



Disparities in health-related quality of life in women undergoing treatment for advanced ovarian cancer: the role of individual-level and contextual social determinants

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Abstract

Purpose Social determinants may influence health-related quality of life (HRQOL) among women with ovarian cancer, potentially creating disparities in clinical outcomes. We investigated the relationship between HRQOL and social determinants of health, including travel distance to access cancer care and health insurance type, among women participating in a randomized trial of primary adjuvant treatment for advanced ovarian cancer.

Methods The Functional Assessment of Cancer Therapy-Ovarian (FACT-O) questionnaire captured HRQOL (physical well-being, functional well-being, ovarian-specific, and trial outcome index [TOI]) prior to chemotherapy (baseline), during the trial, and 84 weeks after initiation of chemotherapy for women with advanced epithelial ovarian, primary peritoneal, or fallopian tube cancer. We constructed bivariate and multivariable linear mixed effects models examining the associations of social determinants of health (individual-level and contextual factors) with HRQOL scores at 84 weeks, clustering participants ($n = 993$) within treatment centers, and Census regions and controlling for baseline HRQOL.

Results Most individual-level (race, age, cancer stage, adverse events) and contextual (travel distance to treatment center, community socioeconomic status) factors were not statistically significantly associated with HRQOL. Compared to participants with private health insurance, other participants had lower mean HRQOL (physical well-being: public insurance, -1.00 (standard error[SE] = 0.49) points, uninsured, -1.93 (SE = 0.63) points; functional well-being: public, -1.29 (SE = 0.59), uninsured, -1.98 (SE = 0.76); ovarian cancer-specific: public, -1.60 (SE = 0.59), uninsured, -1.66 (SE = 0.75); TOI: public, -3.81 (SE = 1.46), uninsured, -5.51 (SE = 1.86); all $p < .05$).

Conclusions Private health insurance was associated with improved HRQOL at the completion of treatment for advanced stage ovarian cancer. Implications of health insurance on HRQOL should be further investigated, particularly among women with ovarian cancer who receive standard of care treatment.

Keywords Health-related quality of life · Social determinants of health · Travel distance · Health insurance · Community health · Ovarian cancer

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Introduction

Over 20,000 women in the USA are diagnosed with ovarian cancer each year. The majority of ovarian cancer cases are diagnosed at an advanced stage, and 5-year survival is poor. Ideal initial treatment includes a combination of surgery and chemotherapy with platinum and taxane-based chemotherapy, which often result in significant toxicity and subsequent reductions in quality of life [1, 2]. Women undergoing ovarian cancer treatment may have lower health-related quality of life (HRQOL) than other women, particularly for certain subdomains of HRQOL and in the short-term after treatment [3–5]. HRQOL is influenced by multiple patient-level factors

and has been associated with disease-specific ovarian cancer outcomes [6].

Social determinants of health, including race, ethnicity, and socioeconomic status (SES), have been linked to disparities in ovarian cancer. Black women and women of lower SES have decreased overall survival following a diagnosis of ovarian cancer [7–11]. Discrepancies in practice patterns have been demonstrated to contribute to disparities in outcomes for this disease, as underserved women are less likely to receive ideal or guideline adherent treatment [8, 9].

Contextual or community factors are also known to play a role in cancer outcomes [12, 13]. Availability of transportation, for example, has been investigated as a contributor to cancer disparities [14, 15]. Cancer patients with higher travel burdens (in terms of distance and time) to their treatment centers often have poorer HRQOL, lower rates of adherence to treatment regimens, and worse survival outcomes [13, 15–17]. Variation in travel burden can pose challenges to cancer patients across the rural-urban continuum, though burdens may be offset by higher quality care at regionalized cancer centers (usually in urban areas) [15, 17]. Other factors, such as insurance status and elderly age, have also been associated with increased travel burden and cancer outcomes in women with gynecologic cancer [16]. Despite the role of social determinants of health in cancer outcomes and disparities, the association between these factors and HRQOL is not well-understood.

In this study, we examined the relationship between HRQOL and individual-level and contextual social determinants among patients enrolled in a clinical trial examining novel therapy for advanced-stage ovarian cancer (including epithelial ovarian, primary peritoneal, or fallopian tube) following their initial diagnosis. Understanding the experiences of women undergoing treatment for ovarian cancer can inform evidence-based health policy and interventions to improve outcomes from this disease.

Methods and materials

Data sources

The present study was a secondary analysis of data from the Gynecologic Oncology Group (GOG)'s randomized trial, protocol GOG-0218 [18]. In brief, participants in the trial were women with stage III or IV ovarian cancer (including epithelial ovarian, primary peritoneal, or fallopian tube) treated with primary surgery. Trial enrollment spanned from October 2005 to June 2009, and participants were randomized to one of three study arms at enrollment. The three study arms consisted of 22 cycles (3 weeks each) of intravenous infusions. Participants were to receive a maximum of 6 cycles of standard chemotherapy with carboplatin and paclitaxel, with the

addition of (1) placebo during cycles 2–22 [arm 1]; (2) bevacizumab during cycles 2–6 and placebo during cycles 7–22 [arm 2]; or (3) bevacizumab during cycles 2–22 [arm 3]. As part of the GOG trial, participants provided demographic and residential information at baseline (at time of enrollment and randomization). In addition, they completed questionnaires five times throughout the treatment period and a sixth time 84 weeks following study enrollment (roughly 6 months after completing 22 cycles of treatment).

The primary protocol (GOG 218) was approved under individual institutional investigation review boards, and all patients signed written informed consent [18]. Data sharing for this secondary analysis was approved by the NRG Oncology Ancillary Studies Committee with the stipulation that no individual patient address information be used in the analysis.

To complement these data, we gathered information on contextual factors of the participants' residential zip codes from the 2000 Census, implemented by the U.S. Census Bureau [19]. Zip codes roughly approximate residents' "communities," although they can be quite large and heterogeneous [20].

Measures

Dependent variables: HRQOL subscale scores

To capture HRQOL, we gathered participants' scores on three subscales (physical well-being [seven items], functional well-being [seven items], ovarian cancer-specific [11 items]) of the Functional Assessment of Cancer Therapy-Ovarian (FACT-O) scale, as well as the trial outcomes index (TOI), i.e., the sum of the three subscales. Each subscale has demonstrated acceptable levels of internal consistency (all $\alpha > 0.70$) and test-retest reliability (all $r > 0.70$), as well as adequate validity [21], and FACT-O has been used commonly in ovarian cancer clinical trials. The TOI describes the summation process of each subscale into one composite score. Responses for each FACT-O item ranged from 0 to 4, with higher values indicating higher quality of life; items were reverse-coded as necessary. Thus, the scores for the physical and functional well-being subscales had a possible range of 0 to 28; the ovarian cancer-specific subscale had a possible range of 0 to 44; and the TOI had a possible range of 0 to 100. The present analysis used HRQOL scores collected at baseline and 84 weeks after enrollment. In the primary study, there were no differences in HRQOL among participants in different treatment arms at 84 weeks post-enrollment (or at baseline) [18], so analyzing HRQOL at this timepoint minimized confounding by study arm and allowed us to examine long-term relationships among the study variables.

Independent variables: individual-level and contextual factors

Individual-level control variables included participant race (white or other), age category (< 65 years or 65+ years), insurance type (private, public [including Medicare, Medicaid, and military insurance], or uninsured [including participants with unknown or other insurance types]), cancer stage (III or IV), and experience of non-hematological adverse events during the trial (grades 3, 4, or 5; yes or no). We excluded hematological adverse events because they were very commonly experienced (74% of all adverse events reported), and patients usually recover from them quickly.

Contextual factors included travel distance and variables measuring social context. Travel distance between each participant's residence and her treatment center (the clinical site participating in the trial where the participant received chemotherapy) was calculated the distance in miles between the centroid of each participant's residential zip code to the centroid of the zip code for her treatment center (using a straight line). Although these estimates do not reflect other factors that affect travel burden (e.g., directness of connecting roads), previous research has indicated high correlations between straight line and road-based measures of travel burden [22]. We categorized this variable into four quartiles based on the observed distribution of travel distance to facilitate comparisons and to minimize the influence of outliers.

We also assembled variables from the US Census characterizing the social context of participants' zip codes as potential correlates of HRQOL: median household income, percent of adults (age 18+ years) with a high school degree or higher, and percent of residents who were non-white. We categorized these variables into quartiles.

Statistical analysis

The original sample included 1873 women from the USA, Canada, South Korea, and Japan, but the current analysis excluded the women who received care outside the USA ($n = 106$). We also excluded women without a valid zip code ($n = 33$) and with missing data for HRQOL at baseline ($n = 341/1734$, response rate = 80.3%), HRQOL at 84 weeks ($n = 394/1393$, response rate = 71.7%), or other covariates ($n = 6$). We generated descriptive statistics of baseline individual-level and contextual factors for participants in the analytic sample.

We evaluated the bivariate associations of travel distance and other individual-level and contextual factors with each HRQOL subscale score at 84 weeks after initiating chemotherapy. Each model controlled for the respective HRQOL subscale score observed at baseline to account for unexplained variation in pretreatment HRQOL. We used linear mixed effects models clustering participants within treatment center zip

codes and U.S. Census regions (Northeast, South, Midwest, or West) to account for non-independence within treatment centers and spatial autocorrelation, respectively [23]. We treated travel distance and the individual-level and contextual factors as fixed effects and clustering variables as random effects. Next, we constructed multivariable models examining the association of the independent variables with HRQOL subscale scores.

Finally, we tested whether Census region moderated the associations observed between the independent variables and HRQOL (i.e., cross-level interactions). We added multiplicative interaction terms for each independent variable (separately) and region to the model and, then, used Wald chi-square tests to evaluate whether each interaction significantly contributed to the models. Because none of the interactions were statistically significant (all $p > .05$), we do not discuss these results further.

NRG Oncology calculated distance metrics prior to data sharing and reviewed study results before publication, to protect patient confidentiality. Analyses were implemented in SAS version 9.3 (Cary, NC) using a two-sided p value of .05.

Results

The final analytic sample was comprised of 993 patients from the USA for whom complete data were available. The majority of participants were white (93.0%), younger than 65 years of age (68.4%), and privately insured (78.9%) (Table 1). Most participants had stage III ovarian cancer (73.9%), and 45.1% experienced an adverse event. (Participants with missing zip code data ($n = 33$) were more likely to lack public or private insurance, while participants with missing HRQOL data ($n = 341$ at baseline and $n = 394$ at 84 weeks) were more likely to be non-white, compared to participants with complete data (Supplementary Table S1)

Across participants' zip codes, the median household income was \$50,019 (standard error [SE] = \$582), 84.3% ($SE = 0.3\%$) of adult residents had a high school degree, and 17.9% ($SE = 0.6\%$) of residents were non-white. Participants lived an average of 37.8 miles ($SE = 4.0$) from the center where they received chemotherapy treatment for ovarian cancer (quartile 1: mean = 3.56 [$SE = 0.13$]; quartile 2: mean = 9.71 [$SE = 0.14$]; quartile 3: mean = 22.10 [$SE = 0.38$]; quartile 4: mean = 115.79 [$SE = 14.97$]). At 84 weeks after beginning their first cycle of ovarian cancer treatment, participants' mean HRQOL subscale scores were 22.2 ($SE = 0.2$) for physical well-being, 20.1 ($SE = 0.2$) for functional well-being, 33.5 ($SE = 0.2$) for ovarian-specific well-being, and 78.9 ($SE = 0.5$) for overall TOI (Table 1). In bivariate models controlling for baseline HRQOL, travel distance quartile was not related to HRQOL subscale scores at 84 weeks (Table 2).

Table 1 Descriptive characteristics of analytic sample ($n = 993$)

Independent variables		
Individual-level factors	<i>n</i>	%
Race		
White	923	93.0
Other	70	7.1
Age group		
< 65 years	679	68.4
65+ years	314	31.6
Insurance type		
Private insurance	783	78.9
Public insurance	141	14.2
Other	69	7.0
Stage		
III	734	73.9
IV	259	26.1
Adverse events ^a		
No	545	54.9
Yes	448	45.1
Contextual factors		
	Mean	<i>SE</i>
Median household income, \$	50,019	582
Adults with a HS degree or higher, (%)	84.3	0.3
Residents who are non-white race, (%)	17.9	0.6
Travel distance, miles	37.8	4.0
HRQOL		
	Mean	<i>SE</i>
Baseline		
Physical well-being subscale	20.9	0.2
Functional well-being subscale	15.3	0.2
Ovarian subscale	29.4	0.2
TOI	65.7	0.5
84 weeks post-cycle 1		
Physical well-being subscale	22.2	0.2
Functional well-being subscale	20.1	0.2
Ovarian subscale	33.5	0.2
TOI	78.9	0.5

^a Grades 3, 4, or 5, excluding hematological events

HRQOL health-related quality of life, TOI trial outcomes index

Race, stage, age, and the experience of an adverse event were not associated with HRQOL. Insurance type was, however, consistently correlated with HRQOL scores; for example, mean physical well-being subscale scores were 0.92 ($SE = 0.45$, $p = .04$) points lower for participants with public insurance and 1.87 ($SE = 0.61$, $p < .01$) points lower for uninsured participants than for participants with private insurance. Similar patterns emerged for the relationship between insurance type and the three other HRQOL scores. In addition, participants living in zip codes in the highest quartile of high school educational attainment had higher mean scores on the functional well-being, ovarian cancer-specific, and TOI

subscales (1.15 [$SE = 0.54$], 1.26 [$SE = 0.54$], and 3.00 [$SE = 1.32$] points higher, respectively, all $p < .05$) compared to participants living in the lowest quartile.

In multivariable analysis, travel distance quartile was not related to HRQOL at 84 weeks after controlling for baseline HRQOL, with one exception: women living in the second quartile of travel distance had lower mean scores for physical well-being than women living in the first quartile (difference = -0.92 , $SE = 0.45$, $p = .04$) (Table 3).

Insurance type remained associated with each HRQOL subscale mean score. Compared to participants with private insurance, mean physical well-being scores were 1.00 ($SE = 0.49$, $p = .04$) points lower for participants with public insurance and 1.93 ($SE = 0.63$, $p < .01$) points lower for uninsured participants (adjusted mean scores: private, 22.8 [$SE = 0.4$]; public, 21.8 [$SE = 0.5$]; uninsured, 20.8 [$SE = 0.7$]). Functional well-being scores were 1.29 ($SE = 0.59$, $p = .03$) points lower for participants with public insurance and 1.98 ($SE = 0.76$, $p = .01$) points lower for uninsured participants (adjusted mean scores: private, 20.5 [$SE = 0.4$]; public, 19.2 [$SE = 0.6$]; uninsured, 18.6 [$SE = 0.8$]). Ovarian cancer-specific HRQOL scores were 1.60 ($SE = 0.59$, $p = .01$) points lower for participants with public insurance and 1.66 ($SE = 0.75$, $p = .03$) points lower for uninsured participants with other insurance (adjusted mean scores: private, 33.7 [$SE = 0.5$]; public, 32.1 [$SE = 0.6$]; uninsured, 32.1 [$SE = 0.8$]). Finally, TOI scores were 3.81 ($SE = 1.46$, $p = .01$) points lower for participants with public insurance and 5.51 ($SE = 1.86$, $p < .01$) points lower for uninsured participants (adjusted mean scores: private, 77.0 [$SE = 1.1$]; public, 73.2 [$SE = 1.5$]; uninsured, 71.5 [$SE = 2.0$]). In all multivariable models, baseline measurements of HRQOL were positively and significantly associated with HRQOL measured at 84 weeks (all $p < .0001$, data not shown).

Discussion

In this study, we evaluated concurrent and prospective HRQOL during the treatment and follow-up of GOG-218, a clinical trial examining the addition of bevacizumab to initial treatment for patients with advanced-stage ovarian cancer [18]. Although bevacizumab mildly compromised HRQOL during chemotherapy, a prolonged effect after chemotherapy completion was not seen [24]. In this secondary analysis of data shared from GOG-0218, we found no differences in HRQOL by race, age, clinical characteristics, travel distance from home to treatment center (measured as straight-line distance between zip code centroids), or zip code characteristics. As the population included in this study was a cohort of women enrolled in a clinical trial for the treatment of advanced ovarian cancer, the study sample was relatively homogenous (more than 90% white, with relatively little variability in zip

Table 2 Bivariate correlates of mean health-related quality of life (HRQOL) subscale scores among women undergoing treatment for ovarian cancer ($n = 993$)

	Physical well-being (range, 0–28)			Functional well-being (range, 0–28)			Ovarian cancer-specific (range, 14–44)			TOI (range, 22–100)		
	est.	SE	<i>p</i>	est.	SE	<i>p</i>	est.	SE	<i>p</i>	est.	SE	<i>p</i>
Individual-level factors												
Race (other v. white)	0.33	0.61	0.59	0.46	0.73	0.53	−0.24	0.73	0.74	0.49	1.80	0.79
Age group (65+ v. < 65 years)	0.12	0.34	0.73	−0.45	0.40	0.27	−0.68	0.40	0.09	−0.99	0.99	0.32
Insurance type (ref: private insurance)												
Public insurance	−0.92	0.45	0.04	−1.38	0.54	0.01	−1.61	0.53	<.01	−3.86	1.32	<.01
Other	−1.87	0.61	<.01	−1.90	0.73	0.01	−1.72	0.73	0.02	−5.45	1.80	<.01
Stage (IV v. III)	0.30	0.36	0.41	−0.38	0.43	0.38	−0.29	0.43	0.49	−0.27	1.06	0.80
Adverse events ^a (yes v. no)	−0.36	0.32	0.25	−0.59	0.38	0.12	−0.52	0.37	0.17	−1.38	0.93	0.14
Contextual factors												
Median household income (quartiles)												
1 (lowest income)	(ref)			(ref)			(ref)			(ref)		
2	0.24	0.45	0.59	1.02	0.54	0.06	1.00	0.54	0.06	2.29	1.32	0.08
3	−0.05	0.45	0.91	0.49	0.54	0.36	−0.02	0.54	0.97	0.37	1.33	0.78
4 (highest income)	0.41	0.45	0.37	1.07	0.54	0.05	0.91	0.55	0.10	2.40	1.34	0.07
Adults with a HS degree or higher (quartiles)												
1 (lowest education)	(ref)			(ref)			(ref)			(ref)		
2	0.57	0.45	0.20	0.85	0.54	0.11	0.55	0.53	0.30	1.97	1.32	0.14
3	0.05	0.45	0.91	0.27	0.54	0.62	−0.06	0.54	0.91	0.19	1.33	0.89
4 (highest education)	0.62	0.45	0.16	1.15	0.54	0.03	1.26	0.54	0.02	3.00	1.32	0.02
Residents who are non-white race (quartiles)												
1 (lowest % non-white)	(ref)			(ref)			(ref)			(ref)		
2	0.40	0.45	0.37	0.29	0.54	0.59	0.11	0.54	0.84	0.78	1.33	0.56
3	−0.27	0.45	0.55	0.23	0.54	0.67	−0.70	0.54	0.20	−0.72	1.34	0.59
4 (highest % non-white)	0.15	0.45	0.73	0.10	0.54	0.86	−0.80	0.55	0.14	−0.55	1.34	0.68
Travel distance (quartiles)												
1 (least distance)	(ref)			(ref)			(ref)			(ref)		
2	−0.80	0.44	0.07	0.17	0.53	0.74	−0.44	0.52	0.40	−1.08	1.30	0.41
3	−0.66	0.44	0.13	0.64	0.53	0.23	−0.27	0.53	0.60	−0.33	1.30	0.80
4 (most distance)	−0.66	0.45	0.14	−0.35	0.53	0.51	0.12	0.54	0.83	−0.92	1.32	0.48

^a Grades 3, 4, or 5, excluding hematological events

Models account for clustering by medical institution and region of the country. Models control for baseline levels of the respective HRQOL measure. TOI trial outcomes index

code characteristics), potentially limiting our ability to detect differences that may be present in the broader population [23].

We did, however, find consistent associations between HRQOL subscale scores and participants' health insurance type. Specifically, women with private insurance had higher HRQOL for all four subscales compared to non-privately insured women at 84 months following their diagnosis. In addition, we noted a graded association between HRQOL and health insurance type, such that women with private insurance had the highest scores, followed by women with public insurance, and finally women with "other" insurance; this latter group (primarily uninsured) may be particularly vulnerable

in terms of HRQOL after ovarian cancer treatment. However, this trend was not statistically significant (all $p > .10$). These findings emerged despite no differences observed in baseline HRQOL by insurance status or zip code median household income, (all $p > 0.50$; data not shown). In absolute terms, the differences in HRQOL associated with insurance type were relatively small, and their clinical significance is not entirely certain. However, previous studies have used 10% of the range to indicate clinically important differences, and the observed associations between HRQOL and insurance type were about half of that magnitude [25]. Additionally, living in a zip code with a higher percentage of

Table 3 Multivariable correlates of health-related quality of life (HRQOL) subscale scores among women undergoing treatment for ovarian cancer ($n = 993$)

	Physical well-being (range, 0–28)			Functional well-being (range, 0–28)			Ovarian cancer-specific (range, 14–44)			TOI (range, 22–100)		
	est.	SE	<i>p</i>	est.	SE	<i>p</i>	est.	SE	<i>p</i>	est.	SE	<i>p</i>
Individual-level factors												
Race (other v. white)	0.36	0.65	0.58	0.63	0.78	0.42	−0.02	0.77	0.98	0.97	1.91	0.61
Age group (65+ v. < 65 years)	0.31	0.37	0.41	−0.20	0.45	0.65	−0.30	0.44	0.49	−0.18	1.10	0.87
Insurance type (ref: private insurance)												
Public insurance	−1.00	0.49	0.04	−1.29	0.59	0.03	−1.60	0.59	0.01	−3.81	1.46	0.01
Other	−1.93	0.63	<.01	−1.98	0.76	0.01	−1.66	0.75	0.03	−5.51	1.86	<.01
Stage (IV v. III)	0.17	0.36	0.64	−0.48	0.44	0.27	−0.42	0.43	0.33	−0.61	1.07	0.57
Adverse events ^a (yes v. no)	−0.34	0.32	0.28	−0.57	0.39	0.14	−0.52	0.38	0.17	−1.33	0.94	0.15
Contextual factors												
Median household income	Overall <i>p</i>		0.91	Overall <i>p</i>		0.45	Overall <i>p</i>		0.14	Overall <i>p</i>		0.35
1 (lowest income)	(ref)			(ref)			(ref)			(ref)		
2	0.14	0.48	0.76	0.81	0.58	0.16	1.04	0.58	0.07	2.03	1.43	0.16
3	−0.05	0.57	0.93	0.09	0.68	0.90	−0.10	0.68	0.88	−0.05	1.68	0.98
4 (highest income)	0.27	0.65	0.68	0.27	0.78	0.73	0.34	0.80	0.67	0.96	1.94	0.62
Adults with a high school degree or higher	Overall <i>p</i>		0.33	Overall <i>p</i>		0.26	Overall <i>p</i>		0.06	Overall <i>p</i>		0.12
1 (lowest education)	(ref)			(ref)			(ref)			(ref)		
2	0.63	0.49	0.20	0.66	0.60	0.27	0.34	0.59	0.56	1.60	1.46	0.27
3	0.04	0.57	0.94	0.16	0.69	0.82	−0.17	0.69	0.81	−0.07	1.69	0.97
4 (highest education)	0.67	0.65	0.30	1.14	0.78	0.15	1.35	0.78	0.08	3.05	1.92	0.11
Residents who are non-white race	Overall <i>p</i>		0.40	Overall <i>p</i>		0.82	Overall <i>p</i>		0.50	Overall <i>p</i>		0.73
1 (lowest non-white %)	(ref)			(ref)			(ref)			(ref)		
2	0.30	0.45	0.50	0.27	0.54	0.62	0.04	0.54	0.94	0.59	1.33	0.66
3	−0.35	0.46	0.44	0.28	0.55	0.60	−0.69	0.55	0.21	−0.45	1.35	0.58
4 (highest non-white %)	0.32	0.50	0.52	0.58	0.60	0.34	−0.37	0.61	0.55	0.51	1.49	0.73
Travel distance (quartiles)	Overall <i>p</i>		0.23	Overall <i>p</i>		0.55	Overall <i>p</i>		0.31	Overall <i>p</i>		0.62
1 (least distance)	(ref)			(ref)			(ref)			(ref)		
2	−0.92	0.45	0.04	0.00	0.55	1.00	−0.81	0.54	0.13	−1.75	1.34	0.19
3	−0.68	0.47	0.14	0.62	0.56	0.27	−0.55	0.56	0.32	−0.65	1.38	0.64
4 (most distance)	−0.51	0.47	0.28	−0.10	0.57	0.87	0.12	0.57	0.83	−0.54	1.40	0.70

^a Grades 3, 4, or 5, excluding hematological events

Each column represents one model. Models account for clustering by medical institution and region of the country. Models control for baseline levels of the respective HRQOL measure. Overall *p* values reflect statistical significance of the joint associations of the four levels of the respective contextual factor. *TOI* trial outcomes index

highly educated adults was associated with higher functional well-being, ovarian-specific, and TOI HRQOL scores in the bivariate analyses, but these coefficients lost statistical significance after controlling for other variables. These results confirm previous research demonstrating associations between ovarian cancer outcomes (including HRQOL) and contextual factors [8, 12–18]. Alternative measures of community characteristics, including better measures of area-level SES, could reveal more robust associations with HRQOL [26].

For women with ovarian cancer, HRQOL is an important outcome both in its own right and because of its association with treatment outcomes [6, 27, 28]. In GOG 218, a five-point

difference in baseline FACT-O TOI score was associated with progression-free survival [29]. In our analysis, the observed relationship between insurance type and HRQOL may have implications for evidence-based health policy [30] and clinical practice. The association between insurance type and HRQOL within this analysis was consistent, despite taking place in the context of a clinical trial, when ability to pay is removed from treatment decisions. Instead, health insurance type in a clinical trial could indicate individual-level socioeconomic status, which we estimated with contextual factors (e.g., zip code, level of income, and education) but were not able to measure directly (i.e., with individual-level measures of income and

education). In addition, health insurance type could reflect access to supportive services outside of the trial; that is, women with private insurance may have had easier access to treatment for pain or psychological symptoms that could have improved their HRQOL [31, 32]. Women with private insurance and, perhaps, higher socioeconomic status, may have been healthier at baseline or had access to greater social support, both of which could impact HRQOL over time [33].

This association, demonstrated in a cohort of women with ovarian cancer enrolled in a clinical trial, likely underestimates the impact of health insurance in the broader population of patients, where insurance coverage is likely more salient. Underinsurance or uninsurance has been demonstrated in previous studies to pose a significant barrier to accessing cancer care, leading to worse cancer-specific outcomes than for insured patients [32, 34]. Even among Medicare beneficiaries, underinsurance influences care as patients without private supplemental insurance have been shown to less likely receive recommended chemotherapy [35]. By addressing gaps between insurance status, social determinants of health, and treatment, the experience of patients with ovarian cancer could be improved.

The strengths of our study include a large sample size of 993 patients, allowing us to examine the associations between HRQOL and several independent variables. HRQOL in the context of social determinants of health among ovarian cancer patients is understudied. This analysis represents a well-controlled longitudinal study to investigate the influence of social determinants on patient outcomes. The results of our analyses were robust to clinical characteristics relevant to HRQOL, increasing our confidence in the validity of the findings. In terms of study limitations, as noted above, data came from a clinical trial population, which varies systematically from the overall patient population. Privately insured and non-Hispanic white women have been historically overrepresented in NCI-funded clinical trials in this disease site [23]. Further, previous research has demonstrated that participants in this clinical trial who had HRQOL data at 84 weeks were healthier with a better overall prognosis than other patients [18, 24]. A more refined analysis could examine the HRQOL and independent variables at each measurement interval during and after active treatment to determine whether these patterns can identify patients who are stabilizing, deteriorating, or improving, thereby highlighting timepoints where supportive care is needed. A related limitation is that we excluded participants with missing data, who may have differed systematically from participants with complete data; alternative approaches to dealing with missing data (e.g., imputation) could have produced different results. Specifically, because HRQOL at baseline was lower among participants who were missing data at 84 weeks than among participants who had data at 84 weeks, our analysis excluded the potentially least healthy ovarian cancer patients, limiting the generalizability of

our findings. We only examined HRQOL in the context of one cancer subtype; HRQOL (and its associations with social determinants of health) likely varies for different cancers. Finally, we were not able to measure exact travel distance from each participant's home to her treatment center due to concerns about patient privacy; additional studies are needed to more accurately capture travel distance and time.

In conclusion, in this secondary analysis of a randomized trial of treatment for ovarian cancer, private health insurance status was associated with statistically significantly higher scores on four subscales of HRQOL compared to other insurance types. This finding was independent of associations observed for clinical characteristics, travel distance, and other individual-level and contextual characteristics. More research is needed on social determinants of health and HRQOL in ovarian cancer, especially analyses of insurance type for those residing in underserved regions in order to inform health policy for cancer patients.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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