


Trends and Racial Disparities in Aggressive End-of-Life Care for a National Sample of Women With Ovarian Cancer

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BACKGROUND: The clinical landscape has moved toward less aggressive end-of-life care for women with ovarian cancer. However, whether there has been a decline in the use of aggressive end-of-life services is unknown. The authors evaluated current national trends and racial disparities in end-of-life care among women with ovarian cancer using the Surveillance, Epidemiology, and End Results–Medicare-linked data set. **METHODS:** In total, 7756 Medicare beneficiaries aged >66 years with ovarian cancer who died between 2007 and 2016 were identified. The authors examined trends and racial disparities in late hospice or no hospice use, >1 emergency department (ED) visit, intensive care unit admission, >1 hospitalization, terminal hospitalization, chemotherapy, and invasive and/or life-extending procedures using multivariable logistic regression. **RESULTS:** The median hospice length of stay did not change over time; however, women were increasingly admitted to the intensive care unit and had multiple ED visits in the last month of life ($P < .001$). Not enrolling in hospice at the end of life and terminal hospitalizations decreased over time ($P < .001$). Non-White women were more likely to receive aggressive end-of-life care, particularly for hospital-related utilization and life-extending procedures, whereas non-Hispanic Black women were more likely to have >1 ED visit (odds ratio, 2.04; 95% CI, 1.57–2.64) or life-extending procedures (odds ratio, 1.89; 95% CI, 1.45–2.48) compared with non-Hispanic White women. **CONCLUSIONS:** Despite clinical guidelines and increasing emphasis on reducing aggressive end-of-life care, the use of aggressive end-of-life care for women with ovarian cancer persists, and care is most aggressive for non-White women. *Cancer* 2021;127:2229–2237. © 2021 American Cancer Society.

KEYWORDS: hospice care, ovarian cancer, racial disparity, terminal care.

INTRODUCTION

Ovarian cancer is a rapidly fatal cancer typically diagnosed at an advanced stage. This makes it an important cancer for evaluating the status of end-of-life care because concerns about care at the end of life are more likely to occur sooner in the course of ovarian cancer care.¹ Clinical consensus suggests that high-quality end-of-life care includes enrollment in hospice when a patient has a prognosis that is <6 months and does not include the receipt of intensive or invasive care.^{2,3} Not meeting these quality standards indicates aggressive end-of-life care.^{4,5}

Previous studies indicated that, despite increasing hospice use over time, end-of-life care for women with ovarian cancer was aggressive and was more aggressive for non-White women.^{6–9} However, these findings reflect trends only through 2007 and, to date, only racial disparities from a single state (Texas) have been examined.^{6,7} Over the past decade, the clinical landscape around end-of-life care has changed. Palliative care was recognized as a specialty in 2006, and the American Society of Clinical Oncology's goal was for palliative care to be integrated into cancer care by 2020.¹⁰ Current guidelines and recommendations by the American Society of Clinical Oncology and the National Academy of Medicine call for palliative care and individualized care for patients with advanced cancer, emphasizing the importance of palliation and quality of life, which, in turn, result in nonaggressive end-of-life care.^{2,10,11}

To fill the gap in our understanding about receipt of end-of-life cancer care in the era of increasing emphasis on palliative care, we evaluated the current state of and trends in end-of-life care among women with ovarian cancer using

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the Surveillance, Epidemiology, and End Results (SEER)-Medicare data set. We assessed trends in the aggressiveness of end-of-life care for women with ovarian cancer between 2007 and 2016 and evaluated whether racial disparities in aggressive end-of-life care exist at a national level.

MATERIALS AND METHODS

Data

For the current analysis, we used data from the linkage of SEER registry data and Medicare claims data from the years 2000 through 2016.¹² The SEER program is comprised of 18 population-based cancer registries, which collect information on all residents of their catchment areas who are diagnosed with invasive cancer. SEER data include patient demographics, tumor characteristics, first course of treatment, and survival. The SEER-Medicare linkage yields treatment and outcomes for roughly 25% of elderly patients with cancer in the United States. Cause-of-death data are attained through a linkage with the National Death Index.¹³

Cohort Selection

Women who were diagnosed between 2000 and 2015 with a first and only primary ovarian cancer and who died between 2007 and 2016 were eligible for this study. Because cause-of-death data are problematic in identifying the underlying cancer cause of death and SEER cancer diagnosis data are very rigorous, we defined our cohort by ovarian cancer diagnosis and restricted it to first and only cancers (with the exception of basal and squamous cell skin carcinomas) to avoid attributing receipt of therapy from another cancer. To facilitate measurement of comorbidity, the sample was restricted to women who were aged >66 years at the time of cancer diagnosis and had complete case information captured by a SEER registry (n = 16,661). To ensure that treatment information was complete, we excluded patients who were not enrolled in both Part A and Part B of Medicare or who were enrolled in a health maintenance organization plan in the 12 months before diagnosis or at any point from the time of diagnosis through the end of study observation (n = 5089). We excluded patients who: had unknown month of diagnosis or death, died within 30 days of diagnosis, were alive before December 2016, had discrepancies between SEER and Medicare birth or death dates, were diagnosed at death or autopsy, had noninvasive disease, had no claims after diagnosis, or had a hospice admission date predating diagnosis (n = 3816). In total, 7756 women with ovarian

cancer were included in our analytic sample (Fig. 1). The Wayne State University Institutional Review Board determined that this study was exempt.

Outcomes

All hospice use, end-of-life treatments, and end-of-life hospital utilization were identified using Medicare claim data from the last 30 days of life (see Supporting Table 1) based on prior definitions and updated with coding according to the International Classification of Diseases, tenth revision.^{6,7} Hospice use measures included failure to enroll in hospice (no hospice), or <3 days of hospice before death (late hospice). Treatment measures included chemotherapy within 14 days of death, life-extending procedures (ventilation, resuscitation, or feeding tubes), and invasive procedures (surgery requiring anesthesia, placement of arterial or central line, endoscopy, interventional radiology procedure, radiotherapy, or pelvic examination with tissue sampling).^{7,14} Hospital utilization measures included >1 emergency department (ED) visit or hospital admission, intensive care unit (ICU) admission, and death in an acute care hospital.^{4,5,15,16} These metrics align with guidelines of the National Quality Forum for quality end-of-life care.^{6,15,17} Independent binary measures for each outcome were created indicating receipt in the month before death.

Exposures

Race/ethnicity (non-Hispanic White [NHW], non-Hispanic Black [NHB], Hispanic, other races) and year of death were our primary exposures of interest. Race/ethnicity was derived by SEER abstractors, with priority given to self-reported information.¹⁸ We calculated a modified Charlson index score for each patient from the 12 months before diagnosis.^{19,20} Census tract poverty was provided by SEER based on the patient's residential address. A priori-identified confounders included: nonurban residence, age of death, time between diagnosis and death (<1 year, 1 to <2 years, or ≥2 years), Charlson comorbidity score (0, 1, 2, or ≥3), census tract poverty (0% to <5%, 5% to <10%, 10% to <20%, 20%-100%, or unknown), and marital status (married or unmarried).

Statistical Analysis

To examine trends over time, the average predicted probability of each binary outcome was calculated using logistic regression to calculate a prediction for each patient in each year with adjustment for patient characteristics and confounders, as detailed previously.⁶ The association of

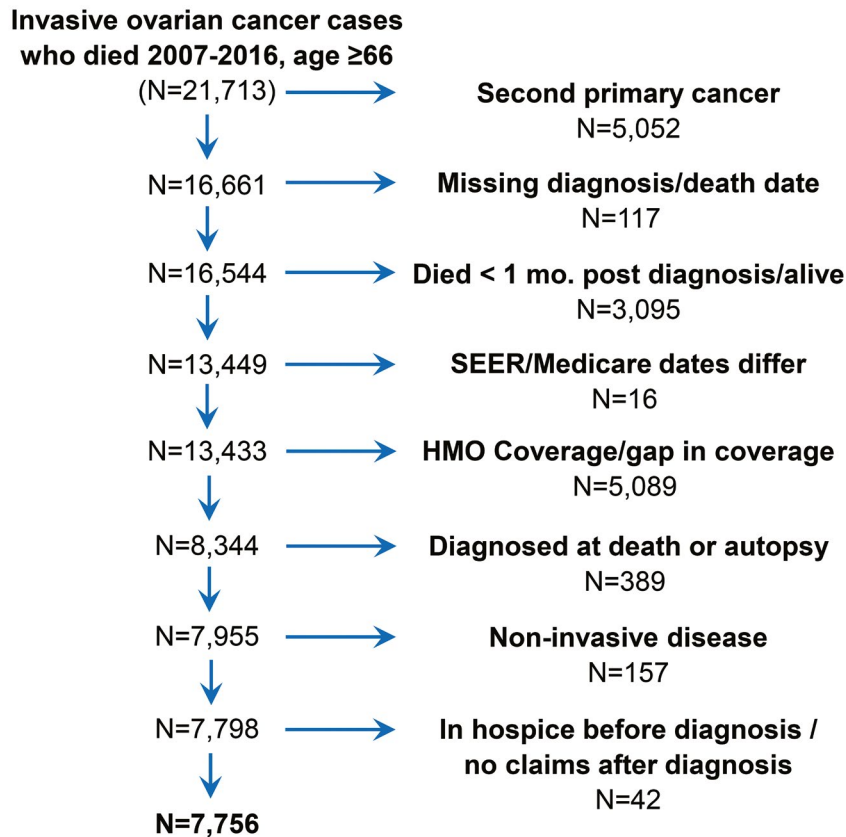


Figure 1. This is a patient exclusion flow diagram from the current study. HMO indicates health maintenance organization; SEER, Surveillance, Epidemiology, and End Results program of the National Cancer Institute.

year and hospice length of stay was evaluated using the Mann-Whitney *U* test because of the skewed distribution. To examine the association between race/ethnicity and each outcome, first, we assessed differences in the bivariate distributions using χ^2 tests. Then, we used multivariable-adjusted logistic regression to estimate the associations between race and receipt of end-of-life care, including hospice use (no hospice, late hospice), inappropriate hospital utilization (>1 ED visit, ICU admission, terminal hospitalization, multiple hospitalizations), and aggressive treatments (life-extending procedures, invasive procedures, chemotherapy), adjusting for poverty, Charlson comorbidity score, marital status, residence, age of death, and years from diagnosis to death. The association of race/ethnicity and hospice length of stay was evaluated using the Mann-Whitney *U* test because of the skewed distribution.

Sensitivity analyses were conducted to assess the robustness of enumerating our cohort based on a first and only ovarian cancer diagnosis. We restricted our cohort in these analyses to women who had a first and only ovarian

cancer and whose cause of death was specified as cancer. We also tested whether findings were consistent when adjusting for stage of diagnosis rather than time between diagnosis and death. All analyses were conducted in SAS version 9.4, and a 2-tailed *P* value <.05 was considered statistically significant.

RESULTS

Most women in the cohort were NHW (84.3%), lived in census tracts with <20% poverty (81%), had no comorbidities (54%), were not currently married (61%), lived in urban areas (97.8%), and survived <2 years after diagnosis (55.3%). The median age of death was 80 years. The median time from diagnosis to death was 20.2 months (Table 1).

The proportion of women who received aggressive end-of-life care varied by race for hospice use, hospital utilization, and treatment receipt (Table 2). Compared with NHW women, approximately 10% more non-White women did not enroll in hospice (*P* < .01). Late

TABLE 1. Demographic and Clinical Characteristics of Women in the Surveillance, Epidemiology, and End Results–Medicare Database With Invasive Ovarian Cancer Who Died Between 2007 and 2016

Characteristic	No. of Women (%) ^a
Race	
Non-Hispanic White	6538 (84.3)
Non-Hispanic Black	505 (6.5)
Hispanic	424 (5.5)
Other ^b	289 (3.7)
Poverty	
0% to <5%	1968 (25.4)
5% to <10%	2065 (26.6)
10% to <20%	2251 (29.0)
20% to 100%	1415 (18.2)
Unknown	57 (0.7)
Year of death	
2007	876 (11.3)
2008	870 (11.2)
2009	814 (10.5)
2010	873 (11.3)
2011	809 (10.4)
2012	709 (9.1)
2013	788 (10.2)
2014	715 (9.2)
2015	746 (9.6)
2016	556 (7.2)
Charlson comorbidity score	
0	4192 (54.0)
1	1871 (24.1)
2	860 (11.1)
≥3	833 (10.7)
Marital status	
Married	3027 (39.0)
Unmarried	4729 (61.0)
Residence	
Urban	7584 (97.8)
Rural	172 (2.2)
Time between diagnosis and death, y	
<1	2841 (36.6)
≥1	1452 (18.7)
≥2	3463 (44.6)
Stage at diagnosis	
Localized/regional	1215 (15.7)
Distant	5870 (75.7)
Unstaged	671 (8.7)
Histology	
Serous	5382 (69.4)
Nonserous	2374 (30.6)
Median age at death, y	80

^aPercentages may not sum to 100% because of rounding.

^bThis group was 78% Asian, 6% Pacific Islander/unknown, 10% American Indian/Alaska Native, and 6% Indian/Pakistani.

enrollment in hospice did not vary by patient race ($P = .62$). A similar pattern was seen in hospital utilization for an ICU stay, terminal hospitalization, and having multiple hospitalizations in the last 30 days of life, and a greater proportion of non-White women used these services compared with NHW women ($P < .01$). In contrast, the proportion of NHB women who had >1 ED visit was double the proportion of NHW women ($P < .01$). Among NHB

women and women in the other races group, the proportion who received life-extending procedures was nearly double that of the proportion of NHW women who received such procedures ($P < .01$). The proportion of women receiving chemotherapy in the last 2 weeks of life did not vary by patient race ($P = .43$).

The adjusted odds of no hospice or late hospice use, inappropriate hospital utilization, and receipt of aggressive treatments for each patient are presented by race in Table 3. Women in the other races group had a 76% greater odds of no hospice enrollment compared with NHW women (odds ratio [OR], 1.76; 95% CI, 1.38-2.24) (Table 3). NHB women had twice the odds of >1 ED visit compared with NHW women (OR, 2.04; 95% CI, 1.57-2.64). NHB women and women in the other races group had 60% higher odds of an ICU stay compared with NHW women (OR, 1.63 [95% CI, 1.32-2.02] vs 1.61 [95% CI, 1.24-2.10], respectively). Women in the other races group had twice the odds of a terminal hospitalization compared with NHW women (OR, 2.10; 95% CI, 1.60-2.76). All non-White women had higher odds of multiple hospitalizations compared with NHW women, and the highest OR was among NHB women (OR, 1.65; 95% CI, 1.24-2.20). The odds of receiving end-of-life chemotherapy did not differ by race. Women in the other races group had twice the odds of receiving a life-extending procedure compared with NHW women (OR, 2.01; 95% CI, 1.45-2.79), and NHB women had 90% higher odds compared with NHW women (OR, 1.89; 95% CI, 1.45-2.48) (Table 3).

The proportion of women who do not enroll in hospice has been declining since 2007 ($P < .01$); however, among enrollees, the proportion enrolling late has not improved ($P = .17$) (Fig. 2A). The proportion of women who had >1 hospitalization in the last month of life has not changed significantly over time. Although the proportion of women dying in the hospital has declined, the number admitted to the ICU has steadily increased, and the proportion with >1 ED visit also has increased (Fig. 2B). Chemotherapy in the last 2 weeks of life and the receipt life-extending procedures have remained stable over time, with 10% of receiving a life-extending procedure and 5% receiving chemotherapy in 2015 and 2016. There is a statistically significant declining trend in the proportion of women receiving invasive procedures; however, approximately 15% of women still underwent 1 such procedure in 2016 (Fig. 2C). The median hospice length of stay was 22 days and did not differ significantly over time ($P = .08$) or by race ($P = .24$).

TABLE 2. Distribution of Hospice Use, Hospital Utilization, and Aggressive End-of-Life Treatments by Race/Ethnicity Among Women With Invasive Ovarian Cancer in the Surveillance, Epidemiology, and End Results–Medicare Database Who Died Between 2007 and 2016

Race	Hospice Use			Aggressive Treatments				Inappropriate Hospital Utilization			
	No Hospice	Late Hospice	Life Extending	Invasive	Chemo	≥2 ED Visit	ICU	Terminal Hospitalization	≥2 Hospitalizations		
NHW	26.8	10.3	8.7	20	5.2	9	19.8	14.4	7.9		
NHB	35.8	10.5	16.4	28.3	6.5	18.2	29.5	23.6	13.9		
Hispanic	34.7	8.3	11.8	24.8	5.9	11.8	27.6	21.2	12.3		
Other	39.8	12.1	16.6	24.9	6.6	15.2	29.1	27	12.1		
P	<.01	.62	<.01	<.01	.43	<.01	<.01	<.01	<.01		

Abbreviations: Chemo, chemotherapy; ED, emergency department; ICU, intensive care unit; NHB, non-Hispanic Black; NHW, non-Hispanic White.

TABLE 3. Adjusted Odds Ratios and 95% CIs of the Association of Race/Ethnicity With Receipt of Aggressive End-of-Life Care for Women in the Surveillance, Epidemiology, and End Results–Medicare Database Who Died With Ovarian Cancer Between 2007 and 2016^a

Race	Hospice Use			Aggressive Treatments				Inappropriate Hospital Utilization			
	No Hospice	Late Hospice	Life-Extending	Invasive	Chemo	≥2 ED Visit	ICU	Terminal Hospitalization	≥2 Hospitalizations		
NHW	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)		
NHB	1.38 (1.13-1.68)	1.02 (0.70-1.50)	1.89 (1.45-2.48)	1.32 (1.07-1.65)	1.21 (0.82-1.79)	2.04 (1.57-2.64)	1.63 (1.32-2.02)	1.62 (1.29-2.04)	1.65 (1.24-2.20)		
Hispanic	1.36 (1.10-1.68)	0.76 (0.49-1.18)	1.27 (0.92-1.73)	1.15 (0.91-1.46)	1.06 (0.69-1.63)	1.23 (0.90-1.68)	1.44 (1.15-1.81)	1.45 (1.13-1.86)	1.45 (1.07-1.98)		
Other	1.76 (1.38-2.24)	1.19 (0.74-1.90)	2.01 (1.45-2.79)	1.23 (0.93-1.63)	1.21 (0.75-1.97)	1.76 (1.26-2.47)	1.61 (1.24-2.10)	2.10 (1.60-2.76)	1.53 (1.06-2.21)		

Abbreviations: aOR, adjusted odds ratio; Chemo, chemotherapy; ED, emergency department; ICU, intensive care unit; NHB, non-Hispanic Black; NHW, non-Hispanic White; Ref, reference group.

^aModels are adjusted for nonurban residence, age of death, time between diagnosis and death, Charlson score, census tract poverty, and marital status.

aOR (95% CI)

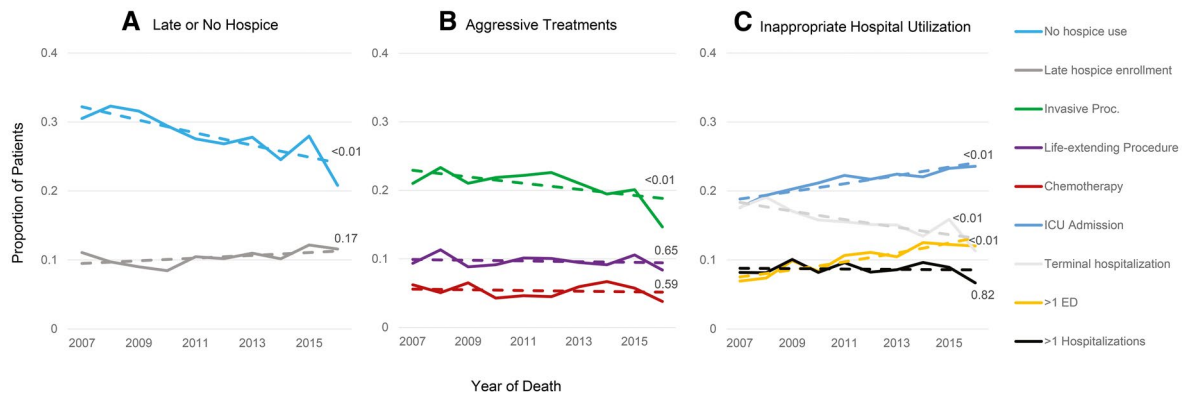


Figure 2. The adjusted yearly proportions of women with invasive ovarian cancer in the Surveillance, Epidemiology, and End Results (SEER)-Medicare database who experienced (A) no or late hospice use, (B) aggressive treatments, and (C) inappropriate hospital utilization in their last month of life are illustrated. Models are adjusted for nonurban residence, age of death, time between diagnosis and death, Charlson score, census tract poverty, and marital status. ED indicates emergency department; ICU, intensive care unit; Invasive Proc., invasive procedures.

Sensitivity Results

In total, 6167 women had a cancer cause of death (results not shown). Medicare records indicate that 556 women died in 2016; however, these women did not have a cause of death available in SEER, so they were excluded from the sensitivity analysis. In the sensitivity analysis for race, we observed the same pattern of results for the associations. The trendline patterns were also the same as those observed when we did not restrict the analysis by cause of death, and annual estimates were not meaningfully different. The greatest difference was observed for hospice services, in which from 4% to 6% fewer women had no hospice enrollment or late hospice enrollment; however, the pattern of declining failure to use hospice and late enrollment was the same. The results were not meaningfully different when the models were adjusted for stage of diagnosis rather than time from diagnosis to death.

DISCUSSION

In this national sample of women with ovarian cancer, the use of aggressive end-of-life care persisted from 2007 through 2016, and there were notable racial disparities. NHB women were approximately twice as likely to have >1 ED visit or a life-extending procedure compared with NHW women. Women in the other races group also were twice as likely as NHW women to have a terminal hospitalization and receive life-extending procedures. Although it has been demonstrated that racial disparities in end-of-life care vary regionally for other cancers,²¹ to our knowledge, this is the first study to demonstrate that racial disparities exist nationally in the use of aggressive end-of-life care for women with ovarian cancer.

Although endorsements for less aggressive end-of-life care and an emphasis on integrating palliative care have increased in recent years, after nearly a decade since Wright et al evaluated trends in aggressive care among women with ovarian cancer, trends in aggressive care persisted from 2007 to 2016.⁶ End-of-life hospital utilization, including ICU and ED use, is climbing. It is equally as concerning that the use of aggressive treatments at the end of life, including chemotherapy and life-extending procedures, has not declined since 2007. Despite more women enrolling in hospice and fewer women dying in the hospital, the median length of hospice stay has not changed over time. Building off the methods used by Wright et al to calculate adjusted annual proportions of aggressive care, we leveraged the rigor and detail of SEER cancer data to define our cohort based on diagnosis of a first and only ovarian cancer, rather than restricting the analysis to an ovarian cancer cause of death. Wright et al previously reported that approximately 50% of women enrolled in hospice in 2007, whereas the rate was closer to 70% in our national sample. This difference may be caused in part by the differential attribution of death among hospice patients, resulting in the inclusion of fewer hospice patients in the cohort studied by Wright and colleagues. The proportion of women enrolling in hospice in our study is very similar to that reported by Taylor et al for women dying of ovarian cancer in the Texas-Medicare data.⁷ We also observed similar results when conducting sensitivity analysis in which the cohort was defined by cancer cause of death. Similar to the patterns observed in other cancers, these results suggest that the use of aggressive end-of-life care persists among women with ovarian

cancer.²²⁻²⁵ Our findings build on these prior studies by including nearly a decade of new data reflecting end-of-life care at a time when there was increased emphasis on improving the quality of this care and expanding it to a national scope.

Our finding that notable racial disparities exist in the use of aggressive end-of-life care among women with ovarian cancer is in line with previous single-state and single-institution studies that reported differences in hospice enrollment and aggressive end-of-life care by race, with the greatest differences observed among NHB women and women of other races.^{7-9,26} In contrast to Taylor et al, we observed slightly lower rates of late hospice enrollment nationally and did not observe a statistically significant difference in late hospice enrollment by race. This may be caused in part by the different racial/ethnic compositions of the 2 cohorts.⁷ Prior research has demonstrated that racial differences in end-of-life care intensity are more pronounced in high-expenditure areas.²¹ In addition, differences in end-of-life care intensity may also reflect regional variations or physician preferences.²⁷⁻²⁹ Although many studies have reported that non-White patients have different end-of-life care preferences than NHW patients, the reasons for these differences are multifaceted and not well understood.³⁰ Future work disentangling these reasons and accounting for social context will be crucial to ensure that patients are receiving care that is in line with decisions they made having an accurate understanding of the implications for both length and quality of life.

In this study, we evaluated hospice use, hospital utilization, and aggressive treatment metrics derived to reflect the high cost care known to result in low quality of life and poorer outcomes.^{4,6,15,31,32} These are important targets for improvement, but the path to reversing these trends and lessening racial disparities is complex. Payment reform models, such as the Oncology Care Model (OCM), have emphasized advanced care planning and early integration of palliative care to prevent aggressive end-of-life care but, to date, have had a limited effect on reducing the use of end-of-life care.^{33,34} After 3 OCM-designated periods, OCM practices have reduced end-of-life hospitalizations but have had no significant impact on ED use, chemotherapy receipt, hospice enrollment, duration of hospice, or timing of hospice.³³ The Medicare Shared Services Program also has not seen a consistent decline in aggressive end-of-life care among participating providers.³⁵ Given the limited impact of these newer payment models to date, future work is needed to also understand patient and physician factors that increase the use of aggressive end-of-life care. The need to focus on patient

and physician factors driving end-of-life utilization is evident in the first OCM progress report, which highlights physician comments regarding reluctance to lose trust from minority and immigrant patients by bringing up advanced care planning and end-of-life discussions. This resulted in physicians leaving it to the patient to bring forward a transition in care goals.³⁴ Physicians may have preconceived ideas of what certain patients will accept for end-of-life care, including that Black patients prefer more aggressive care.³⁶ Without understanding patient and physician factors that influence end-of-life care decisions, efforts to reduce overuse and decrease racial disparities in care aggressiveness, such as tailored interventions, will be limited. This area is particularly important for future studies in ovarian cancer because the pattern of recurrence, poor prognosis, limited treatment options, and loss of sensitivity to chemotherapy make end-of-life care in ovarian cancer somewhat unique.³⁷

Although our study examined national trends in the use of end-of-life care among a large, diverse sample of women with ovarian cancer, it has several potential limitations that warrant comment. First, Medicare coverage begins at age 65 years and is limited to non-health maintenance organization coverage. The generalizability of our findings is limited to older women diagnosed with ovarian cancer and may not reflect all women with Medicare because of the managed care exclusion. In addition, these findings are also generalizable to SEER catchment areas, which are more urban than non-SEER areas. However, our data include a national cohort with >9 years of recent data that reflect care patterns since palliative care became a specialty and since organizations have highlighted the importance of high-quality, less intensive end-of-life care. Second, NHB women are often diagnosed at earlier ages; therefore, the NHB women in our sample may be healthier or better resourced than women who were not included.³⁸ However, this would result in a conservative estimate of the racial differences observed in the study. Third, we combined women with distinct races and ethnicities into an other races group because of small numbers, which limits our ability to assess the diversity and unique experiences of their end-of-life care. Fourth, a change in coding from the ninth to the tenth revision of the International Classification of Diseases coincided with our last year of data, potentially affecting consistency of measurement for the aggressive treatments (invasive and or life-extending procedures and chemotherapy). This may exaggerate the decline in invasive procedures, although we also observed declines based on Current Procedural Terminology coding, which did not change between 2015 and 2016.

Finally, we could not determine the intention behind the procedures received, the patient's preferences in receiving them, or the context for the racial disparities we observed. However, the markers for aggressive care that we used are well established as indicative of the quality of end-of-life care and were designed for measurement from claims data.^{4,5,39} Future studies delving into the mechanisms behind these findings are needed.

Conclusion

Despite guideline recommendations from clinical and quality organizations and emphasis on early palliative care, the quality of end-of-life care for women with ovarian cancer has not improved. A substantial proportion of women are receiving aggressive care, ED and ICU use are increasing, and the risk is even greater among non-White women. These trends suggest that a better understanding of what is driving physician and patient decisions is needed so we can effectively target interventions, inform policies to minimize high-cost/low-value care, and decrease the number of women with ovarian cancer who receive nonevidence-based, aggressive care at the end of their lives.

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CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

AUTHOR CONTRIBUTIONS

Megan A. Mullins: Developed the project idea and design, performed the data analysis, wrote the initial draft, and provided critical revisions. **Julie J. Ruterbusch:** Assisted in the data analysis and provided critical revisions. **Philippa Clarke:** Developed the project idea and design and provided critical revisions. **Shitanshu Uppal:** Developed the project idea and design and provided critical revisions. **Lauren P. Wallner:** Developed the project idea and design and provided critical revisions. **Michele L. Cote:** Developed the project idea and design and provided critical revisions.

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