PHYSICAL SEQUELAE AND DEPRESSIVE SYMPTOMS

IN GYNECOLOGIC CANCER SURVIVORS:

THE ROLE OF MEANING IN LIFE

DISSERTATION

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By

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ABSTRACT

Cancer survivorship research has largely ignored the growing population of gynecologic cancer survivors. The cancer experience may have both negative and positive effects on meaning in life, thus two models are examined. A mediator model is hypothesized where greater problems with the physical sequelae of cancer are associated with lower levels of meaning and, in turn, higher levels of depressive symptoms. Alternatively, meaning in life may moderate the relationship between physical sequelae and depressive symptoms. That is, the physical sequelae of cancer would be associated with higher levels of depressive symptoms, but this relationship would be buffered (lessened) by meaning. Two-hundred and sixty gynecologic cancer patients were studied with a cross-sectional design. Participants completed measures of physical sequelae (physical functioning, quality of life, and symptoms, including fatigue and vaginal changes), depressive symptoms, and the Meaning in Life Scale. Using structural equation modeling, results support a partial mediation effect, as the indirect effect – from Physical Sequelae to Depressive Symptoms through Meaning in Life – was significant ($p < .001$). Results did not support the moderation hypothesis; a difference test indicated that there was no significant difference between those with high versus low levels of meaning in life ($p = .07$). The implications of these findings for future research, clinical screening, and interventions with gynecologic cancer survivors are discussed.

DEDICATION

Dedicated to my family and friends,

the individuals who bring meaning into my life.

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CHAPTER 1

INTRODUCTION

Cancer survival rates continue to rise. The population of cancer survivors is nearing ten million Americans, and ten percent are estimated to be gynecological cancer survivors (NCI, 2004). Research is needed to examine the physical and psychological sequelae of cancer diagnosis and treatment in order to help cancer survivors have the greatest chance of long and healthy lives (Dow, 2003). Following treatment, many cancer survivors endure physical side effects, such as fatigue (Ferrel, Smith, Cullinane, & Melancon, 2003) and poorer physical functioning (Leake, Gurrin, & Hammond, 2001). In addition, the difficulties associated with these outcomes may contribute to psychological distress, including depression (Given, Stommel, Given et al., 1993). A diagnosis of cancer can create an existential plight where all assumptions about the world and one's future, or meaning in life, are challenged. Survivors may continue to face numerous physical, social, emotional, and spiritual after effects, and question meaning in life. Thus the cancer experience in the short and long-term can lead to a search for meaning in some survivors, and those who find more meaning tend to report better adjustment (Schrovers, Ranchor, & Sanderman, 2004; Taylor, Lichtman, & Wood, 1984; Tomich & Helgeson, 2002). Nonetheless, there is little research exploring how the physical and psychological sequelae of the cancer experience are related to meaning in life in cancer survivors. The present study addresses the potential role of meaning in life

in the relationship between physical functioning and quality of life and depressive symptoms in an understudied cancer survivor population – gynecological cancer survivors.

In order to portray the theoretical basis for this study, a review of the physical health problems with which gynecological cancer survivors are confronted is provided. Then, a review of the mental health issues, including depression, faced by cancer survivors, and a background on meaning in life research and its potential influence on adjustment for cancer survivors are presented. Following this, the theoretical connections between physical functioning/quality of life and meaning in life and how they both potentially relate to depressive symptoms in gynecological cancer survivors are explored.

Cancer Survivorship

Understanding the sequelae of the cancer experience for survivors is important. In the United States, gynecologic cancer cases account for 12 percent of all new cancers in women. Of these, 50 percent involve the endometrium or uterus, 30 percent the ovary, 10 percent the cervix, and 10 percent the vulva, vagina, or other genital organs (Jemal et al., 2006). Improved survival rates have been possible through medical advancements, including diagnostic techniques, such as transvaginal ultrasound, advances in cancer therapies, and increases in screening rates, such as the Pap smear for cervical cancer (Li, Samsioe, & Iosif, 1999). Over the past three decades, death rates for gynecologic cancers have significantly declined (42 percent for endometrial cancer; 49 percent for cervical; 27 percent for vaginal and vulvar; and 11 percent for ovarian; Reis, Eisner, Kosary, et al.,

2000). With approximately 80 thousand new gynecologic cancer cases yearly (American Cancer Society, 2005), insight into the effects of physical and psychological functioning among these women in the long-term will be valuable.

While cancer survivors may include anyone who has been diagnosed with cancer and is surviving (Dow, 2003), short-term and long-term survivors may differ in terms of their experiences. Significant psychological and physical morbidity occurs following diagnosis and treatment (for a review see Andersen & Carpenter, 2003). A few studies have examined quality of life outcomes in long-term survivors of adult onset cancers; however, most of these studies have focused on women with breast cancer (for a review see Gotay & Muraoka, 1998). Gynecologic cancer survivors comprise 10 percent of all cancer survivors making them an increasingly important group to study (NCI, 2004). A handful of empirical studies (see below) have documented the physical sequelae and general quality of life concerns among gynecological cancer survivors.

Physical Sequelae of Cancer

Although treatments are aimed at improving health by defeating cancer, they have the potential for side effects and impairment. Many cancer survivors face short-term and long-term physical changes and disabilities as a result of surgery, chemotherapy, and/or radiotherapy.

Surgery. Most gynecologic cancer survivors are treated with some form of surgery. Types of surgery often include total abdominal or modified radical hysterectomy, typically with a bilateral salpingo-oophorectomy for cervical, endometrial, and ovarian disease.

Oophorectomy involves removal of one or both ovaries. The ovaries naturally function to produce eggs for reproduction and the female hormones, estrogen and progesterone, which help regulate the menstrual cycle and pregnancy. If a woman is pre- or peri-menopausal, oophorectomy brings menopause, the end of child bearing, and the possibility of sexual difficulties. For example, oophorectomy can damage the vasocongestive mechanism of genital arousal. (Loescher et al.,1989). In addition, estrogen loss commonly leads to decreased vaginal lubrication during sexual activity and, in turn, dysparenuia (Loesher et al, 1989). Robson and colleagues (2003) conducted a study of 59 women undergoing risk-reducing salpingo-oophorectomy (Robson, Hensely, Baraket, et al., 2003). The mean age of the women was 51 years, 71% were postmenopausal at the time of surgery, and 80% were sexually active post-surgery. Women completed the Symptom checklist (SCL, Ford et al., 1994), MOS SF-36 Health Survey (Ware, Snow, & Kosinski, 1993), and Sexual Functioning Questionnaire-Female (Taylor, Rosen, & Leilbulum, 1994). At an average of 24 months post-surgery, women reported estrogen deprivation symptoms, including vaginal dryness (35%) and dyspareunia (28%). In addition, 58% of the sexually active women reported vaginal dryness as a problem in 50% or more of sexual activities, and 49% reported difficulty achieving orgasm in the majority of sexual activities. Women also reported lack of desire (46%), lack of arousal (43%), and painful penetration (42%). Although not all of these symptoms may be the direct the result of oophorectomy, overall this study demonstrates some of its possible side effects.

Symptoms of estrogen deprivation include hot flashes (Ganz, 2001), which may last four or five years (Finck, Barton, Loprinzi, Quella, & Sloan, 1998). Hot flashes involve temporary periods of flushing, sweating, and a sensation of heat, in addition to possible heart palpitations and anxiety. In a study of 114 postmenopausal breast cancer survivors (49% pre- or peri-menopausal, 27% surgically menopausal, and 24% naturally menopausal at diagnosis), 65 percent reported hot flashes and 59 percent of those with hot flashes rated them as severe (Carpenter et al., 2002). In addition, hot flashes were related to decreased mental and physical quality of life. In another study of 69 breast cancer survivors (an average of 39 months post-diagnosis) and 63 age-matched controls, breast cancer survivors reported significantly more frequent, severe, longer, and distressing hot flashes than controls (Carpenter, Johnson, Wagner, & Andrykowski, 2002). Furthermore, the cancer survivors with severe hot flashes reported significantly greater interference with daily activities, mood disturbance, and negative affect compared to survivors with mild to no hot flashes. While most of the research on hot flashes in cancer survivors has focused on the possibility of chemotherapy induced menopause in breast cancer patients, the treatments (surgery and radiation therapy) used with gynecologic cancer survivors cause complete estrogen loss. Hot flashes can greatly impact a woman's quality of life or functional ability and many women have reported irritability and depression as a result (Finck et al., 1998).

A hysterectomy involves uterine removal and loss of child-bearing potential, as well as possible sexual dysfunction. For women in the reproductive years, fertility issues are prominent. While ovaries can be transposed in the pelvis for some young women for

in vitro fertilization and surrogate parenting, this is not often a realistic alternative for many women, as it has the potential for multiple physical, psychological, and financial complications (Anderson & Lutendorf, 1997). Even with this, there is a high rate of ovarian failure due to interruption of blood flow to or damage to ovaries from other therapies (e.g. chemotherapy; Anderson & Lutgendorf, 1997). Loss of fertility and childbearing abilities can have a varied emotional impact on the survivor.

Surgeries, such as hysterectomy can also lead to problems with sexual functioning. Bergmark and colleagues (1999) conducted a study with 247 women with a history of cervical cancer and 330 controls (Bergmark, Avall-Lundqvist, Dickman, Henningsohn, & Steineck, 1999). Women in the cancer group were treated with hysterectomy only (36%), surgery and radiotherapy (52%), or radiotherapy alone (9%). Both groups reported equivalent amounts of regular intercourse (68% and 72% respectively). However, the cancer survivor group reported significantly more difficulties with vaginal lubrication during sexual intercourse, greater reductions in vaginal length and elasticity, and more dyspareunia than the control group. In addition, in comparison to the control group, the cancer survivor group reported more distress from vaginal changes and their effects on sexual functioning. In general, reports of sexual dysfunction among gynecological cancer survivors varies between 20 and 100 percent (Loescher, Welch-McCaffrey, Leigh, Hoffman, & Meyskens, 1989; Stewart, Wong, Duff, Melancon, & Cheung, 2001), and other forms of treatment can contribute to this

problem, as will be discussed. Finally, loss of the uterus and external scars can lead to sexual identity issues and body image changes (Anderson & Lutgendorf, 1997) making some women feel like less of a woman.

Surgery for vulvar cancer can range from wide local incision to radical vulvectomy (removal of the entire vulva, the external genitalia), and is the most physically deforming gynecologic surgery (Janda, Obermair, Cellas, Crandon, & Trimmel, 2004). Radical vulvectomy includes removal of the distal one-third of the vagina resulting in a shortened vagina and potentially dyspareunia and loss of orgasmic ability (Loescher et al., 1989). Green and colleagues (2000) surveyed 41 women (mean age = 60) after vulvectomy for treatment of vulvar carcinoma or carcinoma *in situ* (Green, Naumann, Elliot, Hall, Higgins, & Grigsby, 2000). Twenty-five of the women were sexually active before surgery, and 18 remained sexually active at the time of the survey. Results indicated that patients had significant body image disturbance, significant decrease in sexual frequency, and significant sexual dysfunction in the DSM-IV categories of sexual aversion disorder, arousal disorder, and hypoactive disorder (Green et al., 2000). In another study, Janda, Obermairi, Cellas, Crandon, and Trimmel (2004) conducted a qualitative assessement of quality of life between two weeks and 39 months since surgery in 15 vulvar cancer patients, 14 of whom had received a radical vulvectomy. The researchers found that patients experienced reductions in quality of life including emotional, physical, and social functioning, sexuality, and body image (Janda et al., 2004).

In addition to sexual difficulties, surgeries, such as vulvectomy, can also contribute to bladder, urinary track, or bowel changes/dysfunction (Janda et al., 2004). Furthermore, in cases where cancer has spread beyond the vulva or there is extensive pelvic disease, pelvic exenteration --surgery to remove the lower colon, rectum, bladder, cervix, vagina, ovaries, and nearby lymph nodes and create stomata (openings) through which urine and stool are passed out of the body -- is often necessary. This surgery changes body function and image by necessitating stoma management and potentially causing skin and odor problems, weight gain, peristomal hernias, electrolyte imbalance (Anderson & Lutgendorf, 1997). For many, it is a life changing experience.

Vaginal cancer, a rarer form of gynecologic disease, most often arises from other gynecologic cancers (Hacker, 2005). It is more common among older women, though approximately ten percent of cases are adenocarcinomas which affect younger women, regardless of whether they were exposed to diethylstilbestrol (DES) in utero (Hacker, 2005). Treatment for vaginal cancer is varied, though radical hysterectomy and partial to radical vaginectomy are common, and pelvic exenteration is performed in cases with more advanced disease or recurrence. In addition, many patients also choose to undergo vaginal reconstruction given the nature of the surgery. Long-term sequelae are similar to those following treatment for cancer of the vulva.

Radiation Therapy. In addition to surgery produced anatomical changes, therapy induced menopause can lead to additional anatomical changes affecting sexual functioning (Knobf, 2001; Loescher et al., 1989; Stewart et al., 2001). In general, survivors report symptoms of dysfunction including inhibited sexual desire or loss of

desire for intercourse (Stewart et al., 2001). Radiation therapy may also cause vaginal

drying, atrophy, stenosis (constriction), and fibrosis triggering sexual dysfunction, and

loss of ovarian function contributes to infertility and loss of hormonal functioning

(Anderson & Lutgendorf, 1997; Loescher et al, 1989). Short-term morbidities include

dietary limitations, diarrhea, and/or constipation. Fistulas, contracted bladder, and others

can be late onset morbidities (Anderson & Lutgendorf, 1997; Loescher et al, 1989).

Chemotherapy. Chemotherapy leads to multiple side effects and toxicities. In the

short-term, hair loss and neurotoxicity are common (Markman, 2005). In addition,

chemotherapy and radiation therapy may interrupt ovarian function triggering increased

risk of osteoporosis (McCarthy, 2004; Shapiro, Menola, & Leboff, 2001), cardiovascular

disease (Loescher et al., 1989; McCarthy, 2004), renal and neurologic problems, as well

as leading to long term energy deficits (Anderson & Lutgendorf, 1997; Loescher et al.,

1989).

Fatigue is a distressing and prolonged side effect affecting between 59 and 100

percent of cancer patients and many survivors (Ferrel et al., 2003; Schwartz, Nail, Chen

et al., 2000). For example, (Loge, Abrahamsen, & Kaasa, 2000) conducted a study with

457 Hodgkin's Disease survivors (44% female) between 3 and 23 years post-treatment

and found that 26 percent of survivors had substantial fatigue for six months or longer.

In another study of 1,957 breast cancer survivors, approximately one third of those

assessed reported more severe fatigue than that reported by age-matched women in the

general population (Bower, Ganz, Desmond et al., 2000). Empirical studies on fatigue in

gynecologic cancer survivors are lacking, but these patients undergo similar treatments

(chemotherapy and radiation therapy) as other cancer survivors, so it is likely that gynecologic cancer survivors also face long-term problems of fatigue and lack of energy (Anderson & Lutgendorf, 1997). One study compared 61 endometrial cancer survivors (5-7 years post-treatment) to 527 healthy postmenopausal women and found that fatigue was a common complaint among the cancer survivor group (Li, Samsioe, & Iosif, 1999; see below for further details on this study).

Overall, gynecologic cancer survivors face numerous and difficult long-term consequences of the cancer experience, and yet they are a relatively neglected research population. Changes such as decreased sexual functioning, dyspareunia, body image concerns, menopausal symptoms, and fatigue are frequent problems facing gynecologic cancer survivors (Loescher et al., 1989), and they appear to be major concerns of this population (Gotay & Muraoka, 1998).

Quality of life in gynecologic cancer survivors.

In addition to findings related to the health and physical functioning problems facing gynecologic cancer survivors, several empirical studies have documented psychological and behavioral concerns among gynecological cancer survivors. However, less is known about such outcomes in the long-term and how the changes in physical functioning and quality of life and psychological sequelae, such as depression, may be related.

Matthews and colleagues (1999) surveyed 220 patients (mean age = 41) diagnosed with clear-cell adenocarcinoma of the vagina or cervix an average of 18 years prior. Patients were treated surgically (89%), in addition to radiotherapy or

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chemotherapy (37%). In addition, 63% had vaginal reconstruction following surgery. Patients were assessed using author-developed measures of health status, coping, and perceived health and quality of life and the Beck Depression Inventory (BDI; Beck & Steer, 1984). Patients reported feeling less healthy than other women their age (46%), that their disease interfered at least moderately with their ability to fulfill life roles (22%), and made it difficult to reach goals (21%). Additionally, patients reported current pelvic pain (12%), urinary incontinence (28%), difficulty initiating urination (17%), recurrent bladder or urinary tract infections (13%), chronic diarrhea (20%), and chronic constipation (15%). Results indicated that 17% of patients were mildly depressed and 9% were moderately or severely depressed. Overall, patients in this study reported favorable health, but a substantial portion continued to experience a range of debilitating somatic symptoms and depressive symptoms several years following their diagnosis and treatment. A high frequency of physical problems was evident, but did not predict psychological distress, possibly due in part to the use of an author-derived measures of psychological functioning and quality of life (Matthews, Aikens, Helmrich, Anderson, Herbst, & Waggoner, 1999).

In another study, Miller, Pittman, Case, and McQuellon (2002) assessed quality of life in 85 gynecologic cancer patients (mean age = 59 years) at least 6 months (median 39 months) from treatment. Seventy-one percent had been treated surgically, 49% with radiotherapy, and 26% with chemotherapy. These patients were compared with an unmatched sample of 42 healthy women (mean age = 56) seeking routine gynecologic care. The authors found that quality of life scores (FACT-G; Cella, Tulsky, & Gray,

1994) were comparable in the cancer and healthy comparison groups; however, functional subscale scores were lower in patients with ovarian cancer, women with fewer years of education, and women with no help at home. Consequently, while quality of life scores were similar for cancer patients and healthy controls, the results suggest that ovarian cancer survivors and those who underwent adjuvant therapy are especially susceptible to quality of life problems (Miller et al., 2002).

Stewart and colleagues (2001) surveyed 200 ovarian cancer survivors (mean age = 55 years) without active disease and at least two years post-treatment (mean 7.2 years post diagnosis). Quality of life and physical functioning were assessed using the items derived from various other quality of life measures. Survivors had been treated with hysterectomy and oophorectomy (98%), chemotherapy (84%), and radiotherapy (22%). Fifty-four percent of survivors reported current pelvic pain or discomfort that they ascribed to their cancer treatment. In addition, 57% reported their sex lives had been affected by cancer and its treatment, and women under age 55 reported a greater sense of loss about sexual functioning and fertility. In spite of these physical symptoms, mental health and energy level were comparable to available norms and most patients reported that the experience of ovarian cancer had changed their life views in a positive way, suggesting that evaluation of the cancer experience in terms of life can impact the relationship between physical functioning difficulties and psychological adjustment difficulties (Stewart, Wong, Duff, Melancon, & Cheung, 2001).

Li, Samsioe, and Iosif (1999) compared 61 endometrial cancer survivors (5-7 years post-treatment) to 527 matched healthy postmenopausal women completing an

author-created questionnaire on quality of life. Treatments for those in the cancer group included surgery only (n=50, 51%), or receipt of adjuvant radiotherapy and/or chemotherapy as well. Two survivor groups were created: older survivors (n=34, mean age=74) and younger survivors (n=27, mean age=56) to facilitate comparison with the relatively young (mean age=55) control group. There was no control group established for older survivors. Sixty-three percent of younger survivors reported significant depressive symptoms. Furthermore, younger patients reported greater depressive symptoms than older patients or controls and feeling more "overstressed" than older patients. Younger patients also reported significantly more stomach discomfort, nausea, and diarrhea, and lower energy levels when compared to controls. There were no significant differences between younger and older patients on these variables. These data illustrated a high frequency of physical problems and psychological distress up to seven years following diagnosis, with younger patients experiencing more distress than older patients (Li, Samsioe, & Iosif, 1999).

In summary, the physical sequelae of treatment are common and persistent (Li et al., 1999; Matthews et al., 1999; Stewart et al., 2001). However, less is known about how survivors adapt to these side effects, although there appears to be a relationship between physical sequelae and psychological functioning, including depressive symptoms.

Psychological Sequelae of Cancer

As noted above in studies on quality of life, psychological distress is a problem for some gynecological cancer survivors. In particular, it appears as though depressive symptoms are in need of attention. Issues such as depression often arise around the time of diagnosis and treatment; however, the late sequelae of cancer and adjustment as a survivor may also be related to depressive symptomatology in gynecological cancer survivors.

Depression. Depressive disorders include Major Depressive Disorder (MDD) and Dysthymic Disorder. Criteria for these two disorders are presented in Appendix A. From a clinical standpoint, it is important to note that individuals may experience subclinical levels of depression, where they do not fully meet the criteria for a disorder, but they exhibit multiple symptoms of depression.

Depression in Cancer Patients. Cancer is one of life's most difficult and dispiriting events leading to physical suffering and psychological distress. While the cancer experience does not always lead to depression, it has been identified as a risk factor for depression (Raison & Miller, 2003). Estimates of depressive symptoms among cancer patients range from 18%-58% (Given et al., 1993). Major depression develops in approximately 25% of cancer patients, and many others suffer at subclinical levels (Kurtz, Kurtz, Stommel, Given, & Given, 2001). Even though the prevalence of psychological disorders, such as depression, is higher among cancer patients than the general population, the symptoms often go unrecognized and untreated, and may be

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disabling and persistent for years post-treatment (Hipkins et al., 2004; Kurtz et al., 2001; Newport & Nemoroff, 1998).

Research has investigated depressive symptoms among cancer patients. For example, Ell and colleagues (2005) assessed 472 breast cancer (53%) and gynecological cancer (47%) patients. Thirty-eight percent were newly diagnosed with recurrent cancer, 51% were in active cancer treatment, and 11% were in active follow-up. Patients completed the Patient Health Questionnaire-9 (PHQ-9), a subset of questions from the PRIME-MD (Pfizer Inc.; Mirander & Cooper, 2004), as a measure of presence of depressive disorders and a subset of items from the Brief Symptom Inventory (BSI; Derogatis, 1993) as a measure of anxiety. Results indicated that 24% of the women met criteria for major depressive disorder. Of those women 71% fell in the moderate range, 38% were in the severe range, and 20% endorsed suicidal ideation. In addition, 15% of women in the sample screened positive for dysthmia. Finally, depression was significantly correlated with anxiety and physical functioning (KPS; Karnofsky & Burchenal, 1949), and fears about treatment side effects were predictive of depression (Ell et al., 2005).

Depression in Cancer Survivors. In addition to depressive symptoms experienced around the time of diagnosis and treatment, cancer survivors, and gynecologic cancer survivors in particular, experience significant reductions in physical functioning and quality of life in the long-term as well, yet examining the psychological outcomes of such changes has been a neglected area of research. Women tend to report higher rates of depression in general (APA, 2000) and they report greater symptom distress and lower

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mental health than male patients (Kurtz et al, 2001), making such an outcome particularly relevant for a group of female cancer survivors.   Several studies have examined depressive symptoms in cancer survivor populations.

Brown and colleagues (2003) assessed 205 cancer patients (48% breast, 52% lung, colon, head and neck, prostate, uterus, ovary, colon, and rectum). Survivors were a mean of nine years since diagnosis and 80 percent were female.   On average, survivors had a CES-D of 20 (16 or higher indicating depression). In a review of long-term breast-cancer survivors between five and thirty years since diagnosis, Gotay and Muraoka (1998) noted women continued to experience anxiety, depression, fear of recurrence, and psychological difficulties with regard to changes in their bodies. Deimling, Kahana, Bowman, and Schaefer (2002) examined 180 older (mean age = 72) long-term (mean of 11 years since diagnosis) breast, colorectal, and prostate cancer survivors. They found that 25 percent of this sample had clinical levels of depression and anxiety and that survivors who had chemotherapy and had more cancer-related symptoms were more depressed.

Saleeba and colleagues (1996) studied 52 breast cancer survivors at least five years (mean = 8.5 years) since diagnosis undergoing routine follow-up care. Survivors were compared to a control group of 88 women undergoing routine low-risk breast cancer screening. Survivors were significantly older (mean age = 54) and less educated (mean = 13 years) than controls (mean age = 45; education = 15); however, age was not a significant covariate for the outcome. Participants completed the BDI and State Trait Anxiety Inventory (STAI; Spielberger, 1983). Covarying for education, analyses

revealed that breast cancer survivors experienced significantly greater levels of depression. There were no significant differences between groups on anxiety levels. This study excluded women who had a history of a DSM-III-R psychiatric diagnosis, which means they may have underestimated the incidence of emotional distress in the population. Nonetheless, it demonstrates that emotional distress, such as depression, can persist in disease-free women five or more years after diagnosis (Saleeba, Wietzner, & Meyers, 1996).

In another study, Zebrack and colleagues (2002) compared 5,736 adult survivors (mean age = 27; 45% female) of childhood leukemia, Hodgkin's disease, and Non-Hodgkin's lymphoma and 2565 sibling controls (mean age 29; 53% female) (Zebrack, Zeltzer, Whitton et al., 2002). Depressive symptoms were assessed using the Brief Symptom Inventory (BSI; Derogatis, 1993) and DSM-IV criteria. Survivors were significantly more likely to report depressive symptoms than sibling controls. In addition, women were more likely to report symptoms of depression than men. Additional variables, such as socioeconomic status and exposure to intensive chemotherapy were also influential. The authors conclude that survivors, particularly females and those with intensive chemotherapy, are at risk for depression (Zebrack et al., 2002).

Depressive Symptoms in Gynecologic Cancer Survivors. A few studies have documented depressive symptoms in the gynecological cancer survivor population. Zabora and colleagues (2001) examined 4, 496 cancer survivors (58% newly diagnosed, 13% between 90 days and one year post-diagnosis, and 30% one or more years from

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diagnosis).   Approximately 28% of the sample was breast cancer patients, while five percent was gynecologic cancer patients. Patients completed the BSI (Derogatis, 1993) and analyses revealed that 30% of gynecologic cancer survivors were considered positive cases for psychological distress, including depression and anxiety (Zabora, BrintzenhofeSzoc, Curbow, Hooker, & Piantadosi, 2001).

In an additional study, 105 women who had underwent major gynecological surgery for carcinoma of the cervix and vulva completed an interview about psycho-social problems and the HADS (Zigmond & Snaith, 1983) between six months and five years post-surgery (mean = 29 months) (Corney, Everett, Howells, & Crowther, 1992). On the HADS, results indicated that 20% of survivors were borderline and 21% were definite symptomatic. On the depression scale, results indicated that 18% of survivors were borderline and 14% were definite symptomatic.   The authors noted that depressive symptoms were a problem for some gynecologic cancer survivors, but that many reported difficulty asking for help, suggesting medical and nursing staff need to be aware of this potential problem (Corney et al., 1992).

It appears as though the cancer experience, even in the long-term, can continue to impact depressive symptomatology. For example, rates of depression among gynecologic cancer survivors range from 9% (Matthews et al, 1999) to 63% (Li et al., 1999). Additional evidence of depressive symptomatology in gynecologic and other cancer survivors will now be presented in relation to the physical sequelae of cancer.

Relationship Between Physical Sequelae and Depressive Symptoms

Figures 1 and 2 demonstrates two models for the current research. Path *a* of these models suggests the physical health and functional problems cancer survivors face may lead to symptoms of depression (see path *a* of Figures 1 & 2). In particular, physical symptoms related to the cancer experience are known to influence adjustment post-treatment (Ganz, 1998; Grassi, 1997). Cancer-related symptoms, such as fatigue and pain, may be difficult to cope with and can leave patients feeling hopeless and depressed. In addition, disabilities related to cancer and its treatment remain an ongoing source of distress during survivorship as physical impairments can generate anger and symptoms related to depression (Welch-McCaffrey, Hoffman, Leigh, Loescher, & Meyskens, 1989). Several studies have explored the relationship between the physical sequelae of cancer and distress, or more specifically, depressive symptoms in cancer patients or survivors.

In the aforementioned study by Li et al. (1999) comparing 61 endometrial cancer survivors (5-7 years post-treatment) to 527 healthy postmenopausal women, cancer survivors experienced more physical symptoms, such as headaches and dizziness, and gastrointestinal symptoms then healthy controls, and many of the survivors were distressed by the experience of such medical complications. As previously mentioned, Deimling et al. (2002) found that 25 percent of a sample of 180 older (mean age = 72) long-term (mean of 11 years since diagnosis) survivors had clinical levels of depression and that survivors with more cancer-related symptoms were more depressed.

Kurtz, Wyatt, & Jurtz (1995) studied 191 cancer survivors (58% breast, 12% uterine, 3% ovarian) who were five or more years from diagnosis, and found that somatic

well-being and sexual functioning were related to psychological well-being (Kurtz et al., 1995). Others have demonstrated that physical symptoms, such as hot flashes, can greatly impact a woman's quality of life or functional ability and many women have reported irritability and depression as a result (Finck et al., 1998).

Weitzner, Meyers, Stuebing, and Saleeba (1997) examined breast cancer survivors (mean age = 54) who had been disease free for at least five years. They found that greater mood disturbance, including depression (BDI; Beck et al., 1961) and anxiety (STAI; Spielberger, Gorsuch, & Lushene, 1970) was associated with poorer quality of life (Ferrans & Powers Quality of Life Index; Ferrans & Powers, 1985), including health functioning and spirituality. This studied excluded women who had a history of a DSM-III-R psychiatric diagnosis, which means they may have underestimated the incidence of emotional distress in the population. Nonetheless, it is apparent that there is a link between health-related quality of life and depression.

As previously mentioned, fatigue is one of the most debilitating and distressing problems facing cancer survivors. Fatigue can make it difficult for survivors to return to work or engage in recreational or social activities. This can affect survivors' quality of life and cause considerable distress. For example, in Loge, Abrahamsen, and Kaasa's (2000) study of 457 Hodgkin's Disease survivors between 3 and 23 years post-treatment, 26 percent of survivors had substantial fatigue (Fatigue Questionnaire; Chalder et al., 1993) for six months or longer, and depression (HADS; Zigmond & Snaith, 1983) was reported more commonly among this subgroup of survivors. Though this study was cross-sectional in nature, a past history of psychiatric problems was not more common

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among the fatigue group adding support to the idea that fatigue is not merely a symptom of psychiatric disorder.   In another study, 1,957 breast cancer survivors (mean age = 55) who were one to five years post-diagnosis, had completed treatment, had no other history of cancer, or no other major disabling medical or psychiatric conditions, were surveyed (Bower et al., 2000). Those reporting more severe fatigue (RAND energy/fatigue subscale; Hays, Sherbourne, & Mazel, 1993) than that reported by age-matched women in the general population, also reported higher levels of depression (CES-D; Radloff, 1977).

In addition to physical symptoms, immobility and having to depend on others to assist in daily activities may have a profound psychological impact on cancer patients. For example, Given et al., (1993) studied 196 cancer patients (53% breast, 10% gynecological).   Findings indicated that patients' immobility (measure derived from MOS; Stewart, Ware, & Brook, 1981), cancer-related symptomatology (McCorkle Symptom Distress Scale; McCorkle, 1988), and dependencies in activities of daily living (OARS Multidimensional Functional Assessment Questionnaire; Filenbaum & Smyer, 1981) affected their levels of depression (CES-D; Radloph, 1977). Similarly, Grassi, Malacarne, Maestri, and Ramelli (1997) examined depressive symptoms (ICD-10; WHO, 1993) and performance status (Karnofsky & Burchenal, 1984) in 113 breast (55%) and other cancer patients one year following diagnosis. The results indicate that 31% of the sample had an ICD-10 diagnosis of depression and that lower performance status was predictive of depression.

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Others have examined the impact of symptom severity and deficits in physical functioning on older persons with cancer (Kurtz et al., 2001). Kurtz et al. (2001) interviewed 420 patients (mean age = 72 years) with breast (43%), colon (22%), prostate (12%), or lung (24%) cancer four to six weeks after surgery and two to four weeks after subsequent chemotherapy or radiation therapy. Higher levels of symptom severity (symptom experience scale; Given, Given, & Stommel, 1994) and greater physical functioning deficits (MOS SF-36; Ware & Shearbourne, 1992) were predictive of higher levels of depressive symptomatology (CES-D; Radloff, 1977). Comorbidity (number of physical comorbid conditions reported) was not predictive of physical functioning deficits. The authors conclude that physical functioning and symptom distress contribute to depressive symptomatology, and stress the need of health care professionals to try and identify these patients for intervention (Kurtz et al., 2001).

Overall, it appears as though there is an important relationship between the physical sequelae of the cancer experience and depressive symptoms in cancer survivors, including gynecological cancer survivors (see Path *a* Figures 1 and 2). Many of these studies support the hypothesis that such physical sequelae can contribute to depressive symptomatology. Knowing this, it is important to also understand what variables may also play a role in this relationship. Some studies have found that social support (Grassi et al., 1997; Lewis, Manne, DuHamel , 2001; Michael et al., 2002) and coping (Sharpe, Sensky, & Allard, 2001; Penedo, Antoni, Schneiderman et al., 2001) are important moderators or mediators. However, additional research suggests that meaning in life may also be influential. In dealing with the physical sequelae of the cancer experience,

existential issues may become more important and the meaning in life may supersede other aspects of daily living (Anderson & Lutgendorf, 1997).

Meaning in Life

A diagnosis of cancer can create an existential plight, and all assumptions about the world and one's future are challenged creating a core spiritual pain. One's system of meaning may be challenged and the constructs of beliefs that once led one's life may be lost along with the physical, social, and psychological losses that may accompany cancer diagnosis and treatment (Doka, 2000).

The cancer experience can affect people in many ways. In addition to the physical and psychological sequelae previously described, the cancer experience can affect people existentially. Most people will at some point encounter existential issues, including loss and death, but those with cancer often deal with them sooner and more intensively than most. In a sample of ethnically-diverse, urban cancer survivors, 40% of patients reported wanting help with finding meaning in life and 28% reported wanting someone with whom to talk about the meaning of life (Moadel, Morgan, Fatone et al., 1999).

Survivors face numerous physical, social, emotional, and even spiritual after effects. Survivors may still question meaning and want to understand why this illness has affected them. This too can challenge prior systems of meaning. For some individuals, new meaning can surface from the experience of cancer. For example, some report strengthened spiritual beliefs or find more value in their own strengths (Doka, 2000). Hence, cancer diagnosis can lead to a search for meaning, and those who find more

meaning tend to report better adjustment (Schroevers, Ranchor, & Sanderman, 2004; Taylor, Lichtman, & Wood, 1984; Tomich & Helgeson, 2002).

The current study examines two common scenarios among cancer survivors. First, it is possible that some survivors find meaning during the initial diagnosis and treatment period and this meaning creates a buffer between the late physical sequelae of survivorship and psychological dysfunction, such as depression. On the other hand, some individuals may continue to search for meaning after the initial cancer experience and the physical debilitation of longer-term survival may interfere with finding meaning, which may exacerbate distress, including depressive symptoms. Nonetheless, there has been little research examining the relationships between late sequelae of cancer diagnosis and treatment and meaning in life.

The Meaning of Meaning. When discussing meaning in life, it is first important to define it, as there are many and varied definitions of meaning in life. Some describe meaning as "…the cognizance of order, coherence, and purpose in one's existence, the pursuit and attainment of worthwhile goals, and an accompanying sense of fulfillment' (Reker & Wong, 1988, pp. 221). Others have suggested that life is meaningful if it is based on a feeling of integration and relatedness (Weisskopf-Joelson, 1968) or a feeling of fulfillment and significance (Maslow, 1964). Still others have suggested that meaninglessness relates to feelings of alienation and nothingness (Camus, 1946). In general, meaning in life seems to depend on a concept of life and a sense of fulfillment related to it (Battista & Almond, 1973). Meaning in life means that one values or believes in something. In addition, it implies that one has an understanding of life.

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Frankl (1963) has suggested, for example, that this understanding represents some goal, function, or purpose for life, for which the individual strives. Hence, a meaningful life implies a positive commitment to some concept of the meaning in life, and this concept gives one the framework from which to view or understand life. In addition, a meaningful life involves fulfilling this concept of life and this fulfillment may be a sense of integration, relatedness, or significance (Battista & Almond, 1973).

For the purpose of the current study, meaning in life is defined by the four distinct yet related dimensions suggested by Jim and colleagues (in press): Harmony and Peace, Life Perspectives, Purpose, and Goals, Benefits of Spirituality, and Confusion and Lessened Meaning (Jim, Purnell, Richardson, Golden-Kreutz, & Andersen, in press). The first dimension, Harmony and Peace, represents positive emotions and thoughts signifying a sense of harmony, serenity, and contentment. The second dimension, Life Perspectives, involves fulfillment related to existing plans and goals in addition to interactions with the world and others. The third dimension, Benefits of Spirituality, is the belief that life fits a greater overall pattern or design existing outside the individual. The final dimension, Confusion and Lessened Meaning, represents negative or confused beliefs about meaning in life.

Meaning in Life and Illness. Sources of meaning vary by individuals, but may include relationships with others, enjoyable activities, personal growth, cultural values and traditions, and helping others, to name a few (Greenstein & Breitbart, 2000). The sequelae of cancer diagnosis and treatment can interfere with individual sources of meaning over long periods of time, thus possibly contributing to depression. Some have

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suggested that having goals on which to focus and feeling part of a larger whole are critically important to finding meaning and coping with life-threatening illness, such as cancer (Greenstein & Breitbart, 2000). Individuals who are able to adapt their goals as cancer survivors may have better psychological adjustment.

The cancer experience, even for survivors can include a great deal of suffering, especially if physical side-effects linger. Frankl (1963) believed that life has meaning under all conditions, even those of suffering. He suggested that suffering creates a search for meaning by providing powerful motivation to make sense of the situation for the sufferer. In addition, he stated that when a person's search for meaning is blocked, existential frustration results, which can eventually lead to 'noogenic neurosis,' a pathological condition characterized by hopelessness, depression, and apathy. Having a feeling of purpose and meaning can aid in alleviating distress caused by illness and its consequences (Greenstein & Breitbart, 2000). For instance, patients who reported a greater degree of meaning in their lives also reported enjoying life more than those with less meaning, even in the case of severe pain or fatigue (Greenstein & Breitbart, 2000). In addition, those who are able to find more meaning within traumatic events appear adapt better to them (Greenstein & Breitbart, 2000).

Research has demonstrated both positive (Taylor, 1983) and negative (Janoff-Bulman, 1989) changes in beliefs following trauma. Individuals may experience changes in activities, priorities, and relationships in a positive way, while views of the self, world, and future may change in both directions. The Assumptive Worlds Perspective can account for negative responses to trauma, such as may be experienced by cancer

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survivors (Janoff-Bulman, 1989). People have certain cognitive assumptions about the world, including the belief that the world is benevolent and meaningful and the belief that the self is worthy and relatively invulnerable to negative events. However, experiencing a life-threatening illness, such as cancer, and dealing with its aftermath, can shatter this perspective. Cancer survivors often feel the world is a more frightening and dangerous place (Bower et al., 2005). For instance, Collins, Taylor, and Skokan (1990) interviewed 55 cancer patients within five years of diagnosis (mean = 3 years). Results indicated that those who reported ongoing threat also reported more negative changes to their views of the self, world, and future. The authors concluded that the assumptive world must be rebuilt and altered to fit new information pertaining to the cancer experience (Collins et al., 1990). In this way, one can see how the struggles of physical sequelae of cancer could interfere with finding positive meaning.

However, some individuals may have a positive outcome to the trauma of the cancer experience. Theorists have proposed that one may attempt to offset the negative consequences of cancer by trying to find benefits in the experience, such as finding meaning, or by believing one is a better person for having survived the experience (Collins et al., 1990). For example, Taylor (1983) found that cancer patients reported new insights about their lives and themselves and that those who experienced positive changes in their values and priorities, experienced better adjustment. Cancer survivors can reprioritize and put more emphasis on relationships, personal growth, and appreciation of life (Tomich and Helgeson, 2002). In a sample of 763 breast cancer survivors assessed longitudinally at one to five and five to ten years after diagnosis,

perceptions of positive meaning and vulnerability (author developed measure based on other measures e.g. Postraumatic Growth Inventory; Concerns about Recurrence Scale) were associated with psychological adjustment (Bower et al., 2005). More specifically, vulnerability was associated with negative affect (subscale CES-D, Radloff, 1977), while positive meaning was associated with positive affect in both cross sectional and longitudinal analyses. These studies further support the idea that those who are able to find meaning from the cancer experience may be protected from psychological distress, while those who still struggle with meaning while experiencing the after effects of illness may be more vulnerable to distress.

Physical Sequelae of Cancer, Meaning in Life, and Depressive Symptoms

Physical Sequelae of Cancer and Meaning in Life (see path *b* Figure 1). It was hypothesized that the physical sequelae of the cancer experience are associated with depressive symptoms in cancer survivors. The physical health and functioning difficulties that accompany long-term cancer survivorship may also be related to distress through a negative relationship with meaning. If survivors are noticing the long-term effects of cancer, they may view the cancer experience as more negative or threatening. For example, events may be interpreted more negatively if the ability to achieve desired goals is impaired (Thompson & Janigian, 1988). As mentioned above, the gynecological cancer experience can result in considerable loss, including loss of organs, loss of fertility, and loss of various functional capacities, to name a few. We hypothesized that trauma and loss such these can threaten meaning in life. Some survivors may have

difficulty making sense of the cancer experience and the loss associated with it, and those who perceive more negative consequences from cancer may find less meaning.

In addition to the cancer experience shattering one's belief system about the self, world, and future, impaired physical health and functioning may hinder survivors from taking part in activities that once provided sources of meaning. For example, sexual dysfunction may alter the dynamics of romantic relationships and lead to a decline in marital satisfaction. This may interfere in meaning previously derived from a survivor's role as a woman or partner. For younger women, infertility may remove meaning once sought through reproduction. Additionally, fatigue can disrupt the survivor's ability to perform not only daily activities of living, but also performance at work, being able to provide for families, and social functioning. This can take away meaning once sought through career development, generativity, and personal relationships.

Meaning in Life as a Buffer (see path b Figure 2). While the late physical sequelae of cancer may cause distress for some individuals, it is possible that others are not as distressed because they may have found meaning earlier in the cancer experience that aids them as they encounter the long term effects of the cancer experience. As mentioned above, the cancer experience brings considerable loss. Some theorists suggest that an important part of resolving loss is to develop an understanding of the event (Frankl, 1963; Janoff-Bulman, 1992; Taylor, 1983). Others suggest people can find benign reasons for loss, or make sense of it within an existing framework of schemas or beliefs about the world (Janoff-Bulman, 1992). For example, some individuals may make sense of events by attributing them to God's will, by assuming some personal

responsibility for an event, or by attributing loss to personal lifestyles or behaviors. Some cancer survivors may resolve their loss as they recover from cancer, and this may protect them from psychological distress as survivors. Some survivors may also find new sources of meaning if impaired physical health and functioning prevent them from taking part in once meaningful activities. By finding new positive and fulfilling sources of meaning, they may again be protected from distress.

Meaning in Life and Depressive Symptoms (see path *c* Figure 1 and path *b* Figure 2). The existential challenge of the cancer experience (challenge to view of self, world, future) is often represented by feelings of hopelessness and depression. The clinical work of Jung, Frankl, and others (Yalom, 1980), suggests that failure to find meaning results in psychopathology, while on the other hand, realization of meaning can be healing. In this way, changes in meaning in life is related to changes in psychological functioning, both positive and negative.

Vickberg and colleagues (2000) noted meaning is associated with reduced concurrent and prospective distress in cancer patients (Vickberg et al., 2000). When cancer has less of an impact on mental-health quality of life, it may be because survivors change their norms or expectations, find improvements in their lives, such as closer interpersonal relationships, or change priorities or life goals (Roberts et al., 1992).

Furthermore, researchers have linked meaning in life to well-being (Zika & Chamberlain, 1992). Zika and Chamberlain (1992) examined this relationship in two samples: 194 mothers of young children (mean age = 29) and 150 older adults (mean age = 69 years; 58% female). They found that meaning in life (using the Purpose in Life test;

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Crumbaugh & Maholick, 1964; Life Regard Index, Battista & Almond, 1973; Sense of Coherence Scale, Antonovsky, 1985) was moderately to strongly correlated with multiple measures of well-being (Mental Health Inventory, Viet & Ware, 1983), including higher order factors, such as psychological distress and well-being, and five lower order factors, anxiety, depression, and loss of behavioral/emotional control, positive and negative affect, and emotional ties, in addition to general life satisfaction. They suggest that the influence of meaning in life on well-being is broad and pervasive, and that people who lack meaning are likely to have problems in many aspects of psychological functioning.

Strawbridge and colleagues (1998) used the 1994 Alameda County Study survey of 2,537 subjects (56% female; mean age = 65 years) to explore the relationship between non-organizational religiosity (prayer and spiritual beliefs), a concept related to meaning in life, and depression. They found that non-organizational religiosity buffered associations between health problems and depression (adapted from PRIME-MD, Spitzer et al., 1994) (Strawbridge,Shema, Cohen, Roberts, & Kaplan, 1998)

Others have found links between spiritual well-being, physical health, and depressive symptoms. For instance, Wenzel and colleagues (2002) conducted a study with 49 stage I-II ovarian cancer survivors who were five or more years (mean = 9) from diagnosis (Wenzel, Donnelly, Fowler et al., 2002). The authors found that 20% of survivors experienced substantial long-term treatment side effects including abdominal pain, gynecologic symptoms, such as vaginal dryness, pain, and cancer-related menopause, and neurotoxicity. In addition, 20% and 23% of patients were below norms for emotional and social functioning, respectively (MOS SF-36; Ware & Sherbourne,

1992). Furthermore, emotional well-being was significantly associated with self-reports of general health and vitality (MOS SF-36; Ware & Sherbourne, 1992) and depressive symptoms (CES-D; Radloff, 1977). Participants reported that the most significant challenge of survivorship was long-term sequelae of treatment, which 20% of patients rated as their primary concern. Furthermore, they found that spiritual well-being was significantly positively associated with mental health, and negatively associated with declining health status. Overall, these results indicate that, while most early-stage ovarian cancer survivors function as well or better than their counterparts who have not experienced cancer, 20 to 23 percent do experience long-term treatment sequelae that are associated with poorer spiritual well-being, traumatic stress and depressive symptoms (Wenzel et al., 2002).

It appears as though some long-term cancer survivors may continue to experience negative physical functioning and quality of life problems that are related to the development of depressive symptoms. On the other hand, other survivors appear to benefit from finding meaning through the cancer experience and fare better psychologically even in the face of late physical effects. Based on what is known about the potential relationships between physical debilitation and meaning in life on depressive symptoms and the importance of studying such an outcome in a gynecological cancer survivor population, the current study was conducted.

Current Study

The current study has two goals. First, it attempts to expand knowledge in the areas of physical functioning/quality of life, meaning in life, and depressive symptoms

among gynecologic cancer survivors. Second, it explores the relationships between these variables in gynecological cancer survivors.

Two competing views of the contribution of meaning in life are tested. Meaning in life may mediate or moderate the relationship between physical functioning and depressive symptoms. It is hypothesized that physical functioning would be associated with levels of depressive symptoms in gynecological cancer survivors and that meaning in life will partially mediate or moderate this relationship. In addition, it is hypothesized that these relationships would still be significant while controlling for a previous history of depression.

A cross-sectional design is used to examine these hypotheses. Patients in active gynecologic oncology follow-up were recruited and interviewed during a visit to their oncologist.   In the current study, physical sequeale is operationalized as follows: physical quality of life (MOS SF-12 Physical Component Score, SF-12 PCS; Ware, Kosinski, & Keller, 1996), gynecologic cancer-specific quality of life (FACT; Cella, Tulsky, & Gray, 1994), treatment toxicity (using Southwest Oncology Group, SWOG, toxicity criteria; Moinpour, Feigl, Mecth, Hayden, Meyskens, & Crowley, 1989), a nurse rated index of performance status (Karnofsky Performance Status, KPS; Karnofsky & Burchenal, 1949), fatigue (Fatigue Symptom Inventory-Revised; FSI; Hann, Jacobsen, Azzarello, Martin, & Curran,1998), and vaginal changes. Meaning in life, the hypothesized mediator or moderator, is measured using a multidimensional measure -- the Meaning in Life Scale (MLS; Jim, Purnell, Richardson, Golden-Kreutz, & Andersen, in press).   Depressive symptomatoloy is the outcome. Measures included to assess

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depressive symptoms include items from the Center for Epidemiologic Studies

Depression Scale (CES-D; Radloff, 1977), and other measures of mood (Profile of Mood

States; POMS; Guadagnoli & Mor, 1989) and mental health functioning (MOS SF-12

Mental Component Score; Ware, Kosinski, & Keller, 1996; PTSD Symptom Checklist-

Civilian version (PCL-C; Weathers et al., 1991).

In addition to the hypothesized relationships between physical cancer sequelae

and meaning of life to depressive symptoms, other potential correlatates and controls are

considered. One known predictor of depressive symptoms is a history of depression. In

order to control for a history of depression, items assessing both major depressive

disorder and dysthymia are added as an additional predictor of current depressive

symptoms. Two categories of importance regarding gynecologic cancer survivorship are

sociodemographic variables and disease/treatment variables. For example, age at

diagnosis has been found to be related to psychosocial difficulties, with younger women

experiencing more than older women in breast cancer (Bowman, Deimling, Smerglia,

Sage, & Kahana, 2003; Cimprich, Ronis, & Martinez-Ramos, 2002; Michael et al., 2002;

Vacek et al., 2003) and gynecology patients (Leake et al., 2001). SES markers such as

years of education (Chan et al., 2001; Miller, Pittman, Case, & McQuellon, 2002) and

employment status (Bloom et al., 2004) have also been associated with poorer quality of

life in gynecologic and breast cancer survivors, respectively. Finally, having a

relationship with a significant other may also be related to the outcome variable (Parker,

Baile, DeMoor, & Cohen, 2003; Vacek, Winstead-Fry, Secker-Walker, Hooper, & Plante,

2003).

Disease and treatment variables may also be influential for depressive symptoms in cancer survivors. For example, more advanced disease in breast cancer survivors is related to poorer mental health (Jacobsen et al., 1998). In addition, extent of surgery is a consistent predictor of global quality of life in gynecologic cancer survivors (Greimel et al., 2002). Finally, length of time since diagnosis and treatment may impact psychological adjustment, even in longer term survivors. Thus, disease and treatment, as well as sociodemographic variables are considered for inclusion in the current study.

Hypotheses.

It is hypothesized that physical functioning, meaning in life, and depressive symptomatology variables are correlated. More specifically, it is hypothesized that greater physical functioning difficulties are associated with higher levels of depressive symptoms (see Figures 1 and 2 path a) and reduced meaning in life (see Figure 1 path *b*). In addition, it is hypothesized that reduced meaning in life is associated with higher levels of depressive symptomatology (see Figure 1 path *c*). It is hypothesized that meaning in life partially mediates the relationship between physical functioning and depressive symptoms (see Figure 1 for conceptual diagram of mediation model). More specifically, it is hypothesized that greater physical functioning difficulties are associated with reduced meaning in life which would, in turn, reflect higher levels of depressive symptomatology.

Conversely, it is hypothesized that meaning in life moderates the relationship between physical functioning and depression symptoms (see Figure 2 for conceptual diagram of the moderator model). More specifically, it is hypothesized that the

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deleterious effects of physical functioning deficits are moderated, in part, by varying

levels of meaning in life perceived by patients (see Figure 2 path *b*).

CHAPTER 2

METHOD

Design

A cross-sectional design was used. Gynecologic cancer survivors (cervical, endometrial, ovarian, vulvar, and other vaginal cancers) were assessed once during a regularly scheduled follow-up appointment. A cancer survivor can be defined as any individual who has been diagnosed with cancer (Dow, 2003); however, a distinction can be made between short and long-term survivors. Two years following cancer diagnosis, the acute stress of diagnosis has ended (Andersen, Anderson, & deProsse, 1989b) and patients resume their pre-cancer routines (Guidozzi, 1993; Klee, Thranov & Machin, 2000b). In addition, after ten years, patients are often entering older adulthood where comorbid conditions are more common, thus making it more complicated to ascribe quality of life concerns to their previous cancer (Lethbridge-Cejku, Schiller, & Bernadel, 2004). Hence in the current sample, time since original diagnosis varies from 2 to 10 years in order to focus on long-term gynecologic cancer survivors as a group.

Participants

Participants include 260 gynecologic cancer patients previously treated at the Ohio State University-affiliated Arthur G. James Cancer Hospital and Richard J. Solove

Research Institute and currently receiving follow-up care with the Division of Gynecologic Oncology, Department of Obstetrics and Gynecology. Exclusion criteria included the following: male (only women have gynecologic cancer), age <20 and >80, other cancer diagnosis, or prior refusal of cancer treatment, organic brain syndrome, significant visual or hearing deficit, major mental illness (e.g. schizophrenia), other mental illness which is not being treated/controlled (e.g. bipolar disorder), mental retardation, deficient ability to speak/read the English language, dementia, and/or current pregnancy.

Procedures

Gynecologic cancer survivors meeting eligibility criteria were identified. Two weeks prior to their clinic appointment, patients were sent a letter providing a written description of the study (i.e. purpose, time commitment, procedures, risks and benefit). Upon their clinic visit, eligible patients were again screened for eligibility and approached for participation in a one-time 60 to 90 minute assessment. Informed consent was obtained from participants using forms approved by the Institutional Review Board. Data collected included interview responses, self-report inventories, medical chart data (e.g. diagnosis, treatment), and medical evaluations. All data were coded by participant number. In conducting the interviews, assessors made every effort to attain data in a private, personal, and non-judgmental manner to minimize the incidence of embarrassment or discomfort. Interviews were conducted individually in consultation rooms available in the clinic. All women were provided with written and verbal information about the psychosocial services generally available at the cancer hospital.

Additionally, special requests (e.g. to see a consulting psychiatrist) made by participants were addressed as part of routine comprehensive care.

Measures

Physical Sequelae of Cancer. Six measures are used to assess physical functioning and the impact of physical functioning on quality of life. These include the following:

Medical Outcomes Study-Short Form 12 Physical Component Summary Score (SF-12 PCS; Ware & Sherbourne, 1992; Ware, Kosinski, & Keller, 1996). The SF-12PCS assessed health-related physical quality of life. The SF-12 assesses eight aspects of quality of life including physical functioning, role functioning-physical, bodily pain, general health perceptions, vitality, social functioning, role functioning-emotional, and mental health. Higher scores reflect better quality of life. The eight primary subscales are summarized into two component scores: the Physical Component Summary (PCS) and the Mental Component Summary (MCS). The SF-12 demonstrates adequate reliability and validity when compared to other similar measures of health-related quality of life. For instance, correlations between scores on the SF-12 and SF-36 range from 0.93 to 0.97. Internal consistency, test-retest reliability, and convergent and discriminant validity coefficients for the SF-12 are similar to those of the SF-36. Two-week test-retest reliability ranges from 0.86 to 0.89 for the PCS (Ware, Kosinski, & Keller, 1996). Internal consistency for the PCS in the present sample is .95.

Functional Assessment of Cancer Therapy (FACT; Cella, Tulsky, & Gray, 1994). The FACT examined quality of life outcomes in the context of cancer. Site- and

symptom-specific quality of life scales have been developed, including the 15-item

FACT-Cx for use with cervical cancer patients, 16-item FACT-En for endometrial cancer

patients, 12-item FACT-O for ovarian cancer patients, and 15-item FACT-V for vulva

patients. Each subscale contains items that reflect the various aspects of coping with a

specific cancer. In the present study, these subscales are used to assess disease-specific

quality of life. Patients endorse each item based on their experience of each

symptom/event during the past seven days. Items are rated on a 5-point Likert scale,

ranging from *0=not at all* to *4=very much.* Following reverse-scoring of negatively

valenced items, responses are weighted and summed. Higher scores reflect better quality

of life. In order to create a FACT score for all participants, the scores for the individual

FACT scales are standardized to create a FACT score. Reliability studies of the FACT-O

indicate 8-week test-retest reliability of 0.81 and internal consistency (alpha) of 0.92 for

the subscale. Tests of convergent and criterion-related validity indicate that the subscale

performs as expected with regard to other measures of QoL, mood, and performance

status (Basen-Engquist et al., 2001). There are currently no published data available on

the reliability and validity of the FACT-Cx, FACT-En, or FACT-V. Internal

consistencies for the individual FACT scales in our sample are as follows: FACT-Cx

(alpha = .83), FACT-En (alpha = .79), FACT-O (alpha = .79), and FACT-V (alpha = .81).

Southwest Oncology Group (SWOG; Moinpour, Feigl, Metch, Hayden,

Meyskens, & Crowley, 1989). During a clinical interview, a research nurse documented

the types and severity of current signs and symptoms. Self-reports of signs/symptoms are

provided for the four body systems most relevant to gynecologic disease: Renal/Bladder,

Gastrointestinal, Endocrine, and Mucosal. Severity ratings using a five-point scale unique to each symptom were used. For example, the scale for gastritis/ulcer (a Gastrointestinal item) includes 0=*none*; 1=*antacid required*; 2=*requires vigorous medical mgmt, no surgery*; 3=*requires surgery for ulcer*; and 4=*perforation, bleeding*. Subscale scores reflect the calculated average of the items for each body system; scores range from 0 to 4, with higher scores indicating more life-threatening symptoms. The subscale scores are summed to obtain an overall toxicity score. The total score ranges from 0 to 16, with a score of 16 indicating life-threatening symptoms in each of the four body systems. Internal consistency in our sample is alpha = 0.68. Six-month test-retest reliability in studies of breast cancer patients who have completed treatment ranges from 0.67 to 0.73 (sample reported in Andersen et al., 2004).

Karnofsky Performance Status rating (KPS; Karnofsky & Burchenal, 1949). The KPS assessed patients' functional status. The scale ranges from 100 (Normal, no complaints, no evidence of disease) to 0 (Dead) with 10-point intervals, each containing differential criteria (e.g., 90=able to carry on normal activity, minor signs/symptoms of disease; 80=normal activity with effort, some signs/symptoms of disease). The lower the score, the more restricted the patient is in the performance of daily and self-care activities. Across cancer studies interrater reliability for the scale ranges from 0.70 to 0.97 (Mor, Laliberte, Morris, & Wiemann, 1984; Wood, Anderson, & Yates, 1981) and many studies have demonstrated predictive validity with significant and high correlation with cancer endpoints (e.g. death, treatment toxicities, etc; Ganz et al., 1988).

Fatigue Symptom Inventory-Revised (FSI: Hann et al., 1998). The FSI is a 14-item measure designed to assess the frequency, severity, and daily pattern of fatigue as well as its impact on ratings of quality of life during the previous week. In the present study, the seven items that comprise the Total Disruption Index (TDI) score are used. Patients rate the degree to which fatigue interfered with a variety of activities during the past week using a 10-point Likert scale, ranging from *0=no interference* to *10=extreme interference*. The score is calculated based by summing the responses to each of the items. Total scores on the TDI range from 0 to 70, with higher scores indicating greater interference. Hann and colleagues (1998) have reported alpha coefficient reliabilities above 0.90 across three groups of women (no history of breast cancer, completed treatment for breast cancer, and active treatment for breast cancer). They have also reported adequate convergent validity for the FSI, with correlations between the TDI and other measures of fatigue and vitality ranging from 0.61 to 0.78 in cancer and healthy groups (Hann et al., 1998). The internal consistency alpha coefficient for the FSITDI is .94 in our sample.

Vaginal Changes. To our knowledge, there are no standardized measures of vaginal changes following gynecologic cancer treatment; therefore, a representative list was devised from the gynecology literature and advice of physician collaborators. Patients are queried about six common vaginal sequelae of treatment (e.g., shortening or narrowing, dryness). In each case, the presence (scored 1) or absence (scored 0) of the

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item is reported. A total score that estimates the degree of vaginal changes is obtained by summing the items. The internal consistency coefficient alpha for the Vaginal Change Score is .71 in our sample.

Meaning in Life. The Meaning in Life Scale is a 21 item, multidimensional measure of meaning (MLS; Jim, et al., in press). Factor analysis reveals that it is comprised of four dimensions: Harmony and Peace (4 items; e.g., "I feel peaceful," "I can reach into myself for comfort"), Life Perspective, Purpose & Goals (7 items; e.g., "I feel more fulfilled and satisfied with life," " I am settled about the future"), Benefits of Spirituality (3 items: e.g., "I find comfort in my faith and spiritual beliefs," "I have strength in my spiritual beliefs"), and Confusion and Lessened Meaning (7 items; "I get confused when I try to understand life," "Life has less meaning"). Scale scores are obtained by rescaling items to a 1 to 6 scale as necessary; reverse scoring negatively worded items (except for the Loss of Meaning scale), and then calculating the mean item response for each scale. Thus, all scales have a score range of 1 to 6. Higher scores indicate greater positive meaning, except for the Loss of Meaning scale, for which higher scores indicate loss of meaning. The Total Meaning score is computed as the sum of scale scores for positive meaning minus the scale score for Loss of Meaning and ranges from -3 to 17. Higher scores indicating greater positive meaning. Coefficient alpha reliability is .93 in the sample.

Depressive Symptomatology. A subset of items from the following measures is used to assess depressive symptomatology:

Center for Epidemiological Studies Depression Scale (CES-D; Comstock & Helsing, 1976; Radloff, 1977; Kohout, Kinan, Evans, & Cornoni-Huntley, 1993). The CES-D Iowa short form consists of 11 items (e.g. "I felt everything I did was an effort," "I felt sad") rated on 3-point Likert scales from *0=hardly ever or never* to *2=much or most of the time.* Women respond based on their feelings during the previous week. Following reverse scoring of positively valenced items, all items are summed with total scores ranging from 0 to 22. Higher scores reflect greater depressive symptoms. Internal consistency is the present sample is 0.82. Unlike other measures of depressive symptoms, the CES-D is relatively unaffected by physical symptoms and is, therefore, commonly used in research with medical patients (Devins et al., 1988).

Medical Outcomes Study-Short Form 12 Mental Health Component Summary (SF-12 MCS; Ware & Sherbourne, 1992; Ware, Kosinski, & Keller, 1996). The SF-12MCS items are scored on a 5-point Likert scale (*1 = all of the time* through *5 = none of the time*). See above for additional details on this measure. Internal consistency for the MCS is .90 in the present sample.

Profile of Mood States (POMS; Guadagnoli & Mor, 1989). The POMS short form is a 14-item measure used to assess mood over the past seven days. The measure is based on the original 65-item POMS (McNair, Lorr, & Droppleman, 1971) and was developed for use with cancer patients. Patients report how they have felt during the past week on a 5-point Likert scale ranging from *0=not at all* to *4=extremely*. The measure

includes a 7-item positive affect subscale (e.g., good-natured), a 7-item negative affect subscale (e.g., panicky), and a 14-item total mood disturbance score. The total score is the sum of the subscale scores (with positive items reverse-scored). It ranges from 0 to 28, with higher scores representing greater mood disturbance. The correlation between scores on the short form and 65-item POMS (alternate-form reliability) is high in our studies (r=.82), consistent with previous research (Guadagnoli & Mor, 1989). Internal consistency, test-retest reliability, and convergent and discriminant validity coefficients for the short form are comparable to those of the long form. Internal consistency this study is .75 for the Total Mood Disturbance score.

PTSD Symptom Checklist-Civilian version (PCLC; Weathers et al., 1991). The PCLC is used to assess PTSD symptomatology. The measure is intended for civilian (i.e., noncombat) populations (Weathers et al., 1991) and has been utilized to assess PTSD symptoms in breast cancer survivors (Andrykowski & Cordova, 1998; Cordova et al., 1995; Shelby, Golden-Kruetz, & Andersen, 2005). The PCL-C consists of 17 items, each corresponding to a specific DSM-IV PTSD symptom. When completing the PCL-C, women will be asked to consider "a stressful experience" and rate how much each symptom has bothered them in the last month. Respondents use a 5-point Likert scale, ranging from *1 = not at all* to *5 = extremely* for each item. Summing the items provides a total score and four subscale scores: Reexperiencing (REEXP), Avoidance (AVD), Numbing (NUMB), Hyperarousal (AROUS), as well as the avoidance and numbing subscales combined (AVDNUMB). The PCL-C total score ranges from 17 to 85). Internal consistency for the PCL-C total score is .94 in the present sample.

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Creation of Depression Parcels. To create observed indicators for the latent

variable of depressive symptomatology, a three step procedure was used. First, a

correlational analyses with the CES-D and all items from the SF-12, POMS, and PCLC

was conducted. A total of 33 items, considered theoretically consistent with the construct

of depression and with a correlation of .40 or greater (p <.001) with the CES-D were

selected for subsequent inclusion in the factor analyses. Second, a factor analysis was

conducted. It was hypothesized that all items would load on a depression factor, so a

one-factor solution was extracted using the Maximun Likelihood discrepancy function

with quartimax rotation. Two- and three-factor solutions were also extracted to test if

there were clusters of depression symptoms (e.g. emotional, behavioral, and physical).

Scree plots, item loadings and communalities, and judgments of factor interpretability

were used to evaluate solutions. While all three factor solutions indicated satisfactory

goodness-of-fit (ps < .001), three items had factor loadings less than .40 for all solutions

and were not considered further. The three factor solution was excluded because no

items had their highest loading on Factor 3. For the two-factor solution, 29 items loaded

on Factor 1, although six of these items loaded slightly higher on Factor 2. The two-

factor solution is presented in Table 1. Examination of the 6 items on Factor 2 suggests

they assess numbing (loss of interest, felt distant or cut off from others, and felt

emotionally numb) and hyperarousal (difficulty concentrating, irritalble/angry, trouble

falling/staying asleep). However, the loadings for these items on Factor 2 versus Factor 1

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suggests they are only marginally different, with an average difference between loadings of less than .07. Inspection of the one-factor solution (see Table 2) revealed that all items loaded satisfactorily, thus the one-factor solution was selected.

Third, to create equivalent "parcels" of symptoms of depression, sequential groupings of every three items were randomly distributed into three parcels. A random shuffle calculator, Graph Pad Software, was used. Included items were reversed scored if necessary and an average standardized score was created for each depression parcel. Internal consistencies of the three depression parcels were .85, .75, and .84 respectively. Inter-correlations of the three depression parcels were .86, .88, and .89. For use in additional analyses, a depression scale was created by using the standardized average of all items used to create the depression parcels. The internal consistency for this scale is .94. The use of the multiple aforementioned measures allowed for a unique, but clinically relevant latent variable to represent depressive symptomatology. While many of the items included assess classic symptoms of depression (felt sad, loss of interest in activities), the variable also represents common clinical aspects of depression, which can include anxiety and hyperarousal symptoms.

Control Variables.

History of Depression. Information about prior episodes of major depression and/or dysthymia was collected. This includes the following items: (1) In the year prior to your cancer diagnosis did you have 2 weeks or more during which you felt sad, blue, depressed, or lost pleasure in things that you usually cared about or enjoyed? And (2)

Have you had 2 years of more in your life when you felt depressed or sad most days, even if you felt okay sometimes?

Sociodemographics. Sociodemographic information collected during the assessment interview includes: age, menopausal status (yes or no), race (Caucasian vs. other), marital status (yes or no), presence of live-in spouse/partner (yes or no), education (years), employment status (yes or no), hours worked per week, and annual household income (in thousands per year).

Disease and treatment. Information regarding disease and treatment was collected through consultation with the medical staff and chart review. Patients are classified by time since diagnosis (years), stage (I through IV) and treatment groups including: surgery (yes or no), chemotherapy (yes or no), and radiotherapy (yes or no). Site is incorporated in similarly: cervix (yes or no), endometrium (yes or no), etc.

Analysis plan

SPSS is used to calculate accrual and descriptive statistics for the sample including sociodemographic and disease and treatment information, in addition to indices of physical functioning and quality of life, meaning in life, and depressive symptoms. Next, Pearson product-moment and point-biserial correlations and one-way ANOVAs determine the inclusion of control variables, such as sociodemographic, disease and treatment modality, and history of depression in the primary analyses. Correlations are conducted with the three depression parcels, and if at least one parcel is correlated with a

hypothesized control variable, the control variable is included. If ANOVAs with additional control variables reveal between group differences concerning the depression parcels, the control variables are included.

Structural equation modeling (AMOS 6.0 software) tests the hypothesized relationships between variables of interest.   For the mediation model, latent variables in the model act as a "predictor," outcome, or mediator of indirect relationships between the predictor and outcome. In specifying the model, Physical Sequelae is an exogenous latent variable (not receiving causal input from other variables). Physical Sequeale is measured by six variables: SF12PCS, FACT, SWOG, KPS, FSITDI, and Vaginal Change Score. Reverse standardized scores are used for the SF12PCS, FACT, and KPS, so that all variables are scored in the same direction, with higher scores indicating greater physical sequelae (i.e. poorer physical functioning).

The outcome variable, Depressive Symptoms, is specified as an endogenous latent variable measured with the three depression parcels. Meaning in life is specified as an endogenous latent variable measured by its four scales from the measure: Harmony and Peace, Life Perspectives, Purpose, and Goals, Benefits of Spirituality, and Confusion and Lessened Meaning. As seen in Figure 4, Meaning in Life is positioned as a mediator between Physical Sequelae and Depressive Symptoms. A direct path from Physical Sequelae to Depressive Symptoms is also included consistent with a partial mediation model. Controls are included as potential correlates of the outcome variable. Controls correlated with Physical Sequelae indicators are represented with a two-way path.

For the test of meaning in life as a moderator, two models are devised, one for

those high in Meaning in Life (High Meaning model) and the other for those low in Meaning in Life (Low Meaning model). Patients with a Total Positive Meaning score at least one-half a standard deviation or above the total sample mean (11.42, SD 2.94) represent the High Meaning group (N = 91; M= 14.39, SD = .89), and patients with a Total Positive Meaning score at minus one-half a standard deviation or below the total sample mean represent the Low Meaning group (N = 73; M = 7.61, SD = 1.83). Data from the "middle" meaning group (N = 96) are not considered further in this analysis. A multi-group analyses using a chi-square difference test to compare models for the two groups indicates if there is any group difference concerning Physical Sequelae as a predictor of Depressive Symptoms. This is done by comparing a constrained model (where all paths are considered equal between the two groups) to an unconstrained model (all parameter estimates are free). Relevant controls are included in the models.

Model estimation is carried out using the raw data as input, in which only 2% of values overall are missing. The maximum likelihood estimation procedure is used to estimate parameters. To provide a metric for the latent constructs and to identify the measurement model, one indicator loading for each latent variable is set to 1.0 in the unstandardized solution. For the mediation model, direct and indirect (mediated by Meaning in Life) effects and their standard errors are estimated. The Sobel test (Sobel, 1982) is used to test the significance of each indirect effect (p <.05). The ability of the model to explain the covariances between variables is evaluated using the Root Mean Square Error of Approximation (RMSEA; Browne & Cudeck, 1992), which considers both fit and parsimony. The 90% confidence interval around the RMSEA point

estimate is considered to indicate good fit to the data if it includes values of .10 or less,

with values less than .06 representing excellent fit (Bryne, 2001; Hu and Bentler, 1998).

CHAPTER 3

RESULTS

Description of the Sample

A study flow diagram is presented in Figure 3. The accrual rate for the sample is 88%. Table 3 provides descriptive data. Descriptively, the present sample is primarily Caucasian (95%), with some college (M = 14.11, SD = 2.76 years), with a mean age of 56.38 (SD = 12.34; range 23 - 80 years). The average household income is $56,200 (SD = $4,200). Women were an average of fours years post-diagnosis, and the majority were survivors of endometrial cancer (51%), followed by ovarian (27%), cervical (18%), and vulvar (4%) cancers. Also, women were primarily diagnosed with stage I (60%) and grade 1 (39%) disease. Most women received some form of surgery (96%). Forty-three percent of women also received chemotherapy and/or 20% received radiation therapy.

Table 4 presents the means and standard deviations for the sample on the physical functioning and quality of life variables. In general, the present sample appears to have moderate functioning in terms of the physical indices, although score ranges indicate a subset of women are experiencing greater difficulties. For example, the mean SF12PCS score 44.27 (12.92) is only slightly lower than the mean of 46.28 (8.68) for females between the ages of 55 and 64 (Ware et al., 2004), although it is considerably lower than

the mean 54.30 (6.22) for a general sample of healthy adults with no chronic conditions. Although there are no known norms for the other physical sequelae measures, the relatively low mean score on the SWOG suggests that few women are experiencing major problems in their renal, gastrointestinal, endocrine, or muscosal systems. However, women are reporting, on average, difficulties with two out of five types of vaginal changes, which could be enough to impact sexual functioning. In addition, the mean score on the KPS was a 78. Women who score an 80 on this measure "perform normal activity with effort and have some signs/symptoms of disease."

Means and standard deviations for the Meaning in Life Scale and subscales are presented in Table 4. Scores on the subscales suggest the present sample has moderate levels of meaning in life comparable to the sample of cancer patients used for the development of the scale (Jim et al., in press).

Table 4 also indicates the percentage of participants who reach the clinically significant cutoff (>10) for depression on the CES-D short form. In the present sample, 10% of survivors meet the clinical cutoff for depression on the CES-D. An additional 11% of the present sample meet the cutoff (>8) for subclinical depression on the CES-D short-form. While there are no clinical cutoffs for the created depression measure, analyses of the average of the combined standardized depression parcel items are consistent with the CES-D data. Eighteen percent of participants fall at one-half a standard deviation or above on this measure.

Control variables

Correlations between the depression parcels and hypothesized control variables

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are shown in Table 5. Significant correlations were found between at least one

depression parcel and age (rs $\geq$ -.22), education (rs $\geq$ -.13), family income (rs $\geq$ -.22), and

history of dysthymia (rs $\geq$ .44) (all ps < .05).   There were no significant correlations

found for menopausal status, race, surgery, chemotherapy, radiation therapy, time since

diagnosis, or a history of major depressive disorder. ANOVAs revealed no significant

between group differences concerning stage (Fs $\leq$ 1.54, ps $\geq$ .17) or disease site (Fs $\leq$

2.11, ps $\geq$ .10) and the three depression parcels.

Mediation Model

The AMOS test of the partial mediation model is presented in Figure 4 and

includes the standardized estimates of parameters in the measurement and structural

models. The model fit the data with a RMSEA of .10 (90% CI = .09-.12). In this model,

the path from Physical Sequelae to Meaning in Life was significant (p < .001), where

those with greater physical sequelae reported lower levels of meaning in life. In addition,

the path from Meaning in Life to Depressive Symptoms was significant (p < .001), with

those reporting less meaning in life, also reporting more depressive symptoms. As

hypothesized, the indirect effect – from Physical Sequelae to Depressive Symptoms

through Meaning in Life – was significant (z = 3.92; p < .001), supporting the view that

Meaning in Life mediates the relationship between Physical Sequelae and Depressive

Symptoms. In addition, the path from Physical Sequelae to Depressive symptoms was

significant (p < .001), supporting the partial mediation hypothesis. That is, patients with

more physical sequelae also report reduced meaning in life, which in turn, is associated

with higher levels of depressive symptoms.

Finally, the significant path weights from Age, Education, and a History of

Dysthymia to Depressive Symptoms (ps< .05) indicate that independent of physical

sequelae, gynecologic cancer survivors at a younger age, with less education, or with a

history of dysthymia reported more symptoms of depression. The path from Family

Income to depressive symptoms was not significant.

Moderation Model

The AMOS test of the moderation model is presented in Figures 5 (High Meaning

Group) and 6 (Low Meaning Group) and includes the standardized estimates of

parameters in the measurement and structural models. For both models, parameter

estimates were significant at the .05 level and in the expected direction for the variables

of interest.

To test for moderation, a comparison between the constrained and unconstrained

model was used. All paths were constrained to be equal for both the High Meaning and

Low Meaning groups, $\chi^2(139) = 294.74$, p< .001, and RMSEA = .083 (95% CI = .070 -

.096). This model was compared to one in which no paths were constrained, $\chi^2(124) =$

271.00, p< .001, and RMSEA = .086 (95% CI = .072 - .099). Contrary to hypotheses, a

difference test indicated that the fit of the constrained model was not significantly

different from the unconstrained model, $\Delta \chi^2(15) = 23.74$, p = .07, but suggested a trend.

In the unconstrained model, differences in key paths of interest were examined. The path

between Physical Sequelae and Depressive Symptoms was significant for both the High

Meaning ($B = .565$, p < .001) and Low Meaning groups ($B = .651$, p < .001). A

difference test comparing models with and without constraints on this path indicated that

they were not significantly different, $\Delta \chi^2(1) = .04$, p = .53. That is, regardless of the level of meaning in life reported by patients, greater physical sequelae were associated with more depressive symptoms.

Other group differences in the models were explored in follow-up analyses. The path between History of Dysthymia and Depressive Symptoms was not significant for the High Meaning group ($B = -.024$, p = .842), but was significant for the Low Meaning group ($B = .310$, p < .01). A difference test comparing models with and without constraints on this path indicated that they were significantly different, $\Delta \chi^2(1) = 3.8$, p < .05. This suggests that a history of dysthymia may be a risk factor for depressive symptoms in those who also report lower levels of meaning. Conversely, individuals with higher levels of meaning may be protected from depressive symptoms, even if they have a history of dysthymia.

For illustration, graphs representing the moderation finding with both the CES-D and the standardized depression score are presented in Figures 7 and 8, respectively. They demonstrate that for patients with a history of dysthymia, having meaning is related to lower levels of depressive symptoms. This finding suggests a potential difference distinguishing dysthymic patients who do or do not report meaning. We hypothesized that some dysthymic patients may have suffered from "double depression" (i.e. having a major depressive episode superimposed on dysthymia). If so, these individuals may also be more likely to report low meaning levels. To test this possibility, follow-up analyses were conducted with the two items assessing a history of depression [In the year prior to your cancer diagnosis did you have 2 weeks or more during which you felt sad, blue,

depressed, or lost pleasure in things that you usually cared about or enjoyed? and, have you had 2 years of more in your life when you felt depressed or sad most days, even if you felt okay sometimes?]. Patients indicating "yes" on both of these items were considered to have a history of double depression. Results indicated that 20% of the sample reported a history of double depression. A follow-up chi-square test was used to test for differences in the frequency of patients with or without a history of double depression who fall in the low or high meaning groups. A $\chi^2(2) = 13.20$, p < .001 reveals those with a history of double depression are significantly more likely to report low levels of meaning (70% falling in the low meaning group) then high levels of meaning (30% falling in high meaning group). This data provides evidence that individuals having a more severe history of depression – that is having a history of major depression superimposed on dysthymia – are more likely to report lower levels of meaning.

Regarding sociodemographics, the path between Age and Depressive Symptoms was not significant for the High Meaning group ($B = .004$, $p = .314$), but was significant for the Low Meaning group ($B = -.01$, $p < .001$). A difference test comparing models with and without constraints on this path indicated that they were not significantly different, but a trend was evident, $\Delta \chi^2(1) = 3.5$, p = .06. The later suggests younger patients reporting lower levels of meaning in life may be at greater risk for depressive symptoms than older patients with low levels of meaning in life. Similarly, the path between Education and Depressive Symptoms was not significant for the High Meaning group ($B = -.007$, $p = .676$), but was significant for the Low Meaning group ($B = -.047$ $p = .10$). A difference test comparing models with and without constraints on this path

indicated that they were not significantly different, $\Delta \chi^2(1) = 2.7$, $p = .10$. The trend suggests among those reporting low meaning, those with "lower" education levels are at higher risk for depressive symptoms. Finally, the path from Family Income to depressive symptoms was not significant for either group (ps > .09).

CHAPTER 4

DISCUSSION

The present study suggests physical sequelae for gynecologic cancer survivors relate to depressive symptomatology. In addition, meaning in life may be a mechanism for this relationship. Results support an interpretation that the depressive symptoms experienced by many survivors as a result of changes in physical functioning and quality of life are due, in part, to the adverse relationship of symptoms with meaning. Physical symptoms may interfere with meaning at personal, professional, and social levels leaving survivors feeling sad, anxious, irritable, or numb. The data do not support a "buffering" role for meaning. That is, high levels of meaning do not appear to lessen the effects of the physical sequelae on depressive symptoms. However, a novel finding emerged: those with a history of dysthymia, who report greater levels of meaning in life, also report fewer depressive symptoms.

Physical Sequelae and Depressive Symptoms

Cancer-related symptoms predict depression in cancer survivors (Deimling et al., 2002). In the present study, the use of a latent variable modeling allowed the representation of several aspects of physical sequelae, including physical functioning, general and gynecologic cancer specific quality of life, and physical symptoms, such as fatigue, vaginal changes, and difficulties in the renal/bladder, gastrointestinal, endocrine,

and mucosal systems, which are particularly relevant for gynecologic cancer patients. Using this representation, the physical sequelae were related to higher levels of depressive symptoms in survivors. Indeed, 10 to 20 percent of the sample may have met criteria for clinical depression.

Meaning as a Mediator

The physical sequelae of the gynecologic cancer experience were related to diminished meaning in life. The mechanism(s) for this relationship are unknown, however, one may be that physical symptoms impact vital sources of meaning. Many gynecologic cancer survivors are still experiencing changes in physical functioning and quality of life. For example, loss of performance abilities or fatigue may interfere with one's ability to work both in and outside of the home, thus altering one's social roles and goals both at home and professionally. Additionally, vaginal changes and decreased sexual functioning may impact a woman's body image and/or relationship with a spouse or significant other. Such changes impacting a woman's sexual self view, relationships, and goals may alter meaning. Also, it may be difficult to adapt one's goals or change exisiting schemas of meaning with the aftermath of cancer. The cancer experience can destroy belief in a world that is benevolent and meaningful, and where one is worthy and relatively invulnerable to negative events (an Assumptive Worlds Perspective; Janoff-Bulman, 1989). Gynecologic cancer survivors may feel the world is a more frightening and dangerous place as they face fear of recurrence or death, adjustments to physical compromise, changes in social roles and relationships, and employment and insurance problems (Bower et al., 2005). Survivors may need help adjusting their schemas of

meaning given the changes and struggles resulting from the physical sequelae of cancer and subsequent loss of meaning.

Lower meaning was, in turn, associated with greater levels of depressive symptoms. The existential challenge of the cancer experience (challenge to view of self, world, future) is often represented by feelings of fear, hopelessness, and depression. Previous research shows that survivors who are able to change their norms or expectations, find improvements in their lives, such as closer interpersonal relationships, or change priorities or life goals have better psychological adjustment (Roberts et al., 1992). On the other hand, individuals who continue to struggle with loss of meaning often feel hopeless and depressed, and experience poorer overall well-being (Yalom, 1980; Zika & Chamberlain, 1992).

Meaning as a Moderator

Unfortunately, for these patients having meaning was not related to fewer depressive symptoms in the face of the physical sequelae of cancer. Previous research has suggested that some cancer survivors may be protected from distress by resolving their losses or finding new sources of meaning if impaired physical health and functioning prevent them from taking part in once meaningful activities (Janoff-Bulman, 1992; Taylor, 1983). Instead, this study suggests that it is difficult to maintain or "recreate" meaning in the face of heightened physical symptoms.

It is important to note, however, that the present study may have been a less than adequate test of meaning in life as a moderator. By using a multi-group analyses, only participants scoring above or below half a standard deviation on meaning in life were

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included, reducing the sample to 164 participants. Experts in structural equation modeling note that a sample size of at least 200 individuals is an appropriate minimum (Kelloway, 1998; Marsh, 1988). In addition, overall the present sample exhibited moderate levels of meaning in life, with scores skewed towards more positive meaning, and many fewer individuals reporting the lowest levels of meaning in life. Thus, the Low Meaning group may have instead represented a "lower meaning" group.

However, data suggest that greater levels of meaning in life may "protect" an individual from current depressive symptoms even if they have a history of dysthymia. This finding may have emerged because the cancer experience may have prompted some patients, including some who had previously suffered from dysthymia, to evaluate the meaning of their lives and find strength, peace, new goals, and a greater appreciation of life in the face of threat. Follow-up analyses revealed that if dysthymic patients had a less severe history of depression (i.e. never experienced "double" depression) they are more likely to find meaning, which may offset depressive symptoms. Such patients may be more able to adapt to the cancer experience by finding meaning. However, there may be other reasons for the re-evaluation of meaning in some dysthymic patients, but not others. For example, dysthymic disorder can be associated with personality disorders including borderline, histrionic, narcissistic, avoidant, and dependent (DSM-IV, APA, 1994). So it is also possible that those without comorbid personality disorders are better able to adapt their ways of thinking in order to find meaning in a difficult time.

Finally, the data suggests that independent of the physical sequelae of cancer, greater meaning in life is associated with fewer depressive symptoms in younger and/or

less educated patients, who tend to be at greater risk for psychological distress (Bowman et al., 2003; Miller et al., 2002; and Vacek et al., 2003). Younger patients may be able to offset depressive symptoms by recreating meaning in their lives. Similarly, patients may vary in their uses of coping strategies, so it is possible that the younger and less educated patients who experience fewer depressive symptoms are utilizing more effective techniques such as active coping, social support, acceptance, and positive reinterpretation, which are predictors of meaning in life (Jim, Richardson, Golden-Kreutz, & Andersen, in press). These are interesting and unique findings and are in need of replication and further study. Together they suggest that cancer survivors who find or maintain meaning through their cancer experience may be able to offset some of the common risk factors for depressive symptoms.

Clinical Implications

These data suggest that 10% of the sample may have suffered from clinical depression, with an additional 11% meeting the cutoff for subclinical depression. Related analyses with the factor analyzed depression items reveal that 18% of participants fall at one-half a standard deviation or above the sample mean, which suggests these participants may also experience anxiety related symptoms as well. Previous studies have found rates of depression as low as 9% (Matthews et al, 1999) and as high as 63% (Li et al., 1999) in gynecologic cancer survivors. Considering all affective disorders that involve depressive episodes, it has been reported that depression affects approximately six percent of the population (Sellick & Crooks, 1999), thus the gynecologic cancer survivors in this and other studies appear to have more difficulties with depression in

comparison to the general population. The rate of depression in the present sample may be an underestimate, however. Absent from the study were patients who did not keep, or did not schedule their follow-up appointments. While the reasons for this may vary, it is possible that some of the patients not sampled are depressed and do not pursue their follow-up health care.

There are important clinical implications of the findings. The outpatient-oncology clinic used to recruit participants for the present study is typical in terms of volume of patients seen annually. It has over 1000 out-patient follow-up visits a year; therefore, with a prevalence rate of 10%-20%, one would expect to see approximately 100-200 cases of depressive disorders per year.   Since a subset of the present sample and likely others (newly diagnosed patients) are experiencing signs of depressive symptoms, use of a screening instrument for depression and anxiety might assist in identifying potential cases and enable appropriate clinical assessment and management.   This may be particularly important for those with a history of dysthymia/double depression, younger age, and lower education who may be at greater risk for depression. Finally, evidence suggests depressive symptomatology is the most consistent psychological predictor of a reduced survival time, making it increasingly important to recognize and address (Brown et al., 2003).

If meaning is a mediator between the physical sequelae of gynecologic cancer and symptoms of depression, patients may need help finding meaning while adjusting emotionally to the physical challenges of survivorship. Clinical interventions that directly address meaning may help alleviate some of the depression and anxiety faced by

gynecologic cancer survivors. Such interventions may help survivors find ways to recreate meaning by replacing sources of meaning lost as a result of physical functioning changes. For example, if a patient has lost the ability to continue one's career, which once gave the patient purpose in life, or a leisure activity, which once gave a patient satisfaction in life, an intervention could help the patient establish other career goals, satisfactions, or new enjoyable activities. Interventions with gynecologic caner patients may also address changes in meaning that result from sexual functioning difficulties or fertility changes that may be impacting relationships with significant others. Finally, interventions addressing meaning may help patients grieve over and accept losses and find comfort and peace while creating new systems of meaning. Future research exploring the present study's implications for screening of depression and anxiety, and clinical interventions addressing meaning in life with gynecologic cancer survivors are needed.

Strengths & Limitations

The present study is the first to examine meaning in life as a mediator of the unique physical challenges faced by gynecologic cancer survivors, in comparison to other cancer populations. The latent variable depression parcels with items that assess classic symptoms of depression, such as feelings of sadness and loss of prior interests, in addition to symptoms, such as anxiety, restlessness, and tension that are commonly present in clinical cases of depression offered important advantages. Many cancer survivors who suffer from depression may also have fears of recurrence or death and anxiety about the many changes and challenges they face. For example, a gynecologic

cancer survivor may feel depressed and anxious about sexual dysfunction or loss of child-bearing abilities, and how this might affect the future of her relationship with her spouse or significant other.   Also, disruption of a survivor's ability to perform daily activities of living, work performance, being able to provide for families, and social functioning could make a survivor feel depressed and anxious, not only about one's ability to care for oneself, but also about one's career, finances, and social roles.

The use of structural equation modeling in the current study had its advantages. Rather than using individual measures, physical sequelae, meaning in life, and depressive symptoms were represented as latent constructs, indicated by multiple valid indicators. These construct estimates are unbiased by correlated measurement errors, allowing for a closer estimate of the "true score" for each and discussion of relationships among latent variables rather than correlations among measures.

It is important to note the limitations of these findings. The modeling analyses imply directionality, which of course, was not demonstrated. The current study relied on the traditional Baron and Kenny (1986) guidelines; however, recent research has suggested that for mediation to occur, the predictor variable has to occur before the mediator, and for moderation to occur, the moderator has to preceed the predictor variable (Kramer & Liernan, 2006). While the current study does not allow for causal implications, the finding of meaning in life as a mediator between the physical sequelae of the gynecologic cancer experience and depressive symptoms is consistent with previous longitudinal research finding evidence for the meaning in life as a mediator between social and physical functioning and distress in breast, colorectal, prostate,

gynecologic, and other cancer survivors (Jim & Andersen, in press).

Also, the present sample is primarily Caucasian with some college education, and middle-class; therefore findings may not generalize to racial minorities or those of a lower educational or economic status. The present study focuses on an important understudied survivor group, yet generalization to other cancer groups is unknown.

Conclusions

Gynecologic cancer patients have been largely neglected in psychosocial research. This study demonstrates that among survivors, many women are adjusting to the cancer experience over time. However, a subset of women experience more severe physical functioning and quality of life deficits, which may directly relate to depressive symptoms, or relate to symptomatology through changes in meaning in life. In other words, even several years after diagnosis and treatment of gynecologic cancer, physical difficulties are associated with reduced meaning, which may, in turn, relate to depressive symptoms. The finding that meaning in life acts as a buffer between a history of dysthymia, and potentially age and education, and current depressive symptoms, is novel. Together the findings from this study recognize the importance of existential issues in the lives of cancer survivors. Survivors carry their cancer experience through their lives. By appreciating the role of meaning in this experience, we can help survivors find new meaning, which is important for their adjustment.

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APPENDIX A

DIAGNOSTIC CRITERIA FOR DEPRESSIVE DISORDERS

Diagnosis of Major Depressive Disorder, Single Episode[1]

A. The person experiences a single major depressive episode:

1. For a major depressive episode a person must have experienced at least five of the nine symptoms below for the same two weeks or more, for most of the time almost every day, and this is a change from his/her prior level of functioning. One of the symptoms must be either (a) depressed mood, or (b) loss of interest.
   a. Depressed mood. For children and adolescents, this may be irritable mood.
   b. A significantly reduced level of interest or pleasure in most or all activities.
   c. A considerable loss or gain of weight (e.g., 5% or more change of weight in a month when not dieting). This may also be an increase or decrease in appetite. For children, they may not gain an expected amount of weight.
   d. Difficulty falling or staying asleep (insomnia), or sleeping more than usual (hypersomnia).
   e. Behavior that is agitated or slowed down. Others should be able to observe this.
   f. Feeling fatigued, or diminished energy.
   g. Thoughts of worthlessness or extreme guilt (not about being ill).
   h. Ability to think, concentrate, or make decisions is reduced.
   i. Frequent thoughts of death or suicide (with or without a specific plan), or attempt of suicide.
2. The persons' symptoms do not indicate a mixed episode.
3. The person's symptoms are a cause of great distress or difficulty in functioning at home, work, or other important areas.
4. The person's symptoms are not caused by substance use (e.g., alcohol, drugs, medication), or a medical disorder.
5. The person's symptoms are not due to normal grief or bereavement over the death of a loved one, they continue for more than two months, or they include great difficulty in functioning, frequent thoughts of worthlessness, thoughts of suicide, symptoms that are psychotic, or behavior that is slowed down (psychomotor retardation).

B. Another disorder does not better explain the major depressive episode.

C. The person has never had a manic, mixed, or a hypomanic Episode (unless an episode was due to a medical disorder or use of a substance).

> **Possible specifiers to describe the episode:**
> Severity: mild, moderate, severe without psychotic features
> Severe With Psychotic Features
> In Partial/Full Remission
> With Catatonic Features
> With Melancholic Features
> With Atypical Features
> With Postpartum Onset

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[1] Summarized from the *Diagnostic and Statistical Manual of Mental Disorders- Fourth Edition*

Diagnosis of Dysthymic Disorder[2]

A. A person has depressed mood for most the time almost every day for at least two years. Children and adolescents may have irritable mood, and the time frame is at least one year.

B. While depressed, a person experiences at least two of the following symptoms:

1. Either overeating or lack of appetite.
2. Sleeping to much or having difficulty sleeping.
3. Fatigue, lack of energy.
4. Poor self-esteem.
5. Difficulty with concentration or decision making.
6. Feeling hopeless.

C. A person has not been free of the symptoms during the two-year time period (one-year for children and adolescents).

D. During the two-year time period (one-year for children and adolescents) there has not been a major depressive episode.

E. A person has not had a manic, mixed, or hypomanic episode.

F. The symptoms are not present only during the presence of another chronic disorder.

G. A medical condition or the use of substances (i.e., alcohol, drugs, medication, toxins) do not cause the symptoms.

H. The person's symptoms are a cause of great distress or difficulty in functioning at home, work, or other important areas.

> **Possible specifiers to describe dysthymia:**
> Early Onset: Dysthymic symptoms begin before the age of 21. This may increase the likelihood of developing later major depressive episodes.
> Late Onset: Dysthymic symptoms begin after the age of 21.
> With Atypical Features: Describes symptoms experienced during the last two years

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[2] Summarized from the *Diagnostic and Statistical Manual of Mental Disorders- Fourth Edition*

APPENDIX B

FIGURES
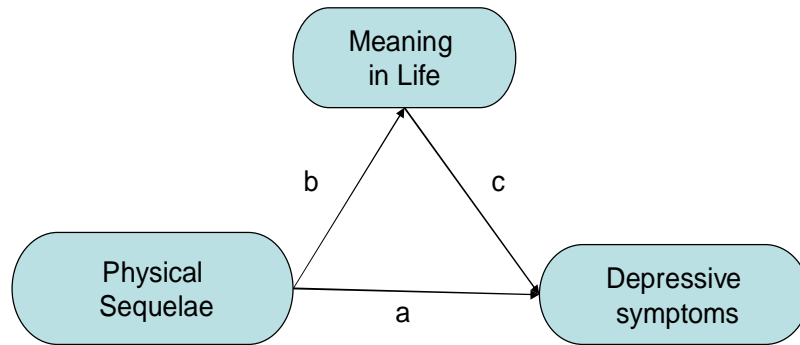
Figure 1. Mediator Model.
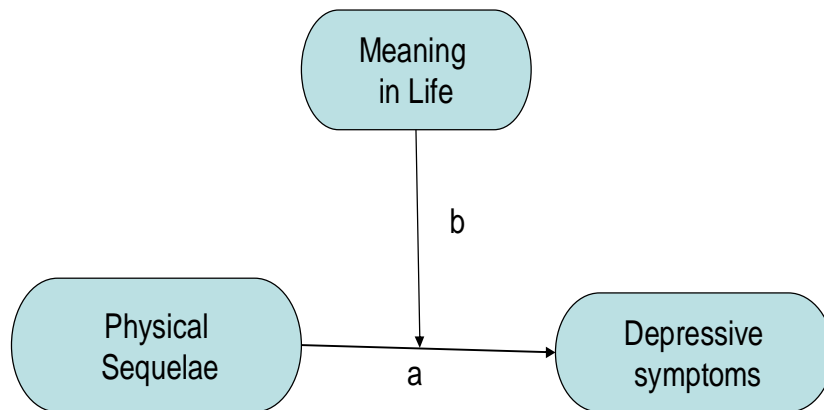
Figure 2. Moderator Model.

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                    ┌─────────────────────────────┐
                    │    Jan 3 – Dec 19, 2005     │
                    │  Follow-up Visits, N = 1059 │
                    └─────────────────────────────┘
```

Jan 3 – Dec 19, 2005
Follow-up Visits, N = 1059

Not Eligible
529 (50%)

Screened Eligible
530 (50%)

Letters sent to all patients screened eligible

Cancel/Reschedule
84 (16%)

No Shows
60 (11%)

Patients Registered
386 (73%)

Excluded/Ineligible
92 (24%)

Eligible
294 (76%)

Refused
34 (12%)

Accrued
260 (88%)
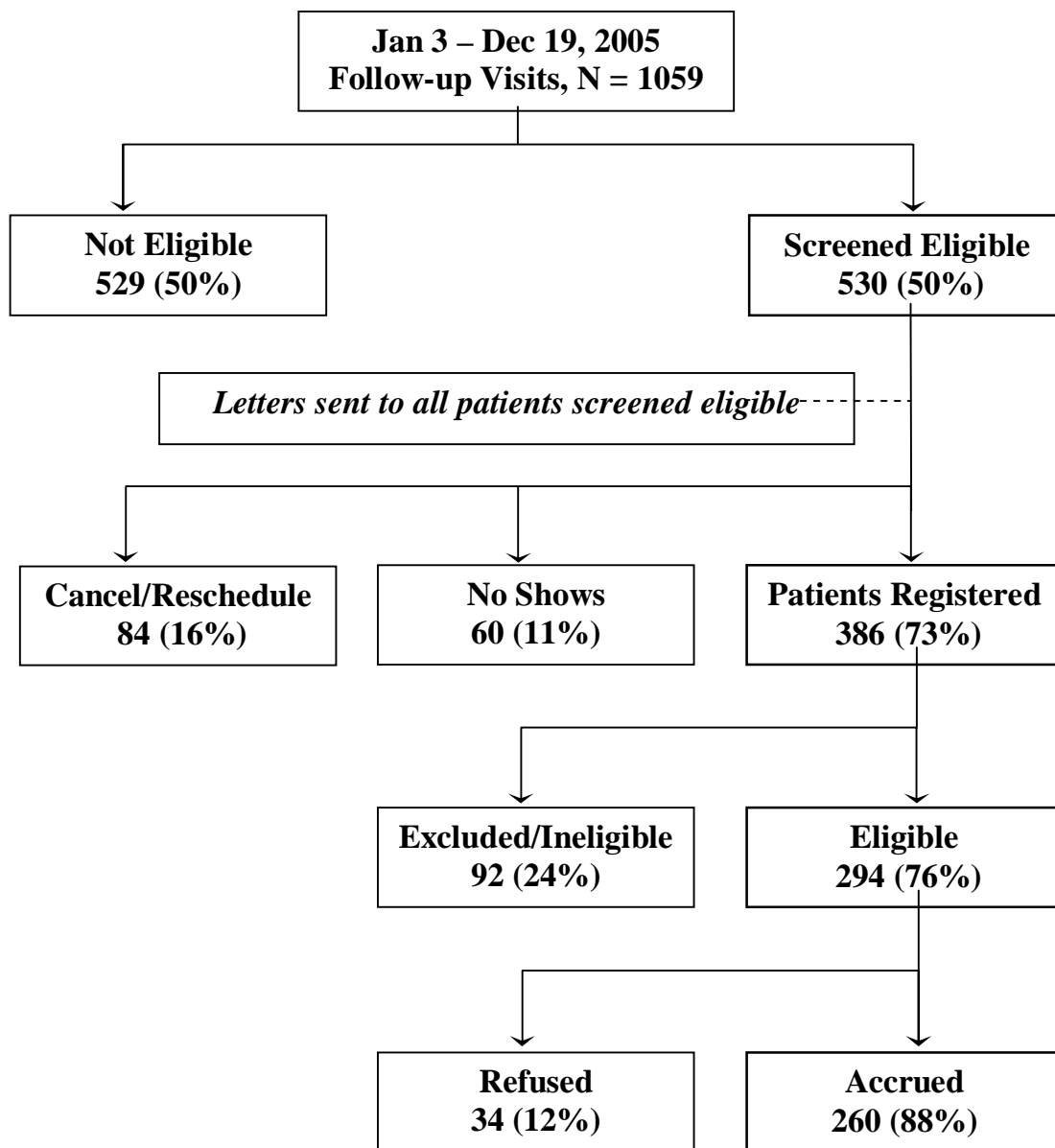
Figure 3. Study Flow.
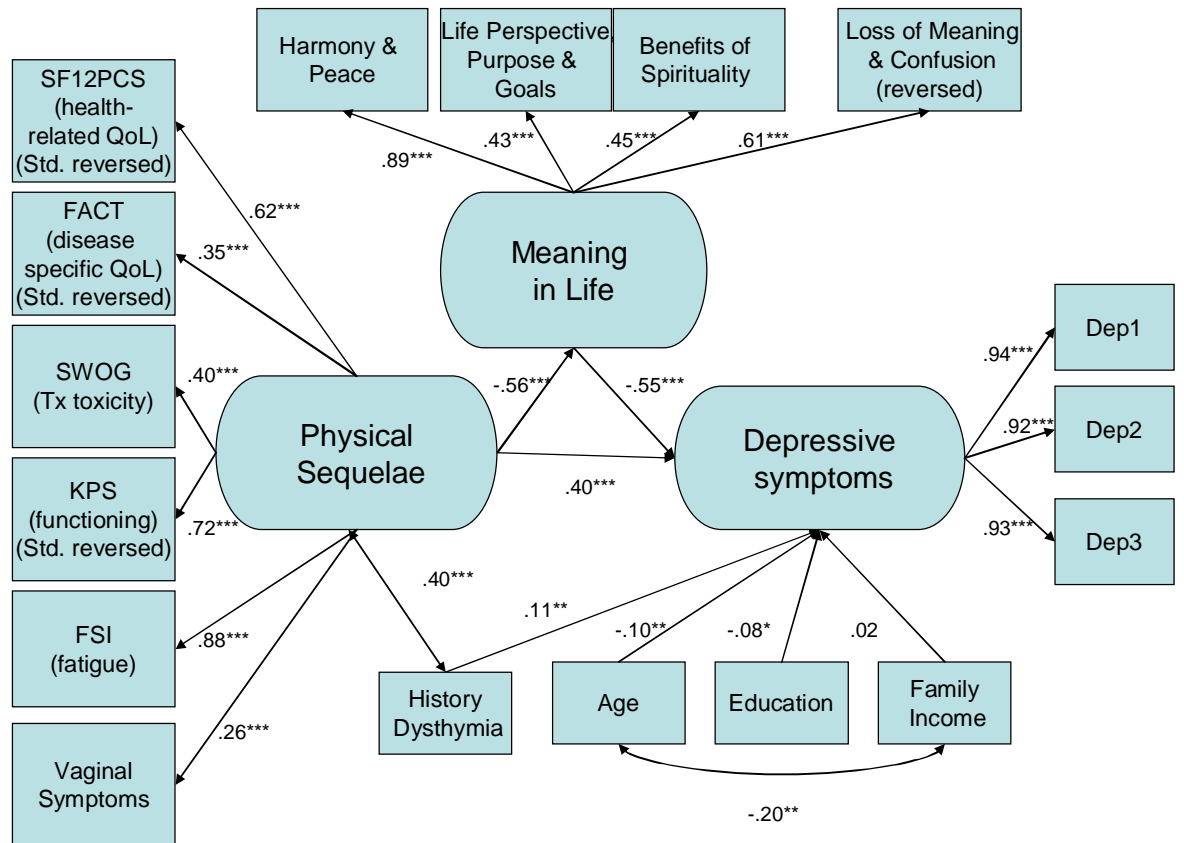
Figure 4. Mediation Path Model.

Figure 5. Moderator Path Model (High Meaning Group).

Figure 6. Moderator Path Model (Low Meaning Group).

Figure 7. Mean CES-D scores with 95% CI for patients with or without a history of dysthymia in the low or high meaning groups.
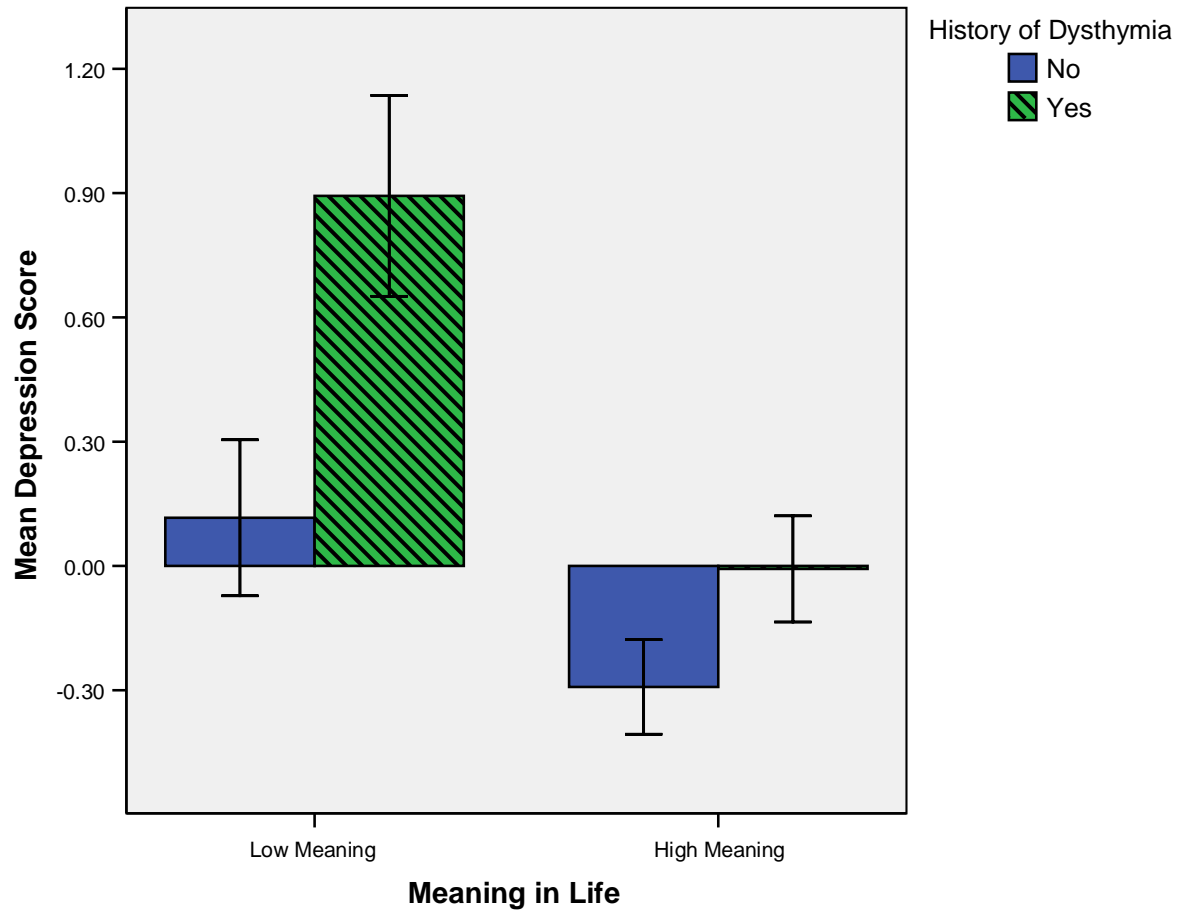
Figure 8. Mean Depression score with 95% CI for patients with or without a history of dysthymia in the low or high meaning groups.

APPENDIX C

TABLES

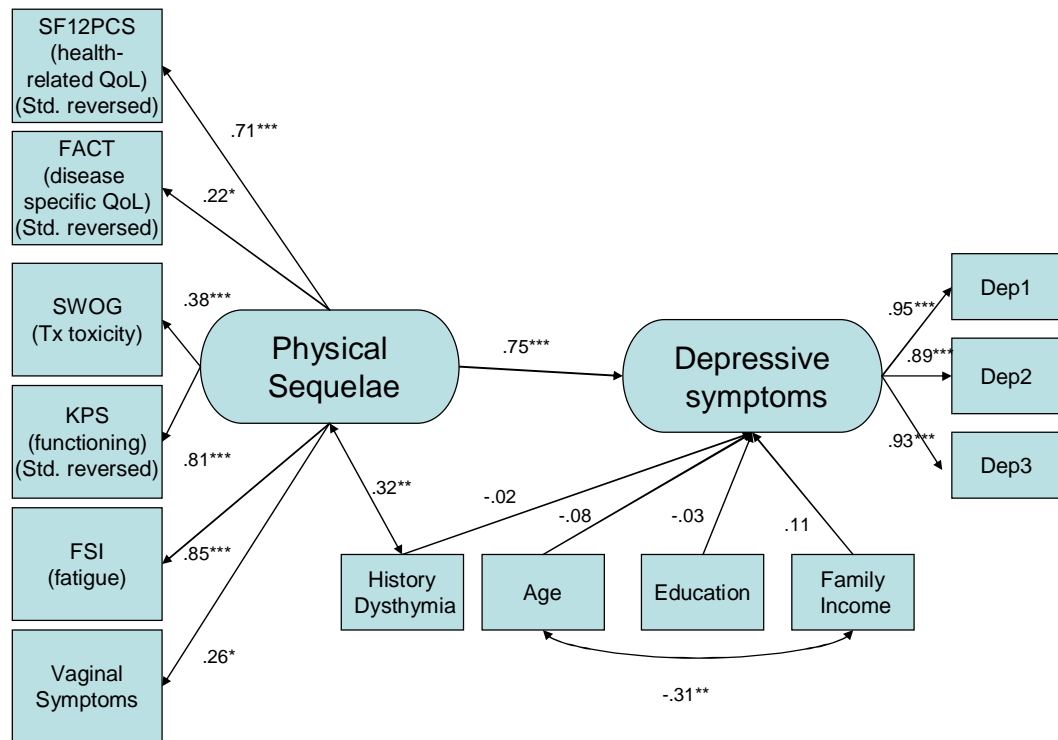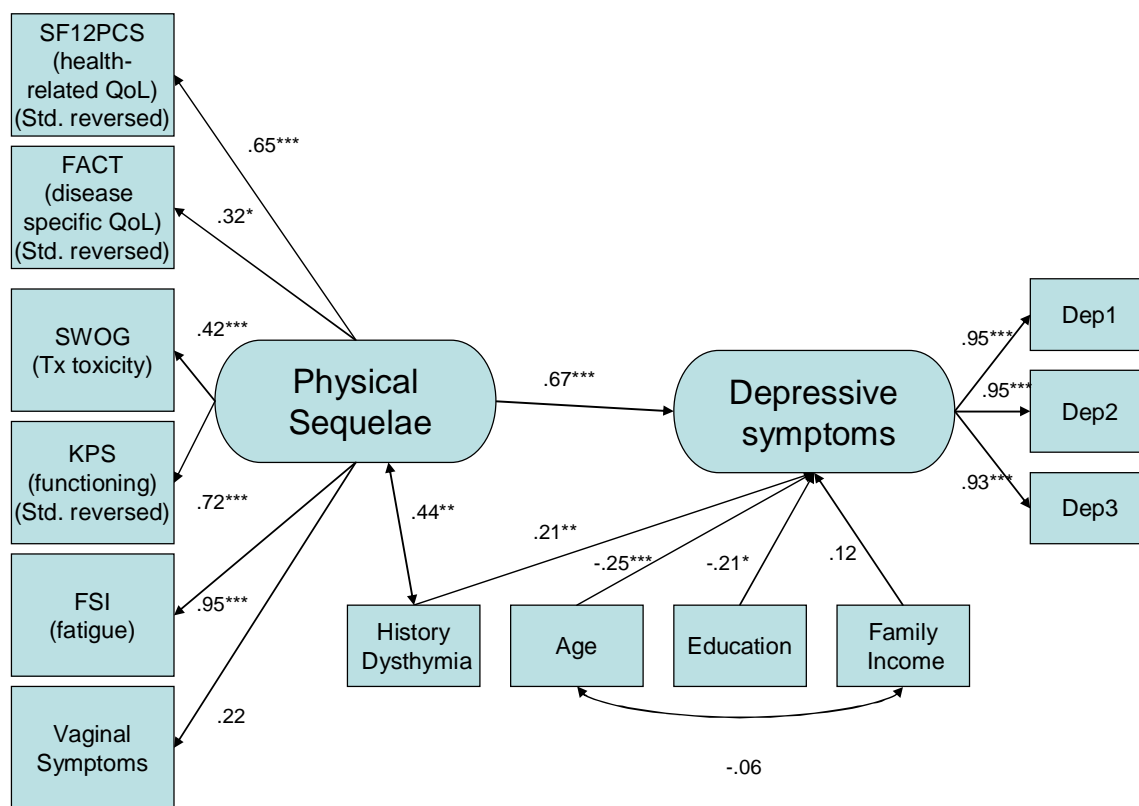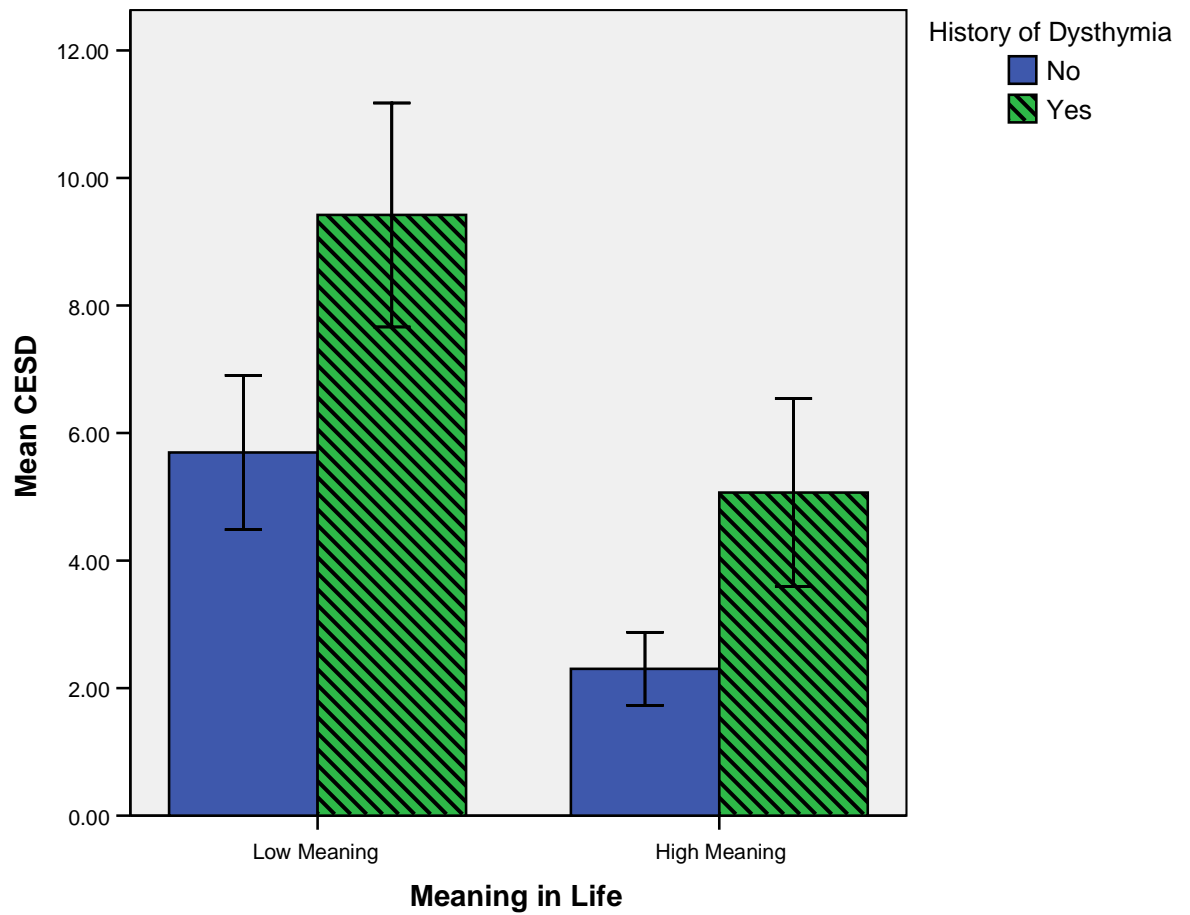| Item	Factor	
	I	II
Felt downhearted & depressed (SF12)	**-.809**	-.121
Felt depressed (CESD)	**.761**	.086
Accomplished less at work because of emotional problems (SF12)	**-.726**	-.006
Felt calm & peaceful (SF12)	**.720**	.053
Felt blue (POMS)	**.704**	
Felt happy (CESD)	**-.682**	.042
Done things less carefully because of emotional problems (SF12)	**-.670**	.061
Felt sad (CESD)	**.627**	.046
Felt relaxed (POMS)	**-.627**	-.010
Physical health or Emotional problems Interfered with social activity (SF12)	**-.616**	.080
Felt on edge (POMS)	**.615**	.106
Felt restless (POMS)	**.614**	-.039
Felt irritable/angry (PCLC)	.485	**.611**
Could not get going (CESD)	**.607**	-.085
Enjoyed life (CESD)	**-.607**	.109
Had a lot of energy (SF12)	**.589**	-.053
Felt anxious (POMS)	**.587**	.064
Loss of interest in activities used to enjoy (PCLC)	.571	**.580**
Had difficulty concentrating (PCLC)	.543	**.570**
Feel distant or cut off from others (PCLC)	.534	**.570**
Felt shaky (POMS)	**.569**	.011
Felt like everything was an effort (CESD)	**.550**	-.065
Felt tense (POMS)	**.549**	.071
Felt emotionally numb (PCLC)	.471	**.547**
Trouble falling/staying asleep (PCLC)	.477	**.544**
Felt lonely (CESD)	**.519**	.196
Had repeated, disturbing dreams of a stressful experience (PCLC)	**.483**	.455
Sleep was restless (CESD)	**.456**	.040
Felt alert (POMS)	**-.433**	.007
Appetite poor was poor (CESD)	.366	-.036
Felt that people disliked me (CESD)	.338	-.002
People were unfriendly (CESD)	.202	.008

Table 1. Two-Factor Solution for Depressive Symptom Items.

Item	Factor I
Felt downhearted & depressed (SF12)	-.814
Felt depressed (CESD)	.761
Felt calm & peaceful (SF12)	.710
Accomplished less at work because of emotional problems (SF12)	-.702
Felt blue (POMS)	.698
Loss of interest in activities used to enjoy (PCLC)	.687
Had difficulty concentrating (PCLC)	.659
Feel distant or cut off from others (PCLC)	.648
Felt happy (CESD)	-.646
Done things less carefully because of emotional problems (SF12)	-.630
Felt on edge (POMS)	.629
Felt sad (CESD)	.624
Felt irritable/angry (PCLC)	.613
Felt relaxed (POMS)	-.611
Trouble falling/staying asleep (PCLC)	.593
Felt anxious (POMS)	.590
Felt restless (POMS)	.589
Felt emotionally numb (PCLC)	.587
Had repeated, disturbing dreams of a stressful experience (PCLC)	.578
Physical health or Emotional problems Interfered with social activity (SF12)	-.571
Could not get going (CESD)	.563
Felt tense (POMS)	.555
Felt shaky (POMS)	.555
Had a lot of energy (SF12)	.554
Enjoyed life (CESD)	-.554
Felt lonely (CESD)	.553
Felt like everything was an effort (CESD)	.513
Sleep was restless (CESD)	.453
Felt alert (POMS)	-.418
Appetite poor was poor (CESD)	.343
Felt that people disliked me (CESD)	.328
People were unfriendly (CESD)	.198

Table 2. One-Factor Solution for Depressive Symptom Items.

Variable	%	N = 260	
		Mean	SD
Sociodemographic			
Age, years		56.38	12.34
Race, % white	95		
Education, years		14.11	2.76
Family Income, thousand $/year		56.20	42.85
Marital status, % married	62		
Significant other, % yes	70		
Disease group			
Cervical, %	18		
Endometrial, %	51		
Ovarian, %	27		
Vulvar, %	4		
Prognostic			
Stage			
I	60		
II	8		
III	23		
IV	4		
Unstaged	5		
Disease Grade			
1	39		
2	25		
3	25		
4	1		
Not determined	10		
Treatment received			
Surgery, % yes	96		
Radiation therapy, % yes	20		
Chemotherapy, % yes	43		
Time since diagnosis, years		4.19	2.04

Table 3. Sociodemographic and disease/treatment characteristics of the sample (N = 260).

Variable	%	Mean	SD
Physical Sequelae			
SF12 Physical Component Summary		44.27	12.92
Functional Assessment of Cancer Therapy Scales			
FACT Cervix		47.00	6.75
FACT Endometrium		57.14	6.38
FACT Ovary		34.94	5.07
FACT Vulvar		44.22	8.91
Southwestern Oncology Toxicity Criteria total		2.14	0.75
Karnofsky Performace Status		78.46	11.22
Fatigue Symptom Inventory		15.37	15.82
Vaginal Change Score		1.62	1.47
Total Positive Meaning		11.42	2.94
Harmony and Peace		3.97	.78
Life Perspective, Purpose an Goals		4.28	1.03
Benefits of Spirituality		5.02	1.26
Loss of Meaning & Confusion		1.86	.90
Center for Epidemiology Depression Scale (Short form)		4.30	3.86
Percent >10 on CES-D (clinical cutoff)	10		
Percent >8 on CES-D (subclinical cutoff)	21		
Average of Standardized Depression Parcel Items	18		
Percent > .5 S.D. above the mean			

Table 4. Means and standard deviations for the Physical Sequelae, Meaning in Life, and Depression measures, and percentages of clinical depression symptom groups.

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	Dep1	Dep2	Dep3	Age	Meno-pausal Status	Race	Marital Status	Signifi-cant Other	Education	Family Income	Surgery	Chemo	Rad	Time Since Diagn.	History MDD	History Dys-thymia
Dep1	1															
Dep2	.87	1														
Dep3	.88	.86	1													
Age	-.23**	-.28**	-.22**	1												
Menopausal Status	.01	-.04	-.08	.29**	1											
Race	-.00	-.08	.00	-.08	.18*	1										
Marital Status	.02	-.01	-.05	-.06	.04	.01	1									
Significant other	.06	-.01	-.03	-.20**	.01	.04	.82**	1								
Education	-.13*	-.12	-.18*	-.09	-.07	-.04	-.04	-.06	1							
Family Income	-.12	-.12	-.22**	.01	.02	.03	.10	.09	-.01	1						
Surgery	.02	.00	-.02	.06	.18*	-.03	.01	.03	.00	.02	1					
Chemo	-.04	-.03	-.02	-.01	.07	.13	-.01	.04	-.06	-.08	.07	1				
Radiation	.00	.01	.04	.00	.07	.11	.05	.05	-.11	.09	-.14*	.14*	1			
Time Since Diagnosis	-.12	-.11	-.12	.04	-.06	.07	.01	-.04	-.06	.17*	.10	.07	.08	1		
History of Major Depression	.10	.08	.03	.01	.01	.12	.05	.04	-.02	.10	.01	-.06	-.12*	-.02	1	
History of Dysthymia	.44**	.45**	.46**	-.12*	.09	.01	-.02	-.00	-.10	-.06	-.04	.07	.03	-.08	-.04	1

Table 5. Correlations between depression parcels and potential control variables.

	DEP1	DEP2	DEP3	SF12 PCS	FACT	SWOG	KPS	FSI	Vaginal Changes	Harmony & Peace	Life Perspectives	Benefits Spirit.	Confusion & Lessened Meaning
DEP1	1												
DEP2	.87***	1											
DEP3	.88***	.86***	1										
SF12PCS	-.29***	-.34***	-.34***	1									
FACT	-.32***	-.34***	-.35***	.18**	1								
SWOG	.26***	.24***	.25***	-.24***	-.21***	1							
KPS	-.40***	-.36***	-.44***	.69***	.20**	-.31***	1						
FSI	.64***	.64***	.68***	-.52***	-.30***	.34***	-.62***	1					
Vaginal Changes	.29***	.26***	.25***	-.08	-.22***	.36***	-.01	.21***	1				
Harmony & Peace	-.71***	-.70***	-.72***	.17**	.34**	-.13*	.28***	-.48***	-.24***	1			
Life Perspectives	-.56***	-.22***	-.24***	.07	.04	-.06	.06	-.10	-.03	.35***	1		
Benefits of Spirituality	.48***	.53***	.54***	-.13*	-.25***	.15*	-.21***	.37***	.10	-.50***	-.38***	1	
Confusion & Lessened Meaning	-.19**	-.21***	-.22***	.04	.16*	-.05	.03	-.16**	-.04	.44***	.44***	-.31***	1

Table 6. Correlations between depression parcels, and observed indicators for Physical Sequelae and Meaning in Life.