

The Sexual Health of Rectal Cancer Patients: A Pilot Study

MSKCC NON-THERAPEUTIC/DIAGNOSTIC PROTOCOL

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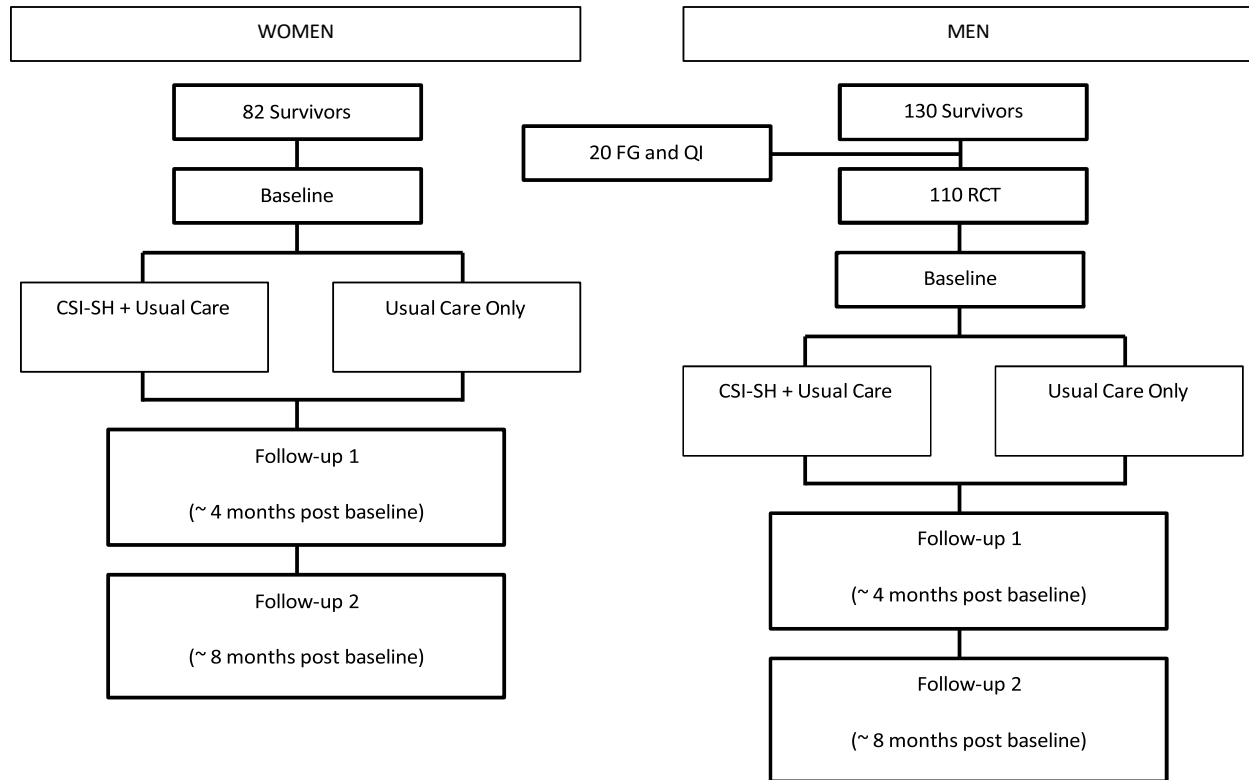
1.0 PROTOCOL SUMMARY AND/OR SCHEMA

The goal of the proposed study is to investigate the feasibility, tolerability, acceptability (including adherence) and efficacy of a sexual health focused intervention, entitled *Cancer Survivorship Intervention-Sexual Health (CSI-SH)*. The primary focus of this intervention is to improve the post-treatment sexual functioning and QOL of male and female rectal cancer (RC) survivors. We are seeking to recruit a total of 192 participants (82 women, 110 men) to the randomized controlled trial (RCT) (this number does not include participants for the qualitative phase).

Patients who are at least 6 months post surgery and/or radiation for stage I-III rectal adenocarcinoma or rectosigmoid cancer with an anastomosis at 15 cm, are at least 6 months post radiation and/or chemotherapy for anal cancer, have no evidence of disease or recurrence, and indicate moderate satisfaction or below on their overall sexual life (a score of “4” or lower on the question “Over the past 4 weeks, how satisfied have you been with your overall sexual life?” for women, and a score of “3” or lower on the question “How would you rate your confidence that you could get and keep an erection” for men). Additionally, men who indicate a “3” or below will be asked an additional criterion question “How much does this problem bother you?” and those indicating a score “2” (a little) or higher will be eligible for this intervention. Based on rectal cancer patients’ clinic and research data, we estimate that 192 participants (110 men and 82 women) will enroll in this study from two sites (Memorial Sloan-Kettering Cancer Center and Mount Sinai School of Medicine). Participants will be stratified according to 1) if they have a permanent stoma or not, and 2) if they have chemotherapy or not. Women will additionally be stratified according to whether or not they are post-menopausal.

Participants will then be randomly assigned to one of the two conditions: 1) CSI-SH plus usual care (UC) or 2) UC only, which is the standard care that patients receive who are not in the intervention. Patients assigned to CSI-SH will receive four individual CSI-SH counseling sessions over a period of approximately two months. The four goals of CSI-SH that will be discussed are: 1) To help rectal cancer survivors understand the phases of the sexual response and common changes in sexuality that many men and women, respectively, experience following rectal cancer treatment (e.g. that some positions may be uncomfortable, painful, or produce disturbing side-effects during intercourse for both women and men, and issues around erectile dysfunction for men); 2) To provide simple strategies to improve sexual function (or sexual rehabilitation) and expand their sexual repertoire; 3) To teach methods for enhancing communication about sexuality in cancer survivorship; and 4) To review the information about available medical resources. Each session focuses on different topics including education about the impact of rectal cancer treatment on sexual health, general distress, coping strategies and specific strategies to increase sexual health. The sessions also include homework assignments which are to be completed in between the sessions. In addition to the counseling sessions, the first three sessions are followed by a booster/trouble-shooting telephone session to help participants enact the strategies and problem solve any barriers to implementation. These booster phone calls will also serve as reminders for strategy practice. Although every effort will be made to complete the booster session in between counseling sessions, if the patient is unavailable to complete the booster calls they may be skipped. Regardless of condition assignment, all participants will be assessed three times: at baseline, approximately four months post-baseline,

and approximately eight months post-baseline. Information from this pilot study will inform interventions to increase sexual health among rectal cancer survivors. This study has high translational promise. If CSI-SH is found to be feasible and efficacious, it could be easily adopted into clinical care.



2.0 OBJECTIVES AND SCIENTIFIC AIMS

The proposed pilot study will test an intervention to enhance rectal cancer survivorship entitled, “Cancer Survivorship Intervention-Sexual Health (CSI-SH)”. The CSI-SH intervention is based on similar interventions with other populations, and will be revised to match the needs and preferences of these survivors. CSI-SH is designed to increase these survivors’ post-treatment sexual functioning and QOL.

- **Primary Aim:** To investigate the feasibility, tolerability, acceptability (including adherence) and efficacy of CSI-SH, a psycho-educational intervention, on the primary outcome of sexual functioning among RC survivors.
- **Secondary Aim:** To investigate the impact of CSI-SH on secondary outcomes: sexual self-schema, cancer specific distress, general distress symptoms, and Quality of Life for all participants, as well as sexual bother for men only.
- **Exploratory Aim:** To explore baseline variables that may influence the effectiveness of CSI-SH (i.e., moderators such as socio-demographic and medical variables).

3.0 BACKGROUND AND RATIONALE

Sexual function after treatment for rectal cancer (RC) has been poorly studied, especially in women. In a review of the literature (e.g., Havenga et al., 1996; Hendren et al., 2005; Mannaerts et al., 2001; Chatwin et al., 2002; Daniels et al., 2006; Latini et al., 2003), we found 20/31 studies evaluating sexual function after therapy included women and only 4/20 included more than 25 women. Further complicating this issue is that less than 15% of patients recall their physicians discussing sexual function pre-operatively, and this appears to be even less frequent in women (6%) (Hendren et al., 2005; Allal et al., 2005). Clearly, based on the existing literature, sexual function in women after rectal cancer therapy is impaired. Several studies report a significant decrease in sexually active women after surgery that ranges from 25%-60% (Havenga et al., 1996; Hendren et al., 2005; Mannaerts et al., 2001; Marijnen et al., 2005; Nesbakken et al., 2000; Pocard et al., 2002; Vironen et al., 2006; Jayne et al., 2005; Engel et al., 2003; Schmidt et al., 2005; Schmidt, Bestmann, & Kremer, 2005).

Most relevant to this proposal are two recent studies. Hendren and colleagues (Hendren et al., 2005) retrospectively surveyed 81 women who had been treated for rectal cancer between 1980 and 2003. The researchers asked these women to complete the Female Sexual Functioning Index (FSFI), an 18-item instrument designed to assess sexual function in women, and the European Organization for Research and Treatment of Cancer Quality of Life (EORTC) instruments as well as answer questions about their pre-operative function. They found that there was a significant decrease in sexual activity after surgery (61% pre vs 32% post) with a mean score on the FSFI of 17.5 (26.55 indicates impairment) suggesting that most women had significant impairment. When evaluating specific issues, women reported problems with libido (41%), arousal (29%), lubrication (56%), orgasm (41%) and dyspareunia (46%). When comparing women who had undergone surgery for rectal cancer to women who had undergone surgery for right colon cancer in a case-controlled analysis, it was evident that women with rectal cancer experienced a great deal more dysfunction. These data reflect the clinical experience of the rectal cancer surgeons with regard to the more frequent sexual problems of female rectal cancer survivors as compared to colon cancer survivors. In addition to the troubling problem of high sexual dysfunction in women, several other lessons were learned from the descriptive study. For example, women, especially older women (>70 years of age) were more likely to not answer questions about sexual function as noted on the EORTC. These data suggest that the addition of the instruments, such as the Female Sexual Functioning Index (FSFI) that include questions about desire and arousal as well as function may be more likely to obtain accurate data across the cohort of women with rectal cancer. This study supports the clinical significance of sexual problems among female rectal cancer patients, and along with their prior work the teams experience enrolling the target population in research and support the inclusion of the FSFI (Rosen, 2000), as well as the EORTC-QLQ 30 – European Organization for the Research and Treatment of Cancer – Quality of Life 30 (Aaronson, 1993) and EORTC-CRC38 – EORTC Colorectal Cancer module (Sprangers, 1999) in the current application. These data suggest that there is a need for interventions designed to help female rectal cancer survivors enhance their sexual functioning.

Sexual dysfunction is also a common problem in male RC survivors. Over 23,000 cases of RC are diagnosed annually among men in the U.S. (American Cancer Society, 2006). As the treatment for RC impacts the parasympathetic and sympathetic nerves responsible for erections

and ejaculation, studies report that as many as 63% of men will have problems with erections and 60% will have difficulty with ejaculation after treatment for rectal cancer (Hendren et al., 2005; Mannaerts et al., 2001; Moriya, 2006). In a recent study of 73 men who had received both radiation and surgery as treatments for their RC, only 10% reported that they could achieve a “quality erection,” and only 10% could ejaculate post-operatively (Mannaerts et al., 2001). Therapy for RC and subsequent dysfunction often translates into a significant decrease in men’s sexual activity (Hendren et al., 2005; Heriot et al., 2005; Marijnen et al., 2005). For example, Hendren and colleagues (2005) reported that of 99 men treated for RC using a nerve sparing surgical technique to preserve functioning, 50% were sexually active post-surgery compared to 91% before surgery; 45% reported that their sex life is worse after treatment, and 47% report a loss of libido.

Men who experience erectile dysfunction (ED) after cancer treatments report significant associated distress and bother. Our data from 231 men following either surgery or radiation for prostate cancer show that ED bother significantly increased post-treatment and remained at consistently high levels throughout the follow-up period (i.e., every 3 months up to 24 months post-treatment) (Nelson, Roth, & Mulhall, 2007). Significant in these data is that even men who returned to “normal” erectile functioning reported greater ED bother post-treatment as compared to pre-treatment. It is also well established in international population-based studies that ED and male sexual dysfunction are associated with higher depressive symptoms (Araujo et al., 1998; Latini et al., 2007; Nelson et al., 2007; Shabsigh et al., 1998; Shiri et al., 2007). Although it is often assumed that older men will be less concerned with sexual functioning, these studies have been conducted in men ranging in age from 40 to 70 years (similar to the age range of men with RC). The bother and distress associated with ED often leads to negative changes in men’s sexual self-schema and loss of intimacy in their relationships, potentially resulting in relationship conflict (Andersen, Cyranowski, & Espindle, 1999; Andersen & van der Does, 1994; Bokhour et al., 2001; Moore et al., 2003). Given data indicating that most (50 to 80%) men do not comply with ongoing medical ED interventions (i.e., pills, injections, vacuum devices) and only 38% of men following treatment found them to be helpful in improving their sex lives (Schover et al., 2002; Sundaram et al., 1997), a psychosocial component appears crucial for effective treatment.

Although there have been no intervention trials specifically designed to target sexual dysfunction among rectal cancer survivors, there are some helpful recommendations for intervention strategies from prior work with other cancer patient populations. For CRC survivors there are also a few specific suggestions such as those found on the National Cancer Institute’s (NCI) and American Cancer Survivors’ (ACS) web pages and in a recent review by Fleming (Consultant). It is important to note that members of the team are also responsible for writing the current ACS booklets “Sexuality and Cancer” for men and women (Schover, Consultant) and the sexuality section under supportive care of the Physicians Desk for the National Cancer Institute (Fleming, Consultant).

Due to the paucity of research with female rectal cancer survivors, we turn to work with breast cancer survivors for further guidance in molding an intervention. Breast cancer is the most common cancer diagnosis in women. Thus, it is not surprising that interventions to address breast cancer survivors’ sexual health have begun to be investigated. Two studies are most relevant to this proposal. The first was recently conducted by Schover and colleagues (2006). They

investigated their peer counseling intervention for African American Breast Cancer Survivors using a wait-list control design. Participants were breast cancer patients at least one year post diagnosis. A workbook was created and divided into three chapters: Menopause and Breast Cancer (i.e., hot flashes, vaginal dryness); Sexuality and Breast Cancer (i.e., feeling unattractive, dating, low sexual desire), and Cancer and Your Family (i.e., fertility and breast cancer treatment). At the end of each chapter, topics were summarized with an index of proposed solutions. Each participant also received a resource list including books and web sites. The intervention was three sessions, each focused on a workbook chapter. There were three assessments: baseline, posttreatment and a 3-month follow-up. At baseline, 65% of the women had an FSFI score below or equal to 26.55, the cut off indicating sexual dysfunction. Following the intervention, significant improvements were noted in overall psychological distress (as measured by the BSI), sexual functioning/satisfaction (FSFI total score) and menopause symptoms (symptom checklist). The intervention was also highly rated in terms of its relevance and impact. This small study (with 60 women) illustrated that a brief intervention using some of the same components/information as in the proposed trial can make a significant impact on women's sexual health.

A second study with breast cancer survivors conducted by Ganz and colleagues (2000) focused on the management of menopausal symptoms. They used a two group design (intervention vs. UC) to investigate the efficacy of a comprehensive menopausal assessment intervention program. As in the current proposal, women in the UC group were not precluded from obtaining care, but were not encouraged to do so (thus this constituted a genuine UC control rather than a no-treatment control). The intervention targeted hot flashes (e.g., pharmacologic), vaginal dryness (e.g., use of lubricants), and urinary incontinence (Kegel exercises). As compared to baseline scores, patients at the 4-month follow-up demonstrated significant improvements in menopausal symptoms and sexual functioning, suggesting that an intervention including multiple strategies (i.e., behavioral strategies and education) can improve breast cancer survivors' sexual functioning. In review articles published by the proposed research team discussing sexual problems and treatment of women following cancer, multiple strategies are recommended (e.g., Krychman et al, 2004; Schover, 2006) including education and behavioral modifications (e.g. use of dilators).

Since research on psychosocial interventions for male RC survivors is similarly scarce, our work with prostate cancer survivors has also informed the current intervention. Prostate cancer is the most common cancer diagnosis in men, and prostate cancer treatments can have a significant impact on sexual functioning. In a recent intervention trial by Schover (consultant) and colleagues (Canada et al., 2005), 51 prostate cancer survivors attended 4 sessions that were designed to address education on prostate cancer, sexual function, options for ED, and sexual communication. The intervention emphasized cognitive behavioral techniques, and detailed handouts and behavioral exercise instructions were sent home with participants. Participants completed assessments at baseline (pre-intervention), 3-months, and then 6-months. At baseline, 31% of the men were using ED treatments, and this number significantly increased to 55% at the 3 month follow-up and 49% at the 6-month follow-up assessment. The International Index of Erectile Function (IIEF) scores showed improvement at the 3-month assessment point. This included total IIEF scores as well as domains for erectile function, intercourse satisfaction, and overall sexual satisfaction. In addition, there was a relatively high drop-out rate in the study, as

39% of the subjects did not complete all treatment sessions. The authors suggest that “booster sessions” be used to help consummate the gains achieved in the therapy.

In addition to the problems experienced by other survivors, rectal cancer survivors may have unique concerns. For example, survivors may need help managing a stoma and its impact on sexuality. For those CRC survivors with a stoma who wish to have sexual intercourse, sexual positions that place no weight on a scar or ostomy can be explored. In addition, for patients with colostomies or ileostomies, the United Ostomy Association prints pamphlets related to resuming sexual activity. As reviewed by Fleming, 2002, CRC survivors, particularly women, have been understudied. However, many of the strategies/information used with other cancer survivors can be included in an intervention for CRC survivors along with specific strategies such as education about how the treatment of rectal cancer uniquely affects sexuality. The research conducted by members of the proposed team and others, provides guidance as to the content of the proposed intervention, CSI-SH (e.g., Schover intervention for breast and prostate (reviewed in the preliminary studies). Thus, CSI-SH is based on prior sexual health interventions, and also includes strategies specific for rectal cancer survivors and is informed further by cognitive processing theory.

Guiding Theoretical Models: In addition to research on sexual health and the team’s past research and clinical experience, the proposed research is theoretically guided by DuHamel and colleagues’ work on applying to cancer a cognitive processing model for adjustment following adverse/traumatic events. DuHamel and her colleagues (DuHamel et al., 2004; Manne et al., 2000; Manne et al., 2002; Manne et al., 2003; Kim et al., 2004) have recently applied this model to understanding the adjustment of mothers of pediatric cancer patients as well as breast cancer patients. This model proposes that when a traumatic event occurs, it can shatter a person’s beliefs about himself/herself and the world. For example, prior to the event a woman may think that the world is a just place and that a strong person could not be victimized. After such an event she may come to think that the world is not just and that she was weak for allowing this to happen. In addition, some people may suppress or avoid thinking about the event, which can lead to an increase in distress such as intrusive thoughts and further avoidance. For example, some men view their ED as a traumatic loss of their “manhood,” and avoid reminders or cues to sexual situations as these situations are distressing, bothersome, lower their self-esteem, and only remind them their “failures.” For both men and women, this type of avoidance often causes withdrawal from sexual contact and intimacy. Ironically, trying to suppress thoughts and avoid reminders can actually lead to an increase in intrusive thoughts and avoidance, impeding psychological adjustment (Lepore et al., 2003; Sundaram et al., 1997).

Much of the work addressing sexual problems in cancer patients and cancer survivors can be considered within this framework – supporting both behavioral and cognitive components for interventions. For example, an early intervention by Robinson et al. (1999), which taught women with gynecological carcinoma treated with radiotherapy how to use vaginal dilators and lubricants as well as how to perform Kegel exercises, found that women who received the intervention had less fear about cancer and sexuality. The results of the study were consistent with a cognitive processing model of adjustment. The cognitive processing model was originally conceived to understand adjustment and stress reactions (i.e., PTSD) after the experience of trauma (i.e. shooting, rape) (Creamer et al., 1990; Creamer et al., 1992; Brewin, 1996) and has been applied by DuHamel and colleagues to coping with cancer (DuHamel et al., 2004; Kim,

DuHamel, Valdimarsdottir, & Bovbjerg, 2004). Based on this model, the therapist in CSI-SH helps the women to assimilate an event into her world view or accommodate her world view to match the event. The proposed intervention may facilitate cognitive processing through counseling, helping a woman to not push fears and intrusive thoughts out of her mind, but rather to talk about them, record them, and ultimately confront them. Discussing the meaning of cancer and its treatment may promote assimilation of cancer treatment and sexual functioning into the woman's world view and reduce her fears. Strategies such as talking about the use of vaginal lubricants and identification of cognitive distortions may normalize the women's experiences, lead to fewer unhelpful thoughts, and reduce cancer specific distress (e.g., intrusive thoughts). Cognitive processing can also involve processing through social interactions. For example, Manne, DuHamel and colleagues (Manne et al., 2000; Manne et al., 2002; Manne et al., 2003) have discussed that talking about an event with a supportive other can facilitate processing. (This has also been studied by other investigators such as Lepore et al., 2000). In the case of CSI-SH, having the survivors use both behavioral strategies (e.g., lubricants, guided imagery, medical treatments and sensate focus) and cognitive processing strategies (challenging dysfunctional thoughts, reducing avoidance, talking with a therapist) may facilitate sexual health as well as psychological adjustment.

In addition to cognitive processing theory, the work of Andersen and colleagues (Anderson et al., 1994, 1998, 1999) also provides some theoretical guidance to our efforts. Her work has indicated the importance of sexual self-concept, or schema in sexual functioning. She and her colleagues define a sexual self-schema as a cognitive generalization about sexual aspects of the self that: a) derived from past experiences, b) manifest in current experiences, c) influential in the processing of sexually relevant social information and d) a source of guidance to future sexual behavior. Andersen and colleagues found that women differ in their sexual self-concepts and hypothesized that having a positive view of the sexual self may be associated with sexual function. They found support for this notion in a study of gynecological cancer patients. After accounting for prior sexual frequency, extent of disease treatment and menopausal status, self-schema was associated with sexual behavior and was also associated in separate analyses with sexual responsiveness (Anderson et al., 1994). The same research team also studied this concept in men, and found that men high on measures of sexual self-schema had less self-inconsistent negative valance words in comparison to those who were lower on sexual self-schema (Andersen et al., 1999). Based on these findings, Anderson has suggested that a schema-guided intervention could enhance sexual self-concept, arousal and behavioral repertoire and lower distress. In the current proposal, we will investigate men's and women's sexual self-schema and explore changes based on CSI-SH.

PRELIMINARY STUDIES

The proposed study reflects our longstanding interest in sexual health and interventions that facilitate quality of life of cancer survivors. Our previous research demonstrates this team's success in working on research that: uses mixed methods (qualitative and quantitative), reduces cancer patients' and cancer survivors' symptoms of distress and improves their QOL, addresses the sexual functioning of cancer patients and cancer survivors, and investigates the sexual and QOL needs of rectal cancer survivors. The team's research expertise in these areas, as well as their clinical work supports the feasibility of the proposed study. The proposed study expands on this work by providing data regarding CSI-SH, a novel intervention designed to match the needs and preferences of rectal cancer survivors

Cultural Sensitivity in Colorectal Cancer Screening in African Americans (AAs):

DuHamel's work includes promoting health behaviors. For example, along with Jandorf and colleagues at MSSM, she has obtained NIH funding (CA104130) to increase Colorectal Cancer screening in AAs. CRC mortality is greater for AAs than for Caucasians. This problem is currently examined in an ongoing randomized clinical trial (RCT) of a stage matched, culturally sensitive intervention to increase participation in CRC screening of AAs age 51 years or older. For this study, as well as others studies (e.g., Erwin et al., 2004; Siporin et al., 2005), DuHamel, Jandorf and their colleagues have used the method of intervention development informed by focus groups. This research supports DuHamel and colleagues' ability to design interventions targeted to the needs of the population.

Barriers to Pain Management: DuHamel and her colleagues have developed a pain communication skills intervention to improve patient-physician communication. Among breast cancer patients they found that of those eligible (e.g., either English or Spanish speaking), 76% agreed to participate and there was less than a 10% attrition rate over 12 weeks (Smith et al., 1999). This study supports the team's experience in recruiting and retaining participants in intervention studies.

Improving Sexual Functioning Among Prostate Survivors: In addition to the recent (2006) intervention with breast cancer survivors (See Background), Schover and colleagues [Canada et al., 2005) conducted a counseling intervention aimed at improving levels of sexual functioning for both the survivor of prostate carcinoma and his partner. Couples were randomized to attend four sessions of counseling together or to have the male attend alone. The sessions included education on prostate carcinoma and sexual function and options to treat erectile dysfunction (ED) in addition to behavioral homework. Attendance by the partner did not affect outcomes. Males completing the intervention demonstrated reduced distress and better sexual function. Females in the intervention showed improved global sexual function at 3-month follow-up. The results of this brief pilot counseling intervention demonstrated gains in sexual function and satisfaction and increased utilization of treatment. We have created the draft manual for the proposed intervention based on the team's clinical, surgical and research experience including this work of Schover. To the best of our knowledge, the proposed CSI-SH intervention is the first sexual health intervention tailored for female survivors of rectal cancer.

ED Bother in Men Following Definitive Treatment for Prostate Cancer: Nelson, Mulhall and their colleagues (Nelson, Roth, & Mulhall, 2007) have expertise in the assessment and treatment of male cancer patients with sexual dysfunction. In one study, 231 patients completed the IIEF-Erectile Function Domain (EFD) questionnaire and a validated questionnaire designed to assess sexual bother associated with ED. These assessments were completed at baseline, and then every 3 months to 24 months postoperatively. Sixty-two percent had radical prostatectomy and the remainder had radiation therapy. Bother scores significantly increased from baseline to 24-month follow-up. Bother scores at 24 months were associated with baseline EFD scores, 24-month EFD scores, and the change in EFD scores between baseline and 24 months. Forty-four percent of men reported a high bother score at 24 months (as compared to 20% reporting high bother at baseline), and bother was evident for men with and without ED. Thus, even men who report "good" erections after surgery are bothered by their erectile functioning. In the proposed study we will explore if the intervention reduces sexual bother.

Prevalence of psychiatric illness in oncology sexual health population : Carter and her colleagues (e.g., Amsterdam, 2006) have expertise in the assessment and treatment of cancer patients with and without psychiatric diagnosis. In one study, a chart review was performed of patients who attended the Sexual Health Program at Memorial Sloan-Kettering Cancer Center. Of the 190 patients, the median age at initial visit was 48 years (range 22-76) and the majority of patients were menopausal (87%). The most common cancer diagnosis was breast cancer. The most frequently encountered sexual complaints were dyspareunia (65%), vaginal dryness (63%), hypoactive desire disorder (46%), and orgasmic dysfunction (7%). At initial presentation, 52 patients (27%) reported having a prior or concurrent psychiatric diagnosis and 72 (38%) were taking an anti-depressant and/or an anxiolytic. This study illustrates that psychiatric conditions are commonly encountered in the oncology population as are the medications to treat them. Because it is well established that these medications are often implicated in sexual dysfunction, in the proposed R21 study we will assess and monitor participants' medications. Although this study illustrates the teams experience with the treatment of sexual problems, the particular problems, preferences and needs of rectal cancer patients have not been systematically assessed or addressed.

Evaluating Bowel Function After Sphincter-Preserving Surgery (SPS) for RC: Temple and colleagues developed an instrument to evaluate bowel function after sphincter-preserving surgery (SPS) (44). Patients who underwent sphincter-preserving surgery between 1997 and 2001 at MSKCC were identified and of the 274 eligible (e.g., over 18 years of age, diagnosed with Stage 1-111 RC, had SPS at MSKCC, and had bowel continuity at time of survey completion), 198 participated in one of the pilot studies that involved examining the test-retest reliability of an instrument (Temple et al., 2005). For one study, 129/184, or 70% responded, with 127 having usable data (two people had much missing data). Of the 127, 67% were male. Participants completed the survey and QoL instruments: EORTC QLQ-C30 – European Organization for the Research and Treatment of Cancer – Quality of Life Questionnaire 30 (Aaronson et al., 1993) and EORTC QLQ-CR38 – EORTC Colorectal Cancer module (Sprangers, te Velde, & Aaronson, 1999). Results indicate that patients who undergo surgery for RC experience worse function if they are treated with radiation. Patients with better function had higher scores on many of the QoL instruments. Temple has subsequently evaluated the role of EORTC-CR38 in identifying patient with functional impairments (Neuman et al., 2007). In addition, Temple and colleagues are collecting data on QoL and sexual functioning of patients who underwent SPS procedures for RC. Using the same measures as proposed in the current trial, (e.g., EORTC QLQ-C30 [Aaronson et al., 1993] and EORTC QLQ-CR38 – EORTC [Sprangers et al., 1999]). Temple and colleagues have recruited 103 RC patients with SPS (57 male patients) (85% of eligible patients) in last 14 months prior to surgery into a prospective IRB protocol. This study illustrates Temple's ongoing research in the functioning and QOL of RC patients. In the current study we don't require that survivors had SPS.

Cognitive Behavioral (CBT) Intervention to Reduce Stress Symptoms in survivors 1-3 years post HSCT:

DuHamel, Redd, and colleagues are currently conducting a multi-site NIH funded clinical trial that is evaluating a 10 session CBT telephone based psychological intervention designed to

reduce cancer survivors' stress symptoms after hematopoietic stem cell transplant. To date, of those who are approached to be in the study, 89% agree to be pre-screened for the trial (e.g., investigation of patients who are 12-36 months post transplant, English speaking), of those who are prescreened and are eligible, 85% agree to be in the study, and 33% are indicated to have distress/stress symptoms (e.g., PTSD) qualifying them for the RCT to reduce these symptoms (a CBT intervention + UC or UC only). All assessments for this trial are conducted over the telephone as proposed for the assessment procedure in this protocol. DuHamel is the Co-PI of the multi-site study and was the PI at MSKCC. This study supports the use of telephone assessments as well as our ability to recruit survivors to an individually focused intervention trial.

Information gained from this pilot R21 study will inform the use of interventions to increase sexual health among female RC survivors. This study has high translational promise. If CSI-SH is found to be efficacious, a larger subsequent trial can be planned, and in the future, it could be easily adopted into clinical care.

4.0 OVERVIEW OF STUDY DESIGN/INTERVENTION

4.1 Design

This is a two year randomized clinical trial examining the feasibility, tolerability, acceptability (including adherence) and efficacy of an intervention designed to improve sexual functioning of survivors of rectal cancer.

We have completed enrollment of female patients and are currently collecting follow up data. Recruitment for male patients is ongoing. Male participants will now be randomized in a 3:1 ratio to either the intervention condition (n = 66) or the control condition (n = 44).

Prior to recruiting to the randomized trial (intervention), we will conduct six qualitative interviews for men and hold at least one focus group (out of three total) to obtain feedback on the content of the intervention. If the survivor is interested he will be scheduled for an individual interview or be offered three possible focus groups dates which will vary in time and day. If they are going to participate in an individual interview, they will be called the day before and reminded of the time and date. Three focus groups with up to 8 participants each will be conducted. Individual interview participants and focus group participants will be reimbursed \$20 for parking (will cover discount parking at MSKCC) and receive \$20 as a small incentive for their individual or focus group participation. Individuals who participate in either a focus group or a qualitative interview will not be randomized. In collaboration with members of the research team, the individual interview will be analyzed by Ms. Shuk who, as illustrated in her biosketch, has contributed to multiple qualitative studies during her tenure at MSKCC. We think that by using these two qualitative methods we will get more range and depth of information (individual interviews) as well as a discussion of shared thoughts and beliefs (focus groups). These focus groups and individual interviews will help identify men's preferences for the means and modes of information delivery, enabling us to develop an effective intervention tailored to their needs and preferences. We will also ask them for their preferences for the name of the intervention although for the current proposal we have labeled it CSI-SH-M. Perhaps most importantly, the focus groups and individual interviews will allow us to investigate barriers and promoters that would impact men's initiation and retention in the RCT study phase. This methodology in the

social sciences is a systematic process for evaluating qualitative data and formulating theoretical propositions emerging from data [52]. Men who participate in the focus groups or individual interviews will be 2 or more years post treatment.

We have concluded the qualitative phase for male participants. In total, we enrolled 20 men to either the focus groups or qualitative interviews.

We originally were recruiting from two sites: Memorial Sloan-Kettering Cancer Center and Mount Sinai School of Medicine). Mount Sinai site was closed on 10/25/2010 due to low recruitment, and we are currently only recruiting from MSKCC.

Using a stratified block design, grouping patients based on 1) presence or absence of a stoma, 2) if patient has chemotherapy or not, and, for women only, 3) if patient is post-menopausal or not. Participants will be randomly assigned to receive either usual care (UC) or Cancer Survivorship Intervention-Sexual Health (CSI-SH). Within each stratum, participants will be randomized with equal probability into either the treatment condition or the standard care condition.

The Project Coordinator (PC) and the Research Study Assistant (RSA) will conduct all telephone survey assessments. Training will include: 1) five hours of didactic lectures about rectal cancer and treatments, 2) training in conducting participant interviews, 3) regular mock interviews to ensure standardization of measures throughout the study. Research study assistant will be blinded to the treatment condition. Dr. Nelson or an unblinded research team member will keep the treatment assignment information and will inform study participants of the condition as well as work with the RSA to inform them when study assessments need to be administered. Dr. DuHamel's previous studies kept RSAs blinded to the treatment condition. We are planning to follow the same procedure with this trial. Research assistants will consent patients and administer questionnaires. Study PI will keep a log of scheduled assessments without reference to the treatment arm.

The RSA, who will be blinded to the treatment condition of the participants, will be responsible for data collection, which takes place prior to the intervention and then approximately four and eight months post-baseline. The timing of these assessments is based on prior research (e.g. 4 months in Ganz, et al., 2000). Please see section 6.0 for a more detailed discussion of recruitment methods.

All assessments will be audio taped. A trained staff member will review 10% of the interviews to ensure consistency, quality control and reliability coding. If the PC or RSA drifts from study procedures, this will be discussed during their ongoing supervision with PI or co-PIs and future monitoring will increase.

Dr. Leslie Schover at MD Andersen Cancer Center, Dr. Megan Fleming at Albert Einstein College of Medicine and Lina Jandorf at Mount Sinai School of Medicine are consultants on this study. Ms. Jandorf will conduct and summarize the focus group and anonymous interview findings. She will continue to assist in the study by reviewing study materials. Ms. Jandorf or Dr. Schover will also participate in treatment fidelity monitoring, as well as in manuscript preparation Dr. Schover will provide expertise in the types of sexual problems typical after

cancer treatment and in the assessment of cancer-related sexual function, as well as in development of appropriate interventions). Dr. Schover will help revise the intervention based on feedback provided by participants who are post treatment for rectal cancer. She will also facilitate the intervention training and monitoring of its process as well as provide ongoing consultation throughout the course of the study. She will participate in dissemination of the results by manuscript preparation. Dr. Fleming will review the materials prior to the study initiation, and will work with Nelson, Carter, Schover, and other members of the team to revise the study materials as needed. She will provide ongoing consultation with regard to the particular issues that may face female survivors of colorectal cancer and any new strategies for increasing their sexual functioning and quality of life.

4.2 Intervention

CSI-SH was developed by the research team and involves four 1-hour individual sessions with three additional telephone booster/review sessions provided in between the four sessions. Sessions can be completed in person or conducted over the phone. Sessions one and two will focus on rehabilitation techniques and tools will be provided and discussed with participants during these first two sessions. This intervention is based on ongoing research on the sexual problems and QOL among rectal cancer patients and survivors, the team's clinical experience, including sexual interventions developed and implemented by collaborator Dr. Leslie Schover, and feedback provided by rectal cancer survivors. Each counseling session lasts about one hour and will be conducted by a trained therapist (Dr. Carter, Dr. Nelson). The sessions also include homework assignments that will be reviewed at the subsequent session. Topics covered in the sessions are reviewed in the booster telephone calls with the participant the following week. These telephone calls serve as a practice reminder for the participant as well as to help the participant reduce any barriers to implementing the session strategies and/or homework. Additionally, participants will be reminded by either telephone or mail of their next appointment to promote adherence to the study. While the current protocol is designed as a single treatment for men and women, with a matched session and homework structure for all participants, session content is appropriately tailored for gender.

Both men's and women's interventions begin with initiation of the collaborative relationship between the patient and therapist and a review of the procedures of the CSI-SH intervention, as well as an overview of the sexual rehabilitation/health process and goals for the intervention. This will include helping RC survivors understand the phases of sexual response and common changes in sexuality that patients may experience after RC treatment. For example, men will be provided with education on why and how erections or ejaculations may be impacted by treatment, while women will be informed about positions that may be uncomfortable or painful without the rectum to cushion the vagina during intercourse. In the first stage of the intervention, the therapist will also conduct a sexual evaluation of the participant and discuss health solutions (e.g., vaginal lubricant and Kegel exercises for women, and planning for ED treatments or coping with the presence of a stoma for men).

Throughout treatment, all participants will be provided with simple strategies to improve sexual function (or sexual rehabilitation) and expand their sexual repertoire. For example,

both men and women will be taught Sensate Focus exercises (i.e., sensual, non-genital touch, later followed by sexual touch that includes genitals, but not to intercourse or orgasm). In addition to providing these behavioral strategies, the therapist will teach methods for enhancing communication about sexuality in cancer survivorship, e.g., how to talk about cancer-related emotions, how to talk about sexual problems, and how to talk about sexual issues (particularly within intimate partner relationships). The therapist will also review information about available medical and/or surgical resources. For men, emphasis will be placed on selection of an ED treatment, and identifying potential barriers to using this treatment. For women, resources discussed may include the ACS Sexuality and Cancer Booklet and/or referral to MSKCC General Gynecology Services.

Based on the strategies and resources discussed, as well as participant willingness to try certain strategies, a treatment plan will be developed with each survivor. Subsequent sessions will begin with an exploration of the patient's behavior and experiences, adherence to the recommended strategies, and discussion of personally feasible ways to implement intervention strategies. All participants will be given homework assignments each session, to be reviewed in the following session. For both men and women, homework will include practicing sexual rehabilitative techniques (including Sensate Focus), identifying potential barriers to treatment, generating possible alternatives, and taking steps to improve communication. For men, an important aspect of the homework is also to assess willingness to try medical ED treatments, and to develop a plan to overcome obstacles to attaining this treatment. As part of the homework, men will complete an ongoing caring diary (i.e., they are asked to do 3 small things every day for 5 days that shows they care for their partner). In-session homework review will serve as an opportunity to track participant progress, assess patient comfort level with the material, and attempt to deal with any reluctance to continue the intervention. For men, reviewing efforts to comply with ED treatment can also facilitate discussion of enjoying sex without firm erection, rekindling lost desire, and feeling pleasure despite ED, identifying negative beliefs about erection problems and challenging these beliefs (e.g., cognitive restructuring). At the end of each session participants will make an appointment for the booster/troubleshooting call for the following week. Each booster call will also be reviewed in the following counseling session. Although every effort will be made to complete the booster session in between counseling sessions, if the patient is unavailable to complete the booster calls they may be skipped.

Treatment will end with a review of 1) the participant's progress with sexual rehabilitation techniques including the homework and the post-session booster/troubleshooting calls, 2) partner or possible future partner issues, 3) specific fears and tips (e.g., for ostomy issues for women and stoma issues for men), 4) the participant's feelings and thoughts about the intervention, and 5) strategies to continue with sexual health in survivorship (and potential barriers to continued ED treatments for men). The therapist will thank the participant for his or her contribution to the study. At this time, participants will be asked to sit in a separate room and complete the Satisfaction with Intervention Scale and the Working Alliance Inventory before they leave the building. The interventionist/educator will complete the Interventionist Satisfaction with CSI-SH. The Principal Investigator will keep the intervention

assignments in a separate data set to ensure that the RSA and PC do not have access to information regarding who received the intervention.

Participants randomized to the Usual Care arm will receive standard care. For women, this is defined as the care that participants who are not in the intervention receive; we will ask these participants what psychosocial care they are receiving to track usual care. For men, “usual care” will consist of a standardized referral to the men’s Sexual Medicine Program at MSKCC and written information in the form of the American Cancer Society (ACS) booklet on Sexuality after Cancer. Individuals randomized to Usual Care will not receive any additional counseling sessions from the study interventionists until they are done with the follow up interviews and then it will be offered to them. Follow up questionnaires will assess all study participants at 4 and 8 months after baseline.

Additionally, participants be asked to complete *Assessment of UC, Mental Health Care Utilization, Medications, and Sexual Health Strategies (HCU)* at baseline and at the completion of the study (4 months follow up) evaluating whether participants in the usual care arm seek other counseling (e.g supportive for sexual issues, psychological) from a variety of sources including nurses, social workers, outpatient psychiatry clinic, etc.

All sessions will be conducted by a qualified mental health professional at Master’s or PhD level with a background in the social sciences, social work, psychology and/or psychiatry.

Training and supervision of the sexual health education sessions will be conducted by the study investigators (Chris Nelson, PhD). All study interventionists will be provided with a treatment manual describing the intervention in detail. To reinforce standardized delivery of the educational sessions, separate, routine dyadic supervision sessions will be led by the study investigators.

5.0 CRITERIA FOR SUBJECT ELIGIBILITY

Assessments given to the participants were designed and validated in English and are not currently available in other languages. Translation of questionnaires into other languages would require reestablishing the reliability and validity of these measures. Therefore, participants must be able to communicate in English to complete the tests.

5.1 Subject Inclusion Criteria

- At least 6 months post radiation and/or surgery for stage I-III rectal adenocarcinoma or rectosigmoid cancer with an anastomosis at 15 cm or below and completed treatment.
- At least 6 months post radiation and/or chemotherapy for anal cancer.
- Have no evidence of disease or recurrence.
- For women: Indicate moderate satisfaction or below on their overall sexual life (a score of “4” or lower on the question “Over the past 4 weeks, how satisfied have you been with your overall sexual life?”)

- For men: indicate a score of “3” or lower on the question “How would you rate your confidence that you could get and keep an erection” for men) and a score of “2” or higher on the question “How much does this problem bother you?”
- In the judgment of the consenting professional, able to communicate in English well enough to work with English speaking interventionists and complete the study assessments.
- Age 21 years or older.

5.2 Subject Exclusion Criteria

- Significant cognitive or psychiatric disturbance sufficient, in the investigator’s judgment, to preclude participation in a psychotherapeutic intervention.
- Are actively participating in protocol 06-151.
- Participated in focus group or qualitative interview.

6.0 RECRUITMENT PLAN

Recruitment Plan (with Limited Waiver of Authorization)

The Research Study Assistants will review the colorectal medical and surgical team’s clinic lists, as well as a DATALINE generate list to identify possible participants. He/she will review the medical record and speak or e-mail with the members of the clinic staff to confirm eligibility. If the survivor is ineligible for the research study, the research staff will destroy all information collected on the patient during the initial conversation and medical records review, except for any information that must be maintained for screening log purposes. If a survivor is eligible, the Research Study Assistant will approach the prospective participant in person at her next clinic visit, or send an invitation letter as outlined below.

During the initial conversation between the investigator/research staff and the patient, the patient may be asked to provide certain health information that is necessary to the recruitment and enrollment process.

Participants may be recruited in one of the following ways as described below:

- 1) During a outpatient clinic visit
- 2) Via a study introduction letter
- 3) Doctor referral, attendings in each respective clinic may also notify the research team of patients they feel may be appropriate for the study.

The research staff will mail an introductory letter to eligible survivors describing the study along with an informed consent form and a study flyer. Physicians will be offered the opportunity to include their signatures on the introductory letter. The outgoing letters may be co-signed by both the physician and the PI or may only contain the PI signatures.

The letter will provide a telephone number for the patient to call if they wish to express non-interest in study participation.

Within one to two weeks of mailing the introductory letter, the RSA will call potential study participants to introduce the study and invite eligible patients to participate. The research assistant will record his or her number of attempts to call eligible patients. If the patient is not available, the research assistant will leave a message with his/her name and phone number indicating he/she is calling to follow up on a letter that was mailed to the participant about research study.

Survivors who are not interested in participating will not be contacted again. Participants who have expressed interest in the study, but who cannot be reached by telephone to complete participation, will be mailed a letter indicating they should contact the research assistant if they are interested in participating in the study. In the event that we have made several unsuccessful phone call attempts to prospective participants, we will mail a letter to them which indicates that they should contact the RSA if they are interested in participating in the study.

After the study is introduced, if the potential participant is interested, a member of the research staff will ask female patients one question (taken from the FSFI) which assesses sexual satisfaction. If the prospective participant's score is a 4 or below (indicating moderate satisfaction or below) the patient will be invited to take part in the study. Male patients will be asked three screening questions to determine their eligibility status: 1) Confidence in obtaining and maintaining an erection (taken from the IIEF); and 2) How bothersome their sexual problem is. Male patients who score a 3 or below on question 2, and a 2 or above on question 3 will be invited to take part in the study. A research study assistant, or one of the investigators who is a consenting professional, will obtain informed consent.

If the survivor expresses interest in the study, and is eligible, the RSA will review the consent form and ask the participant to provide verbal consent over the telephone. Then participants will be called and provided the opportunity to have any additional questions answered and will be asked to complete the baseline interview over the telephone. Participants will be provided with a copy of the assessment battery so they have the option to follow along with the RSA during the phone interview.

For participants who are approached during their outpatient appointment, the RSA will introduce the study, assess the patients interest and obtain written consent.

The screening process for the protocol requires administration of screening questionnaire. In following the Code of Federal Regulations Title 45, Part 46, Subpart A, which states that an IRB may waive the requirement for an investigator to obtain a signed consent form for some or all subjects if it finds that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context, a signed consent a signed consent may not be required for this study. We request to waive consent, in accordance with these regulations, to conduct the screening to identify whether the patient is eligible will not be required for this study.

The study RSA is kept blinded to the participant's treatment condition. Once the participant is randomized, the participant's treatment assignment will be accessed by the study Coordinator and the PI. Participants will be notified of the arm assignment via phone, mail, or e-mail (e-mail).

Participants will only be contacted via e-mail if it is specifically requested. All e-mails will be sent securely using the MSKsecure function (Appendix O).

A consenting professional will consent the patients and administer the questionnaires. All assessments will be audio taped. The RSA will also keep track of the enrolled participants and will provide a list to the investigators during the weekly team meetings. For each of the three assessments (Baseline, 4 Month Follow-up and 8 Month Follow-up) study participants will receive \$10 for each assessment and those in the CSI-SH arm will receive reimbursement for transportation for each face-to-face session. (The Bristol Garage at 300 East 56th street offers special rates to Memorial Sloan-Kettering patients. The Psychiatry Counseling Center is in walking distance of the garage and Memorial Sloan-Kettering provides round-trip jitney service to and from the garage every 20 minutes. The cost for parking for up to four hours is \$17. The Mount Sinai Visitors Parking Garage at 99th Street between Madison and Park Avenue charges \$7.75 per hour and is a walking distance from the East Building at Mount Sinai.) Those patients who are randomized to the UC arm will be offered the intervention after their study participation has been completed. All components of the study will be timed to correspond with medical appointments when possible. Reasons for ineligibility and refusal to participate in the study will be recorded and reported in aggregate format.

For the current study, we plan to recruit African American (AA) and Hispanic/Latino patients to achieve representation similar to the New York City-northern New Jersey-southern Connecticut metropolitan statistical area population of the United States (US Census 2000). Based on the 2000 U.S. Census, the distribution of minority individuals in this metropolitan statistical area is: 59% white, 17% Hispanic/Latino, 15% Black/African American, 7% Asian-American, and 2% other racial/ethnic categories. All minority patients will be over-sampled to assure representation equal to the distribution of minorities in the NYC region. This recruitment goal is consistent with the method of non-proportional quota sampling (e.g., Morrow et al. 2007), which is often used to assure that smaller minority groups are adequately represented in a sample. Non-proportional quota sampling is particularly suitable for preliminary studies because it minimizes sampling bias.

In most cases, the initial contact with prospective participants will be conducted by either the treatment team, investigator, or the research staff working in consultation with the treatment team. The recruitment process outlined above presents no more than minimal risk to the privacy of the patients who are screened and minimal PHI will be maintained as part of a screening log. For these reasons, we seek a (partial) limited waiver of authorization for the purposes of (1) reviewing medical records to identify potential research subjects and obtain information relevant to the enrollment process; (2) conversing with patients regarding possible enrollment; (3) handling of PHI contained within those records and provided by the potential subjects; (4) maintaining information in a screening log of patients approached.

7.0 ASSESSMENT/EVALUATION PLAN

Medical Chart Review: Medical charts will be reviewed at three time points. First, they will be reviewed for eligibility. Second, at baseline to provide medical and treatment information (e.g., radiation and its timing; interval from surgery, surgical factors such as level of anastomosis,

method of reconstruction, permanent stoma), general medical information, medications or hormone replacement status as well as supplement the participants' self-reported usual care. Lastly, they will be reviewed at 8-month follow-up assessment, to provide documentation of any change of information as well as supplement the participants' self-reported UC. In addition to the medical information gathered in the chart review, women's menopausal symptoms (as measured by the menopause checklist) can serve as possible covariates. In addition, participation in prior RC psychosocial research (e.g., protocol 06-151) will be recorded and may serve as a possible covariate.

All participants will complete the following measures at baseline, approximately four months after baseline, and approximately eight months after baseline:

Socio-demographic Information: This form will query demographic data (race, education level, age, employment status, occupation, and marital/partner status). In this pilot RCT, after the baseline assessment, a short version is used in the follow-up assessments to note any changes. (Appendix C, 5 minutes).

Preference for Intervention Delivery, (Cohall et al., 2004): 13 items adapted by DuHamel and colleagues for intervention research with adults will be used to measure participants preferred sources and modes of sexual health information. (Appendix C, 3 minutes).

Impact of Events Scale-Revised (IES-R), (Weiss & Marmar, 1997): The IES-R was developed by Daniel S. Weiss and Charles R. Marmar in 1997 to parallel the DSM-IV criteria for PTSD. The IES-R is similar to the IES in that it is a self-report measure designed to assess current subjective distress for any specific life event. The IES-R has 22 items that tap hyperarousal symptoms, intrusive thoughts and avoidance. Respondents rate each item in the IES-R on a scale of 0 (not at all), 1 (a little bit), 2 (moderately), 3 (quite a bit) and 4 (extremely) according to the past 7 days with regard to cancer and its treatment.

Reliability: In their study of four different population samples, Weiss and Marmar (1997) reported that the internal consistency of the 3 subscales was found to be very high, with intrusion alphas ranging from .87 to .92, avoidance alphas ranging from .84 to .86, and hyperarousal alphas ranging from .79 to .90 (Briere, 1997). Test-Retest Reliability: Test-retest data were available for 2 of the samples in the Weiss and Marmar (1997) study. Data from sample 1 (n = 429) yielded the following test-retest correlation coefficients for the subscales: intrusion = .57, avoidance = .51, hyperarousal = .59. From sample 2 (n = 197) the correlation coefficients were considerably higher: intrusion = .94, avoidance = .89, hyperarousal = .92. It is believed that the shorter interval between assessments and the greater recency of the traumatic event for Sample 2 contributed to the higher coefficients of stability.

Validity: Criterion (or Predictive) Validity: Weiss and Marmar noted that the hyperarousal subscale has good predictive validity with regard to trauma (Briere, 1997). The intrusion and avoidance subscales, which are original IES components, have been shown to detect change in respondents' clinical status over time and detect relevant differences in the response to traumatic events of varying severity (Weiss and Marmar, 1997, Horowitz, Wilner, and Alvarez, 1979). Content Validity: Not available for the hyperarousal subscale. The intrusion and avoidance subscales which are originally IES

items had high endorsements of up to 85% (Horowitz, et al 1979). Construct Validity: Weiss and Marmar (1997) utilized the item-to subscale correlation with that item removed from the subscale generated by the standard alpha coefficient analyses. These were then compared to the cross-subscale Pearson correlations. The results showed that only 1 item ("I had trouble falling asleep") showed a stronger relationship between it and a different subscale. The corrected correlation of this item with its assigned hyperarousal subscale was .71, and its correlation with the intrusion subscale was .79. Nineteen items showed a correlation with their assigned subscale that was higher than with the other subscales; and 2 items ("I had trouble staying asleep," and "I avoided letting myself get upset when I thought about it or was reminded of it") showed a correlation that was equal. The explanations given by Weiss and Marmar (1997) for these results are that the 2 sleep items are very highly correlated, driving a relationship between them in terms of intrusion and hyperarousal; and as to the equal relationship of the avoidance item with the avoidance and intrusion subscales, this may have occurred because the presentation of the thought or the reminder invokes intrusion, and the not dealing with it invokes avoidance. (Appendix C, 5 minutes).

The Brief Symptom Inventory (BSI), (Derogatis & Melisaratos, 1983): consists of 53 items covering nine symptom dimensions: Somatization, Obsession-Compulsion, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic anxiety, Paranoid ideation and Psychoticism; and three global indices of distress: Global Severity Index, Positive Symptom Distress Index, and Positive Symptom Total. The global indices measure current or past level of symptomatology, intensity of symptoms, and number of reported symptoms, respectively.

Reliability: The authors report good internal consistency reliability for the nine dimensions, ranging from .71 on Psychoticism to .85 on Depression. Good internal consistency reliability is supported by several other independent studies (Croog et al., 1986; Aroian & Patsdaughter, 1989 in Derogatis, 1993). No alpha reliability is reported for the three global indices. Test-retest reliability for the nine symptom dimensions ranges from .68 (Somatization) to .91 (Phobic Anxiety), and for the three Global Indices from .87 (PSDI) to .90 (GSI).

Validity: Correlations between the BSI and the Wiggins content scales and the Tryon cluster scores from the MMPI ranged from .30 to .72 with the most relevant score correlations averaging above .50 (Conoley & Kramer, 1989; Derogatis, Rickles, & Rock, 1976 in Derogatis, 1993). Factor analysis results confirmed the a priori construction of the symptom dimensions. In addition, correlations between the BSI and SCL-R-90 were .92 to .99 (Derogatis, 1993). (Appendix C, 8 minutes).

European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire (**EORTC QLQ-C30**) and EORTC Colorectal Cancer-Specific Quality-of-Life Questionnaire Module, (**EORTC QLQ-CR38**), (Engel et al., 2003, Temple, 2005): The EORTC QLQ-C30 and CRC 38 will be used to assess QOL.

EORTC QLQ-C30 is a well-validated instrument that assesses health-related

quality of life in cancer patients. It is composed of 30-items, which factor into scales that evaluate physical functioning and role functioning, as well as emotional, social, and cognitive functioning and global QOL. Three symptom scales measure fatigue, pain, and emesis, while six single items assess financial impact, dyspnea, sleep disturbance, appetite, diarrhea, and constipation. Pearson correlation coefficients demonstrating test-retest reliability for the QLQ-C30 ranged from .63 - .91 depending on the subscale (Hjermstad et. al., 1995). Validity was assessed as inter-scale correlation coefficients. All multi-item scales significantly correlated with each other ($p < .001$) (Fossa, 1994). (Appendix C, 12 minutes).

The EORTC QLQ-CR38 assesses quality of life specifically in colon cancer patients. It is composed of 38-items measuring disease symptoms and treatment-related side effects, with response categories ranging from 1, not at all, to 4, very much. A one week time frame is utilized for all items except the sexuality items, which use a 4 week time frame. The 38 items comprise 9 scales tapping body image, sexual functioning, sexual enjoyment, future perspective, chemotherapy side effects, sexual dysfunction, body image, gastrointestinal defecation and stoma related problems. The measure is designed as a supplement to the core EORTC QLQ-C30 questionnaire, and is not intended for use as a free-standing scale. Using a known-groups comparison, it was established that patients with metastatic disease reported higher scores ($p < .001$). Subscales also correlated with the KPS ($p < .05$) and with weight loss ($p < .01$). When on-treatment performance status was used as a grouping variable, statistically significant differences were established across subscales ($p < .05$). Cronbach α ranged from .38-.91, but was above .70 for 7 of 9 scales. Test re-test reliability coefficients ranged from .53-.92 ($p < .01$) depending on subscale. (Appendix C, administered together with QLQ-C30)

Assessment of UC, Mental Healthcare Utilization, Medications and Sexual Health

Strategies (HUC): We will assess UC by asking specific questions pertaining to recent use of mental health care services and medications. Questions address use of several different types of services (e.g., religious, alternative, support groups, and therapists). (Appendix C, 5 minutes).

Additional measure for women only:

Sexual Self-Schema Scale for Women, (Andersen et al., 1997): The women's sexual self-schema scale contains 26 trait adjectives (i.e. cautious, loving, open-minded) plus 24 adjective fillers (i.e. generous, practical, kind) that are self-rated from 0 (not at all descriptive of me) to 6 (very descriptive of me). It is a cognitive view about sexual aspects of oneself with three dimensions: 1) loving-romantic, 2) direct-open, and 3) embarrassment-conservatism. Internal consistency for the scale is .75. Test-retest reliability indicates stability, with 2-month reliability of .88. (Appendix C, 10 minutes).

Female Sexual Functioning Index (FSFI), (Rosen et al., 2000): Sexual functioning will be assessed by the FSFI, with the total score being the primary outcome. The FSFI is a brief, self-report measure of female sexual function. It is a 19 item multiple-choice questionnaire assessing five domains of sexual function in women: 1) desire and subjective arousal, 2) lubrication, 3) orgasm, 4) satisfaction, and 5) pain/discomfort. The full scale score for sexually dysfunctional women had a mean of 19.2 and SD of 6.63, compared with a mean of 30.5 and SD of 5.29 for controls; 2-4 week test-retest reliability was 0.79 to 0.88 for each subscale. Validation studies on

sexually dysfunctional and matched control women aged 21 to 70 have demonstrated excellent internal consistency (0.89 to 0.97). Discriminant validity was significant for all subscales as well as the summary score. (Appendix C, 10 minutes).

Menopausal Symptom Checklist (MSC), (Ganz et al, 2000): Adapted from the Breast Cancer Prevention Trial Symptom Checklist. The SCL is an instrument devised by the National Surgical Adjuvant Breast Project (NSABP) for the use in the P-1 and P-2 breast cancer chemoprevention trials (Day et al., 1999). It contains 36 items querying a range of physical and psychological symptoms, such as hot flashes and vaginal dryness, as well as symptoms associated with estrogen deprivation. Estrogen levels may influence mood and quality of life. This instrument was successfully administered as part of a baseline QOL assessment to over 9700 participants in the NSABP P1 trial. It has been used in prior research as well as that of the teams. (Appendix C, 8 minutes).

Additional measures for men only:

International Index of Erectile Function (IIEF) (Rosen et al., 1997): The IIEF is a 15-item questionnaire designed to assess erectile functioning. It measures participants' responses on 5- and 6-point Likert Scales. The IIEF demonstrated a high degree of internal consistency for the overall scale (Cronbach's $\alpha = 0.91$) as well as the five factors (Cronbach's α values greater than 0.73). Test-retest reliability was also strong for the total score and the five domain scores. (Appendix C, 10 mins).

Sexual Self-Schema Scale for Men (SSS-M) (Andersen, Cyranowski, & Espindle, 1999): The SSS-M measures individual differences in men's sexual self-schema and includes 27 trait adjectives plus 18 adjective fillers that are self-rated from 0 (not at all descriptive of me) to 6 (very descriptive of me). Similar to the women's version of the scale, the SSS-M contains three dimensions of cognitive views regarding one's sexuality: 1) passionate-romantic, 2) powerful-aggressive, and 3) open-minded-liberal. Internal consistency is .86. Test-retest reliability indicates stability with 9-week reliability of .81. (Appendix C, 10 mins).

Sexual Self-Esteem and Relationship Questionnaire (SEAR), (Cappelleri et al., 2004): The SEAR is a 14-item measure that assesses sexual relationship satisfaction, sexual self-esteem, and overall relationship satisfaction (Manne, DuHamel, & Redd, 2000). This measure was developed for use in men with ED. The items are scored on a 5-point Likert scale with higher scores indicating higher sexual satisfaction and sexual self-esteem. This scale has good internal consistency, Cronbach's α values ranging from .76 to .93 for the total and subscale scores. This scale has also demonstrated good validity and sensitivity to change in men who were treated for ED. (Appendix C, 8 mins).

Sexual Bother: Sexual bother will be assessed with the Sexual Bother (SB) subscale of the Prostate-Health Related QOL (PHR-QOL) questionnaire (Befort et al., 2005). The PHR-QOL questionnaire was developed and validated at Memorial Sloan-Kettering Cancer Center. For the current study, we will only utilize the Sexual Bother subscale. This is a 4-question scale that assesses men on a 5-point Likert scale. The four questions assess how sexual function has impacted close relationships, how big a problem it has been, if the patients have felt ashamed or embarrassed by their sexual function, and if it has impacted their ability to enjoy life. The SB subscale showed good internal consistency with a Cronbach's α of 0.81 and good test-retest reliability with a concordance correlation coefficient of 0.71. (Appendix C, 5 mins).

Additional measures for CSI-SH Participants only: (To be completed after session four).

Patient Satisfaction with CSI-SH: 16- item questionnaire administered to subjects assigned to CSI-SH at the end of the last CSI-SH session only was adapted from a measure used in the investigators' currently/past federally funded intervention studies. Items query subjects' responses to the various components of the intervention (e.g., content, timing and length of sessions). (Appendix C, 16 minutes).

Interventionist Satisfaction with CSI-SH: 12-item questionnaire administered to interventionists at the end of the last CSI-SH session and was adapted from a measure used in the investigators' current/past federally funded intervention studies. Items will query interventionists' responses to the various components of the intervention. (Appendix C, 10 minutes).

Working Alliance Inventory: 12-item self-report scale to assess the therapeutic alliance between patient and interventionist will be analyzed as a potential moderator variable. The Working Alliance Inventory Short Form (Busseri, 2003) will assess the quality of the working relationship between patient and interventionist. Reliability (Inter-item consistency) for this scale is high with alpha estimates ranging from .87 to .93. (Horvath, 1989). (Appendix C, 5 minutes).

Sequence of Assessments: The assessment and intervention schedule will be followed as outlined in the Assessment Schedule. All assessment sessions (baseline, 4 months and 8 months follow up), with the exception of the CSI-SH measures, will be conducted over the telephone by the research staff, who will remain blind to treatment condition. The intervention measure of satisfaction with the intervention and therapeutic alliance will be completed only by the CSI-SH participants after the last session. Therapeutic alliance is only given once as it is considered a possible moderator of the impact of CSI-SH. The study measures will be administered as indicated in the chart below, and the timing of assessments is based on prior research (e.g. Ganz, et al., 2000).

	Baseline at Intervention	Follow up 4 months	Follow up 8 months	After Session 4 (Intervention Group Only)
FOR ALL PARTICIPANTS				
Socio-Demographic	X	X	X	
Preferences for Intervention Delivery	X	X	X	
Impact of Events Scale -Revised	X	X	X	
Brief Symptom Inventory (BSI)	X	X	X	
EORTC QLQ-C30	X	X	X	
EORTC QLQ-CR38	X	X	X	
Assessment of UC, Mental Healthcare Utilization, and Medications (HUC)	X			

Medical Data	X		X	
Treatment Data	X		X	

Tumor Data	X		X	
CSI-SH ONLY				
Patient Satisfaction with CSI-SH				X
Interventionist Satisfaction with CSI-SH				X
Working Alliance Inventory				X

FOR WOMEN ONLY				
Sexual Self Schema Scale for Women	X	X	X	
Female Sexual Functioning Index (FSFI)	X	X	X	
Menopause Symptom Checklist	X	X	X	
FOR MEN ONLY				
International Index of Erectile Function (IIEF)	X	X	X	
Sexual Self-Schema Scale for Men (SSS-M)	X	X	X	
Sexual Self-Esteem and Relationship Questionnaire (SEAR)	X	X	X	
Sexual Bother	X	X	X	

8.0 TOXICITIES/SIDE EFFECTS

There are no physical risks or side effects associated with participation in this study. Psychological risks are limited to possible transient distress related to discussion of the study topics such as sexual problems and symptoms of distress. As study items were chosen to reflect existing concerns, the present study is not expected to markedly increase participants' psychological distress above their routine concerns. Experienced personnel will administer all instruments, and will be supervised by the Principal Investigator. Participants' reactions will be observed and signs of significant distress will be followed up by the PI with attention to presence of any serious psychological concerns.

In the unlikely event of significant acute distress, participants will be referred for evaluation. If a research participant indicates that he or she is acutely suicidal and poses a significant and acute risk of self-harm, this information will be shared with their attending physician so that timely and appropriate psychiatric assessment and care can be provided by the MSKCC Social Work or Psychiatry Service staff.

The Research Staff will review the survey data within 24 hours of completion/receipt of measures and will contact the PI or her Psychiatry Service coverage to evaluate any participants who report severe depression/frequent suicidal ideation.

We have taken several steps to minimize the risk of distress attributable to study participation. Any participant may choose not to answer questions that they do not care to. In addition, our prior research indicates that female rectal survivors do not become distressed in response to direct assessment of sexual functioning, distress, quality of life etc. (Temple et al., 2005, & Temple, In Preparation). In the unlikely event that extreme psychological distress is observed or expressed by a participant in this pilot RCT, one of the following licensed psychologists, Dr Nelson will be present to assess the situation and make appropriate referrals. As MSKCC provides mental health services, individuals may be referred to or seek immediate counseling at the Psychiatry and Behavioral Science Center.

9.0 PRIMARY OUTCOMES

As part of the study, participants will be asked to complete the three study assessments at baseline, 4 months post-baseline and 8 months post-baseline. Participants will also be given brief homework assignments as described in section 4.2 to reinforce skills learned in the intervention. The assessment battery includes standard measures used by the research team in their ongoing research as well as measures that they revised from ongoing work (e.g., the measures of satisfaction with CSI-SH were based on a measure DuHamel and colleagues use in their research of Cognitive Behavior Therapy for symptoms of posttraumatic stress disorder among cancer patients).

- **Primary Aim:** To investigate the feasibility, tolerability, acceptability, and efficacy of CSI-SH, a psycho-educational intervention, on the primary outcome of sexual functioning.

Primary Outcome: Sexual Functioning at 4 and 8 months will be compared to baseline based on Total FSFI and IIEF scores for women and men, respectively. .

JUSTIFICATION: It is our impression that CSI-SH will lead to improved sexual functioning based on prior interventions for other cancer populations (see section 3.0, Background and Preliminary Studies).

Feasibility Outcome: The acceptance rates will be calculated and will indicate feasibility. The intervention will be deemed tolerable if adding CSI-SH to UC does not lead to greater study dropout than UC alone and/or to less adherence to study procedures (e.g., interviews). The adherence with the intervention procedures will also be described such as the number of sessions attended. Satisfaction will be assessed by patient satisfaction and interventionist satisfaction surveys.

JUSTIFICATION: Based on our prior intervention work, it is our impression that CSI-SH will be feasible, tolerable, and acceptable. These issues are critical to address when designing a new intervention. In addition, we need to address these issues in part for preparation of our planned subsequent later stage trial.

- **Secondary Aim:** To investigate the impact of CSI-SH on secondary outcomes: sexual self-schema, cancer specific distress, general distress symptoms, QOL and, for men, sexual bother.

Secondary Outcome: The total *Sexual Self Schema* scores for women and men at the four and 8-month follow-up assessments will be compared to baseline scores. The total scores on the *IES-R*, the *BSI*, the EORTC QLQ-C30, and the EORTC QLQ-CR38 for the four and 8-month follow-up assessments will also be compared to the baseline scores. These analyses will be run three times: one time with only women, one time with only men, and a third time combined. Additionally, scores on 4 and 8-month follow-up assessments of male-specific variables (using the *SEAR* and the Sexual Bother subscale of the *PHR-QOL*) will be compared to baseline scores.

JUSTIFICATION: It is our impression CSI-SH may impact these secondary outcomes as sexual functioning maybe related to sexual self-concept (schema) and distress.

- **Exploratory Aim:** To explore variables that may influence the effectiveness of CSI-SH (i.e., moderators).

Exploratory Outcome: If CSI-SH is found to impact study outcomes, then potential moderators will be explored. Possible moderators include socio-demographic and medical variables as well as the working alliance inventory.

JUSTIFICATION: This exploratory aim will guide possible intervention revision prior to the planned subsequent, larger trial.

10.0 CRITERIA FOR REMOVAL FROM STUDY

A patient may withdraw from the study at any time. A patient may choose not to complete any question and/or battery of questions. A patient who does not complete surveys or misses a session appointment will be rescheduled. If the battery of surveys are not completed for two sequential time points, patients will be called three times on different days and times of day. If they are not reached, patients will be sent a letter inquiring about their desire to continue in the

study. If they do not respond to the letter, they be will considered withdrawn. If a patient develops a recurrence, that patient will be removed from the study because she will be deemed ineligible as outlined in the eligibility criteria.

11.0 BIOSTATISTICS

The overall aim of this study is to pilot test an educational counseling intervention to increase post-treatment sexual functioning and reduce sexual problems of patients treated for rectal cancer. We plan to recruit at least 80 women and 130 men who are at least 6 months post radiation and/or surgery for stage I-III rectal adenocarcinoma or rectosigmoid cancer with an anastomosis at 15 cm or below and completed treatment, at least 6 months post radiation and/or chemotherapy for anal cancer, have no evidence of disease or recurrence, and indicate that they are not very satisfied with their overall sexual life. Patients will be randomized with equal probability into either the experimental intervention condition or the usual care condition, stratified by stoma status (whether they have a permanent stoma or not), chemotherapy, and post-menopausal status. **For male patients only: Participants will be randomized in a 3:1 ratio (intervention: control) to either the intervention condition (n = 66) or the control condition (n = 44).**

Analytic plan for the specific aims are as follows.

- **Primary Aim:** To investigate the feasibility, tolerability, acceptability, adherence and efficacy of CSI-SH, a psycho-educational intervention, on the primary outcome of sexual functioning.

The primary aim will mostly entail the use of descriptive statistics. An important goal of this study is to demonstrate feasibility and obtain preliminary efficacy data for the proposed intervention. We will ascertain aspects of feasibility (e.g., monthly number of consented participants, percentage of patients who consent to participate in the study), tolerability (e.g., therapy completion rate for participants randomized to the intervention condition; retention rate for participants in the usual care condition), adherence (e.g., number of counseling sessions attended), and efficacy of the CSI-SH intervention. Reasons for study ineligibility and refusal will be tabulated (this plan is also stated in Section 6 regarding patient recruitment). Generally, we will use independent sample t-test (for continuous variables) and chi-square test (for categorical variables) to explore potential differences between acceptors and decliners with regard to socio-demographic characteristics, health and medical history to guide the modification and refinement of the CSI-SH intervention.

To estimate the efficacy of the proposed CSI-SH intervention, we will collect preliminary effect size estimates on the outcome of sexual functioning (as measured by the FSFI and IIEF summary scores). The preliminary effect size will be estimated by a univariate two-group repeated-measures analysis of variance to compare the pre-post changes in the FSFI/ IIEF scores across the two treatment conditions (Cohen, 1996).

Statistical Power Considerations. We estimated statistical power with effect sizes of 0.22, 0.30, and 0.50, using a simple, hypothetical complete-case analysis; namely, on the projected number of patients who will have data for the final evaluation. Our sample size estimate showed that, if we recruit at least 80 patients for each (male and female) version of the study, we will have 88% statistical power to detect a standardized between-group variance of 0.30. We used the G*Power computer program to calculate this estimated statistical power (Faul, et al., 1996).

Additional Statistical Considerations for Aim 1. We will monitor recruitment progress periodically to examine barriers to reaching the recruitment target of the recruitment goals for each gender. Steps to boost recruitment will be considered if progress turns out to be slow. This periodic monitoring is consistent with data safety monitoring requirements of our institution. Our own schedule is set at the first 20 recruits, which is 25% of the target recruitment. We believe that this is a sensible plan, in the event that the institutional review does not coincide with this event.

Analyses will be sought to compare FSFI/IEEF scores assessed from our sample with the published data among the general population, individuals with female sexual arousal disorder (Rosen et al., 2000), and patients after rectal cancer treatment (Hendren et al., 2005). In addition to analyzing the FSFI/IEEF scores as numeric variables, these scores will be dichotomized into “abnormal” or “normal” using the clinically significant criterion reported in Hendren et al. (total score < 26, i.e., one standard deviation below the mean of a normal population). We will make necessary statistical adjustments if this dichotomization produces skewed data (Maxwell & Delaney, 1993). Contrasting the FSFI/IEEF scores against the norms will give insight into the severity of sexual dysfunction among patients in our sample. We will also examine the factors that predict impaired sexual function at 8-month follow-up. We will investigate the bivariate and multivariate relationship of patient characteristics (age, previous sexual functioning, partner status), tumor features (location, stage), and treatment (type of surgery, use of radiation), with 4-month FSFI total score.

- **Secondary Aim:** To investigate the impact of CSI-SH on secondary outcomes: sexual self-concept, cancer specific distress, and general distress symptoms, as well as QOL.

We will use repeated-measures ANOVA to gather preliminary effect size estimates on the impact of CSI-SH on secondary outcomes including sexual self-concept, cancer specific distress, and general distress symptoms, as well as QOL. Descriptive statistics will be used to summarize the profiles of these secondary outcomes.

- **Exploratory Aim:** To explore baseline variables that may influence the effectiveness of CSI-SH (i.e., moderators).

Potential moderators will be explored with the data generated from the proposed pilot study. There are no hypotheses for these exploratory analyses. We will include covariates one at a time (e.g., time since treatment) in the repeated-measures ANOVA to examine how the covariates moderate the impact of CSI-SH. Generally, the moderating effects will be tested with an interaction term between the covariate and the treatment group (e.g., time since treatment by group interaction). A statistically significant interaction term supports the moderating effect for

that covariate. Since this proposed study is only a pilot project, we will not attempt to build a full predictive model incorporating all moderating factors together. We are primarily interested in identifying any potential moderators for future research in this area.

Other Considerations Related to Study Attrition. All attempts will be made to keep missing data to a minimum. For example, conducting interviews over the telephone with a trained RSA allows for items not to be unintentionally missed/skipped. More critically, we will determine differential attrition associated with intervention condition (e.g., whether the CSI-SH and UC only conditions are differentially associated with attrition) and with time since surgery (e.g., whether or not patients recruited after 2 years post surgery are more likely to relapse than patients recruited after 5 years post surgery). These analyses will be an integral part of our feasibility aim because such association might have implications for the tolerability or acceptability of the intervention. In order to assess the potential biases introduced by differential attrition between the two treatment arms, a comparison of attrition rates will be included as an ancillary analysis to the primary endpoint comparisons. We do not expect differential attrition because we believe that most withdrawals will be due to cancer relapse. If a CSI-SH study participant drops out of the intervention, they will be asked to voluntarily complete the follow-up assessments, that we may be able to track their experiences on the study scales, include them in the study analyses and discover the reason(s) behind the missed appointment(s). Such information would also inform the study procedures in a future study.

Missing Data Analyses

We will utilize several techniques to address issues associated with attrition including estimating missing data and complete data analysis. We expect that most patients will complete most or all of the assessments. Missing data can be estimated using a number of new, powerful techniques. For this study, we intend to use a multiple imputation procedure described by Schafer and colleagues, (Schafer & Olsen, 1998 ;Schafer & Graham, 2002) which is capable of handling categorical data, continuous data, and any combination of the two. Parameter estimates using this method are unbiased and have standard errors that are typically only slightly larger than those generated by other methods. We will compare results based on imputed data to those based only on completed cases. This comparison allows for an assessment of the extent to which potential biases in imputation may have influenced study results.

Another method is the Pattern-Mixture Model (Hedeker & Gibbons, 1997), which assumes that patients can be grouped into different cohorts according to their typical trajectories of responses and non-responses within each of these cohorts. Membership of these cohorts can be incorporated as dummy covariates as part of testing the intervention effect.

Finally, we can analyze data assuming that those patients who dropped out had no change in their psychological well-being. An intention to treat analysis provides a highly conservative estimate of effect size against which to compare estimates generated by other methods.

12.0 RESEARCH PARTICIPANT REGISTRATION AND RANDOMIZATION PROCEDURES

12.1 Research Participant Registration

Confirm eligibility as defined in the section entitled Criteria for Patient/Subject Eligibility.

Obtain informed consent, by following procedures defined in section entitled Informed Consent Procedures.

During the registration process registering individuals will be required to complete a protocol specific Eligibility Checklist.

All participants must be registered through the Protocol Participant Registration (PPR) Office at Memorial Sloan-Kettering Cancer Center. PPR is available Monday through Friday from 8:30am – 5:30pm at 646-735-8000. Registrations must be submitted via the PPR Electronic Registration System (<http://ppr/>). The completed signature page of the written consent/RA or verbal script/RA, a completed Eligibility Checklist and other relevant documents must be uploaded via the PPR Electronic Registration System.

12.1.1 For Participating Sites: - We are no longer recruiting at MSSM.

Central registration for this study will take place at Memorial Sloan Kettering Cancer Center.

To complete registration and enroll a participant from another institution, the study staff at that site must contact the research staff at MSKCC to notify him/her of the participant registration. The site staff then needs to fax registration/eligibility documents to the Department of Psychiatry and Behavioral Sciences at MSKCC to 212-888-2584.

The following documents must be sent for each enrollment **within 24 hours of the informed consent form being signed:**

- A completed or partially completed MSKCC eligibility checklist
- The signed informed consent and signed HIPAA Authorization form (Research Authorization)
- Supporting source documentation for eligibility questions (laboratory results, pathology report, radiology reports, MD notes, physical exam sheets, medical history, prior treatment records, and EKG report).

Upon receipt, the research staff at Memorial Sloan Kettering Cancer Center will conduct an interim review of all documents. If the eligibility checklist is not complete, the patient will be registered PENDING and the site is responsible for sending a completed form within 30 days of the consent.

If the eligibility checklist is complete, participant meets all criteria, all source documentation is received, the participating site IRB has granted approval for the protocol, and the site is in good standing with MSKCC, the MSK RSA will send the completed registration documents to the MSKCC Protocol Participant Registration (PPR) Office to be enrolled as stated in section 12.1. The participant will be registered.

Once eligibility has been established and the participant is registered, the participant will be assigned an MSKCC Clinical Research Database (CRDB) number (protocol participant number).

This number is unique to the participant and must be written on all data and correspondence for the participant. This protocol participant number will be relayed back to study staff at the registering site via e-mail and will serve as the enrollment confirmation.

12.2 Randomization

Participants from both Memorial Sloan Kettering Cancer Center and Mount Sinai School of Medicine will be stratified (see below) and randomized through CRDB to one of two arms: 1) CSI-SH plus usual care (UC) or 2) UC only. After eligibility is confirmed, patients will be registered in the MSKCC computerized Protocol Participant Registration (PPR) system and randomized using the MSKCC Clinical Research Database (CRDB). Randomization is overseen by the MSKCC Biostatistics Service. Participants will be stratified based on 1) presence or absence of permanent stoma, 2) if they have chemotherapy or not, and for women only, 3) if they are post-menopausal or not. Within each stratum, participants will be randomized with equal probability into either the intervention or the usual care arm. Individuals who participate in a focus group or qualitative interview will be registered through PPR however will not be randomized or stratified.

For male patients only: Participants will be randomized in a 3:1 ratio (intervention: control) to either the intervention condition (n = 66) or the control condition (n = 44).

13.0 DATA MANAGEMENT ISSUES

A Research Study Assistant (RSA) will be assigned to the study at each of the two sites. The responsibilities of the RSA include project compliance, data collection, abstraction and entry, data reporting, regulatory monitoring, problem resolution and prioritization, and coordinating the activities of the protocol study team.

For participants recruited at Mount Sinai School of Medicine, the study personnel will fax the consent forms and eligibility checklists to MSKCC. All assessments and audio recordings obtained at Mount Sinai will also be delivered to MSKCC for filing.

The data collected for this study will be kept in a locked, secured location and will only be accessible to study staff. Data will be stripped of any identifying information. A list, matching participants' names and case numbers will also be kept in a secure area at MSKCC. All questionnaire data completed by participants will be identified only with a study code number. Study findings will be presented in aggregate form only, with no reference made to individual participant's data. The Principal Investigator and her research team will be responsible for identifying, reviewing and reporting all necessary adverse events to the institutional IRB as appropriate. Adverse events are identified through standard, routine protocol review and clinical assessment of each participant in the study. Minimal data set will be maintained in CRDB.

13.1 Quality Assurance

Registration reports will be generated regularly to monitor patient accruals and completeness of registration data. Routine data quality reports will be generated to assess missing and inconsistent data. Accrual rates and extent and accuracy of evaluations and

follow-up will be monitored periodically throughout the study period and potential problems will be brought to the attention of the study team for discussion and action.

Random-sample data quality and protocol compliance audits will be conducted by the study team, at a minimum of two times per year, more frequently if indicated.

13.1.1 Quality Assurance for Participating Sites

Each site participating in the accrual of participants to this protocol will be audited by the staff of the MSKCC study team for protocol and regulatory compliance, data verification and source documentation. Audits may be accomplished in one of two ways: (1) selected participant records can be audited on-site at participating sites or (2) source documents for selected participants will be sent to MSKCC for audit. Audits will usually be determined by participant accrual numbers and rate of accrual, but can also be prompted by reported SAEs or request of Lead PI.

Audits will be conducted at least once shortly after initiation of participant recruitment at a site, annually during the study (or more frequently if indicated), and at the end or closeout of the trial. The number of participants audited will be determined by available time and the complexity of the protocol.

The audit will include a review of source documentation to evaluate compliance for:

- Consent documents and procedures
- Adherence to eligibility criteria
- Protocol defined intervention/interaction
- Required baseline, and if applicable, follow-up interactions
- IRB documents (submitted amendments, annual continuing review reports, SAEs)
- Required specimen submission
- Data submissions to MSKCC: timelines and accuracy

A wrap-up session will be conducted at the outside site and preliminary findings will be discussed with the outside site PI and research team. The preliminary results will be sent to the MSKCC PI.

Each audit will be summarized and a final report will be sent to the PI at the audited participating institution within 30 days of the audit. The report will include a summary of findings, participant by participant case review, specific recommendations on any performance and/or shortcomings and request for corrective action, when necessary. When corrective action is required, the participating institution must reply within 45 days of receipt of audit report with their corrective action plan.

A copy of the audit report and corrective action plan (if applicable) submitted by the outside site must be sent to the MSKCC IRB, CRQA and maintained in the department's protocol regulatory binder.

13.2 Data and Safety Monitoring

The Data and Safety Monitoring (DSM) Plans at Memorial Sloan-Kettering Cancer Center were approved by the National Cancer Institute in September 2001. The plans address the new policies set forth by the NCI in the document entitled "Policy of the National Cancer Institute for Data and Safety Monitoring of Clinical Trials" which can be found at: <http://www.cancer.gov/clinicaltrials/conducting/dsm-guidelines/page1>. The DSM Plans at MSKCC were established and are monitored by the Office of Clinical Research. The MSKCC Data and Safety Monitoring Plans can be found on the MSKCC

Intranet at:

[http://smskpsps9/dept/ocr/OCR%20Website%20Documents/Clinical%20Research%20Quality%20Assurance%20\(CRQA\)/MSKCC%20Data%20and%20Safety%20Monitoring%20Plan.pdf](http://smskpsps9/dept/ocr/OCR%20Website%20Documents/Clinical%20Research%20Quality%20Assurance%20(CRQA)/MSKCC%20Data%20and%20Safety%20Monitoring%20Plan.pdf)

There are several different mechanisms by which clinical trials are monitored for data, safety and quality. There are institutional processes in place for quality assurance (e.g., protocol monitoring, compliance and data verification audits, therapeutic response, and staff education on clinical research QA) and departmental procedures for quality control, plus there are two institutional committees that are responsible for monitoring the activities of our clinical trials programs. The committees: Data and Safety Monitoring Committee (DSMC) for Phase I and II clinical trials, and the Data and Safety Monitoring Board (DSMB) for Phase III clinical trials, report to the Center's Research Council and Institutional Review Board.

During the protocol development and review process, each protocol will be assessed for its level of risk and degree of monitoring required. Every type of protocol (e.g., NIH sponsored, in-house sponsored, industrial sponsored, NCI cooperative group, etc.) will be addressed and the monitoring procedures will be established at the time of protocol activation.

13.3 Regulatory Documentation

Prior to implementing this protocol at MSKCC, the protocol, informed consent form, HIPAA authorization and any other information pertaining to participants must be approved by the MSKCC Institutional Review Board/Privacy Board (IRB/PB). Prior to implementing this protocol at the participating sites, approval for the MSKCC IRB/PB approved protocol must be obtained from the participating site's IRB of Record. The following documents must be provided to MSKCC before the participating site can be initiated and begin enrolling participants:

- Participating Site IRB approval(s) for the protocol, appendices, informed consent form and HIPAA authorization
- Participating Site IRB approved consent form
- Participating Site IRB membership
- Participating Site IRB's Federal Wide Assurance number and OHRP Registration number
- Curriculum vitae/biosketch and medical license (if applicable) for each investigator and consenting professional
- Documentation of Human Subject Research Certification for investigators and key staff members
- Laboratory certifications and normals (if applicable)

Upon receipt of the required documents, MSKCC will formally contact the site and grant permission to proceed with enrollment.

13.3.1 Amendments

Each change to the protocol document must be organized and documented by MSKCC and first approved by the MSKCC IRB/PB. Upon receipt of MSKCC IRB/PB approval, MSKCC will immediately distribute all non expedited amendments to the participating sites, for submission to their local IRBs.

Participating sites must obtain approval from their IRB of record within 90 calendar days of MSKCC IRB/PB approval. If the amendment is the result of a safety issue, sites will not be permitted to continue enrolling new participants until IRB approval has been granted.

The following documents must be provided to MSKCC for each amendment within the stated timelines:

- Participating Site IRB approval
- Participating Site IRB approved informed consent form and HIPAA authorization

13.3.3 Additional IRB Correspondence

Continuing Review Approval

The Continuing Review Approval letter from the participating site's IRB must be submitted to MSKCC at the time re-approval is granted. The most current approved version of the consent form should also be submitted to MSKCC within 7 days of expiration. Failure to submit the re-approval in the stated timeline will result in suspension of study activities.

Deviations and Violations

A protocol deviation on this study is defined as a request to treat a research participant who does not meet all the eligibility criteria, pretreatment evaluation, or who requires alteration in their study plan. If a deviation from this protocol is proposed for a potential or existing participant at MSKCC or a participating site, approval from the MSKCC IRB/PB is required prior to the action. Participating sites should contact the MSKCC PI who will in turn seek approval from the MSKCC IRB/PB.

A protocol violation is anything that occurs with a participant, which deviated from the protocol without prior approval from the MSKCC IRB/PB. For protocol violations that are identified after they occur, the participating site should report to MSKCC as soon as possible. The MSKCC PI will in turn report the violation to the MSKCC IRB/PB.

Participating sites should report deviations and violations to their institution's IRBs as soon as possible per that site's institutional guidelines. Approvals/acknowledgments from the participating site IRB for protocol deviations and violations should be submitted to MSKCC as received.

Other correspondence

Participating sites should submit other correspondence to their institution's IRB according to local guidelines, and submit copies of that correspondence to MSKCC.

13.3.4 Document maintenance

The MSKCC PI and the Participating Site PI will maintain adequate and accurate records to enable the implementation of the protocol to be fully documented and the data to be subsequently verified.

The participating sites will ensure that all participating site IRB correspondence (IRB approval letters referencing protocol version date and amendment number, IRB approved protocol, appendices, consent forms, deviations, violations, and approval of continuing reviews) is maintained in the regulatory binder on site and sent to MSKCC.

A regulatory binder for each site will also be maintained at MSKCC; this binder may be paper or electronic.

After study closure, the investigator will maintain all source documents, study related documents and CRFs for 3 years.

13.4 Noncompliance

If a participating site is found to be noncompliant with the data and regulatory requirements set forth in the protocol document, accrual privileges may be suspended and/or contract payments may be withheld (if applicable), until the outstanding issues have been resolved.

14.0 PROTECTION OF HUMAN SUBJECTS

The proposed research is a low-risk behavioral trial. Although we cannot guarantee that all participants may benefit directly from the intervention, prior cancer survivors often report they enjoy providing researchers with greater knowledge of their experiences in hopes of facilitating the design and improvements of psychosocial interventions. In addition, all participants who meet eligibility criteria will be offered the intervention at no cost to them (those in the usual care arm will be offered CSI-SH after the formal study is over). Overall, the results from this study will investigate the impact of CSI-SH and may improve the clinical care of RC survivors in the future.

The potential risks involve emotional distress that might accompany a patient being asked about the experience of illness or difficulties with sexual functioning. Research staff will carefully monitor each participant's emotional reaction during study interviews, and offer referrals when appropriate. For participants enrolled in CSI-SH their reactions will be monitored during treatment, and the interventionist will seek to address psychological distress in the sessions. Participants will be informed that participation is voluntary and that they have the right to withdraw and/or leave any question blank if they do not feel comfortable answering. Given the potential gains to participants, the ratio of risk to benefit is quite low and reasonable.

Confidentiality of each subject's self-report information and each patient's medical information will be protected with the utmost care. Each study subject will be given a unique numeric identifier upon study entry. Data sheets collected from each subject will be identified solely by a code number. A list matching subject names and code numbers will be maintained separately and kept in a secure area. IRB and HIPAA regulations concerning confidentiality will be strictly enforced. Hardcopies of the original questionnaires will be stored in locked file cabinets.

Through the use of password security measures, restrictions will be applied to each user commensurate with their needs to access the data. Confidential information will not be routinely available to all members of the research team but rather on a 'need to know' basis. All current and new personnel will be instructed in the ethics of electronic data access, as well as receive training in both HIPAA issues and human subjects training.

14.1 Privacy

MSKCC's Privacy Office may allow the use and disclosure of protected health information pursuant to a completed and signed Research Authorization form. The use and disclosure of protected health information will be limited to the individuals described in the Research Authorization form. A Research Authorization form must be completed by the Principal Investigator and approved by the IRB and Privacy Board.

14.2 Serious Adverse Event (SAE) Reporting

Any SAE must be reported to the IRB/PB as soon as possible but no later than 5 calendar days. The IRB/PB requires a Clinical Research Database (CRDB) SAE report be submitted electronically to the SAE Office at sae@mskcc.org containing the following information:

Fields populated from the CRDB:

- Subject's name (generate the report with only initials if it will be sent outside of MSKCC)
- Medical record number
- Disease/histology (if applicable)
- Protocol number and title

Data needing to be entered:

- The date the adverse event occurred
- The adverse event
- Relationship of the adverse event to the treatment (drug, device, or intervention)
- If the AE was expected
- The severity of the AE
- The intervention
- Detailed text that includes the following information:
 - A explanation of how the AE was handled
 - A description of the subject's condition
 - Indication if the subject remains on the study
 - If an amendment will need to be made to the protocol and/or consent form

The PI's signature and the date it was signed are required on the completed report.

There are no physical risks associated with participation. Participants may experience possible mild distress as a result of answering study questions and sharing personal information during the interviews. However, these reactions are usually temporary. If participants become upset as a direct result of answering the questions, they will be

referred to Dr. Carter who is a Ph.D. psychologist, and who will make additional referrals as required. Participants will also be instructed that they may skip any questions that do not wish to answer. Participants endorsing suicidality-related items on the Brief Symptom Inventory (BSI) will be referred to the PI or CO-PIs. In the event that the PI or CO-PIs are not available the patient will be referred to the Psychiatry Fellow on call. If the interventionist determines the participant to be actively suicidal, then they will be offered the necessary services and will be excluded from the study. Such patients will be referred to the MSKCC Psychiatry Service or a local mental health provider from the Department of Psychiatry and Behavioral Science's referral list.

We expect that our patients may be hospitalized related to their cancer. However, due to the nature of our questionnaire/interview study, we will not report hospitalizations or any other events unrelated to the procedures outlined in our protocol as SAEs.

14.3 Serious Adverse Event (SAE) Reporting for Participating Sites

Responsibility of Participating Sites

Participating sites are responsible for reporting all SAEs and grade 4 and 5 unexpected adverse events to the MSKCC PI via fax or e-mail within 3 calendar days of learning of the event. Participating sites should use the SAE Report Template to report SAEs to MSKCC.

SAE contact information for the Coordinating Center is listed below:

- Christian Nelson, PhD: nelsonc@mskcc.org
- Caraline Demirjian, Clinical Research Manager: craigc@mskcc.org

Responsibility of MSKCC

- The MSKCC Research Staff is responsible for submitting all SAEs to the MSKCC IRB as specified in 14.1
- The MSKCC PI is responsible for informing all participating sites about unexpected SAEs and fatalities 30 days of receiving the stamped SAE from the MSKCC IRB/PB.

15.0 INFORMED CONSENT PROCEDURES

Eligible patients will be identified by the research and clinical staff. We will be using a dual method of recruitment: in person in the clinic and via telephone. With the help of clinic staff and approval of the relevant clinician, research study assistants who are consenting professional will approach eligible patients in the clinic. The RSA will explain the study and invite them to participate. Additionally, some eligible survivors will be informed of this research study by introductory letter from their physician at MSKCC and the study investigators. The letter will detail the study and invite them to participate. If study staff do not hear from a participant within two weeks, a phone call will be made to follow-up to see if the individual is interested, and to answer any questions and clarify study procedures. If the individual is interested in taking part, informed consent will be obtained. A copy of the consent will be mailed along with the study letter. All protocols and consent forms are reviewed and approved by the Institutional Review

Board. If a person cannot be reached, the RSA will leave a message with his/her name and phone number, indicating that he/she is calling about a research study.

Before protocol-specified procedures are carried out, consenting professionals will explain full details of the protocol and study procedures as well as the risks involved to participants prior to their inclusion in the study. Participants will also be informed that they are free to withdraw from the study at any time. All participants must sign an IRB/PB-approved consent form indicating their consent to participate. This consent form meets the requirements of the Code of Federal Regulations and the Institutional Review Board/Privacy Board of this Center. The consent form will include the following:

1. The nature and objectives, potential risks and benefits of the intended study.
2. The length of study and the likely follow-up required.
3. Alternatives to the proposed study. (This will include available standard and investigational therapies. In addition, patients will be offered an option of supportive care for therapeutic studies.)
4. The name of the investigator(s) responsible for the protocol.
5. The right of the participant to accept or refuse study interventions/interactions and to withdraw from participation at any time.

Before any protocol-specific procedures can be carried out, the consenting professional will fully explain the aspects of patient privacy concerning research specific information. In addition to signing the IRB Informed Consent, all patients must agree to the Research Authorization component of the informed consent form.

Each participant and consenting professional will sign the consent form if the consent was done in person and/or the consenting professional will sign the verbal script. The patient will be given a full copy of the consent material, which they will keep for their records

15.2 For Participating Centers

The investigators listed on the cover page and their qualified designees at each participating institution may obtain consent and care for the participants according to good clinical practice and protocol guidelines.

Signed copies of the informed consent should be distributed as follows: One copy will be given to the participant to be retained for their personal records. One copy will be maintained on file at the MSKCC. The third copy will be confidentially maintained by the participating institution.

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17.0 APPENDICES

Appendix A1 Interventionist Manual (Women's Version)
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