Published in final edited form as:
Gynecol Oncol. 2009 February ; 112(2): 365–369. doi:10.1016/j.ygyno.2008.10.013.

Smoking and survival among Kentucky women diagnosed with invasive cervical cancer: 1995-2005

Ann L. Coker, PhD[1], **Chris DeSimone, MD**[1], **Katherine S. Eggleston, MSPH**[2], **Claudia Hopenhayn, PhD**[3], **Jaclyn Nee, MPH**[3], and **Thomas Tucker, PhD**[3]

1*University of Kentucky, School of Medicine, Lexington, KY 40506*

2*University of Texas Health Science Center, School of Public Health, Houston Texas 77030*

3*University of Kentucky, College of Public Health and Kentucky Cancer Registry, Lexington, KY 40506*

Abstract

Objectives—To determine whether smokers with cervical cancer were more likely to die from cervical cancer compared with non smokers after adjusting for confounding factors.

Methods—A population-based survival analysis was conducted among 2661 women diagnosed with invasive cervical cancer and reported to the Kentucky Cancer Registry from 1995-2005 and linked with state vital records and the National Death Index through 12/31/2005. A standard Kaplan – Meier approach was used in this survival analysis and Cox Proportional Hazards modeling was used to estimate adjusted hazard [aHR] ratios and 95% confidence intervals [CI] for smoking and survival for all cause and cervical cancer specific cause of death.

Results—Almost half of women diagnosed with cervical cancer (48.6%) were known to be current smokers based the medical record review and reporting to KCR. For another 19.4% no tobacco status was documented (missing) and 32.1% were known non smokers. After adjustment for age and stage at diagnosis, cell type, rural residence, race, insurance coverage, and treatment received, current smoker were 35% more likely to die of any cause (aHR = 1.35; 95% CI = 1.17-1.56) and 21% more likely to die of cervical cancer (aHR = 1.21; 95% CI = 1.01-1.46) compared with known non smoking cases.

Conclusion—These data strongly suggest that smoking reduces cervical cancer survival.

Introduction

Smoking, particularly in combination with high risk HPV types, is etiologically linked to pre-invasive and invasive cancer [1-4]. An emerging literature suggests that smoking may be linked to greater cervical cancer mortality in 3 [5-7] of 5 survival analyses [5-9]. Smoking may interact with high risk HPV types to negatively affect survival. One recent study found that smokers with cervical cancer who were also HPV 18 or 45 positive were four times more likely to die of cervical cancer[8]. Serur [7] found that while smoking was associated with poorer survival among 331 cervical cancer cancers, this association was no longer statistically significant after adjustment for alcohol and drug use. With one exception [6], the studies addressing smoking and cervical cancer prognosis have been relatively small (n<350) and based on clinical samples

Address for Reprints/Corresponding author: Ann L. Coker, ann.coker@uky.edu, 859 323 6758 phone, 859 257 1305 fax.

of women receiving treatment for this disease. Using the population-based Kentucky Cancer Registry (KCR), which is one of few that also collects data on current smoking, we hypothesized that smokers with cervical cancer would be more likely to die from cervical cancer compared with non smokers after adjusting for age and stage at diagnosis, cell type, rural residence, race, insurance coverage, and treatment received. This is the first population-based survival analysis of smoking and cervical cancer reported for women living in the US.

Methods

Study population and data sources

We conducted a population-based survival analysis among 2661 women diagnosed with invasive cervical cancer and reported to the KCR, a state wide population based registry funded by National Cancer Institute's Surveillance Epidemiology and End Results (SEER) program and the Centers for Disease Control and Prevention's National Program of Cancer Registries. The KCR is mandated by legislation passed by the General Assembly in 1990 to record all cases of cancer in the Commonwealth (with the exception of non-melanoma skin cancer). KCR has received gold certification from the North American Association of Central Cancer Registries every year since the formal certification was established, and has over 99% case ascertainment.

We included all invasive cervical cancers reported to KCR from 1995-2005. These dates were selected to include all available cases for survival analyses. KCR maintains active surveillance of case status using linkages with state vital records and the National Death Index. Survival time was calculated using the date of diagnosis and date of death for those deceased. Follow-up time for those still alive at the time of this linkage was calculated using the date of diagnosis and date of last follow-up (12/31/2005). Cases identified by death certificate only were excluded. A standard Kaplan – Meier approach was used in this analysis. Survival follow-up times ranged from 1 – 4503 days. Only primary site invasive cervical cancer cases (ICD-0-3 codes C53.0, C53.1, C53.8, and C53.9 were included in this analysis; the following histology codes were excluded: 9590-9989 (Lymphoma), 9050-9055 (mesothelioma), and 9140 (kaposi sarcoma). Death rates were calculated as the number of deaths divided by 10,000 woman-days of follow up. The Institutional Review Board of the University of Kentucky approved the study protocol.

Smoking status

Data to characterize current tobacco exposure was available from KCR; no information on previous tobacco exposure was available. Categories included cigarette smokers, other tobacco exposure, unknown status, and no tobacco exposure. Because the majority of tobacco exposed women were cigarette smokers (99.1%: 1280 of 1292), we combined the 12 women exposed to other forms of tobacco with cigarette smokers (hereafter smokers). Tobacco exposure was unknown for 515 (19.4%) cases. Because we did not wish to exclude this large proportion of cases from analyses, we retained this group by creating an indicator variable for those with unknown tobacco exposure. Two exposure groups: unknown smokers and smokers were compared with non smokers (n=854). No data are available to describe duration or exposure dose such as pack years of smoking.

Demographic attributes

Additional data from the KCR, originally abstracted from medical records, were used to define age at diagnosis, race/ethnicity, stage at diagnosis, cancer cell type, insurance payor source, rural residence, and treatment received. Race/ethnicity was classified using both race and Spanish/ Hispanic origin and grouped as non-Hispanic White versus all other race/ethnic groupings. KCR utilizes the SEER summary staging guide. Localized stage correspond to

FIGO stages IA_1, IA_2 (excludes carcinoma in situ), regional stage (IB_1 and IB_2) corresponded with FIGO stages IIA and IIB, and distant disease corresponded with FIGO stages IIIA, IIIB, IVA and IVB [10]. A separate indicator variable was used to group those reported with unknown or unstageable disease. Cervical cancer cell types were grouped non-squamous or squamous as the reference group due to established differences in cancer prognosis. Health insurance coverage was grouped for this analysis as private health insurance (including HMO, PPOs, or other private insurance), governmental forms of insurance (e.g. Medicaid, Medicare, TRICARE, Military, or Public Health Service), unknown insurance status, and no insurance or self pay. Beale Codes, published by the US Department of Agriculture, which classify counties as being more urban or more rural, were used to categorize residence at time of diagnosis. Residence in a metro area was defined to include those living in metropolitan counties with populations ranging from less than 250,000 to 1 million. Urban was defined as non-metropolitan areas with populations of at least 2,500. Finally, rural areas were non-metropolitan areas with populations less than 2,500.

Treatment received was available from KCR and included: surgery, chemotherapy, radiation therapy, hormonal therapy, immunotherapy, or other therapy (not specified). Neither the date of therapy, the number of treatments, nor specific therapies were detailed in KCR records. Treatment received was grouped into the following categories which are in general consistent with stage specific treatment recommendation: surgery alone (localized disease), surgery and either chemotherapy, radiation, or other therapy (regional disease), and other therapy yet no surgery (distant). The referent group included those with no treatment or unknown treatment information.

Statistical Analysis

Unadjusted multinomial logistic regression was used to determine demographic and other correlates of known current smokers and unknown tobacco exposure, relative to known non-smokers. Cox proportional hazards modeling was used to estimate the relative rate of dying from any cause as well as cervical cancer. This multivariate survival model was used to examine the relationship between survival time and predictor variables while controlling for sociodemographic factors, cell type, stage and treatment. No assumptions were made about the nature or shape of the hazard function. Finally, we evaluated the effect of smoking on survival by stage at diagnoses for cervical cancer specific mortality and all cause mortality. All data were analyzed using STATA version 9.

Results

Demographic attributes of women diagnosed with cervical cancer and reported to the KCR from 1995-2005 are reported in Table 1. Briefly, the mean age at diagnosis for cervical cancer cases included in this analysis was 50.5 years. The majority of cases were non-Hispanic White women (88.7%) who lived in metropolitan areas (53.1%). The majority of all women diagnosed with cervical cancer had some insurance (41.2% private and 40.4% governmental). Almost half of women diagnosed with cervical cancer (48.6%) were known to be current smokers. For another 19.4% no tobacco status was documented and 32.1% were known non-smokers. The vast majority of cases (80%) had squamous cell carcinoma of the cervix. More than half of the sample were diagnosed with localized disease yet 7.9% had unknown or unstageable disease. Finally, the majority of cases received surgery alone (34.2%) (Table 1).

Relative to non-smokers, current smokers were younger, more likely to live in metropolitan areas, to have governmental or no health insurance, to have squamous cell disease, to be diagnosed with regional relative to localized disease, and to receive other therapy excluding surgery (Table 2). Those missing tobacco exposure data were more likely to be missing other data elements.

Tables 3 and 4 display hazard ratios for all cause and cervical cancer specific mortality using a multivariate model adjusting for confounders. Ethnicity, rural residence and cell type were not associated with all cause survival; however, insurance, stage, and treatment were associated with mortality rates. Women who were current smokers were 35% more likely to die of any cause (aHR = 1.35; 95% CI = 1.17-1.56) and 21% more likely to die of cervical cancer (aHR = 1.21; 95% CI = 1.01-1.46) compared with known non smoking cases. Unknown tobacco exposure was not associated with a survival difference (Table 3).

When examining cervical cancer specific survival by stage at diagnosis, both ethnicity and insurance were associated with mortality rates in women diagnosed in late/regional stages, while cell type was associated with rates in early stage disease. Current smoking was associated with a 23% increased risk of dying from cervical cancer (aHR = 1.23; 95% CI = 1.00-1.53) among those diagnosed beyond localized disease (Table 4). This same pattern was also observed for all cause mortality (aHR = 1.38; 95% CI = 1.15-1.65) data not shown.

Discussion

Findings from this population-based study of smoking and decreased cervical cancer survival are consistent with three of five studies to explore this association [5-7]. While smoking was associated with both all cause (35% increase in mortality) and cervical cancer specific mortality (21% increase in mortality), the association was stronger for all cause mortality. In contrast with Wright [8] we did not have data to characterize the observed interactive effect of smoking and HPV on poorer cervical cancer survival. Further, in contrast with Serur [7], we lacked data to describe alcohol and drug use as confounders for the smoking and survival association.

Why might smoking influence cervical cancer survival? Smoking is well known to be associated with poorer cardiovascular health; thus smokers with cervical cancer may be more likely to die from other smoking associated conditions or these conditions may influence treatment success. Unfortunately we lacked data to describe comorbid conditions by smoking status. Other factors including alcohol use, drug use and SES were factors that were not controlled for in this analysis. However, the use of other demographic factors such as rural residence and payor source may be surrogate markers for SES.

Smoking may result in a more aggressive form of cervical cancer. As reported by Serur [7], we also observed that smokers were younger at cervical cancer diagnosis than were non smokers. Smoking has been associated with earlier onset of HGSIL/SCC ($p<0.01$) [11] and has been linked to more rapid development of CIN 3 among HPV+ women [12]. Taken together, these data suggest that smoking may result in a more aggressive disease, particularly if HPV 18 or 45 is also present [8]. Smoking may influence treatment options and/or treatment effectiveness. Kucera [6] noted that smoking was associated with having more side effects of primary irradiation ($p<0.01$) compared with non smokers. We noted no difference in smoking status and treatment received within stage, yet we lack information on side effects of treatment received or treatment effectiveness.

From a prevention perspective, determining whether smoking cessation improves survival outcomes for women with cervical cancer is important. Smoking cessation has been shown to improve outcomes ranging from cancer to cardiovascular disease survival. Among female ever smokers diagnosed with lung cancer, former smokers experienced a 15% risk reduction for mortality per 10 years of smoking abstinence compared with current smokers [13]. Smoking cessation at cervical cancer diagnosis may benefit patients by changing treatment options and possibly improving survival or quality of life.

Strengths and Weaknesses of the Study

This is the first large population-based study of smoking and cervical cancer survival. Use of a population-based cancer registry rather than a clinic or hospital based sample allows a more complete look at all women diagnosed with cervical cancer whom are seeking care. Data to characterized treatment was abstracted from medical records by hospital-based tumor registrars who provided these data to the Kentucky Cancer Registry. The most recent CDC audit [14] showed a 95.1% overall accuracy rate for KCR data and an internal audit of treatment data found accuracy rate of 94.1% [15]. The use of individual level health insurance as an indicator of socioeconomic status (SES) is a strength relative to prior analyses using Census data as a proxy for SES [16-17]. The availability of 11 years of incidence data resulted in a large sample size (N=2661) which provided good study power.

While we had data to characterize current smoking status, we do not have measures of smoking duration, number of cigarette smoked per day, or former smoking status. Thus we cannot evaluate a possible dose response relationship of smoking and survival. Missing data is always a limitation of analyses based on existing records. In these data, 8% were missing stage at diagnosis, 9.3% were missing insurance status, and 19.4% were missing smoking status. Understandably those missing on stage were more likely to be missing on treatment as well as smoking status. We did not observe a pattern by which missing smoking data was more common by year of diagnosis (p=0.08), patient age (p= 0.62), or rural residence (p=0.33).

Conclusions

Data presented here supports that current tobacco use is associated with increased all cause and cervical cancer specific mortality. Kentucky has the highest current smoking rate in US at 26% and the lowest proportion quitting smoking among ever smokers at 42.5% [18]. Kentucky also has high cervical cancer incidence rates [19]. In concert with high risk HPV, smoking is an established cause of cervical cancer. Additional efforts at both smoking prevention and cessation could decrease cervical cancer mortality.

Acknowledgements

The Kentucky Cancer Registry is supported by funds from both the CDC National Program of Cancer Registries (Grant # 5U58DP000810-02) and the NCI Surveillance Epidemiology and End Results Program (Contract # NO1-PC-54403).

References

1. Herrero R, Brinton LA, Reeves WC, Brenes MM, Tenorio F, de Britton RC, Gaitan E, Garcia M, Rawls WE. Invasive cervical cancer and smoking in Latin America. Journal of the National Cancer Institute 1989;81:205–11. [PubMed: 2536087]
2. Castle PE, Wacholder S, Lorincz A, et al. A prospective study of high-grade cervical neoplasia risk among human papillomavirus-infected women. Journal of the National Cancer Institute 2002;94:1406–1414. [PubMed: 12237286]
3. Tobacco smoke and involuntary smoking. IARC Monograph Evaluation of Carcinogenic Risks to Humans 2004;83:1–1438.
4. Tsai HT, Tsai YM, Yang SF, Wu JY, Chuang HY, Wu TN, Ho CK, Lin CC, Kuo YS, Wu MS. Lifetime cigarette smoke and second-hand smoke and cervical intraepithelial neoplasm-A community-based case-control study. Gynecologic Oncology 2007;105:181–188. [PubMed: 17204311]
5. Waggoner SE, Darcy KM, Fuhrman B, Parham GP, Lucci J 3rd, Monk BJ, Moore DH. Association between cigarette smoking and prognosis in locally advanced cervical carcinoma treated with chemoradiation: A gynecologic oncology group study. Gynecologic Oncology 2006;103:853–858. [PubMed: 16815535]
6. Kucera H, Enzelsberger H, Eppel W, Weghaupt K. Effect of nicotine abuse on treatment results in primary irradiated cervical cancer. Geburtshilfe Frauenheilkd 1986;46:388–90. [PubMed: 3744008]

7. Serur E, Fruchter RG, Maiman M, McGuire J, Arrastia CD, Gibbon D. Age, substance abuse, and survival of patients with cervical carcinoma. Cancer 1995;75:2530–8. [PubMed: 7736398]
8. Wright JD, Li J, Gerhard DS, Zhang Z, Huettner PC, Powell MA, Gibb RK, Herzog TJ, Mutch DG, Trinkaus KM, Rader JS. Human papillomavirus type and tobacco use as predictors of survival in early stage cervical carcinoma. Gynecologic Oncology 2005;98:84–91. [PubMed: 15894364]
9. Fyles A, Voduc D, Syed A, Milosevic M, Pintilie M, Hill R. The effect of smoking on tumor oxygenation and treatment outcome in cervical cancer. Clinical Oncology 2002;14:442–446. [PubMed: 12512963]
10. Young, JLJ.; Roffers, SD.; Ries, LAG.; Fritz, AG.; Hurlbut, AA. SEER Summary Staging Manual - 2000: Codes and Coding Instructions. Bethesda, MD: National Cancer Institute; 2001. NIH Pub. No. 01-4969
11. Matos A, Moutinho J, Pinto D, Medeiros R. The influence of smoking and other cofactors on the time to onset to cervical cancer in a southern European population. European Journal of Cancer Prevention 2005;14:485–91. [PubMed: 16175054]
12. McIntyre-Seltman K, Castle P, Guido R, Schiffman M, Wheeler CW, et al. A. Smoking is a risk factor for cervical intraepithelial neoplasia grade 3 among oncogenic human papillomavirus DNA-positive women with equivocal or mildly abnormal cytology. Cancer Epidemiology Biomarkers and Prevention 2005;14:1165–70.
13. Ebbert JO, Williams BA, Sun Z, Aubry MC, Wampfler JA, Garces YI, et al. Duration of smoking abstinence as a predictor for non-small-cell lung cancer survival in women. Lung Cancer 2005;47:165–72. [PubMed: 15639715]
14. Data Completeness and Quality Audits: Kentucky Cancer Registry (Diagnosis Year 2004). Atlanta, GA: Dept. of Health and Human Services, Centers for Disease Control and Prevention, National program of Cancer Registries; 2006. p. 13
15. Internal Audit of Data Quality, 2006 Cancer Case Records. Lexington, KY: Kentucky Cancer Registry, UK Markey Cancer Center; 2008.
16. Eggleston KS, Coker AL, Williams M, Tortolero-Luna G, Martin JB, Tortolero SR. Socioeconomic Status as a Predictor of Cervical Cancer Survival in Texas, 1995-2001. Journal of Women's Health 2006;15:941–51.
17. 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. Gynecologic Oncology 2006;102:278–284. [PubMed: 16434087]
18. Kuiper N, Malarcher A, Bombard J, Maurice E, Jackson K. State-Specific Prevalence of Cigarette Smoking and Quitting Among Adults --- United States, 2004. Morbidity and Mortality Weekly Reports 2005;54:1124–7.
19. US Cancer Services Working Group. United States Cancer Statistics: 2004 Incidence and Mortality. Atlanta U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; 2007.

Table 1

Demographics of KCR sample of women diagnosed with cervical cancer, 1995-2005

Demographic attribute	N= 2661
Mean age of cases	50.5 ± 16.2
Ethnicity	# (%)
White	2359 (88.7%)
Non white	302 (11.3%)
Rural residence*	
Metro	1413 (53.1%)
Suburban	982 (36.9%)
Rural	266 (10.0%)
Payor source	
Private Insurance	1096 (41.2%)
Government insurance	1074 (40.4%)
Unknown	247 (9.3%)
No insurance / self pay	244 (9.2%)
Smoking status	
Smoker	1280 (48.0%)
Other tobacco user	12 (0.5%)
Unknown tobacco exposure	515 (19.4)
Non smoker	854 (32.1%)
Cervical cancer cell type	
Squamous	2126 (78.9%)
Non squamous	535 (20.1)
Stage	
Localized	1393 (52.4%)
Regional	806 (30.3%)
Distant	251 (9.4%)
Unknown	211 (7.9%)
Treatment received (comprehensive)	
No treatment / unknown treatment	231 (8.7%)
Surgery alone	909 (34.2%)
Surgery + other treatment†	541 (20.3%)
Other treatment†, no surgery	980 (36.8%)

*Rural residence defined using Beale codes: Metro, codes 1-3; Suburban, codes 4-7, Rural, codes 8-9.

†Other treatment includes chemotherapy, radiation, hormone and/or other therapy.

Table 2
Demographics, stage and treatment received by smoking status

	Known Non-smoker # (%) (REF)	Known Current Smoker # (%)[p-value*]	Unknown tobacco status # (%)[p-value*]
	N=854	**N= 1292**	**N= 515**
Age (mean age, STD)	51.9 ±17.6	49.3 ±14.2 **p<0.001**	50.8 ±18.1 p=0.24
Ethnicity			
White	764 (89.5%)	1164 (90.1%)	431 (83.7%)
Non white	90 (10.5%)	128 (9.9%) p=0.64	84 (16.3%) p=0.002
Rural residence†			
Metro	429 (50.2%)	717 (55.5%)	267 (51.8%)
Urban	339 (39.7%)	443 (34.3%)	200 (38.8%)
Rural	86 (10.1%)	132 (10.2%)	48 (9.3%)
p for trend		p= 0.03	p=0.82
Payor source			
Private Insurance	396 (46.4%)	509 (39.4%)	191 (37.1%)
Government insurance	338 (39.6%)	586 (45.4%) **p=0.002**	150 (29.1%) p=0.53
Unknown	49 (5.7%)	49 (3.8%) p=0.24	149 (28.9%) **p<0.001**
No insurance / self pay	71 (8.3%)	148 (11.5%) **p= 0.002**	25 (4.9%) p=0.20
Cervical cancer cell type			
Squamous	621 (72.7%)	1104 (85.4%)	401 (77.9%)
Non squamous	233 (27.3%)	188 (14.6%) **p<0.001**	114 (22.1%) **p=0.03**
Stage at diagnosis			
Localized	480 (56.2%)	650 (50.3%)	263 (51.1%)
Regional	243 (28.4%)	462 (35.8%)	101 (19.6%)
Distant	82 (9.6%)	134 (10.4%)	35 (6.8%)
Unknown	49 (5.7%)	46 (3.5%)	116 (22.5%)
p for trend		p<0.001	p<0.001
Treatment received (comprehensive)			
No treatment / unknown treatment	49 (5.7%)	49 (3.8%)	133 (25.8%)
Surgery alone	317 (37.1%)	404 (31.3%) p=0.26	188 (36.5%) **p<0.001**
Surgery + other treatment*	188 (22.0%)	274 (21.2%) p=0.09	79 (15.3%) **p<0.001**
Other treatment*, no surgery	300 (35.1%)	565 (43.7%) **p=0.003**	115 (22.3%) **p<0.001**

*Chi Square p value, non-tobacco user is the referent.

†Rural residence defined using Beale codes: Metro, codes 1-3; Suburban, codes 4-7, Rural, codes 8-9.

REF = Referent group to whom the (a) known current smokers and (b) unknown tobacco status (missing) groups are compared to each demographic or cancer attributes.

Table 3

Survival analysis: Smoking, all cause, and cervical cancer specific mortality

	All Cause Mortality N=2661		Cervical Cancer Mortality N=2661	
	Death rate (#) *	Adjusted HR†	Death rate (#)*	Adjusted HR†
Smoking status				
Known Non smoker	1.9 (305)	1.0 REF	1.2 (189)	1.0 REF
Known Current Smoker	2.4 (537)	**1.35 (1.17-1.56)**	1.5 (339)	**1.21 (1.01-1.46)**
Unknown tobacco status	1.7 (168)	0.92 (0.75-1.13)	1.1 (111)	0.97 (0.75-1.26)
Age	2.1 (1010)	**1.03 (1.02-1.03)**	1.3 (639)	**1.01 (1.00-1.02)**
Ethnicity				
White	2.1 (892)	1.0 REF	1.3 (555)	1.0 REF
Non-White	2.1 (118)	1.02 (0.83-1.25)	1.5 (84)	1.06 (0.83-1.35)
Rural residence‡				
Metro	2.0 (520)	1.0 REF	1.3 (352)	1.0 REF
Suburb	2.2 (391)	0.94 (0.82-1.08)	1.3 (235)	0.86 (0.72-1.02)
Rural	2.1 (99)	0.99 (0.80-1.24)	1.1 (52)	0.79 (0.59-1.06)
Payor source				
Private Insurance	1.2 (276)	1.0 REF	0.8 (193)	1.0 REF
Government insurance	3.3 (553)	**1.28 (1.09-1.51)**	1.8 (310)	**1.23 (1.00-1.50)**
Unknown	1.9 (91)	1.05 (0.80-1.40)	1.4 (64)	1.07 (0.76-1.51)
No insurance / self pay	2.1 (90)	**1.30 (1.02-1.65)**	1.7 (72)	**1.40 (1.07-1.84)**
Cervical cancer cell type				
Squamous	2.1 (829)	1.0 REF	1.3 (521)	1.0 REF
Non squamous	1.8 (181)	1.05 (0.89-1.24)	1.2 (118)	1.09 (0.88-1.34)
Stage at Diagnosis				
Localized	0.8 (245)	1.0 REF	0.3 (110)	1.0 REF
Regional	4.0 (455)	**2.19 (1.83-2.62)**	2.6 (229)	**2.86 (2.24-3.64)**
Distant	13.4 (207)	**6.20 (5.03-7.64)**	10.5 (162)	**8.73 (6.68-11.41)**
Unknown	2.8 (103)	**1.56 (1.18-2.05)**	1.9 (68)	**2.07 (1.44-2.97)**
Treatment received				
No / unknown treatment	4.0 (138)	1.0 REF	2.5 (86)	1.0 REF
Surgery alone	0.4 (84)	**0.16 (0.12-0.23)**	0.1 (24)	**0.08 (0.05-0.14)**
Surgery + other treatment*	2.1 (215)	**0.45 (0.35-0.59)**	1.4 (141)	**0.48 (0.34-0.67)**
Other treatment*, no surgery	4.4 (573)	**0.54 (0.43-0.70)**	3.0 (388)	**0.56 (0.41-0.77)**

* Death rate is deaths per 10,000 woman days.

† Adjusting for age (continuous), smoking status, ethnicity, rural residence, payor source, cell type, stage, and treatment received.

‡ Rural residence defined using Beale codes: Metro, codes 1-3; Suburban, codes 4-7, Rural, codes 8-9.

Table 4

Survival analysis: Smoking and cervical cancer specific mortality by stage

	Cervical Cancer Mortality (other deaths in denom)			
	Localized Disease, N=1393		Regional / Distant Disease, N=1057	
	Death rate* (#)	Adjusted HR†	Death rate* (#)	Adjusted HR†
Smoking status				
Known Non smoker	0.3 (39)	1.0 REF	3.2 (136)	1.0 REF
Known Current Smoker	0.3 (50)	0.88 (0.57-1.35)	3.9 (271)	**1.23 (1.00-1.53)**
Unknown tobacco status	0.4 (21)	1.21 (0.68-2.15)	3.1 (54)	0.98 (0.71-1.36)
Age	0.3 (110)	**1.00 (0.98-1.01)**	3.6 (461)	**1.01 (1.00-1.02)**
Ethnicity				
White	0.4 (103)	1.0 REF	3.4 (398)	1.0 REF
Non-White	0.2 (7)	0.51 (0.28-1.55)	5.6 (63)	**1.45 (1.10-1.92)**
Rural residence‡				
Metro	0.3 (60)	1.0 REF	3.8 (252)	1.0 REF
Suburb	0.4 (44)	0.86 (0.58-1.28)	3.3 (167)	0.82 (0.66-1.01)
Rural	0.2 (6)	0.47 (0.20-1.11)	3.4 (42)	0.85 (0.61-1.19)
Payor source				
Private Insurance	0.2 (40)	1.0 REF	2.8 (143)	1.0 REF
Government insurance	0.5 (47)	1.51 (0.95-2.39)	3.8 (234)	1.13 (0.89-1.42)
Unknown	0.5 (11)	1.57 (0.72-3.45)	6.7 (29)	**1.86 (1.23-2.81)**
No insurance / self pay	0.4 (12)	1.66 (0.85-3.23)	4.8 (55)	**1.47 (1.07-2.01)**
Cervical cancer cell type				
Squamous	0.3 (80)	1.0 REF	3.6 (388)	1.0 REF
Non squamous	0.4 (30)	**1.56 (1.00-2.43)**	3.3 (73)	1.06 (0.82-1.37)
Treatment received				
No / unknown treatment	0.5 (6)	1.0 REF	15.6 (43)	1.0 REF
Surgery alone	0.04 (9)	**0.13 (0.04-0.42)**	1.7 (11)	**0.13 (0.07-0.25)**
Surgery + other treatment*	0.7 (43)	1.97 (0.70-5.55)	2.6 (87)	**0.17 (0.11-0.24)**
Other treatment*, no surgery	1.4 (52)	**3.83 (1.37-10.74)**	3.7 (320)	**0.21 (0.15-0.30)**

*Death rate is deaths per 10,000 woman days.

†Adjusting for age (continuous, smoking status, ethnicity, rural residence, payor source, cell type, and treatment received.

‡Rural residence defined using Beale codes: Metro, codes 1-3; Suburban, codes 4-7, Rural, codes 8-9.

REF = Referent group