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Prevalence and predictors of depression, pain, and fatigue in older- versus younger-adult cancer survivors

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Abstract

Background: As the number of older adults in the United States continues to grow, there will be increasing demands on health care providers to address the needs of this population. Cancer is of particular importance, with over half of all cancer survivors older than 65 years. In addition, depression, pain, and fatigue are concerns for older adults with cancer and have been linked to poorer physical outcomes.

Methods: For this retrospective chart review, 1012 eligible participants were identified via a query of the Electronic Medical Record for all patients referred to 1 of 4 Survivorship Clinics at Memorial Sloan Kettering Cancer Center. All patients were between the ages of 30 to 55 (younger adults) and >65 (older adults). Depression was measured using the Patient Health Questionnaire-9 (PHQ-9).

Results: The overall rate of depression in this sample of adult cancer survivors was 9.3%. There were no differences in the rates of clinically significant depression (defined as PHQ-9 score ≥10) between younger and older adult cohorts. However, there was a small trend toward higher mean PHQ-9 scores in the younger adult cohort (3.42 vs 2.95; t = 1.763, P = .10). Women reported greater rates of depression and higher pain and fatigue scores. Hispanic/Latino patients also reported significantly greater rates of depression.

Conclusion: There were no observed differences in depression between older and younger adult cancer survivors. Gender and ethnic discrepancies in depression were observed. Future research should focus on understanding the nature of these differences and targeting interventions for the groups most vulnerable to depression after cancer treatment.

KEYWORDS

cancer, depression, fatigue, gender, geriatrics, oncology, pain, PHQ-9, survivorship

1 | INTRODUCTION

As the number of older adults in the United States and internationally continues to grow, there will be increasing demands on health care providers to address the unique needs of this population. This is of particular concern for cancer professionals as cancer is predominantly a disease of the elderly, with more than 50% of cancer survivors in the 65+ age group.[1] This expansion of the older population, coupled with advancements in cancer screening and treatment, has led to an increase in the number of older adult cancer survivors, with greater than 11 million survivors older than 65 years in the United States expected by 2020.[2] Yet the long-term effects of surviving this disease and the psychosocial needs of this growing cohort of older survivors are poorly understood.[3]

Depression is of particular clinical interest in this population, with rates of depression as high as 25% in older adults, well above the general population.[4-11] Depression in older adults in community and primary care medical settings is associated with several important physical, psychosocial, and economic consequences: poor compliance, increased medical care use, and higher rates of mortality.[4-6,10-15] Cancer-specific mortality has also been found to be substantially higher in older patients with a mental disorder, such as Major Depressive

Disorder, compared to those without a mental disorder.[16] Despite its prevalence and impact, depression is often unrecognized in elderly patients[16] because of overlapping symptoms with comorbid medical illness, underreporting of depressive symptoms,[7] the stigma of many physicians that depression is expected in older adults, and an atypical presentation of depressive symptoms (eg, social withdrawal, irritability, somatic complaints, lack of motivation, or anhedonia).[9] Furthermore, older adults seek mental health treatment at a rate lower than any other adult age group and are more likely to seek care from a primary care provider rather than a mental health specialist.[16,17]

Emotional distress is also more common in people with cancer than in the general population, although some literature have found higher distress in younger as opposed to older cancer patients.[12] This literature, however, has not teased apart the different aspects of distress (ie, anxiety versus depression), and data in prostate cancer patients suggest that depression may actually increase with age.[18] One meta-analysis of depression and anxiety in long-term cancer survivors found a prevalence of depression and anxiety of 11.6% and 17.9%, respectively; however they did not compare depression by age of survivors.[19] Studies of depression in long-term cancer survivors have found that older survivors reported depression as much as[20] or even more than younger survivors.[21] A better understanding of how depression affects this aging group of cancer survivors will be critical for improving cancer care in the 21st century.

In addition to depression, pain and fatigue are important clinical outcomes in cancer survivors. There is literature to suggest that fatigue is common among cancer survivors and is linked to poorer physical and psychological outcomes, including depression and sleep disturbance.[22] Pain is also common among cancer survivors, with studies suggesting a prevalence of up to 40% of survivors experiencing pain since diagnosis.[23] Furthermore, older patients may somaticize depressive symptoms, suggesting pain and fatigue may be manifestations of emotional distress.[9]

The goal of the present study is to determine the prevalence of depression in older adult cancer survivors in relation to younger survivors, with the hypothesis that older survivors are a particularly vulnerable group to developing depressive symptoms. In addition, this study aims to compare the levels of pain and fatigue between younger and older adult cancer survivors. Finally, this study also aims to identify additional demographic (ie, gender, ethnicity) predictors of depression, pain, and fatigue among cancer survivors.

2 | METHODS

2.1 | Participants and procedures

This is a retrospective, cross-sectional review of EMR data collected from patients in 1 of 4 Survivorship Clinics at a cancer center in New York City between February 2008 and July 2015. The Survivorship Clinics provide cancer surveillance and health monitoring for patients who completed cancer treatment and are considered to have no evidence of disease. Since this paper focuses on the broad spectrum of survivorship in different cancers, these patients will have been diagnosed in various stages of disease and have had various types of treatments. The purpose of this paper is not to examine variables such as stage of disease or impact of a specific type of treatment. The focus is on those patients who have been treated for cancer and who have no evidence of disease at the time of their visit to the Survivorship Clinics.

As part of their regular Survivorship Clinic Visit, patients complete a (1) Survivor Self-Assessment Form and (2) Patient Health Questionnaire-9 (PHQ-9), which are reviewed by a Nurse Practitioner and scanned into their EMR. We received IRB approval for a waiver of consent to abstract and analyze these archival data. Records eligible for inclusion had a Survivor Self-Assessment Form and PHQ-9 from the date of their initial Survivorship Clinic visit. Patients whose forms were incomplete or who only had forms from follow-up visits were excluded. Other eligibility criteria included: being either 30 to 55 (younger adult cohort) or 65 and older (older adult cohort) on the date of this initial Survivorship visit. We chose to define older adults as age 65 and older for several reasons, including convention in geriatrics health services research, recommendations from special reports,[24] and Medicare definitions. We chose to define the younger adult comparison group as beginning at age 30 to avoid the transition effects of "emerging adulthood" in the twenties and capped the upper age limit at 55 years to keep the 2 age groups distinct and minimize any overlapping effects.

2.2 | Measures

The Survivorship Self-Assessment form included information on demographic variables, exercise, past-month pain and fatigue, and health/cancer screening history. The PHQ-9 is the depression subscale of the full PHQ and includes the 9 DSM-IV criteria that are used to diagnose major depressive disorder.[25] Its psychometrics have been established in diverse general and medical populations.[6,26] Each item is rated 0 (not at all) to 3 (nearly every day) to indicate how much a person has been bothered by each symptom over a 2-week period and summed to produce total scores ranging from 0 to 27. A total score of ≥10 indicates clinically significant depressive symptoms.[27] Pain and fatigue were measured using the Visual Analogue Scale in which participants circled a number between 0 and 10 indicating their self-reported level of pain and fatigue.[28] In addition to these measures, we extracted additional demographic information including age, sex, race, and ethnicity from the EMR.

2.3 | Data analysis

There were no any relevant articles that reported effect sizes appropriate for this study. As this was a data abstraction from existing EMR, this study was limited by data availability rather than recruitment resources. However, recruitment of at least 500 participants in each cohort would be 80% powered to detect an effect size as small as $d = 0.18$ based on a 2-tailed, independent samples t test with .05 significance level.

All data were analyzed using SAS version 9.4 (SAS Institute Inc, Cary, North Carolina). We conducted descriptive analyses for

demographic characteristics. Total PHQ-9 score was calculated as the sum of the 9 individual items, with up to 3 missing items included via substitution by the individual's mean score. Older adults were compared to younger adults on the main study outcomes of depression, pain, and fatigue using *t* tests. We examined the roles of sex and ethnic differences in these main dependent variables using χ^2 tests. Differences in dependent variables across the 4 Survivorship Clinics (henceforth referred to as "Cancer Type") were assessed by analysis of variance. Finally, we fitted linear regression models to identify predictors of depression, pain, and fatigue and to adjust for these effects in the assessment of a potential age-depression association. Predictor variables included age, gender, race, ethnicity, cancer type, and marital/living status. These variables were chosen "a priori" on the basis of the literature demonstrating a relationship between these variables and depressive symptoms.[29-34] Case-wise deletion was used for missing values.

3 | RESULTS

3.1 | Sample characteristics

This sample included 508 older adult and 504 younger adult cancer survivors (Table 1). The mean age of the younger adult cohort was 49.26 (SD = 5.0) and 76.56 (SD = 5.0) for the older adult cohort. Most patients (58.8%) came from the Breast Clinic, followed by Urologic (20.9%), Colorectal (12.6%), and Thoracic (7.8%) clinics. Over half (59.7%) of patients were married and/or living with a partner. Most patients were White (72.9%), and 9.7% identified their ethnicity as Hispanic/Latino.

3.2 | Older versus younger adults

3.2.1 | Depression

Using a cutoff of ≥10 on the PHQ-9 to indicate clinically significant depression, 9.3% of the sample met criteria for depression in the past 2 weeks. Three patients, all in the older adult cohort, were missing more than 3 items on the PHQ-9 and could not be analyzed. There was no significant difference in the rates of depression between older and younger adult cohorts (8.5% vs 10.1%, $\chi^2(1) = .77$, $P = .38$). Mean PHQ-9 scores were compared across age cohorts, with younger adults having higher scores (M = 3.42, SD = 4.56) compared with older adults (M = 2.95, SD = 4.59), although this difference was not significant ($t = 1.63$, $P = .103$).

Each individual item on the PHQ-9 was then assessed independently to determine if older and younger patients experienced different components of depression at different rates. An independent samples *t* test revealed that younger patients reported being bothered more frequently by 1 item, "Feeling bad about yourself/feeling like a failure" ($t = 2.53$, $P = .012$) when compared to older adults. This was the only significant difference found between older and younger adults when each PHQ-9 item was analyzed as a continuous variable. However, because of range and variability considerations, each item was also dichotomized into zero or nonzero values and chi-square associations between each of the dichotomized outcomes to cohort were assessed. This investigation showed that older adults were more likely to report no impairment in feeling down (79% vs 72%; $P = .012$), sleep troubles (63% vs 55%; $P = .014$), feeling tired (55% vs 47%; $P = .014$), poor appetite (82% vs 76%; $P = .038$), feeling bad about themselves (90% vs 82%; $P < .001$), and trouble with concentration (87% vs 81%; $P = .005$) than their younger survivor counterparts. Mean PHQ-9 Total and item scores are reported by age group in Table S1.

TABLE 1 Demographics

Demographics	Younger Adults (N = 504)	Older Adults (N = 508)	All (N = 1012)	Chi-Square (df)	*P* value
Age (M, SD)	49.26 (5.0)	76.56 (5.0)	62.96 (14.5)	N/A	N/A
Female (N, %)	400 (79%)	379 (75%)	779 (77%)	3.23 (1)	0.07
Race					
White	332 (66%)	406 (80%)	738 (73%)	28.07 (3)	<0.001
Black	92 (18%)	58 (11%)	150 (15%)		
Asian	62 (12%)	28 (6%)	90 (9%)		
Other/unknown	18 (4%)	16 (3%)	34 (3%)		
Ethnicity					
Non-Hispanic/Latino	384 (76%)	283 (56%)	667 (66%)	43.56 (2)	<0.001
Hispanic/Latino	54 (11%)	44 (9%)	98 (10%)		
Unknown	66 (13%)	181 (36%)	247 (24%)		
Cancer type					
Breast	351 (70%)	244 (48%)	595 (59%)	95.28 (3)	<0.001
Colorectal	28 (6%)	99 (19%)	127 (13%)		
Thoracic	13 (3%)	66 (13%)	79 (8%)		
Urologic	112 (22%)	99 (19%)	211 (21%)		
Marital/living status					
Married or living with partner	352 (70%)	252 (50%)	604 (60%)	43.18 (2)	<0.001
Not married and living alone	151 (30%)	255 (50%)	406 (40%)		
Missing	1 (<1%)	1 (<1%)	2 (<1%)		

3.2.2 | Pain and fatigue

Pain and fatigue scores both ranged from 0 to 10; mean pain for the sample was 1.71 (SD = 2.63), and mean fatigue was 2.41 (SD = 2.65). Two hundred forty-five survivors (24%) were missing pain scores, and 246 (24%) were missing fatigue scores. There was no significant difference in self-reported levels of pain between younger and older adults. Among the sample as a whole, people who were depressed reported significantly higher levels of both pain (4.03 vs 1.48; $t = -7.57$, $P < .001$) and fatigue (5.74 vs 2.09; $F = -10.81$, $P < .001$). Survivors in the younger cohort reported significantly more fatigue than older survivors (2.66 vs 2.17; $P = .011$); however, this association was not sustained after adjustment for confounders.

3.3 | Gender differences

Women survivors had double the rate of clinically significant depression than men (10.5% vs 5.2%; $\chi^2(1) = 6.152$, $P = .013$). As depicted in Figure 1, mean PHQ-9 scores were significantly higher for women (M = 3.53, SD = 4.83) compared to men (M = 2.03, SD = 3.36; $t = -4.43$, $P < .001$). For individual PHQ item scores, women showed significantly higher scores (all $P < .05$) for little interest or pleasure, feeling down, sleep problems, feeling tired, poor appetite, and trouble concentrating. Women also reported significantly higher levels of pain ($t = 3.99$, $P < .001$) and fatigue ($t = 4.01$, $P < .001$) compared to male survivors.

3.4 | Race and ethnic differences

There were no differences by race in mean PHQ-9 scores or rates of clinically significant depression in this sample. While there were no differences in fatigue scores across race, there were significant differences in mean pain scores ($F(3,766) = 7.44$, $P < .001$) (Figure 1). Pairwise tests indicated that mean self-reported pain scores for Black patients (M = 2.47, SD = 3.15) and other/unknown patients (M = 3.15, SD = 3.34) were significantly different from those of White (M = 1.54, SD = 2.49) and Asian (M = 1.23, SD = 2.06) patients.

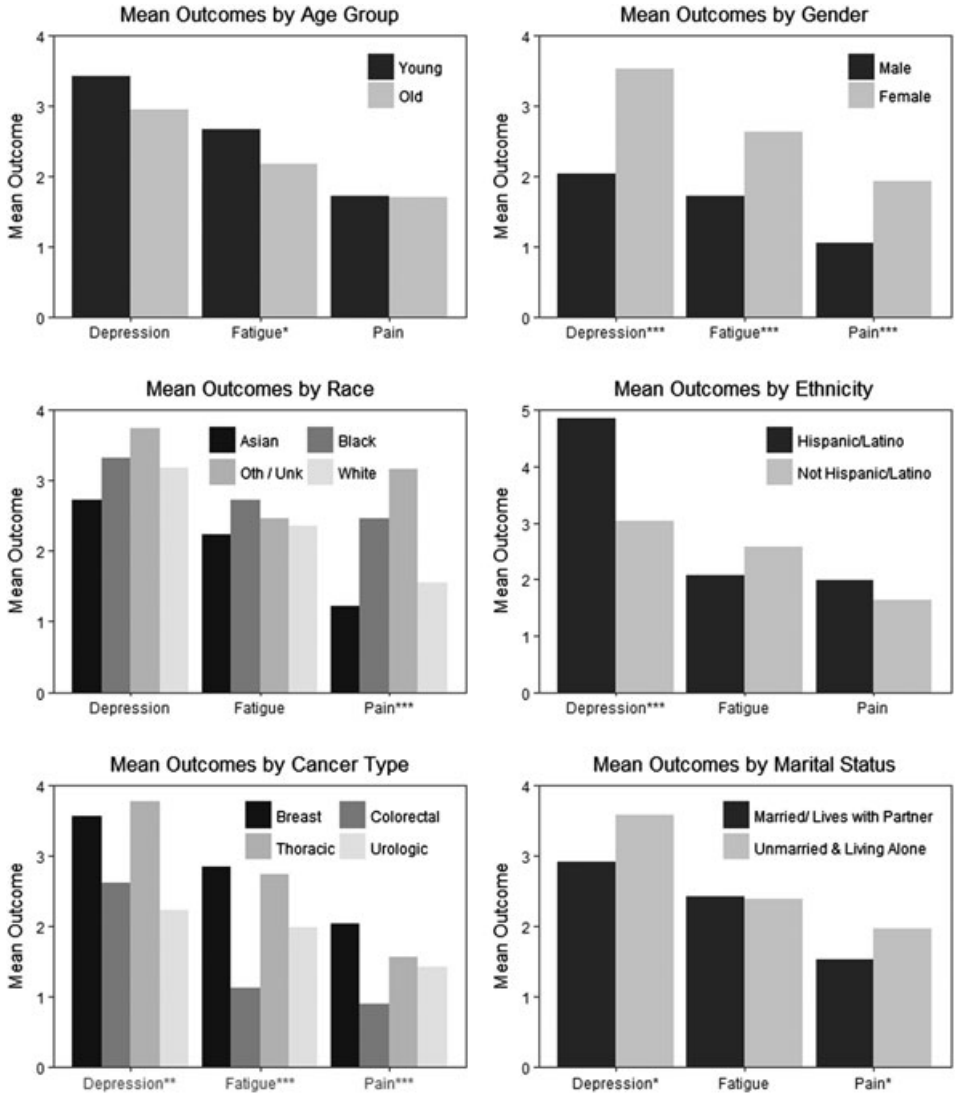

FIGURE 1 Mean depression, fatigue, and pain scores. Note that significant group differences (ie, ANOVA or *t* test) on outcomes are indicated by asterisks (*). * indicates $P < .05$; ** indicates $P < .01$; *** indicates $P < .001$

Patients who identified as ethnically Hispanic/Latino reported significantly higher rates of depression than non-Hispanic/Latino patients (16.3% vs 8.4%; $\chi^2(1, N = 765) = 6.303$, $P = .012$), although ethnicity information was missing or refused for 24% of the study sample. Mean PHQ-9 scores were also significantly greater for Hispanic/Latino (M = 4.84, SD = 6.15) compared to non-Hispanic/Latino patients (M = 3.03, SD = 4.24; $t = -3.69$, $P < .001$). There were no differences in pain or fatigue scores by ethnicity.

3.5 | Other correlates of depression, pain, and fatigue

Cancer type was significantly associated with PHQ-9 score ($F(3,1005) = 5.63$, $P < .01$). Mean PHQ-9 scores for the breast cancer survivors (M = 3.57, SD = 4.90) and thoracic cancer survivors (M = 3.77, SD = 5.70) were significantly different from the urologic cancer survivors (M = 2.22, SD = 3.32). There were also significant differences in pain scores ($F(3,763) = 6.56$, $P < .001$) and fatigue scores ($F(3,762) = 14.83$, $P < .001$), with survivors from the Breast clinic reporting the highest scores for pain and fatigue.

Being currently married and/or living with a partner/spouse was associated with lower rates of depression (7.1% vs 12.6%, $\chi^2(1) = 8.52$, $P = .004$). Mean PHQ-9 scores were also lower for those who were married/living with a partner (M = 2.92, SD = 4.12) compared to those who were not (M = 3.58, SD = 5.19); $t = 2.25$, $P = .03$. Mean pain scores were higher for patients who were unmarried and/or living alone (M = 1.96, SD = 2.78) compared to those who were married/living with a partner (M = 1.53, SD = 2.50; $t = 2.22$, $P = .03$). There were no differences in fatigue scores. Tables with these data on the additional correlates of depression, pain, and fatigue are available on request.

3.6 | Multivariable regression

Given significant associations with one or more outcomes, we adjusted for the aforementioned potential covariates (age, gender, race/ethnicity, cancer type, and marital status) on our main outcome variables of depression, pain, and fatigue (Table 2). This resulted in a reduced effective sample size because of missingness in the ethnicity variable. However, an assessment of bivariate association of all predictors to each of the 3 outcomes showed no differential effects among this subset compared to the larger study sample.

3.6.1 | Depression

In fully adjusted models, a significant association was found between depression and age cohort; younger adults had a PHQ Total average of 0.76 points higher than older adults ($P = .04$) after controlling for confounders. Gender did not remain a significant predictor of mean PHQ-9 Total score, with the average score for women 0.69 points higher than men ($P = .23$). Regarding cancer type, only the thoracic cancer remained a significant predictor of depression, with a mean increase of 1.81 ($P = .02$) compared to urologic. Breast cancer was no longer a significant predictor of depression once predictor variables were included. After adjustment, Hispanic/Latino patients had mean PHQ score 1.70 points higher than non-Hispanic/Latino patients ($P < .001$). Finally, being unmarried and/or living alone also remained a significant predictor, with a score 0.88 points higher than those who were married and/or living with a partner ($P = .02$). Although the model was statistically significant, the *r*-square was only 0.05.

3.6.2 | Pain

After adjustment, only race remained a significant predictor of pain scores, with Black patients having an adjusted mean of 0.81 points

TABLE 2 Unadjusted and adjusted models of depression, pain, and fatigue

		Depression		Pain		Fatigue	
Covariate	**Group**	**Unadjusted Beta**	**Adjusted Beta**	**Unadjustedbeta**	**Adjusted Beta**	**Unadjustedbeta**	**Adjusted Beta**
Age[a]	Older	−0.47	−0.76*	−0.01 (0.97)	0.03	−0.49**	−0.14
Gender	Female	1.50***	0.69	0.87 ***	0.44	0.90***	0.50
Race[b]	Black	0.14	0.02	0.92***	0.81**	0.35	0.26
	Asian	−0.47	−0.11	−0.32	−0.18	−0.13	0.03
	Unk/Oth	0.55	0.41	1.61**	1.65	0.10	0.56
Ethnicity	Hispanic	1.81***	1.70***	0.34	0.13	−0.49	−0.52
Cancer Type[c]	Breast	1.34***	0.48	0.61**	0.23	0.85***	0.56
	Colorectal	0.39	−0.18	−0.54	−0.64	−0.86**	−0.85*
	Thoracic	1.55**	1.81*	0.13	−0.10	0.75*	0.70
Marital/living status	Married/with partner	−0.66*	−0.88*	−0.43*	−0.42	0.05	−0.08
N[d]		763-1009	761	585-767	583	577-766	575
R^2		…	0.04	…	0.45	…	0.46

[a]Younger cohort (ages 30-55) used as reference group.

[b]White racial category used as reference group.

[c]Urologic clinic used as reference group.

[d]Sample size (N) ranges for unadjusted models indicate the minimum and maximum of the 6 models (eg, age or gender) for the given outcome.

*$P < .05$.

**$P < .01$.

***$P < .001$.

higher than Whites (P = .01). Gender, being a breast cancer survivor, and marital/living status were not significant predictors of pain after adjustment for race (Table 2).

3.6.3 | Fatigue

In the adjusted model, age, gender, and being a breast cancer survivor all became nonsignificant predictors of fatigue (Table 2). Being a colorectal cancer survivor remained the only significant predictor of fatigue.

4 | CONCLUSIONS

4.1 | Clinical implications

Our study revealed 3 important findings with significant clinical implications. First, we found no differences in either the prevalence or the severity of depression between younger and older adult cancer survivors; although a moderately statistically significant association emerged for depression after adjustment, the average effect was less than a 1 point difference between the groups. There are a few possible explanations for this finding. First, it may be possible that the PHQ-9 is an inadequate measure of depression among older adults, although previous studies on the sensitivity of brief self-report measures of depression in the elderly have been mixed.[7,35] In addition, it is possible that our location in New York City, a busy urban setting, may preclude some of the social isolation seen in older adults who may live in less dense areas with fewer social services available. Finally, it is possible that because our sample was recruited from Survivorship Clinics, we investigated depression among a higher-functioning, more socially connected group of individuals who are still interested in attending clinic.

Interestingly, the overall rate of depression of 9.3% in this sample of cancer survivors was relatively similar to a sample of adults age 20 and older in New York City, which found a prevalence of major depression of 8% using the CIDI measure.[36] It was also consistent with previous meta-analyses that found an overall prevalence of depression of 11.6% among over 50 000 pooled cancer survivors, and which also found no difference in depression rates among these cancer survivors and healthy controls.[19]

Secondly, we identified significant gender differences in both rates and levels of depression among cancer survivors; however, this effect disappeared after adjustment for confounders. A review article on depression in cancer survivors by Massie[31] found that the literature on gender differences in depression in cancer survivors is inconsistent, with some studies reporting no differences while others found higher rates in both men and women.

Finally, our third important finding was the identification of higher rates of depression among Hispanic/Latino patients compared to non-Hispanic/Latino patients. Of note, we did not have data on primary language spoken or socioeconomic status, so we are unable to determine if this observed difference is explained by other important demographic factors. Some prior literature has found rates of depression in Latina breast cancer survivors over 3 times that of the general population.[37] However, this remains an understudied topic, especially when considering that the US Hispanic population above age 65 is expected to increase over sixfold by 2050, compared to twofold for the non-Hispanic population.[38] Further investigation into the correlates of depression in this population with potential interventions designed specifically for Hispanic/Latino cancer survivors is warranted.

Collectively, these findings have important clinical implications for survivorship clinics. They suggest that routine depression screening is necessary in these clinics, and that age- and culture-appropriate (ie, multiple languages, assessment of social isolation) screening tools are needed to pick up on depression in this population. Given the results indicating higher rates of depression in Hispanic/Latino patients, survivorship clinics should pay specific attention to this population both in screening and in the clinical encounter.

4.2 | Study limitations

The findings of this study should be considered in light of some limitations. First, the use of archival survey data from the EMR means that self-assessment forms were not completed in a controlled research environment by trained research staff and were not always fully complete, leading to missing data. It is possible that survey responders and nonresponders may differ on relevant measurements. While using existing data can be beneficial because it imposes no additional patient burden, it also means that many important correlate variables and/or predictors (eg, social isolation, functional ability, medical comorbidities) may not be included in the dataset, limiting our ability to tease out some of the observed differences. To this end, although the adjusted models for pain and fatigue had r^2 values within a normal range of other psychosocial research, the model for depression showed excessive variation, potentially indicating that another important predictor may have been omitted. Finally, our measures of pain and fatigue were only single-item measures, unlike our measure of depression.

In addition, this study relied on data gathered from patients exclusively in an urban setting who received treatment at a single institution and who were actively involved in a survivorship clinic. It is necessary to replicate these findings in additional settings and include patients who are not followed in a survivorship clinic, as they may be more likely to experience social isolation. Furthermore, it is possible that the PHQ-9 was unable to pick up on the actual burden of depression experienced by the older adults, or the survivor population as a whole, where somatic complaints may be more prevalent than the affective symptoms of depression.[39]

This study also had some notable strengths. We had a large sample that included both older and younger cancer survivors. In addition, we conducted multivariable analyses in addition to bivariate to tease out the complex relationships between predictor variables and our 3 outcomes of interest. Finally, our use of a validated, multi-item measure of depression strengthens our findings and allows us to compare our results to other literature using this measure.

4.3 | Future directions

Overall, this study found relatively low rates of depression in cancer survivors, with no difference observed between younger and older adults. In addition, the findings of gender, racial, and ethnic differences

in depression, pain, and fatigue levels among cancer survivors show possible opportunities for interventions to improve care for the survivorship population. Future work should focus on examining the burden of medical comorbidities experienced by the cancer survivor population and their relationship to depression, pain, and fatigue, which may provide useful information on the correlates of depression in this population.

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CONFLICTS OF INTEREST

The authors report no conflicts of interest.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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