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Kaposi Sarcoma Incidence in Females is nearly Four-Fold Higher in the Lower Rio Grande Valley compared to the Texas Average

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Abstract

The Lower Rio Grande Valley (LRGV) is located on U.S.-Mexican border with a population that is 90% Hispanic (1). Comprised of Hidalgo, Cameron, Starr and Willacy counties, this region has the highest poverty rate and one of the highest incidences of Type 2 diabetes in the United States (2-4). Previous studies demonstrated a high prevalence of Human Herpes Virus 8 (HHV8) in the LRGV (5-7). HHV8 infection has been causally linked to Kaposi Sarcoma (KS) (8). Here, we retrospectively examine the incidence of KS in the LRGV in a set of HIV-negative Hispanic patients. Strikingly, the incidence of KS was higher in LRGV women compared to the Texas state average (nearly four-fold higher in McAllen-Edinburg-Pharr Metro Statistical Area). This unique profile aligns with the increased HHV8 prevalence in the LRGV, suggesting that HHV8 contributes to a high incidence of HIV-negative KS on the U.S.–Mexican border in Texas.

Keywords: Kaposi sarcoma, South Texas, diabetes, HHV8

Abbreviations: Kaposi sarcoma (KS), Lower Rio Grande Valley (LRGV), Human Herpes Virus 8 (HHV8), Acquired Immune Deficiency Syndrome (AIDS), Human Immunodeficiency Virus (HIV)

Introduction

KS is an angio-proliferative neoplasm that gained notoriety during the AIDS (Acquired Immune Deficiency Virus) epidemic in the 1980s in the United States (9-11). In 1982 the KS incidence was 0.5 cases per 100,000 men in the United States, which climbed to its peak in 1989 (9.5 cases per 100,000) (12). KS has declined since the implementation of HAART (Highly Active Antiretroviral Therapy) to treat HIV infection (13-17). The incidence of KS in females has historically been lower compared to men in the United States (7). In 1989 the incidence of KS in females was only 0.14 cases per 100,000 in the United States (3). Therefore, KS cases associated with HIV infection had a disproportionate impact on males; in 1989 there was a 68-fold difference in KS incidence between males and females in the United States (0.14 female cases versus 9.5 male cases per 100,000) (12).

KS was first described by the Hungarian dermatologist Moritz Kaposi in 1872 (18). This *Classic* form of KS was found in Mediterranean men (Italian, Greek, Middle Eastern and Ashkenazi Jewish) (19, 20). *Classic KS* typically has an indolent course allowing affected individuals to live greater than ten years post diagnosis (20). *Endemic* KS has been described in Sub-Saharan Africa (11). This form commonly progresses to lymphadenopathy and affects men, women and children (11). Environmental factors such as parasites, diet and herbs (as well as anti-malarial treatments) contribute to the development of *Endemic KS* (11). The third type of KS is HIV-associated, which can be aggressive with the disease impacting the gastrointestinal tract (21). Treatment of the underlying immuno-deficiency with HAART has improved health outcomes for HIV-related KS (17). A fourth form of KS (*Iatrogenic*) is found in immuno-deficient patients such as transplant recipients and certain cancer patients (13-17).

HHV8 was discovered as a novel herpes virus in 1994 by Moore and Chang (22-24). Subsequent studies showed that HHV8 plays a causative role in the development of KS (25). It is important to note that the vast

majority of HHV8 infected individuals will not develop KS (11). Some populations have a greater than 40% infection rate of HHV8 (Sub-Saharan Africa and Mediterranean populations), but only a fraction of individuals will develop KS (26, 27). HHV8 infection was also significantly associated with the development of ketosis-prone Type 2 diabetes in both Sub-Saharan African and Mediterranean populations (21, 28-39).

Here we present a retrospective study of the incidence of KS in the LRGV, a region with a high prevalence of HHV8 (6). The LRGV is a unique region of South Texas located on the U.S.-Mexican border. The population of the LRGV (90% Hispanic) faces severe socioeconomic challenges, including an extremely high poverty rate, an incidence of Type 2 diabetes double the national average, and federal designation as a medically underserved area (3, 4). An unusually high incidence of non-HIV associated KS, especially in females, was observed in Hidalgo County based on clinical data provided by Texas Oncology (**Table 1**). This prompted us to perform statistical analyses in order to further examine areas in the LRGV for increased KS incidence. We found that Hidalgo County, Texas, had a nearly four-fold higher incidence of female KS compared to the Texas state average (**Fig. 3)**.

Materials and Methods

This work is a retrospective study of seventeen patients seen at an outpatient community cancer center of Texas Oncology located in Hidalgo County, Texas. Patients were evaluated between the years 2011 and 2016. Informed consent was not done due to the retrospective, anonymous nature of the study. The study is IRB exempt according to the UTRGV research code and approved by the UTRGV IRB and Texas Oncology Research Committee (IRB 2017-100-04).

Clinical data was analyzed retrospectively from the electronic medical records (Iknowmed, IKM) of Texas Oncology. De-identified data was provided to researchers at UTRGV for further analysis. All cases presented had KS lesions of the skin confirmed by histopathology. Histological diagnosis was (in most cases) completed by immunohistochemistry staining for HHV8.

The AIDS Clinical Trials Group (ACTG) criteria define complete response (CR) as the absence of any detectable residual lesions. CR was always clinically determined, as patients did not have confirmatory biopsies performed. CR was validated by the lack of progression with consistent long-term follow-up. Relapse was defined as the recurrence of KS after having previously achieved CR (40). Partial response (PR) was defined as a subjective measure of greater or equal to 30% reduction in the size of all lesions.

To more rigorously investigate whether our observed incidence of KS in the LRGV was elevated compared to The State of Texas on average, and nationally, we examined SEER (Surveillance, Epidemiology and End Results Program, National Cancer Institute) and Texas State Cancer Registry (12, 41, 42). The incidence was calculated by taking the number of KS cases (between years 2000-2014) and dividing by the population at risk, and then multiplied by 100,000.

Power Analyses were performed to ensure adequate sample sizes (43). Crude rate was calculated and used for further analysis. The estimate of Incidence Rate Ratio (IRR) was calculated by unconditional maximum likelihood (Wald method) and confidence intervals were calculated using normal approximation (Wald method) [42]. The hypothesis tests on whether the IRR equaled to 1 was also conducted using normal approximation (Wald method) [42]. Calculations were done using *epitools* package in R (https://CRAN.R-project.org/package=epitools) (44, 45).

Results

Evaluation of Clinical Kaposi Sarcoma Data from Hidalgo County Cancer Clinic

KS is commonly associated with HIV infection (14, 17). However, non-HIV associated forms of KS have been found commonly in Africa and Eastern Europe (26). Oncologists in the LRGV noticed a potential spike in non-HIV associated KS in a community cancer clinic in Hidalgo County, Texas. We retrospectively evaluated KS patient data from this clinic (**Table 1**). All cases presented had KS lesions of the skin confirmed by histopathology. All patients were Hispanic; 13 cases were HIV-negative (**Table 1**), whereas 4 cases were HIV-positive. Histological diagnosis was completed by immunohistochemistry staining for HHV8. Of the eleven patients tested for HHV8 virus, all were positive; two patients were not tested for the virus.

The clinical subtype of the thirteen patients with non-HIV KS was as follows: *Classic* (sporadic) KS was found in eleven patients, while two patients had *Iatrogenic* (immunosuppression) KS: one related to chemotherapy for non-Hodgkin lymphoma, and the other was related to immunosuppression with tacrolimus for renal transplant. The stage of all 13 patients with non-HIV KS was nodular. None of the patients had mucosal, lymph node, or visceral involvement by KS. Non-HIV KS lesions were multiple and bilateral at the time of presentation in three patients, and ten patients had solitary, unilateral lesions. The most frequent manifestation of non-HIV KS involved lesions localized to the lower extremity in eight patients, the upper extremity in one patient, and other sites in three patients. Of 11 KS cases from the clinic that were non-HIV associated or non-*Iatrogenic*, three were female (27%), **Table 1**. The high proportion of females with KS in the Hidalgo County Clinic suggested that the female KS incidence in the LRGV may be increased.

Treatment modalities included surgical resection in four patients; radiation therapy in eleven patients; and two patients received chemotherapy. Three patients had combined treatment including both chemotherapy

and radiation. All patients had a complete remission upon treatment received as first line. No patient received α-interferon or other immunomodulatory treatments. None of the patients progressed following the first-line treatment. Recurrent KS occurred in eight patients, with six patients having multiple recurrences at multiple sites. In two patients there was a solitary recurrence. At the end of this retrospective study, eleven of the patients with non-HIV KS were alive, while two had died from non-KS related issues. At the end of the evaluation there were no patients on active treatment for KS.

Female KS in SEER 18 and Texas State

Our clinical evaluation of KS suggested that the incidence of non-HIV associated KS was elevated in the LRGV, especially in females (**Table 1**). To gain insight into whether our observed incidence of KS in the LRGV was elevated compared to the United States on average, we examined SEER (Surveillance, Epidemiology and End Results Program, National Cancer Institute) and Texas Cancer Registry data (12, 41, 42). SEER 9 data used for **Fig. 1 A** included Metro Statistical Area (MSA) and state-level data from Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, and Utah (12). Analysis of SEER data revealed that the male KS incidence in the United States rose sharply in the 1980s and steadily declined to slightly higher than pre-AIDS epidemic incidence levels consistent with previous reports (**Fig. 1 A**). The incidence of KS in females remained low throughout the AIDS epidemic to 2014 (**Fig. 1 A**). Data from SEER 18 (which includes data from Los Angeles, San Jose-Monterey, Rural Georgia, Alaska Native Tumor Registry, Greater California, Greater Georgia, Kentucky, Louisiana, and New Jersey) is depicted in **Fig. 1 B** (12). SEER data indicated that the incidence of KS was 9-fold higher in males compared to females (0.094 KS cases per 100,000 in females and 0.8933 KS cases per 100,000 in males) in 2014, **Fig. 1 B**.

Analysis of our clinical data suggested that there may be a higher incidence of KS in LRGV females compared to SEER 18 data (**Table 1** and **Figs. 1 A-B**). To further investigate KS incidence in LRGV females, we examined data

from the Texas Cancer Registry (41, 42). We sought to determine whether the KS incidence was elevated in females using data from increasingly smaller geographical areas: Texas State, Health Service Regions within Texas, Counties within Texas and MSAs in Texas. At the state level, we found no difference between the female KS incidence in Texas compared to the SEER 18 database; both databases had a female KS incidence of 0.1 per 100,000 using compiled data from 2000-2014 (**Figs. 1 B-E**).

Female KS Incidence in Texas Health Service Region 11 was increased compared to state average

To investigate KS incidence in geographical areas in Texas, we examined data from Health Service Regions obtained from the Texas Cancer Registry (42). The State of Texas is divided into 11 Health Service Regions (HSRs); Region 11 included Hidalgo County (where our initial clinical study was based). The female KS incidences were equal to (or lower than) the state average of 0.1 per 100,000 females in all Texas Health Service Regions investigated with two exceptions: Health Service Regions 8 and 11 (**Fig. 2**). Health Service Region 8 (included the city of San Antonio) had a female incidence of 0.2 per 100,000 from 2000-2014. Health Service Region 11 included cities Corpus Christi, Harlingen and McAllen and had a female KS incidence of 0.3 per 100,000 between years 2000-2014 (**Fig. 2**). The incidence of female KS was 2.53-fold higher in HSR 11 compared to the Texas state average: p-value<0.001, **Table 2**. The male and total KS incidences between HSR 11 and State of Texas were not significantly different, **Table 2**. Males in HSR 11 had a lower KS incidence compared the Texas state average, **Fig. 2 B**. Therefore, it appears that Health Service Region 11 in the LRGV had increased KS incidence in females compared to the Texas state average.

Female KS incidence was increased on the United States-Mexican Border in Texas compared to state average

Given that the female KS incidence was elevated in HSRs 8 and 11, which share a border with Mexico, we examined all Texas HSRs that border Mexico for increased KS (**Fig. 2**). We found increased KS in both males and females in Texas border counties compared to the state average (**Table 2**). The KS difference (Border counties combined versus Texas state) in males was a modest 1.13 fold whereas the difference in females was 1.91 fold (**Table 2,** *p*-value<0.001).

We considered the possibility that the increase in females with KS along the U.S.-Mexican border might not be restricted to Texas. Our intention was to examine KS incidence in all states that share a border with Mexico: Texas, New Mexico, Arizona and California. However, data for New Mexico KS incidence was not available. Therefore, we examined the KS incidence in two additional states that border Mexico (using state-maintained registries): Arizona and California (46-48). Arizona has four counties that share a border with Mexico: Cochise, Pima, Santa Cruz and Yuma (47). We combined data from 2000-2014 for these border counties and examined KS incidence. The KS incidence for the entire population in Arizona was low compared to Texas State: 0.26 per 100,000 overall compared to the Texas average of 0.5 per 100,000 overall. (48). The KS incidence for females in Arizona border counties was 0.06 per 100,000 compared to the Arizona state average for females: 0.04 per 100,000 (**Table 3**); both of these were considerably lower compared to the Texas state average for KS: 0.12 per 100,000 females (**Figs. 2 B-C**). The proportion of KS cases that were female in Arizona border counties compared to Arizona State was higher. Specifically, the male: female KS incidence ratio was 5.81 for Arizona border counties compared to the state ratio of 13.87, *p*-value<0.001, **Table 4**. The KS incidence was also examined in California. The KS incidence in females was the same in border counties compared to the California state female incidence (0.1 compared to 0.11), **Table 4 and Fig. 3 D**. Taken together, our results highlight that there is an increase in the incidence of KS in females along the U.S.-Mexican border in the LRGV. Examination of additional states that share a border with Mexico revealed that Arizona harbors a low incidence of KS overall, with a high proportion of female KS in border counties. California Cancer Registry data indicated that there was not an increase in female KS in border counties.

McAllen-Edinburg-Pharr MSA had almost four-fold increase in Female KS Incidence compared to state average

To further refine the region of Texas that harbored high KS incidence in females, we examined county data. Of 246 counties examined, Hidalgo County in the LRGV had the highest female KS incidence of 0.4 per 100,000 (**Fig. 3 A**) (42). The KS incidence in Hidalgo County men was slightly lower than the Texas state average (0.8 versus 0.9), **Fig. 3 A**. Examination of the McAllen-Edinburg-Pharr MSA (located in Hidalgo County, Texas) found a KS incidence of 0.37 cases per 100,000 in women, which was almost four times greater than the average for women in the United States (0.094 per 100,000) and the Texas state incidence for females (0.1 per 100,000) **Figs. 3 A-C, Table 4,** p-value<0.001. This increase in KS was not observed for men in the McAllen-Edinburg-Pharr MSA, **Figs. 3 A-C**.

Discussion

The United States-Mexican border population found in the LRGV of Texas has a unique public health landscape. This population is genetically unique in that it is 90% Hispanic (5). The LRGV is one of the most economically disadvantaged areas of the country with poverty rates of approximately 36% compared to the United States national average of 14.8% (3, 49, 50). The LRGV has a 30.7% incidence of Type 2 diabetes compared to the United States overall incidence of 12.3% (51). Here we report that the KS incidence is nearly four times higher in females in the McAllen-Pharr-Edinburg MSA compared to Texas and the United States, correlating with the increased incidence of HHV8 found in the LRGV (**Figs. 2-3**) (5).

Genetic factors may play a role in the increased KS found in LRGV females. One possibility is that the genetic variant of HHV8 found in the LRGV is more likely to promote KS. Previous studies showed the minor variant of

ORF K-15 from HHV8 was more commonly found in Hispanic KS patients (78% of patients with the minor HHV8 form were Hispanic compared to 22% who were Caucasian) (6, 7). Additionally, a previous study reported that three women from South Texas (including the San Antonio area) diagnosed with KS had the minor variant of HHV8 *ORF-K15* and were Hispanic (6). Aside from genetic variance of HHV8, one must also consider the genetic differences found in infected patients such as polymorphisms in the *MDM2* gene and genetic changes that would impact immunological response (52-61). For example, the *MDM2* SNP309 T/G genotype was previously found overrepresented among classic KS cases (57). The *MDM2* SNP309 T/G genotype has a reported 1.9-fold increase in MDM2 protein expression (57). One of the primary targets of the MDM2 E3 ubiquitin ligase is the tumor suppressor p53, which is targeted for degradation upon polyubiquitination (62). The *MDM2* SNP309 T/G compromises p53 responses and thereby promotes associated cancers such as KS (57). Thus, the prevalent HHV8 subtype(s), together with the genetic signatures found in the predominantly Hispanic population, may contribute to produce the higher incidence of non-HIV KS found in the LRGV.

The elevated incidence of female KS in the LRGV compared to the Texas state and United States averages underscores the unique epidemiological landscape found this area (**Figs. 2-3**). Infections, poor diet, diabetes, and certain drugs such as anti-malarial therapies may impact the development of KS in HHV8 infected individuals (11). Further investigations are warranted to identify potential environmental factors found in the LRGV that may combine with endemic HHV8 variants and regional genetic backgrounds to impact the incidence of KS in females.

Our initial retrospective study based on clinical data from the LRGV revealed a high incidence of KS in non-HIV infected patients. We found a nearly four-fold increase in KS specifically in females. This increased incidence was found not only in our clinic, but in the McAllen-Edinburg-Pharr MSA, Hidalgo County in Texas, and Health Service Region 11 in Texas. Further studies are needed to elucidate the biological mechanisms that lead to this increase in KS. The incidence of HHV8 infection (including *ORF-K15* genotype) in the LRGV and

neighboring areas should be ascertained. Of note, the overall incidence of KS is actually lower for males in the LRGV compared to the United States and Texas. This finding may be related to the fact that most of the KS patients identified in our study (LRGV) were non-HIV infected, whereas a higher proportion of KS patients in the United States are HIV-infected (63). Therefore, it is likely that the non HIV-infected incidence of KS in males is indeed higher in the LRGV compared to the overall United States. These findings underscore the need for further studies regarding HHV8 incidence and genetic variants in the LRGV.

Figure Legends

Figure 1. KS Incidence in United States and Texas. (A) SEER 9 data is depicted for female, male and all patients with KS between years 1975-2014. The increase in KS was primarily in male patients during the AIDS epidemic. **(B)** SEER 18 data depicted for KS for female, male and all patients between years 2000-2014. (**C**) Texas KS incidence between 2000-2014 (**D-E**) Male: female KS incidence in SEER 18 versus TX. The incidence was calculated by taking the number of KS cases (between years 2000-2014) and dividing by the population at risk multiplied by 100,000.

Figure 2. U.S.-Mexico Border Region has increased KS incidence. (A) Map of KS incidence in TX Health Service Regions. **(B)** KS incidence in Health Service Regions 8, 10 and 11 of Texas. **(C-D)** KS incidence in AZ and CA border counties. The incidence was calculated by taking the number of KS cases (between years 2000-2014) and dividing by the population at risk multiplied by 100,000.

Figure 3. Kaposi Sarcoma is nearly four times higher in females in Hidalgo County and the McAllen-Edinburg-Pharr MSA compared to other cities in Texas. (**A-C**) KS incidences from the Hidalgo County, Texas, and McAllen-Edinburg-Pharr MSA are depicted, showing a nearly four-fold increase in female KS. The

incidence was calculated by taking the number of KS cases (between years 2000-2014) and dividing by the population at risk multiplied by 100,000.

Table 1. Kaposi Sarcoma Clinical Features and Treatment Outcomes in South Texas Clinic

Patient No.	Sex	Race	K.S. Type	Stage	Treatment	Response to Treatment	Recurrence
1	M	Hispanic	Classic (Sporadic)	Nodular	Radiation Therapy & Chemotherapy	Complete Response	Multiple
2	M	Hispanic	Classic (Sporadic)	Nodular	Surgery & Radiation Therapy	Complete Response	Multiple
3	M	Hispanic	Classic (Sporadic)	Nodular	Radiation Therapy	Complete Response	Multiple
4	F	Hispanic	Classic (Sporadic)	Nodular	Radiation Therapy	Complete Response	One Right Foot
5	M	Hispanic	Classic (Sporadic)	Nodular	Radiation Therapy	Complete Response	One Right Leg
6	F	Hispanic	Classic (Sporadic)	Nodular	Surgery	Complete Response	No
7	M	Hispanic	Classic (Sporadic)	Nodular	Radiation Therapy	Complete Response	Multiple
8	F	Hispanic	Classic (Sporadic)	Nodular	Radiation Therapy	Complete Response	Multiple
9	M	Hispanic	Classic (Sporadic)	Nodular	Radiation Therapy	Complete Response	No
10	M	Hispanic	Classic (Sporadic)	Nodular	Radiation Therapy	Complete Response	Multiple
11	M	Hispanic	Iatrogenic (Chemotherapy)	Nodular	Surgery & Radiation Therapy	Complete Response	No
12	M	Hispanic	Iatrogenic (Renal Transplant 1999)	Nodular	Chemotherapy	Complete Response	No
13	M	Hispanic	Classic (Sporadic)	Nodular	Surgery & Radiation Therapy	Complete Response	No
14	M	Hispanic	AIDs-Associated	Solitary Plaque	Radiation Therapy	Complete Response	One Right lower extremity
15	M	Hispanic	AIDs-Associated	N/A	Chemotherapy	Complete Response	One Right Foot
16	M	Hispanic	AIDs-Associated	Diffused			
17	M	Hispanic	AIDs-Associated	Nodular	Surgery	Complete Response	No

Table 2. Kaposi Sarcoma Incidence in Texan Health Service Regions

Populations (in years 2000-2014)	HSR 11		Broder Region (HSRs 8, 10, 11)		HSR 11: Border† (95% CI)	Texas		HSR 11:Texas† (95% CI)	Border: Texas† (95% CI)
	Incidence / Population at risk	**IR**	**Incidence / Population at risk**	**IR**	**IRR**	**Incidence / Population at risk**	**IR**	**IRR**	**IRR**
All	160 / 29,900,802	0.53	451 / 78,629,950	0.57	0.9 (0.74, 1.09) p-value=0.26	1,782/ 357,835,413	0.50	1.08 (0.92, 1.27) p-value=0.34	1.2*** (1.08, 1.34) p-value<0.001
Male	116 / 14,648,644	0.79	369 / 38,545,640	0.96	0.75** (0.6, 0.93) p-value=0.009	1,550 / 177,579,267	0.90	0.9 (0.74, 1.09) p-value=0.27	1.13* (1, 1.27) p-value=0.04
Female	44 / 15,252,158	0.29	82 / 40,084,310	0.2	1.89** (1.22, 2.91) p-value=0.004	232 / 180,256,146	0.13	2.53*** (1.82, 3.52) p-value<0.001	1.91*** (1.46, 2.5) p-value<0.001
Male: Female IRR (95%CI**)	2.74*** (1.94, 3.88) p-value<0.001		4.68*** (3.68, 5.94) p-value<0.001			6.78*** (5.91, 7.79) p-value<0.001			

† The ratios are actually HSR 11: (the rest of Texas other than HSR 11), or Border: (the rest of Texas other than Border), or HSR 11: (the rest of Border area other than HSR 11).

* indicates p-value<0.05, ** indicates p-value<0.01, and *** indicates p-value<0.001

IR: The incidence was calculated by taking the number of KS cases (between years 2000-2014) and dividing by the population at risk, and then multiplied by 100,000.

Table 3. Kaposi sarcoma incidence in Arizona and California Border Counties

State	Populations (in years 2000-2014)	Border Counties†		State		Border: State†† (95% CI)
		Incidence / Population at risk	**IR**	**Incidence / Population at risk**	**IR**	**IRR**
Arizona	**All**	40 / 19,418,600	0.21	236 / 90,422,220	0.26	0.75 (0.53, 1.04) p-value=0.09
	Male	34 / 9,591,635	0.35	220 / 45,012,478	0.49	0.68* (0.47, 0.97) p-value=0.03
	Female	6 / 9,826,965	0.06	16 / 45,409,742	0.04	2.17 (0.79, 5.98) p-value=0.15
	Male: Female IRR (95%CI)	5.81*** (2.43, 13.83) p-value<0.001		13.87*** (8.35, 23.04) p-value<0.001		
California	**All**	389 / 45,302,540†††	0.86	3,836 / 546,166,620	0.69	1.25*** (1.12, 1.39) p-value<0.001
	Male	366 / 22,739,327†††	1.61	3,547 / 271,670,888	1.31	1.26*** (1.13, 1.4) p-value<0.001
	Female	23 / 22,563,213†††	0.1	289 / 274,495,732	0.11	0.97 (0.63, 1.48) p-value=0.87
	Male: Female IRR (95%CI)	15.79*** (10.36, 24.06) p-value<0.001		12.4*** (11, 13.98) p-value<0.001		

†Arizona has 4 border counties including Cochise, Pima, Santa Cruz and Yuma. California has 2 border counties including San Diego and Imperial.

†† The ratios are actually Border Counties: (the rest of State other than Border Counties).

††† Only San Diego is considered, since Imperial does not have reported data.

* indicates p-value<0.05, ** indicates p-value<0.01, and *** indicates p-value<0.001.

IR: The incidence was calculated by taking the number of KS cases (between years 2000-2014) and dividing by the population at risk, and then multiplied by 100,000.

Table 4. Kaposi sarcoma incidence in MSAs in Texas

Populations (in years 2000-2014)	McAllen-Edinburg-Pharr MSA		San Antonio MSA		MEP: SA (95% CI)	Texas		MEP: Texas† (95% CI)	SA: Texas† (95% CI)
	Incidence / Population at risk	**IR**	**Incidence / Population at risk**	**IR**	**IRR**	**Incidence / Population at risk**	**IR**	**IRR**	**IRR**
All	63 / 10,666,164	0.59	202 / 30,154,607	0.67	0.88 (0.66, 1.17) p-value=0.38	1,782/ 357,835,413	0.50	1.19 (0.93, 1.53) p-value=0.17	1.39*** (1.2, 1.61) p-value<0.001
Male	43 / 5,189,783	0.83	179 / 14,786,749	1.21	0.68* (0.49, 0.95) p-value=0.02	1,550 / 177,579,267	0.87	0.95 (0.7, 1.28) p-value=0.72	1.44*** (1.23, 1.68) p-value<0.001
Female	20 / 5,476,381	0.37	23 / 15,367,858	0.15	2.44** (1.34, 4.44) p-value=0.003	232 / 180,256,146	0.12	3.01*** (1.9, 4.76) p-value<0.001	1.18 (0.77, 1.82) p-value=0.44
Male: Female IRR (95%CI**)	2.27** (1.33, 3.86) p-value=0.002		8.09*** (5.23, 12.49) p-value<0.001			6.78*** (5.91, 7.79) p-value<0.001			

† The ratios are actually McAllen-Edinburg-Pharr (MEP): (the rest of Texas other than MEP MSA) or SA: (the rest of Texas other than SA MSA).

* indicates p-value<0.05, ** indicates p-value<0.01, and *** indicates p-value<0.001.

IR: The incidence was calculated by taking the number of KS cases (between years 2000-2014) and dividing by the population at risk, and then multiplied by 100,000.

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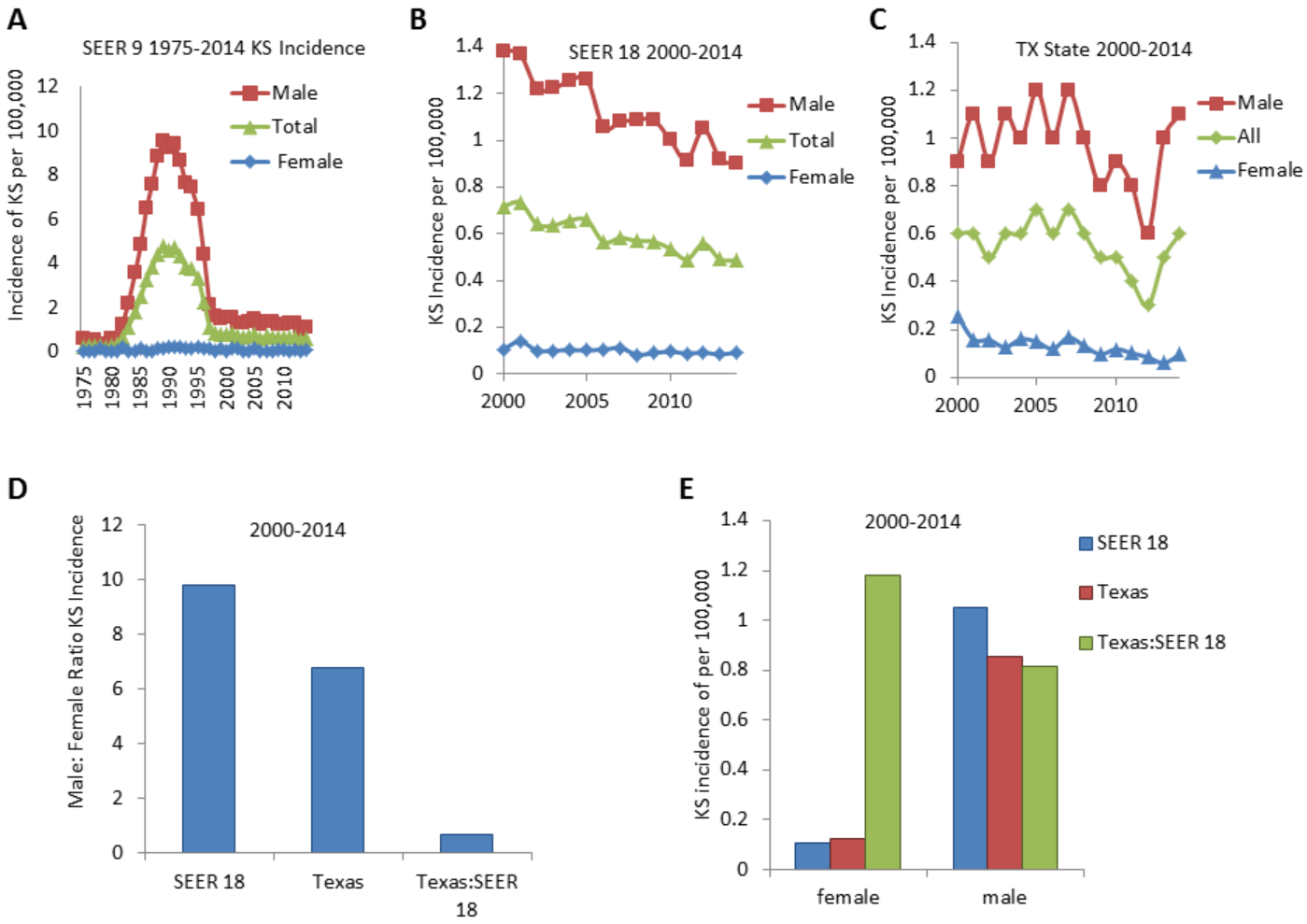
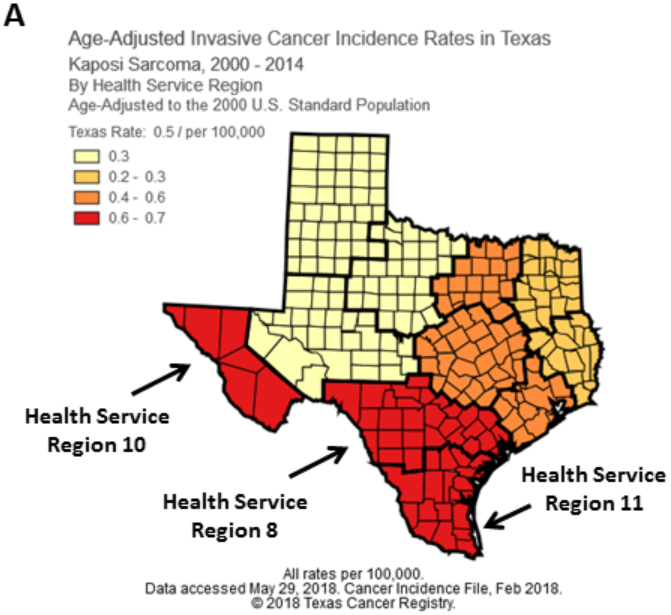

A
SEER 9 1975-2014 KS Incidence
Incidence of KS per 100,000
Male
Total
Female
B
SEER 18 2000-2014
KS Incidence per 100,000
Male
Total
Female
C
TX State 2000-2014
KS Incidence per 100,000
Male
All
Female
D
2000-2014
Male: Female Ratio KS Incidence
SEER 18
Texas
Texas:SEER 18
E
2000-2014
KS incidence of per 100,000
SEER 18
Texas
Texas:SEER 18
female
male

A


Age-Adjusted Invasive Cancer Incidence Rates in Texas
Kaposi Sarcoma, 2000 - 2014
By Health Service Region
Age-Adjusted to the 2000 U.S. Standard Population
Texas Rate: 0.5 / per 100,000
0.3
0.2 - 0.3
0.4 - 0.6
0.6 - 0.7
Health Service Region 10
Health Service Region 8
Health Service Region 11
All rates per 100,000.
Data accessed May 29, 2018. Cancer Incidence File, Feb 2018.
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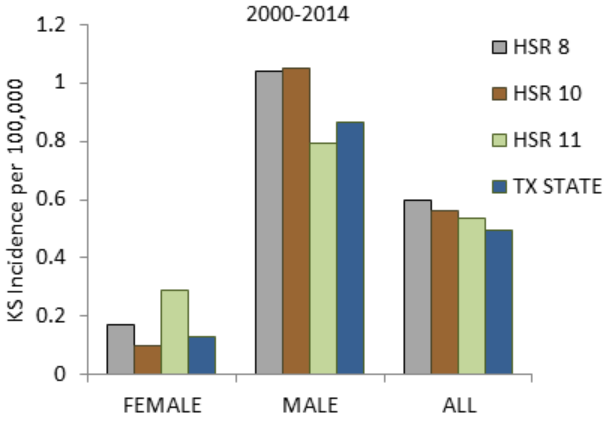
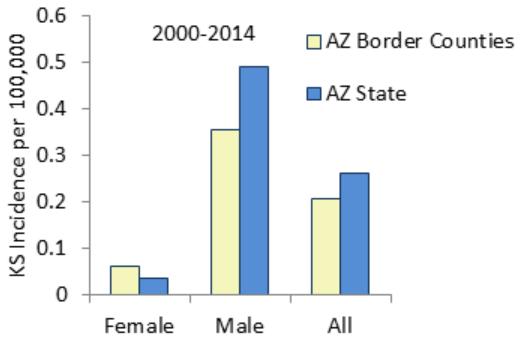
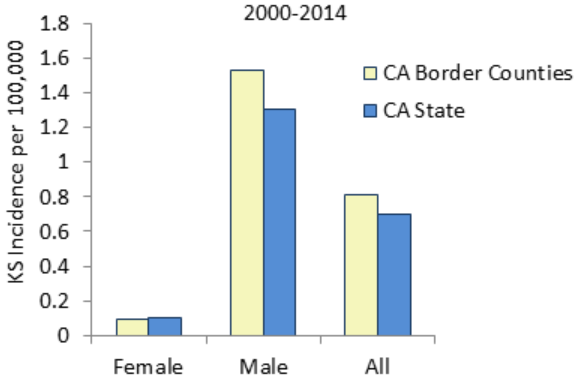
B


2000-2014
KS Incidence per 100,000
1.2
1
0.8
0.6
0.4
0.2
0
HSR 8
HSR 10
HSR 11
TX STATE
FEMALE
MALE
ALL

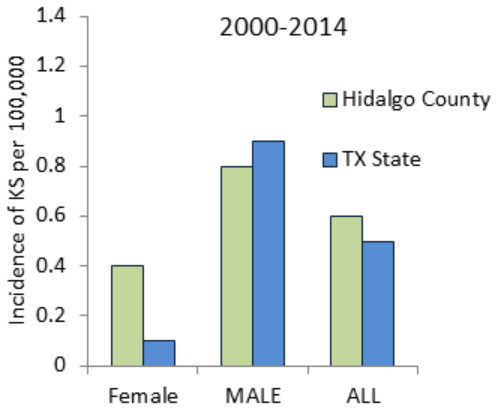
C


2000-2014
KS Incidence per 100,000
0.6
0.5
0.4
0.3
0.2
0.1
0
AZ Border Counties
AZ State
Female
Male
All

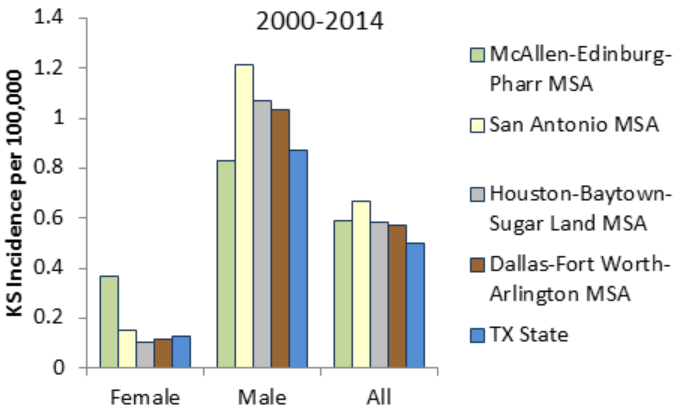
D


2000-2014
KS Incidence per 100,000
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
CA Border Counties
CA State
Female
Male
All

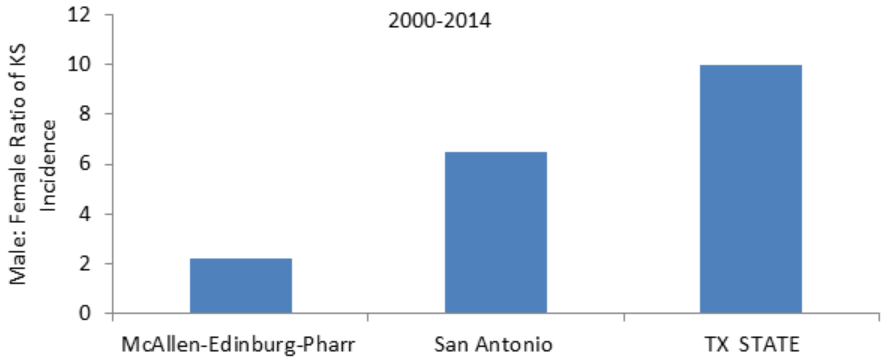
A


2000-2014
Incidence of KS per 100,000
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Hidalgo County
TX State
Female
MALE
ALL

B


2000-2014
KS Incidence per 100,000
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Female
Male
All
McAllen-Edinburg-Pharr MSA
San Antonio MSA
Houston-Baytown-Sugar Land MSA
Dallas-Fort Worth-Arlington MSA
TX State

C


2000-2014
Male: Female Ratio of KS Incidence
12
10
8
6
4
2
0
McAllen-Edinburg-Pharr
San Antonio
TX STATE