Disparities in cancer-specific and overall survival in black women with endometrial cancer: A Medicare-SEER study

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ABSTRACT

Objectives: To examine overall survival (OS) and cancer-specific survival (CSS) for different racial groups of women with surgically staged endometrial cancer by histologic subtype.

Methods: This is a retrospective cohort study of women with stage I-III endometrioid, serous, clear cell, and carcinosarcoma who underwent hysterectomy as primary surgical staging in the 2000–2016 SEER-Medicare database. OS and CSS outcomes were stratified by race (defined as White, Black, Other), stage, and histology. Survival was assessed with descriptive analyses, log-rank tests and unadjusted and adjusted multivariable cox regression models.

Results: Of the 24,142 women identified, 85.5% were White, 8.5% Black, and 6% other races. Receipt of adjuvant therapy differed only for stage III endometrioid: Black women were less likely to receive adjuvant treatment after hysterectomy (61.2% vs. 70.1% White, \( p = 0.03 \)). For stage I, Black women had worse CSS for all histologies other than clear cell in unadjusted and adjusted analyses. For stage II, Black women had worse CSS for endometrioid histology in unadjusted analyses and similar OS. For stage III, Black women with endometrioid carcinoma had worse CSS and OS in unadjusted analyses, but no significant difference in CSS in adjusted analyses. “Other” race showed improved OS for Stage I endometrioid adenocarcinoma without significant differences in outcomes when compared to White women.

Conclusion: Across histologies other than clear cell, Black women diagnosed with stage I endometrial cancer had consistently worse CSS, despite similar receipt of adjuvant therapy. Differences in CSS and OS at higher stages disappeared once accounting for treatment disparities.

1. Introduction

Endometrial cancer is the most common gynecologic cancer with over 66,000 new cases expected to be diagnosed in the United States in 2021 (Cancer Stat Facts, 2021). While the 5-year relative survival rate for women diagnosed with endometrial cancer is over 80% (Cancer Stat Facts, 2021), not all women diagnosed with endometrial cancer can expect similar outcomes (Cote et al., 2015; Bregar et al., 2017). White and Black women are diagnosed with endometrial cancer at similar rates; however Black women are almost twice as likely to die from endometrial cancer (Cancer Stat Facts, 2021; Cote et al., 2015; Bregar et al., 2017).

Research into causes for such disparities have shown many possible etiologies. While racial disparities in endometrial cancer are

Abbreviations: CSS, Cancer-specific survival; OS, Overall survival; SEER, Surveillance Epidemiology and End Results Database; NCCN, National Comprehensive Cancer Network.

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multifactorial, one known factor is that Black women tend to be diagnosed with more aggressive endometrial cancer subtypes and at later stages, which plays a role in their relative prognosis (Sud et al., 2018). Previous studies have also shown that non-White women are less likely to receive National Comprehensive Cancer Network (NCCN) guideline concordant treatment for endometrial cancer. Black women diagnosed with endometrial cancer have been shown to have worse survival rates on a stage for stage basis as well as across histologic subtypes compared to White women (Kaspers et al., 2020; Horne et al., 2020; Huang et al., 2020; Dholakia et al., 2020). Many studies have shown these disparities in outcomes; however, these studies included heterogeneously treated women and were unable to differentiate cancer-specific survival. To develop effective disparity-reducing interventions, there is a need for evidence to compare survival in women who variably received adjuvant chemotherapy and to distinguish racial disparities in overall survival versus cancer specific survival rates (Cheung, 2013; Ruterbusch et al., 2014; Olson et al., 2015).

Our objective was to evaluate how cancer-specific survival (CSS) and overall survival (OS) differs for Black and White women with similar staging and histology when all women are insured and receive primary surgical staging. Understanding the disparities in outcome after primary surgical treatment is vital to improving care of women with endometrial cancer.

2. Methods

Our study is a retrospective cohort study using the Surveillance, Epidemiology, and End Results (SEER)-Medicare Database and included all women diagnosed with endometrial cancer who underwent primary surgical staging with hysterectomy from 2000 to 2015. Follow-up survival data was recorded through 2016. Women in this database are those diagnosed with cancer that are enrolled in Medicare, which includes women 65 or older or those younger with a disability (Warren et al., 2002). Demographic data included race, age, income, geographical region, and Charlson comorbidity index. Data regarding lymph node dissection at the time of surgery, surgery type, cancer histology, grade, FIGO stage, and treatment sequencing were compiled as previously described (Ko et al., 2020). This study was deemed exempt by the University of Pennsylvania Institutional Review Board, IRB # 824,875 (May 2016).

Race information was drawn from the SEER database. For analysis purposes, race-based populations included Black and White. We collapsed all other race entities (including Hispanic, Asian, Native American, other, and unknown) into “Other”, given their comparatively small sample sizes. For the purposes of this study, adjuvant therapy is defined as any patients who receive any combination of chemotherapy or radiation after primary surgical staging of their disease. Adjuvant therapy is currently recommended for women with Stage IB and above endometrioid adenocarcinoma (EAC) endometrial cancer (depending on specific risk factors, including patient age, grade, and the presence of LVS) and Stage IA and above for other histologies per NCCN Guidelines (Abu-Rustum et al., 2021). Survival outcomes included estimated 5-year OS and CSS. Survival outcomes by race were separately calculated for OS and CSS for each stage and histologic subtype. The adjusted OS and CSS models for stage I, II, and III EAC included race, age, geographic region, patient income, Charlson comorbidity index, surgery type, postoperative treatment sequencing, nodes dissection, FIGO substage (where applicable), and tumor grade (where applicable). The adjusted OS and CSS models for stage I, II, and III serous, clear cell, and carcinosarcoma included all the above except sub-stage (Stage IA vs. IB) and grade (not applicable in these histologies).

Descriptive analyses were performed on demographic, clinical, pathologic, and treatment variables using chi-squared test as all variables were defined as categorical. We estimated survival curves using the Kaplan-Meier method. Log rank tests were performed to compare survival differences. Multivariable Cox regression models were used to compare both unadjusted and adjusted relative hazard ratios of survival and their 95% confidence intervals. All statistical tests were two-sided, and differences were considered statistically significant at p ≤ 0.05. We used SAS v9.4 (SAS Institute, Cary, NC) for analyses.

3. Results

3.1. Study Population:

From 2000 to 2015, 24,142 women with stage I-III endometrial cancer undergoing primary hysterectomy were identified, of whom 85.5% were White, 8.6% Black, and 5.9% other. There were 19,351 stage I (80.1%) cases, 1,484 stage II (6.2%), and 3,307 stage III (13.7%) cases. By histology, there were 20,373 EAC (84.4%), 1,994 (8.3%) serous, 433 (1.8%) clear cell, and 1,342 (5.6%) carcinosarcoma cases. Overall, among Black women with endometrial cancer, 64.1% had endometrioid histology, 18.4% serous, 14.1% carcinosarcoma, and 3.5% clear cell, in comparison to White women, of which 86.6% had endometrioid, and only 7.0% serous, 4.7% carcinosarcoma, and 1.6% clear cell. (Table 1) Age at diagnosis was lower for Black women with EAC histology of all stages and for stage I and III serous histology. Black women more frequently resided in the South across all stages and histologies, comprised of a larger proportion in the lowest income bracket (<$40 K/year) and had the greatest proportions residing in metropolitan areas, across all stage and histologies. There was no difference by race for having undergone surgical nodal assessment by race for all stages and histologies aside from stage I endometrioid, where slightly more Black women (63%) underwent nodal dissection compared to White (58.9%) (p < 0.0001). Overall, there were no differences in receipt of adjuvant therapy by race for all stages and histologies, except for stage III EAC: Black women were less likely to receive adjuvant therapy (38% had no adjuvant therapy) compared to 30% for White women and 24% for Other (OR 0.68, p = 0.03). (Table 2)

3.2. Overall survival

Within each stage and with histologies combined, OS was lower for Black women (Stage I log-rank p < 0.0001; Stage II log-rank p = 0.0001; Stage III log-rank p < 0.0001). (Fig. 1) Outcomes are significantly worse for Black women in Stage I EAC (p < 0.0001), serous (p = 0.0004), and carcinosarcoma (p = 0.05), as well as Stage III EAC (p = 0.007). Other races had significantly better OS in stage I EAC (p = 0.02). (Fig. 2)

When stratified by stage and histology, log-rank analyses showed significantly different survival for some stages and histologic subtypes, but not others. For stage I EAC endometrial cancer, Black women had lower probability of 5-year OS (0.78, 95% CI 0.75–0.80) compared to White (0.85, 95% CI 0.84–0.85) or other races (0.85, 95% CI 0.83–0.88). For stage I serous, Black women had a lower OS of 0.52 (95% CI 0.44–0.60), compared to White women (0.67, 95% CI 0.64–0.71), or others (0.77, 95% CI 0.65–0.85). In contrast for stage II, no significant differences in probability of 5-year OS were seen by race (log rank p-values all > 0.05) for any histology. For stage III, significant differences in survival by race were also identified for EAC, where White women had 5-year OS of 0.50 (95% CI 0.47–0.52) compared to Black women (0.38, 95% CI 0.31–0.56), and others (0.57, 95% CI 0.48–0.65).

Table 1

| Total number of cases endometrial cancer by race, stratified by histologic subtype. |
|------------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                   | Total | Endometrioid | Serous | Clear Cell | Carcinosarcoma |
|------------------------------------|-------|--------------|--------|------------|----------------|
| White                              | 20,637| 17,879       | 1,449  | 339        | 970 (4.7%)     |
| Black                              | 2,064 | 1,322 (64.1%)| 379    | 73         | 290 (14.1%)    |
| Other                              | 1,441 | 1,172 (81.3%)| 166    | 21         | 82 (5.7%)      |

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## Table 2

Patient Demographics, sorted by race, stage and histologic subtype.

| STAGE 1 | EAC (n = 17,218) | Serous (n = 1,110) | Clear Cell (n = 262) | Carcinosarcoma (n = 761) |
|---------|-----------------|-------------------|----------------------|-------------------------|
|         | White (n=15,191) | Black (n=1,056)   | Other (n=971)        | White (n=823)           |
|         | White (n=823)   | Black (n=205)     | Other (n=82)         | Black (n=201)           |
|         | Other (n=82)    |                  |                      | Other (n=21)            |
| Age     | <0.0001         | 0.002             | 0.2                  | <0.0001                 |
| 40-69   | 35.1            | 39.8              | 35.5                 | 31                     |
|         | 45.2            | 48.2              | 47.7                 | 47                     |
| 70-79   | 19.7            | 12                | 16.8                 | 22                     |
| 80+     |                  |                  |                      | 14.1                   |
| Stage   | <0.0001         | 0.4               | 0.4                  | 0.01                    |
| IA      | 67.8            | 72.6              | 68.9                 | 70.6                    |
|         | 25.6            | 17.1              | 24.6                 | 20.5                    |
| IB      | 6.6             | 10.2              | 6.5                  | 8.9                     |
| L, NOS  | 13.6            | 13.9              | 12.8                 | 13.8                    |
| Grade   | <0.0001         | 0.001             | 0.001                | 0.001                   |
| 1       | 42.4            | 33.3              | 41.8                 | NA                      |
|         | 31.8            | 31.5              | 30.5                 | NA                      |
|         | 11.2            | 19.2              | 13.8                 | NA                      |
|         | 1                | 2                  | 1.13                 | NA                      |
|         | 13.6            | 13.9              | 12.8                 | NA                      |
| Region  | <0.0001         | <0.0001           | <0.0001              | <0.0001                 |
| Northeast | 24.9            | 25.3              | 12.8                 | 28.6                    |
|         | 14.7            | 14                | 2.4                  | 14.1                    |
|         | 19.1            | 41.9              | 3.3                  | 17.3                    |
| West    | 41.3            | 18.8              | 81.6                 | 45.8                    |
| Charlson| <0.0001         | <0.0001           | 0.3                  | 0.7                     |
| 0       | 67.5            | 51.4              | 58.3                 | 67.2                    |
|         | 21              | 27.1              | 28.2                 | 21.8                    |
|         | 6.8             | 11.2              | 8.8                  | 6.8                     |
| Adj. Treatment | 0.2           | 0.2               | 0.5                  | 0.3                     |
| no adj tx | 75.7            | 74.5              | 76.7                 | 40.3                    |
|         | 21.9            | 21.9              | 20.5                 | 15.7                    |
| CT only | 1.3             | 2.4               | 1.8                  | 26.4                    |
|         | 0.8             | γ                 | γ                    | 9.7                     |
|         | γ               | γ                 | γ                    | 7.2                     |
|         | γ               | γ                 | γ                    | γ                      |
|         | γ               | γ                 | γ                    | γ                      |
| Year of Diagnosis | 0.0003        | 0.05              | 0.9                  | 0.001                   |
| 2000-2008 | 53.3            | 48.7              | 48.4                 | 42.4                    |
| 2009-2015 | 46.7            | 51.3              | 51.6                 | 57.6                    |
| Surgical Modality | <0.0001       | 0.005             | 0.4                  | 0.08                    |
| Not Recorded | 3.8            | 5.6               | 6.8                  | 1.5                     |
| Open    | 54.3            | 61.6              | 52.4                 | 53.2                    |
| Laporoscopic | 22.6            | 15.2              | 22.9                 | 24.4                    |
| Robotic | 11.9            | 11.7              | 10.9                 | 16.2                    |
|         | 4.3             | 3.1               | 4.1                  | 1.9                     |
|         | 3.1             | 3.0               | 2.9                  | 3.0                     |
| Surgeon Type | <0.0001       | 0.001             | 0.7                  | 0.3                     |
| No Record | 4.3             | 6.3               | 7.8                  | 1.7                     |
| GynDec  | 41.7            | 43.5              | 44.3                 | 56.5                    |
| OBGYN   | 51.5            | 49.1              | 46.7                 | 39                     |
| General | 2.5             | γ                 | 1.2                  | γ                       |
| Nodes Examined | 0.0005       | 0.6               | 0.6                  | 0.006                   |
| No      | 40.9            | 36.8              | 35.4                 | 19.7                    |
| Yes     | 58.9            | 63.6              | 64.6                 | 80.2                    |
| Income  | <0.0001         | <0.0001           | 0.001                | <0.0001                 |
| <$40 k  | 21.7            | 53.3              | 21.8                 | 19.3                    |
| $40-$55 k | 25.7            | 23.4              | 24.5                 | 23.8                    |
| $55-$75 k | 24.5            | 15.4              | 25.2                 | 25.2                    |
| $75 k+  | 28.1            | 7.9               | 28.7                 | 31.7                    |
| Metro   | <0.0001         | <0.0001           | 0.001                | <0.0001                 |
| Big Metro | 54.1            | 62.9              | 67.2                 | 54.3                    |
| Metro   | 29.9            | 26.2              | 27.4                 | 29.9                    |
| Other   | 15.9            | 10.9              | 5.4                  | 15.8                    |


| Age | EAC (n=1,121) | Serous (n=162) | Clear Cell (n=48) | Carcinosarcoma (n=153) |
|-----|---------------|----------------|-------------------|------------------------|
|     | White (n=950) | White (n=110) | White (n=48) | P-value | White (n=96) | P-value |
|     | Black (n=106) | Black (n=35) | Black (n=48) |          | Black (n=45) |          |
|     | Other (n=65) | Other (n=17) | Other (n=12) |          | Other (n=12) |          |
| 40-69 | 31.1 | 37.8 | 30.8 | 20.9 | 37.1 | 22.9 | NA | NA | 22.9 | 40.0 |
| 70-79 | 43.1 | 49.1 | 50.8 | 49.1 | 45.7 | 45.8 | NA | NA | 54.2 | >35.5 |
| 80+ | 25.9 | 13.2 | 18.5 | 20.0 | 17.1 | 31.2 | NA | NA | 22.9 | γ |
| Grade | | | | | | | | | | |
| 1 | 0.003 | | | | | | | | | |
| 2 | 0.0008 | | | | | | | | | |
| 3 | 18.4 | >27.3 | 26.2 | NA | NA | NA | NA | NA | NA | NA |
| 4 | 2.3 | γ | γ | NA | NA | NA | NA | NA | NA | NA |
| NOS | 14.4 | 12.3 | 21.5 | NA | NA | NA | NA | NA | NA | NA |
| Region | | | | | | | | | | |
| Northeast | <0.0001 | | | | | | | | | |
| Midwest | 27.5 | 33 | γ | 20 | γ | γ | 25 | NA | NA | 24 | γ |
| South | 13.5 | 10.4 | γ | 18.2 | γ | γ | NA | NA | 16.7 | γ |
| West | 17.4 | 36.8 | γ | 19.1 | 57.1 | γ | NA | NA | 22.9 | 55.6 |
| Charlson | 0.001 | | | | | | | | | |
| 0 | 61.26 | 44.3 | 61.5 | 57.3 | 51.4 | γ | 62.5 | NA | NA | 60.4 | 55.6 |
| 1 | 24 | 30.2 | 29.2 | 19.1 | γ | γ | NA | NA | 26 | 31.1 |
| 2 | 9.47 | 12.3 | γ | 10 | γ | γ | NA | NA | γ | γ |
| 3+ | 5.26 | 13.2 | γ | 13.6 | γ | γ | NA | NA | γ | γ |
| Adj. Treatment | | | | | | | | | | |
| no adj tx | 38.74 | 37.7 | 32.3 | 30 | 34.3 | γ | 25 | NA | NA | 33.3 | 37.8 |
| RT only | 54.84 | 53.8 | 60 | 24.6 | γ | γ | 43.8 | NA | NA | 30.2 | 40.0 |
| CT only | 2.21 | γ | γ | 30.9 | γ | γ | γ | NA | NA | 17.7 | γ |
| RT-CT concurrent | 2.53 | γ | γ | γ | γ | γ | NA | NA | 13.5 | γ |
| RT-CT concurrent, then | | | | | | | | | | |
| CT | γ | γ | γ | γ | γ | γ | NA | NA | γ | γ |
| Sequential RT-CT | γ | γ | γ | γ | γ | γ | NA | NA | γ | γ |
| Sequential CT-RT | γ | γ | γ | γ | γ | γ | NA | NA | γ | γ |
| Sandwich CT-RT-CT | γ | γ | γ | γ | γ | γ | NA | NA | γ | γ |
| CT, then concurrent RT-CT | γ | γ | γ | γ | γ | γ | NA | NA | γ | γ |
| Diagnosis Year | | | | | | | | | | |
| 2000-2008 | 55.2 | 57.6 | 49.2 | 43.6 | 45.7 | γ | 45.8 | NA | NA | 54.2 | 51.1 |
| 2009-2015 | 44.8 | 42.4 | 50.8 | 56.4 | 54.3 | <35.3 | 54.2 | NA | NA | 45.8 | 48.9 |
| Surgical Modality | | | | | | | | | | |
| Not Recorded | 0.0001 | | | | | | | | | |
| Abdominal | 63.4 | 71.7 | 56.9 | 60 | 57.1 | γ | 58.3 | NA | NA | 72.9 | 73.3 |
| Laparoscopic | 17.9 | γ | γ | 14.6 | γ | 70.6 | γ | NA | NA | γ | γ |
| Robotic | 8.4 | γ | γ | 16.4 | γ | γ | γ | NA | NA | γ | γ |
| Vaginal | 3.4 | γ | γ | γ | γ | γ | NA | NA | γ | γ |
| LASH/LAVH | >2.5 | γ | γ | γ | γ | γ | NA | NA | γ | γ |
| Surgeon Type | | | | | | | | | | |
| No Record | 4.6 | γ | γ | γ | γ | γ | γ | NA | NA | γ | γ |
| GynOnc | 46.3 | 38 | 50 | 36.4 | 60 | γ | 50 | NA | NA | 47.1 | 35.1 |
| OBGYN | 46.7 | 50 | 41.1 | 54.6 | γ | γ | 38.1 | NA | NA | 47.1 | 48.7 |
| General | 2.6 | γ | γ | γ | γ | γ | γ | NA | NA | γ | γ |
| Nodes Examined | | | | | | | | | | |
| No | 30.4 | 36.8 | 24.6 | 22.7 | γ | γ | 25 | NA | NA | 24 | 35.6 |
| Yes | 69.6 | 63.2 | 75.4 | 77.3 | >68.5 | <35.2 | 75 | NA | NA | 76 | 64.4 |
| Income | | | | | | | | | | |
| <50k | 23.7 | 50.9 | 29.2 | 22.7 | 60 | γ | 31.3 | NA | NA | 26 | 71.1 |
| $40k to $55k | 26.6 | 24.5 | 24.6 | 28.2 | γ | γ | 25 | NA | NA | 25 | γ |
| $55k to $75k | 24.9 | 13.2 | 24.6 | 20.9 | γ | γ | 27.1 | NA | NA | 26 | γ |
| $75k+ | 24.7 | 11.3 | 21.5 | 28.2 | γ | γ | 27.1 | NA | NA | 22.9 | γ |
| Metropolitan Env | | | | | | | | | | |
| Big Metro | 0.0008 | | | | | | | | | |
| Metro | 50.8 | 63.2 | 71.9 | 56.4 | 57.1 | 88.2 | 43.8 | NA | NA | 48.4 | 55.6 |
| Other | 33 | 28.3 | 25 | 28.2 | γ | γ | 31.3 | NA | NA | 26.3 | γ |
| Adj. Treatment | | | | | | | | | | |
| Adj. Treatment | 0.006 | | | | | | | | | |
| Age | | | | | | | | | | |
| 40-69 | 28.9 | 31.3 | 41.2 | 27.7 | 42.5 | 37.3 | 33.3 | γ | NA | 28.1 | 30.7 | 26.1 |
| 70-79 | 45.9 | 51.3 | 41.2 | 45.4 | 47.5 | 41.8 | 50 | 66.7 | NA | 45.7 | 56.8 | 52.2 |

STAGE III

| Age | EAC (n=2034) | Serous (n=722) | Clear Cell (n=123) | Carcinosarcoma (n=428) |
|-----|---------------|----------------|-------------------|------------------------|
|     | White (n=1738) | Black (n=160) | White (n=90) | P-value | White (n=317) | P-value |
|     | Black (n=136) | Other (n=139) | Other (n=33) |          | Black (n=88) | Other (n=23) |
| 40-69 | 28.9 | 31.3 | 41.2 | 27.7 | 42.5 | 37.3 | 33.3 | γ | NA | 28.1 | 30.7 | 26.1 |
| 70-79 | 45.9 | 51.3 | 41.2 | 45.4 | 47.5 | 41.8 | 50 | 66.7 | NA | 45.7 | 56.8 | 52.2 |
| STAGE III | EAC (n=2034) | Serous (n=722) | Clear Cell (n=123) | Carcinosarcoma (n=428) |
|----------|---------------|---------------|------------------|-------------------|
| White (n=1738) | Black (n=160) | Other (n=136) | White (n=516) | Black (n=139) | Other (n=67) | White (n=90) | Black (n=33) | Other (n=NA) | White (n=317) | Black (n=88) | Other (n=23) |
| Income | | | | | | | | | | | | |
| $75k | 100% | 100% | 100% | 100% | | | | | | | |
| $55k to $75k | 95% | 95% | 85% | 75% | | | | | | | |
| $40k to $55k | 90% | 90% | 70% | 60% | | | | | | | |
| $40k | 85% | 85% | 60% | 50% | | | | | | | |
| Adj. Treatment | | | | | | | | | | | |
| no adj tx | 90% | 90% | 80% | 70% | | | | | | | |
| RT-CT | | | | | | | | | | | |
| concurrent | 80% | 80% | 70% | 60% | | | | | | | |
| Sequential RT-CT | | | | | | | | | | | |
| then CT | 50% | 50% | 40% | 30% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 45% | 45% | 35% | 25% | | | | | | | |
| RT-CT | | | | | | | | | | | |
| CT only | 40% | 40% | 30% | 20% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 35% | 35% | 25% | 15% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 30% | 30% | 20% | 10% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 25% | 25% | 15% | 5% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 20% | 20% | 10% | 0% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 15% | 15% | 5% | 0% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 10% | 10% | 0% | 0% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 5% | 5% | 0% | 0% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 0% | 0% | 0% | 0% | | | | | | | |
| Stage | | | | | | | | | | | |
| IIA | 80% | 80% | 70% | 60% | | | | | | | |
| IIB | | | | | | | | | | | |
| IIC | | | | | | | | | | | |
| IIC2 | | | | | | | | | | | |
| III, NOS | 60% | 60% | 50% | 40% | | | | | | | |
| Grade | | | | | | | | | | | |
| 1 | 100% | 100% | 90% | 80% | | | | | | | |
| 2 | 95% | 95% | 85% | 75% | | | | | | | |
| 3 | 90% | 90% | 80% | 70% | | | | | | | |
| 4 | 85% | 85% | 75% | 65% | | | | | | | |
| Region | | | | | | | | | | | |
| Northeast | 90% | 90% | 80% | 70% | | | | | | | |
| Midwest | 85% | 85% | 75% | 65% | | | | | | | |
| South | 80% | 80% | 70% | 60% | | | | | | | |
| West | 75% | 75% | 65% | 55% | | | | | | | |
| Charlson | | | | | | | | | | | |
| 0 | 75% | 75% | 65% | 55% | | | | | | | |
| 1 | 70% | 70% | 60% | 50% | | | | | | | |
| 2 | 65% | 65% | 55% | 45% | | | | | | | |
| 3+ | 60% | 60% | 50% | 40% | | | | | | | |
| Adj. Treatment | | | | | | | | | | | |
| no adj tx | 85% | 85% | 75% | 65% | | | | | | | |
| RT only | 80% | 80% | 70% | 60% | | | | | | | |
| CT only | 75% | 75% | 65% | 55% | | | | | | | |
| RT-CT | 70% | 70% | 60% | 50% | | | | | | | |
| concurrent | 65% | 65% | 55% | 45% | | | | | | | |
| CT only | 60% | 60% | 50% | 40% | | | | | | | |
| CT | 55% | 55% | 45% | 35% | | | | | | | |
| CT only | 50% | 50% | 40% | 30% | | | | | | | |
| CT | 45% | 45% | 35% | 25% | | | | | | | |
| CT only | 40% | 40% | 30% | 20% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 35% | 35% | 25% | 15% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 30% | 30% | 20% | 10% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 25% | 25% | 15% | 5% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 20% | 20% | 10% | 0% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 15% | 15% | 5% | 0% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 10% | 10% | 0% | 0% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 5% | 5% | 0% | 0% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 0% | 0% | 0% | 0% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 0% | 0% | 0% | 0% | | | | | | | |
| CT | | | | | | | | | | | |
| CT only | 0% | 0% | 0% | 0% | | | | | | | |

(continued on next page)
Demographics of women with endometrial cancer, stratified by stage and histologic subtype are presented. All values represent displayed represent percentages, unless otherwise specified. Abbreviations: NOS- Not otherwise specified, RT- Radiation Therapy, CT- Chemotherapy, LASH- Laparoscopic Assisted Supracervical Hysterectomy, LAVH-Laparoscopic Assisted Vaginal Hysterectomy, GynOnc-Gynecologic Oncologist, OB/GYN- Generalist OB/GYN, General- General Surgeon, Envt- Environment. Groups that had less than 11 patients per group were withheld from reporting, according to SEER-Medicare reporting guidelines, and denoted as “γ” in the table above.

3.3. Cancer-Specific survival

Stage-by-stage, Black women had worse CSS than White women or women of other races (Log-rank ρ < 0.0001 for all stages). (Fig. 1)

When stratified by stage and histology, log-rank analyses showed inconsistently worse CSS for depending on stage and histologic sub-type. For stage I EAC, Black women had lower probability of 5-year CSS of 0.89 (95% CI 0.87–0.91), compared to White (0.94, 95% CI 0.94–0.95) or other races (0.94, 95% CI 0.93–0.96). Similarly, for stage I serous histology, Black women had a lower probability CSS (0.67, 95% CI 0.59–0.74), compared to White women (0.79, 95% CI 0.76–0.82), or others (0.83, 95% CI 0.72–0.90). While no difference was noted for OS, 5-year CSS for Black women with stage I carcinosarcoma was significantly worse (0.52, 95% CI 0.43–0.60) compared to White (0.62, 95% CI 0.58–0.66) and other (0.67, 95% CI 0.50–0.79) women. For stage II, no significant differences in probability of 5-year CSS were seen by race (log rank p-values all > 0.05) for any histology. For stage III, significant differences in survival by race were also identified for EAC, where Black women had worse 5-year CSS (0.48, 95% CI 0.39–0.56) compared to White women (0.61, 95% CI 0.59–0.64), and others (0.66, 95% CI 0.57–0.74). (Table 3)

In unadjusted analyses of Stage 1, Black women were more likely to die from EAC (HR 1.74, 95% CI 1.44–2.10, p < 0.0001), serous (HR 1.61, 95% CI 1.20–2.16, p = 0.002), and carcinosarcoma (HR 1.39, 95% CI 1.06–1.82, p = 0.02) histology. For stage I EAC, Black women with EAC histology had worse CSS (HR 1.57, 95% CI 1.03–2.39, p = 0.04). For stage III, Black women diagnosed with EAC had worse CSS (HR 1.51, 95% CI 1.20–1.91, p = 0.0005). (Table 4)

In adjusted analyses, disparities persisted across stage 1 histologies: stage I EAC (aHR 1.54, 95% CI 1.26–1.89, p < 0.0001), serous (aHR 1.68, 95% CI 1.18–2.39, p = 0.004), and carcinosarcoma (aHR 1.45, 95% CI 1.07–1.98, p = 0.02). There was no significant difference in CSS for stage II EAC (HR 1.26, 95% CI 0.79–2.03, p = 0.3) histology. Disparities for stage III EAC were not seen for CSS in the adjusted analysis (aHR 1.24, 95% CI 0.96–1.61, p = 0.09). (Table 4)

Women of other races did not have significantly different CSS compared to White women for all histologies and stages.

4. Discussion

In our study of over 24,000 women with surgically staged endometrial cancer, Black women diagnosed with stage I endometrial cancer had consistently worse CSS across all histologies other than clear cell, despite similar rates of adjuvant treatment and overall survival. This study provides important evidence on how racial disparities impact survival for a standardized cohort of surgically staged, insured patients. While prior studies have shown that Black women are less likely to undergo surgery (Bregar et al., 2017) or receive appropriate adjuvant care (Huang et al., 2020; Luo et al., 2021), this study evaluates a cohort who had all undergone primary surgical staging, allowing control for differences in treatment approach and highlighting disparities post-treatment.

Most outcome disparities noted in this study are demonstrated in stage I diagnoses. For stage I EAC, Serous, and Carcinosarcoma subtypes, Black women have significantly worse 5-year CSS, despite controlling for comorbidities, age, treatment regimen, and tumor sub-stage/grade (where applicable). This finding supports the hypothesis that disease- and treatment-specific factors play a role in the disparities seen for Black women with endometrial cancer affecting CSS, unlike overall comorbidities that would be expected to impact OS. While we lack data on recurrence, these differences in CSS likely reflect differences in recurrence rates and treatment in recurrence that impact CSS. For example, Black women have been under-enrolled in clinical trials in gynecologic oncology, which are the standard of care in recurrence, limiting their access to cutting edge oncologic care (Scalici et al., 2015; Awad et al., 2020).

These findings build upon prior research where CSS was evaluated as an endpoint within the SEER database, and where Black women have been observed to have worse CSS (Cheung, 2013) that cannot necessarily be explained by difference in rates of comorbidities (Olson et al., 2012). Other studies not using the SEER database have shown that when controlling for comorbidities CSS is still worse for Black women (Ruterbusch et al., 2014), specifically for early-stage diagnoses (Mukerji et al., 2018). This study builds on these hypotheses by showing that when women undergo primary surgical staging and multiple social and therapeutic factors are considered, there are still disparities in outcomes for Black women compared to White women diagnosed with stage I endometrial cancer.

This study, along with its predecessors, points to a need to develop interventions in early-stage endometrial cancer, where Black women
have worse cancer-specific survival, and the largest population of women is affected. Interventions to increase diversity in clinical trials and access to adequate surveillance after primary treatment are essential. Many upstream issues also need to be addressed, such as targeting patient and provider education, screening for irregular bleeding, earlier diagnoses, and treatment in younger women, particularly in Black women given that a greater proportion (ranging from 39 to 47%) were diagnosed in the 40–69 age bracket compared to White women.

Analyzing CSS allows us to determine potential etiologies within the course of the cancer diagnosis itself to help explain disparities and provide actionable interventions. Analyzing CSS within an advanced cohort of endometrial cancer as seen within the stage III endometrioid subgroup demonstrated that CSS could be modified by receipt of adjuvant therapy. Adjuvant therapy likely provides the greatest benefit in survival for advanced cancer cases as opposed to early-stage cancers, and Black women who received less adjuvant therapy had poorer CSS; however, when adjusted for treatment differences by race this effect was ameliorated. This highlights a need to increase receipt of adjuvant therapy in advanced endometrioid populations to improve disparity in CSS. Possible etiologies not studied here include recurrence rates, tumor cell characteristics, and surveillance rates. Recurrence rates are known to be higher for non-Hispanic Black women than White women (Felix et al., 2018). This increased rate of recurrence could be due to many disparities in post-surgical cancer treatment or surveillance and would help explain worse CSS for these patients. Similarly, there may be more to evaluate regarding differences between the types of cancers that form in Black and White women that affect mortality. Analysis of tumor cell characteristics has shown that Black women are noted to have increased upregulation of cell cycle progression, p53 and HER2/NEU signaling that can lead to more aggressive tumor characteristics (Javadian et al., 2021; Kommos et al., 2018). This could contribute to worse cancer specific outcomes in Black women. Further directions for study could involve seeking therapeutic interventions that target more aggressive tumors based on molecular subtyping rather than histology alone to minimize disparities in recurrence rate.

Prior research has also stressed the importance of qualitative research that develops a better understanding of the perspectives of Black women who have been diagnosed with endometrial cancer. The perspective of Black women undergoing screening, diagnosis, treatment, and surveillance for endometrial cancer has been noted to be lacking in research regarding disparities (Doll et al., 2018), and may help guide further interventions that are meant to improve outcomes for these patients. We saw that Black women with advanced endometrioid endometrial cancer received less adjuvant therapy than White women. Multiple factors including the provider offering therapy, patient trust, acceptance and actual receipt of therapy likely play a role and should be further examined to diminish disparities in treatment and associated survival outcomes.

The strengths of this study include its wide variety of demographic and therapeutic data that allows for improved evaluation of how race plays a role in outcomes independent of other factors. It also directly compares OS and CSS for a variety of stages and histologies in a large population of women. Limitations of this study include its generalizability as the data includes women insured through Medicare, which is representative of only women above 65 or those with a prior disability. Black and Hispanic women are more likely to have disabilities leading to Medicare enrollment prior to age 65 (Kaiser and Foundation, 2016), which may lead to their being a population with more co-morbidities and thus lower overall survival in SEER-Medicare. Also, Black women may be underrepresented in this study (8.5% of all patients vs. 12.4% of all Americans), which may be due to known disparities in primary surgical staging or over-representation of white women with early stage endometrioid endometrial cancer. Differentiating between CSS and OS as we do is thus vital to control for such comorbidities. The SEER-
Medicare database, while one of the largest available cancer databases, has a limited sample size for less common histologies, which may affect the ability to detect statistical differences in survival rates within these subclasses. A wide variety of potential confounding factors, including more detailed data on concordant health issues, are not available from this retrospective database. There is similarly a lack of data on hospital and provider data to help understand differences in therapeutics and outcomes on a more granular level.

In further research, it is important to understand race as more than a biological construct and be mindful of factors including social

Fig. 2. Overall Survival by stage and histological sub-type, compared by race. X-axis represents time in months, y-axis represents Overall Survival. White women are denoted in blue, Black women in red, and Other in green. Outcomes are significantly worse for Black women in Stage I EAC (< 0.0001), Serous (p = 0.0004), and Carcinosarcoma (p = 0.05), as well as Stage III EAC (p = 0.007). Other races had significantly better OS in stage I EAC (p = 0.02). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 3 5-year probability of survival (OS and CSS) by race for each stage and histologic subtype.

| Stage | Race | Endometrioid p-value | Serous p-value | Clear Cell p-value | Carcinosarcoma p-value |
|-------|------|----------------------|---------------|--------------------|------------------------|
| Stage I OS | White | 0.85 (0.84–0.85) | <0.0001 | 0.67 (0.64–0.71) | 0.0004 | 0.68 (0.61–0.74) | 0.4 | 0.53 (0.48–0.57) | 0.1 |
| | Black | 0.78 (0.75–0.80) | 0.52 (0.44–0.60) | 0.66 (0.48–0.80) | 0.39 (0.31–0.47) |
| | Other | 0.85 (0.80–0.88) | 0.77 (0.65–0.85) | 0.70 (0.46–0.86) | 0.58 (0.42–0.71) |
| CSS White | 0.94 (0.94–0.95) | <0.0001 | 0.79 (0.76–0.82) | 0.002 | 0.78 (0.71–0.83) | 0.2 | 0.62 (0.58–0.66) | 0.05 |
| | Black | 0.89 (0.87–0.91) | 0.67 (0.59–0.74) | 0.85 (0.67–0.93) | 0.52 (0.43–0.60) |
| | Other | 0.94 (0.93–0.96) | 0.83 (0.72–0.90) | 0.88 (0.59–0.97) | 0.67 (0.50–0.79) |
| Stage II OS | White | 0.70 (0.66–0.73) | 0.47 (0.37–0.57) | 0.58 (0.43–0.70) | 0.8 | 0.28 (0.19–0.38) | 1 |
| | Black | 0.61 (0.51–0.70) | 0.36 (0.20–0.52) | 0.50 (0.06–0.84) | 0.23 (0.12–0.36) |
| | Other | 0.70 (0.56–0.80) | 0.39 (0.16–0.62) | 1.00 (1.00–1.00) | 0.17 (0.03–0.41) |
| CSS White | 0.85 (0.83–0.87) | 0.07 | 0.59 (0.48–0.68) | 0.3 | 0.64 (0.47–0.76) | 0.8 | 0.38 (0.27–0.48) | 0.9 |
| | Black | 0.75 (0.65–0.82) | 0.49 (0.29–0.66) | 0.67 (0.05–0.95) | 0.32 (0.18–0.48) |
| | Other | 0.79 (0.66–0.88) | 0.43 (0.18–0.66) | 1.00 (1.00–1.00) | 0.22 (0.04–0.51) |
| Stage III OS | White | 0.50 (0.47–0.52) | 0.005 | 0.32 (0.28–0.36) | 0.9 | 0.35 (0.25–0.46) | 0.9 | 0.26 (0.21–0.31) | 0.09 |
| | Black | 0.38 (0.31–0.46) | 0.34 (0.26–0.42) | 0.30 (0.16–0.46) | 0.19 (0.12–0.29) |
| | Other | 0.57 (0.48–0.65) | 0.35 (0.23–0.47) | 0.40 (0.05–0.75) | 0.13 (0.03–0.30) |
| CSS White | 0.61 (0.59–0.64) | 0.0009 | 0.41 (0.36–0.45) | 0.8 | 0.47 (0.35–0.58) | 0.8 | 0.33 (0.27–0.38) | 0.4 |
| | Black | 0.48 (0.39–0.56) | 0.43 (0.34–0.52) | 0.46 (0.27–0.63) | 0.29 (0.19–0.40) |
| | Other | 0.66 (0.57–0.74) | 0.42 (0.29–0.55) | 0.53 (0.07–0.86) | 0.20 (0.06–0.40) |

5-year probability of survival (OS and CSS) by race for each stage and histologic subtype are presented, with corresponding 95% CI.
determinants of health and health access upon cancer specific and overall health outcomes to potentially develop interventions that address systems of inequity within healthcare. Further research should explore developing post-treatment interventions within survivorship, surveillance, and treatment of recurrence to reduce disparities. By moving towards prospective studies that test the interventions listed above, we may be able to start seeing improved outcomes for endometrial cancer patients.

**Table 4**

Overall Survival and Cancer Specific Survival, unadjusted and adjusted analyses by race.

| Stages | Endometroid | p-value | Serous | p-value | Clear Cell | p-value | Carcinosarcoma | p-value |
|--------|-------------|---------|--------|---------|------------|---------|----------------|---------|
| Stage I | Unadjusted OS | White | ref | <0.0001 | ref | 1.48(1.19,1.85) | 0.0004 | ref | 0.71(0.41,1.26) | 0.2 | 1.24(1.00,1.55) | 0.05 |
|        | Black | 1.22(1.11,1.36) | 0.03 | 0.77(0.52,1.13) | 0.2 | 0.78(0.39,1.54) | 0.5 | ref | 0.96(0.63,1.45) | 0.8 |
|        | Other | 0.87(0.77,0.99) | 0.3 | 1.74(1.44,2.10) | <0.0001 | ref | ref | ref | 0.77(0.45,1.33) | 0.3 | 0.52(0.16,1.67) | 0.3 | 0.93(0.55,1.58) | 0.8 |
| Unadjusted CSS | White | ref | ref | ref | ref | ref | ref | ref | ref |
|        | Black | 1.74(1.44,2.10) | <0.0001 | ref | ref | 1.61(1.20,2.16) | 0.002 | ref | 0.53(0.21,1.35) | 0.2 | 1.39(1.06,1.82) | 0.02 |
|        | Other | 0.92(0.71,1.19) | 0.5 | 0.83(0.74,0.94) | 0.004 | ref | ref | ref | 0.89(0.05,1.34) | 0.6 | 0.76(0.33,1.74) | 0.5 | 1.36(0.85,2.17) | 0.2 |
| Adjusted OS | White | ref | ref | ref | ref | ref | ref | ref | ref |
|        | Black | 1.11(0.99,1.23) | 0.07 | 1.60(1.24,2.07) | 0.0033 | ref | ref | ref | 1.60(1.24,2.07) | 0.0033 | ref | ref | ref |
|        | Other | 0.85(0.65,1.18) | 0.2 | 0.97(0.54,1.73) | 0.9 | 1.15(0.74,1.43) | 0.2 | 1.15(0.74,1.43) | 0.2 | 1.15(0.74,1.43) | 0.2 | 1.15(0.74,1.43) | 0.2 |
| Stage II | Unadjusted OS | White | ref | 1.51(0.95,2.40) | 0.08 | ref | N/A | ref | ref |
|        | Black | 1.15(0.87,1.51) | 0.3 | ref | ref | ref | ref | ref |
|        | Other | 0.91(0.61,1.34) | 0.6 | 1.30(0.68,2.47) | 0.4 | N/A | ref | ref |
| Unadjusted CSS | White | ref | ref | ref | ref | ref | ref | ref | ref |
|        | Black | 1.57(1.03,2.39) | 0.04 | 1.49(0.85,2.61) | 0.2 | N/A | ref | ref |
|        | Other | 1.41(0.81,2.43) | 0.2 | 1.51(0.74,3.11) | 0.3 | N/A | ref | ref |
| Adjusted OS | White | ref | ref | ref | ref | ref | ref | ref | ref |
|        | Black | 1.95(0.70,1.29) | 0.8 | 1.25(0.67,2.35) | 0.5 | N/A | ref | ref |
|        | Other | 0.96(0.64,1.46) | 0.9 | 1.30(0.60,2.81) | 0.5 | N/A | ref | ref |
| Adjusted CSS | White | ref | ref | ref | ref | ref | ref | ref | ref |
|        | Black | 1.26(0.79,2.03) | 0.3 | 1.71(0.81,3.60) | 0.2 | N/A | ref | ref |
|        | Other | 1.11(0.61,2.01) | 0.7 | 1.63(0.67,4.0) | 0.3 | N/A | ref | ref |
| Stage III | Unadjusted OS | White | ref | 1.01(0.64,1.61) | 0.9 | ref | ref | ref |
|        | Black | 1.32(1.08,1.60) | 0.007 | 0.99(0.80,1.24) | 0.9 | ref | ref | ref |
|        | Other | 0.82(0.65,1.04) | 0.1 | 1.09(0.80,1.47) | 0.6 | N/A | ref | ref |
| Unadjusted CSS | White | ref | ref | ref | ref | ref | ref | ref | ref |
|        | Black | 1.51(1.20,1.91) | 0.0005 | 1.00(0.78,1.29) | 0.9 | ref | ref | ref |
|        | Other | 0.86(0.64,1.15) | 0.3 | 1.13(0.81,1.58) | 0.5 | N/A | ref | ref |
| Adjusted OS | White | ref | ref | ref | ref | ref | ref | ref | ref |
|        | Black | 1.15(0.93,1.43) | 0.2 | 0.90(0.69,1.18) | 0.4 | ref | ref | ref |
|        | Other | 0.88(0.69,1.12) | 0.3 | 1.27(0.92,1.74) | 0.2 | N/A | ref | ref |
| Adjusted CSS | White | ref | ref | ref | ref | ref | ref | ref | ref |
|        | Black | 1.24(0.96,1.61) | 0.09 | 0.88(0.65,1.20) | 0.4 | ref | ref | ref |
|        | Other | 0.90(0.68,1.25) | 0.6 | 1.34(0.94,1.93) | 0.1 | N/A | ref | ref |

Hazard ratios of overall survival and cancer specific survival by race. Values presented are hazard ratios for death (HR, 95% CI). All models defined race by White, Black and Other. White was set as the reference group for all models. All values presented in this table represent the HR for Black women within each respective model. The adjusted OS and CSS models for stage I, II, and III EAC included age, geographic region, patient income, Charlson comorbidity index, surgeon type, post-operative treatment sequencing, nodes dissection, FIGO stage, and tumor grade. The adjusted OS and CSS models for stage I, II, and III serous, clear cell, and carcinosarcoma included all the above except sub-stage and grade (not applicable).

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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