Contents lists available at ScienceDirect

**Gynecologic Oncology** 

# **FI SEVIER**



journal homepage: www.elsevier.com/locate/ygyno

# Rural-urban disparities in psychosocial functioning in epithelial ovarian cancer patients



Rachel Telles <sup>a</sup>, M. Bridget Zimmerman <sup>b</sup>, Premal H. Thaker <sup>c</sup>, George M. Slavich <sup>d</sup>, Edgardo S. Ramirez <sup>e</sup>, Sharaf Zia <sup>f</sup>, Michael J. Goodheart <sup>g,h</sup>, Steven W. Cole <sup>i</sup>, Anil K. Sood <sup>j</sup>, Susan K. Lutgendorf <sup>a,g,h,\*</sup>

<sup>a</sup> Department of Psychological and Brain Sciences, University of Iowa, Iowa City, IA, USA

<sup>b</sup> Department of Preventive Medicine and Biostatistics, University of Iowa, Iowa City, IA, USA

<sup>c</sup> Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Washington University School of Medicine, Saint Louis, MO, USA

<sup>d</sup> Department of Psychiatry and Biobehavioral Sciences, University of California, Los Angeles, CA, USA

<sup>e</sup> Department of Psychology, University of California, Los Angeles, CA, USA

<sup>f</sup> Institute of Clinical and Translational Sciences, University of Iowa Hospital & Clinics, Iowa City, IA, USA

g Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of Iowa, Iowa City, IA, USA

<sup>h</sup> Holden Comprehensive Cancer Center, University of Iowa, Iowa City, IA, USA

<sup>1</sup> Division of Hematology–Oncology, University of California, Los Angeles School of Medicine, Los Angeles, CA, USA

<sup>j</sup> Departments of Gynecologic Oncology, Cancer Biology and Center for RNA Interference and Noncoding RNA, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

# HIGHLIGHTS

• Rural residence is a known risk factor for health disparities in cancer patients.

• Rural ovarian cancer patients show worse recovery in quality of life and distress levels in the year following diagnosis.

· Education levels do not explain differences in trajectories between rural and urban patients.

# ARTICLE INFO

Article history: Received 17 October 2023 Received in revised form 10 January 2024 Accepted 14 January 2024 Available online xxxx

Keywords: Rural urban health disparities Ovarian cancer distress Quality of life Depression Social support

# ABSTRACT

*Objective.* Although rural residence has been related to health disparities in cancer patients, little is known about how rural residence impacts mental health and quality of life (QOL) in ovarian cancer patients over time. This prospective longitudinal study investigated mental health and QOL of ovarian cancer patients in the first-year post-diagnosis.

*Method.* Women with suspected ovarian cancer completed psychosocial surveys pre-surgery, at 6 months and one-year; clinical data were obtained from medical records. Histologically confirmed high grade epithelial ovarian cancer patients were eligible. Rural/urban residence was categorized from patient counties using the USDA Rural-Urban Continuum Codes. Linear mixed effects models examined differences in psychosocial measures over time, adjusting for covariates.

*Results.* Although disparities were not observed at study entry for any psychosocial variable (all *p*-values >0.22), urban patients showed greater improvement in total distress over the year following diagnosis than rural patients (p = 0.025) and were significantly less distressed at one year (p = 0.03). Urban patients had a more consistent QOL improvement than their rural counterparts (p = 0.006). There were no differences in the course of depressive symptoms over the year (p = 0.17). Social support of urban patients at 12 months was significantly higher than that of rural patients (p = 0.04).

*Conclusion.* Rural patients reported less improvement in psychological functioning in the year following diagnosis than their urban counterparts. Clinicians should be aware of rurality as a potential risk factor for ongoing distress. Future studies should examine causes of these health disparities and potential long-term inequities and develop interventions to address these issues.

© 2024 Elsevier Inc. All rights reserved.

\* Corresponding author at: Department of Psychological and Brain Sciences, University of Iowa, G60 Psychological and Brain Sciences Building, Iowa City, IA 52242, USA. *E-mail address:* susan-lutgendorf@uiowa.edu (S.K. Lutgendorf).

#### 1. Introduction

Rural residence has been associated with various health disparities, including increased risk of all-cause mortality [29] and poorer access to healthcare [18]. As many as 61 million (19%) people in the United States live in rural areas as of 2016 [36]. Cancer patients are known to experience significant disparities in diagnosis and treatment depending on their rurality [21]. Despite lower incidence rates, rural populations show higher mortality rates than urban patients across all cancers [43]. Access to treatment is also more limited, with significant travel burden for rural patients to access specialized cancer care [13]. There are also rural-urban disparities in availability of oncology specialties. For example, despite one in five ovarian cancer patients living in rural counties, >99% of gynecologic oncologists in the United States work in metropolitan counties [33], leading to rural health disparities in access [31,42]. Rural gynecologic oncology patients who receive surgery at local hospitals by non-specialists are less likely to receive guidelineadherent care [24]. We have recently reported a survival disparity in rural ovarian cancer patients even when they have received their primary treatment from a gynecologic oncologist in a tertiary-care hospital [27].

To better understand potential contributors to such a survival disparity, we examined contextual factors such as mental health and quality of life (QOL) in our ovarian cancer patients. Mental health concerns are known to contribute to poorer QOL and physical health outcomes for cancer patients [1,11] and may thus contribute to cancer progression, morbidity, and mortality. Prior research on mental health disparities in rural and urban cancer populations has shown mixed results; two large systematic reviews have shown conflicting outcomes, with an older review reporting poorer mental health and QOL for rural cancer patients in most domains [9] and a newer review indicating unmet needs in rural patients but no worse outcomes [38].

Women with ovarian cancer are at high risk for distress and poor mental health [40]. Diagnosis is often delayed due to lack of clear symptoms in early stage disease, and prognosis for advanced disease is generally poor, with a high risk of recurrence and burden of multiple lines of treatment [35]. Previous work from our lab and others has shown that mental health and social support may impact biological and QOL outcomes for these women [3,14,26]. Social support has been shown to be associated with better psychosocial functioning and less overall distress [22]. However, little is known about potential disparities in these domains between rural and urban ovarian cancer patients. Furthermore, few studies have examined trajectories of mental health and QOL over time in rural vs. urban ovarian cancer patients.

To address this knowledge gap, we conducted a prospective longitudinal study, examining differences in psychosocial characteristics prior to initial treatment and over the first-year post-diagnosis in rural vs. urban ovarian cancer patients receiving their primary care in two large midwestern tertiary cancer centers. Additionally, because our prior survival analysis indicated a potential influence of education on the effects of rurality [27], we also performed exploratory analyses adjusting for level of education. Based on our prior results, we hypothesized that rural patients would fair worse than urban patients across the three examined psychosocial characteristics, and that education would explain a significant amount of these differences.

# 2. Method

#### 2.1. Participants

Participants were diagnosed with histologically confirmed high grade primary epithelial ovarian, peritoneal or fallopian tube carcinoma. They were excluded for history of previous cancer, comorbid condition with known immune system effects or systemic steroid use, current pregnancy and inability to accurately answer questions (dementia). All procedures were approved by Institutional Review Boards of participating institutions.

#### 2.2. Procedure

Women were recruited from two large midwestern university hospitals during an initial pre-surgical/neoadjuvant chemotherapy (NAC) clinic visit for pelvic masses suspected for ovarian cancer as part of a larger IRB-approved study on biobehavioral factors and tumor progression. Informed consent was obtained during the clinic visit. Inclusion in the study was confirmed following histological diagnosis of ovarian cancer. Psychosocial surveys were completed between the clinic visit and surgery or initiation of neoadjuvant chemotherapy, at 6 months, and at the one-year follow-up visit. Patients were included if they had data at 2 of the 3 timepoints. The final sample included 261 patients with epithelial ovarian cancer.

#### 2.3. Psychosocial measures

# 2.3.1. Depressive mood

The Center For Epidemiologic Studies Depression Scale (CESD) is a 20 item self-report scale assessing frequency of depressive symptoms over the past seven days [30].

#### 2.3.2. Quality of life

The Functional Assessment of Cancer Therapies (FACT) [10] is a 38 item self-report measure assessing QOL in cancer patients. The FACT-G contains subscales assessing physical (PWB), social/family (SWB), emotional (EWB), and functional (FWB) well-being. The FACT ovarian cancer specific (OCS) scale is a 12-item subscale assessing concerns specific to women with ovarian cancer such as nausea, bloating, sexuality, etc. Participants indicate their functioning over the last 7 days on a 5-point scale, ranging from 0 (*not at all*) to 4 (*very much*). The scale has good reliability and validity [10]. Higher FACT scores indicate better QOL; FACT-G means of the general US adult female population are approximately 80 (SD = 18.6). Five-point score changes in the total scale are considered clinically significant [7].

#### 2.3.3. Distress

The Profile of Mood States short form (POMS-SF) is a well-validated self-report scale consisting of 37 mood adjectives such as "friendly," "tense," and "angry." These are rated on a scale ranging from 0 (*not at all*) to 5 (*extremely*) relating to mood experienced over the last week [16]. A total mood disturbance score (TMD) is obtained by summing all scores of five subscales (anxiety, depression, anger, fatigue, and confusion) and subtracting the final subscale score (vigor) and is considered to be a measure of total distress. General mood disturbance may provide a more holistic measure of emotional distress that is not adequately assessed by depression measures alone, and has been used extensively in studies with cancer patients [23,25].

#### 2.3.4. Social support

The Social Provisions Scale is a 24-item self-report scale measuring the extent to which social relationships are perceived as supportive. The scale has shown acceptable reliability and validity in a variety of populations [17,32].

# 2.4. Clinical and demographic information

Clinical information derived from medical records included age, stage, grade, body mass index (BMI), extent of cytoreduction, histology, neoadjuvant treatment. Demographic information was provided by self-report and included education, income, and relationship status.

Rural/urban residence was categorized from county of residence using the USDA Rural-Urban Continuum Codes (RUCC). This system codes metro counties by area population and non-metro counties by the degree of urbanization and adjacency to non-metro areas. Codes 4–9 are considered non-metro counties [37]. County level classification is as follows: metro counties (1 = 1 million or more; 2 = 250,000 to 1 million; 3 = <250,000) and non-metro counties (4 = 20,000 or more adjacent; 5 = 20,000 or more non-adjacent; 6 = 2500 to 19,999 adjacent; 7 = 2500 to 19,999 nonadjacent; 8  $\leq$  2500 adjacent; 9  $\leq$  2500 nonadjacent).

The Charlson comorbidities index [12] was used to determine extent of comorbidities (non-cancer) and coded as 0, 1, and 2 or more (2+). The index creates a sum score for each individual encompassing all pre-existing medical conditions (e.g., diabetes, heart disease). Comorbidity status was covaried in all analyses.

# 2.5. Statistical analyses

Version 29 of SPSS (IBM Armonk, NY) and version 9.4 of SAS (SAS/ STAT 14.3) (SAS, Cary, NC) were used for data analysis. All distributions were examined for outliers and assumptions of non-normality. Descriptive statistics were used to examine dependent variables, rurality and covariates. Linear mixed model for repeated measures was used in the analysis of the longitudinal data to examine a) mean levels of psychosocial measures at baseline, 6 months, and 12 months, and b) the trajectory of change over time between baseline, 6 months, and 12 months for psychosocial variables according to rural/urban residence. Fixed effects in the model included group, time, and the group X time interaction. In addition, the model adjusted for clinical site, comorbidities, cancer stage (FIGO stage I and II vs. III and IV), age. These models allowed estimation of the relationship of rurality with each psychosocial variable at baseline and at one year, as well as comparison of the trajectories by testing the rurality  $\times$  time interaction effect. Exploratory analyses were conducted adjusting for level of education along with the other covariates to determine whether there was an effect of rurality over and above the effects of education.

# 3. Results

The mean age of participants was 59.9 (range: 27 to 88) years. Respondents were predominantly white, non-Hispanic, and well-educated; more than half (55.1%, N = 140) had completed some college and/or graduate/professional school. About 80.9% (N = 212) were married or living with a partner (See Table 1).

43.7% of Iowa and 30.6% of Washington University patients were rural. There were no significant rural-urban differences in age, disease stage, smoking history, relationship status, or body mass index (BMI: 38% in each residence category were obese or morbidly obese; 30% were overweight), (all *p* values >0.14). Approximately 90% of rural patients made \$80,000 or less; whereas, among urban patients, about 75% were in this category. There was a significant difference in education between rural and urban patients with college graduates or postcollege education accounting for 41% of urban and 19% of rural patients (*p* = 0.0003).

#### 3.1. Psychosocial variables over time in urban vs. rural patients

#### 3.1.1. Distress

At study-entry (pre-diagnosis), rural and urban patients did not differ significantly in levels of distress (p = 0.91), with levels of distress in a moderately elevated range [4]. Linear mixed model analyses adjusting for covariates (site, age, stage, comorbidities) showed significant rural/urban differences in the trajectory of distress between study-entry and 12 months (p = 0.027). As seen in Table 2, whereas both groups of patients showed significant drops in distress between study entry and 6 months (p-values for change over time < 0.0001), by 12 months the distress of urban patients had continued to decrease to approximately one third of the original level (BL: 25.0 to 12 mo: 8.4;

Table 1

Demographic characteristics of the sample.

	Total	Rural	Urban	
Variable	(n = 261)	( <i>n</i> = 101)	(n = 160)	p-value
Study Site, count (%)				
Univ. of Iowa	167 (64.0)	72 (71.3)	95 (59.4)	
Wash. University	94 (36.0)	29 (28.7)	65 (40.6)	0.051
Age, mean [SD]	59.9 [10.6]	59.2 [10.5]	60.4 [10.7]	0.36
Race		. ,		0.71
White	254 (97.3)	99 (98.0)	155 (96.9)	
Black	5 (1.9)	1(1)	4 (2.5)	
Other race	2 (0.8)	1(1)	1 (0.6)	
	. ,	(n = 100)	(n = 159)	
Ethnicity, Non-Hispanic	261 (100)	100 (100)	159 (100)	-
Marital Status	(n = 255)	(n = 99)	(n = 156)	
Married/with partner	206 (80.8)	82 (82.8)	124 (79.5)	0.51
Education	(n = 254)	(n = 100)	(n = 154)	< 0.001
High school or less	94 (37.0)	50 (50.0)	44 (28.6)	
Trade school/some college	78 (30.7)	31 (31.0)	47 (30.5)	
College grad/Postgraduate	82 (32.3)	19 (19.0)	63 (40.9)	
Income	(n = 216)	(n = 85)	(n = 131)	0.015
< \$20,000	33 (15.3)	19 (22.4)	14 (10.7)	
\$20,001-\$50,000	85 (39.4)	32 (37.6)	53 (40.5)	
\$50,001-80,000	59 (27.3)	26 (30.6)	33 (25.2)	
>\$80,000	39 (18.1)	8 (9.4)	31 (23.7)	
Stage	(n = 260)	(n = 100)	(n = 160)	0.50
I	43 (16.5)	18 (18)	25 (15.6)	
II	17 (6.5)	8 (8)	9 (5.6)	
III	171 (65.7)	63 (63)	108 (67.5)	
IV	29 (11.2)	11 (11)	18 (11.3)	
Cytoreduction, Suboptimal	63 (24.1)	27 (26.7)	36 (22.5)	0.44
Serous	200 (76.6)	81 (80.2)	119 (74.4)	0.28
Neoadjuvant therapy	13 (5.0)	6 (5.9)	7 (4.4)	0.57
	(n = 252)	(n = 97)	(n = 155)	
Chemotherapy at 1 year	43 (17.1)	17 (17.5)	26 (16.8)	0.88
	(n = 259)	(n = 101)	(n = 158)	
Body Mass index	28.7 [6.9]	28.7 [6.6]	28.7 [7.2]	0.98
Smoking Status	(n = 257)	(n = 101)	(n = 156)	
Ever smoked	76 (29.6)	35 (34.6)	41 (26.3)	0.15
Comorbidities, non-cancer				0.47
0	195 (74.7)	78 (77.2)	117 (73.1)	
1	55 (21.1)	19 (18.8)	36 (22.5)	
2+	11 (4.2)	4 (4.0)	7 (4.4)	

N of cells are 261 total, 101 rural, 160 urban unless stated otherwise.

University of Iowa patients are 43.1% rural; Washington University patients are 30.9% rural.

All patients included in the study had to have been alive at one year.

p < 0.0001). In contrast, even though rural patients had a significant decrease in distress by 12 months, their level of distress was still elevated (BL: 24.7 to 12 mo: 15.2; p = 0.0003), resulting in a significantly higher overall level of distress in rural patients at 12 months (p = 0.030) (See Table 2 and Fig. 1).

## 3.1.2. Depressive symptoms

At study entry, mean depressive symptoms of the rural patients were consistent with moderate clinical depression (16.57  $\pm$  1.00); whereas, mean depression scores of the urban group were just under the CES-D cutoff of 16 for moderate clinical depression (15.5  $\pm$  0.79). However, these means were not statistically different for urban vs. rural participants (p = 0.35). Using this clinical cutoff, almost 50% of both groups (46% [N = 71] of urban patients and 49% [N = 48] of rural patients) were classified as experiencing moderate clinical depression at study entry, but there was no rural/urban difference in mean depression levels or percentages of depressed patients at that time (*p*-values >0.50). By one year, about one third (29% (N = 25) of rural patients and 24% (N = 27) of urban patients) still met the cut-off for clinical depression. As seen in Table 2, depressive mood of women in both rural and urban patients decreased in a similar pattern over time (p = 0.15) and by 12 months levels of depressive mood of both groups was within the mild range and did not significantly differ (urban 9.3  $\pm$  0.76; rural 11.2  $\pm$  0.96).

#### Table 2

Mean values and mean changes for psychosocial variables by group and time.

	Rural Urban			Difference in Mean Change: Rural-Urban			
	Mean	Mean Change	Mean	Mean Change	Adjusted for Covariates <sup>a</sup>	Adjusted for Covariates <sup>a</sup> and Education	
	(SEM)	(95% CI)	(SEM)	(95% CI)	Difference (95% CI) p-value	Difference (95% CI) p-value	
Distress							
BL	24.7 (2.6)	-	25.0 (2.0)	-			
6 mo	13.1 (2.2)	-11.6 (-16.6, -6.6)**	11.7 (1.8)	-13.3 (-17.2, -9.4)**	1.4 (-5.0, 7.7) 0.67	1.1 (-5.1, 7.3,) 0.72	
12 mo	15.2^ (2.5)	-9.5 (-14.6,-4.4)**	8.4 (1.9)	-16.5 (-20.5,-12.6)**	7.2 (0.7, 13.6,) 0.030	6.8 (0.4, 13.2) 0.038	
				Rurality*Time:	F(2,233) = 3.66, p = 0.027	F(2,229) = 3.34, p = 0.037	
QOL (FACT)							
BL	73.3 (1.6)	_	74.7 (1.3)	_			
6 mo	82.1 (1.4)	8.8 (5.6, 12.0)**	79.7 (1.1)	5.1 (2.5, 7.6)**	3.7 (-0.4, 7.8) 0.079	3.8 (-0.3, 8.0) 0.079	
12 mo	81.3 (1.4)	8.0 (5.0, 11.0)**	84.4 (1.1)	9.7 (7.3, 12.1)**	-1.7 (-5.5, 2.2) 0.40	-1.6(-5.5, 2.2) 0.40	
	· · ·		~ /	Rurality*Time:	F(2,229) = 5.40, p = 0.005	F(2,224) = 5.50, p = 0.005	
FACT-OCS							
BL	32.3 (0.7)	_	32.7 (0.5)	_			
6 mo	33.4 (0.8)	1.1(-0.5, 2.7)	34.7 (0.6)	2.0 (0.7, 3.2)*	-0.9 (-2.9, 1.2) 0.40	-0.8(-2.9, 1.2) 0.43	
12 mo	37.2 (0.5)	4.9 (3.6, 6.3)**	38.4 (0.4)	5.7 (4.7, 6.8)**	-0.8 (-2.5, 0.9) 0.36	-0.7 (-2.4, 1.1) 0.45	
				Rurality*Time:	F(2,420) = 0.53, p = 0.59	F(2,414) = 0.41, p = 0.66	
Social Provisions Scale							
BL	84.9 (0.9)	_	86.3 (0.7)	_			
6 mo	84.9 (0.9)	0.0 (-1.6, 1.7)	84.3 (0.7)	$-2.0(-3.3, -0.6)^*$	2.0 (-0.1, 4.1) 0.064	2.2 (0.0, 4.3) 0.046	
12 mo	82.5^ (0.9)	$-2.4(-3.9, -0.8)^*$	85.1 (0.7)	-1.2(-2.4, 0.1)	-1.2(-3.2, 0.8) 0.24	-1.3(-3.3, 0.7) 0.20	
	· · ·		~ /	Rurality*Time:	F(2,418) = 4.05, p = 0.018	F(2,409) = 4.73, p = 0.009	
Depression							
BL	16.6 (1.0)	_	15.5 (0.8)	_			
6 mo	10.7 (0.9)	-5.9 (-7.7, -3.9)**	10.9 (0.7)	$-4.6(-6.1, -3.1)^{**}$	-1.3 (-3.7, 1.2) 0.30	-1.2 (-3.7, 1.2 0.31	
12 mo	11.2 (1.0)	$-5.4(-7.4, -3.4)^{**}$	9.3 (0.8)	$-6.2(-7.8, -4.6)^{**}$	0.8 (-1.7, 3.3) 0.54	1.0 (-1.5, 3.5) 0.44	
			. ,	Rurality*Time:	F(2,237) = 1.94, p = 0.15	F(2,230) = 2.16, p = 0.12	

significant change from baseline  $p^* < 0.01$ ;  $p^* < 0.0001$ .

^significantly different from urban, adjusted for covariates, p < 0.05.

BL = Baseline.

<sup>a</sup> covariates = site, age, stage, comorbidities.

# 3.1.3. Quality of life

At study entry, total FACT scores of both rural and urban patients were in a moderately impaired range and did not significantly differ (p = 0.38). There were significant differences in the pattern of change of QOL over the course of the 12-month period between rural and urban patients (p = 0.005). As seen in Table 2 this interaction was due to a significant increase in QOL in rural patients from study entry (BL:  $73.30 \pm 1.63$ ) to 6 months ( $82.09 \pm 1.37$ ) with no further increase by 12 months (81.30  $\pm$  1.40). In contrast, the urban group showed a consistent increase in QOL from study entry (BL: 74.57  $\pm$  1.28) to 6 months (79.74  $\pm$  1.09) and again to 12 months (84.34  $\pm$  1.10). Despite differences in trajectories, both groups showed mean increases in QOL by one year that were both statistically and clinically significant. Although urban patients had slightly higher QOL scores at 12 months, the difference in mean scores at 12 months between the two groups was not statistically significant (p = 0.12) and was likely not clinically meaningful [7]. FACT-OCS scores improved in both rural and urban patients between baseline and 12-months and changes did not differ between these groups, either at baseline or over time (see Table 2).

# 3.1.4. Social support

Social support did not significantly differ for rural vs. urban patients at study entry (p = 0.18). Linear mixed model analyses adjusting for covariates showed significant differences in the trajectory of social support over the course of the 12-month period (p = 0.018). Levels of social support remained fairly constant across the study in both groups, with slight, but non-significant drops in social support over time. Social support of urban patients at 12 months ( $85.13 \pm 0.72$ ) was significantly higher than that of rural patients at 12 months ( $82.55 \pm 0.90$ , p = 0.04), although the difference in scores was relatively small (See Table 2).

#### 3.1.5. Education and treatment status

Exploratory analyses were conducted to evaluate the possible contribution of education to differences in psychosocial outcomes. Results are presented in Table 2. Analyses controlling for education showed minimal changes in significance and no changes in directionality or magnitude compared to results without adjusting for education. This suggests that differences observed between rural and urban survivors were not secondary to effects of education. Additional sensitivity analyses were conducted to whether examine differences in active treatment at one year might have affected results. There were no significant differences in number of rural and urban patients on active treatment at one year and inclusion of chemotherapy status at one-year as a covariate in the analyses did not substantially alter the results. This suggests that differences observed here were not due to rural-urban differences in active treatment at a year.

# 4. Discussion

The key findings of this study were that both rural and urban high-grade ovarian cancer patients who had received their initial oncology care in two large midwestern tertiary care NCI designated comprehensive cancer centers reported relatively elevated levels of distress, moderate levels of clinical depression, and moderate impairment in QOL at the time of diagnosis. There were consistent differences in trajectories between patients living in rural vs. urban areas. Rural patients showed significantly poorer resolution of distress over the first-year post-diagnosis and had significantly elevated levels of distress at one year compared to those living in urban areas. Although almost 50% of patients of both groups were in the range of moderate clinical depression at the time of diagnosis, both groups showed similar decreases in



Fig. 1. Distress over the first year following ovarian cancer diagnosis in rural and urban patients. Lines reflect unadjusted within-group means; error bars represent standard error of measurement.

depression over time with mean 12-month levels in the non-clinical range. Although the differences in QOL scores in the two groups were not significantly different at 12 months, urban patients demonstrated a more sustained increase in QOL over time. Additionally, urban patients showed statistically greater increases in social support over time and significantly greater social support than their rural counterparts at 12 months.

The observation that distress differed between rural and urban patients at one-year post-diagnosis is consistent with prior crosssectional research demonstrating poorer mental health and greater distress in rural cancer patients during survivorship [8,28]. However, our prospective longitudinal findings are unique in demonstrating a slower trajectory of recovery from distress at the time of diagnosis in rural patients. Distress includes a variety of negative emotions, including anxiety, anger, confusion, and fatigue, in addition to dysphoria, thus providing a more comprehensive insight into mood. Therefore, although depressed mood alone did not differ in these women by 12 months, examination of a broader range of negative emotions reveals a greater profile of adversity. Whereas a substantial proportion of both groups reported depression in the clinical range pre-diagnosis, both groups showed good recovery by one year to the non-depressed range.

Psychological outcomes in cancer patients are thought to be determined by a combination of the challenges a patient experiences and the resources they possess to cope with those challenges [2]. The results described here suggest that the stress and burden may not differ at the time of diagnosis between rural and urban patients, but that rural residence is a risk factor for greater distress over the course of treatment and recovery for ovarian cancer patients. One potential explanation for the differences observed is that resources available to these patients may differ according to where they reside. Rural-urban disparities in healthcare have been attributed to causes such as differences in socioeconomic status [41], education levels [28], and ability to access services [6]. Indeed, we noted differences in both education and income between rural and urban patients which may have affected their ability to access healthcare, nutrition, and exercise, and their understanding of treatment recommendations. Exploratory analyses adjusting for education indicated that the rural-urban differences were maintained over and above the effects of education. As we have previously noted, rural patients received less of their follow-up care at tertiary care centers during the first year following diagnosis [27] which may have influenced their outcomes. Rural residents are at increased risk for many chronic illnesses and have higher rates of many risk factors, including smoking rates, obesity, lack of health insurance coverage, and lower incomes as compared to their urban counterparts [20]. While differences in social support observed at one year were small, they were significant, and may represent a growing disparity over the year that contributes to differences in distress and quality of life.

Efforts to increase telehealth options for psychological interventions have been increasing, particularly following the COVID-19 pandemic [34]. However, there remain significant infrastructure disparities in internet access for rural residents—the so-called "digital divide" [39]. Broadband internet access is significantly more limited in rural areas as compared to urban areas [19], with broadband penetration rates ranging from 59.9% to 82.7% in rural areas as compared to 96.0% in urban counties. This disparity may render telehealth interventions potentially less accessible for a population which would benefit greatly from their successful implementation. Future research on improvements to telehealth for rural areas, including improving broadband access within health centers themselves, incorporating multiple forms of telehealth (e.g. both phone visits and video visits), and public policy and education on broadband access is warranted.

#### 4.1. Limitations

Several limitations should be noted. The women studied here came from midwestern sites and may not reflect broader rurality across the United States. It is possible that effects and disparities of rurality vary by rural location in ways that are not captured in the current study. For example, all of the patients in this study received their initial treatment at a tertiary care academic center from gynecologic oncologists. This is often not the case for rural patients. Additionally, this study sample is composed of largely older non-Hispanic Whites and thus does not describe how these disparities may be affected by intersectionality concerns such as ethnic and racial diversity. Intersectionality describes compounding harm that results from multiple overlapping identities that may individually be at risk [15]. More diverse samples such as minoritized groups may experience significantly more hardship or lessened access to services than is described here. These patients were followed only to one-year post-diagnosis, where differences in OOL and social support were modest. However, the differences in trajectories suggest that there may be potentially larger differences emerging beyond one year after diagnosis and affecting longer term functioning. It will be important to examine these disparities beyond one year to understand potentially larger differences in these psychosocial factors.

Rurality was assessed here using USDA RUCC classifications. These classifications are made at a county level, which lacks some granularity compared to other potential measures of rurality. However, USDA RUCC classification was used due to its availability in publicly available SEER data and relative stability in definitions and classifications over time. Future research should examine findings noted here using more granular classifications of rurality as well.

Analyses here examined the potential for education to explain these differences, but rural/urban disparities were maintained independent of education. Education is frequently used as a proxy variable for socioeconomic status (SES) but is an imperfect measurement of SES [5]. Income data was not reported by a large number of participants here; income disparity may explain differences observed here between rural and urban participants, as there were significant differences in income among those who reported it. Other potential social determinants of health that were not assessed include transportation, food insecurity, utility insecurity, or intimate partner violence, among others. It is possible that these may contribute to the findings described here.

# 4.2. Clinical implications and conclusion

In conclusion, although differences may not be apparent at the time of diagnosis, clinicians should be aware of rurality as a potential risk factor for psychosocial impairments, particularly distress, and potentially for QOL, over the course of treatment and recovery for ovarian cancer patients. Here, rural patients showed impaired recovery in QOL and distress and poorer social support as compared to their urban counterparts over the year following diagnosis. Future research should evaluate longterm mental health disparities in rural ovarian cancer patients that may persist beyond one year following diagnosis.

Written informed consent was obtained from the patients for publication of this report and accompanying images.

#### Conflicts of interest and source of funding

This project was supported in part by NIH grants CA193249 and CA140933 (SL), T32GM108540 (SL), CA109298 (AKS), P30CA086862 (PI George Weiner) and the American Cancer Society (AKS). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

# **CRediT authorship contribution statement**

Rachel Telles: Conceptualization, Writing – original draft, Writing – review & editing. M. Bridget Zimmerman: Conceptualization, Formal analysis, Methodology, Writing – review & editing. Premal H. Thaker: Conceptualization, Investigation, Resources, Supervision, Writing – review & editing. George M. Slavich: Writing – review & editing. Edgardo S. Ramirez: Conceptualization, Writing – review & editing. Sharaf Zia: Data curation, Writing – review & editing. Michael J. Goodheart: Investigation, Resources, Writing – review & editing. Steven W. Cole: Investigation, Writing – review & editing. Susan K. Lutgendorf: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing.

# **Declaration of competing interest**

Dr. Thaker has done consulting for, Zentalis, Verastem, Immunon, Seagen, Novocure, Caris, R-Pharm, Merck, and Glaxo Smith Kline and Astra Zeneca, has research funding from Merck and Glaxo Smith Kline, and is a Immunon shareholder; Dr. Sood has done consulting for Merck and Kiyatec, has had research funding from M-Trap, and is a Biopath shareholder; Dr. Lutgendorf is a shareholder of Abbvie; other authors declare no potential conflicts of interest.

# References

- B.L. Andersen, H.-C. Yang, W.B. Farrar, D.M. Golden-Kreutz, C.F. Emery, L.M. Thornton, D.C. Young, W.E. Carson, Psychologic intervention improves survival for breast cancer patients a randomized clinical trial, Cancer 113 (12) (2008) 3450–3458, https://doi.org/10.1002/cncr.23969.
- [2] M.A. Andrykowski, E. Lykins, A. Floyd, Psychological health in cancer survivors, Semin. Oncol. Nurs. 24 (3) (2008) 193–201, https://doi.org/10.1016/j.soncn.2008. 05.007.
- [3] E. Arden-Close, Y. Gidron, R. Moss-Morris, Psychological distress and its correlates in ovarian cancer: a systematic review, Psycho-Oncology 17 (11) (2008) 1061–1072, https://doi.org/10.1002/pon.1363.
- [4] F. Baker, M. Denniston, J. Zabora, A. Polland, W.N. Dudley, A POMS short form for cancer patients: psychometric and structural evaluation, Psycho-Oncology 11 (4) (2002) 273–281, https://doi.org/10.1002/pon.564.
- [5] P. Braveman, C. Cubbin, K. Marchi, S. Egerter, G. Chavez, Measuring socioeconomic status/position in studies of racial/ethnic disparities: maternal and infant health, Public Health Rep. 116 (5) (2001) 449–463, https://doi.org/10.1093/phr/116.5.449.
- [6] G.A. Brenes, S.C. Danhauer, M.F. Lyles, P.E. Hogan, M.E. Miller, Barriers to mental health treatment in rural older adults, Am. J. Geriatr. Psychiatry 23 (11) (2015) 1172–1178, https://doi.org/10.1016/j.jagp.2015.06.002.
- [7] P.S. Brucker, K. Yost, J. Cashy, K. Webster, D. Cella, General population and Cancer patient norms for the functional assessment of cancer therapy-general (FACT-G), Eval. Health Prof. 28 (2) (2005) 192–211, https://doi.org/10.1177/01632787 05275341.
- [8] J.L. Burris, M. Andrykowski, Disparities in mental health between rural and nonrural cancer survivors: a preliminary study, Psycho-Oncology 19 (6) (2010) 637–645, https://doi.org/10.1002/pon.1600.
- [9] P.N. Butow, F. Phillips, J. Schweder, K. White, C. Underhill, D. Goldstein, on behalf of the Clinical Oncological Society of Australia, Psychosocial well-being and supportive care needs of cancer patients living in urban and rural/regional areas: a systematic review, Support Care Cancer 20 (1) (2012) 1–22, https://doi.org/10.1007/s00520-011-1270-1.
- [10] D.F. Cella, D.S. Tulsky, G. Gray, B. Sarafian, E. Linn, A. Bonomi, M. Silberman, S.B. Yellen, P. Winicour, J. Brannon, The functional assessment of cancer therapy scale: development and validation of the general measure, J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol. 11 (3) (1993) 570–579, https://doi.org/10.1200/JCO.1993.11.3.570.
- [11] A. Chang, E.K. Sloan, M.H. Antoni, J.M. Knight, R. Telles, S.K. Lutgendorf, Biobehavioral pathways and cancer progression: insights for improving well-being and Cancer outcomes, Integr. Cancer Ther. 21 (2022) 15347354221096081, https://doi. org/10.1177/15347354221096081.
- [12] M.E. Charlson, P. Pompei, K.L. Ales, C.R. MacKenzie, A new method of classifying prognostic comorbidity in longitudinal studies: development and validation, J. Chronic Dis. 40 (5) (1987) 373–383, https://doi.org/10.1016/0021-9681(87)90171-8.
- [13] X. Chen, H. Orom, J.L. Hay, E.A. Waters, E. Schofield, Y. Li, M.T. Kiviniemi, Differences in rural and urban health information access and use, J. Rural. Health 35 (3) (2019) 405–417, https://doi.org/10.1111/jrh.12335.
- [14] E.S. Costanzo, S.K. Lutgendorf, A.K. Sood, B. Anderson, J. Sorosky, D.M. Lubaroff, Psychosocial factors and interleukin-6 among women with advanced ovarian cancer, Cancer 104 (2) (2005) 305–313, https://doi.org/10.1002/cncr.21147.

- [15] K. Crenshaw, Demarginalizing the intersection of race and sex: a black feminist critique of antidiscrimination doctrine, feminist theory and antiracist politics, U. Chi. Legal F. 1989 (1989) 139.
- [16] S.L. Curran, M.A. Andrykowski, J.L. Studts, Short form of the profile of mood states (POMS-SF): psychometric information, Psychol. Assess. 7 (1) (1995) 80–83, https://doi.org/10.1037/1040-3590.7.1.80.
- [17] C.E. Cutrona, Social support and stress in the transition to parenthood, J. Abnorm. Psychol. 93 (1984) 378–390, https://doi.org/10.1037/0021-843X.93.4.378.
- [18] N. Douthit, S. Kiv, T. Dwolatzky, S. Biswas, Exposing some important barriers to health care access in the rural USA, Public Health 129 (6) (2015) 611–620, https://doi.org/10.1016/i.puhe.2015.04.001.
- [19] C. Drake, Y. Zhang, K.H. Chaiyachati, D. Polsky, The limitations of poor broadband internet access for telemedicine use in rural America: an observational study, Ann. Intern. Med. 171 (5) (2019) 382–384, https://doi.org/10.7326/M19-0283.
- [20] M.S. Eberhardt, E.R. Pamuk, The importance of place of residence: examining health in rural and nonrural areas, Am. J. Public Health 94 (10) (2004) 1682–1686, https:// doi.org/10.2105/AJPH.94.10.1682.
- [21] M. Hashibe, A.C. Kirchhoff, D. Kepka, J. Kim, M. Millar, C. Sweeney, K. Herget, M. Monroe, N.L. Henry, A.-M. Lopez, K. Mooney, Disparities in cancer survival and incidence by metropolitan versus rural residence in Utah, Cancer Med. 7 (4) (2018) 1490–1497, https://doi.org/10.1002/cam4.1382.
- [22] E.M. Hill, Quality of life and mental health among women with ovarian cancer: examining the role of emotional and instrumental social support seeking, Psychol. Health Med. 21 (5) (2016) 551–561, https://doi.org/10.1080/13548506.2015. 1109674.
- [23] C. Kamen, K.M. Mustian, C. Heckler, M.C. Janelsins, L.J. Peppone, S. Mohile, J.M. McMahon, R. Lord, P.J. Flynn, M. Weiss, D. Spiegel, G.R. Morrow, The association between partner support and psychological distress among prostate cancer survivors in a nationwide study, J. Cancer Surviv. 9 (3) (2015) 492–499, https://doi.org/10. 1007/s11764-015-0425-3.
- [24] S. Karanth, M.E. Fowler, X. Mao, L.E. Wilson, B. Huang, M. Pisu, A. Potosky, T. Tucker, T. Akinyemiju, Race, socioeconomic status, and health-care access disparities in ovarian cancer treatment and mortality: systematic review and Meta-analysis, JNCI Cancer Spectrum 3 (4) (2019) pkz084, https://doi.org/10.1093/jncics/pkz084.
- [25] C. Koopman, K. Angell, J.M. Turner-Cobb, M.A. Kreshka, P. Donnelly, R. McCoy, A. Turkseven, K. Graddy, J. Giese-Davis, D. Spiegel, Distress, coping, and social support among rural women recently diagnosed with primary breast cancer, Breast J. 7 (1) (2001) 25–33, https://doi.org/10.1046/j.1524-4741.2001.007001025.x.
- [26] S.K. Lutgendorf, K. De Geest, D. Bender, A. Ahmed, M.J. Goodheart, L. Dahmoush, M.B. Zimmerman, F.J. Penedo, J.A. Lucci, P. Ganjei-Azar, P.H. Thaker, L. Mendez, D.M. Lubaroff, G.M. Slavich, S.W. Cole, A.K. Sood, Social influences on clinical outcomes of patients with ovarian cancer, J. Clin. Oncol. 30 (23) (2012) 2885–2890, https:// doi.org/10.1200/JCO.2011.39.4411.
- [27] S.K. Lutgendorf, E. Ramirez, A. Schrepf, M.C. Valentine, M. Charlton, M.B. Zimmerman, M.J. Goodheart, S. Zia, A.K. Sood, P.H. Thaker, Rural residence is related to shorter survival in epithelial ovarian cancer patients, Gynecol. Oncol. 163 (1) (2021) 22–28, https://doi.org/10.1016/j.ygyno.2021.07.035.
- [28] S. Portero de la Cruz, J. Cebrino, Rural-urban differences in common mental disorders, functional limitation and social support among adults with cancer: a population-based study in Spain, J. Clin. Med. 11 (10) (2022), https://doi.org/10. 3390/jcm11102742 Article 10.

- [29] J.C. Probst, W.E. Zahnd, P. Hung, J.M. Eberth, E.L. Crouch, M.A. Merrell, Rural-urban mortality disparities: variations across causes of death and race/ethnicity, 2013–2017, Am. J. Public Health 110 (9) (2020) 1325–1327, https://doi.org/10. 2105/AJPH.2020.305703.
- [30] L.S. Radloff, The CES-D scale: a self-report depression scale for research in the general population, Appl. Psychol. Meas. 1 (3) (1977) 385–401, https://doi.org/10. 1177/014662167700100306.
- [31] S. Ricci, A.I. Tergas, K. Long Roche, M.G. Fairbairn, K.L. Levinson, S.C. Dowdy, R.E. Bristow, M. Lopez, K. Slaughter, K. Moore, A.N. Fader, Geographic disparities in the distribution of the U.S. gynecologic oncology workforce: a Society of Gynecologic Oncology study, Gynecol. Oncol. Rep. 22 (2017) 100–104, https://doi.org/10.1016/ j.gore.2017.11.006.
- [32] D. Russell, C.E. Cutrona, J. Rose, K. Yurko, Social and emotional loneliness: an examination of Weiss's typology of loneliness, J. Pers. Soc. Psychol. 46 (6) (1984) 1313–1321, https://doi.org/10.1037/0022-3514.46.6.1313.
- [33] S.L. Stewart, S.H. Rim, T.B. Richards, Gynecologic oncologists and ovarian cancer treatment: avenues for improved survival, J. Women's Health 20 (9) (2011) 1257–1260, https://doi.org/10.1089/jwh.2011.3053.
- [34] J. Torous, S. Bucci, I.H. Bell, L.V. Kessing, M. Faurholt-Jepsen, P. Whelan, A.F. Carvalho, M. Keshavan, J. Linardon, J. Firth, The growing field of digital psychiatry: current evidence and the future of apps, social media, chatbots, and virtual reality, World Psychiatry 20 (3) (2021) 318–335, https://doi.org/10.1002/wps.20883.
- [35] K.F. Trivers, J.R. Patterson, K.B. Roland, J.L. Rodriguez, Issues of ovarian cancer survivors in the USA: a literature review, Support Care Cancer 21 (10) (2013) 2889–2898, https://doi.org/10.1007/s00520-013-1893-5.
- [36] U.S. Census Bureau, Understanding and Using American Community Survey Data, 2020.
- [37] USDA ERS Rural-Urban Continuum Codes, Retrieved August 8, 2022, from 2013. https://www.ers.usda.gov/data-products/rural-urban-continuum-codes.aspx.
- [38] S.R. van der Kruk, P. Butow, I. Mesters, T. Boyle, I. Olver, K. White, S. Sabesan, R. Zielinski, B.A. Chan, K. Spronk, P. Grimison, C. Underhill, L. Kirsten, K.M. Gunn, on behalf of the Clinical Oncological Society of Australia, Psychosocial well-being and supportive care needs of cancer patients and survivors living in rural or regional areas: a systematic review from 2010 to 2021, Support Care Cancer 30 (2) (2022) 1021–1064, https://doi.org/10.1007/s00520-021-06440-1.
- [39] J.-Y. Wang, K. Bennett, J. Probst, Subdividing the digital divide: differences in internet access and use among rural residents with medical limitations, J. Med. Internet Res. 13 (1) (2011), e1534, https://doi.org/10.2196/jmir.1534.
- [40] S. Watts, P. Prescott, J. Mason, N. McLeod, G. Lewith, Depression and anxiety in ovarian cancer: a systematic review and meta-analysis of prevalence rates, BMJ Open 5 (11) (2015), e007618, https://doi.org/10.1136/bmjopen-2015-007618.
- [41] K.E. Weaver, A.M. Geiger, L. Lu, L.D. Case, Rural-urban disparities in health status among US cancer survivors, Cancer 119 (5) (2013) 1050–1057, https://doi.org/10. 1002/cncr.27840.
- [42] K. Weeks, C.F. Lynch, M. West, R. Carnahan, M. O'Rorke, J. Oleson, M. McDonald, S.L. Stewart, M. Charlton, Rural disparities in surgical care from gynecologic oncologists among Midwestern ovarian cancer patients, Gynecol. Oncol. 160 (2) (2021) 477–484, https://doi.org/10.1016/j.ygyno.2020.11.006.
- [43] W.E. Zahnd, A.J. Fogleman, W.D. Jenkins, Rural-urban disparities in stage of diagnosis among cancers with preventive opportunities, Am. J. Prev. Med. 54 (5) (2018) 688–698, https://doi.org/10.1016/j.amepre.2018.01.021.