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Worse Depression Profiles Are Associated With Higher Symptom Burden and Poorer Quality of Life in Patients With Gynecologic Cancer

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Abstract

Background: Depression is a pervasive symptom in patients with gynecological cancer undergoing chemotherapy.

Objectives: Purposes were to identify subgroups of patients with distinct depression profiles and evaluate for differences in demographic and clinical characteristics, severity of common symptoms, and quality of life (QOL) outcomes among these subgroups.

Methods: Patients with gynecological cancer (n=231) completed the Center for Epidemiologic Studies Depression Scale six times over two cycles of chemotherapy. All of the other measures were completed prior to the second or third cycle of chemotherapy. Latent profile analysis was done to identify the distinct depression profiles. Differences were evaluated using parametric and non-parametric tests.

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Results: Three distinct profiles were identified: Low (60.1%), High (35.1%), and Very High (4.8%). Compared to Low class, the other two classes had lower functional status and were more likely to self-report a diagnosis of depression. Patients in the two worse profiles reported a higher comorbidity burden, higher levels of trait and state anxiety, sleep disturbance and fatigue, as well as lower levels of cognitive function, and poorer QOL. State and trait anxiety, evening fatigue, and sleep disturbance scores exhibit a "dose-response effect" (i.e., as the depression profile worsened, the severity of these symptoms increased).

Conclusions: Almost 40% of our sample experienced high or very high levels of depression across two cycles of chemotherapy.

Implications for Practice: Clinicians can use the identified risk factors to identify high risk and provide tailored psychological interventions aimed to decrease symptom burden and prevent decrements in QOL.

Introduction

Depression occurs in 23% to 52% of patients with gynecological cancer,[1–3] which is higher than the 10.4% reported for women in the general population.[4] Unrelieved clinical depression during chemotherapy is associated with increased suffering,[5] poorer adherence with treatments,[6] reduced quality of life (QOL),[7] poorer prognosis,[6] and increases in healthcare costs.[8] Of note, subsyndromal depression (i.e., clinically significant symptoms of depression without meeting the diagnostic criteria for major depression) is common in patients with gynecological cancer and increases their risk for a major depressive disorder.[9] While multiple factors can contribute to the development and/or exacerbation of depression in these patients,[3,10] little is known about specific modifiable risk factors during receipt of chemotherapy. Without this knowledge, high risk patients cannot be identified and targeted interventions initiated.

Only five longitudinal studies have examined the occurrence, severity, and risk factors for depression in patients with gynecological cancer undergoing chemotherapy.[11–15] In a study that assessed patients with ovarian cancer during and for 6 months after the completion of chemotherapy,[11] depression decreased over time. In another study of patients with advanced ovarian cancer,[12] depression scores did not change from prior to surgery through to the fourth course of chemotherapy. Risk factors associated with higher depression scores included fewer number of live births, history of an abortion, and higher levels of CA125. In another study,[13] compared to healthy women, depression scores in patients with ovarian cancer were significantly higher prior to chemotherapy and decreased following one cycle. Younger age was the only risk factor associated with higher levels of depression.

In a study that followed patients with gynecological cancer for nine months,[14] poorer functional status at enrollment was associated with higher levels of depression over time. Additional risk factors for higher levels of depression at enrollment included younger age, White ethnicity, and a history of ovarian cancer recurrence. In the fifth study,[15] 18.5% of patients with ovarian cancer had depression scores above the clinically meaningful cut point on the Center for Epidemiologic Studies Depression Scale (CES-D) before, during, and after

chemotherapy and these scores did not change over time. Risk factors associated with more severe depression included lower self-efficacy and higher symptom distress scores.

These longitudinal studies provide some insights into the occurrence of and the risk factors for depression in patients with gynecological cancer receiving chemotherapy. However, none of them evaluated a comprehensive list of risk factors, as well as the impact of depression on QOL. In addition, only two studies reported on associations between depression and symptom distress[15] or functional status.[14] This gap in knowledge regarding associations between depression and common symptoms associated with cancer and its treatments (e.g., fatigue, sleep disturbance) warrants additional investigation because evidence suggests that the co-occurrence of multiple symptoms can have synergistic effects on patients' functional status and QOL outcomes.[16]

Of note, because four of the previous studies included only women with ovarian cancer,[11–13,15] little is known about changes in depression in a more heterogeneous sample of patients with various types of gynecologic cancer. Finally, none of these studies used a person-centered analytic approach (e.g., latent profile analysis [LPA]) to evaluate for inter-individual variability in depression. Therefore, the purpose of this study, in a sample of patients with gynecological cancer undergoing chemotherapy (n = 231), was to identify subgroups of patients with distinct depression profiles. In addition, differences in demographic and clinical characteristics, severity of common symptoms, and QOL outcomes among these subgroups were evaluated. The identification of modifiable and non-modifiable risk factors for depression will help clinicians to identify the most vulnerable patients who warrant referrals for psychological services.

Methods

Patients and Settings

This study is part of a larger, longitudinal study of the symptom experience of oncology outpatients receiving chemotherapy that used the Theory of Symptom Management as its theoretical framework.[17] Briefly, patients were ≥18 years of age; had a diagnosis of breast, gastrointestinal, gynecological, or lung cancer; had received chemotherapy within the preceding four weeks; were scheduled to receive at least two additional cycles of chemotherapy; were able to read, write, and understand English; and provided written informed consent. Patients were recruited from two Comprehensive Cancer Centers, one Veteran's Affairs hospital, and four community-based oncology programs during their first or second cycle of chemotherapy.

Study Procedures

Study was approved by the Institutional Review Board at each of the study sites. Of the 2234 patients approached, 1343 consented to participate. Patients were approached in the infusion unit during their first or second cycle of chemotherapy by a research nurse who explained the study procedures and obtained informed consent. The major reason for refusal was being overwhelmed by their cancer treatments. Patients completed the CES-D a total of six times over two chemotherapy cycles (i.e., prior to chemotherapy administration,

approximately 1 week after chemotherapy administration, and approximately 2 weeks after chemotherapy administration). All of the other measures were completed at enrollment (i.e., prior to the second or third cycle of chemotherapy). For this analysis, data from patients with gynecological cancer (n = 231) who had complete data on the depression measure were evaluated.

Instruments

Demographic and clinical measures—Patients completed a demographic questionnaire that obtained information on age, gender, ethnicity, marital status, living arrangements, education, employment status, and income. In addition, they completed the Karnofsky Performance Status (KPS) scale which is widely used to evaluate functional status in patients with cancer.[18] Patients rated their functional status using the KPS scale that ranged from 30 (I feel severely disabled and need to be hospitalized) to 100 (I feel normal; I have no complaints or symptoms).

The Self-Administered Comorbidity Questionnaire (SCQ) consists of 13 common medical conditions simplified into language that can be understood without prior medical knowledge.[19] Patients indicated if they had the condition; if they received treatment for it (proxy for disease severity) and if it limits their activities (indication of functional limitations). For each condition, the patient can receive a maximum of 3 points. The total SCQ score ranges from 0 to 39.

Alcohol Use Disorders Identification Test (AUDIT) is a 10-item questionnaire that assesses alcohol consumption, alcohol dependence, and the consequences of alcohol abuse in the last 12 months. The AUDIT gives a total score that ranges between 0 and 40. Scores of 8 or more are defined as hazardous use and scores of 16 or more are defined as use of alcohol that is likely to be harmful to health.[20,21] In this study, its Cronbach's alpha was 0.63.

The MAX-2 score was used to evaluate the toxicity of the various chemotherapy regimens based on the most toxic drug in the regimen.[22] Scores can range from 0 to 1 with a higher score indicating a worse toxicity profile. Medical records were reviewed for disease and treatment information.

Depression measure—The 20-item CES-D evaluates the major symptoms in the clinical syndrome of depression.[23] A total score can range from 0 to 60, with scores of ≥16 indicating the need for individuals to seek clinical evaluation for depression. Its Cronbach's alpha was 0.89.

Other symptom measures

The 20 items on the Spielberger Trait-State Anxiety Inventories (STAI-T and STAI-S) were rated from 1 to 4.[24] The STAI-S measures a person's temporary anxiety response to a specific situation or how anxious or tense a person is "right now" in a specific situation. The STAI-T measures a person's predisposition to anxiety as part of one's personality. Cutoff scores of ≥ 31.8 and ≥ 32.2 indicate high levels of trait and state anxiety, respectively. Cronbach's alphas for the STAI-T and STAI-S were .92 and .96, respectively.

The 18-item Lee Fatigue Scale (LFS) was designed to assess physical fatigue and energy.[25] Each item was rated on a 0 to 10 numeric rating scale (NRS). Total fatigue and energy scores were calculated as the mean of the 13 fatigue items and the 5 energy items, respectively. Higher scores indicate greater fatigue severity and higher levels of energy. Using separate LFS questionnaires, patients were asked to rate each item based on how they felt within 30 minutes of awakening (i.e., morning fatigue, morning energy) and prior to going to bed (i.e., evening fatigue, evening energy). The LFS has established cut-off scores for clinically meaningful levels of fatigue (i.e., ≥3.2 for morning fatigue, ≥5.6 for evening fatigue) and energy (i.e., ≤6.2 for morning energy, ≤3.5 for evening energy).[26] Cronbach's alphas were 0.96 for morning and 0.93 for evening fatigue and 0.95 for morning and 0.93 for evening energy.

The 21-item General Sleep Disturbance Scale (GSDS) was designed to assess various aspects of sleep disturbance. Each item was rated on a 0 (never) to 7 (everyday) NRS. The GSDS total score ranges from 0 (no disturbance) to 147 (extreme sleep disturbance).[27–29] A GSDS total score of 343 indicate a significant level of sleep disturbance that warrants clinical evaluation and management.[26] In this study, Cronbach's alpha for the GSDS total score was 0.83.

The 16-item Attentional Function Index (i.e., AFI) was designed to assesses an individual's perceived effectiveness in performing daily activities that are supported by attention, working memory, and executive functions (e.g., setting goals, planning and carrying out tasks). A higher total mean score on a 0 to 10 NRS indicates greater capacity to direct attention.[30] Clinically meaningful cutpoints for attentional function are as follows: <5.0 low function, 5.0 to 7.5 moderate function, >7.5 high function.[31] Cronbach's alpha for the AFI was 0.93.

Worst pain severity was assessed using the Brief Pain Inventory (BPI).[32] Patients were asked to indicate whether they were generally bothered by pain (yes/no). Those who were bothered by pain noted if their pain was or was not associated with cancer. In addition, they rated worst pain severity in the past 24 hours using a 0 (no pain) to 10 (worst pain imaginable) numeric rating scale (NRS) and completed the pain interference score of the BPI.

QOL measures—QOL was evaluated using generic (i.e., Medical Outcomes Study-Short Form-12 [SF-12][33]) and disease-specific (i.e., QOL-Patient Version [QOL-PV][34]) measures. The individual items on the SF-12 were evaluated and the instrument was scored into two components (i.e., physical component summary [PCS] and mental component summary [MCS] scores). QOL-PV measures four dimensions of QOL (i.e., physical, psychological, social, spiritual well-being), as well as a total QOL score. For both measures, higher scores indicate a better QOL.

Data Analysis

LPA was used to identify unobserved subgroups of patients (i.e., latent classes) with distinct depression profiles over the six assessments using the patients' CES-D scores. LPA was performed using Mplus version 8.4.[35] Estimation was carried out with full information maximum likelihood with standard errors and a Chi square test that is robust

to non-normality and non-independence of observations ("estimator=MLR"). Model fit was evaluated to identify the solution that best characterized the observed latent class structure with the Bayesian Information Criterion, Vuong-Lo-Mendell-Rubin likelihood ratio test, entropy, and latent class percentages that were large enough to be reliable.[35,36] Missing data were accommodated for with the use of the Expectation-Maximization algorithm.[37]

All of the other data were analyzed using SPSS version 28 (IBM Corporation, Armonk, NY). Differences among the depression latent classes in demographic and clinical characteristics, symptom severity scores, and QOL outcomes at enrollment were evaluated using parametric (e.g., analysis of variance) and nonparametric (e.g., Kruskal Wallis) tests. Bonferroni corrected p-value of <.017 was considered statistically significant for the pairwise contrasts (i.e., .05/3 possible pairwise contrasts).

Results

Latent profile analysis

As noted in Table 1, a three-class solution was selected based on the fit indices. Using the CES-D clinically meaningful cutoff score of ≥16,[23] as shown in Figure 1, the depression classes were labeled: "Low depression" (60.1%, Low); "High depression" (35.1%, High); and "Very High depression" (4.8%, Very High). Except for the Very High class, patients in the other two classes had depression scores that increased slightly at the second and fifth assessments (i.e., following the administration of chemotherapy). For the Very High class, depression scores remained relatively stable across the six assessments.

Differences in demographic and clinical characteristics

Compared to the Low class, the High class was more likely to be younger; had fewer years of education; was less likely to be employed; and was more likely to have a lower annual household income (Table 2). Compared to the Low class, the Very High class was more likely to have child care responsibilities and was more likely to self-report a diagnosis of ulcer or stomach disease. Compared to the Low class, the other two classes had lower functional status and were more likely to self-report a diagnosis of depression. Compared to the Low and High classes, the Very High class was less likely to have had prior cancer treatments and was more likely to self-report a diagnosis of lung disease, kidney disease, and back pain. In addition, significant differences were found among the three latent classes in total number of comorbid conditions and SCQ scores (i.e., Low < High < Very High).

Differences in common symptoms

As shown in Table 3, significant differences were found among the three latent classes for trait and state anxiety, evening fatigue, and sleep disturbance (i.e., Low < High < Very High). Compared to the Low class, the other two classes reported higher levels of morning fatigue, lower levels of cognitive function, the occurrence of both non-cancer and cancer pain, and higher pain interference scores. Compared to the Low class, the High class reported lower levels of evening energy. Compared to the Low class, the Very High class reported lower levels of morning energy.

Differences in QOL outcomes

For the SF-12's physical functioning, role physical, bodily pain, general health, vitality, and social functioning domains, compared to the Low class, the other two classes reported lower scores (Figure 2). Significant differences were found among the three latent classes for role emotional, mental health, and MCS scores (i.e., Low > High > Very High). For the PCS domain, compared to the Low class, patients in the High class reported lower scores.

Significant differences were found among the three latent classes for the QOL-PV's psychological and total QOL scores (i.e., Low > High > Very High; Figure 3). For the physical and social well-being domains, compared to the Low class, the other two classes reported lower scores. For the spiritual well-being domain, compared to the Low class, the Very High class reported lower scores.

Discussion

This study is the first to use LPA to identify subgroups of patients with gynecological cancer with distinct depression profiles and to evaluate for associated modifiable and non-modifiable risk factors. Based on the clinically meaningful cutoff score for the CES-D, 39.9% of our patients experienced high or very high levels of depression across two cycles of chemotherapy i.e., 35.1% and 4.8% in the High and Very High classes, respectively). Our occurrence rate is at the higher end of the 23% to 52% reported in previous reviews.[1–3] These differences may be related to the symptom measures used; the timing of the assessments; and/or the methods used to determine occurrence rates. Of note, the mean CES-D score at enrollment for our Very High class (i.e., 36.7) was approximately 2.3 times higher than the cutoff score of ≥16. In addition, a large percentage of women in the two highest classes self-reported a diagnosis of depression.

In terms of changes in depression scores over time, our findings are consistent with previous longitudinal studies,[11,13,14] in that the Low and High classes' CES-D scores increased slightly at the second and fifth assessments (i.e., approximately 1 week after chemotherapy administration). In contrast, the Very High class's scores remained relatively consistent (Figure 1). Additional research is warranted to confirm these cyclic variations, before, during, and following the completion of chemotherapy.

Demographic and clinical characteristics

While younger age, lower levels of education, being unemployed, and having a lower annual income were primarily non-modifiable risk factors associated with membership in the High class (Table 2), similar trends were seen in the Very High class compared to the Low class. The lack of significance may be related to the small number of patients (n = 11) in the Very High class. Consistent with previous reports,[3,13,14,38] younger women with gynecological cancer had higher rates of depression. One plausible explanation for this association is that the site of the cancer and associated treatments have adverse effects on sexual and hormonal functions.[39] Therefore, younger women who experience premature menopause;[39] alterations in sexual activity;[3,38] and/or sexual dysfunction may become depressed.[38] Equally plausible,

significant changes in body image may contribute to higher levels of depression in younger patients.[40]

Having child care responsibilities was the only distinct demographic characteristic associated with membership in the Very High class. This finding, that is consistent with younger age, may be related to the psychological burden of having to care for younger children while facing a potentially life-threatening condition (e.g., sadness at potentially not seeing one's children reach adulthood). Equally important, being unemployed and having a lower annual income were risk factors associated with membership in the High class. As noted in prior reports,[41,42] receipt of chemotherapy interferes with patients' ability to work and contributes to financial toxicity. In addition, the enormous financial cost of cancer treatments[43] and a higher symptom burden[42,44] may exacerbate financial hardship due to patients' inability to remain employed. Given that oncology patients with a lower socioeconomic status are less likely to be referred to specialized mental health services,[45] clinicians should screen patients for both depression and financial toxicity and initiate appropriate referrals to social services.

Compared to the Low class, women in the other two classes had a higher number of comorbidities, higher comorbidity burden, a poorer functional status, and higher rates of a self-reported diagnosis of depression (Table 2). Consistent with a previous study of multimorbidity in patients with gynecological cancer,[46] a dose-response effect was seen in the SCQ scores (i.e., measure of comorbidity burden) among our depression classes. Equally important, women in the Very High class self-reported higher rates of lung disease, kidney disease, and back pain that may complicate the receipt of chemotherapy.

Consistent with this high comorbidity burden, women in our two highest classes reported KPS scores that suggest that they "can care for themselves but are not able to carry on normal activity or do normal work." A similar association was found between depression and performance status in a study of patients with breast and gynecological cancers.[47] These findings warrant careful consideration because oncology patients who experience multimorbidity have a two to four times increase in the odds of reporting depression,[47] lower functional status,[47] poorer QOL,[48] and increased mortality.[48] While multimorbidity may not be a modifiable risk factor, optimal management of women's chronic conditions and referrals to physical therapy to improve functional status are warranted.

It should be noted that a large number of patients in the High and Very High classes self-reported a diagnosis of depression. This association validates the LPA findings and suggests that the CES-D score can be used to screen these vulnerable patients who warrant referral to psychological services. While detailed information on our patients' use of antidepressants is not available, the high rates of the depression in our sample may be related to the fact that less than 12% of women with gynecological cancer receive pharmacological treatment for depression and that only 5% are referred for counseling or participate in a cancer support group.[47]

Symptom severity

Our findings highlight important associations between depression and the severity of other common symptoms in patients with gynecological cancer. For all of the symptoms except decrements in morning and evening energy, our two higher classes had worse scores (Table 3). Furthermore, the severity scores for state and trait anxiety, morning and evening fatigue, and sleep disturbance were above the clinically meaningful cutoff scores. In addition, the differences between the Low and High classes, as well as between the Low and Very High classes, represent not only statistically significant but clinically meaningful differences in symptom severity scores (i.e., effect sizes ranged from 0.51 [morning fatigue] to 1.0 [trait and state anxiety]).[49] These findings suggest additive or synergistic interactions among these symptoms.

Equally important, the state and trait anxiety, evening fatigue, and sleep disturbance scores demonstrated a “dose response effect” in that as the depression profile worsened, the severity of these symptoms increased significantly. Our findings are consistent with studies of the general population that found dose response relationships between depression and both anxiety[50] and sleep disturbance.[51] Of note, while no studies have evaluated for a dose response effect between depression and fatigue, in our previous study of patients with gastrointestinal cancer,[52] depression scores increased as the evening fatigue profiles worsened. Given that our study is the first to describe dose response relationships between depression and anxiety, fatigue, and sleep disturbance in patients with gynecological cancer undergoing chemotherapy, additional studies need to confirm these findings and evaluate common and distinct underlying mechanisms.

In terms of pain, compared to the 26.3% of women in the Low class, 50% and 63.6% of the patients in the High and Very High depression classes, respectively, reported the occurrence of both non-cancer and cancer pain. In addition, patients with the worst two profiles had moderate to severe levels of pain interference associated with routine activities (e.g., normal work, walking activity; Table 3). Our findings are consistent with previous studies that found an association between depression and pain.[53,54] For example, in a study that examined factors associated with depression in patients with cervical cancer,[53] women who reported high pain scores were more likely to report depression. In another study that evaluated for associations between pain and depression,[54] patients with advanced cancer who reported pain were 4.2 times more likely to report depression.

One plausible explanation for the association between depression and other common symptoms is that the receipt of chemotherapy results in dysregulation of common inflammatory and neurotransmission pathways.[55] For example, in patients with heterogenous types of cancer, elevations in proinflammatory cytokines (e.g., interleukin 6 (IL6)) were associated with higher levels of depression,[56] anxiety,[57,58] sleep disturbance,[56,59] fatigue,[56,59] and pain,[56] as well as poorer cognitive function.[60] Equally important, altered levels of monoamine neurotransmitters (e.g., serotonin, dopamine) were associated with higher levels of anxiety,[61] fatigue,[62] depression,[61] and sleep disturbance.[61]

An equally plausible explanation for these relationships is stress. While albeit limited, evidence suggests that increases in levels of stress in oncology patients were associated with

higher levels of depression, anxiety, fatigue, sleep disturbance, and pain. For example, in a study of patients with head and neck cancer,[63] higher levels of all five symptoms were associated with a flattened cortisol slope. Additional research is warranted to determine the mechanisms that may contribute to the development and/or exacerbation of a higher symptom burden in patients with gynecological cancer who report multiple common symptoms associated with cancer and its treatments. This knowledge will assist with the development of tailored interventions that can target multiple symptoms simultaneously and improve patients' QOL.

QOL outcomes

Consistent with prior research,[64,65] our High and Very High classes reported worse scores for all of the QOL domains on both the general and disease-specific measures (Figures 2 and 3). Furthermore, patients in the High and Very High classes reported PCS and MCS scores of less than 50, that were lower than the normative score for the general population.[34] These findings highlight how depression can have a negative impact on both physical and psychological well-being.[64]

A cancer diagnosis and associated treatments can result in significant role changes and disruptions in daily activities that are risk factors for depression.[64] In addition, patients with gynecological cancer often receive chemotherapy regimens that are associated with the occurrence of multiple common symptoms that effect all aspects of their daily life. Taken together, our findings suggest that clinicians need to screen patients on a routine basis and provide tailored interventions to decrease symptom burden and prevent decrements in QOL.

Limitations

Several limitations warrant consideration. First, our sample was relatively homogenous in terms race/ethnicity, education, and income, so our findings may not generalize to all patients with gynecologic cancer. Second, given the relatively small sample sizes for the various types of gynecologic cancer, future studies can use LPA to replicate these findings within different types of gynecologic cancer (e.g., ovarian, uterine). Third, information was not collected on the use of antidepressants and other symptom management interventions that would have assisted with the interpretation of our findings. Lastly, given that depression was measured over only two cycles of chemotherapy, additional longitudinal studies are needed to evaluate for changes in this symptom from prior to through the completion of chemotherapy, as well as for associations between depression and various modifiable risk factors (e.g., occurrence of common symptoms) that may change over time.

Conclusions

Despite these limitations, our findings suggest that a high percentage of patients with gynecological cancer undergoing chemotherapy experience clinically meaningful levels of depression that impacts their QOL. Of note, while various demographic and clinical characteristics, as well as the occurrence of common symptoms were associated with depression, additional longitudinal studies need to explore other potential risk factors (e.g., stress, personality, coping mechanisms) that may contribute to depression in these patients.

In addition, future research needs to evaluate for additive or synergistic interactions between depression and the occurrence of other symptoms. Equally important, the common and distinct molecular mechanisms that may underlie depression and the occurrence of multiple common symptoms warrant evaluation.

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Implications for Practice

Given that the risk for depression remains increased for years after a cancer diagnosis,[46] clinicians need to perform systematic and comprehensive assessments of depression, including a diagnostic interview,[66] to identify vulnerable patients. Equally important, clinicians need to refer patients who report subsyndromal and high levels of depression to psychosocial services. Based on the findings regarding modifiable risk factors, several clinical implications warrant consideration. Given the high levels of comorbidity and decrements in functional status, many of these patients warrant referrals to physical therapy. Equally important, because all of the patient subgroups had clinically meaningful levels of sleep disturbance, clinicians need to educate patients about how to improve their sleep habits.[67] In addition, patients with pain may benefit from education about how to optimize their administration of pharmacologic and nonpharmacologic interventions.

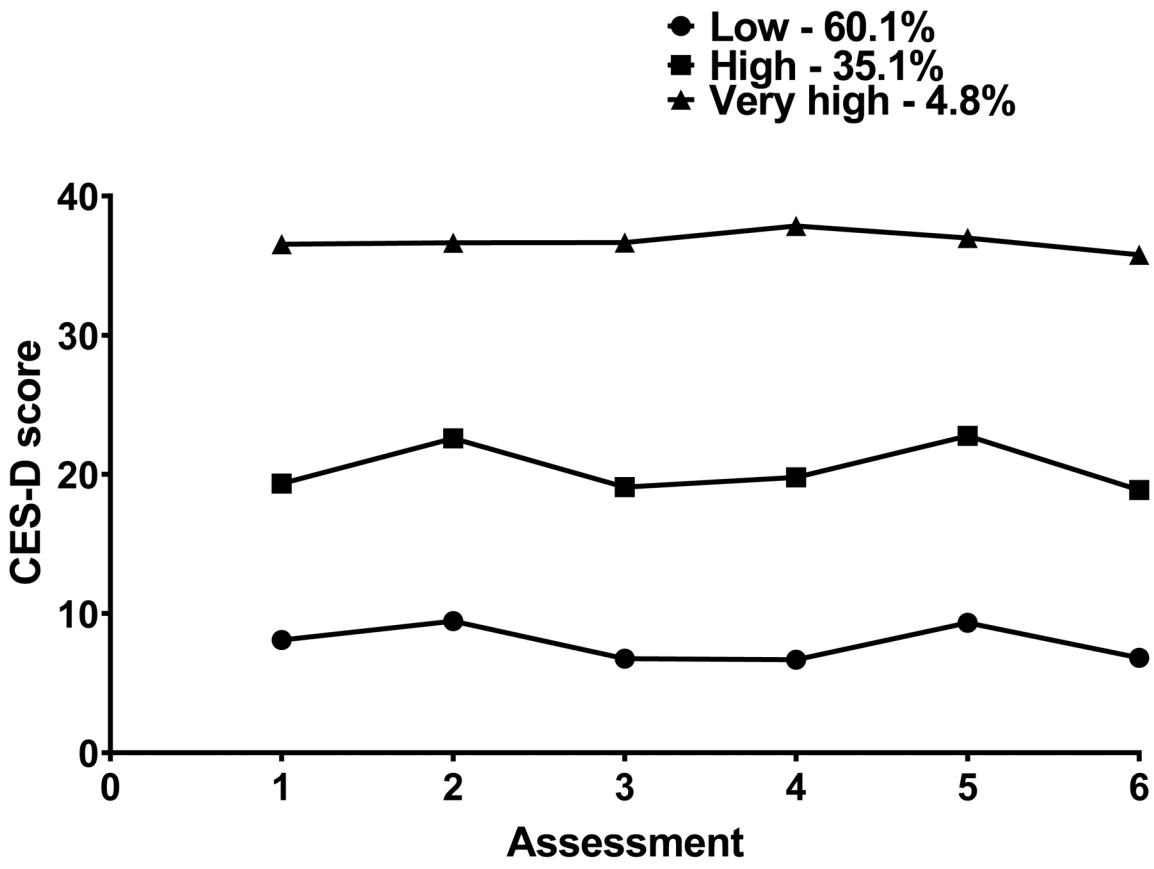

Figure 1.

Depression trajectories for the three latent classes. The latent classes were named based on the Center for Epidemiologic Studies Depression Scale clinically meaningful cutoff score of ≥16.0 as Low (60.1%), High (35.1%), and Very High (4.8%).

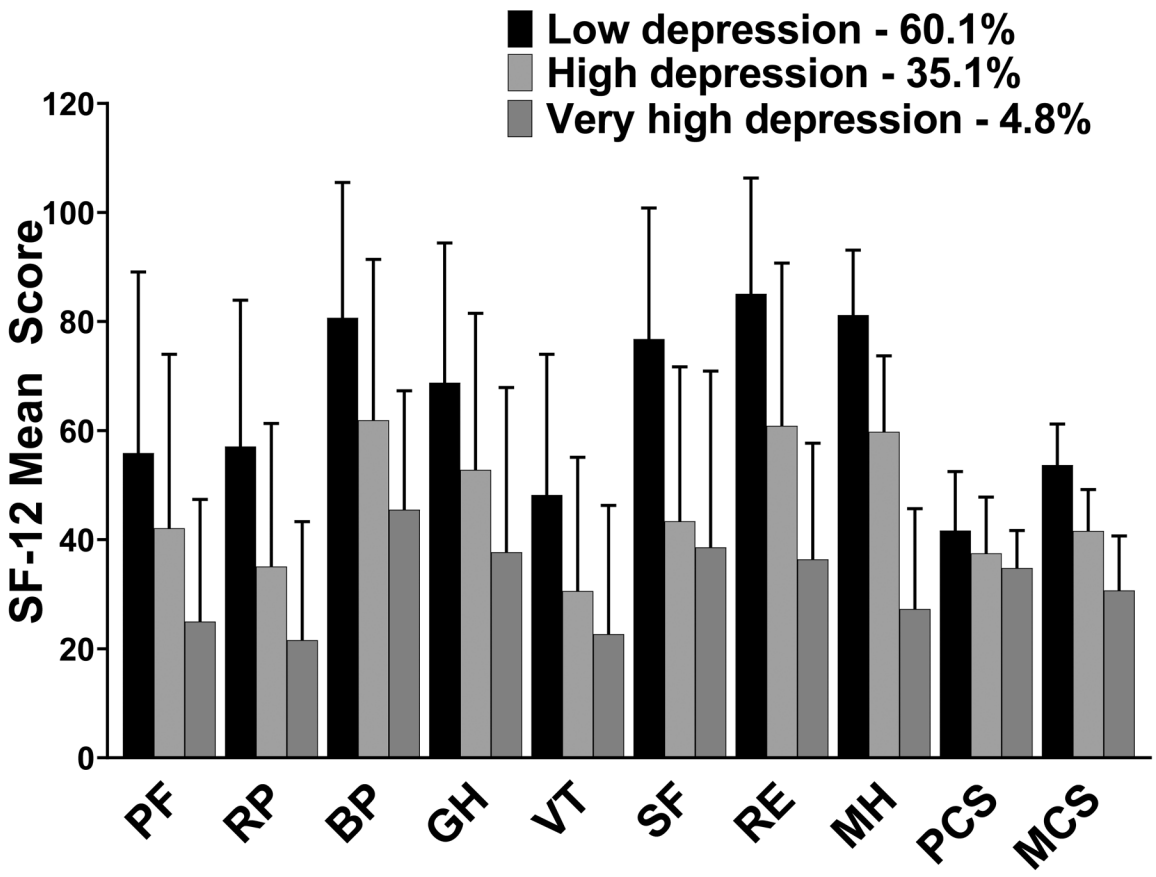

Figure 2.

Differences in Medical Outcomes Study-Short Form 12 (SF-12) physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), mental health (ME), physical component summary (PCS), and mental component summary (MCS) scores among the depression latent classes. All values are plotted as means ± SDs. For the RE, MH, and MCS scores, post hoc contrasts demonstrated significant differences among the classes that followed the same pattern (i.e., Low > High > Very High classes; all, $p < .05$). For the PF, RP, BP, GH, VT, and SF scores, post hoc contrasts demonstrated that the differences among the classes were as follows: Low > High and Very High classes (all, $p < .05$). For the PCS score, the post hoc contrast demonstrated that the Low class had a higher score than the High class ($p < .05$).

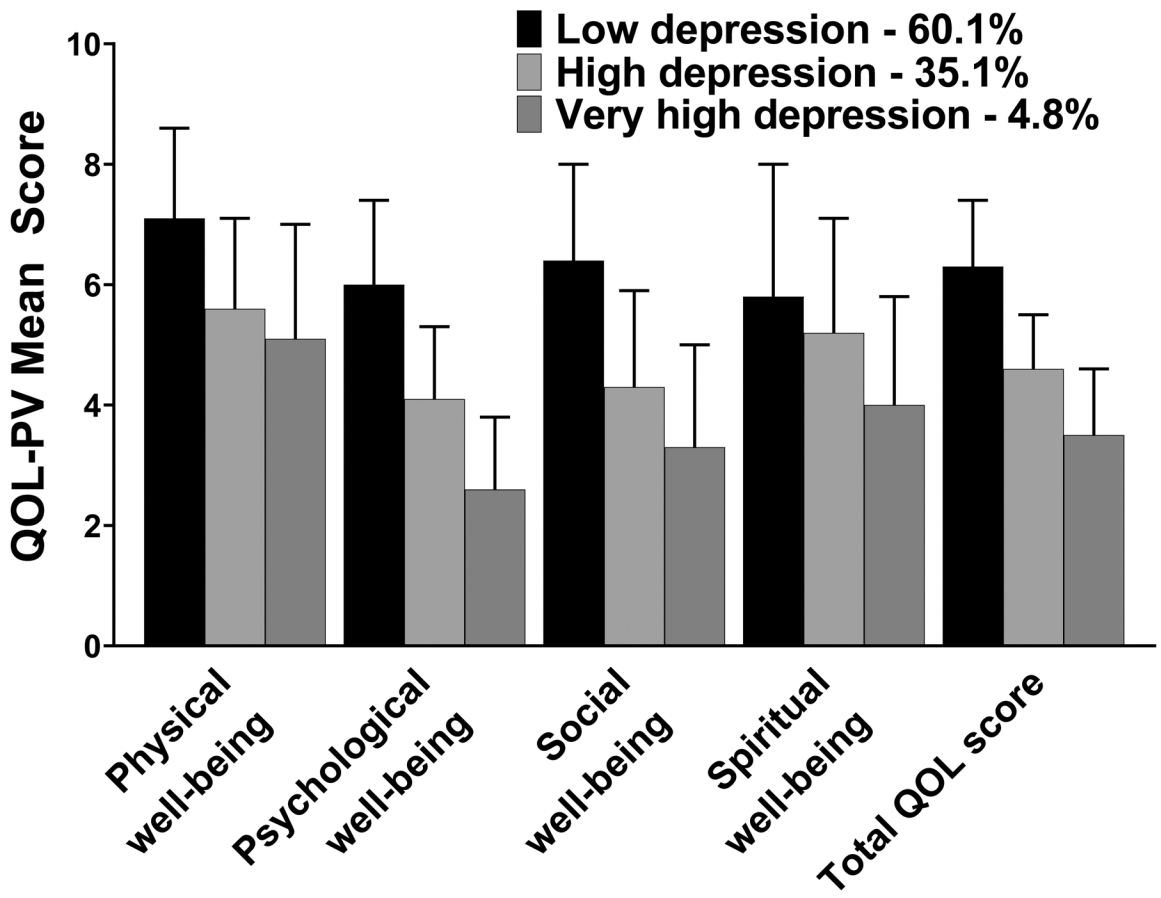

Figure 3.

Differences in Quality-of-Life Scale–Patient Version (QOL-PV) scores for the physical, psychological, social, and spiritual well-being domains as well as total quality of life (QOL) among the depression latent classes. All values are plotted as means ± SDs. For the psychological domain and QOL total scores, post hoc contrasts demonstrated that significant differences among the classes followed the same pattern (i.e., Low > High > Very High class; both, $p < .05$). For the physical and social well-being domains, post hoc contrasts demonstrated that the differences among the classes were as follows: Low > High and Very High classes (both, $p < .05$). For the spiritual well-being domain, the post hoc contrasts demonstrated that the differences among the classes were as follows: Low class > Very High class ($p < .05$).

Table 1.

Latent Profile Solutions and Fit Indices for One through Four Classes for Center for Epidemiologic Studies Scale Scores

Model	LL	AIC	BIC	Entropy	VLMR
1 Class	−4457.59	8939.17	8980.48	n/a	n/a
2 Class	−4136.06	8310.13	8375.53	0.88	643.05[a]
3 Class[a]	−4009.63	8071.25	8160.76	0.93	252.87[c]
4 Class	−3939.81	7945.62	8059.22	0.88	ns

Baseline entropy and VLMR are not applicable for the one-class solution.

[a]The 3-class solution was selected because the BIC for that solution was lower than the BIC for the 2-class solution. In addition, the VLMR was significant for the 3-class solution, indicating that three classes fit the data better than two classes. Although the BIC was smaller for the 4-class than for the 3-class solution, the VLMR for 4-classes was not significant, indicating that too many classes had been extracted.

[b]$p < .10$.

[c]$p < .05$.

Abbreviations: AIC, Akaike's Information Criterion; BIC, Bayesian Information Criterion; LL, log-likelihood; n/a, not applicable; ns, not significant; VLMR, Vuong-Lo-Mendell-Rubin likelihood ratio test for the K vs. K-1 model.

Table 2.

Differences in Demographic and Clinical Characteristics Among the Depression Latent Classes

Characteristic	Low Depression (0) 60.1% (n=139)	High Depression (1) 35.1% (n=81)	Very High Depression (2) 4.8% (n=11)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)	61.6 (12.1)	56.6 (13.3)	54.9 (10.2)	F=4.89, p=.008 0 > 1
Education (years)	16.4 (2.9)	15.4 (2.8)	16.2 (2.2)	F=3.22, p=.042 0 > 1
Body mass index (kg/m^2)	26.8 (5.8)	28.3 (7.7)	26.9 (6.8)	F=1.36, p=.258
Alcohol Use Disorders Identification Test score	2.5 (1.6)	3.1 (2.5)	4.0 (4.0)	F=2.81, p=.063
Karnofsky Performance Status score	81.9 (11.7)	73.8 (11.7)	70.9 (9.4)	F=14.28, p<.001 0 > 1 and 2
Number of comorbid conditions	2.1 (1.1)	2.6 (1.5)	4.1 (2.4)	F=12.26, p<.001 0 < 1 < 2
Self-administered Comorbidity Questionnaire score	4.7 (2.3)	6.0 (3.7)	9.7 (5.7)	F=16.13, p<.001 0 < 1 < 2
Time since diagnosis (years)	2.1 (3.0)	2.2 (4.4)	1.0 (1.5)	KW=2.81, p=.245
Time since diagnosis (years, median)	0.53	0.50	0.38	
Number of prior cancer treatments	1.9 (1.2)	1.7 (1.0)	1.5 (1.4)	F=0.88, p=.417
Number of metastatic sites including lymph node involvement[a]	1.5 (1.3)	1.5 (1.3)	1.7 (1.5)	F=0.23, p=.797
Number of metastatic sites excluding lymph node involvement	1.0 (1.1)	1.0 (1.1)	1.5 (1.4)	F=0.75, p=.472
MAX2 score	0.15 (0.06)	0.16 (0.06)	0.12 (0.06)	F=1.92, p=.149
	% (n)	% (n)	% (n)	
Self-reported ethnicity				
White	79.0 (109)	74.0 (57)	72.7 (8)	
Asian or Pacific Islander	10.1 (14)	6.5 (5)	9.1 (1)	X^2=4.56, p=.602
Black	2.9 (4)	5.2 (4)	0.0 (0)	
Hispanic, Mixed, or Other	8.0 (11)	14.3 (11)	18.2 (2)	
Married or partnered (% yes)	56.3 (76)	53.8 (42)	45.5 (5)	X^2=0.54, p=.764
Lives alone (% yes)	30.9 (42)	36.7 (29)	54.5 (6)	X^2=2.91, p=.233
Currently employed (% yes)	37.7 (52)	20.0 (16)	27.3 (3)	X^2=7.48, p=.024 0 > 1

Characteristic	Low Depression (0) 60.1% (n=139)	High Depression (1) 35.1% (n=81)	Very High Depression (2) 4.8% (n=11)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Annual household income				KW=10.42, p=.005 0 < 1
Less than $30,000[b]	11.1 (14)	27.0 (20)	44.4 (4)	
$30,000 to $70,000	25.4 (32)	31.1 (23)	22.2 (2)	
$70,000 to $100,000	20.6 (26)	12.2 (9)	0.0 (0)	
Greater than $100,000	42.9 (54)	29.7 (22)	33.3 (3)	
Child care responsibilities (% yes)	6.5 (9)	13.6 (11)	27.3 (3)	X^2=6.75, p=.034 0 < 2
Elder care responsibilities (% yes)	6.4 (8)	12.2 (9)	9.1 (1)	X^2=1.97, p=.373
Past or current history of smoking (% yes)	33.8 (46)	37.5 (30)	18.2 (2)	X^2=1.64, p=.440
Exercise on a regular basis (% yes)	74.6 (103)	65.4 (51)	70.0 (7)	X^2=2.09, p=.352
Specific comorbid conditions				
Heart disease	5.0 (7)	6.2 (5)	0.0 (0)	X^2=0.77, p=.681
High blood pressure	33.8 (47)	28.4 (23)	63.6 (7)	X^2=5.45, p=.066
Lung disease	2.2 (3)	2.5 (2)	18.2 (2)	X^2=9.04, p=.011 0 and 1 < 2
Diabetes	3.6 (5)	8.6 (7)	0.0 (0)	X^2=3.28, p=.194
Ulcer or stomach disease	3.6 (5)	6.2 (5)	27.3 (3)	X^2=10.83, p=.004 0 < 2
Kidney disease	2.9 (4)	1.2 (1)	18.2 (2)	X^2=9.49, p=.009 0 and 1 < 2
Liver disease	2.2 (3)	2.5 (2)	0.0 (0)	X^2=0.28, p=.870
Anemia or blood disease	13.7 (19)	17.3 (14)	36.4 (4)	X^2=4.05, p=.132
Depression	7.9 (11)	39.5 (32)	72.7 (8)	X^2=46.91, p<.001 0 < 1 and 2
Osteoarthritis	15.1 (21)	19.8 (16)	9.1 (1)	X^2=1.26, p=.533
Back pain	20.9 (29)	27.2 (22)	63.6 (7)	X^2=10.20, p=.006 0 and 1 < 2
Rheumatoid arthritis	2.2 (3)	2.5 (2)	9.1 (1)	X^2=1.95, p=.378
Type of gynecological cancer				X^2=1.73, p=.785
Ovarian	57.6 (80)	51.9 (42)	72.7 (8)	

Characteristic	Low Depression (0) 60.1% (n=139)	High Depression (1) 35.1% (n=81)	Very High Depression (2) 4.8% (n=11)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Uterine	28.1 (39)	32.1 (26)	18.2 (2)	
Other	12.9 (18)	13.6 (11)	9.1 (1)	
Prior cancer treatment				X^2=25.72, p<.001
No prior treatment	2.2 (3)	2.6 (2)	27.3 (3)	0 and 1 < 2
Only surgery, CTX, or RT	54.3 (75)	55.1 (43)	36.4 (4)	NS
Surgery and CTX, or surgery and RT, or CTX and RT	38.4 (53)	28.2 (22)	27.3 (3)	NS
Surgery and CTX and RT	5.1 (7)	14.1 (11)	9.1 (1)	NS
Metastatic sites				X^2=2.64, p=.853
No metastasis	26.1 (36)	26.9 (21)	36.4 (4)	
Only lymph node metastasis	14.5 (20)	11.5 (9)	0.0 (0)	
Only metastatic disease in other sites	31.2 (43)	29.5 (23)	36.4 (4)	
Metastatic disease in lymph nodes and other sites	28.3 (39)	32.1 (25)	27.3 (3)	
Receipt of targeted therapy				X^2=2.33, p=.312
No	71.2 (99)	75.9 (60)	90.9 (10)	
Yes	28.8 (40)	24.1 (19)	9.1 (1)	
CTX regimen				X^2=3.96, p=.412
Only CTX	71.2 (99)	75.9 (60)	90.9 (10)	
Only targeted therapy	6.5 (9)	3.8 (3)	9.1 (1)	
Both CTX and targeted therapy	6.5 (31)	6.5 (16)	0.0 (0)	
Cycle length				KW=1.34, p=.511
14-day cycle	5.8 (8)	4.9 (4)	0.0 (0)	
21-day cycle	78.4 (109)	85.2 (69)	81.8 (9)	
28-day cycle	15.8 (22)	9.9 (8)	18.2 (2)	
Emetogenicity of the CTX regimen				KW=0.16, p=.922
Minimal/low	17.3 (24)	21.0 (17)	18.2 (2)	
Moderate	77.0 (107)	69.1 (56)	81.8 (9)	
High	5.8 (8)	9.9 (8)	0.0 (0)	
Antiemetic regimen				X^2=2.99, p=.810

Characteristic	Low Depression (0) 60.1% (n=139)	High Depression (1) 35.1% (n=81)	Very High Depression (2) 4.8% (n=11)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
None	10.5 (14)	10.1 (8)	18.2 (2)	
Steroid alone or serotonin receptor antagonist alone	27.1 (36)	26.6 (21)	27.3 (3)	
Serotonin receptor antagonist and steroid	48.9 (65)	46.8 (37)	27.3 (3)	
NK-1 receptor antagonist and two other antiemetics	13.5 (18)	16.5 (13)	27.3 (3)	

[a] Total number of metastatic sites evaluated was 9.

[b] Reference group.

Abbreviations: CTX, chemotherapy; kg, kilograms; KW, Kruskal Wallis; m^2, meters squared; pw, pairwise; n/a, not applicable; NK-1, neurokinin-1; NS, not significant; RT, radiation therapy; SD, standard deviation.

Table 3.

Differences in Co-Occurring Symptom Severity Scores Among the Depression Latent Classes

Symptoms[a]	**Low Depression (0) 60.1 % (n=139)**	**High Depression (1) 35.1% (n=81)**	**Very High Depression (2) 4.8% (n=11)**	**Statistics**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	
Trait anxiety (≥31.8)	30.7 (7.4)	41.5 (7.5)	57.3 (10.8)	F=95.51, p<.001 0 < 1 < 2
State anxiety (≥32.2)	28.1 (7.7)	40.0 (9.5)	62.2 (10.0)	F=112.56, p<.001 0 < 1 < 2
Morning fatigue (≥3.2)	2.3 (1.8)	4.3 (2.1)	5.0 (2.8)	F=30.39, p<.001 0 < 1 and 2
Evening fatigue (≥5.6)	5.1 (1.9)	5.8 (2.0)	7.4 (1.7)	F=9.32, p<.001 0 < 1 < 2
Morning energy (≤6.2)	4.6 (2.2)	3.9 (2.1)	2.9 (1.5)	F=4.61, p=.011 0 > 2
Evening energy (≤3.5)	3.8 (2.0)	3.0 (1.6)	3.1 (2.4)	F=5.14, p=.007 0 > 1
Sleep disturbance (≥43.0)	48.5 (19.2)	60.3 (17.1)	74.8 (19.0)	F=17.57, p<.001 0 < 1 < 2
Attentional function (<5.0 = Low, 5 to 7.5 = Moderate, >7.5 = High)	6.8 (1.6)	5.2 (1.5)	4.4 (1.1)	F=34.45, p<.001 0 > 1 and 2
	% (n)	% (n)	% (n)	
Types of pain				X^2=23.24, p<.001
None	29.9 (41)	10.0 (8)	0.0 (0)	0 > 1
Only non-cancer pain	13.1 (18)	10.0 (8)	18.2 (2)	NS
Only cancer pain	30.7 (42)	30.0 (24)	18.2 (2)	NS
Both non-cancer and cancer pain	26.3 (36)	50.0 (40)	63.6 (7)	0 < 1 and 2
For the patients with pain	Mean (SD)	Mean (SD)	Mean (SD)	
Worst pain intensity score	5.7 (2.5)	6.1 (2.6)	6.1 (2.3)	F=0.34, p=.712
Mean pain interference score	2.2 (1.9)	4.0 (2.5)	4.8 (3.2)	F=17.01, p<.001 0 < 1 and 2

Abbreviation: SD, standard deviation.

[a]Clinically meaningful cutoff scores.