Information about you and your health is personal and private. Generally, it cannot be obtained without your written permission. By signing this form, you are providing that permission and your information may be obtained and used in accordance with this informed consent and as required or allowed by law. This means that researchers may obtain information regarding your past medical history, as well as specimens and samples from previous health care providers such as hospitals and labs.

4. What are the risks to participating in this study?

There are risks to taking part in any research study. However, this particular study does not have any physical risks. You may find it upsetting to answer some of the items on the questionnaire. The research assistant will be available to you during your participation in the study. If you feel upset by any aspect of the study, the research assistant, along with your oncologist, will be available to talk with you. We can arrange for you to meet with our psychologist for additional counseling if needed.

Major known risks to participating in this research study include:

- Disclosure of sensitive personal information may result is a loss of privacy
- Possible emotional distress due to personal questions
- Significant amount of time required to complete questionnaires (online and/or in person)

5. Will being in this study benefit me in any way?

Taking part in this research study may or may not benefit you. We hope the information learned from this research study will provide more information about how a mobile app intervention can improve our management of sexual health symptoms for stem cell transplant survivors.

We do not know if taking part in this study will benefit you. This study may help researchers learn information that could help people in the future.

6. What are my options?

If you decide to participate, please sign and date at the end of this form.

We will give you a copy and you can refer to this consent form at any time during the research study.

If you choose not to participate in this research study, the research doctors will discuss other treatment options with you and/or refer you back to your primary doctor.

A. WHY IS THIS RESEARCH STUDY BEING DONE?

This research study is being done to evaluate whether the use of a mobile app can help transplant survivors experiencing sexual health problems.

In this research study, we are:

- Testing whether using the mobile app is feasible in addressing sexual health problems in transplant survivors.
- The app is called "SHIFT: Sexual Health and Intimacy Following Transplant." It was developed by clinicians at MGH.
- Previous research shows that mobile apps can be effective in helping people with issues like anxiety and we want to see if we can similarly address sexual health problems.
- We are hoping to learn if using the app to address sexual health problems is acceptable and useful to transplant survivors.

The main purpose of this study is to compare two types of care – the mobile app intervention versus enhanced standard care which includes having a one-time visit with a transplant clinician to conduct a brief medical examination and asses the needs for medications or treatments to address sexual health problems.

B. WHAT OTHER OPTIONS ARE THERE?

Instead of being in this research study, you have other options which may include the following:

- Decide not to participate in this research study.
- Participate in another research study.

If you choose not to participate, are not eligible to participate, or withdraw from this research study, this will not affect your present or future care and will not cause any penalty or loss of benefits to which you are otherwise entitled.

We encourage you to take some time to think this over, to discuss it with other people and your primary doctor, and to ask questions now and at any time in the future.

C. WHAT IS INVOLVED IN THE RESEARCH STUDY?

Before the research starts: Prior to signing this consent form, our research team reviewed your medical record to determine that you were eligible to participate in this research study. We also asked your oncology team for permission to approach you to participate in the study.

After you sign this consent form: You will first be asked to answer a few questions about yourself on a laptop tablet computer, such as your race, ethnicity, religion, relationship status, education, income, and living situation.

You will then be asked to complete a baseline questionnaire on the laptop which contains questions about your mood, quality of life (including your general, physical, social, and emotional well-being), and sexual function. If you are not able to use the laptop, you may fill out the baseline questions on paper.

Assignment to study group:

Because no one knows which of the study option is best, you will be randomized into one of the study groups:

- Enhanced Standard Care
- Multimodal Intervention mobile app to address sexual health problems

Randomization means that you are put into a group by chance. It is like flipping a coin. Neither you nor your doctor will choose which arm you are assigned to. You will have an equal chance of being placed in either group.

Study procedures:

If you are randomized to enhanced standard care:

- You will receive standard oncology care by your oncology team
- You will attend a clinic visit with a transplant clinician specializing in sexual health who will conduct a brief examination and assess the need for any treatments or medications to address your sexual health problems.
- You will be asked to complete study questionnaires on the laptop computer at 8 and 12 weeks after enrolling in the study. These questionnaires are expected to take up to 20 minutes each. You will have the option of completing these questionnaires during one of your routine clinic visits, or remotely through a secure web link or over the phone, or through the mail.

If you are randomized to the Multimodal Intervention app:

- You will receive standard oncology care by your oncology team.
- You will attend a clinic visit with a transplant clinician specializing in sexual health who will conduct a brief examination and assess the

need for any treatments or medications to address your sexual health problems.

- You will be provided with instructions on how to use the mobile app. You will be asked if you have your own iPad that you would be willing to use for the study. If you don't have an iPad, you will be provided with an iPad that allows you to engage with the mobile app at your convenience at home over an eight-week period.
- You will be asked to complete study questionnaires on the laptop computer at 8 and 12 weeks after enrolling in the study. These questionnaires are expected to take up to 20 minutes each. You will have the option of completing these questionnaires during one of your routine clinic visits, or remotely through a secure web link, or over the phone, or through the mail.

After the last assessment:
Your oncologist, as well as the research team, will be available to discuss any questions or concerns that you may have. Once you complete the last questionnaire you will not be contacted by us again. We would like to keep track of your medical condition by reviewing your electronic medical record for the next 2 years.

D. WHAT ARE THE RISKS OR DISCOMFORTS OF THE RESEARCH STUDY?

There are risks to taking part in any research study. However, this particular study does not have any physical risks. You may find it upsetting to answer some of the items on the questionnaire. The research assistant will be available to you during your participation in the study. If you feel upset by any aspect of the study, the research assistant, along with your oncologist, will be available to talk with you. We can arrange for you to meet with our psychologist for additional counseling if needed.

There is also a small risk of a breach of confidentiality.

During the research study, you will be provided with any new information that may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

E. WHAT WILL HAPPEN IF I AM REMOVED FROM THE STUDY OR DECIDE TO END MY PARTICIPATION IN THE RESEARCH?

You may be taken off the research study for any reason including:

- It is considered to be in your best interest
- The study treatment or procedures are found to be unsafe or ineffective
- There is any problem with following study treatments and procedures
- Your condition worsens
- A decision is made to end the study
- Or for other unforeseen reasons that make it necessary to stop your participation in the research study

You can also choose to stop participating in the research study at any time. Tell the research doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop. Leaving the research study will not affect your medical care outside of the research study.

F. WILL I BE PAID TO TAKE PART IN THIS RESEARCH STUDY?

You will not be paid for participating in this study.

G. WHO IS SUPPORTING THIS RESEARCH?

Massachusetts General Hospital is supporting this research study by providing funding.

H. WHAT ARE YOUR COSTS?

Taking part in this research study will not lead to added costs to you or your insurance company. You will not be billed or incur any co-pays for your visit with the transplant clinician to address sexual health problems as part of this study.

I. WHAT HAPPENS IF I AM INJURED OR BECOME SICK BECAUSE I TOOK PART IN THIS RESEARCH STUDY?

If you think you have been injured as a result of taking part in this research study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent form.

The treating hospital will offer you the care needed to treat injuries directly resulting from taking part in this research. These treatments may be billed to you or your insurance company. You will be responsible for deductibles, co-payments and co-insurance. There are no plans to pay you or give you other compensation for the injury.

You do not give up your legal rights by signing this form.

We will need to collect certain personal information about you for insurance or payment reporting purposes, such as your name, date of birth, gender, social security number or Medicare identification number and information related to this research study. We may be required to report this information to the Centers for Medicare & Medicaid Services. We will not use this information for any other purpose.

If you go to the Emergency Room or to another hospital or doctor it is important that you tell them that you are in this research. If possible, you should give them a copy of this consent form.

J. WHOM DO I CONTACT IF I HAVE QUESTIONS ABOUT THE RESEARCH STUDY?

If you have questions about the study, please contact the research doctor or study staff as listed below:

Massachusetts General Hospital:

- Areej El-Jawahri, MD: (617) 726-2000, beeper #18734
- 24-hour contact: Areej El-Jawahri, MD: (617) 726-2000, beeper #18734

For questions about your rights as a research participant, please contact a representative of the Office for Human Research Studies at Dana-Farber Cancer Institute (617) 632-3029. This can include questions about your participation in the study, concerns about the study, a research related injury, or if you feel/felt under pressure to enroll in this research study or to continue to participate in this research study.

K. RETURN OF RESEARCH RESULTS

Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will not *contact you to let you know what they have found.*

L. CLINICALTRIALS.GOV (CT.GOV)

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.

M. CONFIDENTIALITY

We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data.

Medical information created by this research study may become part of your hospital medical record and may be forwarded to your primary doctor. Information that does not become part of your medical record will be stored in your study file. It may also become part of a DF/HCC research database called CORIS.

The questionnaires will not become part of your medical record but will be stored in a research file with a specific study code identifier without your name.

Your answers to all the survey questionnaires will remain confidential.

The study team plans to publish the results of this research study and when we do, we may be asked to make the data we collect available to other researchers. We will not include information that identifies you in any publications or to the researchers who request the data to do additional research.

There is a risk that deidentified research data that is shared with outside collaborators may be reidentified. When deidentified data and specimens are shared with outside collaborators agreements limit what the outside collaborators can do with the information to help prevent reidentification.

N. GENETIC RESEARCH

This research will not involve genomic or germline testing.

O. PRIVACY OF PROTECTED HEALTH INFORMATION (HIPAA AUTHORIZATION)

The Health Insurance Portability and Accountability Act (HIPAA) is a federal law that requires Dana-Farber/Harvard Cancer Center (DF/HCC) and its affiliated research doctors, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions ("protected health information"). If you enroll in this research study, your "protected health information" will be used and shared with others as explained below.

1. What protected health information about me will be used or shared with others during this research?

- Existing medical records, including mental health records.
- New health information created from study-related tests, procedures, visits, and/or questionnaires

2. Why will protected information about me be used or shared with others?

The main reasons include the following:

- To conduct and oversee the research described earlier in this form;
- To ensure the research meets legal, institutional, and accreditation requirements;
- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm); and
- To provide the study sponsor with information arising from an adverse event or other event that relates to the safety or toxicity of the drug(s) used in the study and for the purpose of this or other research relating the study drug(s) and their use in cancer;
- To better understand the diseases being studied and to improve the design of future studies; and,

- Other reasons may include for treatment, payment, or health care operations. For example, some medical information produced by this research study may become part of your hospital medical record because the information may be necessary for your medical care. (You will also be given a notice for use and sharing of protected health information.)

3. Who will use or share protected health information about me?

- DF/HCC and its affiliated research doctors and entities participating in the research will use and share your protected health information. In addition, other DF/HCC offices that deal with research oversight, billing or quality assurance will be able to use and share your protected health information.

4. With whom outside of DF/HCC may my protected health information be shared?

While all reasonable efforts will be made to protect the confidentiality of your protected health information, it may also be shared with the following entities:

- Outside individuals or entities that have a need to access this information to perform functions relating to the conduct of this research such as analysis by outside laboratories on behalf of DF/HCC and its affiliates (for example, data storage companies, insurers, or legal advisors).
- The sponsor of the study, its subcontractors, representatives, business partners, and its agents.
- Other research doctors and medical centers participating in this research, if applicable
- Federal and state agencies (for example, the Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes. A qualified representative of the FDA and the National Cancer Institute may review your medical records.
- Hospital accrediting agencies
- A data safety monitoring board organized to oversee this research, if applicable

Some who may receive your protected health information may not have to satisfy the privacy rules and requirements. They, in fact, may share your information with others without your permission.

5. For how long will protected health information about me be used or shared with others?

    - There is no scheduled date at which your protected health information that is being used or shared for this research will be destroyed, because research is an ongoing process.

6. Statement of privacy rights:

    - You have the right to withdraw your permission for the research doctors and participating DF/HCC entities to use or share your protected health information. We will not be able to withdraw all the information that already has been used or shared with others to carry out related activities such as oversight, or that is needed to ensure quality of the study. To withdraw your permission, you must do so in writing by contacting the researcher listed above in the section: "Whom do I contact if I have questions about the research study?"
    - You have the right to request access to your protected health information that is used or shared during this research and that is related to your treatment or payment for your treatment, but you may access this information only after the study is completed. To request this information, please contact the researcher listed above in the section: "Whom do I contact if I have questions about the research study?"

P. DOCUMENTATION OF CONSENT

My signature below indicates:

- I have had enough time to read the consent and think about participating in this study;
- I have had all of my questions answered to my satisfaction;
- I am willing to participate in this study;
- I have been told that my participation is voluntary and I can withdraw at any time

_____ _____

Signature of Participant or Legally Authorized Representative — Date

_____

Relationship of Legally Authorized Representative to Participant

My signature below indicates:

- I have had enough time to read the consent and think about participating in this study;
- I have had all of my questions answered to my satisfaction;
- I am willing to participate in this study;
- I have been told that my participation is voluntary and I can withdraw at any time

_____ _____

Second Signature of Legally Authorized Representative Date

_____

Relationship of Legally Authorized Representative to Participant

To be completed by person obtaining consent:

Adult Participant

The consent discussion was initiated on _____ (date).

Signature of individual obtaining consent: _____

Printed name of above: _____

Date: _____

☐ A copy of this signed consent form will be given to the participant or legally authorized representative.

☐ 1) The participant is an adult and provided consent to participate.

☐ 1a) Participant (or legally authorized representative) is a non-English speaker and signed the translated Short Form in lieu of English consent document:

As someone who understands both English and the language spoken by the participant, I interpreted and/or witnessed, in the participant's language, the researcher's presentation of the English consent form. The participant was given the opportunity to ask questions.

Signature of Interpreter/Witness: _____

Printed Name of Interpreter/Witness: _____

Date: _____

☐ 1b) Participant is physically unable to sign the consent form because:

☐ The participant is illiterate.

☐ The participant has a physical disability.

☐ Other (please describe): _____

The consent form was presented to the participant who was given the opportunity to ask questions and who communicated agreement to participate in the research.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

☐ 2) The participant is an adult who lacks capacity to provide consent and his/her legally authorized representative:

☐ 2a) gave permission for the adult participant to participate

☐ 2b) did not give permission for the adult participant to participate

42.0 Appendix L

< Date>

<First Name> <Last Name>
<Address 1>
<City>, <State> <ZIP>

ID Number: <xxxxxx>

Dear <First Name>,

We are writing to you because you have undergone a bone marrow or blood stem cell transplant. As part of the Dana Farber Harvard Cancer Center Bone Marrow Transplant Survivorship Initiative, we have created a research program to address patient concerns regarding sexual health and intimacy after transplant. Prior studies have shown that many patients who have gone through transplant struggle with issues pertaining to their sexual health and intimacy, which are not adequately addressed in clinical practice. These issues can be distressing to patients and their loved ones. The study doctors want to know if the use of a mobile app focused on improving sexual function may improve your overall care.

This research program is designed for all transplant survivors. The program includes:

1. A consultation visit with a transplant clinician trained to comprehensively address your sexual health and intimacy needs
2. The use of a mobile app on an iPad to reinforce the treatment plan that was discussed during the consultation visit. If you do not have an iPad, the research team will provide you with one
3. Three brief questionnaires to understand your sexual health concerns and overall quality of life

If you are at all interested in this program and would like to hear more, please reply to this gateway message or contact the following research coordinator:

<Research Coordinator Name> (<Research Coordinator Email> / <Research Coordinator Phone>)

We hope you are doing well and look forward to hearing from you!

Cordially,

Areej El-Jawahri MD

Director, BMT Survivorship Program

43.0 Appendix M

Qualitative Interview Guide for Patients

INTRODUCTION

You recently took part in a study that was designed to improve the sexual function and quality of life of patients who have undergone stem cell transplantation through the use of a mobile intervention application (the SHIFT app). We are now interested to know about your satisfaction with different aspects of the SHIFT app so that we can continue to shape how to best provide it to patients. There is no right or wrong answer. Your answers will be kept confidential and will not affect your participation in future research studies or your access to medical care.

I would like to audio-record this interview because I will not be able to write all of this information down. The interview will be transcribed word for word and will allow us to capture your thoughts and feelings in your own words. No identifying information, such as your name or names of others, will be included in the transcript. This interview will take approximately 30 minutes to complete.

- Do I have your permission to audio record this interview?
- Before we start, do you have any questions about what we are doing here today?

GENERAL EXPERIENCE

I will begin by asking about your general experience using the SHIFT mobile app.

1. How difficult was it to use the SHIFT app?

A. Difficult B. Not Difficult C. Not sure	Additional Comments:

2. How helpful was the SHIFT app in addressing your sexual health and intimacy concerns?

A. Helpful B. Not helpful C. Not sure	Additional Comments:

3. What did you like most about the SHIFT app?

4. What did you like least about the SHIFT app?

5. How satisfied were you with the mobile app format overall?

A. Satisfied
B. Not Satisfied
C. Not sure

Additional Comments:

6. During this study, you accessed the SHIFT mobile app using an i-pad. How convenient was it to use an i-pad to access the app?

A. Convenient
B. Not convenient
C. Not sure

Additional Comments:

7. Did you experience any technical difficulties while using the SHIFT app?

A. Yes
B. No
C. Not sure

Additional Comments:

8. How do you feel about the length of the modules in the SHIFT app?

9. If you did not complete the SHIFT app, were there any reasons that made you decide to not complete the entire SHIFT app?

10. How do you feel about the duration of the allotted 8-week period over which you were to complete the app modules?

A. Too long
B. Too short
C. Just right

Additional Comments:

11. Throughout the SHIFT app, you may have played games to reinforce your learning. How helpful were these games?

A. Helpful
B. Not helpful
C. Not sure

Additional Comments:

12. How do you feel about the frequency of the games in the SHIFT app?

A. Too little

Additional Comments:

B. Just right

C. Too much

13. What were the games that you liked the most in the SHIFT app?

14. What were the games that you liked the least in the SHIFT app?

15. How could we modify the SHIFT app to increase your engagement with the content?

APP CONTENT

Now I am going to ask some questions about the specific material covered in the app. We would like to ask you your opinion about the content of the app:

1. *Education about sexual health and intimacy*
   The app included educational content regarding the causes of sexual health problems after transplant and expected trajectory of sexual health recovery.

   A. How helpful was it to have this educational content?

   A. Helpful

Additional Comments:

B. Not helpful

C. Not sure

B. How difficult was it to understand the educational content?

A. Difficult

B. Not difficult

C. Not sure

Additional Comments:

C. Were there remaining topics that you wished were addressed regarding sexual health and intimacy?

2. *Communication about your sexual health concerns*
The app included information on how to best communicate with your medical team and your partner regarding your sexual health concerns.

A. How helpful was the content focused on communication with your medical team?

A. Helpful

B. Not helpful

C. Not sure

Additional Comments:

B. How helpful was the content focused on communication with your partner about your sexual health concerns?

A. Helpful

B. Not helpful

C. Not sure

Additional Comments:

C. Do you have additional feedback about the modules focused on communication in the SHIFT app?

3. *Intimacy exercises:*
The app incorporated multiple exercises to improve physical and non-physical intimacy, such as pleasure mapping, sensate focus exercise, exposure tower, and intimacy chest

A. How helpful were these intimacy exercises?

A. Helpful
B. Not helpful
C. Not sure

Additional Comments:

B. How often did you use the intimacy exercises that you learned from the SHIFT app?

A. Often
B. Not Often
C. Not sure

Additional Comments:

C. What were the intimacy exercises that you liked the most in the SHIFT app?

D. What were the intimacy exercises that you liked the least in the SHIFT app?

E. Any additional feedback regarding the intimacy exercises in the SHIFT app?

4. *Coping with sexual health and intimacy concerns*
The SHIFT app focused on helping you cope most effectively with your sexual health concerns. The app discussed problem-focused and emotion-focused coping strategies to address your sexual health concerns.

A. How helpful were the coping strategies in the SHIFT app?

A. Helpful
B. Not helpful
C. Not sure

Additional Comments:

B. How often did you use the coping strategies (i.e. such as mindfulness, acceptance) that you learned from the SHIFT app?

A. Often
B. Not Often
C. Not sure

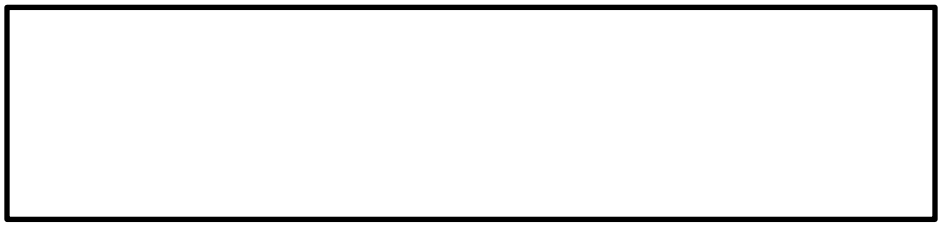
Additional Comments:

C. What coping strategies you found most useful in the SHIFT app?

D. What coping strategies you found least useful in the SHIFT app?

E. Any additional feedback regarding the intimacy exercises in the SHIFT app?

Is there anything else you would like to add that we have not discussed?



We have now reached the end of this interview. Thank you for being a part of the study. We appreciate your thoughtful responses and participation in research.