

# UCSF

## UC San Francisco Previously Published Works

### Title

Understanding cervical cancer after the age of routine screening: Characteristics of cases, treatment, and survival in the United States

### Permalink

<https://escholarship.org/uc/item/8kn435b1>

### Journal

Gynecologic Oncology, 165(1)

### ISSN

0090-8258

### Authors

Lichter, Katie E  
Levinson, Kimberly  
Hammer, Anne  
[et al.](#)

### Publication Date

2022-04-01

### DOI

10.1016/j.ygyno.2022.01.017

Peer reviewed



Published in final edited form as:

*Gynecol Oncol.* 2022 April ; 165(1): 67–74. doi:10.1016/j.ygyno.2022.01.017.

## Understanding cervical cancer after the age of routine screening: characteristics of cases, treatment, and survival in the United States

Katie E. Lichter, MD MPH<sup>1</sup>, Kimberly Levinson, MD MPH<sup>2</sup>, Anne Hammer, MD PhD<sup>3,4</sup>,  
Melissa H. Lippitt, MD MPH<sup>2</sup>, Anne F. Rositch, PhD MSPH<sup>5,\*</sup>

<sup>1</sup>Department of Radiation Oncology, University of California San Francisco, 505 Parnassus Ave San Francisco, CA 94143.

<sup>2</sup>Kelly Gynecologic Oncology Division, Department of Gynecology and Obstetrics, Johns Hopkins University School of Medicine, 600 N Wolfe St, Baltimore, MD 21287.

<sup>3</sup>Department of Obstetrics and Gynecology, Gødstrup Hospital, Gl. Landevej 61, 7400 Herning, Denmark

<sup>4</sup>Department of Clinical Medicine, Palle Juul Jensens Boulevard 99, Aarhus University, Denmark

<sup>5</sup>Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, 615 N Wolfe Street, Baltimore, MD 21205.

### Abstract

**Objective:** Given that cervical cancer incidence rates do not decline in women >65, there is generally limited screening, and these women have a poor prognosis, it is imperative to better understand this population. We aim to describe the characteristics, treatment, and survival of women >65 diagnosed with cervical cancer.

**Methods:** SEER-Medicare 2004–2013 data was used to describe 2,274 patients >65 diagnosed with cervical cancer. Five-year cancer-specific survival was estimated using the Kaplan-Meier method. Multivariable Poisson and Cox regression analyses identified characteristics associated with treatment and mortality.

---

\*Corresponding author at: Johns Hopkins Bloomberg School of Public Health 615 N Wolfe Street Baltimore, MD 21205, arositch@jhu.edu.

Author Contribution:

Katie Lichter: Conceptualization, Methodology, Software, Formal Analysis, Writing- Original draft, Writing- Reviewing and Editing

Kimberly Levinson: Conceptualization, Methodology, Supervision, Writing- Reviewing and Editing

Anne Hammer: Writing- Original draft, Writing- Reviewing and Editing, Supervision

Melissa Lippitt: Methodology, Software, Data Curation, Writing- Reviewing and Editing Anne Rositch: Conceptualization, Methodology, Supervision, Writing- Reviewing and Editing, Project administration, Funding acquisition.

**Publisher's Disclaimer:** This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflict of interest

The authors have no conflicts of interest to declare

Supplementary data

Supplementary material

**Results:** The median age was 76.1 years, with nearly one-third of cases occurring in women >80 years. Most patients were non-Hispanic White (64.8%), had comorbidity scores  $\geq 1$  (53.9%) and squamous histology (66.3%). Most women were diagnosed at stage II or higher (62.7%), including nearly one-quarter at Stage IV (23.1%). Nearly 15% of patients were not treated (14.6%). Lack of treatment was associated with oldest age (>80), comorbidity scores  $\geq 3$ , and stage IV disease. Five-year cancer-specific survival was 50%. Increasing age and stage at diagnosis were significantly associated with lower cancer-specific survival whereas treatment was strongly associated with increased survival.

**Conclusion:** Most women >65 with cervical cancer are diagnosed with locally advanced or metastatic disease and many do not receive treatment. Survival is improved with early-stage diagnosis and treatment. These findings, coupled with the fact that women >65 constitute an increasing proportion of the population, highlight the need to re-evaluate screening and treatment practices in this population to detect cervical cancer at earlier stages and increase survival.

### Keywords

Cervical cancer; elderly; older; disparities; mortality; Surveillance, Epidemiology, and End Results (SEER); SEER-Medicare

---

## INTRODUCTION

In 2021, an estimated 14,480 women in the United States will be diagnosed with cervical cancer.<sup>1</sup> Approximately 20% of these cases will be diagnosed among women aged >65, most of whom will have exited routine cervical cancer screening per current screening recommendations.<sup>2,3</sup> Although incidence rates of cervical cancer have been declining in the United States (US) over the past five decades, this is not the case for rates among women over the age of 65, especially for minorities.<sup>4-6</sup> After accounting for hysterectomy prevalence, cervical cancer incidence and mortality rates in women older than 65 were recently found to be 80% higher than previously reported.<sup>7</sup> Due to population growth and increased life expectancy, it is estimated that the number of women over 65 years will increase by 23% over the next 10 years,<sup>8</sup> and it is therefore imperative to better understand this large cohort of older women who remain at risk for cervical cancer.

Compared to younger women, women >65 are more likely to present with advanced stage disease at diagnosis and have higher rates of comorbidities.<sup>6,9-12</sup> Moreover, older women are less likely to receive aggressive therapy, and may receive insufficient treatment at times, despite growing evidence that they can often tolerate treatment well.<sup>13</sup> Taken together, these factors likely contribute to the high mortality rate observed among women in this older age group.<sup>3,14,15</sup>

To date, knowledge on characteristics and prognosis of older women diagnosed with cervical cancer remains limited. Given the high incidence and mortality and limited screening in this population, coupled with the fact that it will take decades before we see an impact of HPV vaccination in this age group, it is imperative to better understand cervical cancer in this population. Thus, using SEER-Medicare data, we aimed to describe characteristics and treatment of older women diagnosed with cervical cancer and the impact of these factors

on cancer-specific survival. These data are essential to help identify targeted subpopulations and specific interventions that can reduce cervical cancer morbidity and mortality in older women.

## METHODS

### Data Sources

This study is a retrospective analysis of the Surveillance, Epidemiology, and End Results registry (SEER)-linked Medicare dataset approved by The Johns Hopkins Bloomberg School of Public Health Institutional Review Board. This analysis focuses on cervical cancer cases in women >65 years old, as reported by the SEER registry from 2004 through 2013, with linked Medicare enrollment files and Medicare claims, including follow-up data through 2015. The SEER-Medicare dataset links two large population-based sources of data, providing information about Medicare beneficiaries with cancer. The SEER program, administered by the National Cancer Institute (NCI), includes population-based tumor registries in 11 geographical areas: the metropolitan areas of San Francisco/Oakland, Detroit, Atlanta, and Seattle; Los Angeles county; the San Jose–Monterey area; and the states of Connecticut, Iowa, New Mexico, Utah, and Hawaii.<sup>16</sup> Medicare covers approximately 97% of individuals aged 65 and older.<sup>17</sup> The claims data provides information on health care services that patients obtain through Medicare.

### Study Population

The study included women aged >65 years who were diagnosed with cervical cancer between January 1, 2004, to December 31, 2013 and were accounted for in both SEER and Medicare datasets. Women were excluded if they did not have complete Medicare claims data which requires women to have both Medicare Parts A and B for at least 12 months prior to diagnosis (thus removing women <66 so we could have data on comorbidities prior to incident cancer diagnosis). This also excludes women who had health maintenance organization (HMO) medical insurance coverage. Additionally, women were excluded if they did not have a recorded month of diagnosis, had multiple malignancies or if their cancer was only diagnosed on autopsy or death certificate. Women were followed from time of diagnosis to date of death or end of the study period in December 2015. Area of residence was obtained using SEER's rural-urban continuum code population definitions: large metropolitan areas as metro areas of >1 million people, metro areas of 250,000 – 1 million, urban as population of 20,000 or more adjacent to a metro area, and less urban/rural as <20,000 people or not adjacent to a metropolitan area.

### Patient and tumor characteristics and treatment identification

SEER data were used to obtain demographic and clinical information including patients' age at diagnosis, year of diagnosis, marital status at diagnosis, area of residence. SEER data on race/ethnicity was recoded to include Hispanic ethnicity. Additionally, tumor characteristics including histology and American Joint Committee on Cancer (AJCC) stage were extracted from SEER. Medicare claims from the 12 months prior to diagnosis were used to ascertain comorbid conditions. Comorbidity scores were calculated using the Klabunde-modified Charlson comorbidity index scale.<sup>17</sup>

Treatment was defined as receipt of any surgery (e.g., cone biopsy, hysterectomy, radical hysterectomy), radiation therapy, or chemotherapy. Cancer-specific surgical treatment was identified in the SEER dataset. Given known limitations related to completeness of other cancer treatments<sup>18</sup>, all non-surgical cervical cancer treatments were identified through Medicare claims data using ICD-9 diagnosis codes, Common Procedural Terminology (CPT) codes, Healthcare Common Procedure Coding System (HCPCS) codes, and revenue center codes. A variable for chemoradiation was created and coded to include cases where the start date of chemotherapy and radiation were within 14 days of one another.

### Statistical analysis

Descriptive statistics were used to highlight patient, tumor, and treatment characteristics. Poisson and cox regression models were used to evaluate factors potentially associated with receipt of treatment and risk of death within 5 years, respectively. Univariate analyses were first performed, followed by multivariate analysis including purposeful selection of factors with p-values of < 0.10 or with known clinical significance. Adherence to the proportional hazards assumption was confirmed with log–log plots. No collinearity was noted between any of the factors in the final model. Women contributed time at risk from date of diagnosis until loss to follow-up, death, or administratively at the end of the study period December 31, 2015. Cancer-specific survival rates were estimated using the Kaplan-Meier method.<sup>19</sup> Stratified Kaplan-Meier curves were used to compare survival among subgroups based on patient and tumor characteristics. The resulting relative survival curves were compared using log-likelihood statistics. All tests were 2-sided, and p-values <0.05 were considered statistically significant. All statistical analyses were performed using STATA version 15 (StataCorp, College Station, TX).

## RESULTS

### Patient and Tumor Characteristics

A total of 2,274 women were identified from the SEER-Medicare dataset and met study inclusion criteria (Figure 1). The median age at cervical cancer diagnosis was 76.1 years (interquartile range [IQR] 68.6 – 83.6 years; Table 1). Cases were equally distributed by age with nearly one-third of cases occurring in the youngest (aged 66–70 years) and oldest (>80 years) age groups. The majority of patients were non-Hispanic White (64.8%), had comorbidity scores  $\leq 1$  (53.9%), and resided in metropolitan areas (81.8%). Cervical cancer cases in this population were predominately squamous cell carcinomas (SCC) (66.3%) with 17.5% adenocarcinomas (AC). Most were diagnosed as AJCC stage II or higher (62.7%), including nearly one-quarter of women diagnosed at Stage IV (23.1%).

Subtle but important differences by race and distribution of histologic subtypes over time were observed (Appendix A). Women with AC (75.1%) and were more likely to be diagnosed with stage I disease (31.6%). Over time, women were more likely to be diagnosed with AC, with AC accounting for 16.8% in early years (2004–2006) and 19.0% in later years (2010–2013) (Appendix B).

## Receipt of Treatment

Nearly 15% of patients received no cancer-specific treatment (14.6%; Table 1). Among the 85% of women who received treatment, the most common regimen was surgery with adjuvant chemotherapy and/or radiotherapy (41.9%), followed by radiotherapy alone for 18.8% of women. Treatment rates were lowest among women >80 (76.0%; Table 2), those with 3 or more comorbidities (73.7%), non-AC/non-SCC histology (73.4%), and those with stage IV (76.7%) or unknown stage disease (63.3%).

Receipt of treatment varied within the cohort based on patient and disease characteristics (Table 2). On univariate analysis, women >80 were less likely to receive treatment compared to women who were aged 66–70 (RR 0.83 [95% CI 0.74 – 0.94]), and those with a comorbidity score of 3 were less likely to receive treatment compared to those with no comorbidities (RR 0.81 [95% CI 0.70 – 0.94]). Additionally, women with advanced stage disease (AJCC Stage IV; RR 0.82 [95% CI 0.72 – 0.93]), and those with unknown stage (RR 0.67 [95% CI 0.57 – 0.80]), were less likely to receive treatment compared to those with Stage I disease. After considering potential confounders, women aged >80, those with a comorbidity score of 3, and those diagnosed at stage IV and unknown stage were still significantly less likely to receive treatment. Among women with Stage I disease, 34 (6.1%) did not receive treatment, of whom most were >80 (64.7%) and had comorbidity scores >1 (61.8%). No differences in receipt of treatment were observed across race, marital status, area of residence, and histology.

## Cancer specific survival

The median survival time following cervical cancer diagnosis was 56 months, and 5-year cancer-specific survival was 49.5% (95% CI: 47.5% – 51.6%). Five-year cancer-specific survival decreased significantly for each sequential age group ( $p < 0.01$ ; Figure 2A): 58.4% for women ages 66–70, 53.4% for ages 71–75 years, 44.4% for ages 76–80, and 40.3% for women aged >80 years. Additionally, Black women had significantly lower 5-year cancer-specific survival compared to all other races/ethnicities ( $p = 0.01$ ; Figure 2B): 44.6% for Black women, 49.6% for White, Non-Hispanic women, 51.2% for ‘other’ races/ethnicities, and 56.1% for White, Hispanics. The 5-year cancer-specific survival was comparable between SCC and AC (52.9% and 49.9%, respectively,  $p = 0.61$ ;) but ‘other’ histologic subtypes had significantly lower survival at 35.4% ( $p < 0.01$ ; Figure 2C). The 5-year cancer-specific survival decreased with increasing stage of disease at diagnosis ( $p < 0.01$ ; Figure 2D): 78.9% for Stage I, 60.0% for Stage II, 47.2% for Stage III, and only 18.9% for those diagnosed with Stage IV disease. Those with unknown stage also had low 5-year cancer-specific survival (38.5%). Overall survival rates revealed similar findings, although overall survival rates were lower (data not shown).

## Risk factors associated with cancer-specific survival

Various patient and disease characteristics were found to be associated with cancer-specific survival in this cohort (Table 3). On univariate analysis, lower cancer-specific survival was associated with older ages (ages 76–80=HR 0.66 (95% CI 0.54 – 0.81) and >80=HR 0.58 (95% CI 0.49 – 0.70), compared to ages 66–70. Women with ‘other’ histology types had a lower cancer-specific survival compared to those with SCC [HR 0.60 (95% CI 0.53 – 0.71)].

Increasing stage at diagnosis was also associated with lower cancer-specific survival; women with Stage II (HR 0.50; 95% CI 0.38 – 0.65), III (HR 0.32; 95% CI 0.25 – 0.41), and IV (HR 0.14; 95% CI 0.11 – 0.17) disease all had lower cancer-specific survival compared to those with Stage I disease. All forms of treatment, except for chemotherapy alone (which was rare), were associated with much higher cancer-specific survival compared to no receipt of treatment. This included: surgery + chemotherapy/radiation (HR 2.56; 95% CI 1.53 – 2.63), chemoradiation (HR 2.32; 95% CI 1.81 – 2.94), surgery only (HR 6.67; 95% CI 4.76 – 10.0), and radiation only (HR 1.45; 95% CI 1.19 – 1.79). Lower cancer-specific survival was observed for Black women (HR 0.83; 95% CI 0.69 – 0.99) although this association was attenuated and no longer significant after multivariable adjustment (HR 0.95; 95% CI 0.81 – 1.11). Factors found to be significant after adjustment included age >80 (HR 0.77; 95% CI 0.64 – 0.91), residing in a metropolitan area (HR 0.85; 95% CI 0.75 – 0.99), other histology (HR 0.73; 95% CI 0.62 – 0.85), and higher stage disease (Stage II HR 0.53 95% CI 0.41 – 0.68, Stage III HR 0.35 95% CI 0.28 – 0.44), and Stage IV HR 0.16 95% CI 0.13 – 0.21).

## DISCUSSION

Using SEER-Medicare data we identified a total of 2,147 women aged >65 who were diagnosed with cervical cancer. Most women were diagnosed with locally advanced or metastatic disease, and 5-year cancer-specific survival was only 50%. Nearly 15% of cervical cancers went untreated, with important differences by age, stage, and comorbidities. Lowest survival rates were observed among older women, and women with advanced stage disease. Importantly, even after accounting for older age, treatment was associated with an increased survival rate. These findings, coupled with the fact that women aged >65 constitute an increasing proportion of the US population and remain at-risk for cervical cancer into their 80's, highlight the need to re-evaluate screening and treatment practices in this population.

Similar to previous studies among older US women<sup>15,20</sup> from 2006 to 2012, nearly 1/6 of women in the present study did not receive any treatment. In the present analysis, women aged 80 years and older remained less likely to receive treatment compared to women aged <80 years after adjusting for important factors such as stage at diagnosis and comorbidities, suggesting that age itself is associated with decreased likelihood of receiving treatment. It remains unclear if these women declined or were not offered treatment; however, this is consistent with previous studies showing that, stage for stage, women >65 are treated less aggressively compared to women <65.<sup>11</sup> For example, older women are less likely to undergo extensive surgery, such as radical hysterectomy and pelvic lymphadenectomy, compared to younger women.<sup>15,21</sup> Furthermore, we suspect the consistent lack of treatment among older women across studies<sup>20,22</sup> can be partially explained by high rates of comorbidities<sup>12,23–25</sup> and high proportion of stage IV disease compared to younger women. Historically, older individuals with geriatric conditions and comorbidity have been underrepresented in trials and studies.<sup>26</sup> Further research focusing on this population is imperative to better elucidate the complex interplay between age, stage at presentation and comorbidities.<sup>27</sup>



Given that screening is associated with a significantly reduced risk of cervical cancer, advanced stage disease, and death from the disease<sup>28</sup> the discontinuation of screening at age 65 for the majority of women may play a role in the late stage at diagnosis and subsequently more difficult treatment decisions and outcomes in this population. Unfortunately, we were unable to retrieve information on previous screening history from SEER-Medicare linked data but previous studies report that about 25–50% of women diagnosed with cervical cancer had adequate screening prior to exiting.<sup>29–31</sup> Furthermore, research has shown that screening prior to exiting is associated with a decreased risk of cervical cancer after age 65<sup>24,32,33</sup>, and a decreased risk of advanced stage disease.<sup>34</sup> Coupled with the fact that the life expectancy is increasing, and the number of women with an intact cervix is increasing as a result of declining hysterectomy incidence rates,<sup>35</sup> these findings may also suggest a need to continue screening beyond the age of 65.<sup>36</sup> On the other hand, due to atrophy and the retraction of the transformation zone into the cervical canal in older women, false negative screening and diagnostic work-up of screen-positive women is very challenging.<sup>37</sup> Thus, further research is needed to better understand the impact of screening in this population and to improve the effectiveness of screening programs for older women.

Like treatment, survival rates also declined significantly with increasing age, from 54.5% in women aged 66–70 to 37.4% in women aged 80 years and older. Although older women were more likely to be diagnosed with advanced stage disease, less likely to receive treatment, have a higher comorbidity score, and more likely to be diagnosed with other histologic subtypes, risk of cervical cancer death remained higher among older women after adjusting for these variables. This persistently elevated risk of cancer mortality may be due to other clinically important factors, such as type of treatment (e.g., surgery, radiotherapy, chemotherapy, etc.) and premature cessation of treatment because of side effects or patient wishes, which were not accounted for in this study. Thus, more studies are needed to explore potential explanations for these findings to improve survival, especially given the increasing life expectancy in the general population.

Unlike previous studies of women diagnosed with cancer > 25 years<sup>38</sup> we found no statistical differences in receipt of treatment across race/ethnicity but 5-year cancer-specific survival did vary from a high of 56% in White Hispanic to 45% in Black women. Mechanisms behind racial disparities in survival are likely multifactorial and related to patient factors (i.e., socio-economic status, comorbidity, etc.), provider factors (screening, surgery, quality of treatment, etc.)<sup>39,40</sup>, and disease factors (histology, stage, etc.). In the present study, there were minor differences in stage at presentation, but Black women were more likely to be diagnosed with ‘other’ histologic subtypes which are known to be more aggressive and associated with lower survival rates. Thus, further investigation into the relationship between various histologic subtypes and stage at presentation and how these and care-related factors relate to racial disparities.

In our study, 5-year survival rates were similar between AC and SCC but significantly lower among women diagnosed with other histologic subtypes. Previous literature comparing AC to SCC has found AC to be more aggressive and associated with poorer prognosis<sup>41–43</sup> compared to SCC. However, there may have been too few AC cases in our study to detect a statistically significant difference. Conversely, it is not surprising that other histologies



had lower survival, given that several subtypes are known to be more aggressive and often diagnosed at later stages, including small cell, papillary SCC, and mucinous carcinoma.<sup>44</sup> Even after adjusting for potential confounders in our study, survival was still significantly lower among other histologic subtypes compared to SCC, highlighting a potential need to explore new treatment options for these subtypes that are often underrepresented in clinical trials due to small case numbers.

We recognize our study is subject to limitations. The SEER dataset is limited to eleven SEER regions that may not adequately represent the entire U.S. population, which may affect the generalizability of our findings if cases, treatment, or survival patterns from other regions differ from those included here. In addition, we acknowledge the limitations of using the Medicare database to calculate comorbidity scores and the potential risk of misclassification of medical conditions due to reliance on ICD-9 codes. Additionally, there may be coding errors and disruptions in observed rates due to coding transition/errors. Other limitations of using ICD-9 codes include possible unmeasured confounding, misclassification bias, missing data, and changing participant eligibility over time that stem from not using data created or collected to answer a specific research question. On the other hand, the use of the SEER-Medicare linked data provides a large sample size for robust statistical analysis and together provide extensive treatment information. Additionally, our analysis calculates cancer-specific survival, providing accurate information about the women in this population who are dying of cancer versus other age-related conditions, which is especially important to understanding the cancer outcomes in this population.

In conclusion, both treatment and survival decline significantly with increasing age, which partly may be attributed to a higher proportion of advanced stage disease at diagnosis in older women. Given that cervical cancer screening is associated with a significantly reduced risk of cervical cancer, particularly advanced stage disease and death from the disease, even among women older than 65, our findings highlight a need to re-evaluate the appropriate age to exit routine screening.<sup>36</sup> Furthermore, future studies may be necessary to explore how to improve diagnostic work-up of women who screen positive, as this would allow for earlier detection of disease thereby increasing likelihood of receiving (less aggressive) treatment and improving survival. Given that the proportion of the population over the age of 65 continues to grow, it will take decades to see the impact of the HPV vaccine in this age group<sup>35</sup>, and life expectancy is increasing, the burden of disease among older women will continue to increase. Therefore, further evaluation of screening, diagnostic, and treatment practices in this population are critical in order to increase survival and keep up with advances in medical care and population health that have now afforded women a longer life.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgements

This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors. The authors acknowledge the efforts of the National Cancer Institute; the

Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc.; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database.

### Funding

This research was supported, in part, by the JHMI Cigarette Restitution Fund and the Johns Hopkins Cervical Cancer SPORE (P50 CA098252-16, P.I.: TC Wu) to AF Rositch.

### Data availability

The data that support the findings of this study are available from the corresponding author, AR upon reasonable request.

### ABBREVIATION

<b>SEER</b>	Surveillance, Epidemiology, and End Results registry
<b>AJCC</b>	American Joint Committee on Cancer
<b>CPT</b>	Common Procedural Terminology
<b>HCPCS</b>	Healthcare Common Procedure Coding System
<b>AC</b>	adenocarcinoma
<b>SCC</b>	squamous cell carcinoma
<b>HR</b>	hazard ratio
<b>RR</b>	relative risk

### REFERENCES

1. Cervical Cancer Statistics | Key Facts About Cervical Cancer. Accessed August 23, 2021. <https://www.cancer.org/cancer/cervical-cancer/about/key-statistics.html>
2. Fontham ETH, Wolf AMD, Church TR, et al. Cervical cancer screening for individuals at average risk: 2020 guideline update from the American Cancer Society. *CA Cancer J Clin.*2020;70(5):321–346. doi:10.3322/caac.21628 [PubMed: 32729638]
3. Saslow D, Solomon D, Lawson HW, et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. *Am J Clin Pathol.* 2012;137(4):516–542. doi:10.1309/AJCPTGD94EVR SJCG [PubMed: 22431528]
4. Yoo W, Kim S, Huh WK, et al. Recent trends in racial and regional disparities in cervical cancer incidence and mortality in United States. *PLoS ONE.* 2017;12(2):e0172548. doi:10.1371/journal.pone.0172548 [PubMed: 28234949]
5. Mandelblatt JS, Yabroff KR. Breast and cervical cancer screening for older women: recommendations and challenges for the 21st century. *J Am Med Womens Assoc.* 1972. 2000;55(4):210–215. [PubMed: 10935354]
6. Rositch AF, Nowak RG, Gravitt PE. Increased age and race-specific incidence of cervical cancer after correction for hysterectomy prevalence in the United States from 2000 to 2009. *Cancer.* 2014;120(13):2032–2038. doi:10.1002/cncr.28548 [PubMed: 24821088]
7. Beavis AL, Gravitt PE, Rositch AF. Hysterectomy-corrected cervical cancer mortality rates reveal a larger racial disparity in the United States. *Cancer.* 2017;123(6):1044–1050. doi:10.1002/cncr.30507 [PubMed: 28112816]

8. Bureau UC. Population Projections. The United States Census Bureau. Accessed November 29, 2020. <https://www.census.gov/programs-surveys/popproj.html>
9. Coker AL, Du XL, Fang S, Eggleston KS. Socioeconomic status and cervical cancer survival among older women: Findings from the SEER–Medicare linked data cohorts. *Gynecol Oncol.* 2006;102(2):278–284. doi:10.1016/j.ygyno.2005.12.016 [PubMed: 16434087]
10. Lababidi S, McQuerry KJ, Duan R, Johnson MS, Fredericks T, Baldwin L. Incidence and Characteristics of Cervical Cancer in Elderly Women [3Q]. *Obstet Gynecol.* 2018;131:184S. doi:10.1097/01.AOG.0000533216.91272.ad
11. Quinn BA, Deng X, Colton A, Bandyopadhyay D, Carter JS, Fields EC. Increasing age predicts poor cervical cancer prognosis with subsequent effect on treatment and overall survival. *Brachytherapy.* 2019;18(1):29–37. doi:10.1016/j.brachy.2018.08.016 [PubMed: 30361045]
12. Brun J, Stoven-Camou D, Trouette R, Lopez M, Chene G, Hocké C. Survival and prognosis of women with invasive cervical cancer according to age. *Gynecol Oncol.* 2003;91:395–401. doi:10.1016/S0090-8258(03)00501-8 [PubMed: 14599872]
13. Elit L. Cervical cancer in the older woman. *Maturitas.* 2014;78(3):160–167. doi:10.1016/j.maturitas.2014.04.018 [PubMed: 24861965]
14. Xie S, Pan S, Zou S, Zhu H, Zhu X. Characteristics and Treatments of Patients Aged 65 Years or Over with Cervical Cancer. *Clin Interv Aging.* 2020;15:841–851. doi:10.2147/CIA.S255305 [PubMed: 32606624]
15. Nogueira-Rodrigues A, de Melo AC, Garces AHI, et al. Patterns of Care and Outcome of Elderly Women Diagnosed With Cervical Cancer in the Developing World. *Int J Gynecol Cancer Off J Int Gynecol Cancer Soc.* 2016;26(7):1246–1251. doi:10.1097/IGC.0000000000000756
16. Warren JL, Klabunde CN, Schrag D, Bach PB, Riley GF. Overview of the SEER-Medicare data: content, research applications, and generalizability to the United States elderly population. *Med Care.* 2002;40(8 Suppl):IV-3–18. doi:10.1097/01.MLR.0000020942.47004.03
17. Potosky AL, Riley GF, Lubitz JD, Mentnech RM, Kessler LG. Potential for cancer related health services research using a linked Medicare-tumor registry database. *Med Care.* 1993;31(8):732–748. [PubMed: 8336512]
18. Noone AM, Lund JL, Mariotto A, et al. Comparison of SEER Treatment Data With Medicare Claims. *Med Care.* 2016;54(9):e55–e64. doi:10.1097/MLR.000000000000073 [PubMed: 24638121]
19. Sawaya GF, Sung HY, Kearney KA, et al. Advancing Age and Cervical Cancer Screening and Prognosis. *J Am Geriatr Soc.* 2001;49(11):1499–1504. doi:10.1046/j.1532-5415.2001.4911243.x [PubMed: 11890589]
20. Coker AL, Du XL, Fang S, Eggleston KS. Socioeconomic status and cervical cancer survival among older women: findings from the SEER-Medicare linked data cohorts. *Gynecol Oncol.* 2006;102(2):278–284. doi:10.1016/j.ygyno.2005.12.016 [PubMed: 16434087]
21. Wright JD, Gibb RK, Geevarghese S, et al. Cervical carcinoma in the elderly. *Cancer.* 2005;103(1):85–91. doi:10.1002/cncr.20751 [PubMed: 15540239]
22. Sharma C, Deutsch I, Horowitz DP, et al. Patterns of care and treatment outcomes for elderly women with cervical cancer. *Cancer.* 2012;118(14):3618–3626. doi:10.1002/cncr.26589 [PubMed: 22038773]
23. Mitchell PA, Waggoner S, Rotmensch J, Mundt AJ. Cervical cancer in the elderly treated with radiation therapy. *Gynecol Oncol.* 1998;71(2):291–298. doi:10.1006/gyno.1998.5180 [PubMed: 9826474]
24. Hammer A, Soegaard V, Maimburg RD, Blaakaer J. Cervical cancer screening history prior to a diagnosis of cervical cancer in Danish women aged 60 years and older-A national cohort study. *Cancer Med.* 2019;8(1):418–427. doi:10.1002/cam4.1926 [PubMed: 30600650]
25. Feldman S, Cook E, Davis M, et al. Cervical Cancer Incidence Among Elderly Women in Massachusetts Compared With Younger Women. *J Low Genit Tract Dis.* 2018;22(4):314–317. doi:10.1097/LGT.0000000000000435 [PubMed: 30256336]
26. Scher KS, Hurria A. Under-representation of older adults in cancer registration trials: known problem, little progress. *J Clin Oncol Off J Am Soc Clin Oncol.* 2012;30(17):2036–2038. doi:10.1200/JCO.2012.41.6727

27. United Nations, Department of Economic and Social Affairs, Population Division. World Population Ageing: 2017 Highlights.; 2017. Accessed August 25, 2021. [https://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2017\\_Highlights.pdf](https://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2017_Highlights.pdf)
28. Landy R, Pesola F, Castañón A, Sasieni P. Impact of cervical screening on cervical cancer mortality: estimation using stage-specific results from a nested case-control study. *Br J Cancer*. 2016;115(9):1140–1146. doi:10.1038/bjc.2016.290 [PubMed: 27632376]
29. Yost S, Hoekstra A. Cervical cancer in women over 65: An analysis of screening. *Gynecol Oncol Rep*. 2018;25:48–51. doi:10.1016/j.gore.2018.05.010 [PubMed: 30023421]
30. Castañón A, Landy R, Cuzick J, Sasieni P. Cervical screening at age 50–64 years and the risk of cervical cancer at age 65 years and older: population-based case control study. *PLoS Med*. 2014;11(1):e1001585. doi:10.1371/journal.pmed.1001585 [PubMed: 24453946]
31. Dinkelspiel H, Fetterman B, Poitras N, et al. Screening history preceding a diagnosis of cervical cancer in women age 65 and older. *Gynecol Oncol*. 2012;126(2):203–206. doi:10.1016/j.ygyno.2012.04.037 [PubMed: 22561038]
32. Castañón A, Landy R, Cuzick J, Sasieni P. Cervical screening at age 50–64 years and the risk of cervical cancer at age 65 years and older: population-based case control study. *PLoS Med*. 2014;11(1):e1001585. doi:10.1371/journal.pmed.1001585 [PubMed: 24453946]
33. Kaminen A, Weinmann S, Shy KK, Glass AG, Weiss NS. Efficacy of screening in preventing cervical cancer among older women. *Cancer Causes Control*. 2013;24(9):1653–1660. doi:10.1007/s10552-013-0239-4 [PubMed: 23744043]
34. Landy R, Pesola F, Castañón A, Sasieni P. Impact of cervical screening on cervical cancer mortality: estimation using stage-specific results from a nested case-control study. *Br J Cancer*. 2016;115(9):1140–1146. doi:10.1038/bjc.2016.290 [PubMed: 27632376]
35. Simms KT, Yuill S, Killen J, et al. Historical and projected hysterectomy rates in the USA: Implications for future observed cervical cancer rates and evaluating prevention interventions. *Gynecol Oncol*. 2020;158(3):710–718. doi:10.1016/j.ygyno.2020.05.030 [PubMed: 32723676]
36. Dilley S, Huh W, Blechter B, Rositch AF. It's time to re-evaluate cervical Cancer screening after age 65. *Gynecol Oncol*. 2021;0(0). doi:10.1016/j.ygyno.2021.04.027
37. Gustafson LW, Petersen LK, Bor P, Andersen B, Hammer A. Cervical cancer prevention among older women - challenges in screening, diagnostic workup and treatment. *Acta Obstet Gynecol Scand*. 2021;100(8):1364–1368. doi:10.1111/aogs.14162 [PubMed: 33866548]
38. Du XL, Lin CC, Johnson NJ, Altekruze S. Effects of individual-level socioeconomic factors on racial disparities in cancer treatment and survival. *Cancer*. 2011;117(14):3242–3251. doi:10.1002/cncr.25854 [PubMed: 21264829]
39. Johnson NL, Head KJ, Scott SF, Zimet GD. Persistent Disparities in Cervical Cancer Screening Uptake: Knowledge and Sociodemographic Determinants of Papanicolaou and Human Papillomavirus Testing Among Women in the United States. *Public Health Rep Wash DC* 1974. 2020;135(4):483–491. doi:10.1177/0033354920925094
40. Ford S, Tarraf W, Williams KP, Roman LA, Leach R. Differences in cervical cancer screening and follow-up for black and white women in the United States. *Gynecol Oncol*. 2021;160(2):369–374. doi:10.1016/j.ygyno.2020.11.027 [PubMed: 33323276]
41. Jung EJ, Byun JM, Kim YN, et al. Cervical Adenocarcinoma Has a Poorer Prognosis and a Higher Propensity for Distant Recurrence Than Squamous Cell Carcinoma. *Int J Gynecol Cancer Off J Int Gynecol Cancer Soc*. 2017;27(6):1228–1236. doi:10.1097/IGC.0000000000001009
42. Hu K, Wang W, Liu X, Meng Q, Zhang F. Comparison of treatment outcomes between squamous cell carcinoma and adenocarcinoma of cervix after definitive radiotherapy or concurrent chemoradiotherapy. *Radiat Oncol Lond Engl*. 2018;13(1):249. doi:10.1186/s13014-018-1197-5
43. Chen RJ, Lin YH, Chen CA, Huang SC, Chow SN, Hsieh CY. Influence of histologic type and age on survival rates for invasive cervical carcinoma in Taiwan. *Gynecol Oncol*. 1999;73(2):184–190. doi:10.1006/gyno.1999.5364 [PubMed: 10329032]
44. Maniar KWJ. Pathology of Cervical Carcinoma | GLOWM. In: *Glob. Libr. Women's Med*; 2017. Accessed December 20, 2021. [http://www.glowm.com/section-view/heading/Pathology of Cervical Carcinoma/item/230](http://www.glowm.com/section-view/heading/Pathology%20of%20Cervical%20Carcinoma/item/230)

**NOVELTY AND IMPACT STATEMENT**

In SEER-Medicare linked data from 2004 – 2013, most women >65 with cervical cancer were diagnosed with locally advanced or metastatic disease. Both receipt of treatment and survival decreased with increasing age. These findings, coupled with the fact that women aged >65 constitute an increasing proportion of the population, highlight the need to re-evaluate screening and treatment practices in older women to detect cervical cancer at earlier stages and increase survival.

Author Manuscript

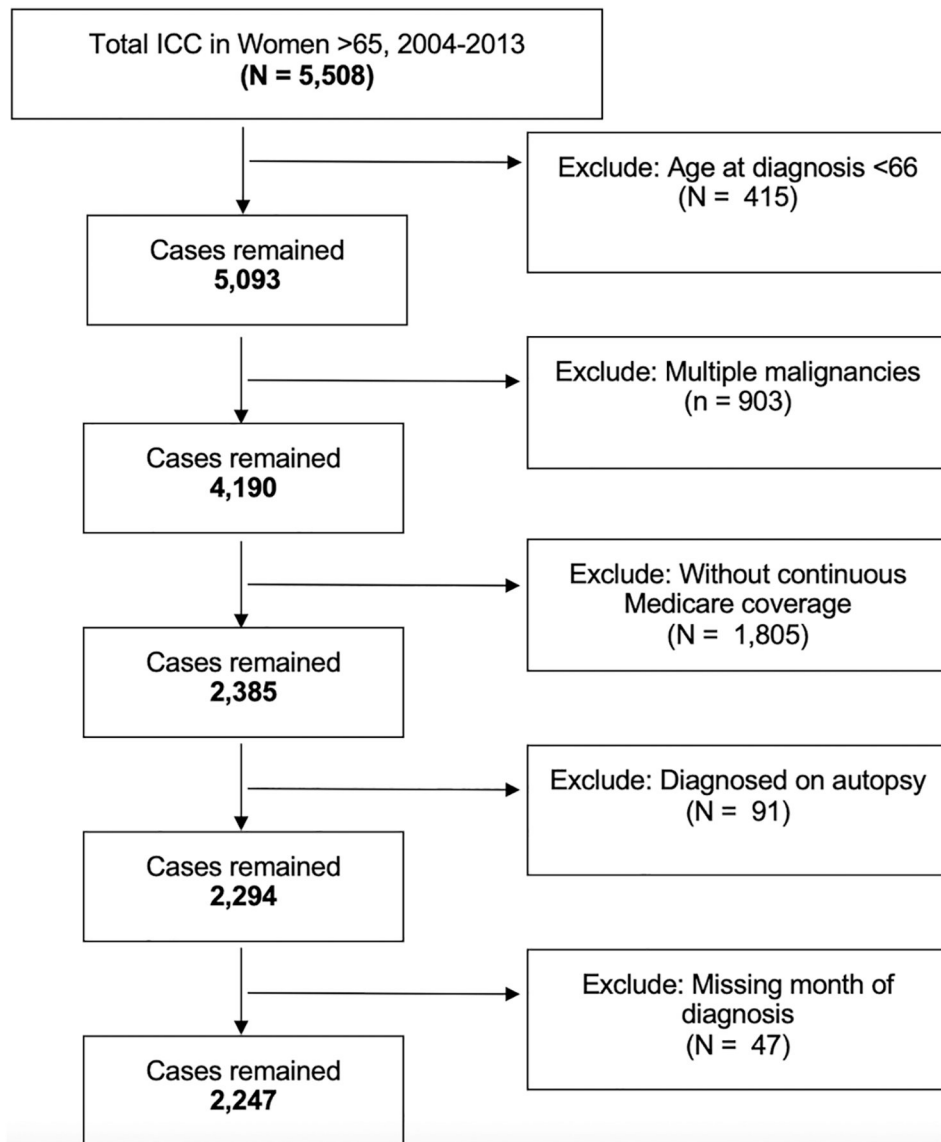
Author Manuscript

Author Manuscript

Author Manuscript

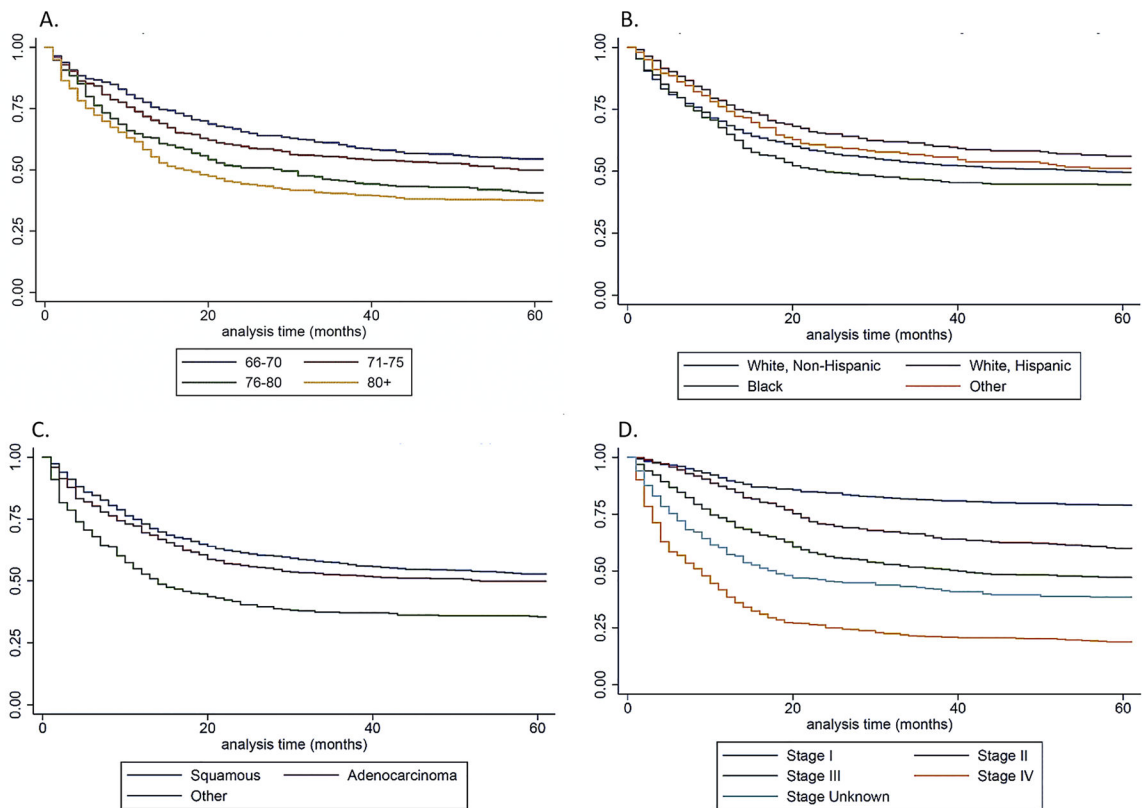
### Highlights

- Most women >65 years with cervical cancer were diagnosed at stage II or higher (63%), including 23% at Stage IV.
- Nearly 15% of patients weren't treated, which was associated with age>80, comorbidity scores  $\geq 3$ , and stage IV disease.
- 5-year cancer-specific survival was 50% overall and treatment was associated with higher cancer-specific survival.
- Increasing age and stage at diagnosis were associated with lower cancer-specific survival.



**Figure 1 -**  
Flow chart of selection of the study population.





**Figure 2,**  
**A-D - Cervical cancer 5-year cancer specific survival for women >65 years of age who were diagnosed between 2004–2013 in the SEER-Medicare database.**

A. Survival, by age at diagnosis (years)					
Age (years)	Number of patients	Events/deaths	5-Yr Cancer-Specific Survival	95% CI	Log-rank
66–70	663	276	58.4%	54.5% – 62.0%	p < 0.01
71–75	541	252	53.4%	49.1% – 57.5%	
76–80	417	232	44.4%	39.6% – 49.1%	
>80	626	374	40.3%	36.4% – 44.1%	

B. Survival, by race/ethnicity.					
Race/ethnicity	Number of patients	Events/deaths	5-Yr Cancer-Specific Survival	95% CI	Log-rank
White, Non-Hispanic	1455	734	49.6%	47.0% – 52.1%	p = 0.02
White, Hispanic	223	98	56.1%	49.3% – 62.3%	
Black	368	204	44.6%	39.4% – 50.0%	
Other	201	98	51.2%	44.1% – 57.9%	

C. Survival, by tumor histology.					
Tumor Histology	Number of patients	Events/deaths	5-Yr Cancer-Specific Survival	95% CI	Log-rank
SCC	1490	702	52.9%	50.3% – 55.4%	p = 0.16 <sup>+</sup>
AC	393	197	49.9%	44.8% – 54.7%	
Other	364	235	35.4%	30.1% – 40.4%	p < 0.01 <sup>*</sup>

D. Survival, by stage.					
AJCC Stage	Number of patients	Events/deaths	5-Yr Cancer-Specific Survival	95% CI	Log-rank
Stage I	555	117	78.9%	75.3% – 82.1%	p < 0.01
Stage II	375	150	60.0%	54.9% – 64.8%	
Stage III	515	272	47.2%	42.8% – 51.4%	
Stage IV	519	421	18.9%	15.6% – 22.4%	
Unknown	283	174	38.5%	32.9% – 44.2%	

Abbreviations: SCC, squamous cell carcinoma; AC, adenocarcinoma.

\* Log-rank comparing squamous and adenocarcinoma survival curves only

<sup>+</sup> Log-rank comparing all three tumor histology survival curves

**Table 1:**Patient, tumor, and treatment characteristics of patients >65 years of age diagnosed with cervical cancer.<sup>a</sup>

Characteristic	Total, n=2,247 (%)
Age at diagnosis (years)	
66–70	663 (29.5)
71–75	541 (24.1)
76–80	417 (18.6)
>80	626 (27.9)
Race/Ethnicity	
Non-Hispanic White	1455 (64.8)
Hispanic White	223 (9.9)
Black <sup>b</sup>	368 (16.4)
Other <sup>c</sup>	201 (9.0)
Year of Diagnosis	
2004–2006	702 (31.2)
2007–2009	671 (29.9)
2010 – 2013	874 (38.9)
Comorbidity Index Score	
0	1035 (46.1)
1	490 (21.8)
2	249 (11.1)
3	312 (13.9)
Unknown <sup>d</sup>	161 (7.2)
Marital Status	
Single/Not Married	1476 (65.7)
Married	634 (28.2)
Unknown	137 (6.1)
Area of Residence	
Large Metropolitan	1218 (54.2)
Metropolitan	620 (27.6)
Urban	123 (5.5)
Less Urban/Rural	286 (12.8)
Tumor Histology	
SCC	1490 (66.3)
AC	393 (17.5)
Other <sup>e</sup>	364 (16.2)
AJCC Stage (6th edition) <sup>f</sup>	
Stage I	555 (24.7)
Stage II	375 (16.7)
Stage III	515 (22.9)

Characteristic	Total, n=2,247 (%)
Stage IV	519 (23.1)
Unknown/Unavailable <sup>g</sup>	283 (12.6)
Treatment	
No Treatment	329 (14.6)
Surgery + Chemotherapy or Radiation	942 (41.9)
Chemoradiation	239 (10.6)
Surgery Only	275 (12.2)
Chemotherapy Only	40 (1.8)
Radiation Therapy Only	422 (18.8)

Abbreviations: SCC, squamous cell carcinoma; AC, adenocarcinoma.

<sup>a</sup>Source: SEER-Medicare 2004–2013 linked database.

<sup>b</sup>Includes both Hispanic (n=3) and non-Hispanic Blacks (n=365)

<sup>c</sup>Other includes: American Indian/AK Native. Asian/Pacific Islander. Variable is independent of Hispanic ethnicity.

<sup>d</sup>Patients without Medicare hospital data required to calculate the co-morbidity scores were categorized as 'Unknown'.

<sup>e</sup>Other includes: Unspecified neoplasms (n=43), epithelial neoplasms NOS (n=147), complex epithelial neoplasms (n=61), basal cell neoplasms (n=6), cystic, mucinous, and serous neoplasms (n=62), nevi and melanomas (n=15), soft tissue tumors and sarcomas (n=3), myomatous neoplasms (n=5), complex mixed and stromal neoplasms (n=28), mesonephromas (n=1), and gliomas (n= 1), and miscellaneous tumors (n=1)

<sup>f</sup>SEER Modified AJCC 6th Edition - Derived by algorithm from extent of disease (EOD). Not available for all years or for all sites. The modified version stages cases that would be un-staged under strict AJCC staging rules.

<sup>g</sup>Includes variables that had a recode scheme was not yet available for analysis of patient staging.

**Table 2:**

Patient and tumor variables associated with receipt of treatment<sup>a</sup> for women >65 years of age diagnosed with cervical cancer.<sup>b</sup>

Variable	Received Treatment <sup>a</sup> n = 1,918 (%)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Age at Diagnosis			
66–70	603 (91.0)	1.00 (Reference)	1.00 (Reference)
71–75	480 (88.7)	0.98 (0.87 – 1.10)	0.98 (0.87 – 1.11)
76–80	359 (86.1)	0.94 (0.83 – 1.08)	0.96 (0.84 – 1.10)
>80	476 (76.0)	0.83 (0.74 – 0.94)	0.87 (0.77 – 0.98)
Race/Ethnicity			
White, Non-Hispanic	1234 (84.9)	1.00 (Reference)	1.00 (Reference)
White, Hispanic	200 (89.7)	1.05 (0.91 – 1.23)	1.04 (0.89– 1.20)
Black <sup>c</sup>	303 (82.3)	0.97 (0.86 – 1.10)	1.01 (0.89 – 1.14)
Other <sup>d</sup>	181 (90.0)	1.06 (0.91 – 1.24)	1.07 (0.91 – 1.24)
Comorbidity Index			
0	739 (71.4)	1.00 (Reference)	1.00 (Reference)
1	429 (87.6)	0.97 (0.86 – 1.08)	0.97 (0.87 – 1.09)
2	197 (79.1)	0.87 (0.75 – 1.02)	0.89 (0.76 – 1.04)
3	230 (73.7)	0.81 (0.70 – 0.94)	0.85 (0.73 – 0.98)
Unknown <sup>e</sup>	125 (77.6)	0.86 (0.71 – 1.03)	0.86 (0.71 – 1.03)
Marital Status			
Single/Not Married	1242 (84.1)	1.00 (Reference)	1.00 (Reference)
Married	575 (90.7)	1.08 (0.98 – 1.19)	1.02 (0.93 – 1.14)
Unknown	101 (73.7)	0.88 (0.72 – 1.07)	0.92 (0.75 – 1.13)
Area of Residence			
Large Metropolitan	1003 (82.3)	1.00 (Reference)	1.00 (Reference)
Metropolitan	532 (85.8)	1.01 (0.91 – 1.12)	1.00 (0.90 – 1.12)
Urban	102 (82.9)	0.98 (0.78 – 1.20)	0.98 (0.80 – 1.20)
Less Urban/Rural	250 (87.4)	1.03 (0.90 – 1.18)	1.04 (0.90 – 1.19)
Tumor Histology			
SCC	1317 (88.4)	1.00 (Reference)	1.00 (Reference)
AC	334 (85.0)	0.96 (0.85 – 1.08)	0.97 (0.86 – 1.09)
Other <sup>f</sup>	267 (73.4)	0.83 (0.73 – 0.95)	0.90 (0.79 – 1.03)
AJCC Stage (6th edition) <sup>g</sup>			
Stage I	521 (93.9)	1.00 (Reference)	1.00 (Reference)
Stage II	356 (94.9)	1.01 (0.88 – 1.16)	1.01 (0.88 – 1.16)
Stage III	464 (90.1)	0.96 (0.85 – 1.09)	0.96 (0.85 – 1.09)
Stage IV	398 (76.7)	0.82 (0.72 – 0.93)	0.84 (0.73 – 0.96)
Unknown <sup>h</sup>	179 (63.3)	0.67 (0.57 – 0.80)	0.72 (0.60 – 0.85)

Abbreviations: RR, relative risk; CI, confidence interval; SCC, squamous cell carcinoma; AC, adenocarcinoma.

<sup>a</sup>Treatment is defined as receipt of a single treatment or combination of surgery, chemotherapy, and/or radiation.

<sup>b</sup>Source: SEER-Medicare 2004–2013 linked database.

<sup>c</sup>Includes both Hispanic (n=3) and non-Hispanic Blacks (n=365)

<sup>d</sup>Other includes: American Indian/AK Native. Asian/Pacific Islander. Variable is independent of Hispanic ethnicity.

<sup>e</sup>Patients without Medicare hospital data required to calculate the co-morbidity scores were categorized as 'Unknown'.

<sup>f</sup>Other includes: Unspecified neoplasms (n=43), epithelial neoplasms NOS (n=147), complex epithelial neoplasms (n=61), basal cell neoplasms (n=6), cystic, mucinous, and serous neoplasms (n=62), nevi and melanomas (n=15), soft tissue tumors and sarcomas (n=3), myomatous neoplasms (n=5), complex mixed and stromal neoplasms (n=28), mesonephromas (n=1), and gliomas (n= 1), and miscellaneous tumors (n=1)

<sup>g</sup>SEER Modified AJCC 6th Edition - Derived by algorithm from extent of disease (EOD). Not available for all years or for all sites. The modified version stages cases that would be un-staged under strict AJCC staging rules.

<sup>h</sup>Includes variables that had a recode scheme was not yet available for analysis of patient staging.

**Table 3:**

Risk factors associated with cancer specific survival for women >65 years of age diagnosed with cervical cancer.<sup>a</sup>

Characteristic	Total, n=2,247	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Age at Diagnosis			
66–70	663	1.00 (Reference)	1.00 (Reference)
71–75	541	0.85 (0.72 – 1.01)	0.90 (0.76 – 1.07)
76–80	417	0.65 (0.54 – 0.77)	0.71 (0.59 – 0.85)
>80	626	0.56 (0.48 – 0.66)	0.77 (0.64 – 0.91)
Race/Ethnicity			
Non-Hispanic White	1455	1.00 (Reference)	1.00 (Reference)
Hispanic White	223	1.26 (1.02 – 1.56)	1.12 (0.91 – 1.39)
Black <sup>b</sup>	368	0.87 (0.75 – 1.02)	0.95 (0.81 – 1.11)
Other <sup>c</sup>	201	1.10 (0.89 – 1.35)	1.07 (0.86 – 1.33)
Comorbidity Index			
0	702	1.00 (Reference)	1.00 (Reference)
1	671	0.89 (0.76 – 1.03)	0.94 (0.81 – 1.10)
2	874	0.93 (0.76 – 1.14)	1.13 (0.92 – 1.39)
3		0.76 (0.64 – 0.91)	1.03 (0.85 – 1.23)
Unknown <sup>d</sup>	1035	0.75 (0.60 – 0.93)	0.95 (0.76 – 1.20)
Marital Status			
Single/Unmarried	490	1.00 (Reference)	1.00 (Reference)
Married	249	1.28 (1.11 – 1.46)	1.08 (0.93 – 1.24)
Unknown	312	1.07 (0.83 – 1.37)	1.14 (0.89 – 1.47)
Area of Residence			
Large Metropolitan	1476	1.00 (Reference)	1.00 (Reference)
Metropolitan	634	0.92 (0.80 – 1.05)	0.86 (0.75 – 0.99)
Urban	137	0.93 (0.71 – 1.20)	0.95 (0.73 – 1.24)
Less Urban/Rural		0.91 (0.76 – 1.08)	0.90 (0.75 – 1.08)
Tumor Histology			
SCC	1218	1.00 (Reference)	1.00 (Reference)
AC	620	0.90 (0.76 – 1.05)	0.89 (0.76 – 1.05)
Other <sup>e</sup>	123	0.57 (0.49 – 0.66)	0.73 (0.62 – 0.85)
AJCC Stage (6th edition) <sup>f</sup>			
Stage I	286	1.00 (Reference)	1.00 (Reference)
Stage II	555	0.49 (0.38 – 0.62)	0.53 (0.41 – 0.68)
Stage III	375	0.32 (0.26 – 0.40)	0.35 (0.28 – 0.44)
Stage IV	519	0.13 (0.11 – 0.16)	0.16 (0.13 – 0.21)
Unknown <sup>g</sup>	283	0.24 (0.19 – 0.30)	0.34 (0.26 – 0.44)
Treatment			



Characteristic	Total, n=2,247	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
No Treatment	329	1.00 (Reference)	1.00 (Reference)
Surgery + Chemotherapy/Radiation	942	2.73 (2.33 – 3.21)	2.08 (1.74 – 2.50)
Chemoradiation	239	2.43 (1.95 – 3.03)	1.79 (1.40 – 2.28)
Surgery Only	275	6.16 (4.62 – 8.22)	2.46 (1.80 – 3.38)
Chemotherapy Only	40	1.01 (0.69 – 1.46)	1.25 (0.85 – 1.84)
Radiation therapy Only	422	1.43 (1.20 – 1.70)	1.24 (1.03 – 1.49)

Abbreviations: HR, hazard ratio; SCC, squamous cell carcinoma; AC, adenocarcinoma.

<sup>a</sup>Source: SEER-Medicare 2004–2013 linked database.

<sup>b</sup>Includes both Hispanic (n=3) and non-Hispanic Blacks (n=365)

<sup>c</sup>Other includes: American Indian/AK Native. Asian/Pacific Islander. Variable is independent of Hispanic ethnicity.

<sup>d</sup>Patients without Medicare hospital data required to calculate the co-morbidity scores were categorized as 'Unknown'.

<sup>e</sup>Other includes: Unspecified neoplasms (n=43), epithelial neoplasms NOS (n=147), complex epithelial neoplasms (n=61), basal cell neoplasms (n=6), cystic, mucinous, and serous neoplasms (n=62), nevi and melanomas (n=15), soft tissue tumors and sarcomas (n=3), myomatous neoplasms (n=5), complex mixed and stromal neoplasms (n=28), mesonephromas (n=1), and gliomas (n= 1), and miscellaneous tumors (n=1)

<sup>f</sup>SEER Modified AJCC 6th Edition - Derived by algorithm from extent of disease (EOD). Not available for all years or for all sites. The modified version stages cases that would be un-staged under strict AJCC staging rules.

<sup>g</sup>Includes variables that had a recode scheme was not yet available for analysis of patient staging.