

## Supplementary Online Content

Clarke MA, Devesa SS, Hammer A, Wentzensen N. Racial and ethnic differences in hysterectomy-corrected uterine corpus cancer mortality by stage and histologic subtype. *JAMA Oncol*. Published online May 5, 2022. doi:10.1001/jamaoncol.2022.0009

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This supplementary material has been provided by the authors to give readers additional information about their work.

## eMethods

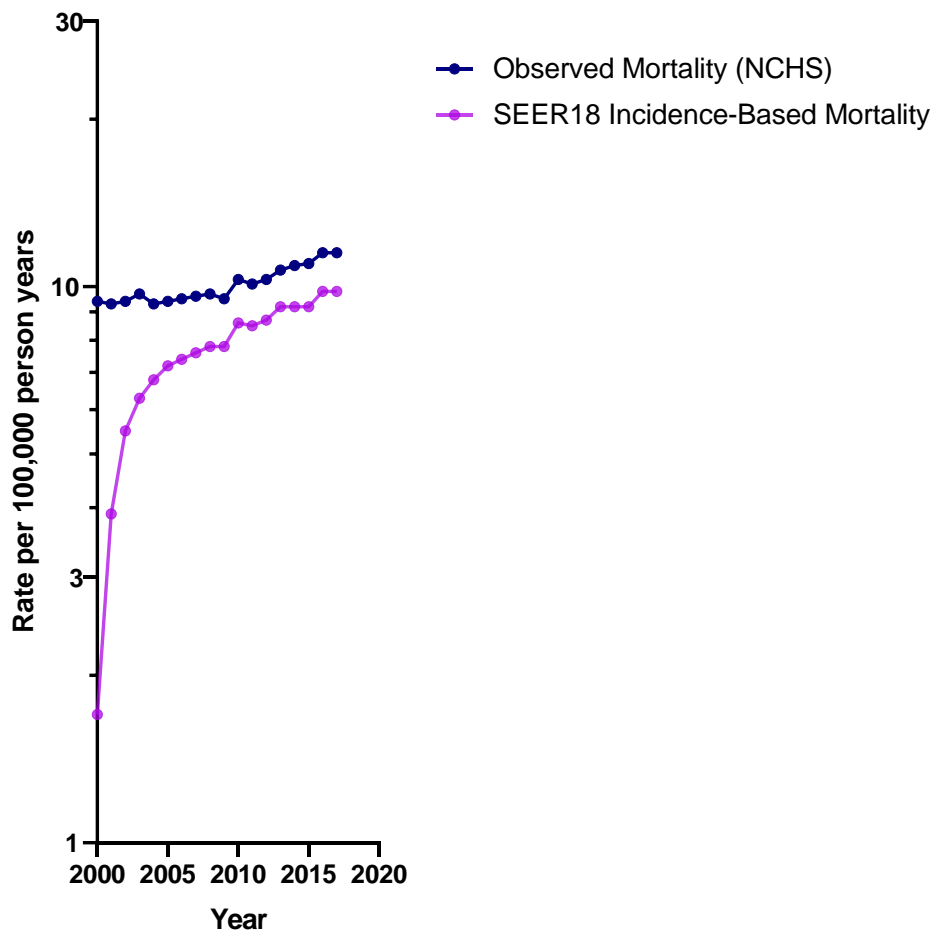
### **Comparison of Observed Corpus and Uterus, NOS deaths in the SEER Mortality Database and in the SEER18 Incidence-Based Mortality Database**

The SEER18 Incidence-Based Mortality database includes deaths that occurred between 2000 and 2017 among cancer cases registered in 18 SEER registries, covering approximately 26% of the U.S. population. Standard mortality analyses in SEER are based on causes of death ascertained from death certificates obtained by the National Center for Health Statistics (NCHS). These death certificates have no information on tumor characteristics beyond the cancer site. In the incidence-based mortality file, uterine cancer deaths can be linked to incident uterine cancer cases registered in SEER, allowing evaluation of mortality rates according to tumor characteristics such as histology and stage. Due to the lag time between cancer diagnosis and death, sufficient follow-up time is needed to obtain reliable mortality estimates. Incidence-based mortality rates may be severely underestimated in the initial years following cancer diagnosis. Specifically, uterine cancer deaths occurring between 2000 and 2017, particularly in the earlier years, may have been among cases diagnosed prior to 2000, when incidence data were not available from all 18 registries. Therefore, to determine the appropriate time window for our incidence-based mortality analysis, we compared incidence-based uterine cancer mortality rates (using the selection criteria described in the Methods section of the manuscript) to the observed uterine cancer mortality rates (death certificate data from NCHS mortality file, restricted to SEER18 registries) from 2000 to 2017. As shown in eFigure 1, the incidence-based mortality rate trends became parallel to the observed NCHS mortality rates by 2010; therefore, we allowed for 10 years of follow-up of incident cases to ensure that incidence-based mortality rates capture almost all uterine cancer deaths in our analysis, and present incidence-based mortality rates only for 2010 to 2017.

### **Reallocation of Adenocarcinoma NOS Deaths**

We reclassified deaths attributed to Adenocarcinoma NOS histology to account for changes in pathology reporting (moving from more general, non-specific categories to reporting more specific histology results) in recent years. Grouping Adenocarcinoma NOS cases separately, or with Endometrioid subtypes, which has been done in many studies, would lead to biased estimates since the changes in Adenocarcinoma NOS (decreasing in both incidence and mortality) do not reflect true changes in incidence and mortality, but are secondary to changes in pathology reporting over time. This is particularly true for an incidence-based mortality analysis, where non-Endometrioid subtypes constitute a greater proportion of overall uterine cancer deaths compared to incident cases.

To reclassify deaths attributed to Adenocarcinoma NOS as either Endometrioid or Non-endometrioid, we calculated the distribution of deaths occurring in cases diagnosed with Endometrioid and Non-Endometrioid histology by year, age group, race and ethnicity, and stage, respectively. Then we applied the proportions of endometrioid and non-endometrioid deaths to the total number of deaths from Adenocarcinoma, NOS within each stratum. For example, among non-Hispanic Whites aged 65-69 years in 2016 with localized disease, the proportion of deaths from Endometrioid cancers is 68% and the proportion of deaths from Non-Endometrioid cancers is 32%. When applying these proportions to the 15 cases of adenocarcinoma in that strata, 10 deaths would be reclassified as Endometrioid and 5 deaths would be reclassified as Non-Endometrioid.

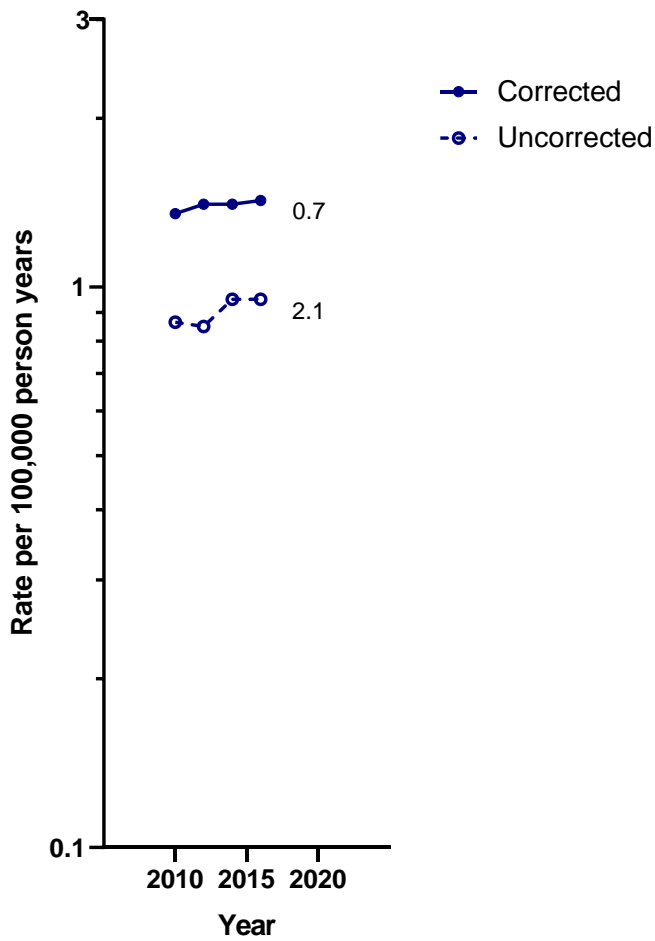


**eFigure 1. Corpus and Uterus, NOS Cancer Observed NCHS Mortality and Incidence-Based Mortality, SEER18 (2000-2017).** Trends in age-adjusted observed NCHS mortality and incidence-based mortality rates of microscopically confirmed uterine corpus cancer, among US women aged 40 to 85+ years. Rates are shown separately for National Center for Health Statistics (NCHS) Mortality estimates (death certificate only data, shown in solid navy circles) and SEER Incidence-Based Mortality estimates (corpus and uterus, NOS cases linked to corpus and uterus, NOS deaths, shown in solid pink circles). A follow-up period of 10 years for incident cases was determined based on when incidence-based mortality rates were parallel with mortality rates (approximately in 2010).

eTable 1. Histologic Subtype Groupings among Corpus and Uterus, NOS Cancer Deaths in SEER18 Incidence-Based Mortality File, 2010-2017, (N=16,797)**^		
Histologic Subtype	Histology	Count
Endometrioid	8050/3: Papillary carcinoma, NOS	11
Endometrioid	8141/3: Scirrhus adenocarcinoma	1
Endometrioid	8210/3: Adenocarcinoma in adenomatous polyp	39
Endometrioid	8260/3: Papillary adenocarcinoma, NOS	48
Endometrioid	8261/3: Adenocarcinoma in villous adenoma	1
Endometrioid	8262/3: Villous adenocarcinoma	3
Endometrioid	8263/3: Adenocarcinoma in tubulovillous adenoma	6
Endometrioid	8380/3: Endometrioid carcinoma	5,857
Endometrioid	8381/3: Endometrioid adenofibroma, malignant	2
Endometrioid	8382/3: Endometrioid adenocarcinoma, secretory variant	15
Endometrioid	8383/3: Endometrioid adenocarcinoma, ciliated cell variant	5
Endometrioid	8440/3: Cystadenocarcinoma, NOS	3
Endometrioid	8480/3: Mucinous adenocarcinoma	55
Endometrioid	8481/3: Mucin-producing adenocarcinoma	5
Endometrioid	8560/3: Adenosquamous carcinoma	131
Endometrioid	8570/3: Adenocarcinoma with squamous metaplasia	94
<b>Total Endometrioid</b>		<b>6,276</b>
Non-Endometrioid	8255/3: Adenocarcinoma with mixed subtypes	93
Non-Endometrioid	8310/3: Clear cell adenocarcinoma, NOS	493
Non-Endometrioid	8323/3: Mixed cell adenocarcinoma	1,171
Non-Endometrioid	8441/3: Serous cystadenocarcinoma, NOS	1,476
Non-Endometrioid	8460/3: Papillary serous cystadenocarcinoma	1,055
Non-Endometrioid	8461/3: Serous surface papillary carcinoma	116
Non-Endometrioid	8950/3: Mullerian mixed tumor	782
Non-Endometrioid	8951/3: Mesodermal mixed tumor	52
Non-Endometrioid	8980/3: Carcinosarcoma, NOS	1,738
Non-Endometrioid	8981/3: Carcinosarcoma, embryonal	2
<b>Total Non-Endometrioid</b>		<b>6,978</b>
Sarcomas	8800/3: Sarcoma, NOS	140
Sarcomas	8801/3: Spindle cell sarcoma	12
Sarcomas	8802/3: Giant cell sarcoma	12
Sarcomas	8804/3: Epithelioid sarcoma	5
Sarcomas	8805/3: Undifferentiated sarcoma	48
Sarcomas	8840/3: Myxosarcoma	1
Sarcomas	8850/3: Liposarcoma, NOS	1
Sarcomas	8890/3: Leiomyosarcoma, NOS	843
Sarcomas	8891/3: Epithelioid leiomyosarcoma	38

Sarcomas	8895/3: Myosarcoma	1
Sarcomas	8896/3: Myxoid leiomyosarcoma	26
Sarcomas	8900/3: Rhabdomyosarcoma, NOS	27
Sarcomas	8901/3: Pleomorphic rhabdomyosarcoma, adult type	9
Sarcomas	8902/3: Mixed type rhabdomyosarcoma	3
Sarcomas	8910/3: Embryonal rhabdomyosarcoma, NOS	1
Sarcomas	8912/3: Spindle cell rhabdomyosarcoma	1
Sarcomas	8920/3: Alveolar rhabdomyosarcoma	2
Sarcomas	8930/3: Endometrial stromal sarcoma, NOS	258
Sarcomas	8931/3: Endometrial stromal sarcoma, low grade	43
Sarcomas	8933/3: Adenosarcoma	108
Sarcomas	8935/3: Stromal sarcoma, NOS	34
Sarcomas	9120/3: Hemangiosarcoma	1
<b>Total Sarcomas</b>		1,614
<b>Adenocarcinoma, NOS<sup>#</sup></b>	8140/3: Adenocarcinoma, NOS	1,128
Other	8000/3: Neoplasm, malignant	108
Other	8004/3: Malignant tumor, spindle cell type	1
Other	8005/3: Malignant tumor, clear cell type	1
Other	8010/3: Carcinoma, NOS	365
Other	8012/3: Large cell carcinoma, NOS	4
Other	8013/3: Large cell neuroendocrine carcinoma	7
Other	8015/3: Glassy cell carcinoma	1
Other	8020/3: Carcinoma, undifferentiated, NOS	116
Other	8021/3: Carcinoma, anaplastic, NOS	1
Other	8022/3: Pleomorphic carcinoma	1
Other	8030/3: Giant cell and spindle cell carcinoma	1
Other	8031/3: Giant cell carcinoma	1
Other	8032/3: Spindle cell carcinoma, NOS	3
Other	8033/3: Pseudosarcomatous carcinoma	6
Other	8041/3: Small cell carcinoma, NOS	27
Other	8045/3: Combined small cell carcinoma	3
Other	8046/3: Non-small cell carcinoma	11
Other	8052/3: Papillary squamous cell carcinoma	1
Other	8070/3: Squamous cell carcinoma, NOS	38
Other	8071/3: Squamous cell carcinoma, keratinizing, NOS	4
Other	8072/3: Squamous cell carcinoma, large cell, nonkeratinizing, NOS	2
Other	8074/3: Squamous cell carcinoma, spindle cell	1
Other	8082/3: Lymphoepithelial carcinoma	1
Other	8130/3: Papillary transitional cell carcinoma	3
Other	8200/3: Adenoid cystic carcinoma	1

Other	8240/3: Carcinoid tumor, NOS	1
Other	8244/3: Mixed adenoneuroendocrine carcinoma (ICD-O-3 update)	1
Other	8246/3: Neuroendocrine carcinoma, NOS	52
Other	8290/3: Oxyphilic adenocarcinoma	1
Other	8313/3: Clear cell adenocarcinofibroma	1
Other	8410/3: Sebaceous adenocarcinoma	1
Other	8450/3: Papillary cystadenocarcinoma, NOS	2
Other	8482/3: Mucinous adenocarcinoma, endocervical type	1
Other	8510/3: Medullary carcinoma, NOS	1
Other	8574/3: Adenocarcinoma with neuroendocrine differentiation	12
Other	8575/3: Metaplastic carcinoma, NOS	1
Other	8806/3: Desmoplastic small round cell tumor	1
Other	8830/3: Malignant fibrous histiocytoma	1
Other	8940/3: Mixed tumor, malignant, NOS	2
Other	8963/3: Malignant rhabdoid tumor	3
Other	9014/3: Serous adenocarcinofibroma	2
Other	9110/3: Mesonephroma, malignant	4
Other	9364/3: Peripheral neuroectodermal tumor	2
Other	9473/3: Primitive neuroectodermal tumor	4
<b>Total Other</b>		<b>803</b>
<b>Total</b>		<b>16,797</b>
<p>*Includes microscopically confirmed cases of invasive corpus uteri and uterine corpus not otherwise specified (NOS) cancers using the first matching record from the SEER 18 Incidence-Based Mortality database</p> <p>^Histologic diagnoses were defined by the third edition of the International Classification of Diseases for Oncology histology codes</p> <p># Deaths caused by adenocarcinoma NOS (n=1,128), were reclassified according to the observed distribution of endometrioid and non-endometrioid deaths by year, age, race, and ethnicity as previously described.(3)</p>		



**eFigure 2. Uterine Sarcoma Incidence-Based Mortality, SEER18 (2010-2017), Uncorrected and Corrected for Hysterectomy.** Trends in age-adjusted incidence-based mortality rates of microscopically confirmed uterine sarcomas uncorrected (hollow circle) and corrected (solid circle) for hysterectomy prevalence, among US women aged 40 to 85+ years. Rates are based on two-year averages, all trends are summarized by a single annual percentage change estimate.



eTable 2. Uterine Cancer Incidence-Based Mortality Rates by Year (2010 and 2017), Subtype, and Race and Ethnicity, Uncorrected and Corrected for Hysterectomy, SEER18						
	Uncorrected Incidence-Based Mortality Rates			Corrected Incidence-Based Mortality Rates		
	2010	2017	Corresponding APC <sup>^</sup>	2010	2017	Corresponding APC <sup>^</sup>
<b>All Uterine Cancers</b>	8.6	9.8	2.2*	14.9	16.7	1.8*
<b>Endometrioid Subtypes</b>	3.5	4.0	1.3*	6.1	6.7	0.8
<b>Non-Endometrioid Subtypes</b>	3.8	4.5	3.0*	6.6	7.8	2.7*
<b>All Uterine Cancers</b>						
Hispanic	7.4	8.8	3.8*	11.6	13.6	3.5*
Non-Hispanic Asian/Pac. Islander	6.5	7.9	3.1	8.6	10.5	3.1
Non-Hispanic Black	13.8	16.4	2.8*	27.4	31.8	2.2
Non-Hispanic White	8.3	9.1	1.7*	14.8	15.9	1.4*
<b>Endometrioid Subtypes</b>						
Hispanic	3.0	3.3	0.3	4.7	5.0	-0.2
Non-Hispanic Asian/Pac. Islander	2.0	3.1	4.6	2.7	4.1	4.3
Non-Hispanic Black	4.0	3.9	1.5	8.1	7.6	-1.8
Non-Hispanic White	3.8	4.2	1.1	6.7	7.3	1.1
<b>Non-Endometrioid Subtypes</b>						
Hispanic	3.4	4.1	7.1*	5.4	6.6	6.7*
Non-Hispanic Asian/Pac. Islander	2.7	3.6	3.5*	3.7	4.9	3.4*
Non-Hispanic Black	7.7	10.1	3.6*	15.4	19.9	3.5*
Non-Hispanic White	3.4	3.7	1.5*	6.1	6.7	1.5*
<b>Sarcomas</b>	0.9	0.9		1.5	1.4	

<sup>^</sup>Refers to the corresponding APC for the entire time period; values for non-Hispanic Asian/Pacific Islanders for all uterine cancers and for non-Hispanic Blacks for all uterine cancers and nonendometrioid subtypes correspond to average APCs \*P<0.05

Abbreviations: Pac. Is, Pacific Islander; APC, Annual Percentage Change

Incidence-Based Mortality rates were age adjusted to the 2000 US standard population and expressed per 100,000 person-years.