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ORIGINAL ARTICLE

# Physical Sequelae and Depressive Symptoms in Gynecologic Cancer Survivors: Meaning in Life as a Mediator

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**Abstract**
***Background*** Continuing symptoms and poor health following cancer treatments may alter meaning in life for cancer survivors. Gynecologic cancer survivors are particularly troubled with physical sequelae. In addition, for the most common sites of disease, such as breast and gynecologic cancers, the prevalence of depression is also high.
***Purpose*** This study tests meaning in life as a mechanism for the relationship between physical symptoms and depressive symptoms.
***Methods*** Gynecologic cancer survivors ($N$=260) participated. Measures of physical sequelae (nurse rated symptoms/signs, patient-reported gynecologic symptoms), meaning in life (harmony, life purpose, spirituality, and conversely, confusion and loss), and depressive symptoms were obtained at the time of a routine clinical follow-up visit 2–10 years following the completion of treatment. Latent variables were defined, and structural equation modeling tested a mediator model.
***Results*** Analyses support partial mediation. That is, survivors with more physical sequelae also reported lower levels of meaning in life, which was associated with higher levels of depressive symptoms.
***Conclusions*** Gynecologic cancer patients have been neglected in psychosocial research, and findings highlight the importance of existential issues in their lives. While many adjust well, those with persistent physical functioning deficits may experience depressive symptoms. By appreciating the role of meaning in their experience, we may help survivors foster their own growth and perspectives important for their future.

**Keywords** Meaning · Depression · Gynecologic cancer · Survivor · Symptoms

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## Introduction

Cancer survival rates continue to rise, and there are more than 10 million cancer survivors in the USA [1]. In general, cancer survivors adjust well as they recover [2, 3], with many reporting benefits from the cancer experience [4]. Still, there is potential for morbidities and impairments. These can include, for example, neurological, vascular, cardiac, pulmonary, urologic, and gastrointestinal conditions [5, 6]. For example, compared to healthy postmenopausal women, endometrial cancer survivors experience more physical symptoms, and many report distress from continuing medical complications [7]. Due to physical disabilities, some survivors become dependent upon others, which may have a profound psychological impact [8, 9].

As the experience of physical sequelae is often linked to distress, it would be important to discover what variables might play a mediating role. Research has focused on one such possibility—meaning in life [10]. Meaning can include feelings of integration and relatedness [11], fulfillment and significance [12, 13], understanding, or having some goal, function, or purpose for life toward which the individual strives [14, 15]. Meaning is also thought of as one perceiving life as part of a larger picture [16]. Data suggest that meaning in life may indeed mediate the relationship between physical status and distress. First, in a cross-sectional study of cancer survivors, Jim and

Andersen [17] found meaning to be a partial mediator for the effects of both physical and social functioning impairments on heightened distress. Next, in a longitudinal study with breast cancer survivors, physical functioning difficulties and social functioning impairments at 18 months postdiagnosis predicted lower levels of meaning in life at 24 months, which, in turn, predicted distress at 30 months. There, meaning fully mediated the effects of social functioning on distress and was a significant, partial mediator for the effects of physical functioning difficulties on distress.

The current cross-sectional study expands prior research on the importance of meaning in life as it specifically relates to depressive symptoms by focusing on a new patient sample of exclusively gynecologic cancer survivors and the unique physical burdens following their cancer treatment. The majority receives radical pelvic and genital surgeries in addition to any radiation or chemotherapy treatments that follow, and there are high rates of bladder, urinary tract, or bowel complications [18]. As more than 40% are less than 50 when diagnosed, many undergo premature menopause, with the attendant end of child bearing and beginning of estrogen deprivation effects (e.g., hot flashes, increased risk of osteoporosis, vaginal dryness, and others) [19, 20]. Gynecologic patients are at substantial risk for sexual morbidity. For those who were once sexually active, problems of lowered desire, arousal difficulties, and dyspareunia accompany significant declines in sexual activity [6]. With this complexity of physical health challenges, understanding variables that might lessen distress for patients is important [21].

Figure 1 displays a hypothesized model and suggests that health problems increase an individual's vulnerability to psychological difficulties. Patients can be vulnerable to psychological distress (see path a) and reduced meaning in life (path b). With multiple symptoms—lymphedema, pain, sexual dysfunction—and losses—bodily organs, infertility—the meaning one derives from life may significantly change. Survivors may have difficulty making sense of the cancer experience and the losses associated with it [4]. Frankl [14] suggested that suffering creates a search for meaning by providing powerful motivation for the sufferer to understand the situation. However, when a person's search for meaning is blocked, existential frustration may result, leading to hopelessness, depression, and apathy. Related but stronger positions are those of Jung [22] and Yalom [23], who offered that the failure to find meaning results in psychopathology. Thus, the model suggests that reduced meaning in life may be associated with psychological distress (path c).

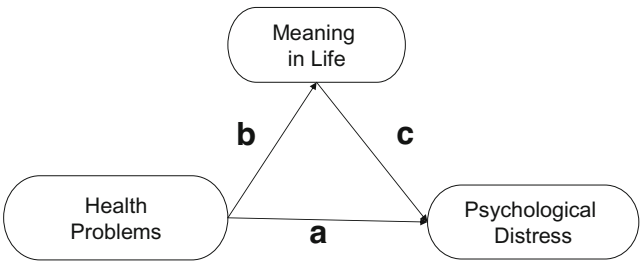


**Fig. 1** A hypothesized model of the relationships between meaning in life, health problems, and psychological distress

The model is tested with gynecologic cancer survivors. The constructs are operationalized with multiple indicators, creating latent variables for structural equation modeling. For health problems, patients' functional status and symptoms/signs were evaluated by a research nurse, and then patients also reported on gynecologic cancer-specific disruptions. Meaning is operationalized by patients' feelings of harmony and peace in life, judgments that one's life has purpose and obtainable goals, and, for some, spiritual feelings that bring meaning to life [17]. In addition, confusion and loss of meaning are also assessed [24]. For psychological distress, depression is the latent variable. Estimates of depression among gynecologic cancer survivors range from 9% [25] to 63% [7], which is higher than that of 6% for the general US population [26]. Symptoms of depression (low mood, guilt) as well as other symptoms (anxiety, restlessness, and tension) common among those with major depressive disorder are included. Risk factors for depressive symptoms—a history of major depressive disorder and dysthymia—are included as controls along with sociodemographic and disease/treatment variables found to covary with distress in gynecologic cancer patients (e.g., age [27], education [2], and extent of disease/treatment [28]). In summary, structural equation modeling is used to test the relationships among physical health, meaning, and depression, with the critical test being the magnitude of an indirect effect of health on depression via meaning (paths b and c) relative to the more direct route of path a.

## Materials and Methods

### Procedures

Gynecologic cancer survivors returning for routine follow-up at a university-affiliated comprehensive cancer center outpatient clinic were eligible. To reduce variability, only patients completing treatment 2 and 10 years previously and currently without evidence of disease were sought (after 2 years, the acute stress of diagnosis has ended [29], but patients may not yet be experiencing the comorbid conditions common in older adulthood that would make it more complicated to ascribe quality-of-life concerns to their previous cancer [30]). Exclusion criteria included the following: age less than 20 or greater than 85 years, other

cancer diagnosis, prior refusal of cancer treatment, organic brain syndrome, significant visual or hearing deficit, major or untreated mental illness (e.g., schizophrenia), mental retardation, deficient ability to speak/read the English language, dementia, and/or current pregnancy.

Two weeks prior to a follow-up appointment, a letter describing the study (i.e., purpose, procedures, risks, and benefits) was sent to patients. Upon their clinic visit, patients were screened, and those remaining eligible were approached. During 12 months of accrual, 294 consecutive gynecologic cancer patients were found eligible, and 260 (88%) were enrolled. Participants completed a 60- to 90-min assessment consisting of an interview, questionnaire completion with a female research assistant, and a health assessment with an oncology nurse.

## Participants

Patients were an average of 4 years postdiagnosis ($M$=4.19, SD=2.04) and survivors of endometrial (51%), ovarian (27%), cervical (18%), or vulvar (4%) cancers. This site distribution corresponds to national data [1] for gynecologic cancers. Sixty percent of patients were diagnosed with stage I disease, and the majority was treated with surgery (96%), with some also receiving chemotherapy (43%) and/or radiation therapy (20%). The sample was primarily Caucasian (95%) and late middle aged ($M$=56, SD=12, range 23–83 years). Seventy percent of the women reported having a spouse or partner. Overall, the group reported having some postsecondary education ($M$=14, SD=3 years) and an annual household income of $56,200 (SD=$4,200).

## Measures for Latent Variables

### *Physical Sequelae*

Six measures were used. A research nurse completed measures 1 and 2 during a clinical interview, and measures 3–6 were patient reported. (1) The types and severity of signs/symptoms of the four body systems most relevant to gynecologic disease—renal/bladder, gastrointestinal, endocrine, and mucosal—were used [31]. A five-point severity rating scale unique to each symptom was used. Items within a system were summed and averaged, with scores ranging from 0 to 4, and the four system scores were totaled for an overall toxicity score ranging from 0 to 16. Internal consistency was 0.68. (2) The Karnofsky Performance Status rating (KPS; [32]) assessed patients' functional status. The scale ranges from 100 (normal, no complaints, no evidence of disease) to 0 (dead) with ten-point intervals.

(3) The Medical Outcomes Study-Short Form 12 Physical Component Summary Score (SF-12 PCS; [33, 34]) uses 12 items to assess disruption in quality of life due to physical symptoms and impairments. Items come from eight scales: physical functioning, role functioning—physical, bodily pain, general health perceptions, vitality, social functioning, role functioning—emotional, and mental health, which are weighted differentially to comprise a PCS score. For the present sample, internal consistency is 0.95. (4) Scores from the site- and symptom- specific quality of life Functional Assessment of Cancer Therapy (FACT; [35]) scales, the 15-item cervical (FACT-Cx; score range 0–60), 16-item endometrial (FACT-En; score range 0–64), 12-item ovarian (FACT-O; score range 0–48), and 15-item vulva subscales (FACT-V; score range 0–60), were used. Across the scales, there are nine common items and three to seven site specific. Items are rated on a five-point scale ranging from 0=not at all to 4=very much. Patients completed the appropriate disease-specific scale, and then all scores were standardized to yield an equivalent metric across patients. Higher scores reflect better quality of life. Internal consistencies were as follows: FACT-Cx (0.83), FACT-En (0.79), FACT-O (0.79), and FACT-V (0.81). (5) The Fatigue Symptom Inventory—Revised (FSI; [36]) assesses the frequency and severity of fatigue. The seven-item total disruption index score ranging from 0 to 70 was used. The internal consistency was 0.94. (6) Vaginal changes were assessed. Patients were queried about the presence (scored 1) or absence (scored 0) of five common vaginal sequelae of treatment (e.g., shortening or narrowing, dryness). Items were summed for a total score (ranging from 0 to 5) estimating the degree of vaginal change. Internal consistency is 0.71.

### *Meaning in Life*

The Meaning in Life Scale is a 21-item measure (MLS; [24]), which conceptualizes meaning as a multidimensional construct present when one has a sense of purpose, coherence, and fulfillment in life and holds beliefs that life has value. Confirmatory factor analysis reveals that it is comprised of four dimensions: harmony and peace (four items; e.g., "I feel peaceful," "I can reach into myself for comfort"), life perspective, purpose, and goals (seven items; e.g., "I feel more fulfilled and satisfied with life," "I am settled about the future"), benefits of spirituality (three items: e.g., "I find comfort in my faith and spiritual beliefs," "I have strength in my spiritual beliefs"), and confusion and lessened meaning (seven items; "I get confused when I try to understand life," "Life has less meaning"). Scale intercorrelations range from −0.31 to −0.50, and internal consistency in the present sample is 0.93. The measure is convergent but not overlapping with measures of mental health (e.g., $r$=0.58 with the SF-36 Mental Health Component score), shows discriminent validity ($r$=0.11 with SF-36 Physical Health Component),

and has negligible correlations with sociodemographic variables (e.g., age, education; $r \pm 0.03$–$0.09$). Two-week test–retest reliability is 0.80 [14].

### *Depression*

According to the Diagnostic and Statistical Manual (DSM-IV; [37]), symptoms of major depressive disorder include depressed mood, anhedonia, appetite and sleep changes, psychomotor agitation or retardation, loss of energy, difficulty concentrating, feelings of guilt/worthlessness, and suicidal ideation. To create multiple observed indicators and include this range of symptoms (particularly anxiety-related ones), a three-step procedure was used. First, the Center for Epidemiological Studies Depression Scale (CES-D; [38–40]) Iowa short form was used as the primary measure. It consists of 11 depressive symptom items (e.g., "I felt....sad, depressed, lonely") with an internal consistency of 0.82. Next, items from three additional measures were considered: (1) The Medical Outcomes Study—Short Form 12 Mental Health Component Summary (SF-12 MCS; [33, 34]). See above for additional details on this measure. (2) The Profile of Mood States (POMS; [41]) short form is a 14-item measure used to assess mood over the past 7 days, plus eight items from the Anxiety–Tension subscale of the original POMS [42] version were considered. (3) The post-traumatic stress disorder (PTSD) Symptom Checklist—Civilian version (PCL-C; [43]) that assessed PTSD symptomatology was used. The PCL-C consists of 17 items, each corresponding to anxiety-related PTSD symptoms [37].

The CES-D was used as the depressive symptom standard, and correlations between the CES-D and items from the SF-12 MCS, POMS, and PCL-C were examined. Items with a correlation of 0.40 or greater ($p<0.001$) and theoretically consistent with DSM-IV depression criteria were identified ($n=33$). Next, a factor analysis was conducted. It was hypothesized that all 33 items would load on a single depression factor. Maximum likelihood discrepancy function with quartimax rotation, scree plots, item loadings, communalities, and judgments of factor interpretability were used to evaluate the solution. The solution adequately fit the data (root mean square error of approximation [RMSEA]=0.09). Three items had factor loadings less than 0.40 and were not considered further. The remaining 30 items were used for the latent variable of depression. As a latent variable needs at least three indicators [44], the third step created equivalent depression "parcels." With the 30 items, three-item, sequential groupings were randomly distributed [45] into three groups/parcels. Internal consistencies of the parcels were 0.85, 0.75, and 0.84, and intercorrelations were 0.86, 0.88, and 0.89. Thus, three reliable indicators were determined. In scoring, an average standardized score was used for each.

## Control Variables

### *Risk for Depression*

Two items assessed a history prior to cancer diagnosis of depression (i.e., a period of 2 weeks of feeling sad, blue, depressed, or having lost pleasure in things usually cared about or enjoyed) and dysthymia (i.e., a period of 2 or more years where felt depressed or sad most days, despite feeling "okay" sometimes).

### *Sociodemographic and Disease/Treatment Information*

Descriptive variables included age, menopausal status (yes or no), race (Caucasian or other), marital status (yes or no), presence of live-in spouse/partner (yes or no), education (years), employment status (yes or no), and annual household income (in thousands per year). Disease and treatment information included time since diagnosis (years), stage of disease at diagnosis (I through IV), site (cervix [yes or no], endometrium [yes or no], etc.), and treatment received: surgery (yes or no), chemotherapy (yes or no), and radiotherapy (yes or no).

## Analytic Strategy

Structural equation modeling (AMOS 6.0 software; [46]) tested the hypothesized relationships (see Fig. 2). In specifying the model, physical sequelae was an exogenous latent variable. Reverse standardized scores were used for the SF-12 PCS, FACT, and KPS, so that all variables were scored in the same direction, with higher scores indicating greater physical sequelae (i.e., poorer physical functioning). Meaning in life is specified as an endogenous latent variable using the four scales from the MLS. The outcome variable, depression, was specified as an endogenous latent variable measured with the three ten-item symptom parcels. Controls were included if they were significantly correlated with the outcome. Control variables that correlated with other variables were represented with a two-way path.

Full-information maximum likelihood estimation of parameters was conducted using raw data as input (less than 2% of values missing). To provide a metric for the latent constructs and to identify the measurement model, one indicator loading for each latent variable was set to 1.0 in the unstandardized solution. Direct and indirect effects and their standard errors were estimated, and the Sobel test [47] determined the significance of each indirect effect ($\alpha=0.05$). The model's ability to explain the covariances between variables was evaluated with two fit indices. RMSEA [48] 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

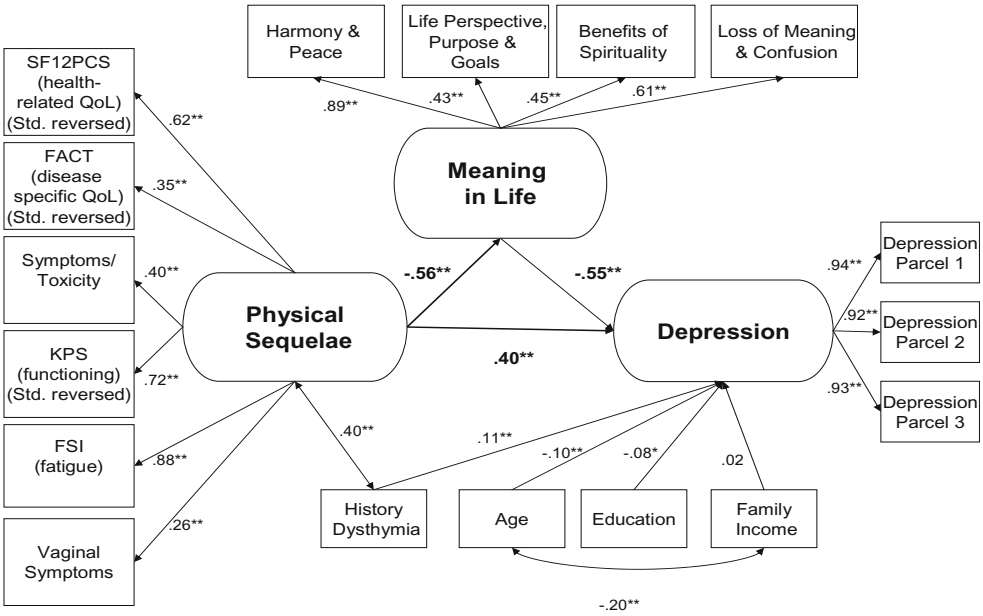


**Fig. 2** The model of the hypothesized relationships tested by structural equation modeling

values of 0.10 or less, with values less than 0.06 representing excellent fit. For the comparative fit index (CFI, [49]), 0.90 is regarded as indicating good fit and 0.95 or greater as excellent fit [50, 51].

## Results

### Description of the Sample and Preliminary Analyses

Table 1 presents the means and standard deviations for the sample on the measured variables as well as possible score ranges. In general, patients reported quality-of-life impairments due to physical functioning. The group mean (44.3) was one half the standard deviation below the population mean of 50. Scores on the meaning subscales are comparable to those from cancer patients sampled for scale development [24]. Regarding depressive symptomatology, the mean score of the CES-D (4.30) was within the normal range, but inspection of individual scores showed that 21% of the sample had significant symptomatology. Eleven percent of the patients had scores within the subclinical range (scores >8), and an additional 10% of patients scored in the clinical range (scores >10; [40]).

Preliminary analyses were conducted examining the control variables. First, analyses of variance were con-

**Table 1** Means and standard deviations for the measured physical sequelae, meaning, and depressive symptom variables

| Measured variable | Mean | SD | Possible range |
|---|---|---|---|
| Physical sequelae | | | |
| SF-12 PCS | 44.27 | 12.92 | |
| FACT scales | | | |
| FACT-Cx | 47.00 | 6.75 | 0–60 |
| FACT-En | 57.14 | 6.38 | 0–64 |
| FACT-O | 34.94 | 5.07 | 0–48 |
| FACT-V | 44.22 | 8.91 | 0–60 |
| Signs and symptoms (nurse rated) | 2.14 | 0.75 | 0–3 |
| KPS (nurse rated) | 78.46 | 11.22 | 0–100 |
| FSI | 15.37 | 15.82 | 0–70 |
| Vaginal change score | 1.62 | 1.47 | 0–5 |
| Total positive meaning | 11.42 | 2.94 | −3–17 |
| Harmony and peace | 3.97 | 0.78 | 1–6 |
| Life perspective, purpose, and goals | 4.28 | 1.03 | 1–6 |
| Benefits of spirituality | 5.02 | 1.26 | 1–6 |
| Loss of meaning and confusion | 1.86 | 0.90 | 1–6 |
| Center for Epidemiology Depression Scale—short form | 4.30 | 3.86 | 0–22 |

ducted with categorical variables and revealed no significant group differences between disease site ($F \leq 2.11$, $p \geq 0.10$), stage of disease ($F \leq 1.54$, $p \geq 0.17$), type of cancer treatment received ($F < 0.48$, $p > 0.48$), or time since diagnosis ($F < 0.77$, $p > 0.91$) on scores for the three depression parcels. Secondly, correlations were examined (see Table 2). Significant correlations were found between the depression parcels and age ($r \geq -0.22$), education ($r \geq -0.13$), family income ($r \geq -0.22$), and history of dysthymia ($r \geq 0.44$; all $p < .05$), where patients who were younger, less educated, had lower income, and/or a history of depression were more likely to report more depressive symptoms.

### Mediation Model

The AMOS test of the partial mediation model is presented in Fig. 2. The standardized estimates of the parameters in the measurement and structural models and, for simplicity, only the significant correlations among exogenous variables are reported. The model fits the data with a RMSEA of 0.10 (90% confidence interval=0.09–0.12) and a CFI of 0.89, and the overall effect size ($R^2$) for the outcome, depression, is 0.80. Thus, both indices were on the boundaries for desirable fit estimates. In comparing the indices, RMSEA rewards for model parsimony (fewer parameters), whereas CFI is sensitive to larger sample sizes and complex models [49]. This model, however, accounts for control variables, as well as indicators of latent variables, making it complex. The model demonstrates valuable local fit with the majority of the standardized regression weights being greater than 0.45 and in the hypothesized directions [52]. Significant path weights (all $p < 0.001$) between the observed indicators and the latent variables demonstrate that all indicators provided successful representations of the latent variables.

In this model, the path from physical sequelae to meaning in life was significant ($p < 0.001$), indicating that reports of higher levels of physical sequelae and disruption from them were associated with reports of lower levels of meaning in life. In addition, the path from meaning in life to depression was significant ($p < 0.001$), with those reporting less meaning in life also reporting more depressive symptoms. As hypothesized, the indirect effect from physical sequelae to depression through meaning in life was significant ($z = 3.92$; $p < 0.001$), suggesting meaning in life as a mediator of the relationship between physical sequelae and depression. Finally, the path from physical sequelae to depression was also significant ($p < 0.001$), indicating partial mediation.

Lastly, the significant path weights from age, education, and a history of dysthymia to depression ($p < 0.05$) indicate that, independent of physical sequelae or meaning, gynecologic cancer patients who were younger, less educated, or with a history of dysthymia reported more symptoms of depression.

### Post-hoc Analyses

The structural equation modeling used here implies directionality in the hypothesis of meaning as a mediator of the relationship between physical sequelae and depressive symptoms. These are cross-sectional data, however, not longitudinal. Acknowledging this, confidence in a statistical test of mediation would be enhanced if it could be demonstrated that the above findings have stronger support than a test of the converse relationships. That is, a similar analysis could be performed testing depressive symptoms as a mediator of the relationship between physical sequelae and meaning. We performed these analyses and then compared the two models. The Akaike information criterion (AIC; [49]) can be used to compare models, and the one with the lower AIC is preferred. Moreover, Burnham and Anderson [49] suggested that a difference in AIC of 4 to 7 corresponds, roughly, to "95% confidence" in the superiority of one model over another. The AIC for the hypothesized model is 577.55, and the AIC for the reversed model is 602.48, with the difference between models being 24. Thus, support for the proposed model was obtained.

## Discussion

Finding (or regaining) meaning in one's life may benefit cancer survivors by providing fulfillment and satisfaction, new perspectives or life goals, and a sense of peace or harmony with life or offering a spiritual presence. However, these data suggest that survivors facing physical challenges may face difficulties capturing meaning or may even experience meaning losses. Moreover, lowered meaning may covary with impaired mental health, as illustrated here with heightened depressive symptoms. We discuss these findings and their implications.

Among quality-of-life studies with cancer survivors, most studies have focused on disease sites other than gynecologic despite their high risk for morbidity [6, 19]. Recently [53], the National Cancer Institute described a "critical need" for more physiologic, psychological, social, and behavioral information about long-term survivorship in all cancer groups but noted gynecologic cancer patients in particular. In this study, the use of latent variable modeling allowed the representation of their general and disease-specific physical morbidities and disruption due to them. While patient reports were used, an experienced gynecology oncology clinical nurse specialist provided symptom/sign evaluations as well as functional ratings. With their complex physical health challenges, understanding variables that might lessen distress for patients is important as psychosocial difficulties can arise even when there is no psychiatric comorbidity, such as major depression or

**Table 2** Correlations between observed indicators for depression, physical sequelae, and meaning in life latent variables

| | DEP1 | DEP2 | DEP3 | SF-12 PCS | FACT | Symptoms/ toxicity | KPS | FSI | Vaginal changes | Harmony and peace | Life perspectives | Benefits of spirituality | Confusion and lessened meaning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DEP1 | 1 | | | | | | | | | | | | |
| DEP2 | 0.87*** | 1 | | | | | | | | | | | |
| DEP3 | 0.88*** | 0.86*** | 1 | | | | | | | | | | |
| SF-12 PCS | −0.29*** | −0.34*** | −0.34*** | 1 | | | | | | | | | |
| FACT | −0.32*** | −0.34*** | −0.35*** | 0.18** | 1 | | | | | | | | |
| Symptoms/ toxicity | 0.26*** | 0.24*** | 0.25*** | −0.24*** | −0.21*** | 1 | | | | | | | |
| KPS | −0.40*** | −0.36*** | −0.44*** | 0.69*** | 0.20** | −0.31*** | 1 | | | | | | |
| FSI | 0.64*** | 0.64*** | 0.68*** | −0.52*** | −0.30*** | 0.34*** | −0.62*** | 1 | | | | | |
| Vaginal changes | 0.29*** | 0.26*** | 0.25*** | −0.08 | −0.22*** | 0.36*** | −0.01 | 0.21*** | 1 | | | | |
| Harmony and peace | −0.71*** | −0.70*** | −0.72*** | 0.17** | 0.34** | −0.13* | 0.28*** | −0.48*** | −0.24*** | 1 | | | |
| Life perspectives | −0.26*** | −0.22*** | −0.24*** | 0.07 | 0.04 | −0.06 | 0.06 | −0.10 | −0.03 | 0.35*** | 1 | | |
| Benefits of spirituality | 0.48*** | 0.53*** | 0.54*** | −0.13* | −0.25*** | 0.15* | −0.21*** | 0.37*** | 0.10 | −0.50*** | −0.38*** | 1 | |
| Confusion and lessened meaning | −0.19** | −0.21*** | −0.22*** | 0.04 | 0.16* | −0.05 | 0.03 | −0.16** | −0.04 | 0.44*** | 0.44*** | −0.31*** | 1 |

*DEP1–3* Depression parcels 1–3, *SF-12 PCS* The Medical Outcomes Study—Short Form 12 Physical Component Summary Score, *FACT* Functional Assessment of Cancer Therapy score, *KPS* Karnofsky Performance Status rating, *FSI* Fatigue Symptom Inventory—Revised score

*$p<0.05$, **$p<0.01$, ***$p<0.001$

generalized anxiety disorders [54–56]. The significant relationship between physical sequelae and concurrent depressive symptoms for these patients is consistent with data from other investigators [8, 57].

Of larger magnitude than the relationship of physical sequelae with depression was that between physical sequelae and lowered meaning. Individuals searching for meaning after cancer may be disheartened when physical symptoms/signs continue, worsen, or emerge late. The evaluation of these patients' physical status likely reflects a stabilized course, as patients were assessed an average of 4 years post-therapy, with the shortest interval being 2 years. Limitations in the capacity to resume life as it was (or how it was anticipated to be) may bring lack of fulfillment, feelings of dissatisfaction with one's current life, and disappointments when physical limits or debilitation interferes. Gynecologic patients report fatigue that is life disrupting as do many other cancer patients [58, 59], but their higher incidence of sexual difficulties distinguish their survivorship [60]. Vaginal changes, as assessed here, covary with decreased sexual functioning [61] and may negatively impact a woman's view of herself as a sexual person [61, 62]. Thus, there are many changes that may alter meaning for gynecologic survivors, some unique to their disease and others not.

The existential challenge of the cancer experience—challenging one's view of the self, the world, and one's future—may increase the likelihood of poorer quality of life and well-being [23, 63]. Among these survivors, lowered levels of meaning were associated with greater levels of depressive symptoms. As these are cross-sectional data, we do not know the temporal order of the relationship, but we hypothesized meaning loss preceding depression. Test of the reverse relationship, depression predicting meaning, suggests that the hypothesized model is parsimonious. Regardless, what is clear is that more than 20% of these survivors were at heightened risk for major depressive disorder, which is substantially higher than the estimated base rate of 6% in the general population [26]. We also note that the frequency of significant depressive symptomatology may be an underestimate for patients from this clinic, as those who did not schedule, did not keep, or did not return for follow-up did not participate. While the reasons for this may vary, mood-related difficulties might be contributory for some.

The relationship among physical sequelae, meaning loss, and higher levels of depressive symptoms may be viewed, in part, in the broader context of high rates of mood and anxiety disorders generally found among the medically ill. For example, rates of depression range from 9% in outpatient clinics to 30% or more among the hospitalized [64]. It is not surprising to note that the diagnosis of a life-threatening illness can be a risk factor for a depressive episode or an anxiety attack [65]. Indeed, the lifetime prevalence of any psychiatric disorder for those with chronic illness is higher—42%—than is found for the general population (i.e., 33% [66]). With the two most common killers—heart disease and cancer—mental disorders among patients are well above the base rate [67] and are linked to disease course, morbidity, and death. The greatest study has focused on depression, anxiety, and coronary heart disease (e.g., [68–71]). By contrast, much less is known about depression and anxiety in the context of cancer, even though both disorders are more prevalent among cancer patients than among coronary heart disease patients as well as any other chronic illness patient group [65].

Despite the physical impairments that cancer and aging may bring, they need not lead, inevitably, to loss of meaning. It is premature to suggest from these data that interventions should be designed and tested to help patients with this issue. However, there are data that may be germane. Lee et al. [72] randomized breast and colorectal cancer patients to a meaning–making coping strategies intervention versus routine care, and intervention patients reported higher self-esteem, optimism, and self-efficacy compared to the control group [72]. Others have tested "positive psychotherapy," utilizing resilience building exercises that have a meaning component, with patients with mild to moderate depression [73]. These studies provide early, suggestive data that efforts to enhance meaning (or stem meaning losses) may have beneficial effects on patients' moods and well-being.

We note the methodological aspects of the study. The use of convergent measures enabled the use of structural equation modeling. SEM can provide unbiased construct estimates, allowing for the discussion of relationships among latent entities rather than correlations among measures. This was particularly advantageous for the physical sequelae-latent variable. Similarly for depression, the CES-D taps classic symptoms of sad mood, low motivation, etc., but the additional items included agitation, difficulties in concentrating, etc., which are seen in clinical cases and identified in the DSM-IV criteria for major depression. In the hypothesized model, the a priori tests of direct and indirect effects were significant, but the fit estimates suggest the need for replication and/or future modifications, and research considering additional variables or alternative constructs would be valuable. We do not know the relevance of these data to non-Caucasian racial/ethnic groups. We would, however, expect the findings to be generally relevant to female cancer survivors as the mean age and socioeconomic level of the sample approaches population estimates. For example, the median education level (≤14 years) is the same as that attained by 58% of the adult females in Ohio. Regarding family

income, the estimate of $56,200 for this sample is roughly $10,000 above the median for Ohio ($43,500) but comparable to the US median ($55,800). The latter two variables are important in cancer, and data show them to be more relevant than race alone [74]. Our results suggest that income and education were correlated negatively with depressive symptoms, consistent with related data from breast cancer patients [75].

In summary, the data bring to light the importance of existential issues in the lives of cancer survivors. Survivors carry their cancer experience and for some, the continuing burden of negative treatment effects, through their lives. When this happens, patients may struggle with finding and retaining new life perspectives and goals for their future. In combination, patients may become additionally vulnerable to depressive symptoms. Clarifying these relationships may be an important step in assisting patients to cope effectively with cancer.

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