PROTOCOL TITLE: *Development and Piloting an Avatar-based Intervention to Support Patients Undergoing Stem Cell Transplantation*

PRINCIPAL INVESTIGATOR (PI)

Gregory Abel, MD MPH
Dana-Farber Cancer Institute, Department of Medical Oncology
450 Brookline Avenue, Boston, MA 02215
Phone: 617-632-1906
gregory_abel@dfci.harvard.edu

CO-INVESTIGATOR:

Amar Harry Kelkar, MD
Dana-Farber Cancer Institute, Department of Medical Oncology
450 Brookline Avenue, Boston, MA 02215
Phone: 857-215-6105
amarh_kelkar@dfci.harvard.edu

VERSION NUMBER: V1.1

DATE: 8/24/2022

Table of Contents

1.0 Objectives

1.1 **Aim 1: Modify care.coach, an existing inpatient bedside digital relational agent to enhance the well-being, safety, and outcomes of patients undergoing hematopoietic cell transplantation (HCT).** We will convene a focus group consisting of HCT nurse navigators, inpatient HCT nurses, and HCT physicians and extenders to determine appropriate modifications to the care.coach health coaching protocols and technology setup for the inpatient HCT setting, including development of educational modules that will be provided to patients undergoing HCT.

1.2 **Aim 2: Iteratively pilot the modified avatar agent in three cohorts of six patients each.** We will assess the feasibility of the patient education and relational functions of the digital avatar.

2.0 Background

2.1 Among patients who undergo reduced intensity conditioning stem cell transplantation (RIC), relatively lengthy inpatient stays are routine for pre-HCT conditioning and receipt of donor cells. As those who receive this type of transplant tend to be older (60 to 75) and/or have baseline comorbidities, the inpatient stay can be difficult. Indeed, in-house delirium is one of the most frequent and distressing complications, even though it is typically a treatable, reversible syndrome.

The incidence of delirium in cancer patients undergoing myeloablative HCT is about 50%, and the presence of delirium at any point during hospitalization after transplantation has been shown to be highly predictive of mortality (odds ratio = 14).[1] Also, the medications and side effects that accompany RIC HCT place this population at high risk for falls, and sustained low platelet counts following transplant exacerbate risk of death in the event of a fall.[2] Many risk factors for falls among HCT patients correspond to risk factors for delirium and preventing delirium in cancer patients can also prevent falls.[3]Moreover, HCT often experience stress, anxiety, anger, depression, insomnia and loneliness, with the percentage of depressed patients increasing more than two-fold after 2 weeks of isolation. Among HCT patients, research has shown that loneliness during hospital stay is negatively associated with overall quality of life six months after transplant, reducing both social and functional well-being, increasing difficulty of managing disease symptoms six months after transplant, and increasing ratio of neutrophil to monocyte counts 30 days after transplant (an indicator of poorer survival rate).[4]

Inpatient non-pharmacological interventions that have been implemented to improve the quality of life (QOL) of pediatric and adult HCT patients include psychoeducational, exercise, and mindfulness interventions, all of which hold

potential to outcomes during patients' hospital stay. In a multimodal study, individualized psychoeducation was provided to HCT patients 5 days a week alongside other interventions; patients showed an improvement for a variety of symptoms.[5-7] Individualized and supervised exercises routines, such as daily dynamic exercises, stretching exercises, resistance training and progressive relaxation training, have been implemented and well received in both pediatric and adult HSCT settings.[6,7] Mindfulness mediation (MM) practices can be easily provided to patients and have the potential to relieve patient distress.[5] Although sleep interventions have been implemented in a wide variety of inpatient populations, they have not specifically been studied in the inpatient HCT population.[8] Since different sleep interventions may better serve some populations more than others, it is unclear which sleep interventions may be the most beneficial to HSCT patients.[8]

Indeed, a combination of psychoeducational, exercise, sleep, and mindfulness interventions could be applied in HCT patient settings simultaneously with the goal to improve patient QOL and to potentially improve patient outcomes. Moreover, for RIC HCT, post-HCT changes in lifestyle are complex, including nutrition, hydration, transplant medications, home disinfection, socialization, and others. For this population, the Health Belief Model[5,] and Prochaska's Transtheoretical model of change[6] would argue that patients who are hospitalized and waiting for their HCT to occur would be highly motivated to learn about these items being in the "groundwork for change/take action" phase while admitted.

care.coach™ provides a care support and health coaching platform in which a patient-facing interface is a digital relational agent, appearing on a tablet device as a dog or cat avatar to enable a non-judgmental, positive emotional connection for inpatients during their stay. Each avatar is controlled directly by a 24x7, world-wide team of trained humans known as "health advocates," who are background checked, psychometrically screened, and receive specialized training (non-medical). Each health advocate can cost-effectively monitor and engage 12 or more patients sequentially (2 simultaneously) through audio/visual feeds from the patient's device and send text commands which are converted into the avatar's voice through a speech synthesis engine. The health advocates are guided by a software-driven expert system embedded into their work interface, which implements evidence-based clinical protocols to support patient self-management and care coordination.

Pace University conducted a clinical pilot of the care.coach technology in 2016 at Jamaica Hospital Medical Center with 95 hospitalized (medical/surgical) older adults at high falls or delirium risk.[9] Mean age was 76.5 years, with 55% female, 46% African-American, and 44% speaking English as a second language.[9] Typical length of stay was 3-6 days. On average, the avatars performed 71.3 observational check-ins, 61 minutes of

engagement using 11.5 images or audio files, and 6.5 protocol-driven tasks per patient, per day, based on certain protocols derived from the Hospital Elder Life Program (HELP).[9] Compared to randomized control patients with a daily nurse student visit (n=54), intervention patients with our bedside avatar (n=41) showed a significantly greater reduction in delirium score (CAM, p=0.003) and loneliness (UCLA-LS, p=0.008). The primary intervention unit had 0.9 falls per 1000-patient days during the 3-month study period, compared to 6.5 on the control unit (86% reduction in fall rate).[9] University of Washington has published 3 peer-reviewed papers about how the avatars help reduce loneliness, increase social support through informational, affectionate, and positive social interaction mechanisms, and decrease depressive symptoms among older adults in the community, including those with mild cognitive impairment.[10-12] Quality improvement projects with care.coach health plan customers have also reported high patient and provider satisfaction, and reduced anxiety based on GAD-7 surveys.[10-12]

In summary, digital conversational agents provided to patients offer potential benefits to patients including a reduction in delirium, and this technology has not been offered to patients in HCT settings. We propose to pilot this technology after modifying it to include educational protocols tailored to the needs of RIC HCT patients additionally offering education in post-HCT home care.

2.2 **Draft care.coach Clinical Protocols**: The following protocols will be developed into lessons that will be presented by the avatar.

[1] Diet & Hydration

- Hydration reminder, question
    - Importance of staying hydrated to maintain kidney health, drinking at least 2 liters of fluid per day with the goal of 2-3 liters per day (aiming for non-caffeinated beverages)
- Meal rating, enjoyment
- Permitted outside foods (during inpatient transplant)
    - Beverages : canned sodas, juices, flavored drinks, nutritional supplements
    - Canned items: canned foods EXCEPT grapefruit, canned vegetables, canned soups and stews (portioned sized)
    - Cookies, crackers, and snacks : all individually portioned packages cookies, crackers, and chips, individually packaged pies and cakes that are commercial, shelf-stable products
    - Candy : individually wrapped hard candy and candy bars
    - Frozen entrees: Only frozen entrees that are individual portion-sized, remain frozen during transport to you, and have been cooked at BWH, either by room service or in the floor microwave

- Inquiry about (healthy) eating habits/plans, fruits & vegetables (at home after transplant)
    - Vegetables: May eat fresh vegetables, raw or uncooked, as long as they are washed well EXCEPT FOR raw broccoli and cauliflower
    - Frozen vegetables: May eat frozen vegetables, raw or uncooked, as long as they have been washed well EXCEPT FOR broccoli and cauliflower which must be cooked and cannot be eaten raw
    - Canned vegetables: Can eat and do not have to be cleaned or cooked
    - Vegetable drinks : May eat if they are pasteurized
    - Fruits: Do not eat grapefruit or grapefruit juice, Seville oranges or marmalade made with Seville oranges
    - Fresh Fruits: can eat fresh fruits as long as they are washed well EXCEPT fresh berries (must be cooked completely). No cracks or bruises
    - Frozen fruits: May eat cooked or raw as long as they are washed well EXCEPT fresh berries (must be cooked completely). No cracks or bruises
    - Dried Fruits: May eat dried fruits
    - Canned Fruits: May eat, without washing or cooking
    - Fruit Cups: Can eat fruit cups packaged and pasteurized at the factory. You do not have to wash or cook fruit cups packed at the factory.
    - Fruit Drinks: Can drink fruit drinks if they are pasteurized
    - DO NOT EAT HONEY
- Food Safety (at home after transplant)
    - Reminder to check expiration dates before opening frozen or canned vegetables or vegetable juices
    - Vegetable cans, boxes, and bags should have no rips, dents
    - Wash bags, boxes, and cans before opening frozen or canned vegetables or vegetable juices
    - Clean the can opener before using it
    - Do not eat food prepared at friends' or family's houses. Do not eat out or eat takeout.
- Diabetes-related diet questions

[2] Physical Exercise [ambulation]

- Education about energy saving techniques, platelet precautions with activity and the overall importance of daily mobility to prevent fatigue/deconditioning
- Mobility assessment to determine levels (5) of ambulation, types of exercises (seated, standing, in bed)
- Otago exercises (home-based balance, strength exercises for older adults)
- Exercise arms, feet, hands, neck, hip, leg lifts, toe/calf raises

- Inquiry about ambulation, going for a walk, exercise for the day

[3] Orientation/confusion/delirium
- Focused attention questions
- Confusion assessment (CAM) questions
- Orientation questions
- Cognitive impairment (MoCA) questions
- 5 senses countdown

[4] Non-pharmacological pain/anxiety management,
- Comfort level assessment/question(s)
- Evening meditation, guided imagery
- Simple breathing exercise, relaxation

[5] Sleep
- Encourage to go back to sleep if after 11PM

[6] Toileting/fall risk assessment
- Inquiry if need to use the bathroom (call nurse to assist if yes)
- Reminders – ambulatory device/assistive tech (cane, glasses, hearing aids), ask for assistance, do not rush, proper footwear, sleep in the center of the bed
- Falls check
- Tips for lowering your risk for falling
    - Wear non-skid socks or supportive footwear
    - Taking time with positional changes
    - Notifying staff if you have sudden onset of dizziness
    - Ensuring there is adequate lighting before getting up

[7] Psychosocial Support & Staff communication.
- Depression/mood question(s)
- Companionship/loneliness (FS/UCLA) question(s)
- Stress, worry, nervousness, anger question(s)
- "Fun facts", patient education
- Establish urgent call criteria
- Interactive games
- Music, images, audiobooks

[8] HCT Medication Resources
- Tacrolimus
- Sirolimus
- Mycophenolate mofetil

- Levofloxacin
- Acyclovir
- Atovaquone
- Bactrim
- Ursodiol

[9] Catheter Care

- Preparation to flushing catheter
    - Each lumen (small tube within your catheter) of central line catheter will need to be flushed once a day with 0.9% saline flush. The following steps can be used for either a PICC or a Hickman Central Line.
    - MUST wash hands prior, may choose not to wear gloves
- Steps to flushing catheter, which are as follows:
    1. Clean your worktable with a disinfectant wipe
    2. Gather supplies
        a. Catheter caps
        b. Alcohol wipes
        c. Prefilled 10mL .9% saline flush
        d. Gloves (optional)
        e. Alcohol cover (Curos)
    3. Wash hands well with soap and water OR use an alcohol-based hand sanitizer
    4. Dry your hand with a clean paper towel
    5. If you have been taught to or want to use gloves, put them on now
    6. Take the flush syringe from the package
    7. Hold the syringe up in the air with the plunger pointing to the floor
    8. Tape the syringe so that any air bubbles rise to the top
    9. Take off the syringe cap
    10. Push the plunger to the 10mL mark. This will take out any air and extra flush from the syringe. Some flush may drop out.
    11. Hold the syringe upright and do not let the syringe touch anything
    12. Do you have a green alcohol cover over your catheter cap OR do you NOT have a green alcohol cover over your catheter cap
        a. IF YES:
            i. Remove the green alcohol cover only, do not reuse
            ii. Leave the catheter cap in place
            iii. Do not let the end of the catheter cap touch anything, including your body
        b. IF NO
            i. Open the alcohol wipe
            ii. Scrub the catheter cap with the alcohol wipe for at least 10 seconds

iii. Let it dry completely
iv. Do not let the end of the catheter cap touch anything, including your body after it has been cleaned

13. Hold the catheter cap
14. Put in and screw the flush syringe onto the end of the catheter cap
15. Open the clamp on the catheter
16. Flush the line with the saline using a push pause method. The turbulence helps to keep your line clear.
17. Firmly push 1cc then pause
18. Continue to push 1cc and pause until the line is flushed with al 10 ccs
    a. If it is hard to push the flush, check to make sure the clamp is open. If it was clamped, open the clamp
    b. If it is still hard to push, STOP. Do not push the flush. Close the clamp. Unscrew and remove the syringe. Call your doctor or Oncology Nurse Navigator.
19. Do not use force to flush
20. Be sure that the clamp is over wording " clamp here"
21. Clos ethe clamp on the catheter. You should here a click.
22. Hold the catheter cap tightly and unscrew the syringe form the catheter. Be careful not to loosen the catheter cap form the catheter.
23. Always check to be sure the catheter cap is on tight
24. Put a new green alcohol cover over the catheter cap.
25. Now flush all other lumens of the catheter.
26. After you flush all of your lumens, throw your supplies away.

3.0 Inclusion and Exclusion Criteria

3.1 Aim 1: Screening and Eligibility

We will convene one focus group with 8-10 participants who are DFCI/BWH HCT nurse navigators, inpatient HCT nurses, and HCT physicians and extenders (NP/PA).

Eligibility for Aim 1:

- Inclusion Criteria
    - Age 18+.
    - DFCI/HCC *HCT nurse navigators, inpatient HCT nurses, and HCT physicians and extenders (NP/PA).*

3.2 Aim 2: Screening and Eligibility

Potential patients will be identified and screened through provider referral as identified in the transplant team's weekly (Friday afternoon) clinical meeting.

Screening and recruitment will be conducted by a trained research assistants (RA) who will utilize HIPAA-compliant and DFCI IRB approved patient approach procedures. Potential patients will be approached and consented upon inpatient admission for RIC HCT.

Eligibility for Aim 2:

- Inclusion Criteria:
  - Age 18+.
  - Admitted for reduced-intensity conditioning (RIC) allogeneic HCT (prior to day 0, generally day -7).

- Exclusion Criteria:
  - Deemed by clinical staff or RA to be unable to converse with an avatar, due to:
    - Severe, uncorrectable hearing impairment and simultaneous severe, uncorrectable vision impairment.
    - Severe speech impairment that precludes understanding by staff (and by extension, by the avatar).
    - Not fluent in English.

4.0 Study-Wide Number of Subjects

Aim 1: This is a single-site study, located at Dana-Farber/BWH Cancer Center. We anticipate 8-10 participants for the focus group.

Aim 2: This is a single-site study, located at Dana-Farber/BWH Cancer Center. We anticipate enrolling 3 cohorts of 6 patients for a total of 18 participants.

5.0 Study-Wide Recruitment Methods

Aim 1: Potential participants will be Dana-Farber/BWH Cancer Center staff. Department directories will be used to identify potential participants, who will be initially recruited by email and follow up contacts will be by phone and/or in person.

Aim 2: All eligible patients as defined in Section 3.0 will be met by a trained RA soon after inpatient admission. This RA will be responsible for obtaining informed consent, as outlined in Section 23.0. All participants will be entered into the Clinical Trials Management System (CTMS) OnCore per DF/HCC guidance as per DF/HCC Policy REGIST-101.

6.0 Study Timelines

Aim 1: Prior to enrollment of the initial cohort of patients, we will convene a one-time 60minute focus group led by Anna Revette PhD (annac_revette@dfci.harvard.edu), a Senior Research Scientist in qualitative research, to discuss perspectives and opinions on implementing care.coach technology for HCT patients including education domains to include, frequency of avatar interactions, and anticipated staff concerns. This analysis will inform changes to be applied to the avatar, including script adjustments, prior to introducing the technology to patients in Aim 2.

Aim 2: We will complete the initial implementation of multiple HCT-related avatar changes across each of the categories in Section 2.2 and integrate them into an overall program schedule within 3 months. In the next 6 months, the HCT avatar program will then be piloted and iteratively improved through a phased, iterative user acceptance study with 3 consecutive cohorts of 6 RIC HCT patients each, receiving the avatar for up to 3 weeks per cohort (or patient discharge). After each cohort, user feedback will be gathered in the post-pilot survey (one week after disenrollment; see Appendix A), and protocol completion and patient-avatar engagement data will be analyzed.

7.0 Study Endpoints

7.1 Aim 1: Modifications to an avatar-based human-staffed artificial intelligence technology platform for use in an inpatient HCT setting, derived from thematic analyses of a focus group of DF/BWH Cancer Center HCT nurse navigators, inpatient HCT nurses, and HCT physicians and extenders (as described in Section 8.4)

7.2 Aim 2: PRIMARY: Retention rate in protocol from enrollment to hospital discharge or three weeks (whichever comes first). SECONDARY: Patient satisfaction rate with avatar in the final cohort; rate of completion of 80% of the HCT educational modules; rate of completion of post-pilot survey.

8.0 Procedures Involved

8.1 **Design/Study Type**

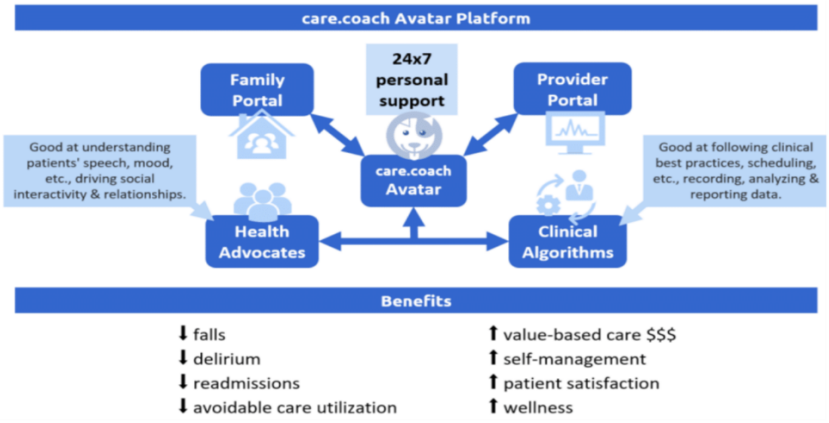
Aim 1: Focus group.

Aim 2: Single-arm feasibility pilot, with 3 cohorts of 6 patients (18 total).

8.2 **care.coach**

care.coach is a "human-in the-loop" conversational agent (avatar) used to interact and converse with patients through natural dialogue and text-to-speech software that is powered by a team of trained human staff, called health advocates. A summary of the platform is shown in Figure 1. Note that the Family Portal and Provider Portal depicted in this figure are features from the commercial care.coach device that will not be activated for the purposes of this study. These features provide patient-avatar interaction summaries to the providers and, if approved by the patient, to family members.

Figure 1. care.coach Avatar Platform



The care.coach patient-facing interface appears as a virtual animal avatar on a touch-screen handheld device. Patients interact with the avatar by speaking with it or tapping the avatar on the screen. This simple interface allows many users to be engaged effectively. The avatar has two states: awake and asleep. When the avatar is visually sleeping, the audiovisual (AV) stream is offline. To awaken the avatar on-demand, it must be tapped on the touchscreen device. When the avatar is visually awake, the care.coach staff-monitored AV stream will become active. Several times per day, the avatar will attempt to engage the patient spontaneously to provide key reminders, such as for hydration or activity, and initiate patient education modules.

If a patient participant is not available, does not respond, or the participant requests privacy, the avatar will go back to sleep. Whenever the avatar is visually awake, care.coach staff members monitor the AV streams from the avatar device to hear, see and interpret what users are saying and what is happening in the environment. This enables the care.coach staff to speak to study participants

appropriately and have genuinely natural, contextually relevant interactions and conversations. What the avatar says is guided by software protocols for consistency, speed, and automation, but is overseen and directly controlled ("supervised") by care.coach staff to ensure that the avatar talks with patients in a sensible, appropriate, and empathic manner. In the case of an emergency when communicating with the avatar, the care.coach team will contact the unit coordinator (number will be provided at patient enrollment) and ask for the nurse assigned. A removable cover will be provided for the camera if patients desire at time of enrollment.

Health advocates contribute to the system their human abilities for natural language processing and compassionate conversational responses to help each avatar build personal relationships. While health advocates are not clinicians, they have a minimum set of certifications (Section 8.3).

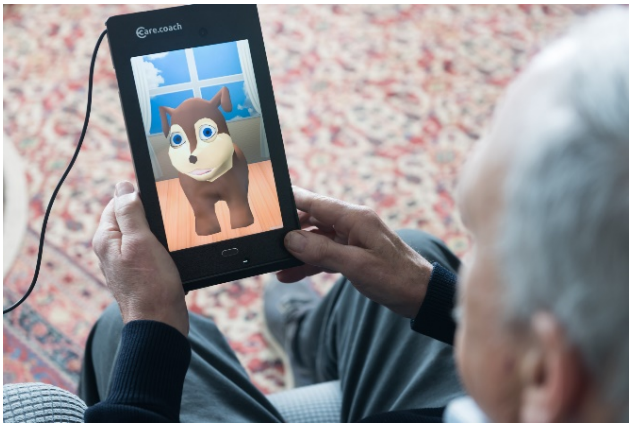


***Figure 2**: patient using the "tap to wake" feature on avatar*

Additionally, the abilities are augmented through a software-driven system embedded into the work interface, which guides participants through modules that aim to mitigate falls and delirium, executing cognitive exercises. Modules have been reviewed by principal investigators and will be adapted to best serve patients who have undergone RIC HCT. An analysis of the focus group on Aim 1 will result in the re-review and further improvement of these modules.

8.3 care.coach Health Advocate Training

The health advocates who staff the avatar system must each complete the following screening mechanisms and training certifications (or their equivalents deemed by care.coach, as specific training courses and providers become outdated/available from time-to-time), through several online learning platforms, over the course of approximately 65 hours:

1. care.coach psychometric, technical, skills-based, and face-to-face interview assessment

2. InfoCubic international background check
3. Registered Nurses' Association of Ontario delirium, dementia and depression course
4. National Institutes of Health privacy and ethics course for human subjects research
5. MGB basic motivational interviewing class
6. care.coach technology, patient support, information security, and job shadowing training

The qualification process is stringent, and the proportion of health advocate job applicants who successfully complete all the required certifications and are hired is only about 1%. For the proposed project, each health advocate will also attend a specific one-hour training about RIC HCT provided by Drs. Abel and Kelkar.

8.4 **Study Procedures**

In Aim 1, a focus group consisting of focus group consisting of DF/BWH Cancer Center HCT nurse navigators, inpatient HCT nurses, and HCT physicians and extenders will he held to discuss the feasibility and benefits of implementing an avatar-based artificial intelligence system in an inpatient HCT setting (See Appendix B for draft script). The care.coach technology as described in Section 8.2 will be presented to the focus group. Following this introduction, a guided discussion will be held discussing the feasibility and benefits of providing this technoloigy to HCT patients. Participants will receive $50 gift cards for participation. The findings of this focus group will further shape the development of educational scripts incorporated into the care.coach technology.

In Aim 2, the care.coach device will be provided to a total of 18 patients (3 cohorts of 6 patients) who fall within the eligibility requirements outlined in Section 3.2 and who consent to participating in the study. Participants will receive the device while admitted at the Brigham and Women's Hospital for RIC HCT, and the device will be collected by study staff prior to discharge.

8.5 **Aim 2 Study Calendar**

Table 1. Study Calendar

Study Procedures	Baseline	Day 5 (± 2)	-1 to 0 days prior to discharge	One week after pilot (+ 5 days)
Informed Consent of participant	X			
Demographic data: self-report and EHR review	X			
Setting up avatar device	X			
RA check in		X	X	
Disenroll patients and retrieve avatar device from participants			X	

Post-pilot survey				X

9.0 Data and Specimen Banking

9.1 **Data Collected by care.coach:** Only meta-data will be collected through the avatar device. care.coach will be provided with a first-name, study-assigned patient number, and in-hospital location for safety functions, but will not be provided with other PHI. Upon completion of the study, name and in-hospital location data will be decoupled from other data and destroyed by care-coach. Audiovisual streams are recorded for immediate language processing and understanding but will not be stored post-processing. See Appendix C for care.coach security protocols.

9.2 **Data Collected by Dana-Farber:** No specimens will be collected or stored as part of this study. We will collect data on feasibility outcomes (retention, satisfaction, completion of modules) via post-pilot survey administered by the RA in person, at first follow up at Dana-Farber after discharge, or via telephone (Appendix A). Components of post-pilot survey questions on technology usability (Q1-19) were adapted from a published system usability scale.[13] Questions on self-efficacy (Q20-28) were directly adapted from the General Self-Efficacy Scale.[14] The remaining questions were newly developed for this study. Data will also be collected on patient demographics, transplant characteristics (type of transplant, donor characteristics, conditioning, GVHD prophylaxis, antibiotic prophylaxis, status of prior infectious diseases), and transplant outcomes (incidence and severity of GVHD, other infectious and non-infectious complications, relapse, survival). PHI will be stored with these data to allow for monitoring of long-term outcomes. Data will be stored on a secure server at DFCI up to 5 years from completion of the last study conducted as part of this project (dependent on whether we proceed to the Phase 2 study). One year after completion of the study, long-term analyses, and publication of deidentified findings, all PHI will be destroyed.

9.3 **Data Storage:** No specimens will be stored.

9.4 **Data Sharing:** Aggregated de-identified post-protocol survey data will be shared with care.coach; care.coach meta-data will not be shared with DFCI.

10.0 Data Management and Confidentiality

10.1 **Data Analysis:**

Aim 1: This will be a qualitative study, consisting of a focus group of 8-10 subjects consisting of DF/BWH Cancer Center HCT nurse navigators, inpatient HCT nurses, and HCT physicians and extenders. The objective of Aim 1 is to use this focus group to identify key educational topics of interest, frequency of check-ins with the study patients, transplant treatment groups most likely to benefit from the avatar, timing of avatar device delivery, length of time with the avatar, and other potential uses for the avatar. After enrollment (as described in Section 5.0), we will undertake the focus group using a semi-structured guide (Appendix C), in which we will present each topic and ask for feedback. The focus group will be conducted either virtually using videoconference software or on-site at DFCI depending on the current state of the pandemic at the time of the focus group. The session will last approximately 60 minutes, will be audio-recorded, and will be transcribed verbatim. The interview guide will be further developed by the investigators, and we will consult the Dana-Farber/Harvard Cancer Center (DF/HCC) Survey and Data Management Core for help in reviewing our final guide (although we will run the focus groups ourselves). We will explore the themes listed in the Table in Appendix C, which have been developed based on areas of highest need in our transplant program to improve patient experience and outcomes. We will request feedback from the group about the utility of different transplant education topics, frequency of interruptions, and other potential uses of the avatar and recommendations for modifications to improve usability, feasibility, and utility of the avatar. In addition to soliciting feedback from all participants, we will perform in-depth explorations of components of the avatar functions for which each type of participant is considered a topical expert. For example, we will seek advice on optimal timing and frequency of patient interruptions from bedside transplant nurses who are most closely involved in direct patient care and are most familiar with patient needs and attention spans. The investigators will analyze all transcribed interviews through an interactive approach using framework analysis.[15] Using techniques we have refined in prior work,[16,17] two team members will review transcripts independently using an electronic research journal (NVivo 12 Pro) to create a coding matrix, after which they will compare results until reliability and interpretive consistency of coding is established (80% agreement). We will keep a thorough audit trail that will allow for other team members to carefully review and confirm that conclusions clearly flow from the coding, thus enhancing interpretive rigor and credibility. The study team will integrate

findings from the focus group into the functions of the avatar to optimize the device functions for our patients.

Aim 2: We will enroll 18 patients in a single-arm pilot/feasibility study testing the care.coach avatar. The goal of the study is to determine if the avatar achieves the prespecified usability and feasibility outcome goals. As is common for HCT studies,[18] the following covariates will be collected for each enrolled patient from hospital records and analyzed in conjunction with survey data collected by study RAs, with the support of the consulting biostatistician: incidence of delirium, falls, falls with injury, and sitter utilization, length of stay, use of benzodiazepines and sedatives, fluid "ins/outs" and meal fractions from nursing notes, in-hospital weights, neutrophil and platelet counts at fixed durations post-transplant, and incidence and severity of transplant-related complications including graft failure, graft-versus-host disease (GVHD), thrombotic microangiopathies (TMA), venous thrombosis, hemorrhage, acute infections and viral reactivations, idiopathic pneumonia syndromes, vaso-occlusive disease (VOD), cytokine release syndrome, mucositis, engraftment syndromes, and posterior reversible encephalopathy syndrome (PRES). Demographic variables between groups, including age, gender, education, and race/ethnicity collected upon enrollment will be compared to confirm equivalency and randomization. Primary and secondary usability and feasibility outcomes are summarized in Table 1. Each metric will be analyzed using paired t-tests to compare between groups and analysis of covariance to adjust for possible differences in demographics or initial assessments (baseline) between groups. Binary measures will entail chi-squared comparisons of proportions between groups. All data will be analyzed using the Statistical Package for Social Sciences software (SPSS, Inc. Chicago, IL). Statistical significance will be defined as $p \leq 0.05$.

Table 2. Usability and Feasibility Outcomes

Usability and Feasibility Outcomes	Estimated Percentage Usability or Feasibility
Determine the feasibility of retaining 18 patients in the protocol from enrollment to hospital discharge or three weeks (whichever comes first).	66%
Determine the patient satisfaction rate in the final cohort.	80%
Determine the rate of completion of the HCT educational modules.	75%
Determine the rate of completion of the post-pilot survey within one week of discharge.	90%

10.2 **Sample Size:**

Aim 1: Aim 1. We selected a focus group size of 8-10 subjects. As per Krueger and Casey's "Focus groups: A practical guide for applied research," the ideal size of a focus group is 8-10 subjects because participants in a smaller focus group may feel pressure to talk more than they would otherwise, while larger focus groups will limit detail of participants' responses who may feel pressure to share airtime.[19]

Aim 2: A sample size of 18 patients was selected to achieve three goals. First, we estimated 162 RIC transplants per year over the past three years, with approximately 33% (54 patients) being performed inpatient, and estimated that approximately 33% could be enrolled, resulting in an achievable pilot sample size of 18 patients. Second, we ensured that the "rule of 10" for binary outcomes, wherein at least 10 participants per arm allows for reliable estimates in pilot studies (10 total in a single arm pilot, such as ours), was met.[20] Third, we wanted to ensure that there were sufficient patients in three smaller cohorts to allow for an iterative process of improving the technology over the course of the pilot study, as per the guidance from the NIH SBIR process. With six patients per cohort, we should be able to achieve sufficient data for assessing usability.[21]

10.3 **Milestones and Success Criteria:**

PRIMARY: Retention rate in protocol from enrollment to hospital discharge or three weeks (whichever comes first) of over 66%.

SECONDARY: Patient satisfaction rate with avatar in the final cohort of 80%; rate of completion of 80% of the HCT educational modules of 75%; rate of completion of post- pilot survey within 1 week of discharge of 90%.

10.4 **Risk Mitigation and Alternative Strategies:** After each group of 5 we will assess patient feedback and modify the avatar program; this iterative design will allow for rapid protocol improvements to be deployed to new patients in subsequent cohorts to move towards achieving the success criteria above. In case outcomes are disappointing during the first cohort, we may switch to a more frequent iteration rate, in conjunction with the advice of our consulting biostatistician.

11.0 Withdrawal of Subjects

Subjects are able to withdraw from the study at any point. They will be given study team contact information to withdraw after agreeing to participate and will be able to terminate their participation in the focus group or interview at any point. Their demographic information will not be used at that point; for focus group participants, it will not be possible to remove their data from the audio transcription; for individual interviewees,

their interview data will be deleted. Subject withdrawal reason(s) will be attempted to be obtained. In certain situations, such as severe encephalopathy or critical illness, patients may be withdrawn from the trial by the investigators due to inability to utilize and interact with the digital avatar device.

12.0 Risks to Subjects

12.1 Anticipated Risks

Aim 1: Anticipated risks to participants include the potential risk of compromise of participant confidentiality due to use of video conferencing groups. For the focus group associated risks, the study team will explain to participants the procedures that will be employed to ensure privacy and confidentiality, and situations such as the focus group discussions where these are not entirely possible. Procedures that will be taken to ensure confidentiality include de-identifying all the data collected from the focus group and storing in a password encoded database.

Aim 2: Anticipated risks to participants include the potential risk of compromise of participant confidentiality and loss of confidentiality of their data collected by the DFCI investigators. Psychological risks include embarrassment and stigmatization if there is inadvertent disclosure of confidential information, and distress due to losing a friendship with the avatar at the end of the hospital stay. While it is very common to develop a friendship with the avatar and ending such a relationship is generally a negative experience, due to the context of the relatively short-term hospital stay, it is expected that patients will overall be happy to be discharged and they will not be led to believe that the avatar will be with them for the long-term.

12.2 Unanticipated Risks

Any unanticipated event will be reported to the OHRS. All human subjects will be informed of their right to stop participation at any time. Subjects will be notified of their right not to answer any questions or choosing to no longer participate. If a participant experiences distress, they can contact Dr. Gregory Abel at gregory_abel@dfci.harvard.edu or 617-632-1906 or Dr. Amar Kelkar at amarh_kelkar@dfci.harvard.edu.

12.0 Potential Benefits to Subjects

Aim 1: There is no direct benefit expected for participants except for the $50 gift card.

Aim 2: Participants may potentially benefit from participating in the study by being exposed to educational modules pertaining to their care as well as receiving psychosocial support via the avatar. Participants in the third cohort will receive a $20 Dana-Farber gift card for completion of at least 4 out of 7 educational modules presented by the device to assess the impact of this potential benefit when planning the subsequent randomized trial.

13.0 Community-Based Participatory Research

Not applicable.

14.0 Sharing of Results with Subjects

Given constraints on study resources and the exploratory nature of the study, we do not plan to disseminate study findings or individual results directly to participants; however, participants will hopefully be able to view publications that arise from this study in oncology journals.

15.0 Setting

Aim 1: Participants will be selected and recruited purposively via recruitment emails. The focus group will be held over a secured Zoom conference call to abide by social distancing guidelines outlined by the CDC during the COVID-19 pandemic.

Aim 2: Potentially eligible patients identified in weekly transplant sign-out round meetings will be approached and those who consent will be given the device at the time of their admission for RIC HCT at Brigham and Women's Hospital.

16.0 Resources Available

DFCI: Drs. Abel and Dr. Kelkar both have experience with care delivery research. The study will be supported by our research assistants Isabella Kallassy and Dillon Clancy.

17.0 Prior Approvals

Aim 1: We will request a waiver documentation of informed consent, although all elements of informed consent will be included in the focus group script. (Appendix B).

Aim 2: N/A.

18.0 Recruitment Methods

Aim 1: HCT nurse navigators, inpatient HCT nurses, and HCT physicians and extenders will be selected and recruited purposively via recruitment emails

Aim 2: We will use weekly transplant sign-out meetings to identify potentially eligible patients. Communication with all potential participants will contain all the elements of informed consent and potential participants will also be made aware that the study team will keep personal identifiers confidential by removing identifying information from interview transcripts. Patient information will be kept in a database that is password protected and utilized only at DFCI. This will ensure that ineligible patients are not contacted and will limit the number of non-participants affected.

19.0 Local Number of Subjects

Aim 1: 8-10 participants for the focus group.

Aim 2: 3 cohorts of 6 patients for a total of 18 participants.

20.0 Provisions to Protect the Privacy Interests of Subjects

Subjects' demographic data will be deidentified, as described above, and contact information will be stored on a secured database on a password-protected computer accessible only to DFCI study team personnel. Participants will be informed of the steps taken to secure their data privacy during the consent process.

21.0 Compensation for Research-Related Injury

This research involves minimal risk to subjects; therefore, this is not applicable.

22.0 Economic Burden to Subjects

We anticipate no additional costs to subjects for enrollment in this study.

23.0 Consent Process

Those unable to consent for themselves are not involved in this research. Informed consent will be required for all participants.

Aim 1: As this Aim is minimal risk and involves no procedures for which written documentation of consent is normally required outside of the research context, we request that written documentation of consent be waived. Oral consent language is included in all recruitment communications with participants (see appendices). The PI will be present at each focus group and interview to obtain oral consent.

Participants will be shown the script on the video conference screen, which includes all elements of informed consent (Appendix B). Participants will be asked to verbally confirm their consent at the time of the meeting. This verbal confirmation will serve as documentation of consent. We request that written documentation of consent be waived.

Aim 2: Informed consent will be required for all participants in the study. The RA will document consent with the participant's wet-ink signature. All participants will receive a copy of the completed consent form for their records.

24.0 Process to Document Consent in Writing

25.1. Aim 1: This research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context. As such, we request that the IRB waive the requirement to obtain written documentation of consent. During all participant contacts, all the required elements of informed consent will be included, as are outlined in the Appendices.

25.2. Aim 2: We will be obtaining written consent for this study per SOP: Informed Consent Process (CON-100). Once a potentially eligible subject is admitted, the RA will approach the subject. If the subject is interested, the RA will document consent with the participant's wet-ink signature. The RA will consent the first 6 patients under the supervision of either Dr. Kelkar or Dr. Abel.

25.0 Drugs or Devices

N/A.

26.0 Appendices – Attached Separately in Individual Files

A: Post-Pilot Survey Draft
B: Focus Group Script Draft
C: Security Details

References:

1. Laino C: Delirium Often Misdiagnosed in Stem Cell Transplant Patients, Screening Warranted. Oncology times 27:20-22, 2005
2. Ueki S, Ikegame K, Kozawa M, et al: Risk Analysis of Falls in Patients Undergoing Allogeneic Hematopoietic Stem Cell Transplantation. Clinical journal of oncology nursing 18:396-399, 2014
3. Pautex S, Herrmann FR, Zulian GB: Factors associated with falls in patients with cancer hospitalized for palliative care. Journal of palliative medicine 11:878-884, 2008
4. Mosher CE, Lepore SJ, Wu L, et al: Social correlates of distress following hematopoietic stem cell transplantation: Exploring the role of loneliness and cognitive processing. Journal of health psychology 17:1022-1032, 2012
5. Bauer-Wu S, Sullivan AM, Rosenbaum E, et al: Facing the Challenges of Hematopoietic Stem Cell Transplantation With Mindfulness Meditation: A Pilot Study. Integrative Cancer Therapies 7:62-69, 2008
6. Bogg TFT, Broderick C, Shaw P, et al: Feasibility of an inpatient exercise intervention for children undergoing hematopoietic stem cell transplant. Pediatric Transplantation 19:925-931, 2015
7. Jarden M, Nelausen K, Hovgaard D, et al: The Effect of a Multimodal Intervention on Treatment-Related Symptoms in Patients Undergoing Hematopoietic Stem Cell Transplantation: A Randomized Controlled Trial. Journal of Pain and Symptom Management 38:174-190, 2009
8. Tamrat R, Huynh-Le M-P, Goyal M: Non-Pharmacologic Interventions to Improve the Sleep of Hospitalized Patients: A Systematic Review. Journal of General Internal Medicine 29:788-795, 2014
9. Bott N, Wexler S, Drury L, et al: A Protocol-Driven, Bedside Digital Conversational Agent to Support Nurse Teams and Mitigate Risks of Hospitalization in Older Adults: Case Control Pre-Post Study. J Med Internet Res 21:e13440, 2019
10. Machesney D, Wexler SS, Chen T, et al: Gerontechnology Companion: Virutal pets for dementia patients, IEEE, pp 1-3
11. Demiris G, Thompson HJ, Lazar A, et al: Evaluation of a Digital Companion for Older Adults with Mild Cognitive Impairment. AMIA ... Annual Symposium proceedings 2016:496-503, 2016
12. Chi N-C, Sparks O, Lin S-Y, et al: Pilot testing a digital pet avatar for older adults. Geriatric nursing (New York) 38:542-547, 2017
13. Brooke J: SUS - A quick and dirty usability scale,
14. Schwarzer R, Jerusalem M: Generalized Self-Efficacy Scale, in J. Weinman SW, & M. Johnston (ed): Measures in health psychology: A user's portfolio. Windsor, UK, NFER-NELSON, 1995, pp 35-37
15. Pope C, Ziebland S, Mays N: Qualitative research in health care. Analysing qualitative data. Bmj 320:114-6, 2000
16. Odejide OO, Salas Coronado DY, Watts CD, et al: End-of-Life Care for Blood Cancers: A Series of Focus Groups With Hematologic Oncologists. Journal of Oncology Practice 10:e396-e403, 2014

17. Henckel C, Revette A, Huntington SF, et al: Perspectives Regarding Hospice Services and Transfusion Access: Focus Groups With Blood Cancer Patients and Bereaved Caregivers. J Pain Symptom Manage 59:1195-1203.e4, 2020

18. Rahul Banerjee; Amar Kelkar M: The Toxicities of Allogeneic Transplantation: What Fellows Need to Know, in Hematopoiesis (ed). www.hematology.org

19. Krueger R, Casey M: Focus groups: A practical guide for applied research (ed 4th edition). New York, NY, SAGE Publications, Inc, 2008

20. van Belle G: Statistical Rules of Thumb (ed 2nd). New York, NY, John Wiley & Sons, Inc, 2008

21. Nie Q, Nguyen L, Myers D, et al: Design guidance for video chat system to support social engagement for older adults with and without mild cognitive impairment. Gerontechnology 20:1-15, 2020

Appendix A: Post-Pilot Survey

Hello,

Thank you for participating in this study evaluating the care.coach avatar.

My name is ***. We met when you were first enrolled in the study. As we mentioned in enrollment, I'm calling/stopping by to review a brief survey on your experience with the care.coach avatar.

We appreciate your time and help with this study!

CONTINUE

POST-PILOT SURVEY

Technology Usability

1. Regardless of prior choice, my ideal care.coach avatar is a:
    a. Dog
    b. Cat
    c. Other Animal
    d. Human

2. I find the avatar easy to use.
    a. Likert Scale (Strongly Agree to Strongly Disagree) ("on a scale of 1 to 5")

3. What do you like best about the avatar?
    a. Write-in

4. What did you like least about the avatar?
    a. Write-in

5. I like the appearance of the avatar.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

6. I had difficulty waking the avatar.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

7. My conversation with the avatar was clear and understandable.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

8. I felt like I was speaking to a person while using the avatar.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

9. Roughly, what percentage of your (insert number) hospital days did you want to use the avatar?
    a. Scale of percentages (by 10% intervals)

10. The avatar interacted with me an appropriate number of times per day to encourage healthy habits such as eating, drinking, medications, and physical activity.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

11. Did you ever turn off or use the cover for the avatar?
    a. Yes/No

12. Did you feel like your privacy was impacted negatively by the presence of the avatar?
    a. Yes/No

13. I felt safer in the hospital because of the avatar.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

14. I would use the avatar again in the hospital.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

15. I would use the avatar at home after discharge if it were available.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

16. I would use the avatar before I was admitted to the hospital to prepare for my stay and treatment.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

17. Using the avatar was fun.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

18. Using the avatar was an enjoyable challenge.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

19. I would recommend the avatar to others.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

Self-Efficacy

20. I can always manage to solve difficult problems if I try hard enough
    a. Likert Scale (Strongly Agree to Strongly Disagree)

21. It is easy for me to stick to my aims and accomplish my goals.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

22. I am confident that I could deal efficiently with unexpected events.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

23. Thanks to my resourcefulness, I know how to handle unforeseen situations.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

24. I can solve most problems if I invest the necessary effort.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

25. I can remain calm when facing difficulties because I can rely on my coping abilities.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

26. When I am confronted with a problem, I can usually find several solutions.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

27. If I am in trouble, I can usually think of a solution.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

28. I can usually handle whatever comes my way.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

Educational Modules

29. Since leaving the hospital after my transplant …
    a. I know the most common side effects of my transplant to watch out for.
        i. Likert Scale (Strongly Agree to Strongly Disagree)

    b. I feel comfortable with the dosage and timing of my transplant medications.
        i. Likert Scale (Strongly Agree to Strongly Disagree)

    c. I feel comfortable recognizing situations where I might be at high risk for infections.
        i. Likert Scale (Strongly Agree to Strongly Disagree)

    d. I feel comfortable shopping for food that I can safely eat.
        i. Likert Scale (Strongly Agree to Strongly Disagree)

    e. I feel comfortable with the protocols for cleaning my home.
        i. Likert Scale (Strongly Agree to Strongly Disagree)

    f. I know the situations when I need to call my transplant team.
        i. Likert Scale (Strongly Agree to Strongly Disagree)

Loneliness/Isolation

30. When did you choose to engage with the avatar? [select as many as appropriate]
    a. Never without prompting
    b. Education
    c. Passing Time
    d. Loneliness
    e. Anxiety
    f. Exercise
    g. Other

31. I felt less bored/lonely/anxious in the hospital due to the avatar.
    a. Likert Scale (Strongly Agree to Strongly Disagree)

32. With which did the avatar help the most?
    a. Boredom/Loneliness/Anxiety

Artificial Intelligence

33. Did you feel respected when speaking to the avatar?
    a. Yes/No

34. Did you trust what the avatar was saying?
    a. Yes/No

35. Did you at times forget that you were talking to an avatar?
    a. Yes/No

36. Did that bother you?
    a. Yes/No

Thank you for taking the time to participate in our survey!

Appendix B: Focus Group Script Draft

Introduction and Welcome

Welcome and thank you for taking the time to be part of this focus group session. We are working on a study to determine appropriate modifications to care.coach, an avatar-based care support platform, for the inpatient HCT setting. The information from this discussion will be used to develop educational modules that will be provided to patients undergoing HCT.

This session is being audio recorded because we don't want to miss any of your comments. People often say very helpful things in these discussions, and we can't write fast enough to get them all down. You can introduce your name as you would like to be called, but there will be no names attached to comments in our reports. We also ask each of you to keep everything that is discussed today confidential. To prevent feedback and distraction, we ask that each of you please turn off your cell phones so that the session is not interrupted and, if you are not already in a quiet place, please move to one if you are able. For recording purposes, it is best if we speak one at a time.

My role here, as the moderator, is to guide the discussion by asking questions and listening. I will be asking you some questions that we have developed, and we are interested in your thoughts. There are no wrong answers and we do not expect everyone to agree, but rather it is important to know if people have differing points of view. Please know, however, that you can skip any question you do not wish to answer. I will also occasionally interrupt and move us to a new topic to keep us on time, thank you for your understanding if this occurs. I will turn on the audio-recorder now. Let us begin the discussion.

Topics: [Moderator will ask questions that probe the following themes]

1. Educational topics that should be incorporated into the avatar?
   … Diet selection, exercise, medication use, common symptoms, when to call for help, catheter flushing, others?
2. Check-in frequency?
   … At meal times only? Morning? Afternoon? Night? Total number of check-ins per day?
3. Which populations would most benefit?
   …Older patients? Younger? RIC? MAC? Specific regimens?
4. When should care.coach be given to patients?
   …Before the transplant admission? On the date of admission for transplant? On the date of transplant? Several days after transplant? Other?
5. When should care.coach be taken back from the patient?
   …On the date of transplant? Several days after transplant? At the time of discharge? At the time of completion of the educational modules? Other?
6. What other functions do you think this technology could be used for?