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**Title:** Trends and racial disparities in aggressive end of life care for a national sample of women with ovarian cancer

**Running Title:** End of life care trends and disparities

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**Precis:** Despite the recent emphasis on reducing aggressive end of life care, no/late hospice use, aggressive treatment, and inappropriate hospital utilization persist among women with ovarian cancer who are at the end of life, and this care is most aggressive for Nonwhite women.

### **ABSTRACT**

**Background:** The clinical landscape has moved towards 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. We evaluated current national trends and racial disparities in end-of-life care among women with ovarian cancer, using the Surveillance, Epidemiology and End Results (SEER) linked Medicare dataset.

**Methods:** We identified 7,756 Medicare beneficiaries over age 66 with ovarian cancer dying between 2007 and 2016. We examined trends and racial disparities in late or no hospice use, more than one emergency department (ED) visit, intensive care unit (ICU) admission, more than one 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 ICU 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 ( $p < .001$ ). Nonwhite 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 visits (OR 2.04 CI 1.57-2.64) or life extending procedures (OR 1.89 CI 1.45-2.48) compared to 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 Nonwhite women.

**Key Words:** hospice care, ovarian cancer, terminal care, racial disparity

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## 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, as end-of-life concerns are more likely to occur sooner in the course of cancer care.<sup>1</sup> Clinical consensus suggests high-quality end-of-life care includes enrollment in hospice when a patient has a prognosis that is less than six months, and does not include receipt of intensive or invasive care.<sup>2,3</sup> Not meeting these quality standards indicates aggressive end-of-life care.<sup>4,5</sup>

Prior studies have found that despite increasing hospice use over time, end of life care for women with ovarian cancer was aggressive, and that end-of-life care was more aggressive for non-white women.<sup>6-9</sup> However, these findings reflect trends only through 2007, and to date, only examine racial disparities from a single state (Texas).<sup>6,7</sup> 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 (ASCO) goal was for palliative care to be integrated into cancer care by 2020.<sup>10</sup> Current guidelines and recommendations by ASCO 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 non-aggressive end-of-life care.<sup>2,10,11</sup>

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

## **METHODS**

### *Data*

This analysis used data from the linkage of SEER registry data and Medicare claims data from years 2000-2016.<sup>12</sup> The SEER program is comprised of 18 population-based cancer registries collecting information on all residents of their catchment areas who are diagnosed with invasive cancer. SEER data includes patient demographics, tumor characteristics, first course of treatment, and survival. The SEER-Medicare linkage yields treatment and outcomes for roughly 25% of elderly cancer patients in the US. Cause of death data is attained through a linkage with the National Death Index.<sup>13</sup>

### *Cohort Selection*

Women 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 is problematic in identifying the underlying cancer cause of death and SEER cancer diagnosis data is very rigorous, we defined our cohort by ovarian cancer diagnosis and restricted to first and only cancers (with the exception of basal and squamous cell skin carcinomas) in order to avoid attributing receipt of therapy from another cancer. To facilitate measurement of comorbidity, the sample was restricted to women over age 66 at the time of cancer diagnosis, who had complete case information captured by a SEER registry (n=16,661). To ensure complete treatment information, we excluded patients who were not enrolled in both Part A and Part B Medicare, or who were enrolled in an HMO plan in the 12 months prior to diagnosis, or at any point from the time of diagnosis through the end of study observation (n=5,089). We excluded cases with: unknown month of diagnosis or death, death within 30 days of diagnosis, alive before December 2016, discrepancies between SEER and Medicare birth or death dates, diagnosis at death or autopsy, non-invasive disease, no claims after diagnosis, and hospice admission date predating diagnosis (n=3,816). In total, 7,756 women with ovarian cancer were

included in our analytic sample (Figure 1). The Wayne State University Institutional Review Board determined the 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 (Supplemental Table S1) based on prior definitions and updated with ICD10 coding.<sup>6,7</sup> Hospice use measures included failure to enroll in hospice (no hospice), or less than 3 days of hospice prior to 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, pelvic exam with tissue sampling).<sup>7,14</sup> Hospital utilization measures included >1 ED) visit or hospital admission, ICU) admission, and death in an acute care hospital.<sup>4,5,15,16</sup> These metrics align with NQF guidelines for quality end-of-life care.<sup>6,15,17</sup> 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.<sup>18</sup> We calculated a modified Charlson Index score for each patient from the 12 months prior to diagnosis.<sup>19,20</sup> Census tract poverty was provided by SEER based on patient's residential address. A priori-identified confounders included: non-urban residence, age of death, time between diagnosis and death (<1 year, 1-<2 years, 2+ years), Charlson score (0,1,2,3+), census tract poverty (0-<5%, 5-<10%, 10-<20%, 20-100%, unknown) and marital status (married/unmarried).

### *Statistical Analysis*

To examine trends over time, the average predicted probability of each binary outcome was calculated using logistic regression, making a prediction for each subject in each year with adjustment for patient characteristics and confounders as detailed previously.<sup>6</sup> The association of year and hospice length of stay was evaluated with the Mann-Whitney U test due to the skewed distribution. To examine the association between race/ethnicity and each outcome, we

first assessed differences in the bivariate distributions using chi-squared tests. We then 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 with the Mann-Whitney U test because of the skewed distribution.

Sensitivity analyses were conducted to assess the robustness of enumerating our cohort based on first and only ovarian cancer diagnosis. We restricted our cohort in these analyses to women with first and only ovarian cancer 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 two-tailed p-value of <0.05 was considered statistically significant.

## RESULTS

The majority of the cohort was Non-Hispanic White (NHW) (84.3%), lived in census tracts with less than 20% poverty (81%), had no co-morbidities (54%), were not currently married (61%), lived in urban areas (97.8%), and survived less than 2 years after diagnosis (55.3%). The median age of death was 80. The median time from diagnosis to death was 20.2 months (Table 1).

The proportion of women with aggressive end-of-life care varied by race for hospice use, hospital utilization, and treatment receipt (Table 2). Compared to NHW women, approximately 10% more nonwhite women did not enroll in hospice ( $p < 0.01$ ). Late enrollment in hospice did not vary by patient race ( $p = 0.62$ ). 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 where a greater proportion of nonwhite women used these services compared to NHW women ( $p < 0.01$ ). In contrast, the proportion of NHB women with >1 ED visits was double the proportion of NHW women ( $p < 0.01$ ). NHB and other races grouped women had nearly double the proportion of women receiving a life extending procedure compared to NHW ( $p < 0.01$ ). The proportion of women receiving chemotherapy in the last two weeks of life did not vary by patient race ( $p = 0.43$ ).

Adjusted odds of no or late hospice use, inappropriate hospital utilization, and receipt of aggressive treatments for each patient race are presented in Table 3. Other races grouped women had a 76% greater odds of no hospice enrollment compared to NHW (OR 1.76 CI 1.38-2.24) (Table 3). NHB women had twice the odds of >1 ED visits compared to NHW women (OR 2.04 CI 1.57-2.64). NHB and Other race women had 60% higher odds of an ICU stay when compared to NHW (OR 1.63 CI 1.32-2.02; OR 1.61 CI 1.24-2.10 respectively). Other races grouped women had twice the odds of a terminal hospitalization compared to NHW (OR 2.10 CI 1.60- 2.76). All nonwhite women had higher odds of multiple hospitalizations compared to NHW, with the highest for NHB (OR 1.65 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 NHW of receiving a life extending procedure, (OR 2.01 CI 1.45-2.79) and NHB had 90% higher odds compared to NHW (OR 1.89 CI 1.45-2.48) (Table 3).

The proportion of women not enrolling in hospice has been declining since 2007 ( $p < 0.01$ ), but among enrollees, the proportion enrolling late has not improved ( $p = 0.17$ ) (Figure 2A). The proportion of women with more than one 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 increased (Figure 2B). Chemotherapy in the last two weeks of life and receiving 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, but around 15% of women still had one in 2016 (Figure 2C). Median hospice length of stay was 22 days, and did not differ significantly over time ( $p = 0.08$ ) or by race ( $p = 0.24$ ).

### *Sensitivity Results*

6,167 women had a cancer cause of death (results not shown). Medicare records indicate 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 saw the same pattern of results for the associations. The trendline patterns were also the same as when we did not restrict by cause of death, and annual estimates were not meaningfully different. The most difference was seen for hospice services where 4-6% 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. Results were not meaningfully different when 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 2007-2016, and there were notable racial disparities. NHB women were approximately twice as likely to have >1 ED visit or a life extending procedure compared to NHW women. The Other races group was also twice as likely as NHW to have a terminal hospitalization and receive life extending procedures. While racial disparities in end of life care have been shown to vary regionally for other cancers,<sup>21</sup> to our knowledge, this is the first study to demonstrate that racial disparities exist in the use aggressive end-of-life care for women with ovarian cancer nationally.

Despite endorsements for less aggressive end-of-life care and an emphasis on integrating palliative care increasing 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.<sup>6</sup> End of life hospital utilization, including ICU and ED utilization, is climbing. Equally as concerning, aggressive treatments at the end of life, including chemotherapy and life-extending procedures, have 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 employed 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 first and only ovarian cancer, rather than restricting to ovarian cancer cause of death. Wright et al. previously found about 50% of women enrolling in hospice in 2007, whereas we found closer to 70% in our national sample. This difference could in part be due to differential attribution of death among hospice patients resulting in fewer hospice patients being included in Wright et al's cohort. The proportion of women enrolling in hospice in our study is very similar to those reported by Taylor et al. for women dying of ovarian cancer in Texas-Medicare.<sup>7</sup> We also found similar results when conducting sensitivity analysis defining the cohort by cancer cause of death. Similar to patterns seen in other cancers, these results suggest that the use of aggressive end of life care persists among women with ovarian cancer.<sup>22-25</sup> Our findings build upon these prior studies by

including nearly a decade of new data reflecting end of life care in a time with increased emphasis on improving the quality of this care, and expanding 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 institution studies which found differences in hospice enrollment and aggressive end of life care by race, with the largest differences seen among NHB and Other races group women.<sup>7,8,26,27</sup> In contrast to Taylor et al., we found slightly lower rates of late hospice enrollment nationally, and did not see a statistically significant difference in late hospice enrollment by race. This may in part be due to the different racial/ethnic compositions of the two cohorts.<sup>7</sup> Prior research has shown that racial differences in end-of-life care intensity are more pronounced in high expenditure areas.<sup>21</sup> In addition, differences in end of life care intensity may also reflect regional variation, or physician preferences.<sup>28-30</sup> Although many studies have found that nonwhite patients have different end of life care preferences than NHW patients, the reasons for these differences are multifaceted and not well understood.<sup>31</sup> Future work disentangling these reasons and accounting for social context is 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 high cost care known to result in low quality of life and poorer outcomes.<sup>6,15,32-34</sup> 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 in order to prevent aggressive end-of-life care, but to date have had limited impact on reducing end of life utilization.<sup>35,36</sup> After three periods, OCM practices have reduced end of life hospitalizations, but had no significant impact on ED use, chemotherapy receipt, hospice enrollment duration of hospice or timing of hospice.<sup>35</sup> The Medicare Shared Services Program has also not seen consistent decline in aggressive end of life care among participating providers.<sup>37</sup> Given the limited impact of these newer payment models to date, future work is needed to also understand patient and physician-factors, which 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 highlighting 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.<sup>36</sup> Physicians may have preconceived ideas of what certain patients will accept for end-of-life care, including that black patients prefer more aggressive care.<sup>38</sup> 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.<sup>39</sup>

While our study examined national trends in end of life care utilization among a large, diverse sample of women with ovarian cancer, this study has several potential limitations that warrant comment. First, Medicare coverage begins at age 65 and is limited to non-HMO coverage. . The generalizability of our findings is limited to older women diagnosed with ovarian cancer and may not reflect all women with Medicare due to the managed care exclusion. Additionally, these findings are also generalizable to SEER catchment areas, which are more urban than non-SEER areas. However, our data includes a national cohort with over 9 years of recent data that reflect care patterns since palliative care became a specialty and 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 are not included.<sup>40</sup> However, this would result in a conservative estimate of the racial differences found in this study. Third, we combined women with distinct races and ethnicities into an Other races group due to small numbers, which limits our ability to assess the diversity and unique experiences of their end of life care. Fourth, a change from ICD9 to ICD10 coding coincided with our last year of data, potentially impacting 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 saw declines based on CPT coding which did not change between 2015 and 2016. Finally, we cannot determine the intention behind procedures received, the patient's preferences in receiving them, nor the context for the racial disparities we see. However, the markers for aggressive care that we used are well established as indicative of quality of end-of-life care and designed for measurement from claims data.<sup>5,32,41</sup> 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, end of life quality of 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 higher among nonwhite women. These trends suggest 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 receiving non-evidence based aggressive care at the end of their lives.

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## TABLE AND FIGURE LEGENDS

Table 1: Demographic and clinical characteristics of women in SEER-Medicare with invasive ovarian cancer dying between 2007 and 2016.

Table 2: Distribution of hospice use, hospital utilization and aggressive end of life treatments by race/ethnicity among women with invasive ovarian cancer in SEER-Medicare who died between 2007 and 2016.

Table 3: Adjusted Odds Ratios and 95% Confidence Intervals of the association of race/ethnicity with receipt of aggressive end of life care for women in SEER-Medicare dying with ovarian cancer between 2007 and 2016. Models are adjusted for non-urban residence, age of death, time between diagnosis and death, Charlson score, census tract poverty and marital status.

Figure 1: Patient exclusion flow diagram.

Figure 2: Adjusted yearly proportion of women with invasive ovarian cancer in SEER-Medicare who experienced no or late hospice use (2A), aggressive treatments (2B), and inappropriate hospital utilization (2C) in their last month of life. Models are adjusted for non-urban residence, age of death, time between diagnosis and death, Charlson score, census tract poverty and marital status.

Supplemental Table 1: Medicare claims codes for aggressive treatments and inappropriate hospital utilization.

**Table 1:** Demographic and clinical characteristics of women in SEER-Medicare with invasive ovarian cancer dying between 2007 and 2016.

	N	% <sup>a</sup>
<b>Race</b>		
Non-Hispanic White	6,538	84.3
Non-Hispanic Black	505	6.5
Hispanic	424	5.5
Other <sup>b</sup>	289	3.7
<b>Poverty</b>		
0-<5%	1,968	25.4
5 -<10%	2,065	26.6
10-<20	2,251	29.0
20 to 100	1,415	18.2
Unknown	57	0.7
<b>Year of Death</b>		
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
<b>Charlson Comorbidity Score</b>		
0	4,192	54.0
1	1,871	24.1
2	860	11.1
3+	833	10.7
<b>Marital Status</b>		
Married	3,027	39.0
Unmarried	4,729	61.0
<b>Residence</b>		
Urban	7,584	97.8
Rural	172	2.2

<b>Years Between Diagnosis and Death</b>		
<1	2,841	36.6
1+	1,452	18.7
2+	3,463	44.6
<b>Stage at Diagnosis</b>		
Localized/Regional	1215	15.7
Distant	5870	75.7
Unstaged	671	8.7
<b>Histology</b>		
Serous	5382	69.4
Nonserous	2374	30.6
<b>Median Age at Death</b>		80

a. May not sum to 100 due to rounding

b. This group is 78% Asian, 5% Pacific Islander, 10% American Indian/Alaska Native, 6% Indian/Pakistani, 1% unknown

**Table 2:** Distribution of hospice use, hospital utilization and aggressive end of life treatments by race/ethnicity among women with invasive ovarian cancer in SEER-Medicare who died between 2007 and 2016

Race	Hospice Use		Aggressive Treatments			Inappropriate Hospital Utilization			
	No Hospice	Late Hospice	Life Extending	Invasive	Chemo	2+ ED	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	<0.01	0.62	<0.01	<0.01	0.43	<0.01	<0.01	<0.01	<0.01

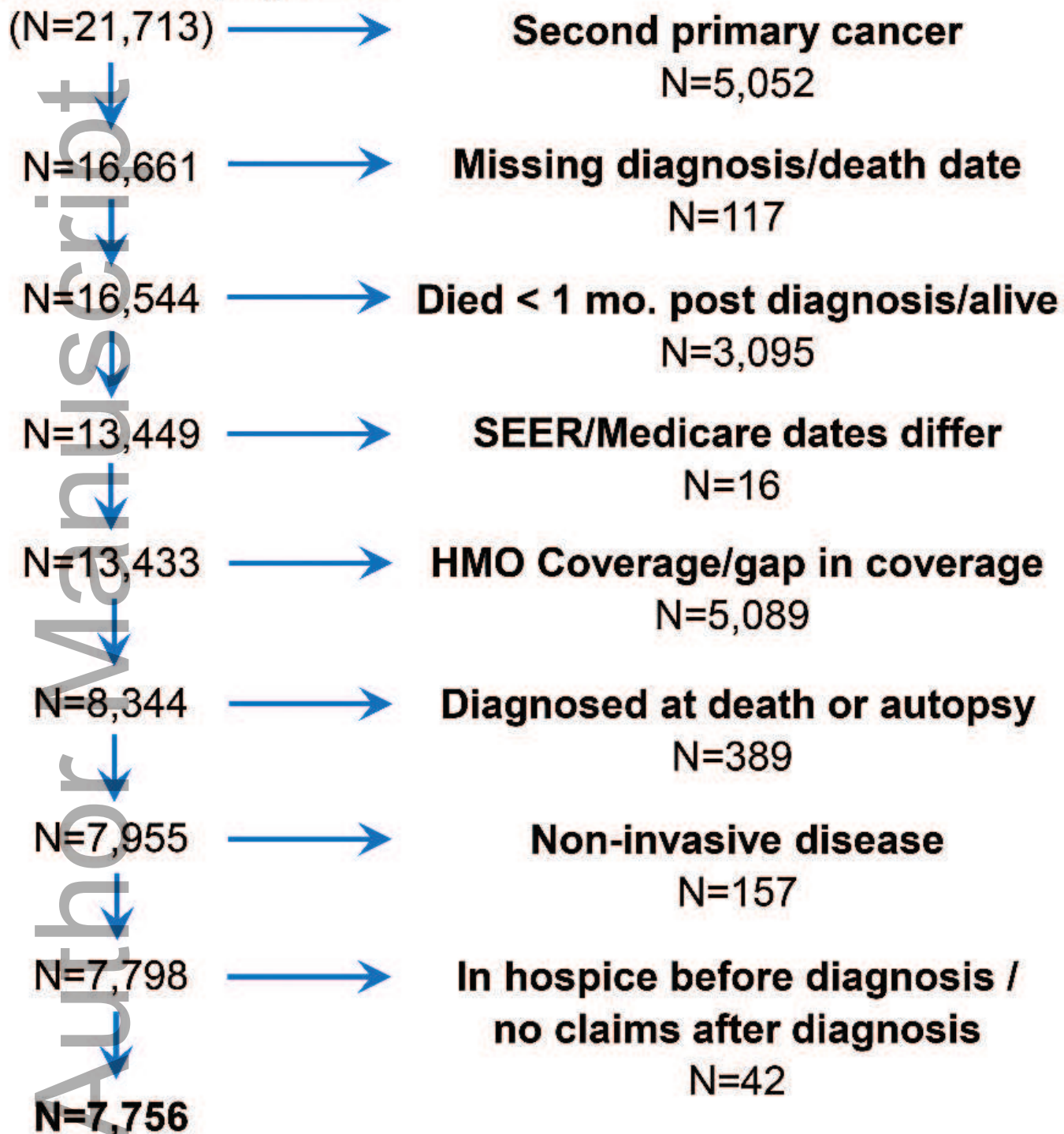
**Table 3:** Adjusted Odds Ratios and 95% Confidence Intervals of the association of race/ethnicity with receipt of aggressive end of life care for women in SEER-Medicare dying with ovarian cancer between 2007 and 2016. Models are adjusted for non-urban residence, age of death, time between diagnosis and death, Charlson score, census tract poverty and marital status.

Race	Hospice Use		Aggressive Treatments			Inappropriate Hospital Utilization			
	No Hospice	Late Hospice	Life Extending	Invasive	Chemo	2+ ED	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)

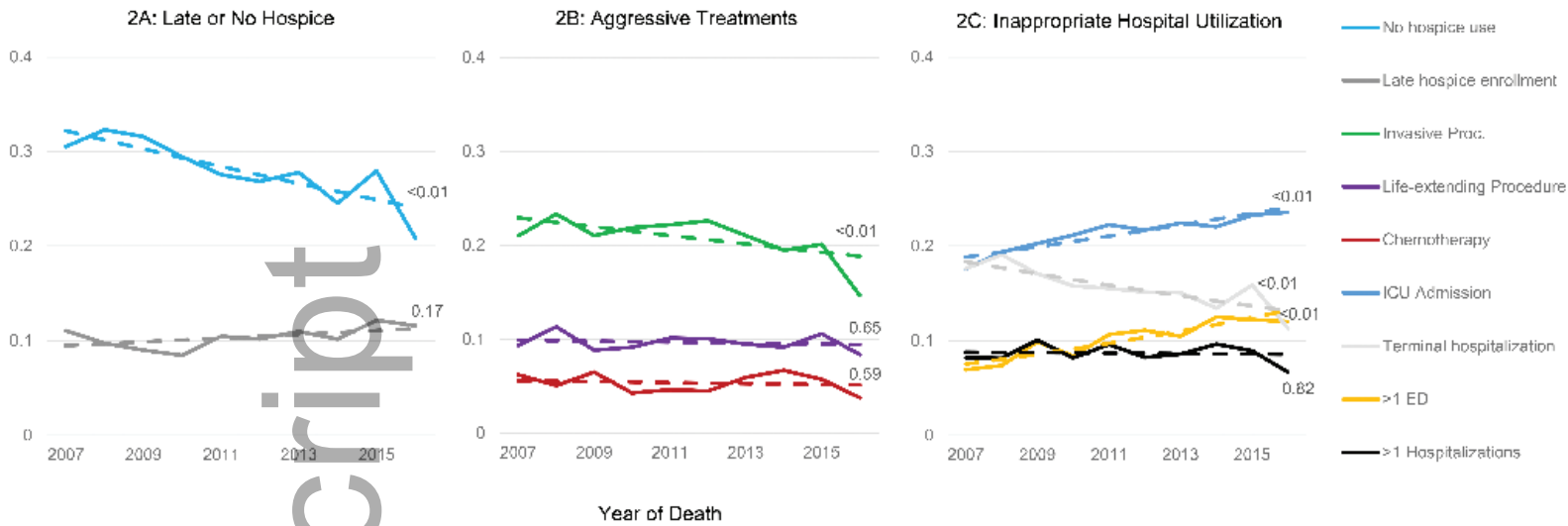
Other	1.76 (1.38, 2.24)	1.19 (0.74, 1.90)	2.01 (1.45, 2.79)	1.23 (0.93, 1.63)	1.21 (0.75, 1.97)	1.76 (1.26, 2.47)	1.61 (1.24, 2.10)	2.10 (1.60, 2.76)	1.53 (1.06, 2.21)
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**Invasive ovarian cancer cases  
who died 2007-2016, age ≥66**



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