Project Title: Promoting Cancer Symptom Management in Older Adults
Grant Number: 1R15NR015851-01
NT #: NA
Date of original submission: 12/11/2019
Date of update with cover sheet: 08/09/2021

A. SPECIFIC AIMS

This research addresses the critical need to improve symptom self-management of chemotherapy-induced nausea and vomiting (CINV) among older (≥ 65) adults by developing and testing an avatar-based Serious Game (SG) designed to build CINV self-management skills. Older adults undergoing cancer treatment are at high risk for progressive severe effects resulting from nausea and vomiting[1-4] such as fluid and electrolyte imbalances, dehydration, muscle weakness, generalized fatigue, weight loss, dizziness, altered mental status, low blood pressure, changes in cardiac function, falls, and non-adherence with treatment plans. CINV is among the top five reasons why patients call their doctor while under treatment for cancer[5, 6] and has shown to lead to increased use of resources (e.g., unplanned emergency department (ED) and/or hospital admissions).[7] Severe CINV-related symptoms occur in up to 80% of older adults undergoing chemotherapy treatment,[2] resulting in high direct and indirect costs.[8, 9] Additionally, quality of life (QOL) and daily functioning are greatly reduced with CINV.[10] Guidelines exist for treating CINV; [11, 12] however, anti-emetics are often under-prescribed in the elderly[3] and, to our knowledge, there is no evidence regarding older adults' use of anti-emetics or non-pharmacologic self-management strategies at home or within structured CINV intervention programs. Because of the increased risk for treatment-related toxicity, there is a significant need for effective educational strategies that assist older adults in making self-management decisions and taking action against CINV.

The Common Sense Model of illness provides a framework explaining how older adults with cancer make decisions regarding symptom self-management. Actions taken are related to a person's beliefs (cognitive representation) about the identity, cause, timeline, consequences, and ability of the symptom to be controlled or cured.[13, 14] *Older people are able to identify a symptom and attribute it to cancer;[15, 16] however, barriers to taking action to self-manage symptoms include beliefs about symptom consequences[17] and the symptom's ability to be controlled or cured.* Our intervention addresses these barriers to self-managing symptoms by actively engaging older adults in a simulated gaming experience, where an avatar experiences positive or negative outcomes, based on the player's symptom self-management decisions. Our preliminary data suggests that such an intervention is needed, feasible, and acceptable to older adults in order to mitigate the challenges of self-managing symptoms of cancer treatment. This project is planned in two phases: Phase I will consist of the design and development of an interactive avatar-based Serious Game that will engage and prepare older adults to make CINV self-care decisions. Phase II will be a two-arm, randomized clinical trial comparing the newly developed simulation system, **e**lectronic **S**ymptom **Se**lf-**M**anagement **T**raining- CINV (eSSET-CINV) with attention control. Once shown to be effective, this novel educational strategy can be widely disseminated for use at the bedside and be adapted to educate older adults on self-management strategies for other cancer-related symptoms with negative outcomes.

Research AIMS are:

Phase I: Game prototype and production

1. Identify real-life scenarios involving CINV incidence, self-management, and consequences using a peer Community Advisory Board of older adults who have undergone cancer treatment, their family members, and oncology nurses to design and develop a serious game for CINV self-care decision making.
2. Identify design aspects and elements of eSSET-CINV game play, audio, and visual avatar development that have the greatest appeal for older adults with cancer.

Phase II: Game prototype testing

1. Estimate effect size of the eSSET-CINV in changing patient outcomes: cognitive representation, self-management behaviors, CINV severity, QOL, and resource use.
2. Examine differences in cognitive representation, self-management behaviors, CINV severity, QOL, and resource use between, and within, the intervention and attention control groups.
3. Obtain preliminary data regarding the feasibility and acceptability of the game in older adults experiencing CINV.

This study builds on the investigators' prior work in older adults' cancer symptom experience and gaming.[15, 16, 18-21] The eSSET-CINV intervention is expected to have a *positive impact* on the self-management choices related to CINV. Participants will use knowledge gained during game play to manage their own care resulting observable changes in outcomes: cognitive representation, self-management behaviors, CINV severity, QOL, and resource use.

RESEARCH STRATEGY

B. SIGNIFICANCE

Adults ages 65 and older represent 13.3% (41.4 million people) of our population.[22] By 2040, older adults will represent 21% of the population.[22] However, older adults account for the majority of cancer diagnoses.[23] With an increasing older population, the number of older adults with cancer will also increase, taxing limited healthcare resources. These factors make managing cancer in older adults a healthcare priority.[24, 25] Complications from cancer treatment are more common in older adults with cancer compared to younger adults.[26] Aging and associated limitations in organ systems that prolong plasma levels of chemotherapy (e.g., renal, gastrointestinal, and liver dysfunction[1, 27, 28]) and increase risk of treatment-related toxicity and poor outcomes in older adults include co-morbidity, poly-pharmacy, functional and physical limitations, nutrition, emotional status, and social support (caregiver).[1, 24] Because of this increased risk for treatment-related toxicity due to severe CINV, there is a significant need for effective educational strategies that assist older adults in making self-management decisions and taking action against CINV that are rooted in their beliefs about that symptom.

The significance of the proposed intervention lies in its ability to allow older adults to visualize the consequences of self-management decisions and reframe cognitive representation. It can result in improved control of CINV. This intervention educates older adults to more effectively self-manage symptoms at home, optimizing quality of life. eSSET-CINV is poised to reduce healthcare costs by decreasing use of resources (unplanned ED or hospital admissions) for CINV due to poor symptom management.

Conceptual Framework for Intervention Development and Testing

Phase I: **Game prototype and production**. Phase I will consist of the design, development, and production of the serious game: eSSET-CINV. Game design will be guided by the principles of serious gaming and a user-centered approach that involves the older cancer patient at all stages of development to ensure ease of use and value to the player (patient).[29, 30] Serious Gaming is a well-established method designed to support learning and change health-related behavior by engaging individuals in an entertaining experience.[31-33] It is also consistent with the representational approach to behavior change used in Phase II of this project. Serious gaming capitalizes on fun while promoting change.[32] Social cognitive theory[34] is the most widely used theory for game design[31] and can provide behavior change as a result from enhancing skills and confidence in using the new behavior while receiving feedback about these new skills. By introducing training to reinforcing positive self-management strategies related to CINV early in the treatment trajectory, the risk for negative sequela and unnecessary costs associated with unplanned hospital admission due to severe CINV will be reduced.

Our proposed eSSET-CINV intervention will use an electronic format (study-provided tablet or laptop computer) to deliver a game that promotes cognitive reframing of CINV and effective self-management. Five older adults who have undergone cancer treatment with emetogenic chemotherapy, three family caregivers, and two oncology nurses who have experience managing CINV will be involved as co-designers (Community Advisory Board [CAB]) as the game is developed and refined. The CAB will be convened at the start of the study and will assist the principal investigator (PI) in developing real-life CINV scenarios to be used in eSSET:CINV. Focus groups will allow the CAB to discuss their experiences with CINV. These experiences will provide the foundation for CINV scenarios for the game. Subsequent focus groups will validate scenarios, provide feedback to game designers, and allow for game testing

Phase II: **Game prototype testing**. Phase II is guided by a representational approach to educational interventions and grounded in the Common Sense Model of Illness (CSM) which asserts that illness-related beliefs frame how older adults make decisions about self-management of illness and treatment-related symptoms.[35] Action is related to a person's beliefs (cognitive representation) about the identity, cause, timeline, consequences, and ability of the symptom to be controlled or cured.[13, 14] Representations developed from past experiences guide self-management of illness or symptoms, and incorrect representations can lead to consequences such as delays in seeking care and/or non-adherence to prescribed or recommended treatments.[13, 35, 36] Beliefs about consequences are important predictors of self-management.[36] Older adults' beliefs regarding their ability to cure or control a symptom also determine the likelihood of self- management.[37] People who do not believe a symptom has consequences or that their actions will lead to positive outcome likely do nothing to self-manage.[36]

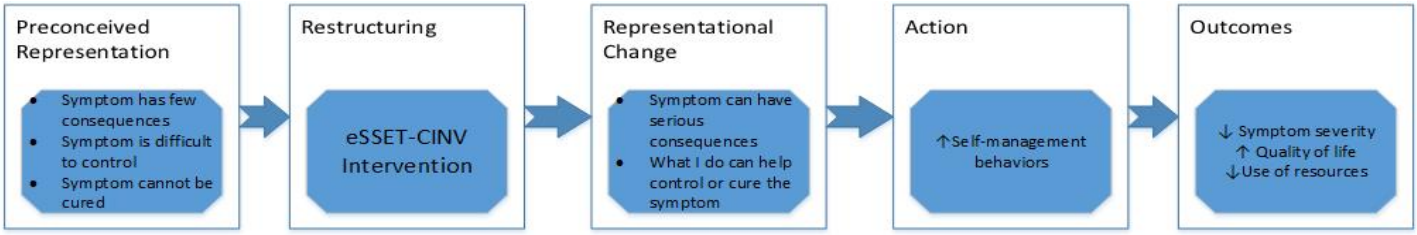
Studies have demonstrated that older adults are less responsive than younger people to symptoms, including those that might indicate a serious condition.[35] The tendency to minimize symptoms and their impact has

been seen in breast cancer survivors[38] and the elderly with symptoms related to myocardial infarction.[39] Many older people interpret symptoms as part of aging, leading them to delay seeking treatment.[35] Adults of all ages may normalize symptoms and subsequently minimize the significance of their symptoms on their health, leading to delays in treatment.[40] Further, cancer patients worry more over symptoms that indicate worsening disease, compared to symptoms that they interpret as a sign that chemotherapy is working to kill the cancer.[41] Other reasons for delayed treatment in the elderly include being uncertain about the symptom's severity or seriousness and believing that treatment or management is not possible.[39] Interventions that specifically address people's illness or symptom representations may be able to alter their response to illness.[36]

A representational approach: 1) assesses a person's illness or symptom representation (beliefs), 2) seeks to restructure existing representations, and 3) elicits a conceptual change in which learning can occur.[42, 43] During a representational intervention, symptom beliefs are assessed, misperceptions and gaps are explored and corrected, new information is introduced and processed to replace old misperceptions, and new goals and strategies are set.[43] The representational approach has been successful in improving outcomes related to cancer pain,[43] end-of-life communication,[44] end stage renal disease, and symptom distress.[45] It is also being tested online to help women with recurrent ovarian cancer manage symptoms.[43]

As shown in the overall study model (Figure 1), older adults begin treatment for cancer with a preconceived cognitive representation about chemotherapy treatment-related symptoms. The eSSET-CINV intervention is designed to restructure the older adult's known erroneous representations and introduce new information regarding the efficacy of using self-management strategies for CINV. We propose that "a picture paints a thousand words" and images are more powerful than the written word. In the proposed approach, visualizing CINV consequences (positive and negative) experienced by the character in the game as a result of symptom management decisions, coupled with discussion with a nurse, will help the older adult reframe his or her cognitive representation, set new goals, prompt use of self-management strategies for CINV, and improve outcomes. We hypothesize that through the eSSET-CINV intervention, older adults undergoing treatment with emetogenic chemotherapy who reframe their CINV cognitive representation will engage in more effective symptom self-management behaviors, resulting in decreased CINV severity, increased QOL, and decreased resource use.

Figure 1: Overall Study Model: Representational Framework



Background

Approximately 63% of all cancers are diagnosed in people age 65 and older.[46] In addition, most older adults report at least one co-morbid condition (e.g. arthritis, heart disease, diabetes).[47] Older people with a history of cancer report more comorbid conditions compared to people without cancer (7 versus 5, respectively); however symptoms related to comorbid conditions are not unique to people with cancer.[48] While cancer treatment often results in a myriad of treatment-related symptoms, symptoms may be more related to comorbid illnesses instead of cancer and its treatment.[48] In addition, symptoms from comorbid conditions may be present at diagnosis, making the onset of some cancer treatment-related symptoms difficult to discern (e.g., fatigue, bowel disturbances, sleep disturbances, pain).

Nausea is a frequent, readily identifiable side effect of cancer treatment. Up to 64% of adults being treated for cancer report delayed nausea, and 33% report acute nausea.[10] In addition, patients who developed nausea at cycle 1 are more likely to report it in subsequent cycles.[10] While pharmacologic and non-pharmacologic practice guidelines for prevention and treatment of CINV in adults exist (see Figure 2),[11, 12, 49] *none are specific to treating older adults*. To our knowledge, *few studies* have examined the effectiveness of any CINV self-management strategy in older adults. Only one intervention study for CINV was found that included the elderly as a specific group(n=23); this study demonstrated that palonosetron-a 5-HT3 receptor antagonist, plus dexamethasone is safe and effective at reducing moderate acute and delayed CINV in this population.[2] *This study will address these gaps by examining the effects of an interactive intervention for CINV (eSSET-CINV)*

in older cancer patients to reinforce the use of self-management strategies based on clinical guidelines and recommendations.

Self-management of CINV in older adults is unknown

Printed patient education material for CINV based on the treatment and prevention guidelines are routinely provided to new patients and their family members so they can self-manage CINV at home. *No studies* were found that examined older adults' use of CINV self-management strategies based on these guidelines. Studies have reported that adults (age 18 and older) in China experienced an average of 14 treatment-related symptoms and used 16 to 21 self-management strategies per week.[50] Another study from China reported that cancer patients used an average of 8.56 strategies for managing CINV and reported low to moderate relief. Strategies used by this sample included dietary (e.g., small frequent meals) and environmental (e.g., avoid smells) modification, psychological strategies (e.g., relaxation), acupuncture/pressure, and taking anti-emetics.

Figure 2: Common Recommended CINV Interventions

Pharmacologic: Antiemetic therapy as prescribed by MD
Non-Pharmacologic:
Nutrition: Eat- dry food, small meals, bland and easy to digest foods. Sit up after eating. Avoid cooking odors, spicy and greasy foods.
Hydration: 8 to 12 cups of liquid per day. Drink even if not thirsty. Include liquids like soup, ice pops, flavored ices, gelatin. Limit caffeine products
Complementary: Relaxation, yoga, behavioral therapy (distraction, meditation), guided imagery, controlled breathing, environmental changes, acupuncture/acupressure

Patients who experienced more severe or prolonged CINV engaged in more types self-management behaviors. However, timing (preventive versus active management) of the self-management behaviors was unknown. Patients treated in an outpatient setting reported using fewer self-management behaviors than those treated in inpatient settings. Regarding CINV relief, those with delayed CINV or greater symptom distress reported less relief[51] indicating the more severe the CINV, the less likely it is to be relieved. *Because there are no studies that specifically focus on the older cancer patient with either acute or prolonged CINV, one goal of the proposed intervention is to help older adults identify and manage CINV in the early stages to reduce negative consequences.*

In related symptom and self-management literature, studies show that other cancer treatment-related symptoms (fatigue, chemotherapy-induced peripheral neuropathy) are generally accepted or perceived as inevitable. Most adults modify their activities to reduce the impact of symptoms rather than actively engage in self-management behaviors.[52-55] Perceived control influences self-management. A qualitative study of perceived control and self-care in colorectal cancer patients found that some people believed symptoms were expected and had to be endured. Others believed nurses were responsible for managing treatment-related symptoms and doubted their personal ability to make an impact on a symptom. Some patients believed they should be active in their own care, but those who engaged in self-care believed they could make a difference and symptoms were temporary.[37] While these beliefs have not been well studied, it is reasonable to apply these attitudes and behaviors to other symptoms such as CINV. Older adults may be using strategies to minimize the impact of CINV on daily life rather than treat the symptom itself. How they make decisions to use symptom self-management recommendations is unknown. *Through the examination of differences in self-management strategies used between the intervention and attention control groups, this study will identify pharmacologic and non-pharmacologic self-management strategies used by older adults receiving cancer treatment with emetogenic chemotherapy and describe the magnitude of effect (i.e., effect size) of those strategies in managing or reducing CINV.*

Symptoms and QOL in older adults with cancer are related

The literature related to CINV and QOL in older adults is extremely limited and unclear. One study reported significant declines in QOL and functioning in adults (mean age 56 years) with both acute and delayed CINV over 3 treatment cycles.[10] Other studies have shown that older adults receiving cancer treatment report functional loss,[56] and adults with more treatment-related symptoms report poorer functioning and QOL.[57, 58] However, other studies have not appreciated a decline in QOL in older adults with CINV under treatment for lung cancer.[59] *This study will further the knowledge related to quality of life and the symptom experience in older adults undergoing treatment for cancer with emetogenic chemotherapy.*

Older adults are unique learners and need non-generic intervention

Teaching older adults about self-care is critical to improving chemotherapy-related outcomes from CINV.[60] While some healthcare providers believe that intellectual capacity declines in older age, research shows that intellectual functioning is maintained by older adults[61]. Most older adults do not experience dementia.[62] Adult teaching theories emphasize the independence of the learner and the importance of being ready and motivated to learn.[63] While most teaching strategies for educating older adults apply to written material (e.g., using large print, lower reading levels)[62, 64, 65] these strategies can be applied to novel methods of education, such as

technology-based programs. Effective educational strategies for older adults focus on "must know" concepts[62] such as self-care activities. In addition, practicing new skills is essential[62, 66] to produce patterns of behavior[66] and may be an effective way to introduce and reinforce new information and learning. The use of storytelling by either using the patient's own experiences as a learning tool, or introducing new stories is also an effective means of promoting learning in elders.[67] By eliciting stories from older adults, healthcare providers can better understand how older cancer patients cope with illness and suggest more effective strategies. *The proposed intervention will improve learning by introducing a "story" about a character experiencing CINV that older adults can relate to and then transfer knowledge gained from the intervention into their own lives. Images of positive and negative consequences (termed "after-imaging"[60]) related to CINV symptom management may be retained by the older adult after playing the game and going home to manage their own symptoms.*

Serious Game education in older adults has potential to improve learning

Serious gaming has been used mostly in children and adolescents with diabetes[68-70] and depression,[71] adults with chronic pain,[72] and for various topics in medical education to teach decision making in women's health,[73] surgical skills,[74] disaster preparedness[75] and surrogate decision making.[20] New applications in older adults include interventions involving "exergaming" for balance in residents of assisted living facilities. Exergaming has shown to be safe and potentially effective at encouraging physical activity using the Wii Fit game system.[72, 76-78] Other interactive technologies being used with older adults include use of avatars and interactive touchscreen technology for diabetes education,[79] and mobile devices to promote activity in sedentary elders.[80] Studies that have used technology including avatars report that they are well liked by older adults.[79, 81]

The success of these technology-based interventions in older populations, combined with our preliminary work[82], suggests eSSET-CINV has the potential to be feasible and acceptable to the older cancer patient. *This study will address the limitations of previous studies by intervening during active chemotherapy treatment when side effects are likely to be at their worst. In addition, eSSET-CINV can be used in the outpatient chemotherapy setting before treatment, requiring no additional use of healthcare resources or patient travel.*

Innovation

This application proposes the development of a *novel serious game* that will *educate and engage* older cancer patients, through their interactions with avatars, to reframe their cognitive representation of CINV, increase CINV self-management behaviors, reduce CINV severity, improve overall QOL, and reduce healthcare resource use. This proposed project addresses NIH research priorities by investigating the use of serious gaming to facilitate changes in cancer symptom self-management through health behaviors and improved health outcomes in an understudied population. This approach departs from traditional methods of education (passive receipt of information) because *our game uses simulation and gaming technology to engage older adults in active learning (game playing) instead of passive learning (traditional printed patient education material) to improve CINV self-management at home.* Our methodology eschews a "one size fits all" approach common to standard adult patient education and is expected to dynamically challenge older adults' core representations about controlling symptoms. The intervention *targets known barriers to symptom self-management (cognitive representation related to symptom consequence, and cure/control) in older adults and seeks to change these representations and promote self-management behaviors. This game allows older adults to learn by actively reframing misperceptions and using new knowledge to practice making self-management decisions in a safe environment before they attempt to manage CINV at home.* In contrast to interventions that are developed by healthcare professionals from their own perception of patient need, our method of game development *involves a Community Advisory Board (CAB) that included older adults with cancer who have undergone treatment with emetogenic chemotherapy, family members and oncology nurses who have had experience with treatment-related side effects such as CINV. The CAB is crucial to developing an intervention based on real life experiences that is mature, relatable, practical and salient for their peers.* Finally, this study seeks to *address the numerous gaps in the literature regarding older adults, CINV, cognitive representation, and self-management behaviors.* If the eSSET-CINV intervention is shown to be effective in this population, the intervention can be easily adapted to educate older adults about self-managing other treatment-related symptoms (e.g., fatigue, sleep disturbances).

C. APPROACH:

Team:

Dr**. Vicki Loerzel** (VL, PI) is an Oncology Certified Nurse with over 20 years of oncology experience. Since 2004, Dr. Loerzel has been the project director and research nurse on an NINR funded RCT (R01) and the PI on several small funded studies investigating the symptom experience of older adults with cancer. Dr. Loerzel

has a long-standing history with the UF Health Cancer Center- Orlando at Orlando Health and has excellent experience in recruiting and retaining older adults in research. Her qualitative and descriptive quantitative research focusing on older cancer survivors and adults with cancer, symptom experience, and cognitive representation provide foundation for this study. She is a new investigator to NIH; however, she has extensive research administration experience to lead this team. In addition, Co-I Clochesy and consultant Given will also provide support to the PI.

Dr. **John M. Clochesy** (JC, Co-I) is an expert in developing and adapting serious games for health in different patient populations with over 20 years of experience as a PI. These interventions have improved outcomes by reducing health disparities using simulation-based avatars to promote self-efficacy in self-management of healthcare providers from medically and socially disenfranchised groups (eSMART-HD) and reducing depressive symptoms in young adults (eSMART-MH). A current study focuses on avatar-based decision support for surrogate decision makers (eSMARTT). Clochesy has also served as a mentor to several researchers developing serious games for different populations. Loerzel and Clochesy are well known to each other through alumni events with Case Western Reserve University and through conference meetings and reside in the same region, permitting them to work closely in the execution of this project.

Dr. **Barbara Given** (BG, Consultant) is an expert in older people with cancer, cancer symptom management, and cancer intervention research with over 30 years of intervention research for symptom management and funding from the National Institutes of Health. Her current intervention research is using technology (eCancer- A technological approach to symptom management from home to practice; Text messaging to improve adherence to oral chemotherapy agents) to help patients receiving chemotherapy self-manage the severity of their symptoms at home so they can continue to adhere to medications. Given has served as a mentor to numerous researchers in oncology for a variety of topics. Given and Loerzel are known to each other through common research interests and the development of this project.

Dr. **Xin Yan** (XY) will work as Biostatistician for statistical design, analysis and interpretations of results. Dr. Yan has 20 years of experience in design and analysis of more than 70 clinical trials (Phase I through Phase IV) in various therapeutic areas. He has been PI for several funded research projects in design and analysis of clinical trials and Co-PI for NIH funded research projects. Loerzel and Yan have worked closely together during the development of this proposal.

Ms. **Patricia Geddie** (PG) is an Advanced Oncology Clinical Nurse Specialist at the UF Health Cancer Center-Orlando, has over 28 years of clinical oncology experience and is a doctoral student at the UCF College of Nursing. Geddie has expertise in the symptom experience of older adults undergoing treatment for cancer. She has extensive experience recruiting and retaining older adults for research. She will be the study's research nurse and have primary responsibility for recruitment, enrollment, data collection and intervention delivery. Loerzel and Geddie are well known to each other through the Central Florida ONS Chapter, previous working relationship, and partnership on several pilot studies in preparation for this proposal.

Our team will be supported by **Eileen Smith** (ES, Co-I) of **E2i Creative Studios** (E2i)**,** a media lab within the University of Central Florida's Institute for Simulation and Training (IST). E2i has created several avatar-based training systems in partnership with nursing (DRAMA-RAMA[83]) and has collaborated with Loerzel in pilot focus groups in preparation for this study.

Nursing students will be an integral part of the team and will be active research assistants (RAs) throughout this study. All students will receive training in research and will be required to undergo CITI training as required by the UCF Institutional Review Board. All students will be educated on cancer chemotherapy side effects and self-management behaviors prior to working with research subjects. In phase I, students will be trained to participate in focus groups (e.g., note taking), analyze focus group data (e.g., review transcripts, code, and develop themes), and pre-test the eSETT:CINV game. In phase II, students will be trained in the following: 1) data base setup, data entry, and cleaning; 2) conduct follow-up phone calls and data collection; and 3) develop a questionnaire to elicit feedback about the games appeal and usability. Pre-nursing students, undergraduate Honors in the Major students, and graduate students have a strong record of research within our college with many students conducting their own research or working on faculty projects. Students engaged in this project will be exposed to cutting-edge technology and patient education and have opportunities to publish and present their work related to this project at university, local, and regional research conferences. This project will provide a research foundation that they can use for their own research careers.

Preliminary Studies:

Symptom experience and cognitive misperceptions: Dr. Loerzel (PI) initially investigated QOL and the symptom experience of older breast cancer survivors and found that older breast cancer survivors experienced high QOL while experiencing treatment-related symptoms.[18, 38, 84] These women accepted symptoms as "part of life," a belief that prompted their decision to not manage current symptoms.[16] Grounded theory research, funded by the American Nurses Foundation, found that older breast cancer survivors "pushed" cancer into the background using a process involving: expecting illness with aging, keeping cancer in perspective, and sensing a partnership in the fight against breast cancer. Again, women minimized their experience with breast cancer, choosing to focus on the positive aspects of their recovery, not lingering treatment-related symptoms. While symptoms were present, older women rarely volunteered their experience with symptoms.[15] Following these studies, Dr. Loerzel used a mixed method approach in a series of small funded studies to examine the symptom experience and cognitive representation of older people with cancer. In one pilot study, Loerzel found that older breast cancer survivors (N=9) within a year of completing treatment reported an average of 6 (range 3-9) cancer treatment-related symptoms. The most common long-term symptoms were sleep disturbances, pain and fatigue. *Contrary to prior studies[17], this study identified cognitive misperceptions in symptom cause, consequence, and ability to control/cure the symptom.*[85] In another pilot study, older adults (n=43) under treatment for cancer reported an average of 7 (range 2-13) symptoms. Twenty-five percent reported CINV as one of the most bothersome symptoms with a mean symptom severity rating of 6.8 on a 0 to 10 scale. This *study again identified cognitive misperceptions in symptom consequence and ability to control/cure symptoms.*[86] In addition, *there was poor self- management of CINV* with only 33.3% of older adults actively managing it with medication. Medication was rated moderately effective at managing CINV.[87] *In summary, these studies indicate that older adults with cancer experience multiple treatment-related symptoms throughout the cancer treatment trajectory. Older adults do little to manage symptoms (including CINV) due to cognitive misperceptions related to symptom consequences and ability to be controlled/cured.*

Current standard education is overwhelming, technology accepted by older adults: Currently, Dr. Loerzel, Ms. Geddie, and Ms. Smith collaborate on a study using qualitative focus groups to evaluate current education strategies for older adults and explore new approaches for educating older adults with cancer. Preliminary data suggest that older adults consider standard symptom patient education: 1) overwhelming; 2) difficult to prioritize; and 3) challenging to apply to their own care. Older adults value engaging others in conversation (peers and MD) and learning from other patients experiences. This current study and prior studies indicate that *most older adults use technology, including playing electronic games (e.g., Words with Friends, Solitaire, Candy Crush) on a daily basis and are receptive to new technology based educational interventions above and beyond typical written handouts.*[82]

Experience with Novel Technology

The proposed application builds on the collective experience of our team to develop a serious game for managing CINV using the Unity 3d gaming platform. Based on prior experience in game design and development, Dr. Clochesy (eSMART-HD[20]; eSMART-MH[19]) and Ms. Smith (DRAMA-RAMA[83]) will lead the team in developing an interactive decision making game for CINV using avatars and CINV scenarios. The CINV game scenarios will be developed in partnership with the CAB. Educational and CINV self-management content for the scenarios will be created by Dr. Loerzel and Ms. Geddie using common recommended CINV interventions (Figure 2).[11, 12]

In summary, these multiple preliminary studies and experiences informed our decision to focus on developing a technology-based intervention to help older adults restructure existing cognitive representations and promote a conceptual change in which learning can occur. This intervention will introduce new information about CINVs ability to be managed (cured/controlled) at home by providing visual cues to the consequences (positive and negative) of using CINV self-care strategies.

Research Design and Methods

Design: This project incorporates qualitative and quantitative research designs. Phase I consists of three focus groups with the CAB who have personal and professional experience with CINV and can identify realistic scenarios and educational content to build the game. Phase II is a two-arm randomized trial to establish effect size of the intervention. Nursing students, as research assistants (RAs), will be involved in both phases of this study.

Phase I: Game design and production: The goal of phase I in this proposed research is to design and develop a serious game that offers older adults practical skills to reframe cognitive representation of CINV, reduce CINV severity, enhance CINV self-management behaviors, reduce healthcare resource use, and improve overall QOL. This game will put the user in the center of the action and focus on a specific outcome.[33] It will also affect motivation to self-manage CINV.[33] Phase I will be guided by a formative evaluation (FE) process[88] using a Community Advisory Board (CAB) and principles of serious game design (Figure 3).[31, 32, 68, 89] The FE process will allow the team to present the project's status, talk about changes, observe and capture feedback during play testing of the emerging learning scenario, and receive objective feedback from the CAB as to the project's progress. Members of the CAB will participate in 3 focus groups. Focus Group 1: Participants will be asked to describe their personal and professional experiences (incidence, self-management, perceived and actual consequences) with CINV in order to begin building realistic game scenarios. In addition, standard CINV interventions[11] such as taking antiemetic's, eating small frequent meals, and staying hydrated (Figure 2) will be used to guide the emerging scenarios and self-management choices made by the player that may lead to positive or negative outcomes. Focus Group 2: Participants will validate themes from the first focus group and provide feedback on game scenario context related to CINV, character development, reality of the setting, scripts, self-management choices and subsequent outcomes. Focus Group 3: Participants will pre-test the game and provide feedback on game consistency, usefulness, likelihood of changing symptom representation related to CINVs ability to be cured/controlled, engagement, entertainment factor, and potential "dose" of the intervention.

Figure 3: Principles of Serious Gaming

- Knowledge sets stage for behavioral change
- Practicing skills leads to self-mastery
- Modeling is an effective way to learn new skills
- Tailored games facilitate character identification
- Game must be entertaining

All focus groups will be digitally audiotaped, transcribed verbatim, and uploaded into HyperRESEARCH™ software for content analysis. Under the guidance of the PI, student RAs will take notes during the focus groups and be involved in data analysis and game pre-testing. The focus groups will be held at the E2i lab in the UCF Institute for Simulation and Training.

Phase I outcomes: The primary outcome of this phase is the development of an interactive dialogue system that allows older adults to progress through a serious game through interacting with characters inside the game. The main form of participant interaction is making dialogue decisions at specific times in a serious game. When a virtual character is asked a question, the participants can pick which response they feel is most appropriate. This function behaves much like the popular "choose your own adventure" books where readers pick the direction in which a story progresses. Interactive dialogue systems allow for the participant to follow an intended story, while still making decisions of how the story unfolds. Another benefit of this approach is that the participant can engage in the serious game multiple times and explore varying story arcs. The main design priority is planning for all possible paths in the experience (scenarios). For this project, we propose to have an "either/or" approach to the types of decisions participants can make in the game, thus witnessing the effect of their choice. For example, the avatar will show early signs of CINV (e.g., mild queasiness, not wanting to eat or drink). The decisions a player could make include: 1) no management (wait it out), 2) self-manage with prescribed medication, or 3) self-manage with distraction techniques. Once the player makes a choice, the avatar will show the consequences of their decision (e.g., progressive nausea leading to vomiting, controlled nausea and being able to do normal activities, or persistent mild nausea). The player will be led through progressive scenarios based on their decisions and asked to make self-management choices at different time points until the avatars CINV is either controlled or a serious effect such as dehydration and/or fall at home leads to an unplanned ED or hospital admission.

Recruitment of CAB: Sampling will be purposive. The CAB will consist of 5 older adults who have finished cancer treatment with chemotherapy within the past 3 years, 3 family caregivers, and 2 oncology staff nurses who deliver chemotherapy treatments. Older adults and caregivers are the critical voice of the target audience, and oncology trained nurses are important to verify accuracy of recommended CINV self-management strategies within the game and current treatment center discharge instructions. To the greatest extent possible, all CAB members will be present at each focus group. CAB members will provide input for scenarios (incidence, self-management, perceived and actual consequences) based on their experiences with CINV. Older adults will be recruited from a pool of approximately 109 participants from the PIs prior research studies who agreed to be contacted for further research.

Names will be randomly drawn from this pool; an invitation to participate will be mailed in batches of 10

until target numbers are reached. Nurses will be recruited from the UF Health Cancer Center-Orlando chemotherapy treatment center. Retention will be enhanced by offering a $50 stipend/gift card to the CAB members for each focus group they participate in. Informed consent and participant characteristics (e.g., age, gender, race, educational level, CINV experience) information will be collected from all CAB members.

Phase II - Game prototype testing

Phase II will use a prospective 2-group randomized, longitudinal design to evaluate effect size of the intervention, examine group differences and evaluate game appeal. Patients who meet the inclusion criteria will be randomly assigned into the intervention group or control group at a 1:1 ratio. All participants will be followed for four chemotherapy cycles (approximately 4 months).

Setting: The outpatient treatment center at the UF Health Cancer Center-Orlando will be the primary site for enrollment due to its long-standing relationship with these researchers. In 2013, UF Health Cancer Center-Orlando saw approximately 4,694 patients. Of these 2,573 patients were age 65 or older, and 565 of these patients received outpatient chemotherapy. These numbers indicate an ample sampling pool of older adults.

Sample size: The target sample is older adults receiving emetogenic chemotherapy for the first time. Sixty-six participants will be enrolled if they meet the following **inclusion criteria**: age 65 and older, newly diagnosed with any cancer, treatment with any chemotherapeutic agent with a moderate to severe emetic potential (on a 3- or 4- week cycle), proficient in English, and have a telephone. **Exclusion criteria** include: previous diagnosis and treatment for cancer, advanced or end stage disease with a palliative intent, visually or hearing impaired. Dementia or cognitive impairment is not a concern with the population since they have already been cognitively screened in order to consent to treatment at this cancer center. There will be no exclusion based on gender or racial/ethnic status. Retention of all participants will be enhanced by the following strategies 1) weekly telephone follow-up phone calls by the RA; 2) a $50 incentive/gift card at the end of the study period; and 3) attention control group offered eSSET-CINV at the end of the study. We will oversample by 20% in order to account for attrition.

Phase II Procedures:

Recruitment and randomization: Successful recruitment and retention strategies previously established by the team will be used during this phase.[7, 15, 16, 18, 90] Convenience sampling, followed by randomization will be used. All new patients will be screened for eligibility by the Research Nurse (RN-PG) using the Sunrise XA - electronic medical record system used by Orlando Health. Eligible patients will be approached by the RN at their first chemotherapy appointment and asked to participate. This timing is not expected to add to or create patient anxiety. Patients usually wait 30 to 60 minutes for lab results and chemotherapy to be delivered. Participating may act as a distraction, thus reducing anxiety. In addition, patients have already received standard written education regarding treatment effects and will expect CINV as a possible effect of treatment. Written informed consent will be obtained in a private area of the clinic open to the RN. A signed copy of the consent will be given to the patient. Once informed consent is obtained, baseline measures will be completed, and participants will be randomized (Intervention Group [IG] and Attention Control Group [ACG]) to either group by choosing an envelope with a group assignment.

Table 1: Intervention schema

	Pre-treatment		First Treatment Visit			Post - treatment
	Standard written patient education at *admission to cancer center*	**Standard** written patient education at *treatment planning visit*	**ENROLL/ RANDOMIZE**	**eSSET-CINV Intervention:** **1)** Game **2)** Decision discussion with research nurse	**Standard** review of written patient education on side effects	**Follow-up** phone call
All subjects	x	x	**IG**	x	x	x
			ACG		x	x

Note: IG= Intervention Group, ACG=Attention Control Group

Participants in each group will receive **standard care**: 1) *on admission* to the cancer center (receipt of standard written educational materials that patients are instructed to bring to each appointment), 2) *at a treatment planning visit* (receipt of specific handouts regarding treatment and potential side effects, and 3) *at time of treatment* (verbal review of chemotherapy and symptom handouts by treatment center nurses). See Table 1 for an outline of standard education and eSSET-CINV intervention.

Study Variables

Independent variable: Intervention versus Attention Control group

1) Intervention Group

The intervention will consist of two parts: 1) the eSSET-CINV game and 2) decision discussion with research nurse (RN). The game will be administered by the RN. Participants will play the game at the outpatient treatment center prior to their first chemotherapy treatment using either a study-provided laptop or smart tablet using headphones to ensure privacy and limit distraction. Please see Table 2 for the eSSET-CINV intervention process. At the end of game play, the RN will engage the participant in a discussion about the self-management choices the player made and suggest changes or discuss possible outcomes based on different choices. For example, if the player chose not to treat the avatar's mild nausea and vomiting occurred, the RN would discuss more effective self-management choices as outlined in Figure 3.

The players will be allowed to play the game as many times as they choose during that chemotherapy visit in order to practice making decisions and visualizing consequences and outcomes. Once the participant is discharged home, a student RA, blinded to the treatment group, will call participants weekly to see how they are doing and remind them to record self-management data. To reduce bias, a scripted interview form will be used. Student RAs will instruct the participant to follow cancer center procedures and call their oncologist if they are having problems or have questions.

Table 2: eSSET-CINV Intervention process	
1	Game introduction and orientation
2	Choose avatar
3	Avatar discharged home after treatment
4	Avatar begins to experience nausea
5	Player makes self-management decisions
6	Avatar responds based on player decisions
7	Avatar experience continues with periodic nausea as player continues to make self-management decisions
8	Game ends when avatar achieves goal of mild or no nausea or has an unplanned ED or hospital admission
9	Discussion of decision choices with Research Nurse

Intervention fidelity. eSSET-CINV will be presented and delivered by the same RN each time. The RN will base the discussion on common self-management options (Figure 3). Minor interruptions (< 10 minutes) to game play will be recorded and participants will resume game play where they left off. Technology malfunctions (e.g,. system crash or frozen screen) will be recorded and participants will be asked to start eSSET-CINV over. For players with caregivers, caregiver involvement (e.g., helping, prompting) in the game will be recorded for subgroup analysis.

2) Attention Control Group

Participants in the control group will receive: 1) standard care; 2) follow-up phone calls from the student RAs to remind them to record self-management data; and 3) the opportunity to play eSSET:CINV at the end of the study period. During the follow-up phone calls, the student RAs will instruct the participant to follow cancer center procedures and call their oncologist if they are having problems or have questions. Contamination between groups is not expected since participants are likely scheduled for chemotherapy at different times and receiving treatment in different areas of the treatment center.

Co-variates

Participant characteristics: Demographic and experiential characteristics that may influence CINV and ability to self-manage this symptom will be measured at T1 (baseline). Demographics include: age, gender, comorbidity information, education level, and income level. Experiential characteristics include: cancer diagnosis and stage, chemotherapy regimen with antiemetics, discharge antiemetic prescriptions, use of the Internet to research symptom management information, and caregiver presence (yes/no) and involvement at home. All cancer information will be collected from the patient's electronic medical record by the RN. Delays in chemotherapy treatment and rationale for delay will also be recorded at each time point by the RN.

Dependent Variables

An overview of study variables, measures and data collection timeline are presented in Table 3. Data will be collected for 4 treatment cycles (3 or 4 months depending on cycle length). Questionnaires will use a paper/pencil format with enlarged font and be entered into Excel™ software.

1) **Symptom severity:** The *Symptom Representation Questionnaire (SRQ)*[91] , a 24-item self-report measure will be used to identify presence and severity of common treatment-related symptoms (0-10 Likert scale), including nausea and vomiting (N/V). This measure asks respondents to think about their symptoms over the past week.

2) **Cognitive representation:** The *Symptom Representation Questionnaire (SRQ)*[91] has an additional 15 questions to assess cognitive representation (identity, cause, timeline, consequences, and cure/control) or beliefs about specific symptoms (0-4 agreement scale). This measure includes subscales for symptom cause (2 questions), timeline (3 questions), cure/control (3 questions), and consequence (6 questions). Only the cognitive representation of nausea will be evaluated. This tool is reliable with alpha co-efficients from 0.63 to 0.88 for the subscales.[91] The cognitive representation questions will be modified at baseline to assess participants' beliefs about potential CINV consequences and their ability to be controlled/cured. Subsequent data collection time points will focus on current cognitive representations.

3) **Self-management behaviors:** An investigator-developed *Symptom Management Checklist [SMC]* will measure CINV: 1) self-management behaviors and 2) prevention behaviors. Participants will complete this daily at home between chemotherapy cycles. When experiencing CINV, the participant will use the SMC to record: 1) *CINV severity* (0-10 Likert scale) prior to self-management, 2) the *type* of self-management strategies used and, 3) the strategies *perceived helpfulness* in reducing nausea (0-10 Likert scale). Preventative self-management activities for CINV will also be recorded. All self-management strategies are coded (e.g,. "MED"= taking antiemetic, "DIS"- using distraction), and the participants will fill in the strategy code they are using on the form. To lessen the risk of the SMC becoming an intervention for the Control Group, all participants will be asked to record self-management behaviors of other common treatment-related symptoms (i.e. fatigue, mouth/throat sores). The SMC will be collected by the research nurse at chemotherapy cycles 2, 3 and 4.

Table 3: Summary of dependent variables, measures and data collection time points

		Data Collection Time points			
Dependent Variable/Outcomes	**Measure**	**T1 Baseline**	**T2 Cycle 2**	**T3 Cycle 3**	**T4 Cycle 4**
Symptom severity	SRQ- patient report	x	x	x	x
Cognitive representation	SRQ-patient report	x	x	x	x
Self-management behaviors*	SMC- patient report		x	x	x
Resource Use	Patient report		x	x	x
QOL	EORTC-patient report	x	x	x	x

*Note: self-management behaviors will be recorded daily by participants, but collected by the research nurse at each treatment visit

4) **Health-related Quality of Life-** The EORTC-30[92] will measure QOL at each treatment cycle. This frequency is consistent with others studies that have measured QOL in older adults over time.[59, 93]. This well-known scale includes 5 functional scales, 3 symptom scales, and 6 single items using a 4-point Likert scale ("not at all" to "very much"), and 2 global health/QOL items using a 7-point Likert scale ("very poor" to "excellent"). Higher scores on the functional and health/QOL scale indicate better functioning, while higher scores on the symptom-related scales and items indicate higher symptoms. Reliabilities (Cronbach's alphas) range from 0.52 (role functioning scale) to 0.89 (QOL).[92]
5) **Resource Use:** Any unplanned Emergency Department or hospital admission will be recorded via participant report using a dichotomous (Y/N) variable at each follow-up phone contact and treatment visit. Follow-up questions about the reason for the admission, length of time for admission and treatment will also be asked. The report will be verified by medical record review whenever possible.

Additional Outcomes:

Game appeal: Under the guidance of the PI, student RAs will develop and pre-test a short survey to evaluate game appeal at the first follow-up phone call. Using a 4-point agreement scale, participants will be asked the extent to which the agree or disagree with statements regarding ease of game play, game likability, clarity of self-management choices, usefulness in educating about CINV consequences and ability to be controlled/cured, and realism (setting and scenario). Additional comments about the game will be recorded.

Willingness to recommend the game will be assessed using one item: Would you recommend this game to other older adults about to start chemotherapy treatment (yes/no)? This will be collected at Cycle 4 (T4).

DATA ANALYSIS

Phase I: Game prototype and production

AIM 1: Identify real-life scenarios involving CINV incidence, self-management, and consequences using a peer Community Advisory Board of older adults who have undergone cancer treatment, their family members, and oncology nurses to design and develop a serious game for CINV self-care decision making.

AIM 2: Identify design aspects and elements of eSSET-CINV game play, audio, and visual avatar development that have the greatest appeal for older adults with cancer.

Data from focus groups will be digitally audio-recorded and transcribed. Methods consistent with classic content analysis will be used to analyze data from the focus groups and will begin immediately after each focus group.[94] The focus group recordings will be reviewed by the PI and student RAs and content analysis will be conducted to thematically categorize responses. Data will be de-identified in analysis-no names will be used. In order to eliminate bias, the analysis will remain grounded in the data. Themes will be created and coded using language similar to what the participants use. These codes will then be grouped by similarity and used to summarize feedback about the game and suggestions for improvement.[94] The notes taken by the RAs during and after the focus groups will serve as a "trail of evidence" to increase the trustworthiness of the data and confirm final findings. Data are not intended to be generalized but will answer specific study AIMS.

Phase II: Game prototype testing

Preliminary data analysis: Descriptive statistics will be provided to characterize the study participants for all demographic and experiential variables at baseline and at each treatment cycle time point. Summary tables will be provided to present participant characteristics (e.g., gender, age group, race), major study variables, game appeal, and willingness to recommend game to others. Internal consistency of study measures will be checked and evaluated to ensure data quality. Effort will be taken as much as possible to avoid missing data. If there are significant missing data that may impact analysis results, the multiple imputation method may be used for the analysis of primary endpoint. All statistical analyses will be performed using Statistical Application Packages (SAS®), version 9.4.

Principle data analysis: The primary endpoints for the study are N/V severity score and the number of self-management behaviors. The secondary endpoints are ED/hospital admission and QOL. Summary statistics for the primary and secondary endpoints will be provided. The t-test will be used if the normality of the endpoint can be confirmed. Otherwise, the Wilcoxon Rank-Sum test will be used to assess the difference between the two groups at each treatment cycle time point.

AIM 1: Estimate effect size of the eSSET-CINV in changing patient outcomes: cognitive representation, self-management behaviors, CINV severity, QOL, and resource use. The effect size of N/V severity score will be estimated using the Cohen's d, which is defined as the difference between two means divided by a standard deviation for the data.

AIM 2: Examine differences in cognitive representation, self-management behaviors, CINV severity, QOL, and resource use, between, and within, the intervention and attention control groups. For the primary endpoints, the data will be collected over 4 treatment cycles, and the method of analysis of longitudinal data will be used to compare the difference between intervention and control groups over time. The generalized estimating equation (GEE) approach may be used to enhance the robustness of the estimation of model parameters when the ideal working correlation structure is difficult to pre-specify. In the longitudinal model treatment cycle time, interaction of time and treatment, or both, whenever feasible, may be added into the model to assess the time effect on treatment difference.

The one-way repeated measures ANOVA will be used to assess the difference between the two groups. The mixed effect model may be used as exploratory analysis to account for unobservable variations from each individual patient. In addition, comparisons between two groups at each treatment cycle time point will be performed for all primary and secondary endpoints. For this particular comparison, the univariate normality of each endpoint will be assessed graphically at each treatment cycle time point. An appropriate time window will be determined to define the treatment cycles for the study.

AIM 3: Obtain preliminary data regarding the feasibility and acceptability of the game in older adults experiencing CINV. Feasibility- Computer science and digital media undergraduate students will work under the direction of Ms. Smith and Dr. Loerzel to identify patterns in game play data (e.g., self-management decisions, scenario patterns of progression), time to game completion, and number of times the game was played (intervention dose). The RN will track any instance of game play interruptions or

malfunction. This data will be summarized with descriptive statistics. Game Appeal: Responses to the game appeal and willingness to recommend questions will be scored and summed using descriptive statistics. Additional comments about the game will be recorded and analyzed for themes.

Sample size and statistical power:

Based on the assumption of a nausea severity mean score of 6.20, range from 2 to 9, a standard deviation of 2.44, and a clinically meaningful difference in mean nausea severity score of one between the intervention and control groups, with 90% power, the required sample size is 33 participants for each group, yielding a total sample size of 66 for the study. To reduce the patient selection bias, single-blinded randomization may be used whenever feasible. Due to lack of available data from prior research the sample size for secondary endpoints is not possible for the study at first stage. However, the power statistical analysis will be assessed when data become available from the planned study.

Potential challenges and strategies for addressing:

Although prior research participants have agreed to be contacted for future research projects, it is possible, that we will not be able to recruit enough CAB members for phase I. In that unlikely event, we would recruit additional CAB members from the UF Health Cancer Center who recently completed treatment. Challenges related to creating a credible educational game (e.g., does not appeal to older people, unrelatable characters/avatars) will be minimized through the partnership of the CAB who will lend credibility to the scenarios for CINV. Prototypes will be created first so credibility issues can be addressed and corrected in phase I focus groups. In addition, Dr. Clochesy (Co-I) and our partners at E2i have a successful history of game development for many different populations and settings. Challenges inherent to having team members at a distance will be addressed through face-to-face meetings at critical time-points related to each phase of the project. Team meetings will be scheduled for every 2 to 3 weeks and distance team members will have the option to Skype into those meetings.

Student engagement in clinical research: The PI, Dr. Loerzel has involved undergraduate and graduate students in prior clinical research and has the necessary experience and expertise to guide them through this innovative project. Students will be involved in all phases of this project. Their participation in this project will expose them to cutting-edge technology and opportunities to build multidisciplinary connections.

Study Start-up and Training: During the first 3 months of the study, ES will hire the technical team for game development, and VL will hire UCF CON nursing students as RAs. At the start of each study phase, VL will provide appropriate staff training and education for the RAs on the following topics: Collaborative IRB Training Initiative (CITI), human subject protection, CINV, CINV self-management behaviors, conducting focus groups, coding and analyzing qualitative data, collecting data during follow-up phone calls. Regular team meetings will be held with investigators, consultants, and study staff to ensure study protocols are maintained (Table 4).

Table 4: Project Timeline

Activity	Year	1				2				3			
	Quarter	1	2	3	4	1	2	3	4	1	2	3	4
Project startup		x											
Team meeting prior to game development		x											
RA training (both phases)			x			x							
Phase I - CAB recruitment			x										
Phase I - Focus groups, game development, and initial testing				x	x								
Phase II - Participant recruitment and enrolment, data collection, intervention delivery					x	x	x	x	x	x			
Phase II - Database set up					x								
Phase II - Data entry and cleaning					x	x	x	x	x	x			
Phase II - Data analysis								x	x	x	x		
Dissemination and final grant reports										x	x	x	x

REFERENCES- USE SEPARATE DOCUMENT

1. Jakobsen JN, Herrstedt J. Prevention of chemotherapy-induced nausea and vomiting in elderly cancer patients. **Crit Rev Oncol Hematol**. Sep 2009;71(3):214-221.
2. Massa E, Astara G, Madeddu C, et al. Palonosetron plus dexamethasone effectively prevents acute and delayed chemotherapy-induced nausea and vomiting following highly or moderately emetogenic chemotherapy in pre-treated patients who have failed to respond to a previous antiemetic treatment: comparison between elderly and non-elderly patient response. **Crit Rev Oncol Hematol**. Apr 2009;70(1):83-91.
3. Gridelli C. Same old story> Do we need to modify our supportive care treatment of elderly cancer patients? Focus on anti-emetics. **Drugs and Aging**. 2004;21(13):825-832.
4. Naeim A, Aapro M, Subbarao R, Balducci L. Supportive Care Considerations for Older Adults With Cancer. **Journal Of Clinical Oncology: Official Journal Of The American Society Of Clinical Oncology**. 2014.
5. Reid J, Porter S. Utility, caller, and patient profile of a novel chemotherapy telephone helpline service within a regional cancer centre in northern ireland. **Cancer Nursing**. 2011;34(3):E27-32.
6. Flannery M, McAndrews L, Stein KF. Telephone calls by individuals with cancer. **Oncol Nurs Forum**. Sep 2013;40(5):464-471.
7. Geddie P. Family caregiver knowledge, patient related factors and unplanned hospital admissions in older adults with cancer.

; In preparation.

8. Shih Y-CT, Xu Y, Etting LS. Costs of uncontrolled chemotherapy induced nausea and vomiting among working-age cancer patients receiving highly or moderately emetogenic chemptherapy. **Cancer** 2007;110(3):678-685.
9. Carlotto A, Hogsett VL, Maiorini EM, Razulis JG, Sonis ST. The economic burden of toxicities associated with cancer treatment: review of the literature and analysis of nausea and vomiting, diarrhoea, oral mucositis and fatigue. **Pharmacoeconomics**. Sep 2013;31(9):753-766.
10. Cohen L, de Moor CA, Eisenberg P, Ming EE, Hu H. Chemotherapy-induced nausea and vomiting: incidence and impact on patient quality of life at community oncology settings. **Support Care Cancer**. May 2007;15(5):497-503.
11. National Cancer Institute. Managing chemotherapy side effects: Nausea and Vomiting. Available at: http://www.cancer.gov/cancertopics/coping/physicaleffects#Nausea+and+Vomiting, 2014.
12. Tipton JM, McDaniel RW, Barbour L, et al. Putting evidence into practice: evidence-based interventions to prevent, manage, and treat chemotherapy-induced nausea and vomiting. **Clin J Oncol Nurs**. Feb 2007;11(1):69-78.
13. Leventhal H, Brissette I, Leventhal EA. The common-sense model of self-regulation of health and illness. In: Cameron LD, Leventhal H, eds. The self-regulation of health and illness behavior. New York: Routledge; 2003:42-63.
14. Prohaska TR, Keller ML, Leventhal EA, Leventhal H. Impact of symptoms and aging attribution on emotions and coping. **Health Psychology**. 1987;6(6):495-514.
15. Loerzel VW, Aroian K. "A bump in the road": older women's views on surviving breast cancer. **J Psychosoc Oncol**. 2013;31(1):65-82.
16. Loerzel VW, Aroian K. Post-treatment concerns of older women with early stage breast cancer. **Cancer Nursing**. 2012 35(2).
17. Royer HR, Phelan CH, Heidrich SM. Older breast cancer survivors' symptom beliefs. **Oncol Nurs Forum**. Jul 2009;36(4):463-470.
18. Loerzel VW, McNees P, Powel LL, Su X, Meneses K. Quality of life in older women with early stage breast cancer in the first year of survivorship. **Oncology Nursing Forum**. 2008;35(6):924-932.
19. Pinto MD, Hickman RL, Clochesy J, Buchner M. Avatar-based depression self-management technology: promising approach to improve depressive symptoms among young adults... Self-Management Resource Training for Mental Health (eSMART-MH). **Applied Nursing Research**. 2013;26(1):45-48.
20. Clochesy JM, Buchner M, Hickman RL, Pinto MD, Znamenak K. Creating a serious game for health. **Journal of Health and Human Service Administration**. In press.

21. Hickman RL, Clochesy JM, Pinto MD, Burant C, Pignatiello G. Impact of serious games for health on chronic disease self-management: preliminary efficacy among community dwelling adults with hypertension. **Journal of Health and Human Service Administration**. In press.

22. Genetic testing for breast and ovarian cancer susceptibility: evaluating direct-to-consumer marketing--Atlanta, Denver, Raleigh-Durham, and Seattle, 2003. **MMWR. Morbidity And Mortality Weekly Report**. 2004;53(27):603-606.

23. American Cancer Society. Estimated New Cancer Cases by Sex and Age (Years), 2014. Available at: http://www.cancer.org/research/cancerfactsstatistics/cancerfactsfigures2014/index, 2014.

24. Balducci L, Colloca G, Cesari M, Gambassi G. Assessment and treatment of elderly patients with cancer. **Surg Oncol**. Sep 2010;19(3):117-123.

25. Given B, Given CW. Cancer treatment in older adults: implications for psychosocial research. **J Am Geriatr Soc**. Nov 2009;57 Suppl 2:S283-285.

26. Balducci L, Stanta G. Cancer in the frail patient. A coming epidemic. **Hematology Oncology Clinics of North America**. Feb 2000;14(1):235-250, xi.

27. Sehl M, Sawhney R, Naeim A. Physiologic aspects of aging: impact on cancer management and decision making, part II. **Cancer J**. Nov-Dec 2005;11(6):461-473.

28. Sawhney R, Sehl M, Naeim A. Physiologic aspects of aging: impact on cancer management and decision making, part I. **Cancer Journal (Sudbury, Mass.)**. 2005;11(6):449-460.

29. Dabbs AD, Myers BA, MCCurry KR, et al. User-centered design and interactive health technologies for patients. **CIN: Computers, Informatics, Nursing**. 2009;27(3):175-183.

30. Henderson VA, Barr KL, An LC, et al. Community-based participatory research and user-centered design in a diabetes medication information and decision tool. **Prog Community Health Partnersh**. Summer 2013;7(2):171-184.

31. Baranowski T, Buday R, Thompson DI, Baranowski J. Playing for real: video games and stories for health-related behavior change. **Am J Prev Med**. Jan 2008;34(1):74-82.

32. Thompson D. Designing serious video games for health behavior change: current status and future directions. **J Diabetes Sci Technol**. Jul 2012;6(4):807-811.

33. McCallum S. Gamification and serious games for personalized health. **Studies In Health Technology And Informatics**. 2012;177:85-96.

34. Bandura A. Social cognitive theory: An agentic perspective. **Asian Journal of Social Psychology**. 1999;2(1):21-41.

35. Leventhal EA, Prohaska TR. Age, symptom interpretation, and health behavior. **Journal of the American Geriatric Society**. 1986;34:186-191.

36. Cameron LD, Moss-Morris R. Illness-Related Cognition and Behaviour In: Kaptein A, Weinman J, eds. Health psychology: An introduction. Oxford, UK.: Blackwell Publishers; 2004:84-110.

37. Kidd L, Hubbard G, O'Carroll R, Kearney N. Perceived control and involvement in self care in patients with colorectal cancer. **J Clin Nurs**. Aug 2009;18(16):2292-2300.

38. Loerzel VW, Aroian K. Posttreatment concerns of older women with early-stage breast cancer. **Cancer Nurs**. Mar-Apr 2012;35(2):83-88.

39. Ryan CJ, Zerwic JJ. Perceptions of symptoms of myocardial infarction related to health care seeking behaviors in the elderly. **Journal of Cardiovascular Nursing**. 2003;18(3):184-196.

40. Kessler D, Lloyd K, Lewis G, Gray DP. Cross sectional study of symptom attributiuon and recognition of depression and anxiety in primary care. **BMJ**. 1999;318:436-440.

41. Nerenz DR, Levbenthal H, Love RR, Ringler KE. Psychological aspects of cancer chemotherapy. **International Review of Applied Psychology**. 1984;33:521-529.

42. Donovan HS, Ward S. A representational approach to patient education. **Journal of Nursing Scholarship**. 2001;33(3):211-216.

43. Donovan HS, Ward SE, Song M, Heidrich SM, Gunnarsdottir S, Phillips CM. An update on the representational approach to patient education. **Journal of Nursing Scholarship**. 2007;39(3):259-265.

44. Song M-K, Ward SE, Happ MB, et al. Randomized controlled trial of SPIRIT: An effective approach to preparing African-American dialysis patients and families for end of life. **Reserach in Nursing & Health**. 2009;32:260-273.

45. Heidrich SM, Brown RL, Egan JJ, et al. An individualized representational intervention to improve symptom management (IRIS) in older breast cancer survivors: three pilot studies. **Oncol Nurs Forum**. May 2009;36(3):E133-143.

46. Institute NC. SEER stat fact sheet: All cancer sites. Available at: http://seer.cancer.gov/statfacts/html/all.html.

47. U.S. Department of Health and Human Services. A profile of older Americans: 2012. Available at: http://www.aoa.gov/AoARoot/%28S%282ch3qw55k1qylo45dbihar2u%29%29/Aging_Statistics/Profile/index.aspx, 2014.

48. Bender CM, Engberg SJ, Donovan HS, et al. Symptom clusters in adults with chronic health problems and cancer as a comorbidity. **Oncol Nurs Forum**. Jan 2008;35(1):E1-E11.

49. Basch E, Prestrud AA, Hesketh PJ, Kris MG, Somerfield MR, Lyman GH. Antiemetic Use in Oncology: Updated Guideline Recommendations from ASCO. **Am Soc Clin Oncol Educ Book**. 2012;32:532-540.

50. Chou F-y, Dodd M, Abrams D, Padilla G. Symptoms, self-care, and quality of life of Chinese American patients with cancer. **Oncology Nursing Forum**. 2007;34(6):1162-1167.

51. Lou Y, Yates P, McCarthy A, Wang HM. Self-management of chemotherapy-related nausea and vomiting: a cross-sectional survey of Chinese cancer patients. **Cancer Nurs**. Mar-Apr 2014;37(2):126-138.

52. Closs SJ, Staples V, Reid I, Bennett MI, Briggs M. Managing the symptoms of neuropathic pain: an exploration of patients' experiences. **J Pain Symptom Manage**. Oct 2007;34(4):422-433.

53. Fitch MI, Mings D, Lee A. Exploring patient experiences and self-initiated strategies for living with cancer-related fatigue. **Can Oncol Nurs J**. Summer 2008;18(3):124-140.

54. Speck RM, DeMichele A, Farrar JT, et al. Scope of symptoms and self-management strategies for chemotherapy-induced peripheral neuropathy in breast cancer patients. **Support Care Cancer**. Oct 2012;20(10):2433-2439.

55. Spichiger E, Rieder E, Muller-Frohlich C, Kesselring A. Fatigue in patients undergoing chemotherapy, their self-care and the role of health professionals: a qualitative study. **Eur J Oncol Nurs**. Apr 2012;16(2):165-171.

56. Goodwin JA. Older adults' functional performance loss and adaptation during chemotherapy. **Geriatric Nursing (New York, N.Y.)**. 2007;28(6):370-376.

57. Cheng KKF, Yeung RMW. Symptom distress in older adults during cancer therapy: Impact on performance status and quality of life. **Journal of Geriatric Oncology**. 1// 2013;4(1):71-77.

58. Miaskowski C, Cooper BA, Paul SM, et al. Subgroups of patients with cancer with different symptom experiences and quality-of-life outcomes: a cluster analysis. **Oncology Nursing Forum**. 2006;33(5):E79-E89.

59. Park S, Kim IR, Baek KK, et al. Prospective analysis of quality of life in elderly patients treated with adjuvant chemotherapy for non-small-cell lung cancer. **Annals Of Oncology: Official Journal Of The European Society For Medical Oncology / ESMO**. 2013;24(6):1630-1639.

60. Rigdon AS. Development of patient education for older adults receicing chemotherapy. **Clinical Journal of Oncology Nursing**. 2010;14(4):433-441.

61. Merriam SB, Caffarella RS, Baumgartner LM. **Learning in adulthood: A comprehensive guide**. 3rd ed. San Francisco, CA: Jossey-Bass; 2007.

62. Zurakowski T, Taylor M, Bradway C. Effective teaching strategies for the older adult with urologic concerns. **Urol Nurs**. Oct 2006;26(5):355-360.

63. Knowles M. **Applying modern principles of adult learning**. San Francisco, CA: Jossey-Bass, Inc.; 1984.

64. Billek-Sawhney B, Reicherter EA. Literacy and the older adult: Educational considerations for Health Professionals. **Topics in Geriatric Rehabilitation**. 2005;21(4):275-281.

65. Speros CI. More than words: promoting health literacy in older adults. **Online Journal of Issues in Nursing**. 2009;14(3):6-6.

66. Fenter PC. Unxderstanding the role of practice in learning for geriatric individuals. **Topics in Geriatric Rehabilitation**. 2002;17(4):11-32.

67. Sorrell JM. Storytelling as an educaitonal strategy for older adults with chronic illnesses. **Jorunal of Psychosocial Nursing**. 2008;46(7):19-22.

68. Thompson D, Baranowski T, Buday R, et al. Serious Video Games for Health: How Behavioral Science Guided the Development of a Serious Video Game. **Simul Gaming**. Aug 1 2010;41(4):587-606.
69. Lieberman D. Management of chronic pediatric diseases with interactive health games: Theory and research findings. **Journal of Ambulatory Care Management**. 2001;24(1):26-38.
70. Aoki N, Ohta S, Masuda H, et al. Edutainment tools for initial education of type-1 diabetes mellitus: initial diabetes education with fun. **Studies In Health Technology And Informatics**. 2004;107(Pt 2):855-859.
71. Pinto MD, Hickman RL, Jr., Clochesy J, Buchner M. Avatar-based depression self-management technology: promising approach to improve depressive symptoms among young adults. **Appl Nurs Res**. Feb 2013;26(1):45-48.
72. Jansen-Kosterink SM, Huis In 't Veld RMHA, Schönauer C, Kaufmann H, Hermens HJ, Vollenbroek-Hutten MMR. A Serious Exergame for Patients Suffering from Chronic Musculoskeletal Back and Neck Pain: A Pilot Study. **Games For Health Journal**. 2013;2(5):299-307.
73. de Wit-Zuurendonk LD, Oei SG. Serious gaming in women's health care. **BJOG: An International Journal Of Obstetrics And Gynaecology**. 2011;118 Suppl 3:17-21.
74. Graafland M, Schraagen JM, Schijven MP. Systematic review of serious games for medical education and surgical skills training. **The British Journal Of Surgery**. 2012;99(10):1322-1330.
75. Breslin P, McGowan C, Pecheux B, Sudol R. Serious gaming. Advanced computer simulation games help to transform healthcare and disaster preparedness. **Health Management Technology**. 2007;28(10):14.
76. Malliot P, Perrot A, Hartley A. Effects of interactive physcial-activity video-game training on physical and cognitive function in older adults. **Psychology & Aging**. 2012;27(3):589-600.
77. Wüest S, Borghese NA, Pirovano M, Mainetti R, van de Langenberg R, de Bruin ED. Usability and Effects of an Exergame-Based Balance Training Program. **Games For Health Journal**. 2014;3(2):106-114.
78. Chao Y-Y, Scherer YK, Wu Y-W, Lucke KT, Montgomery CA. The feasibility of an intervention combining self-efficacy theory and Wii Fit exergames in assisted living residents: A pilot study. **Geriatric Nursing**. 2013;34(5):377-382.
79. Finkelstein J, Bedra M. Avatar-based Interactive Diabetes Education in Older Adults.
80. King AC, Hekler EB, Grieco LA, et al. Harnessing Different Motivational Frames via Mobile Phones to Promote Daily Physical Activity and Reduce Sedentary Behavior in Aging Adults.
81. Green-Hamann S, Eichhorn KC, Sherblom JC. An Exploration of Why People Participate in Second Life Social Support Groups.
82. Loerzel VW, Geddie P, Smith E. Perceptions of cancer education: Older adults with cancer. In preparation.
83. Norris AE, Hughes C, Hecht M, Peragallo N, Nickerson D. Randomized trial of a peer resistance skill-building game for Hispanic early adolescent girls. **Nurs Res**. Jan-Feb 2013;62(1):25-35.
84. Loerzel VW. Dimensions of well-being in older breast cancer survivors. Paper presented at: 10th Annual Conference on Cancer Nursing, 2009; Orlando, FL.
85. Loerzel VW. An exploration of symptom representation: Older breast cancer survivors. In preparation.
86. Loerzel VW, Geddie P. Cognitive representation of treatment-related symptoms in older adults with cancer. In preparation.
87. Loerzel VW. Self-management strategies for treatment-related symptoms in older adults with cancer. In preparation.
88. Stetler CB, Legro MW, Wallace CM, et al. The role of formative evaluation in implementaion research and the QUERI experience. **Journal of General Internal Medicine**. 2006;21:S1-8.
89. Lewis M. Analysis of the roles of "serious games" in helping teach health-related knowledge and skills and in changing behavior. **Journal of Diabetes Science and Technology**. 2007;1(6):918-920.
90. Geddie P. Nursing assessment of family caregiver knowledge and action tool (NAFKAT): Development and psychometric testing. in preparation.
91. Donovan HS, Ward SE, Sherwood P, Serlin RC. Evaluation of the symptom representation questionnaire (SRQ) for assessing cancer-related symptoms. **Journal of Pain & Symptom Management**. 2008;35(3):242-257.

92. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. **Journal of the National Cancer Institute**. Mar 3 1993;85(5):365-376.
93. Scarpa M, Di Cristofaro L, Cortinovis M, et al. Minimally invasive surgery for colorectal cancer: quality of life and satisfaction with care in elderly patients. **Surgical Endoscopy**. 2013;27(8):2911-2920.
94. Schilling J. On the pragmatics of qualitative assessment. **European Journal of Psychological Assessment**. 2006;22(1):28-37.